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): November 23, 2021

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 Global 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 November 23, 2021, Tonix Pharmaceuticals Holding Corp. (the "Company") issued a press release announcing the U.S. Food and Drug Administration ("FDA") cleared the Investigational New Drug ("IND") Application to support the initiation of a Phase 2 study of the Company's TNX-1900 (intranasal potentiated oxytocin) product candidate for the prevention of migraine headache in chronic migraineurs. 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 November 23, 2021, the Company announced that the FDA cleared the IND Application to support the initiation of a Phase 2 study of TNX-1900 for the prevention of migraine headache in chronic migraineurs. The program is expected to qualify for the 505(b)(2) pathway for FDA approval, which is available to new formulations of an approved drug. The Company believes that by engaging and stimulating oxytocin receptors in the trigeminal ganglia, TNX-1900 has the potential to help chronic migraine sufferers. TNX-1900 contains magnesium, which potentiates the action of oxytocin at oxytocin receptors in animal models. The Company expects to begin enrollment in the TNX-1900 Phase 2 study in the second half of 2022, and plans to develop TNX-1900 for craniofacial pain and insulin resistance.

The Company updated its expectation for topline data from the Phase 3 RALLY study for its TNX-102 SL product candidate for the management of fibromyalgia to be the first quarter of 2022, and the commencement of another Phase 3 study for the management of fibromyalgia to occur in first half of 2022. The Company also updated its expectation for the commencement of a first-in-human clinical study for its TNX-2100 SARS-CoV-2 functional T cell immunity skin test product candidate to be the first quarter of 2022.

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 intellectual property rights and protections related to TNX-1700, 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 November 23, 2021
99.02	Corporate Presentation by the Company for November 2021
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: November 23, 2021

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

Exhibit 99.01

Tonix Pharmaceuticals Announces FDA Clearance of the IND for Potentiated Intranasal Oxytocin (TNX-1900) for the Prevention of Migraine Headache in Chronic Migraineurs

Approximately Four Million in U.S. Suffer from Chronic Migraine

Development of TNX-1900 Also Planned for Treatment of Episodic Migraine, Craniofacial Pain and Insulin Resistance

CHATHAM, NJ, November 23, 2021 (GLOBE NEWSWIRE) – 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 the initiation of a Phase 2 study of TNX-1900* (intranasal potentiated oxytocin) for the prevention of migraine headache in chronic migraineurs. The program is expected to qualify for the 505(b)(2) pathway for FDA approval, which is available to new formulations of an approved drug.

"We are excited to have received the FDA's IND clearance to begin clinical trials for TNX-1900 in prevention of migraine headaches in chronic migraineurs," said Seth Lederman, M.D., President and CEO of Tonix. "An estimated four million individuals in the United States suffer from chronic migraine. We believe that by engaging and stimulating oxytocin receptors in the trigeminal ganglia, TNX-1900 has the potential to help chronic migraine sufferers. TNX-1900 contains magnesium, which potentiates the action of oxytocin at oxytocin receptors in animal models. We expect to begin enrollment in the TNX-1900 Phase 2 study in the second half of 2022." Dr. Lederman added, "We also plan to develop TNX-1900 for craniofacial pain as well as insulin resistance. A related intranasal potentiated oxytocin product candidate, TNX-2900*, is under development for the treatment of Prader-Willi syndrome."

**TNX-1900 and TNX-2900 are investigational new drugs and have not been approved for any indication.*

About Migraine

Migraine is a neurological condition that manifests in throbbing headache, often on one side of the head, that lasts at least four hours. It can also be accompanied by nausea, vomiting, visual disturbances, and sensitivity to bright light, strong smells, and loud noises[1]. Epidemiological studies indicate that globally, approximately 1.2 billion individuals suffer from migraines annually.[2] In the U.S., approximately 39 million Americans suffer from migraines and among these individuals, approximately four million experience chronic migraines (15 or more headache days per month).[2]

About TNX-1900

TNX-1900 (intranasal potentiated oxytocin) is a proprietary formulation of oxytocin in development as a candidate for prophylaxis of chronic migraine and for the treatment of craniofacial pain, insulin resistance and related conditions. In 2020, TNX-1900 was acquired from Trigemina, Inc. and licensed from Stanford University. TNX-1900 is a drug-device combination product, based on an intranasal actuator device that delivers oxytocin into the nose. Oxytocin is a naturally occurring human hormone that acts as a neurotransmitter in the brain. Oxytocin has no recognized addiction potential. It has been observed that low oxytocin levels in the body can lead to increase in migraine headache frequency, and that increased oxytocin levels can relieve migraine headaches. Certain other chronic pain conditions are also associated with decreased oxytocin levels. Migraine attacks are caused, in part, by the activity of pain-sensing trigeminal nerve cells which, when activated, release of CGRP which binds to receptors on other nerve cells and starts a cascade of events that is believed to result in headache. Oxytocin when delivered via the nasal route, concentrates in the trigeminal system[3] resulting in binding of oxytocin to receptors on neurons in the trigeminal system, inhibiting transmission of pain signals and the release of CGRP.[4] Blocking CGRP release is a distinct mechanism compared with CGRP antagonist and anti-CGRP antibody drugs, which block the binding of CGRP to its receptor. With TNX-1900, the addition of magnesium to the oxytocin formula enhances oxytocin receptor binding[5] as well as its effects on trigeminal neurons and craniofacial analgesic effects in animal models[7]. Intranasal oxytocin has been well tolerated in several clinical trials in both adults and children[6]. Targeted nasal delivery results in low systemic exposure and lower risk of non-nervous system, off-target effects which could potentially occur with systemic CGRP antagonists such as ant-CGRP antiibodies[8]. For example, CGRP has roles in dilating blood vessels in response to ischemia, including in the heart. We believe nasally targeted delivery of oxytocin could translate into selective blockade of CGRP release in the trigeminal ganglion and not throughout the body, which could be a potential safety advantage over systemic CGRP inhibition. In addition, daily dosing is more quickly reversible, in contrast to monthly or quarterly dosing, as is the case with anti-CGRP antibodies, giving physicians and their patients greater control. We intend to initiate a Phase 2 study in chronic migraine in the second half of 2022. We also plan to develop TNX-1900 for treatment of episodic migraine, craniofacial pain and insulin resistance. Tonix has a license with the University of Geneva to use TNX-1900 for the treatment of insulin resistance and related conditions. TNX-2900* is another intranasal potentiated oxytocin-based therapeutic candidate, being developed for the treatment of Prader-Willi syndrome, or PWS. The technology for TNX-2900 was licensed from the French National Institute of Health and Medical Research. PWS, an orphan condition, is a rare genetic disorder of failure to thrive in infancy, associated with uncontrolled appetite later in childhood.

[1] https://www.mayoclinic.org/diseases-conditions/migraine-headache/symptoms-causes/syc-20360201

[2] Burch et al., *Migraine: Epidemiology, Burden, and Comorbidity,* Neurol Clin 37 (2019) 631–649.

[3] Yeomans DC, et al. *Transl Psychiatry*. 2021. 11(1):388.

[4] Tzabazis A, et al. *Cephalalgia*. 2016. 36(10):943-50.

[5] Antoni FA and Chadio SE. *Biochem J.* 1989. 257(2):611-4.

[6] Yeomans, DC et al. 2017. US patent US2017368095

[7] Cai Q, et al., *Psychiatry Clin Neurosci*. 2018. Mar;72(3):140-151.

[8] MaassenVanDenBrink A, et al. *Trends Pharmacol Sci.* 2016. 37(9):779-788

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 primarily composed of immunology and central nervous system (CNS) product candidates. Tonix's immunology portfolio includes COVID-19-related product candidates to prevent and treat COVID-19, to treat Long COVID as well as to detect functional T cell immunity to SARS-CoV-2. 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[1] (cyclobenzaprine HCl sublingual tablets), is in mid-Phase 3 development for the management of fibromyalgia. TNX-1300[2] is a biologic designed to treat cocaine intoxication that is expected to start a Phase 2 trial before year end. Tonix's lead vaccine candidate for COVID-19, TNX-1800[3], is a live replicating vaccine based on Tonix's

recombinant pox vaccine (RPV) platform to protect against COVID-19, primarily by eliciting a T cell response. Tonix expects to start a Phase 1 study in humans in the second half of 2022. Tonix is developing TNX-2100[4], an *in vivo* diagnostic to measure the presence of functional T cell immunity to SARS-CoV-2 and intends to initiate a first-in-human clinical study in the first quarter of 2022. TNX-3500[5] (sangivamycin) is a small molecule antiviral drug to treat acute COVID-19 and is in the pre-IND stage of development. Finally, TNX-102 SL is a small molecule drug being developed to treat Long COVID, a chronic post-COVID condition, and is also in the pre-IND stage. Tonix expects to conduct a Phase 2 study in Long COVID in the first half of 2022. Tonix's immunology portfolio also includes biologics to address immunosuppression, cancer, and autoimmune diseases.

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

[2] *TNX-1300 is an investigational new biologic at the pre-IND stage of development and has not been approved for any indication.*

[3] *TNX-1800 is an investigational new biologic and has not been approved for any indication. TNX-1800 is based on TNX-801, live horsepox virus vaccine for percutaneous administration, which is 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-2100 is an investigational new biologic and has 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.*

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 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, 2020, as filed with the Securities and Exchange Commission (the "SEC") on March 15, 2021, and periodic reports filed with the SEC on or after the date thereof. All 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, 2020, as filed with the Securities and Exchange Commission (the "SEC") on March 15, 2021, 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

ADVANCING THE SCIENCE AND UNDERSTANDING OF DISEASES

by developing **innovative therapies** that improve **population health**

by focusing on **unmet needs** in patient care

OUR STRATEGY

Using our integrated development engine, we advance innovative programs across multiple therapeutic areas into the clinic while maximizing asset potential

TONIX PHARMACEUTICALS

PIPELINE
COVID, BIODEFENSE & IMMUNOLOGY PORTFOLIO

COVID, BIODEFENSE AND IMMUNOLOGY PORTFOLIO

CANDIDATES	PORTFOLIO & INDICATION	STATUS / NEXT MILESTONE
	COVID	
TNX-1800	COVID-19 Vaccine[1]	Phase 1 start - 2H 2022
TNX-102 SL	Long COVID-19 (Post-Acute Sequelae of COVID-19 or PASC)[2]	Phase 2 start – 1H 2022
TNX-2100	SARS-CoV-2 Diagnostic for T-Cell Immunity[3]	First-in-human study – Q1 2022
TNX-3500	COVID-19 Antiviral[4]	Preclinical
	BioDefense	
TNX-801[5]	Smallpox and monkeypox preventing vaccine	Preclinical
TNX-701	Radioprotection	Preclinical
	Immunology & Oncology	
TNX-1500[6]	Organ Transplant Rejection/ Autoimmune Conditions	Phase 1 start – 2H 2022
TNX-1700[7]	Gastric and pancreatic cancers	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 vector.
[2]Pre-IND (Investigational New Drug) meeting with the FDA completed; Company plans to file IND to support Phase 2 study in subset of patients whose symptoms overlap with fibromyalgia.
[3]In vivo diagnostic: SARS-CoV-2 peptide epitope mixtures for intradermal administration to measure delayed-type hypersensitivity to SARS-CoV-2.
[4]Sangivamycin for injection.
[5]Live attenuated vaccine based on horsepox virus
[6]anti-CD40L humanized monoclonal antibody
[7]Recombinant trefoil factor 2 (rTFF2) based protein; licensed from Columbia University

TONIX PHARMACEUTICALS

PIPELINE
CNS PORTFOLIO

CNS PORTFOLIO

Candidates	INDICATION	STATUS / NEXT MILESTONE
	CNS	
TNX-102 SL[1]	Fibromyalgia (FM) Posttraumatic Stress Disorder (PTSD) Long COVID (PASC[2])	Mid-Phase 3 Phase 2 start – 1Q 2022 Phase 2 start – 1H 2022[3]
TNX-1300[4]	Cocaine Intoxication / Overdose	Phase 2 start – 4Q 2021
TNX-1900[5]	Migraine and Craniofacial Pain	Phase 2 start – 2H 2022[6]
TNX-2900[7]	Prader-Willi Syndrome	Preclinical
TNX-601 CR	Depression, PTSD, Neurocognitive Dysfunction from Steroids	Phase 2 start – 1H 2022[8]
TNX-1600[9]	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 an investigational new drug and has not been approved for any indication. Long COVID/PASC program is also included in the COVID-19 Portfolio. Additional indications of Agitation in Alzheimer's Disease (AAD) and Alcohol Use Disorder (AUD) are Phase 2 ready.
[2]Post-Acute Sequelae of COVID-19.
[3]Pre-IND (Investigational New Drug) meeting with the FDA completed; Company plans to file IND to support Phase 2 study in patients whose symptoms overlap with fibromyalgia
[4]TNX-1300 (double-mutant cocaine esterase) is an investigational new biologic and has not been approved for any indication; licensed from Columbia University.
[5]Acquired from Trigemina; license agreement with Stanford University; IND cleared
[6]A Phase 2 trial under an investigator-initiated IND has been completed in the U.S. using TNX-1900; Phase 2 expected to start 2H'22
[7]Co-exclusive license agreement with French National Institute of Health and Medical Research (Inserm)
[8]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 1H 2022
[9]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

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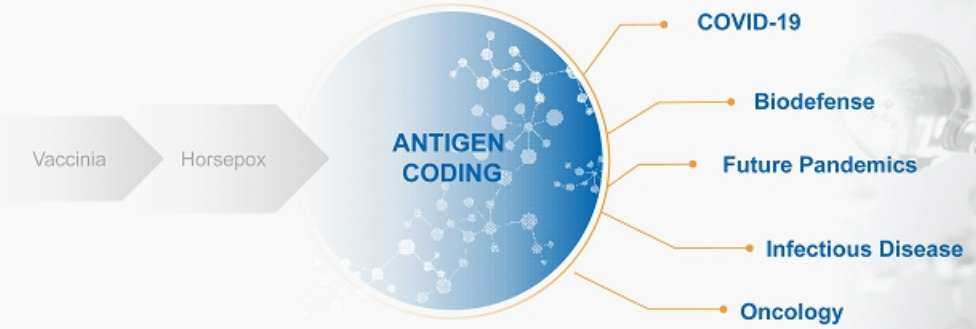
KEY CANDIDATES: COVID, BIODEFENSE & IMMUNOLOGY

RECOMBINANT POX VACCINE (RPV) PLATFORM:
NEW VACCINE TECHNOLOGY FOR EMERGING DISEASES



COVID, BIODEFENSE AND IMMUNOLOGY PORTFOLIO

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

TONIX PHARMACEUTICALS

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RPV PLATFORM PROFILE

COVID, BIODEFENSE AND IMMUNOLOGY PORTFOLIO

POTENTIALLY LONGER DURABILITY DUE TO POX-ENGINEERED ARCHITECTURE

- Enables broad CD8+ T-cell response, resulting in strong immune response

PROGRAMMABLE VECTOR DESIGN FOR USE IN DIFFERENT DISEASE MODELS

- Responsive to new variants
- Wide range of clinical applications: pandemic, biodefense, infectious disease, smallpox, oncology

VIRUS-BASED SCIENCE IS WELL ESTABLISHED

- Streamlined development
- Ability to vertically integrate development and manufacturing
- Highly concentrated non–cold-chain products

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8

RPV PLATFORM & COVID-19 VACCINE
INTERNAL DEVELOPMENT & MANUFACTURING CAPABILITIES

COVID, BIODEFENSE AND IMMUNOLOGY 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; currently BSL-2 but being converted to BSL-3
- Status: Operational; acquisition completed on October 1st, 2021

Advanced Development Center (ADC) – New Bedford, MA
- Function: Development and clinical scale manufacturing of live-virus vaccines to support Phase 1 and Phase 2 trials
- Description: ~45,000 square feet, under construction, planned BSL-2
- Status: Expected to be operational in first half 2022

Architectural Rendering

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

TONIX PHARMACEUTICALS

TNX-1800 COVID-19 VACCINE
RPV PLATFORM DEVELOPMENT PROGRAM

COVID, BIODEFENSE AND IMMUNOLOGY PORTFOLIO

ESTABLISHES RPV PLATFORM
- Encodes a protein from SARS-CoV-2, the cause of COVID-19
- Provides a novel, variant-reflexive alternative to mRNA products

ANIMAL TESTING WITH SOUTHERN RESEARCH INSTITUTE
- Non-human primate immune response: positive results reported in Q4 2020
- Non-human primate CoV-2 challenge testing: positive data reported in Q1 2021

MANUFACTURING AGREEMENT WITH FUJIFILM DIOSYNTH
- Development for GMP manufacturing for human trials
- GMP clinical supply expected to be ready for human trials in 2H 2022

Patents Filed

DEVELOPMENT PROGRAM

Market Entry: COVID-19 Vaccine

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

Status: Preclinical

Next Steps: 2H 2022 Initiate Phase 1 Study

TONIX PHARMACEUTICALS

RPV PLATFORM: WHAT MAKES TNX-1800 DIFFERENT FROM MRNA VACCINES

CRITERIA	mRNA VACCINES	TNX-1800*
Number of shots	Two	One
Duration	8 months	Years / decades
Boosters	Recommended	Likely not required
Protection from variants	Variants	Expected
Forward transmission	Unknown for variants like delta	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-1800 show in table represent expectations.*

COVID, BIODEFENSE AND IMMUNOLOGY PORTFOLIO

TONIX PHARMACEUTICALS

US TRENDS IN COVID-19 VACCINE BOOSTER DEVELOPMENT

CURRENT US GOVERNMENT STANCE IS BOOSTERS MAY BE NEEDED POST- PFIZER OR MODERNA VACCINATION[1]

- CDC, FDA, White House, COVID-19 Response Team stated that immunity wanes and booster vaccines should be used in certain cases
- FDA has authorized and CDC approved a single booster shot of the Pfizer-BioNTech and Moderna COVID-19 vaccines for Americans age 18 and older, six months after second dose
- FDA has authorized a single booster shot of the J&J vaccine for everyone who received the initial J&J vaccine two or more months ago

IMPORTANCE OF TESTING PROTECTIVE IMMUNITY

- Personalized approach to determine need for vaccine boosters
- More cost effective
- Reduces risk with unnecessary vaccination
- One-size-fits-all booster strategy is expensive and likely unsustainable

[1]www.cdc.gov/media/releases/2021/s0818-covid-19-booster-shots.html

COVID, BIODEFENSE AND IMMUNOLOGY PORTFOLIO

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ASSESSING ANTI-SARS-COV-2 PROTECTIVE IMMUNITY

COVID, BIODEFENSE AND IMMUNOLOGY PORTFOLIO

TWO TYPES OF IMMUNITY

- *Antibodies* – can be measured in a blood test, but anti-SARS-CoV-2 antibodies are not predictive of protection
- *T cell* – can be measured in a blood test, but requires sophisticated lab, unknown if predictive

NEUTRALIZING ANTIBODIES – APPEAR TO CORRELATE WITH PROTECTION[1]

- Not part of standard antibody tests
- Requires culture of antibodies with live SARS-CoV-2; possibly "pseudo-type" assays

FUNCTIONAL T CELL IMMUNITY

- *in vivo* – classic skin test – correlation with protection under investigation[2,3]

[1]Krammer, F. (2021) Nature Medicine. 27:1145–1153. https://www.nature.com/articles/s41591-021-01432-4.pdf
[2]Barrios, Y et al. Clinical Immunol. (2021) 226:108730
[3]Barrios, Y et al. Vaccines (2021) 9:575

TONIX PHARMACEUTICALS

TNX-2100*: SARS-COV-2 DIAGNOSTIC TO MEASURE T-CELL IMMUNITY

COVID, BIODEFENSE AND IMMUNOLOGY PORTFOLIO

MEASURES THE PRESENCE AND STRENGTH OF FUNCTIONAL IN VIVO T-CELL IMMUNITY

- Designed to elicit delayed-type hypersensitivity in individuals who have been exposed to SARS-CoV-2 or successfully vaccinated
- SARS-CoV-2 epitope peptide mixtures for intradermal administration (Skin Test)

POTENTIALLY SCALABLE FOR WIDESPREAD USE

- Many tests† for T-cell immunity to SARS-CoV-2 require specialized laboratories and are not amendable to standardization
- Adaptive Biotech's T Detect™ COVID-19 test received FDA EUA based on genetic analysis of T-cell receptors

DEVELOPMENT PLANS

- Q1 2022: Plan to initiate first-in-human clinical testing
- Patents filed

*TNX-2100 is in the pre-IND stage of development and has not been approved for any indication.
†Intracellular cytokine staining (ICS) measured by flow cytometry after in vitro stimulation of purified peripheral blood mononuclear cells.

TONIX PHARMACEUTICALS

TNX-3500*: COVID-19 ANTIVIRAL TREATMENT
SANGIVAMYCIN

COVID, BIODEFENSE AND IMMUNOLOGY PORTFOLIO

PROFILE

New variants heighten need for therapeutics

NIH Treatment Guidelines for COVID-19 are mixed on use of remdesivir

Potential monotherapy antiviral[1]
- 65 times more potent than remdesivir in inhibiting SARS-CoV-2 in cell culture infectivity studies (dose to achieve IC_{90})

Potential combination therapy with remdesivir[1]
- TNX-3500 antiviral effect is additive when combined with remdesivir and reduces the amount of each drug necessary for an IC_{90}
- Combination therapies for other viruses have reduced the emergence of drug resistant viral strains

Patents Filed

DEVELOPMENT PROGRAM

Market Entry: COVID-19 Antiviral

Additional Indications: MERS, Ebola, Lassa, Oncology

Status: Preclinical

Next Steps: Q4 2021 Initiate Animal Studies

MERS = Middle East Respiratory Syndrome; NIH = National Institutes of Health; PK = pharmacokinetics.

*TNX-3500 is in the pre-IND stage of development and has not been approved for any indication.

1. Bennett RP et al. *Viruses*. 2020;13(1):52. doi: 10.3390/v13010052.
2. Data on file, live virus BSL-4 testing conducted by NIAID in collaboration with OyaGen.

[1]Bennett, RP et al. *JCI Insight*. 2021 in press preview 10.1172/jci.insight.153165

TONIX PHARMACEUTICALS

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

COVID, BIODEFENSE AND IMMUNOLOGY PORTFOLIO

PROFILE

Long COVID or Post-acute Sequelae of COVID-19 (PASC[1]) – What is it?

- 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

To address the urgent need for PASC therapies, Congress awarded the National Institutes of Health $1.15 billion to study Long COVID.[3]

Patents Issued

DEVELOPMENT PROGRAM

Market Entry: Long COVID (PASC)

Status: Clinical – pre-IND; FDA minutes from pre-IND meeting received in Q3 2021

Next Steps: Start Phase 2 study for treating subset of Long COVID patients whose symptoms overlap with fibromyalgia in 1H 2022

[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.
[3]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-1500
NEXT GENERATION CD40 LIGAND ANTIBODY

COVID BIODEFENSE AND IMMUNOLOGY PORTFOLIO

THE CD40-CD40L PATHWAY IS A PIVOTAL IMMUNE SYSTEM MODULATOR AND IS A WELL-ESTABLISHED AND PROMISING TREATMENT TARGET TO MORE SAFELY PREVENT ALLOGRAFT REJECTION[1]

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: Re-engineered to better modulate the binding of FcγR while preserving FcRn function

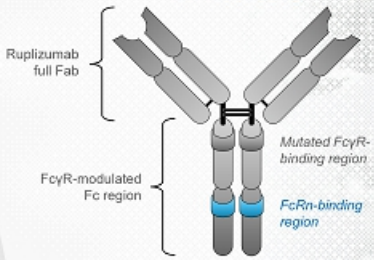
- Expected to deliver efficacy without compromising safety

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

Next Steps: 2H 2022 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

TONIX PHARMACEUTICALS

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

TONIX PHARMACEUTICALS

KEY CANDIDATES: CNS

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

Status: One Positive Phase 3 study (RELIEF) Completed

Next Steps: Second Phase 3 Study: Clinical phase completed; topline data expected 1Q 2022; Confirmatory Phase 3 planned 1H 2022

TONIX PHARMACEUTICALS

TNX-102 SL: FIBROMYALGIA
CYCLOBENZAPRINE PROTECTIC® SUBLINGUAL TABLETS PROGRAM UPDATE

CNS PORTFOLIO

Phase 3 Study, RALLY (F306)

- July 2021: Tonix stopped enrollment in the RALLY study following an unblinded, pre planned interim analysis by the Independent Data Monitoring Committee (IDMC).
- Based on interim analysis results of the first 50% (n=336) enrolled participants, the IDMC recommended stopping the trial as TNX-102 SL is unlikely to demonstrate a statistically significant improvement in the primary endpoint.
- Clinical phase of study completed, with 514 participants enrolled overall – 399 completers; topline results expected 1Q 2022
- Confirmatory Phase 3 study (F307) planned 1H 2022

Following analysis of F306 results, including pharmacogenetic comparison of F304 and F306, Tonix may modify F307 protocol

TNX 102-SL Development Beyond Fibromyalgia

- Development efforts continue in PTSD, Agitation in Alzheimer's, Alcohol Use Disorder, Long COVID

TONIX PHARMACEUTICALS

TNX-601 CR: PSYCHIATRY
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

Patents Issued

DEVELOPMENT PROGRAM

Market Entry: Major Depressive Disorder

Additional Indications: PTSD, Neurocognitive Disorder From Corticosteroids

Status: Clinical – pre-IND

Next Steps: 1H 2022 Initiate Phase 2 Trial

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]

One billion individuals worldwide suffer from migraines

Patents Issued

DEVELOPMENT PROGRAM

Market Entry: Chronic Migraine

Additional Indications: Acute Migraine, Craniofacial Pain, Insulin Resistance

Status: Clinical – IND cleared[3]

Next Steps: 2H 2022 Initiate Phase 2 Trial

1. Tzabazis et al., 2017.
2. Antoni and Chadio, 1989.
3. A Phase 2 trial under an investigator-initiated IND has been completed in the U.S. using TNX-1900

CGRP = calcitonin gene-related peptide.

TONIX PHARMACEUTICALS

TNX-2900: PRADER-WILLI SYNDROME
INTRANASAL POTENTIATED OXYTOCIN (OT) WITH MAGNESIUM

CNS PORTFOLIO

PROFILE

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

- Orphan disease occurring in 1 in 15,000 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, Orphan Hyperphagia Conditions

Status: pre-IND

Next Steps: Submit applications to the FDA for Orphan Drug and Fast Track designations for TNX-2900

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: Q4 2021 Initiate Trial

FDA Breakthrough Therapy Designation

TONIX PHARMACEUTICALS

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.


FUTURE OUTLOOK
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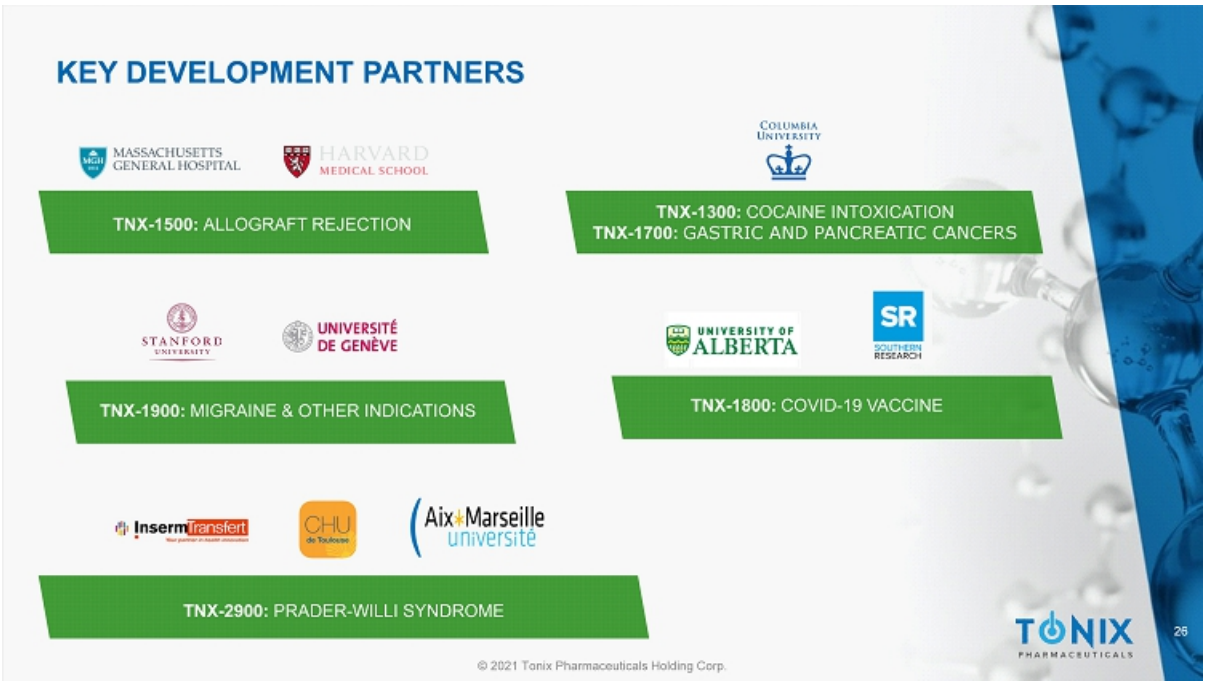
KEY DEVELOPMENT PARTNERS
MASSACHUSETTS GENERAL HOSPITAL
HARVARD MEDICAL SCHOOL
TNX-1500: ALLOGRAFT REJECTION
COLUMBIA UNIVERSITY
TNX-1300: COCAINE INTOXICATION
TNX-1700: GASTRIC AND PANCREATIC CANCERS
STANFORD UNIVERSITY
UNIVERSITÉ DE GENÈVE
TNX-1900: MIGRAINE & OTHER INDICATIONS
UNIVERSITY OF ALBERTA
SR SOUTHERN RESEARCH
TNX-1800: COVID-19 VACCINE
InsermTransfert
CHU de Toulouse
Aix Marseille université
TNX-2900: PRADER-WILLI SYNDROME
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MILESTONES:
RECENTLY COMPLETED AND UPCOMING*

- ☑ 4th Quarter 2020 Positive topline data from TNX-102 SL Phase 3 F304/RELIEF study in fibromyalgia reported
- ☑ 1st Quarter 2021 Non-human primate positive efficacy data from TNX-1800 in COVID-19 models reported

Data

- ❑ **1st Quarter 2022 Topline data from TNX-102 SL Phase 3 F306/RALLY study in fibromyalgia expected**

Expected Clinical Trial Initiations

- ❑ **4th Quarter 2021 Phase 2 OL safety study start of TNX-1300 in ED setting for cocaine intoxication**
- ❑ **1st Quarter 2022 First-in-human clinical study start of TNX-2100 for SARS-CoV-2 skin test**
- ❑ **1st Quarter 2022 Phase 2 study start of TNX-102 SL for the treatment of PTSD in Kenya**
- ❑ **1st Half 2022 Phase 3 study start of TNX-102 SL for the management of fibromyalgia**
- ❑ **1st Half 2022 Phase 2 study start of TNX-102 SL for the treatment of Long COVID**
- ❑ **1st Half 2022 Phase 2 study start of TNX-601 CR for the treatment of major depressive disorder**
- ❑ **2nd Half 2022 Phase 2 study start of TNX-1900 for the treatment of migraine**
- ❑ **2nd Half 2022 Phase 1 study start of TNX-1800 for COVID-19**
- ❑ **2nd Half 2022 Phase 1 study start of TNX-1500 for prevention of allograft rejection**

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

TONIX PHARMACEUTICALS

MANAGEMENT TEAM

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Co-Founder, CEO & Chairman

TARGENT · Fusilev (levoleucovorin) for injection · vela

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Jessica Morris
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THANK YOU
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