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): October 3, 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 October 3, 2022, Tonix Pharmaceuticals Holding Corp. (the "Company") announced that the U.S. Food and Drug Administration (the "FDA") cleared the Investigational New Drug ("IND") application to support a Phase 2 clinical trial with the Company's TNX-601 ER (tianeptine hemioxalate extended-release tablets) product candidate, a once-daily formulation of tianeptine as a potential treatment for major depressive disorder ("MDD"). A copy of the press release which discusses this matter is furnished hereto as Exhibit 99.01, and incorporated herein by reference.

The Company updated its investor presentation, which is used to conduct meetings with investors, stockholders and analysts and at investor conferences, and which the Company intends to place on its website, which may contain nonpublic information. A copy of the presentation 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 October 3, 2022, the Company announced that the FDA cleared the IND application to support a Phase 2 clinical trial with the Company's TNX-601 ER product candidate as a potential treatment for MDD. The Company expects to initiate the Phase 2 trial in MDD in the first quarter of 2023, with the potential for additional future indications in posttraumatic stress disorder and neurocognitive dysfunction from corticosteroids. The study is expected to be a registration-quality, potentially pivotal, Phase 2, 6-week, randomized, double-blind, placebo-controlled, parallel-group study to evaluate the efficacy, safety, and tolerability of TNX-601 ER monotherapy in male and female subjects aged 18 to 65 years (inclusive), with current MDD as defined by DSM-5 criteria at screening and a Montgomery-Åsberg Depression Rating Scale (MADRS) total score $\geq$ 25 at baseline. A total of 300 participants are planned to be randomized to two treatment arms across approximately 30 clinical trial sites in the U.S. The study is expected to have a single unblinded interim analysis for sample size re-estimation when the study has results of the first 50% of efficacy evaluable patients, pending agreement on the comprehensive statistical analysis plan with the FDA.

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 October 3, 2022
99.02	Corporate Presentation by the Company for October 2022
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: October 3, 2022

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

Exhibit 99.01

Tonix Pharmaceuticals Announces IND Clearance for TNX-601 ER as a Potential Treatment for Major Depressive Disorder

TNX-601 ER, Tianeptine Hemioxalate, is an Extended-Release Tablet for Once-a-Day Dosing

Phase 2 Clinical Trial of TNX-601 ER Expected to Start First Quarter 2023

CHATHAM, N.J., October 3, 2022 – Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a clinical-stage biopharmaceutical company, today announced 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-601 ER (tianeptine hemioxalate extended-release tablets), a once-daily formulation of tianeptine as a potential treatment for major depressive disorder (MDD)[1]. Tianeptine is a new molecular entity in the U.S. that is being developed under the 505(b)(1) pathway. Tianeptine sodium (amorphous) immediate release (IR) tablets have been available in Europe and many countries in Asia and Latin America for the treatment of depression over more than three decades since it was first marketed in France in 1989. Tianeptine's activity is mechanistically distinct from traditional monoaminergic treatments for depression available in the U.S. including the selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), monoamine oxidase inhibitors (MAOIs), and tricyclic antidepressants (TCAs).

"This is an important milestone as we advance TNX-601 ER into clinical development," said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals. "TNX-601 ER is a novel, oral, extended-release once-daily tablet. Studies from across the globe conducted over more than 30 years show that immediate-release (IR) tianeptine sodium formulations have comparable efficacy to SSRIs and TCAs, fewer drug-drug interactions, and are associated with a lower incidence of sexual dysfunction compared with SSRIs, SNRIs and TCAs. We expect that our new once-daily formulation will maintain these properties while also providing convenience and adherence advantages over the three-times-a-day dosing of these IR tianeptine sodium products. We expect to initiate the Phase 2 trial in MDD in the first quarter of 2023, with the potential for additional future indications in posttraumatic stress disorder and neurocognitive dysfunction from corticosteroids."

TNX-601 ER is being developed as a monotherapy and first-line treatment for MDD. No tianeptine-containing product has been approved by the FDA. The proposed mechanism of action of TNX-601 ER is distinct from traditional monoaminergic antidepressants, in that its principal mechanism in MDD is believed to be through indirect modulation of glutamatergic neurotransmission. It is notable that in multiple placebo-controlled and comparative studies that tianeptine demonstrates efficacy on par with both SSRIs and tricyclic antidepressants, while showing a more favorable tolerability profile, lacking the sedative, autonomic, cardiovascular and side effects on memory and attention of TCAs and a low incidence of sexual side effects, nausea, and sleep disruption as compared with SSRIs.[2,3]

In addition to its glutamatergic properties, tianeptine has weak μ-opioid receptor agonist properties and has been linked to illicit misuse at much higher doses than those reported to be effective in the treatment of MDD[4]. Previously, Tonix was developing a naloxone-containing tablet, TNX-601 CR (tianeptine oxalate and naloxone controlled-release) for MDD, that was designed to mitigate the risk of parenteral abuse. TNX-601 ER is also designed with abuse deterrent properties but without the μ-opioid receptor antagonist naloxone. The abuse-deterrent properties include gel forming polymers which impede extraction for illicit misuse. In addition, the tablet's hardness makes it difficult to crush, cut or grind to fine particle size, which hinders efforts to misuse by nasal insufflation or intravenous route.

[1]TNX-601 ER is an investigational new drug and is not approved for any indication

[2]McEwen, B.S., et al. Neurobiological properties of the antidepressant tianeptine. *Molecular Psychiatry* 2010, *15*, 237-249.

[3]Paparrigopoulos, T.J., et al. Sleep and antidepressant medication. *WPA Bulletin on Depression* 2007, *11* (33), 7-11.

[4]Lauhan, R., et al. Tianeptine abuse and dependence: case report and literature review. *Psychosomatics* 2018, *59* (6), 547–553.

About the Phase 2 Study

Tonix is proposing to conduct a registration-quality, potentially pivotal, Phase 2, 6-week, randomized, double-blind, placebo-controlled, parallel-group study, to evaluate the efficacy, safety, and tolerability of TNX-601 ER monotherapy in male and female subjects aged 18 to 65 years (inclusive), with current MDD as defined by DSM-5 criteria at screening and a Montgomery-Åsberg Depression Rating Scale (MADRS) total score ≥ 25 at baseline. A total of 300 participants are planned to be randomized to two treatment arms across approximately 30 clinical trial sites in the U.S. The study is expected to have a single unblinded interim analysis for sample size re-estimation when the study has results of the first 50% of efficacy evaluable patients, pending agreement on the comprehensive statistical analysis plan with the FDA.

About Depression

According to the National Institute of Mental Health, an estimated 21 million adults in the U.S. in 2020 experienced at least one major depressive episode[1], with highest prevalence among individuals aged 18-25 at a rate of 17.0%. For approximately 2.5 million adults in the U.S., adjunctive therapies are necessary for depression treatment.[2,3] Depression is a condition characterized by symptoms such as a depressed mood or loss of interest or pleasure in daily activities most of the time for two weeks or more, accompanied by appetite changes, sleep disturbances, motor restlessness or retardation, loss of energy, feelings of worthlessness or excessive guilt, poor concentration, and suicidal thoughts and behaviors. These symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning. The majority of people who suffer from depression do not respond adequately to initial antidepressant therapy.[4]

[1]Data Courtesy of SAMHSA on Past Year Prevalence of Major Depressive Episode Among U.S. Adults (2020). Retrieved from http://www.nimh.nih.gov/health/statistics/major-depression.shtml

[2]IMS NSP, NPA, NDTI MAT-24-month data through Aug 2017.

[3]Kubitz N, et al. (2013) *PLOS One*,. 8(10):e76882. doi: 10.1371/journal.pone.0076882. PMID: 24204694.

[4]Rush AJ, et al. (2007) *Am J. Psychiatry* 163:11, pp. 1905-1917 (STAR*D Study).

About TNX-601 ER

TNX-601 ER is a novel oral formulation of tianeptine hemioxalate designed for once-daily daytime dosing that is now in the IND (Investigational New Drug) stage of development for the treatment of MDD. Tianeptine sodium (amorphous) immediate release (dosed three times daily) was first marketed for depression in France in 1989 and has been available for decades in Europe, Russia, Asia, and Latin America for the treatment of depression. Tianeptine sodium has an established safety profile from decades of use in these jurisdictions. Currently there is no tianeptine-containing product approved in the U.S. and no extended-release tianeptine product approved in any jurisdiction. Tonix discovered a novel hemioxalate salt of tianeptine that may provide improved stability, consistency, and manufacturability compared to known salt forms of tianeptine. Tianeptine is believed to work in depression as an indirect modulator of the glutamatergic system, without direct binding NMDA, AMPA or kainate receptors. Tianeptine reverses stress induced increases in AMPA receptor trafficking, restoring hippocampal long-term potentiation and reversing the neuroplastic changes from stress and corticosteroid exposure. Tianeptine and its MC5 metabolite are also weak μ-opioid receptor agonists, that present a potential abuse liability if illicitly misused in large quantities (8-80 times the therapeutic dose for depression). In patients who were prescribed tianeptine for depression, the French Transparency Committee found an incidence of misuse of approximately 1 case per 1,000 patients treated[1] suggesting low abuse liability when used at the antidepressant dose in patients prescribed tianeptine for depression. Clinical trials have shown that cessation of a therapeutic course of tianeptine did not appear to result in dependence or withdrawal symptoms following 6-weeks[2,3,4–6], 3-months[7], or 12-months[8] of treatment. Tianeptine's reported pro-cognitive and anxiolytic effects as well as its ability to attenuate the neuropathological effects of excessive stress responses suggest that it may also be used to treat posttraumatic stress disorder. TNX-601 ER is expected to have patent protection through 2037.

[1]Haute Authorite de Sante; Transparency Committee Opinion. Stablon 12.5 Mg, Coated Tablet, Re- Assessment of Actual Benefit at the Request of the Transparency Committee. December 5, 2012.

[2]Emsley, R., et al. *J. Clin. Psychiatry* **2018**, *79* (4)

[3]Bonierbale M, et al. *Curr Med Res Opin* **2003**, *19*(2):114-124.[4]Guelfi, J. D., et al. *Neuropsychobiology* **1989**, *22* (1), 41–48.

[5]Invernizzi, G. et al., *Neuropsychobiology* **1994**, *30* (2–3), 85–93.

[6]Lepine, J. P., et al. *Hum. Psychopharmacol.* **2001**, *16* (3), 219–227.

[7]Guelfi, J. D. et al., *Neuropsychobiology* **1992**, *25* (3), 140–148.

[8]Lôo, H. et al., *Br. J. Psychiatry. Suppl.* **1992**, No. 15, 61–65.

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. TNX-601 ER (tianeptine hemioxalate extended-release tablets) is a once-daily formulation of tianeptine being developed as a potential treatment for major depressive disorder (MDD) with a Phase 2 study expected to be initiated in the first quarter of 2023. 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.

**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 at www.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

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.

TONIX PHARMACEUTICALS

What We Do

OUR MISSION

Tonix Pharmaceuticals is committed to improving population health by inventing and developing innovative therapies and vaccines, through broad in-house capabilities and creative collaborations, to help address important unmet needs.

OUR VISION

Tonix Pharmaceuticals strives to be a leader in providing novel drug therapies and vaccines to improve population health around the world.

TONIX PHARMACEUTICALS

Milestones: Recently Completed and Upcoming*

- ☑ 1st Quarter 2022 — Topline data from Phase 3 RALLY study of TNX-102 SL for the management of fibromyalgia
- ☑ 2nd Quarter 2022 — Phase 3 RESILIENT study start of TNX-102 SL for the management of fibromyalgia
- ☑ 3rd Quarter 2022 — Phase 2 PREVAIL study start of TNX-102 SL for the treatment of Long COVID

Expected Data

- ❑ 2nd Quarter 2023 — Interim analysis results of Phase 3 RESILIENT study of TNX-102 SL in fibromyalgia
- ❑ 1st Half 2023 — Interim analysis results of Phase 2 PREVAIL study of TNX-102 SL in Long COVID

Expected Clinical Trial Initiations

- ❑ 4th Quarter 2022 — Phase 2 study start of TNX-102 SL for the treatment of PTSD in Kenya
- ❑ 4th Quarter 2022 — Phase 2 study start of TNX-1900 for the treatment of migraine
- ❑ 1st Quarter 2023 — Phase 2 study start of TNX-1300 for the treatment of cocaine intoxication
- ❑ 1st Quarter 2023 — Phase 2 study start of TNX-601 ER for the treatment of major depressive disorder
- ❑ 1st Half 2023 — Phase 1 study start of TNX-1500 for prevention of allograft rejection
- ❑ 1st Half 2023 — Phase 1 study start of TNX-801 for prevention of monkeypox and smallpox in Kenya

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

TONIX PHARMACEUTICALS

Pipeline
Central Nervous System (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 4Q 2022 Start Phase 2
TNX-1300[3]	Cocaine Intoxication *FDA Breakthrough Designation*	Mid-Phase 2, Targeted 1Q 2023 Start
TNX-1900[4]	Migraine, Craniofacial Pain and Binge Eating Disorder	Phase 2, Targeted 4Q 2022 Start[5]
TNX-601 ER	Depression, PTSD, Neurocognitive Disorder from Steroids	Phase 2, Targeted 1Q 2023 Start[6]
TNX-1600[7]	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). Both indications are Phase 2 ready.
[2]Post-Acute Sequelae of COVID-19.
[3]TNX-1300 (double-mutant cocaine esterase) was licensed from Columbia University.
[4]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.
[5]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 4Q 2022
[6]A Phase 1 trial for formulation development was completed outside of the U.S; Phase 2 expected to start 1Q 2023
[7]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.

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)

Pipeline
Immunology and Immuno-Oncology portfolio

CANDIDATES*	INDICATION	STATUS / NEXT MILESTONE
TNX-1500[1]	Organ Transplant Rejection/ Autoimmune Conditions	Phase 1, Targeted 1H 2023 Start
TNX-1700[2]	Gastric and colorectal cancers	Preclinical

**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

Pipeline
Infectious Disease Portfolio

CANDIDATES*	INDICATION	STATUS / NEXT MILESTONE
TNX-801[1]	Smallpox and monkeypox vaccine	Phase 1, Targeted 1H 2023 Start
TNX-1850[2]	COVID-19 Vaccine (horsepox-based live virus vaccine)	Preclinical
TNX-2300[3]	COVID-19 Vaccine	Preclinical
TNX-3600[4]	COVID-19 Therapeutic Platform (monoclonal antibodies)	Preclinical
TNX-3700[5]	COVID-19 Vaccine (zinc nanoparticle mRNA technology)	Preclinical

INFECTIOUS DISEASE PORTFOLIO

**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-1850 is based on the BA.2 variant spike protein.
[3]Live attenuated vaccine based on bovine parainfluenza (BPI) virus
[4]Fully human monoclonal antibody generated from COVID-19 convalescent patients
[5]COVID vaccine based on mRNA in zinc nanoparticle (ZNP) formulation with CD40L molecular trigger

TONIX PHARMACEUTICALS

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 is currently enrolling

Next Steps: Interim analysis results expected 2Q 2023

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

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[2]
- 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

Patents Issued

DEVELOPMENT PROGRAM

Market Entry: Long COVID (PASC)

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

Status: Phase 2 study PREVAIL is currently enrolling

Next Steps: Interim analysis results expected 1H 2023

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

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

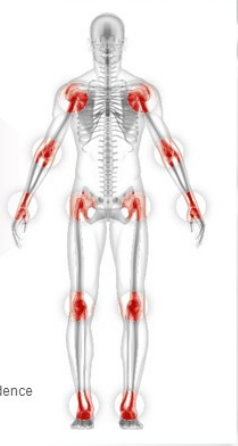
TONIX PHARMACEUTICALS

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 myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS).
- In August 2022, the HHS released the *National Research Action Plan on Long COVID*[1] which endorses the connection between Long COVID and chronic fatigue syndrome.

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 irritable bowel syndrome (IBS) in 10% to 20% of those exposed



[1]Department 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.
[2]Blomberg J, et al. Front Immunol. 2018;9:229. Published 2018 Feb 15.
[3]Warren JW, et al. Urology. 2008;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.

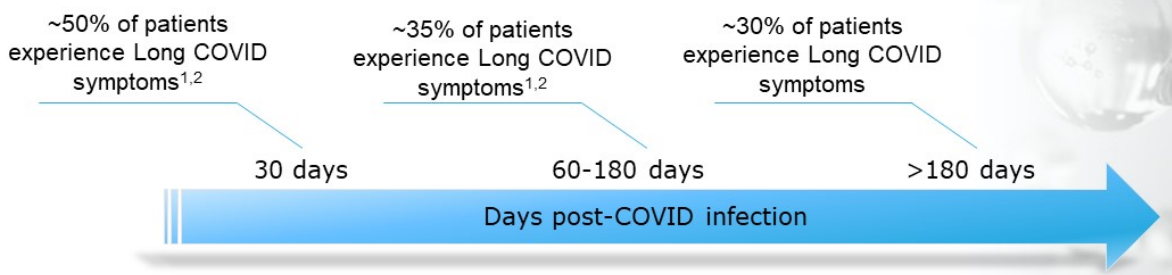
TNX-102 SL: Long COVID
a.k.a Post-Acute Sequelae of SARS-CoV-2 Infection (PASC)

- Long COVID is a heterogeneous condition that displays elements of nociplastic pain in many individuals, who experience otherwise unexplained[1-2]:

- 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]Bierle 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.
[2]Moghimi, 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.

Prevalence of Long COVID
~30% of Recovered SARS-CoV-2 Patients after 6 Months



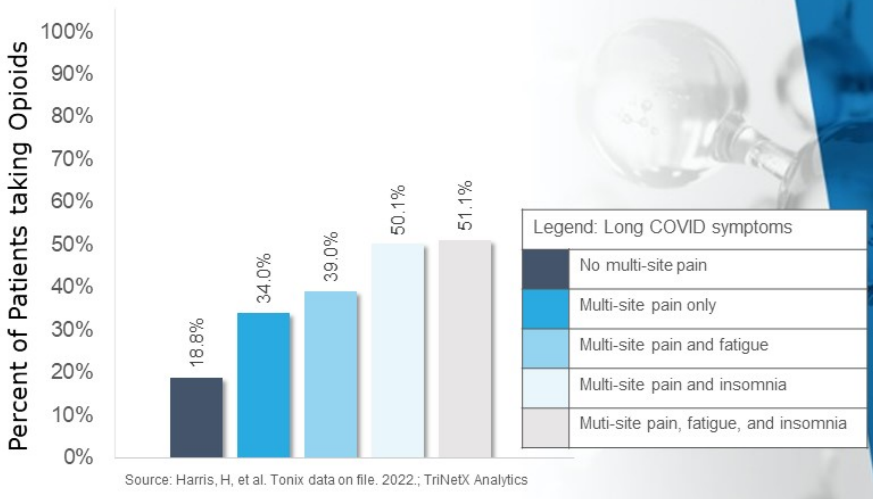
Long COVID (PASC) is more prevalent among patients[1,2]:

- 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.

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[1-2]



Source: Harris, H, et al. Tonix data on file. 2022.; TriNetX Analytics

[1]Shah, A, et al. *MMWR Morb Mortal Wkly Rep*. 2017;66:265–269.
[2]U.S. Department of Labor

TNX 102 SL*: Posttraumatic Stress disorder (PTSD)
Cyclobenzaprine Protectic® Sublingual Tablets

CNS PORTFOLIO

PROFILE

PTSD is a serious chronic psychiatric illness

- Defined as maladaptive prolonged stress response which occurs after experiencing severely injurious traumatic event(s)

Affects approximately 12 million Americans adults[1,2]

Large unmet clinical need and limited effective therapies available

- Advances in pharmacological treatments beyond the currently approved SSRIs (e.g., Zoloft® (sertraline), Paxil® (paroxetine)) are needed[3]

Patents Issued

DEVELOPMENT PROGRAM

Market Entry: PTSD

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

Status: One Phase 2 study (AtEase) completed

Two Phase 3 studies (HONOR, RECOVERY) conducted

Next Steps: 4Q 2022 Initiate Phase 2 Trial in Kenya

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

[1]Goldstein RB, et al. The epidemiology of DSM-5 posttraumatic stress disorder in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions-III. Soc Psychiatry Psychiatr Epidemiol. 2016;51(8):1137-1148.
[2]Pietrzak RH, et al. Prevalence and Axis I comorbidity of full and partial posttraumatic stress disorder in the United States: results from Wave 2 of the National Epidemiologic Survey on Alcohol and Related Conditions. J Anxiety Disord. 2011;25(3):456-465.
[3]Cain, C. K., et al. Targeting memory processes with drugs to prevent or cure PTSD. Expert Opin Investig Drugs. 2012; 21(9), 1323-1350

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

Status: Mid-Phase 2

Next Steps: Initiate a new Phase 2 single-blind, placebo-controlled, randomized, potentially pivotal study in 1Q 2023, pending FDA agreement.

FDA Breakthrough Therapy Designation

Awarded Cooperative Agreement Grant from National Institute on Drug Abuse (NIDA)

*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-601 ER*: Depression
Tianeptine Hemioxalate Extended-Release Tablets

CNS PORTFOLIO

PROFILE

A novel, oral, extended-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

Treatment effect of tianeptine in depression is well-established

Patents Issued

DEVELOPMENT PROGRAM

Market Entry: Major Depressive Disorder

Additional Indications: PTSD, Neurocognitive Disorder From Corticosteroids

Status: Phase 2 ready

Next Steps: 1Q 2023 Initiate Phase 2 Trial

*TNX-601 ER 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

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: Phase 2 ready[4]

Next Steps: 4Q 2022 Initiate Phase 2 Trial and Investigator Initiated Phase 2 Trial in Binge Eating Disorder

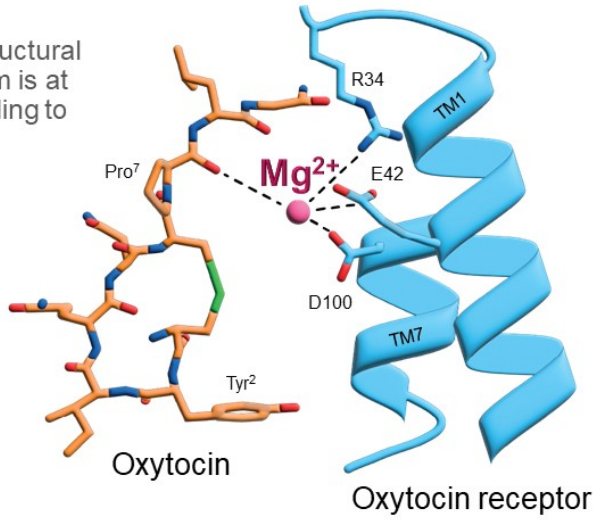
*TNX-1900 has not been approved for any indication.
CGRP = calcitonin gene-related peptide.

[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: PMC1135023.
[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.

TONIX PHARMACEUTICALS

TNX-1900 for Migraine
Magnesium (Mg^{2+}) is at the Core of Oxytocin Binding[1]

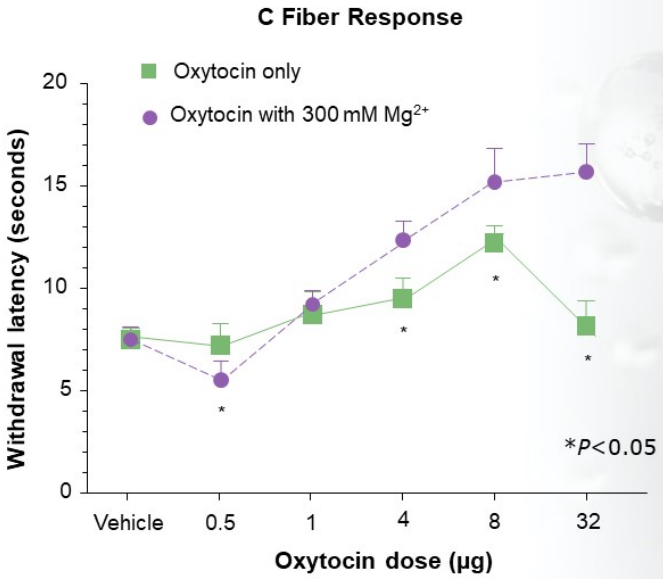
TNX-1900 contains magnesium: Recent structural studies show magnesium is at the core of oxytocin binding to oxytocin receptor[1]



[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-1900 for Migraine
Addition of Mg2+ Augments Oxytocin-Induced Analgesia in Animal Model

***in vivo* effect of Mg^{2+} ion addition with intranasal oxytocin-induced craniofacial analgesia on the withdrawal response time to noxious heat stimulation of the cheek of pre-inflamed rat**



Bharadwaj VN, et al. *Pharmaceutics.* 2022;14(5):1105.

TNX-2900*: Prader-Willi Syndrome
Intranasal Potentiated Oxytocin (OT) with Magnesium

PROFILE

Prader-Willi Syndrome is the most common genetic cause of life-threatening childhood obesity

- Rare disease occurring in 1 in 10,000 to 1 in 30,000 births

Symptoms include lack of suckling as infants, poor muscle strength, and constant hunger (hyperphagia)

- In animal models, OT has improved suckling and suppressed hunger
  - Tonix's patented potentiated OT formulation is believed to increase specificity for OT receptors relative to off-target vasopressin receptors

Patents Issued

DEVELOPMENT PROGRAM

Market Entry: Prader-Willi Syndrome

Additional Indications: Rare Hyperphagia Conditions

Status: Preclinical, granted orphan drug designation by FDA

Next Steps: pre-IND Meeting to seek agreement on development plans

*TNX-2900 is in the pre-IND stage of development and has not been approved for any indication.

TNX-1500*: Prevention of Allograft Rejection
Next Generation α-CD40 Ligand (CD40L) Antibody

THE CD40-CD40L pathway is a pivotal immune system modulator and a well-established and promising treatment target

First Generation: Development halted due to thromboembolic (TE) complications—blood clots—traced to Fc gamma receptor (FcγR)

Second Generation: Eliminated the FcγR TE complication but *potency and half life was reduced, limiting utility*

Third Generation (TNX-1500): Re-engineered to better modulate the binding of FcγR while preserving FcRn function

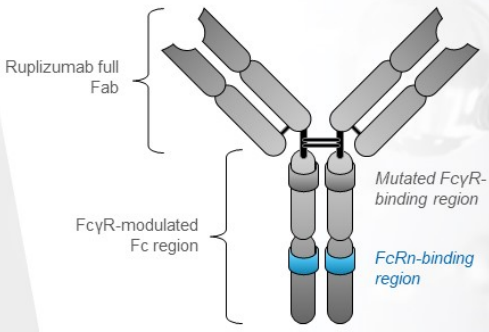
- Expected to deliver efficacy without compromising safety

Status: Preclinical; collaborations ongoing with Mass General Hospital on heart and kidney transplantation in non-human primates

Next Steps: 1H 2023 Initiate Phase 1 Study

Patents Filed

SELECTIVELY MODIFIED anti-CD40L AB



Contains the full ruplizumab Fab and the engineered Fc region that modulates FcγR-binding, while preserving FcRn function.

*TNX-1500 is in the pre-IND stage of development and has not been approved for any indication.

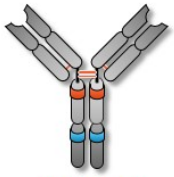
IMMUNOLOGY PORTFOLIO

[1]Camilleri B, et al. *Exp Clin Transplant.* 2016;14(5):471-483.

TONIX PHARMACEUTICALS

Third-Generation α-CD40L
Engineered to Decrease Risk of Thrombosis

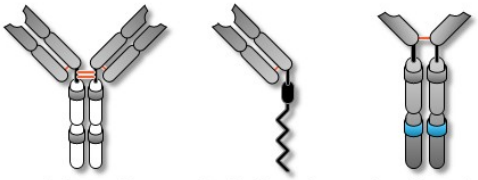
First-generation
anti-CD40L mAbs



Ruplizumab

Constant fragment (Fc) domain interacted with FcγRIIA (CD32A), which suggested a mechanism for the increased risk of thrombosis.[1,2]

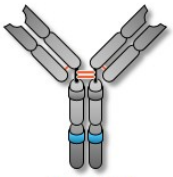
Second-generation
anti-CD40L mAbs



Aglycosyl Ruplizumab *Dapirolizumab* *Letolizumab*

Second-generation anti-CD40L mAbs exhibited dramatically reduced binding to FcγRIIA[3-5] but had other issues, including decreased efficacy.[6-8]

Third-generation
anti-CD40L mAbs*



TNX-1500

TNX-1500 is engineered to target CD40L therapeutically while reducing FcγRIIA binding and thereby lowering the potential for thrombosis.[1-8]

*Sanofi's SAR441344 and Eledon's tegoprubart (f.k.a., AT-1501) also are F_c-modified

[1]Inwald DP, et al. *Circ Res*. 2003;92(9):1041-1048.
[2]Robles-Carrillo L, et al. *J Immunol*. 2010;185(3):1577-1583.
[3]Shock A, et al. *Arthritis Res Ther*. 2015;17(1):234.
[4]Xie JH, et al. *J Immunol*. 2014;192(9):4083-4092.
[5]Ferrant JL, et al. *Int Immunol*. 2004;16(11):1583-1594.
[6]ClinicalTrials.gov identifier: NCT02273960. Updated July 16, 2019. Accessed June 1, 2021. https://clinicaltrials.gov/ct2/show/results/NCT02273960?view=results
[7]Walters J, *Biocentury*; October 26, (2018). https://www.biocentury.com/article/298908/biogen-ucb-report-phase-iib-miss-for-lupus-candidate-dapirolizumab
[8]Company data.

Development and Regulatory Strategy

- **1st Indication – Kidney allotransplantation (human to human)**
  - Replacement for nephrotoxic CNI's (calcineurin inhibitors, *e.g.* Prograf® (tacrolimus)[1], Neoral® (cyclosporin)[2]
  - Similar development path to the successful development of BMS's Nulojix® (belatacept)[3], CTLA-4/Ig biologic
  - Clinical development may combine with Nulojix or Rapamune® (rapamycin/sirolimus)[4]
- **2nd Indication – Heart or kidney xenotransplant (pig to human)**
  - CD40L:CD40 blockade considered essential
  - The engineered pig organ is also considered a biologic
- **3rd Indication –Lou Gehrig's Disease, or ALS[5]**
  - Animal models show strong activity; competitor Eledon (ELDN) is pursuing ALS as primary indication
- **4th Indication (and beyond) – Autoimmune disease (e.g., Systemic Lupus Erythematosus, Rheumatoid Arthritis, Progressive Systemic Sclerosis)**
  - These indications require large studies; SLE and RA would represent very large target markets

[1]http://www.accessdata.fda.gov/drugsatfda_docs/label/2009/050708s027,050709s021lbl.pdf
[2]http://www.novartis.us/sites/www.novartis.us/files/neoral.pdf
[3]https://packageinserts.bms.com/pi/pi_nulojix.pdf
[4]https://labeling.pfizer.com/showlabeling.aspx?id=139
[5]Amyotrophic Lateral Sclerosis

TNX-1700*: Gastric and Colorectal cancers
Stabilized Recombinant Trefoil Factor 2 (rTFF2)

IMMUNOLOGY PORTFOLIO

POTENTIAL NEW CANCER TREATMENT

- TNX-1700 (rTFF2) has effects on cancer by altering the tumor micro-environment
- Mechanism of action: suppresses myeloid-derived suppressor cells and activates anti-cancer CD8+ T cells
- Potential synergy with anti-PD-1 or anti-PD-L1 monoclonal antibodies (mAbs)

PRECLINICAL EVIDENCE FOR INHIBITING GROWTH OF CANCER CELLS

- Data showed that TFF2-CTP augmented the efficacy of mAb anti-PD-1 therapy. Anti-PD-1 in combination with TFF2-CTP showed greater anti-tumor activity in PD-L1-overexpressing mice.

LICENSED FROM COLUMBIA UNIVERSITY

- Developing in partnership under sponsored research agreement

Patents Filed

DEVELOPMENT PROGRAM

Market Entry: Gastric and colorectal cancers

Status: Preclinical

Next Steps: Animal studies ongoing

*TNX-1700 is in the pre-IND stage of development and has not been approved for any indication.

TONIX PHARMACEUTICALS

TONIX PHARMACEUTICALS

INFECTIOUS DISEASE: KEY CANDIDATES

TNX-801: Monkeypox and Smallpox Vaccine
Live Virus Platform Development Program

APPLICATION OF LIVE VIRUS PLATFORM

- TNX-801 is a cloned version of horsepox[1] (without any insert) purified from cell culture
- In addition to being a potential addition to the U.S. Strategic National Stockpile, TNX-801serves as the basis for the RPV/horsepox platform

ANIMAL TESTING OF TNX-801 WITH SOUTHERN RESEARCH INSTITUTE

- Non-human primate monkeypox challenge testing: positive data reported in 1Q 2020[2]

DEVELOPED IN COLLABORATION WITH UNIVERSITY OF ALBERTA

- Proprietary synthetic biology approach and vector system

Patents Filed

DEVELOPMENT PROGRAM

Market Entry: Monkeypox and Smallpox Vaccine

Status: Preclinical, Pre-IND

Next Steps: Developing GMP manufacturing for TNX-801; initiate Phase 1 Trial, 1H 2023 in Kenya

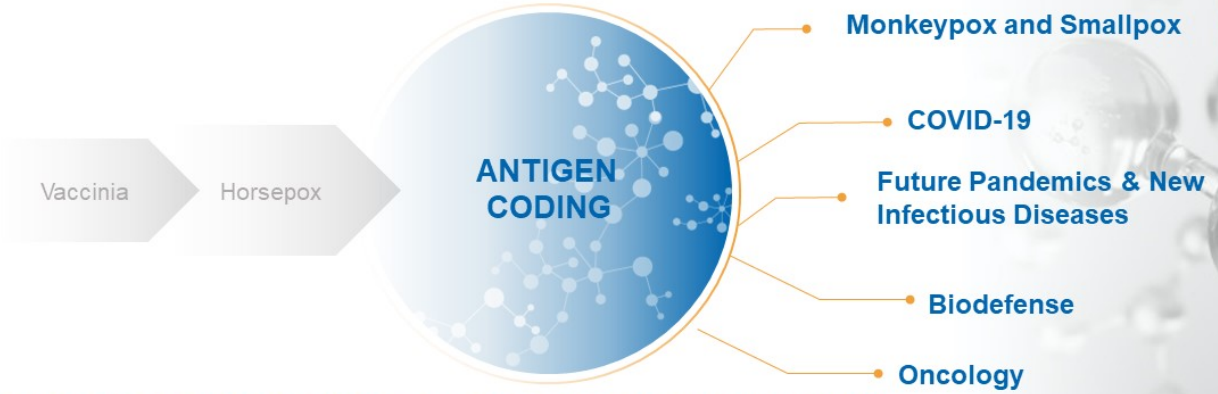
*TNX-801 is in the pre-IND stage of development and has not been approved for any indication.

INFECTIOUS DISEASE PORTFOLIO

[1]Noyce RS, et al. Construction of an infectious horsepox virus vaccine from chemically synthesized DNA fragments. PLoS One. 2018 Jan 19;13(1):e0188453.
[2]Noyce, RS, et al. Synthetic Chimeric Horsepox Virus (scHPXV) Vaccination Protects Macaques from Monkeypox* Presented as a poster at the American Society of Microbiology BioThreats Conference - January 29, 2020, Arlington, VA. (https://content.equisolve.net/tonixpharma/media/10929ac27f4fb5f5204f5cf41d59a121.pdf)

TONIX PHARMACEUTICALS

Live Virus Vaccine Platform: Recombinant Pox Vaccine (RPV)
Technology for Emerging Infectious Diseases and Oncolytics



RPV VECTOR BELIEVED SIMILAR TO EDWARD JENNER'S VACCINE[1-3]

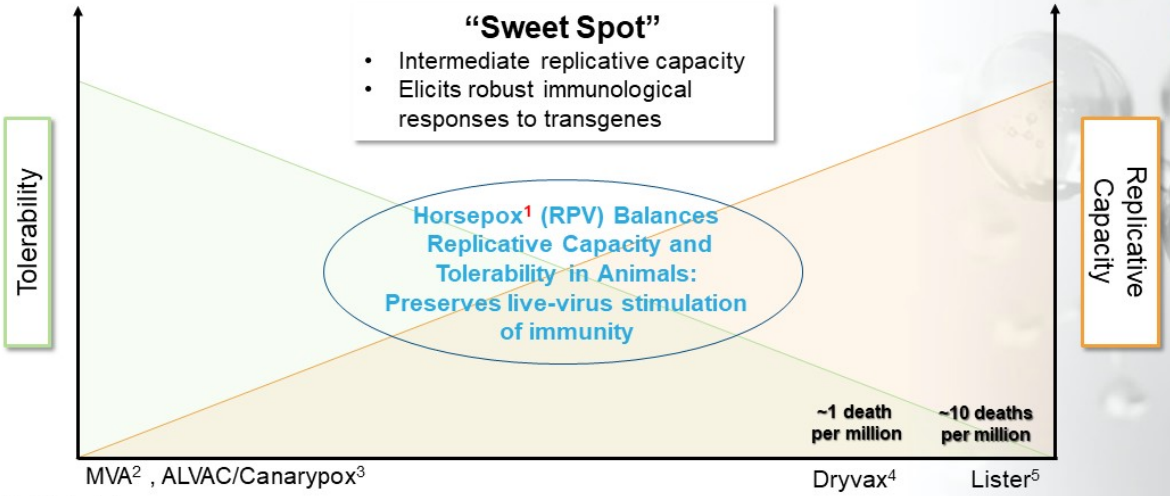
Using Proven Science To Address Challenging Disease States, We Have Created A Programmable Technology Platform Aimed At Combating Future Threats To Public Health

INFECTIOUS DISEASE PORTFOLIO

[1]Shrick, L. N Engl J Med 2017; 377:1491-1492. DOI: 10.1056/NEJMc1707600
[2]Esparza, J. Vaccine. 2020 Jun 19; 38(30): 4773–4779. doi: 10.1016/j.vaccine.2020.05.037
[3]Brinkmann, A. Genome Biol. 2020; 21: 286. doi: 10.1186/s13059-020-02202-0

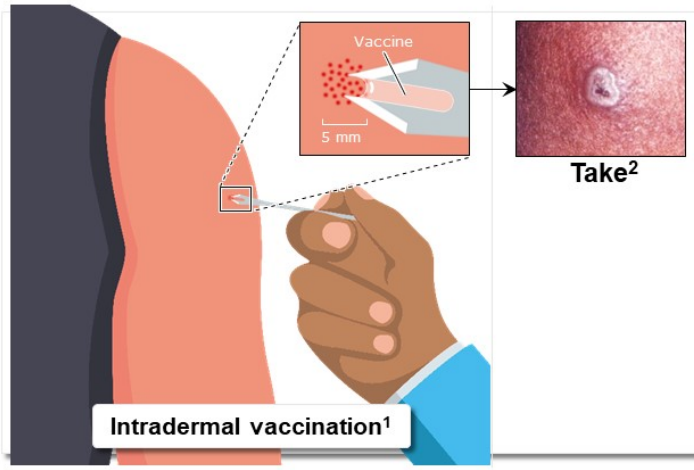
TONIX PHARMACEUTICALS

Spectrum of Pox-Virus Replicative Capacity
Horsepox Has Lower Replicative Capacity in Human Cells



MVA = Modified Vaccinia virus Ankara
[1]Tonix Pharmaceuticals. June 1, 2022. Accessed Sept 30, 2022. ir.tonixpharma.com/news-events/press-releases/detail/1318/tonix-pharmaceuticals-announces-issuance-of-u-s-patent-for
[2]Volz A, et al. *Adv Virus Res.* 2017;97:187-243.
[3]Kim, JH, et al, Annual Review of Medicine 2015, 66: 423-437.
[4]Belongia EA, et al. *Clin Med Res.* 2003;1(2):87-92.
[5]Kretzschmar M, et al. *PLoS Med.* 2006;3(8):e272.

Vaccinia and Horsepox Induce a Skin Reaction Called a "Take"
Described by Dr. Edward Jenner



- **Biomarker of protection**
  - Smallpox was eradicated using this marker
  - Revaccination indicated for recipients without "take"
- **Measure of T cell immunity**
  - No need for blood draws or complex laboratory studies
  - No other functional T cell assay is approved or in clinical use for vaccination

*Example of major cutaneous reaction, or "take," resulting from a replication-competent live-virus vaccine with intradermal delivery, indicating successful vaccination[1,2]

[1]Fulginiti VA, et al. *Clin Infect Dis.* 2003;37(2):241-250.
[2]Centers for Disease Control and Prevention. Accessed April 15, 2020. https://phil.cdc.gov/Details.aspx?pid=3276

TNX-1850*: COVID-19 Vaccine
Live Virus Platform Development Program

APPLICATION OF LIVE VIRUS PLATFORM

- First version TNX-1800 encodes spike protein from SARS-CoV-2, Wuhan strain
- Planned new version TNX-1850 encode spike protein from SARS-CoV-2 BA.2 strain[1]

ANIMAL TESTING OF TNX-1800 WITH SOUTHERN RESEARCH INSTITUTE

- Non-human primate immune response: positive results reported in 4Q 2020
- Non-human primate CoV-2 challenge testing: positive data reported in 1Q 2021

DEVELOPED IN COLLABORATION WITH UNIVERSITY OF ALBERTA

- Proprietary synthetic biology approach and vector system

Patents Filed

DEVELOPMENT PROGRAM

Market Entry: COVID-19 Vaccine

Additional Indications: Future Pandemic, Infectious Disease, Smallpox, Cancer

Status: Preclinical

Next Steps: Developing TNX-1850 (BA.2) version

*TNX-1850 is in the pre-IND stage of development and has not been approved for any indication.

[1]Brennan, Z. *Endpoints* March 2, 2022 (https://endpts.com/weaker-omicron-variant-is-great-news-for-the-world-but-bad-news-for-covid-related-clinical-trials/)

INFECTIOUS DISEASE PORTFOLIO

TONIX PHARMACEUTICALS

Live Virus Platform: What Makes TNX-1850 Different from mRNA Vaccines

CRITERIA	mRNA VACCINES	TNX-1850
Number of shots	Two	One
Duration	6 months	Years / decades
Boosters	Recommended	Likely not required
Protection from variants	Decreased	Expected
Forward transmission	Unknown for variants	Likely prevents
Biomarker	None	Yes – "Take"
Manufacturing	Complex	Conventional
Glass-sparing packaging	No	Yes
Shipping and storage	Cold chain	Standard refrigeration
Protection from smallpox	No	Yes

** Characterizations of TNX-1850 shown in table represent expectations.*

INFECTIOUS DISEASE PORTFOLIO

TONIX PHARMACEUTICALS

TNX-2300*: COVID-19 Vaccine
Live Virus Vaccine Based on Bovine Parainfluenza (BPI) Virus

LIVE VIRUS VACCINE[1-5]

- Previously has been shown to be an effective antigen delivery vector in humans, notably well tolerated in infants and children
- Vector is well suited for mucosal immunization using a nasal atomizer, but it can also be delivered parenterally

ANIMAL TESTING OF TNX-2300 ONGOING

- Non-human primate immune response: positive results reported in 4Q 2020
- Non-human primate CoV-2 challenge testing: positive data reported in 1Q 2021

DEVELOPED IN COLLABORATION WITH KANSAS STATE UNIVERSITY (KSU)

- Uses a novel live attenuated vaccine vector platform, BPI, and the CD40-ligand to stimulate T cell immunity

Patents Filed

DEVELOPMENT PROGRAM

Market Entry: COVID-19 Vaccine

Additional Indications: Future Pandemic, Infectious Diseases

Status: Preclinical

Next Steps: Animal studies with KSU to test the effect of co-expression of the CD40-ligand, also known as CD154 or 5c8 antigen, to stimulate T cell immunity.

*TNX-2300 is in the pre-IND stage of development and has not been approved for any indication.

INFECTIOUS DISEASE PORTFOLIO

[1]Halle, AA *et al. J Gen. Virology* (2003) 84:2153–2162; [2]Halle, AA *et al. J Virology* (2000) 74 (24): 11626–11635; [3]Karron RA *et al. J Inf Dis* (1995) 171: 1107-14; [4]Karron RA *et al. Vaccine* (2012) 30: 3975– 3981; [5]Schmidt AC *et al. J Virology* (2001) 75(10): 4594–4603

TONIX PHARMACEUTICALS

TNX-3600*: COVID-19 Therapeutics
Fully Human Monoclonal Antibody Platform

PROFILE

Collaboration with Columbia University

Human monoclonal antibodies (mAbs) generated from COVID-19 convalescent patients

Potential monotherapies

- Plan to seek indication similar to current EUA therapeutic mAbs for treating individuals with mild-to-moderate COVID-19 who are at high risk for progression to severe disease

Potential combination therapy with other antibodies

- Combination therapies for other anti-CoV-2 monoclonal antibodies are believed to have reduced the emergence of drug resistant viral strains

Given the unpredictable trajectory of the SARS-CoV-2 virus and new variants[1], we seek to contribute to a broad set of monoclonal antibodies from a variety of patients, that can be scaled up quickly and potentially combined with other monoclonal antibodies.

DEVELOPMENT PROGRAM

Market Entry: COVID-19 Therapeutic

Additional Indications: Symptomatic COVID in patients with risk factors for poor outcome

Status: Preclinical

Next Steps: Study inhibition of SARS CoV-2 variants in tissue culture

*TNX-3600 is in the pre-IND stage of development and has not been approved for any indication.

INFECTIOUS DISEASE PORTFOLIO

[1]Waltz, E. Nature. "Does the World Need an Omicron Vaccine?" 28 Jan 2022 https://www.nature.com/articles/d41586-022-00199-z

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TNX-3700*: COVID-19 Vaccine
Zinc Nanoparticle (ZNP) Formulation for mRNA Vaccines

INFECTIOUS DISEASE PORTFOLIO

PROFILE

Collaboration with Kansas State University

ZNP technology is a potential replacement for the Lipid Nanoparticle (LNP) technology of current mRNA vaccines

Potential improved stability
- Plan to seek initial indications as booster, similar to the current EUA and FDA approved mRNA vaccines
- Improved stability would facilitate shipping and storage

Addresses limitations in current mRNA vaccines which require ultra-cold storage and shipping
- Stability issues limit use in less developed countries

Patents Filed

DEVELOPMENT PROGRAM

Market Entry: Booster for COVID-19 Vaccines

Additional Indications: COVID-19 vaccine for naïve individuals

Status: Preclinical

Next Steps: Research at K-State on CoV-2 spike based vaccine in tissue culture and animals

*TNX-3700 is in the pre-IND stage of development and has not been approved for any indication.

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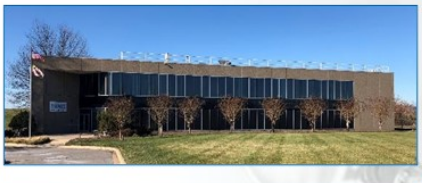
Live Virus RPV Platform
Internal Development & Manufacturing Capabilities

INFECTIOUS DISEASE PORTFOLIO

Infectious Disease R&D Center (RDC) – Frederick, MD
- Function: Accelerated development of vaccines and antiviral drugs against COVID-19, its variants and other infectious diseases
- Description: ~48,000 square feet, BSL-2 with some areas designated BSL-3
- Status: Operational

Advanced Development Center (ADC) – North Dartmouth, MA
- Function: Development and clinical scale manufacturing of live-virus vaccines
- Description: ~45,000 square feet, BSL-2
- Status: Partially operational as of 2Q 2022

Commercial Manufacturing Center (CMC) – Hamilton, MT
- Function: Phase 3 and Commercial scale manufacturing of live-virus vaccines
- Description: ~44 acre green field site, planned BSL-2
- Status: Planning for site enabling work in 2022



Architectural Rendering

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American Pandemic Preparedness Plan (AP3)

- **"Platforms" – Foundation of Pandemic Response**
  - Key element of AP3 from White House Office of Science and Technology Policy or OSTP[1,2]
    - 100 days to human trials
    - Technologies that do not require sterile injection

- **TNX-801/TNX-1850 (live virus RPV) platform addresses OSTP requirements[1,2]**
  - Our goal is to be able to test new live virus vaccines against novel pathogens within the 100 days of obtaining sequence
    - RDC is equipped to make new vaccines
    - ADC will be equipped to make clinical trial material
    - CMC is planned to make commercial scale material

[1] Sept 3, 2021 (https://www.whitehouse.gov/wp-content/uploads/2021/09/American-Pandemic-Preparedness-Transforming-Our-Capabilities-Final-For-Web.pdf)
[2] Sept 3, 2021 (https://www.whitehouse.gov/briefing-room/statements-releases/2021/09/03/fact-sheet-biden-administration-to-transform-capabilities-for-pandemic-preparedness/)

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-1850: COVID-19 VACCINE

Kansas State University

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

Milestones: Recently Completed and Upcoming*

- ☑ 1st Quarter 2022 — Topline data from Phase 3 RALLY study of TNX-102 SL for the management of fibromyalgia
- ☑ 2nd Quarter 2022 — Phase 3 RESILIENT study start of TNX-102 SL for the management of fibromyalgia
- ☑ 3rd Quarter 2022 — Phase 2 PREVAIL study start of TNX-102 SL for the treatment of Long COVID

Expected Data

- ❑ 2nd Quarter 2023 — Interim analysis results of Phase 3 RESILIENT study of TNX-102 SL in fibromyalgia
- ❑ 1st Half 2023 — Interim analysis results of Phase 2 PREVAIL study of TNX-102 SL in Long COVID

Expected Clinical Trial Initiations

- ❑ 4th Quarter 2022 — Phase 2 study start of TNX-102 SL for the treatment of PTSD in Kenya
- ❑ 4th Quarter 2022 — Phase 2 study start of TNX-1900 for the treatment of migraine
- ❑ 1st Quarter 2023 — Phase 2 study start of TNX-1300 for the treatment of cocaine intoxication
- ❑ 1st Quarter 2023 — Phase 2 study start of TNX-601 ER for the treatment of major depressive disorder
- ❑ 1st Half 2023 — Phase 1 study start of TNX-1500 for prevention of allograft rejection
- ❑ 1st Half 2023 — Phase 1 study start of TNX-801 for prevention of monkeypox and smallpox in Kenya

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

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