**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): May 9, 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 2.02 Results of Operations and Financial Condition**

On May 9, 2022, Tonix Pharmaceuticals Holding Corp. (the "Company") announced its operating results for the quarter ended March 31, 2022. A copy of the press release that discusses these matters is filed as Exhibit 99.01 to, and incorporated by reference in, this report.

**Item 7.01 Regulation FD Disclosure.**

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 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 9.01 Financial Statements and Exhibits.**

(d)

| **Exhibit No.** | **Description.** |
|---|---|
| 99.01 | Press release of the Company, dated May 9, 2022 |
| 99.02 | Corporate Presentation by the Company for May 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: May 9, 2022

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

**Exhibit 99.1**

**Tonix Pharmaceuticals Reports First Quarter 2022 Financial Results and Operational Highlights**

*Fibromyalgia Phase 3 Trial of TNX-102 SL Enrollment Initiated; Results from Interim Analysis Expected First Quarter 2023*

*Long COVID IND Cleared for TNX-102 SL; Phase 2 Trial Expected to Initiate Second Quarter 2022*

*Three Additional CNS Programs Expected to Initiate Phase 2 Studies in 2022: TNX-1300 for Cocaine Intoxication, TNX-1900 for Chronic Migraine and TNX-102 SL for PTSD*

*FDA Granted Orphan-Drug Designation for TNX-2900 for Treatment of Prader-Willi Syndrome*

*Organ Transplantation Phase 1 Study of TNX-1500 Expected to Initiate Second Half 2022*

*Cash and Cash Equivalents Totaled Approximately $140 Million at March 31, 2022*

CHATHAM, N.J., May 9, 2022 (GLOBE NEWSWIRE) – Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a clinical-stage biopharmaceutical company, today announced financial results for the first quarter ended March 31, 2022, and provided an overview of recent operational highlights.

“Tonix is making meaningful strides developing our rich portfolio of high impact product candidates,” said Seth Lederman, M.D., Chief Executive Officer of Tonix. “By the end of this year, we expect to have five central nervous system (CNS) programs in the clinic, led by our most advanced program, TNX-102 SL (cyclobenzaprine HCl sublingual tablets) for fibromyalgia, which is in mid-Phase 3 development. Enrollment has begun for TNX-102 SL in a registration-enabling-Phase 3 clinical trial. TNX-102 SL trials in Long COVID and PTSD are also expected to initiate enrollment in the second quarter of 2022.”

Dr. Lederman continued, “Long COVID is a growing problem because it is a chronic condition experienced by approximately 30% of people who recover from COVID-19. There is no currently approved treatment for this condition. We recently reported data from a retrospective observational study of U.S. adults that shows that 35% of Long COVID sufferers who experience multi-site pain are turning to addictive opioids. We are excited to study TNX-102 SL for this condition, since TNX-102 SL is a centrally-acting, non-addictive analgesic which is intended for chronic use. We look forward to starting our Phase 2 study for Long COVID with multi-site pain imminently.”

Gregory Sullivan, M.D., Chief Medical Officer of Tonix said, “We are excited by the opportunities ahead for our rich pipeline of CNS, rare disease, immunology and infectious disease product candidates. TNX-1300 (recombinant double mutant cocaine esterase) is expected to start enrolling in a Phase 2 trial in the second quarter of 2022 for emergency department treatment of cocaine intoxication, and TNX-1900 (intranasal potentiated oxytocin) is expected to enter the clinic in the second half of 2022 for the prevention of migraines in chronic migraineurs. In addition to the CNS programs, we expect to begin a Phase 1 study of TNX-1500, a monoclonal antibody targeting CD40 ligand, also known as CD154, which will initially be developed to prevent organ transplant rejection and, ultimately, to treat autoimmune conditions. We continue to progress our infectious disease portfolio, which is led by our smallpox vaccine, TNX-801 (live horsepox virus vaccine). We are also developing the live-virus vectored COVID-19 vaccines, TNX-1840 and TNX-1850 that are designed to express the spike proteins from the omicron and BA.2 variants, respectively.”

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**Recent Highlights—Key Product Candidates***

*Central Nervous System (CNS) Pipeline*

*TNX-102 SL (cyclobenzaprine HCl sublingual tablet): small molecule for the management of fibromyalgia (FM)*

- In April 2022, Tonix initiated enrollment in the RESILIENT study, a double-blind, randomized, placebo-controlled, potentially pivotal Phase 3 study of TNX-102 SL for the management of fibromyalgia. The two-arm trial is expected to enroll approximately 470 participants in the U.S. Results from a planned interim analysis are expected first quarter 2023.

- In March 2022, Tonix reported topline data from its second Phase 3 study, RALLY. As expected, based on interim analysis results reported in July 2021, TNX-102 SL did not achieve statistical significance over placebo on the primary endpoint of reduction in daily pain ($p$=0.115). Tonix reported the interim analysis of RALLY in July 2021 in which the independent data monitoring committee recommended stopping the study for futility. The Company therefore stopped enrollment of new participants while continuing those participating at that time to completion. Topline data revealed that an unexpected number of adverse event related discontinuations in both drug and placebo treated groups may have contributed to the statistical miss.

- Tonix reported positive results on the primary endpoint of reduction in daily pain ($p$=0.010) from the Phase 3 RELIEF study for the management of fibromyalgia in December 2020.

*TNX-102 SL for the treatment of Long COVID, also known as Post-Acute Sequelae of COVID-19 (PASC)*

- In April 2022, Tonix announced the U.S. Food and Drug Administration (FDA) cleared the Investigational New Drug (IND) application to support a Phase 2 clinical study with TNX-102 SL as a potential treatment for a subset of patients with Long COVID with multi-site pain and will utilize a daily pain diary as the primary endpoint. The Phase 2 trial is expected to start second quarter 2022.

- In April 2022, Tonix announced results of a retrospective observational database study of over 50,000 adult U.S. patients with Long COVID. Results showed that over 40% of patients had fibromyalgia-like multi-site pain. These findings support the feasibility of the planned Phase 2 study which will enroll Long COVID patients with multi-site pain.

- The retrospective observational database study also revealed a high rate of opioid use in Long COVID patients with multi-site pain. These findings raise concerns about development of opioid use disorder in Long COVID patients who find nowhere else to turn for symptom relief, adding to an existing national health crisis resulting from chronic use of opioids.

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*TNX-102 SL for the treatment of Posttraumatic Stress Disorder (PTSD)*

- Tonix expects to begin enrolling a Phase 2 study of TNX-102 SL in police in Kenya in the second quarter of 2022. The new PTSD study will use one month look-back CAPS-5 as the primary endpoint rather than one week look-back as was used in prior studies after a clinical guidance meeting with the FDA.

*TNX-1300 (recombinant double mutant cocaine esterase): biologic for life-threatening cocaine intoxication*

- Tonix expects to initiate a Phase 2 open-label safety study of TNX-1300 in an emergency department setting in the second quarter of 2022. TNX-1300 was licensed from Columbia University. A positive Phase 2a study of volunteer cocaine users in a controlled laboratory setting has been previously completed. TNX-1300 has been granted Breakthrough Therapy designation by the FDA.

*TNX-1900 (intranasal potentiated oxytocin): small peptide for migraine, craniofacial pain, insulin resistance and related disorders, and binge eating disorder*

- In late 2021, Tonix received IND clearance from the FDA to support the initiation of a Phase 2 study of TNX-1900 for the prevention of migraine headache in chronic migraineurs. The 505(b)(2) pathway for FDA approval is expected to be acceptable for this program since intravenous oxytocin is FDA approved and widely used to induce labor in pregnancy. The Company continues to expect to begin enrollment in the second half of 2022.

- In March 2022, Tonix entered into an agreement with Massachusetts General Hospital to evaluate TNX-1900 in an investigator-initiated Phase 2 clinical trial as a potential treatment for binge eating disorder. The Phase 2 clinical trial is expected to start in the second half of 2022.

- Tonix's proprietary formulation includes magnesium (Mg), which has been reported to potentiate the binding of oxytocin to the oxytocin receptor. Further evidence for the role of Mg in potentiating the effects of oxytocin at the oxytocin receptor were published by a third party[1].

*TNX-601 CR (tianeptine oxalate and naloxone controlled-release tablets): small molecule for the treatment of major depressive disorder, PTSD and neurocognitive dysfunction associated with corticosteroid use.*

- Based on official minutes from a pre-IND meeting with the FDA, the Company expects to initiate a Phase 2 study for the treatment of major depressive disorder (depression) in the first quarter of 2023. Tonix previously completed a Phase 1 trial for formulation development outside of the U.S.

<u>*Rare Disease Pipeline*</u>

*TNX-2900 (intranasal potentiated oxytocin): small peptide for the treatment of Prader-Willi syndrome (PWS)*

- TNX-2900 received Orphan-Drug designation by the FDA for the treatment of PWS in March 2022.

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- In February 2022, Tonix entered into a sponsored research agreement with Inserm (the French National Institute of Health and Medical Research) and Aix-Marseille Université to study oxytocin in the genetically engineered mouse model of Prader-Willi syndrome, a rare genetic disorder that causes distinct, but related pathological eating disorders in newborns versus adolescents and young adults.

<u>*Immunology Pipeline*</u>

*TNX-1500 (anti-CD40L monoclonal antibody): third generation monoclonal antibody for prophylaxis of organ transplant rejection and treatment of autoimmune disorders.*

- Tonix expects to start a Phase 1 study in the second half of 2022. Preliminary results from ongoing experiments in heart and kidney transplants in non-human primates at Massachusetts General Hospital indicate that TNX-1500 appears to have monotherapy efficacy in promoting rejection-free transplant organ acceptance and no evidence of thrombosis, a serious safety concern that was present in earlier generations of anti-CD40L antibodies, has been observed.

<u>*Infectious Disease Pipeline*</u>

*TNX-801 (live horsepox virus vaccine for percutaneous administration): vaccine against smallpox and monkeypox designed as a single-administration vaccine to elicit T cell immunity*

- Tonix previously reported protection of non-human primates from a monkeypox challenge[2]. TNX-801 is less virulent than traditional vaccinia vaccines in mice[3]

*TNX-1840 /-1850 (live virus vaccines based on Tonix's recombinant pox virus vector): COVID-19 vaccines designed as single-administration vaccines to elicit T cell immunity*

- Because the omicron and BA.2 variants have out-competed the ancestral Wuhan strain, Tonix is now planning new versions of the TNX-1800 vaccine: TNX-1840 and TNX-1850, that are designed to express spike protein from the omicron and BA.2 variants, respectively. TNX-1840 and TNX-1850 are next-generation COVID-19 vaccines using live virus technology designed to primarily elicit a T cell response believed to result in longer durability of protection and to potentially block forward transmission.

*TNX-3700: COVID-19 mRNA vaccine candidate using a zinc nanoparticle (ZNP) formulation*

- In January 2022, Tonix entered into an exclusive option and research collaboration with Kansas State University (K-State) to develop ZNP mRNA vaccines that replace the lipid nanoparticle (LNP) technology in current mRNA COVID-19 vaccines. The new ZNP technology has the potential to confer increased stability to mRNA vaccines over a wide range of temperatures, addressing limits to rapid global deployment.

*TNX-2300: Live virus vaccine based on a bovine parainfluenza virus vector to protect against COVID-19*

- In April 2022, Tonix announced a new preclinical research agreement with K-State to develop a vaccine candidate, TNX-2300, for the prevention of COVID-19 that utilizes a novel live virus vaccine vector platform. The candidate will also test the efficacy of co-expression of the CD40-ligand to stimulate T cell immunity.

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- TNX-2300 is designed to potentially stimulate immunity against the SARS-CoV-2 spike protein. The research is being directed by Dr. Waithaka Mwangi, Kansas State University, Department of Diagnostic Medicine/Pathobiology, who is the inventor of the new technology. In addition, K-State has granted Tonix an option for an exclusive license for the clinical and commercial use of K-State's intellectual property associated with coronavirus vaccines under this relationship.

*TNX-2100 (diagnostic skin test): SARS-CoV-2 epitope peptide mixtures for intradermal administration to measure the delayed-type hypersensitivity (DTH) reaction to SARS-CoV-2*

- Tonix initiated enrollment in a dose-finding clinical study for TNX-2100 in early January 2022. However, due to the current COVID landscape in which the U.S. Centers for Disease Control and Prevention (CDC) reports[4] that approximately 60% of adults and approximately 75% of children and adolescents in the U.S. have been infected with SARS-CoV-2, and the current U.S. strategy of reducing or eliminating control measures such as mask-mandates, lockdowns or surveillance, Tonix has stopped enrollment in the study and is terminating further development in the U.S.

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

[1] *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 (2022). https://doi.org/10.1038/s41594-022-00728-4*

[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)*

[3] *Noyce RS, et al. Construction of an infectious horsepox virus vaccine from chemically synthesized DNA fragments. PLoS One. 2018 Jan 19;13(1): e0188453.*

[4] *Clarke KE, et al. Seroprevalence of Infection-Induced SARS-CoV-2 Antibodies — United States, September 2021–February 2022. MMWR Morb Mortal Wkly Rep 2022;71:606-608. DOI: http://dx.doi.org/10.15585/mmwr.mm7117e3*

**Recent Highlights--Financial**

As of March 31, 2022, Tonix had $140.4 million of cash and cash equivalents, compared to $178.7 million as of December 31, 2021. Subsequent to March 31, 2022, the Company sold 33.9 million shares of common stock in at-the-market offerings (ATM) sales under a Sales Agreement with A.G.P./Alliance Global Partners, for net proceeds of approximately $6.8 million. Additionally, the Company sold 13.0 million shares of common stock under the Purchase Agreement with Lincoln Park for net proceeds of approximately $2.0 million.

Cash used in operations was approximately $31.1 million for the first quarter ended March 31, 2022, compared to $21.1 million for the first quarter ended March 31, 2021. The increase in primarily due to an increase in research and development (R&D) expense, general and administrative (G&A) expense, and increases in working capital. Capital expenditures were approximately $20.2 million for the first quarter ending March 31, 2022 compared to $0.5 million for the first quarter ended March 31, 2021. The increase was primarily due to the continued buildout of the Advanced Development Center in North Dartmouth, Mass.

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First Quarter 2022 Financial Results

R&D expenses for the first quarter of 2022 were $18.4 million, compared to $15.3 million for the same period in 2021. This increase is predominately due to employee-related expenses and non-clinical expenses. We continue to expect R&D expenses to increase during 2022 as we move our clinical development programs forward and invest in our development pipeline.

G&A expenses for the first quarter of 2022 were $8.0 million, compared to $5.4 million for the same period in 2021. The increase is primarily due to employee-related expenses.

Net loss per common share was $26.4 million, or $0.05 per share, basic and diluted, for the first quarter of 2022, compared to net loss of $20.7 million, or $0.07 per share, basic and diluted, for the first quarter of 2021. The basic and diluted weighted average common shares outstanding for the first quarter of 2022 was 522,060,899, compared to 290,106,510 shares for the first quarter of 2021.

**About Tonix Pharmaceuticals Holding Corp.[1]**

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 first quarter of 2023. TNX-102 SL is also being developed to treat Long COVID, a chronic post-acute COVID-19 condition. Tonix expects to initiate a Phase 2 study in Long COVID in the second quarter of 2022. TNX-1300 (cocaine esterase) is a biologic designed to treat cocaine intoxication that is expected to start a Phase 2 trial in the second quarter of 2022. TNX-1300 has been granted Breakthrough Therapy Designation by the FDA. Finally, 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 second half of 2022. Tonix's rare disease portfolio includes TNX-2900 (intranasal potentiated oxytocin) for the treatment of Prader-Willi syndrome. TNX-2900 has been granted Orphan-Drug Designation by the FDA. Tonix's immunology portfolio includes biologics to address organ transplant rejection, autoimmunity and cancer, including TNX-1500 which is a humanized monoclonal antibody targeting CD40-ligand being developed for the prevention of allograft and xenograft rejection and for the treatment of autoimmune diseases. A Phase 1 study of TNX-1500 is expected to be initiated in the second half of 2022. Tonix's infectious disease pipeline consists of a vaccine in development to prevent smallpox and monkeypox called TNX-801, next-generation vaccines to prevent COVID-19, and a platform to make fully human monoclonal antibodies to treat COVID-19. Tonix's lead vaccine candidates for COVID-19 are TNX-1840 and TNX-1850, which are live virus vaccines based on Tonix's recombinant pox live virus vector vaccine platform.

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

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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.

**TONIX PHARMACEUTICALS HOLDING CORP.**
**CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS**
**(In Thousands, Except Share and Per Share Amounts)**
**(unaudited)**

| | Three Months Ended March 31, | |
|---|---|---|
| | **2022** | **2021** |
| COSTS AND EXPENSES: | | |
| Research and development | $ 18,422 | $ 15,327 |
| General and administrative | 8,014 | 5,409 |
| | 26,436 | 20,736 |
| Operating loss | (26,436) | (20,736) |
| Interest and other income, net | 19 | 83 |
| Net loss | $ (26,417) | $ (20,653) |
| Net loss per common share, basic and diluted | $ (0.05) | $ (0.07) |
| Weighted average common shares outstanding, basic and diluted | 522,060,899 | 290,106,510 |

**TONIX PHARMACEUTICALS HOLDING CORP.**
**CONDENSED CONSOLIDATED BALANCE SHEETS**
**(In Thousands)**
**(Unaudited)**

| | **March 31, 2022** | **December 31, 2021[1]** |
|---|---|---|
| **Assets** | | |
| Cash and cash equivalents | $ 140,435 | $ 178,660 |
| Prepaid expenses and other | 12,554 | 10,389 |
| Total current assets | 152,989 | 189,049 |
| Other non-current assets | 70,727 | 51 ,851 |
| Total assets | $ 223,716 | $ 240,900 |
| | | |
| **Liabilities and stockholders' equity** | | |
| Total liabilities | $ 15,759 | $ 22,183 |
| Stockholders' equity | 207,957 | 218,717 |
| Total liabilities and stockholders' equity | $ 223,716 | $ 240,900 |

[1]The condensed consolidated balance sheet for the year ended December 31, 2021 has been derived from the audited financial statements but do not include all of the information and footnotes required by accounting principles generally accepted in the United States for complete financial statements.

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**Exhibit 99.2**


## 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.

## 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





## Pipeline:
## Central Nervous System (CNS) Portfolio



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

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

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

## Pipeline
## Immunology and Immuno-Oncology portfolio

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

IMMUNOLOGY PORTFOLIO

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



TONIX PHARMACEUTICALS



## Pipeline
## Infectious Disease Portfolio

| CANDIDATES* | INDICATION | STATUS / NEXT MILESTONE |
|---|---|---|
| TNX-801[1] | Smallpox and monkeypox vaccine | Preclinical |
| TNX-1840/TNX-1850[2] | COVID-19 Vaccine (horsepox-based live virus vaccine) | Preclinical |
| TNX-2300[3] | COVID-19 Vaccine | Preclinical |
| TNX-3500[4] | COVID-19 Antiviral | Preclinical |
| TNX-3600[5] | COVID-19 Therapeutic Platform (monoclonal antibodies) | Preclinical |
| TNX-3700[6] | 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-1840 is based on the omicron variant spike protein. TNX-1850 is based on the BA.2 variant spike protein.
[3]Live attenuated vaccine based on bovine parainfluenza (BPI) virus
[4]Sangivamycin for injection; licensed from OyaGen, Inc.
[5]Fully human monoclonal antibody generated from COVID-19 convalescent patients
[6]anti-CD40LCOVID vaccine based on mRNA in zinc nanoparticle (ZNP) formulation



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## Pipeline
## Rare Disease Portfolio

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

RARE DISEASE PORTFOLIO

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



TONIX PHARMACEUTICALS



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## TNX-102 SL*: Fibromyalgia
## Cyclobenzaprine Protectic® Sublingual tablets

CNS PORTFOLIO

### PROFILE

**A unique formulation of cyclobenzaprine designed to optimize delivery and absorption**

**Innovative and proprietary PROTECTIC® Rapid drug exposure following nighttime administration**

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

**Clinical trial program designed to examine treatment of core Fibromyalgia symptoms**

***Patents Issued***

### DEVELOPMENT PROGRAM

**Market Entry:** Fibromyalgia

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

**Status:** One Positive Phase 3 study RELIEF Completed

Second Phase 3 study RALLY missed primary endpoint

Confirmatory Phase 3 study RESILIENT (F307) is currently enrolling

**Next Steps:** Interim analysis results expected 1Q 2023

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

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## TNX-102 SL: Fibromyalgia
## Program Update

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

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

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

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

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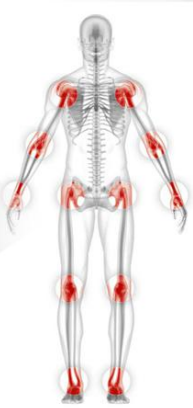
## Role of Infections in Triggering Fibromyalgia or Chronic fatigue (CFS)-Like Illnesses

**Infection initiates an autoreactive process, which affects several functions, including brain and energy metabolism[1-6]**

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




[1]Blomberg J, et al. Front Immunol. 2018;9:229. Published 2018 Feb 15.
[2]Warren JW, et al. Urology. 2008;71(6):1085-1090.
[3]Buskila D, et al. Autoimmun Rev. 2008;8(1):41-43.
[4]Hickie I, et al. BMJ. 2006;333(7568):575.
[5]Parry SD, et al. Am J Gastroenterol. 2003;98(9):1970-1975.
[6]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)

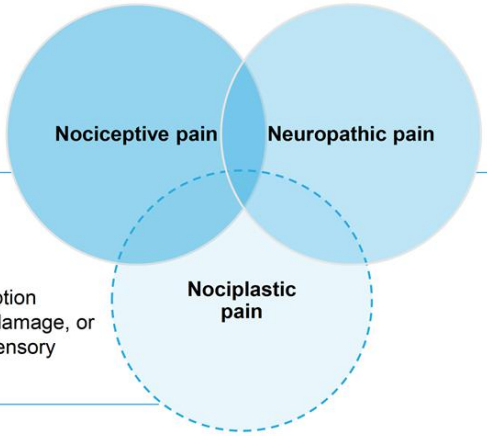
- Long COVID is a heterogeneous condition that displays elements of nociplastic pain in many individuals, who experience otherwise unexplained[1-2]:


- 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.

## New Classification for Central Pain: Nociplastic Pain[1]

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




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

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

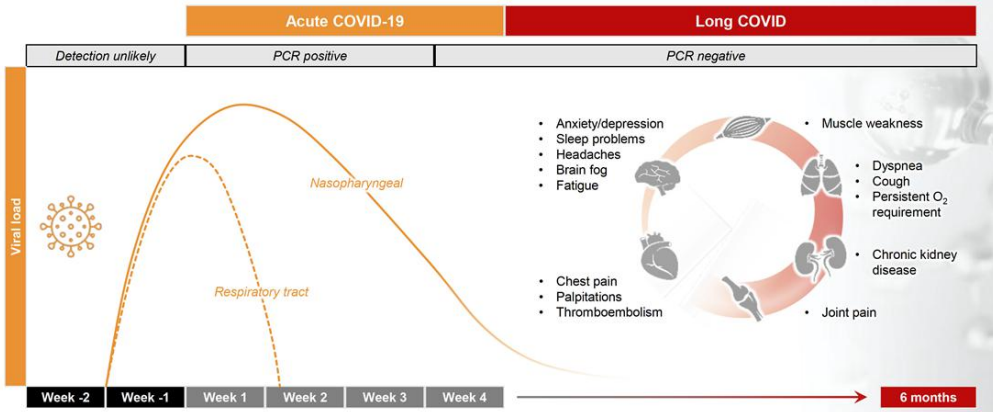
[1]Trouvin AP, et al. *Best Pract Res Clin Rheumatol*. 2019;33(3):101415.





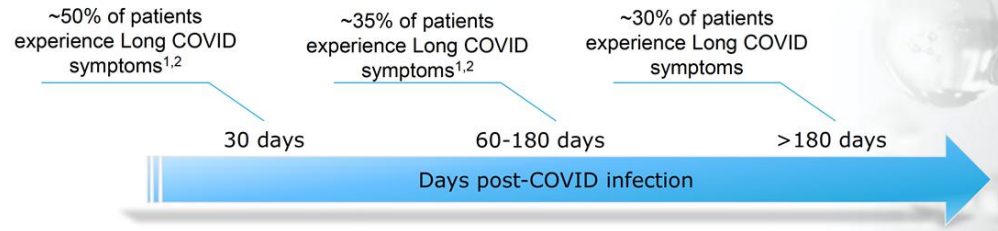


## Timeline of Long COVID After Acute COVID-19 Post-Viral Syndrome[1-3]




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

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




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

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

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



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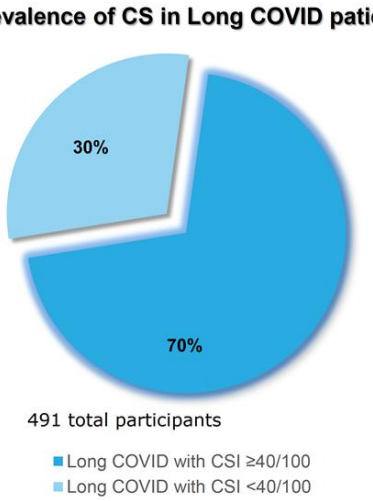
## Rate of Central Sensitization (CS) in Long COVID survey
## CS Symptoms reported in 70%[1]

70% of Long COVID participants had CS symptoms (CSI[2]>=40/100)

65% of Long COVID participants had severe CS symptoms




[1]Goudman, L, et al. *J of Clin Med*. 2021;10(23):5594.
[2]CSI = Central Sensitization Inventory



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## Long COVID Patients in TriNetX Study[1]
## Retrospective Observational Database Study

**TriNetX Dataworks USA Network[2]:**

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

| | Patients | HCOs |
|---|---|---|
| Network | 75,241,815 | 48 |
| COVID diagnosis (PCR+) and Age 18-65 | 1,004,258 | 47 |
| Cannot have other specified viral infection | 931,837 | 47 |
| At least 1 encounter ≤180 days post-index | 260,082 | 47 |
| Long COVID symptoms days 91-180 | **52,322** | 45 |

PCR = Polymerase Chain Reaction
Encounter = Interaction with healthcare provider in network

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



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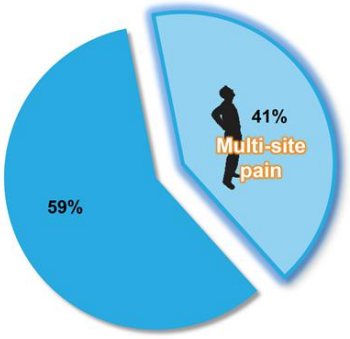
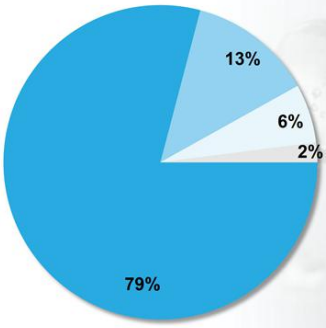
## Long COVID Patients in TriNetX study[1]
## Fibromyalgia-like Symptoms (Multi-Site Pain) in Over 40% of Patients[1,2]

52,322 total Long COVID patients




| |
|---|
| Multi-site pain |
| No multi-site pain |

21,694 total FM-like Long COVID patients




| |
|---|
| Multi-site pain only |
| Multi-site pain and fatigue |
| Multi-site pain and insomnia |
| Multi-site pain, fatigue, and insomnia |

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



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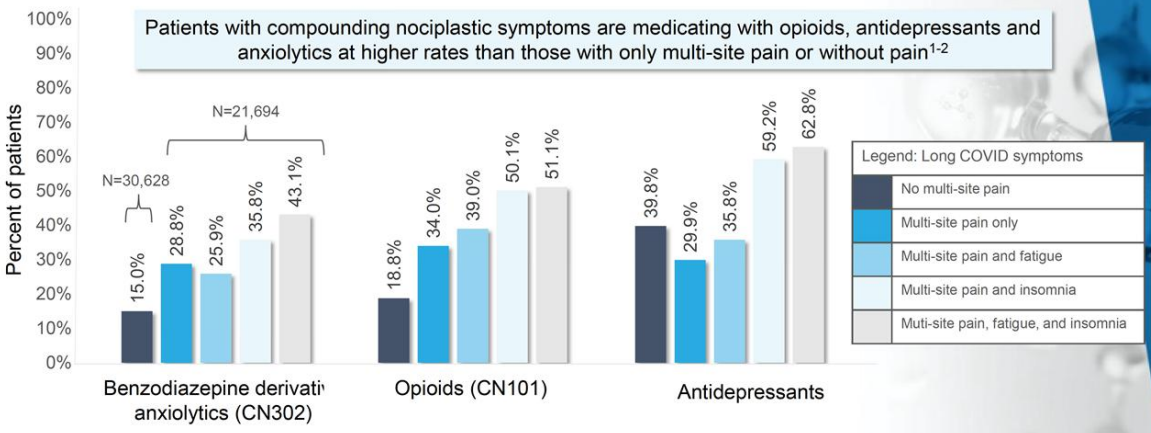
## Long COVID Patients in TriNetX Study[1]
## Recorded Medication Use, Days 91-180




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



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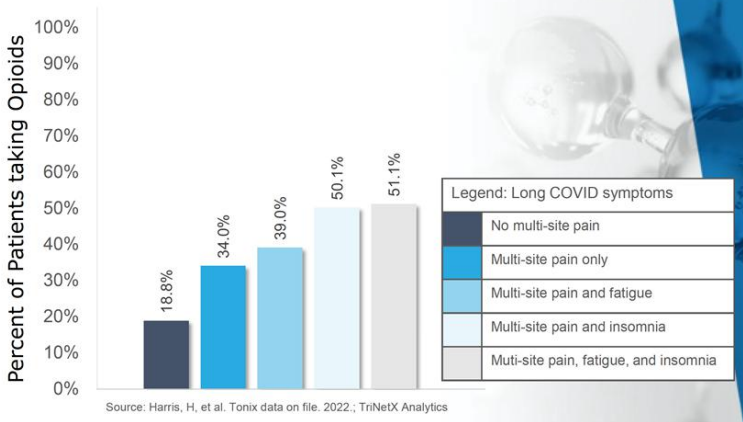
## Rate of Opioid Use in Long COVID Patients
## Potential Health Concern

- 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



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## Significant Financial Impact of Long COVID for Households and Economies

- 25% of Long COVID patients are unable to return to work[1]
- Over 250,000 Quality Adjusted Life-Years (QUALYS) will be lost due to Long COVID in the UK[2]
- $23.3 billion is estimated to be paid by the UK government to avoid QUALY losses due to Long COVID[2]

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







## Long COVID Presidential Memorandum
## President Biden – April 5, 2022[1]

**Policy**

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

**Organizing Government Wide Response**

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

**National Research Action Plane**

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

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

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

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

## Long COVID and Vaccination
## Recent Reports[1]

**Vaccination may not change risk of Long COVID after Breakthrough COVID-19**

- A retrospective cohort study of 10,024 breakthrough infection in the US showed no benefit of vaccination in decreasing Long COVID after breakthrough infection[1]
  - Vaccination has benefits in decreased symptoms of acute breakthrough COVID
- A UK study (different vaccines than are used in US) showed a ~50% reduction in Long COVID after breakthrough COVID[2]

**Herd immunity concept may not apply to COVID-19**

- Dr. Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases (NIAID) has written[3]
  - "'Classical' herd immunity, leading to disease eradication or elimination, almost certainly is an unattainable goal"
  - Prior discussion about COVID not disrupting most people's lives was focused on herd immunity
  - For other viruses, herd immunity occurs when "natural infection with a pathogen" reaches a "community circulation [that] is reduced below the level of significant public health threat."

[1]Taquet, M et al. (2022) "Six-month sequelae of post-vaccination SARS-CoV-2 infection: A retrospective cohort study of 10,024 breakthrough infections. "Brain, Behavior, and Immunity," 103, 154-162, https://doi.org/10.1016/j.bbi.2022.04.013.
[2]Antonelli, M et al. (2022) "Risk factors and disease profile of post-vaccination SARS-CoV-2 infection in UK users of the COVID Symptom Study app: a prospective, community-based, nested, case-control study," Lancet Infectious Diseases, 22(1) 43-55, https://doi.org/10.1016/S1473-3099(21)00460-6.
[3] David M Morens, DM, Folkers, GK and Fauci, AS. "The Concept of Classical Herd Immunity May Not Apply to COVID-19", *The Journal of Infectious Diseases*, 2022;, jiac109, https://doi.org/10.1093/infdis/jiac109



CNS PORTFOLIO

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## TNX-102 SL*: Long COVID (PASC)
## Cyclobenzaprine Protectic® Sublingual Tablets

### 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

**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 –IND clearance granted

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

*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.
[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. 

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## Opportunities to Expand TNX-102 SL to Other Indications

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**Role of sleep disturbance more established in common psychiatric and neurological/pain disorders**

- Recognized as a core symptom of many of these disorders
- Traditional sleep medications, which increase sleep quantity, may not provide benefit (benzodiazepines in major depression) or are contraindicated

**Psychiatric Disorders**
- Stress Disorders (PTSD)
- Mood Disorders (Depression)
- Anxiety Disorders
- Addiction (Alcohol Use Disorder)

**Psychiatric Symptoms of Neurological Disorders**
- Agitation in Alzheimer's
- Psychosis in Parkinson's, Alzheimer's and other dementias

**Chronic Pain States**
- Chronic wide-spread pain (fibromyalgia)
- Osteoarthritis

**Growing recognition that there are many disorders where sleep disturbances may have a role in the pathophysiology (cardiovascular, metabolic, neurologic)**

- Sleep quality plays a homeostatic role *in several disorders*

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## TNX-1300*: Cocaine Intoxication
## Cocaine Esterase (CocE)

CNS PORTFOLIO

PROFILE

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

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

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

**CocE is a recombinant protein that degrades cocaine in the bloodstream**

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

***Patents Issued***

DEVELOPMENT PROGRAM

**Market Entry:** Cocaine Intoxication

**Additional Indications:** Cocaine Overdose

**Status:** Phase 2 Open Label

**Next Steps:** 2Q 2022 Initiate Trial

***FDA Breakthrough Therapy Designation***

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

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

TONIX PHARMACEUTICALS

## TNX-1900*: Migraine
## Intranasal Potentiated Oxytocin (OT) with Magnesium

CNS PORTFOLIO

### PROFILE

**Intranasal OT has potential utility in treating migraine[1]**

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

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

**One billion individuals worldwide suffer from migraines**

***Patents Issued***

### DEVELOPMENT PROGRAM

**Market Entry:** Chronic Migraine

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

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

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

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

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



TONIX PHARMACEUTICALS



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

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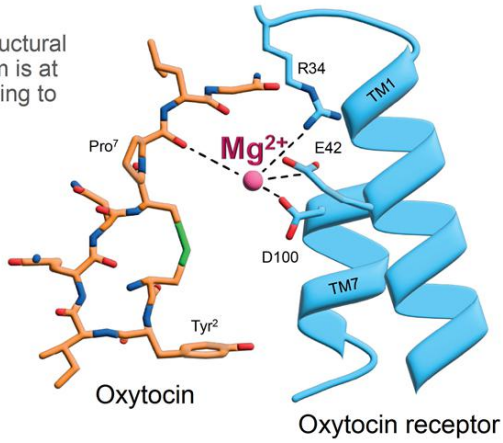
**TNX-1900 contains magnesium:** Recent structural studies show magnesium is at the core of oxytocin binding to oxytocin receptor[1]




[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



TONIX PHARMACEUTICALS

## TNX-601 CR*: Depression
## Tianeptine Oxalate and Naloxone

CNS PORTFOLIO

### PROFILE

**A novel, oral, controlled release once-daily tablet**

**Mechanistically different from traditional monoaminergic treatments for depression**

**Indirectly modulates the glutamatergic system**

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

**Naloxone added to deter parenteral abuse**

**Treatment effect of tianeptine in depression is well-established**

***Patents Issued***

### DEVELOPMENT PROGRAM

**Market Entry:** Major Depressive Disorder

**Additional Indications:** PTSD, Neurocognitive Disorder From Corticosteroids

**Status:** pre-IND

**Next Steps:** 1Q 2023 Initiate Phase 2 Trial

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

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

TONIX PHARMACEUTICALS





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## TNX-1500 ($\alpha$-CD40L mAb): Prophylaxis of Transplant Rejection
## Potential Treatment for Autoimmune Conditions



**Pre-IND Candidate**

**Targeted as a first-line monotherapy for autoimmunity and add-on therapy for preventing and treating organ transplant rejection**

- Distinct mechanism of action (MOA)—TNX-1500 blocks T cell helper function

**New molecular entity, biologic**

- US Patient Protection and Affordable Care Act provides 12 years of exclusivity for biologics

**Patent applications directed to composition of matter**

- Expected patent protection through 2039

**Significant Unmet Need**

**Clinical evidence for anti-CD40L mAbs in the treatment of systemic lupus erythematosus (SLE) and allogeneic kidney transplant**

- Several studies have shown anti-CD40L to be active in the treatment of human SLE[1-3] and transplant rejection[4,5]

[1]Huang W, et al. *Arthritis Rheum*. 2002;46(6):1554-1562.
[2]Boumpas DT, et al. *Arthritis Rheum*. 2003;48(3):719-727.
[3]Grammer AC, et al. *J Clin Invest*. 2003;112(10):1506-1520.
[4]Kawai T, et al. *Nat Med*. 2000;6(2):114.
[5]Koyama I, et al. *Transplantation*. 2004;77(3):460-462.





## TNX-1500 ($\alpha$-CD40 Ligand)
## Market Opportunity



**OPPORTUNITY**

| Organ transplant rejection drugs | Kidney transplants: 24,000/year/US[2] | Autoimmune Lupus: 1.5 M patients in US[4] | Autoimmune Disease |
|---|---|---|---|
| **$4.7 billion[1]** | **$5.54 billion[3]** | **1.87 billion[5]** | **$149.4 billion[6]** |

[1]Global market as of 2018 (https://www.biospace.com/article/organ-transplant-rejection-medications-market-drug-companies-focus-on-improving-long-term-outcome-of-new-drugs/)
[2]Wang, Jeffrey H. and Hart, Allyson. *Kidney360* November 2021; 2(11) 1836-1839
[3]Global market as of 2020 (https://www.grandviewresearch.com/industry-analysis/transplantation-market)
[4]https://www.lupus.org/resources/lupus-facts-and-statistics
[5]Global market as of 2020 (https://www.globenewswire.com/news-release/2021/02/18/2177637/0/en/Global-Lupus-Therapeutics-Market-Is-Expected-to-Reach-USD-3-62-Billion-by-2028-Fior-Markets.html)
[6]Anticipated market size by 2025 (https://www.prnewswire.com/news-releases/the-global-autoimmune-disease-therapeutics-market-size-is-expected-to-reach-149-4-billion-by-2025--rising-at-a-market-growth-of-4-34-cagr-during-the-forecast-period-300902336.html)

## About CD40L (also called CD154)

- **CD40L is a transiently expressed T cell surface molecule and is also called CD154[1-4]**
  - Predominantly expressed by T cells and interacts with CD40 on B cells and macrophages
- **Mediates T cell helper function[1-4]**
  - Activates B cells for humoral (antibody-mediated) immune response
  - Activates macrophages and dendritic cells
  - Provides T cell help to activated CD8+ T cells
- **X-linked hyper-IgM syndrome is caused by a defective CD40L gene[5-6]**
  - Lack of T helper function with only IgM serum antibodies but no IgG or IgE because T cells are required for B cell isotype switching
  - If maintained on gamma globulin, patients are otherwise healthy
- **Member of the TNFα superfamily[4]**
  - TNFα and RANKL are other family members and are drug targets for approved products


[1]Lederman S, et al. *J Exp Med.* 1992;175(4):1091-1101.
[2]Lederman S, et al. *J Immunol.* 1992;149(12):3817-3826.
[3]Lederman S, et al. *J Immunol.* 1994;152(5):2163-2171.
[4]Covey LR, et al. *Mol Immunol.* 1994;31(6):471-484.
[5]Ramesh N, et al. *Int Immunol.* 1993;5(7):769-773.
[6]Callard RE, et al. *J Immunol.* 1994;153(7):3295-3306.








## TNX-1500*: Prevention of Allograft Rejection
## Next Generation $\alpha$-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

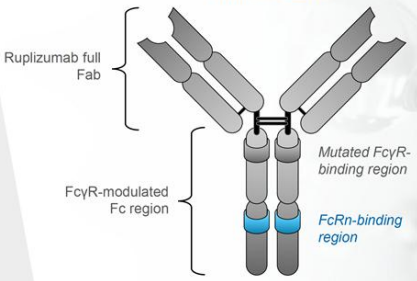
- Expected to deliver efficacy without compromising safety

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

**Next Steps:** 2H 2022 Initiate Phase 1 Study

***Patents Filed***

SELECTIVELY MODIFIED anti-CD40L AB



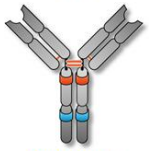

Contains the full ruplizumab Fab and the engineered Fc region that modulates FcγR-binding, while preserving FcRn function.

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

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

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

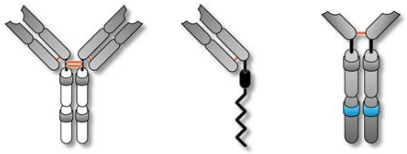
**First-generation anti-CD40L mAbs**



*Ruplizumab*

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

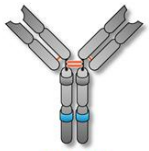
**Second-generation anti-CD40L mAbs**



*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]Waters J, *Biocentury*; October 26, (2018).
[8]Company data.





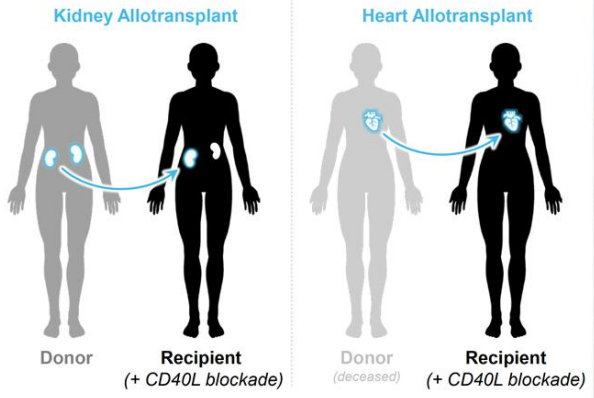

TONIX PHARMACEUTICALS



## α-CD40L Treatment to Prevent Allograft Rejection

- Calcineurin inhibitors (CNIs), mainly tacrolimus, are the cornerstone of immunosuppressive therapy[1,2]
- However, CNIs cause irreversible and progressive deterioration of kidney function in all types of solid organ transplants[3,4]
- Costimulation blockade (anti-CD40L in particular) may be more effective at protecting allografts than CNIs[5]

**Concept for Human-to-Human Allotransplantation[1,2]**





[1]Enderby C, et al. *Am J Manag Care*. 2015;21(1 Suppl):s12-s23.
[2]Camilleri B, et al. *Exp Clin Transplant*. 2016;14(5):471-483.
[3]Naesens M, et al. *Clin J Am Soc Nephrol*. 2009;4(2):481-508.
[4]Nankivell BJ, et al. *N Engl J Med*. 2003;349(24):2326-2333.
[5]Cooper DKC, et al. *Blood Purif*. 2018;45(1-3):254-259.



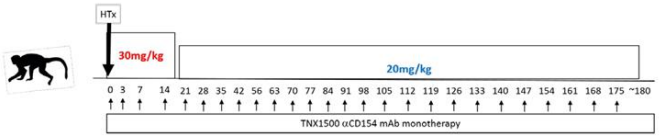



TONIX PHARMACEUTICALS

## Non-Human Primate Heart Heterotopic Allograft Study

### Dr. Richard Pierson, Mass General Hospital

- **TNX-1500 monotherapy consistently (4/5 heart transplants) prevents heart transplant rejection[1]**
  - Graft acceptance without acute cellular injury[2] or chronic antibody injury[3] through day 180
  - Prolonged acceptance after cessation of therapy (in progress)




- **Similar activity to chimeric hu5c8[4] during treatment phase in prior studies[5]**
  - Last dose of hu5c8 was day 84
- **No thrombosis observed**
  - Thrombosis was observed with hu5c8 in prior studies

[1]TNX-1500 dosed at 30 mg/kg twice weekly on days 0, 3, 7, and 14; 20 mg/kg weekly from days 21 to 175
[2]H&E staining
[3]C4d immunohistochemistry
[4]Mouse-human IgG1κ chimeric anti-CD154
[5]TNX-1500 dosed at 30 mg/kg twice weekly on days 0, 3, 7, and 14; 10 mg/kg weekly on days 21, 28, 35 and 42; 20 mg/kg monthly on days 56 and 84.



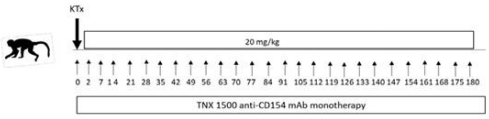


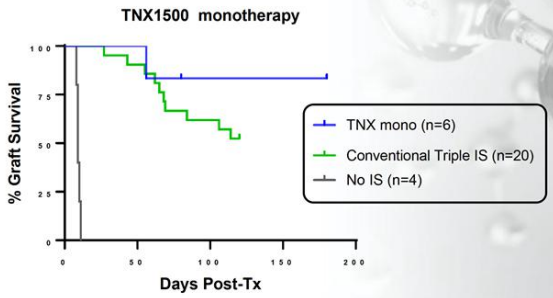


## Non-Human Primate Kidney Allo-Transplantation Study

### Dr. Tatsuo Kawai, Mass General Hospital

- **TNX-1500 monotherapy consistently (5/6 kidney transplants) prevents kidney transplant rejection[1]**
  - Six recipients were treated with TNX-1500 monotherapy[1]
  - No rejection was observed in 5/6 recipients through day 180
  - Superior to results with conventional triple drug immunosuppressive regimen[2]




- **No thrombosis observed**
  - Thrombosis was observed with hu5c8 in prior studies

[1]TNX-1500 monotherapy dosed at 20 mg/kg on days 0, 2, 7 and weekly until Day 180 (6 months)
[2]Tacrolimus, MMF and steroids

## Tolerance Induction with Donor Bone Marrow Transplantation

**Induction of "mixed chimerism" induces allograft tolerance**

- Long-lasting, durable tolerance—specifically to donor tissues
- Initial protocols required that the recipient's mature T cells be severely depleted

**Tolerance induction via "mixed chimerism" allows long-term kidney transplant survival in humans without maintenance immunosuppression[1-2]**

- Combined kidney and bone marrow transplantation (CKBMT)

**Non-myeloablative conditioning for induction of mixed chimerism is being developed**

- Mixed chimerism and tolerance can be induced even without complete T cell depletion using costimulatory pathway blockade using anti-CD40L mAb and/or CTLA-4-Ig
- Prof. Tatsuo Kawai showed addition of CD40L blockade to the conditioning regimen facilitates induction of mixed chimerism and renal allograft tolerance[3]

[1]Kawai T, et al. *N Engl J Med*. 2008;358(4):353-361.
[2]Kawai T, et al. *Am J Transplant*. 2014;14(7):1599-1611.
[3]Kawai, T et al. *Am J Transplant*. 2004;4(9):1391-1398.





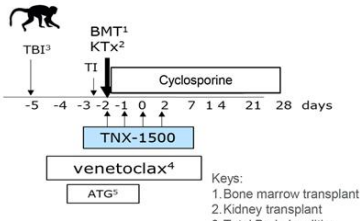


## Non-Human Primate Combined Kidney and Bone marrow Transplantation (CKBMT) with TNX-1500 induced allograft tolerance
### Dr. Tatsuo Kawai, Mass General Hospital

A. CONDITIONING REGIMEN FOR BONE MARROW & KIDNEY TX

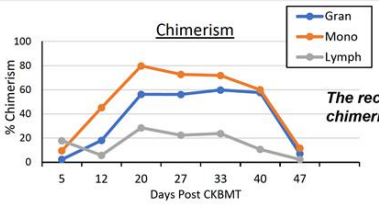
The nonhuman primate recipient received the conditioning regimen that includes low dose total body irradiation (TBI, 1.5Gy), thymic irradiation (TI, 7Gy), venetoclax and ATG. The recipients then received combined kidney and bone marrow (BM) transplantation (CKBMT), after which treated with TNX-1500 (20mg/kg X 4 doses) and cyclosporine (28 days). No immunosuppression was given after day 28.

***No immunosuppression after day 28***



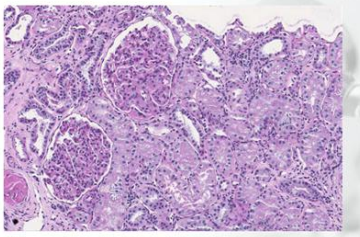

Keys:
1. Bone marrow transplant
2. Kidney transplant
3. Total Body Irradition
4. Venclexta®
5. Thymoglobulin®

B. DONOR BLOOD CELLS TRANSIENTLY EXPANDED AFTER TRANSPLANT




***The recipient developed multilineage chimerism until day 47***

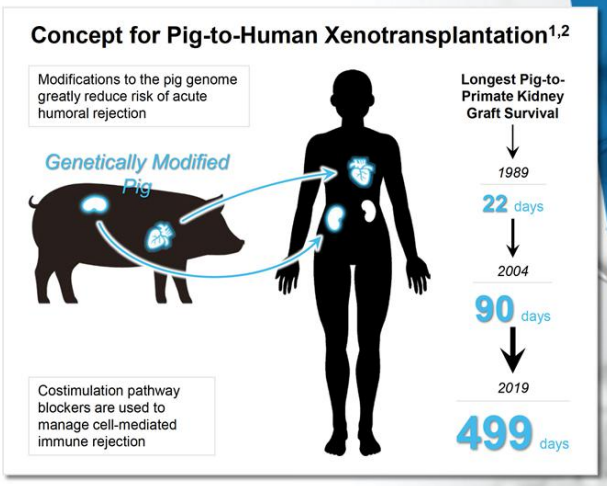
C. KIDNEY BIOPSY AT ONE YEAR SHOWING NO REJECTION



The recipient achieved long-term immunosuppression-free renal allograft survival (> one year). The picture shows renal allograft biopsy taken at one year after transplantation, showing no signs of rejection.

## $\alpha$-CD40L Beyond Allografts: Xenografts

- Allotransplantation is limited by a critical shortage of human organs; **pig-to-human xenotransplantation offers a promising alternative**[1,2]
- Costimulation blockade (anti-CD40L in particular) is more effective at protecting xenografts than CNIs[2]
- Blockade of CD40-CD40L has been associated with some of the longest pig-to-primate xenograft survivals[1,3]




[1]Samy KP, et al. *J Immunol Res*. 2017;2017:8415205.
[2]Cooper DKC, et al. *Blood Purif*. 2018;45(1-3):254-259.
[3]Längin, M. et al. Consistent success in life-supporting porcine cardiac xenotransplantation. *Nature* 564, 430–433 (2018)





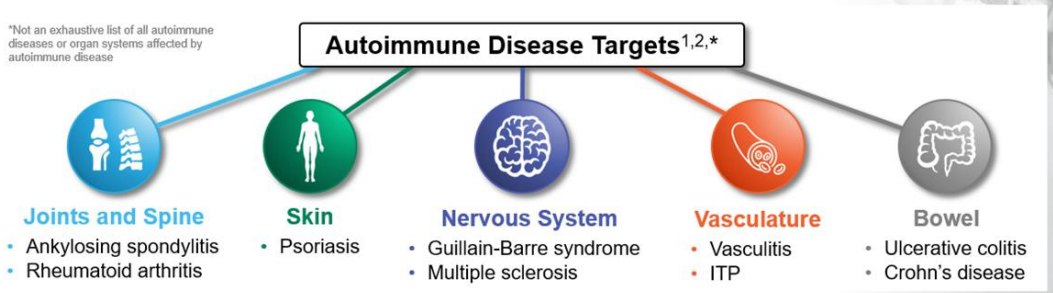


## Recent Xenotransplant Headlines

| | | |
|---|---|---|
| The New York Times<br>**"In a First, Surgeons Attached a Pig Kidney to a Human, and It Worked"**<br>Roni Caryn Rabin<br>*October 19, 2021* | THE WALL STREET JOURNAL.<br>**"Saved by a Pig's Heart"**<br>The Editorial Board<br>*January 12, 2022* | THE WALL STREET JOURNAL.<br>**"Pig Kidneys Transplanted Into Brain-Dead Man as Patients Face Organ Shortages"**<br>Amy Dockser Marcus<br>*January 20, 2022* |
| THE WALL STREET JOURNAL.<br>**"The Next Pig Thing in Medicine"**<br>Sally Satel<br>*February 9, 2022* | THE NEW YORKER<br>**"The Medical Miracle of a Pig's Heart in a Human Body"**<br>Rivka Galchen<br>*February 21, 2022* | THE WALL STREET JOURNAL.<br>**"The Patient Who Received a Pig Heart Dies Two Months After Transplant"**<br>Allison Prang<br>*March 9, 2022* |

## $\alpha$-CD40L Beyond Transplantation: Autoimmunity

- Autoimmune diseases are also characterized by immune system activity that attacks "self," which can damage various parts of the body[1,2]
- First-generation anti-CD40L Abs showed evidence of efficacy in autoimmunity before trials were halted due to thromboembolic events[3]




[1]Li P, et al. *Front Pharmacol*. 2017;8:460.
[2]WebMD. Accessed March 3, 2020. https://www.webmd.com/a-to-z-guides/autoimmune-diseases
[3]Tocoian A, et al. *Lupus*. 2015;24(10):1045-1056.







## TNX-1500: Key Considerations

- TNX-1500 may be used in large markets that are not currently well served
- There is a long history of use of monoclonal antibodies
- Tonix has engineered a safer, potentially more efficacious molecule than previous anti-CD40L mAbs
- Intellectual property is in place (composition of matter)
- Manufacturing (CMC) is in progress

**Key milestones:**

- Pre-IND meeting (FDA) 2Q 2022; Phase 1 2H 2022
- Autoimmune disorders – Planning INDs

## 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







## TNF$\alpha$ Superfamily Members are Targeted by mAbs

- CD40L is a member of the Tumor Necrosis Factor (TNFα) Superfamily[1]
- Other TNFα Superfamily members have proven to be effective targets for antagonist (blocking) mAbs[2]

**anti-TNFα mAbs for the treatment of certain autoimmune conditions**

- infliximab (Remicade®)
- adalimumab (Humira®)

**TNFα antagonist receptor fusion protein**

- etanercept (Enbrel®)

**anti-RANKL (CD254) mAb for the treatment of osteoporosis, treatment-induced bone loss, metastases to bone, and giant cell tumor of bone**

- denosumab (Prolia® or Xgeva®)

**No mAb against CD40L has been licensed *anywhere* in the world**

[1]Covey, L.R., et al. *Mol. Immunol.* 31:471-484. 1994. PMID: 7514269.
[2]Remicade® and Simponi® are trademarks of Janssen; Humira® is a trademark of AbbVie; Cimzia® is a trademark of UCB; Enbrel® is a trademark of Amgen; and Prolia® and Xgeva® are trademarks of Amgen.

## Recent mAb Transactions

**2020 September**

**Immunomedics acquired by Gilead for $21B[1]**

- TRODELVY™ (sacituzum ab govitecan-hziy) is an anti-Trop-2 antibody-drug conjugate (ADC) approved for triple-negative breast cancer

**October**

**Momenta acquired by Johnson & Johnson for $6.5B[2]**

- Nipocalimab (M281) is a clinically validated anti-FcRn antibody with a rare pediatric disease designation from the US FDA
- J&J called nipocalimab "a pipeline in a product"

**2021 January**

**Kymab acquired by Sanofi for $1.1B[3]**

- Is an anti-Ox40L for the treatment of autoimmune disease

**Viela Bio acquired by Horizon for $3B[3]**

- UPLIZNA® (inebilizumab-cdon) is an anti-CD19 (B-cell-depleting) antibody approved for the treatment of neuromyelitis optica spectrum disorder (NMOSD), which is a rare and severe autoimmune disease
- VIB4920 anti-CD40L is Viela's second program

**2022 March**

**Sanofi and IGM Biosciences announce collaboration deal that could surpass $6B[4]**

- The two companies will partner on immunoglobulin M (IgM) antibody agonists against three cancer targets and three immunology/inflammation targets

[1]Gilead. September 13, 2020. Accessed June 3, 2021. https://www.gilead.com/news-and-press/press-room/press-releases/2020/9/gilead-sciences-to-acquire-immunomedics
[2]Johnson & Johnson. October 1, 2020. Accessed June 3, 2021. https://www.jnj.com/johnson-johnson-completes-acquisition-of-momenta-pharmaceuticals-inc
[3]Business Wire. February 1, 2021. Accessed June 3, 2021. https://www.businesswire.com/news/home/20210201005296/en/Horizon-Therapeutics-plc-to-Acquire-Viela-Bio-Inc.-to-Significantly-Expand-Development-Pipeline-and-Grow-Rare-Disease-Medicine-Portfolio
[4]BioSpace. March 29, 2022. Accessed March 29, 2022. https://www.biospace.com/article/sanofi-and-igm-partner-on-oncology-and-immunology-in-deal-worth-more-than-6-billion/







## Monoclonal Antibodies (mAbs) Represent 4 of Top 10 Products by 2021 Sales

- Over 100 mAbs have been approved by the US FDA, and significant growth potential remains[1]
- Global mAb market is projected to grow from $179B in 2021 to $452B in 2028 at a CAGR of 14.1%[2]

### TOP 10 DRUGS BY GLOBAL SALES IN 2021

| | | |
|---|---|---|
| 1. Comirnaty | | $36.8 B[3] |
| 2. Humira | anti-TNFα mAb | $20.7 B[4] |
| 3. Spikevax | | $17.7 B[5] |
| 4. Keytruda | anti-PD-1 mAb | $17.2 B[6] |
| 5. Revlimid | | $12.8 B[7] |
| 6. Eliquis | | $10.8 B[8] |
| 7. Stelara | anti-IL12/23 | $9.1 B[9] |
| 8. Biktarvy | | $8.6 B[10] |
| 9. Eylea | anti-VEGF | $5.8 B[11] |
| 10. Imbruvica | | $5.4 B[12] |

[1]Mullard A. May 5, 2021. Accessed February 24, 2022. (https://www.nature.com/articles/d41573-021-00079-7)
[2]Forbes Business Insights. August 2021. Accessed February 24, 2022. (https://www.fortunebusinessinsights.com/monoclonal-antibody-therapy-market-102734)
[3]https://s28.q4cdn.com/781576035/files/doc_financials/2021/q4/Q4-2021-PFE-Earnings-Release.pdf
[4]https://news.abbvie.com/news/press-releases/abbvie-reports-full-year-and-fourth-quarter-2021-financial-results.htm
[5]https://s29.q4cdn.com/745959723/files/doc_news/Moderna-Reports-Fourth-Quarter-and-Fiscal-Year-2021-Financial-Results-and-Provides-Business-Updates-2022.pdf
[6]https://www.merck.com/news/merck-announces-fourth-quarter-and-full-year-2021-financial-results/
[7]https://news.bms.com/news/corporate-financial/2022/Bristol-Myers-Squibb-Reports-Fourth-Quarter-and-Full-Year-Financial-Results-for-2021/default.aspx
[8]https://news.bms.com/news/corporate-financial/2022/Bristol-Myers-Squibb-Reports-Fourth-Quarter-and-Full-Year-Financial-Results-for-2021/default.aspx
[9]https://johnsonandjohnson.gcs-web.com/news-releases/news-release-details/johnson-johnson-reports-q4-and-full-year-2021-results
[10]https://investors.gilead.com/news-releases/news-release-details/gilead-sciences-announces-fourth-quarter-and-full-year-2021
[11]https://investor.regeneron.com/news-releases/news-release-details/regeneron-reports-fourth-quarter-and-full-year-2021-financial
[12]https://news.abbvie.com/news/press-releases/abbvie-reports-full-year-and-fourth-quarter-2021-financial-results.htm#:~:text=Global%20Imbruvica%20net%20revenues%20were%20%241.385%20billion%2C%20a%20decrease%20of%20en t%20on%20an%20operational%20basis.

## 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 GROWHT 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





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## TNX-801: Smallpox and Monkeypox 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-801 will support recognition of the RPV/horsepox platform

### ANIMAL TESTING OF TNX-1800 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:** Smallpox and Monkeypox Vaccine

**Status:** Preclinical, Pre-IND

**Next Steps:** Developing GMP manufacturing for TNX-801 (horsepox)

*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



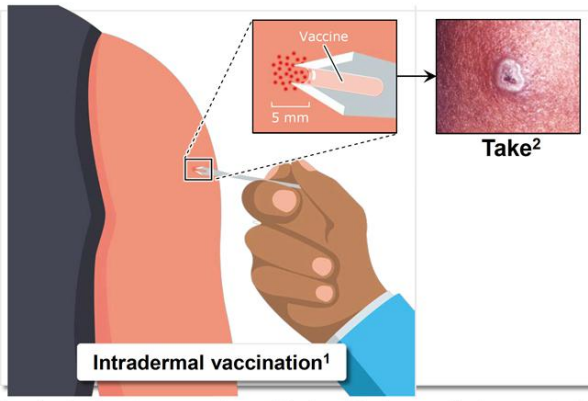
## Live Virus Vaccines: Development Rationale

- **Control of smallpox, measles, mumps, rubella, chickenpox and other viral conditions**
  - Prevent forward transmission
- **Effective in eliciting durable or long-term immunity**
- **Economical to manufacture at scale**
  - Low dose because replication amplifies dose *in vivo*
  - Single shot administration
- **Standard refrigeration required for shipping and storage**
- **Live virus vaccines are the oldest vaccine technology**
  - Starting with Edward Jenner's smallpox vaccine, the first vaccine, eradicated smallpox

INFECTIOUS DISEASE PORTFOLIO

TONIX PHARMACEUTICALS

## 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







## Live Virus Recombinant Pox Vaccine (RPV) Platform Profile

**POTENTIALLY LONGER DURABILITY DUE TO POX-ENGINEERED ARCHITECTURE**

- Live virus vaccines present unique "danger signals" resulting in strong immune response

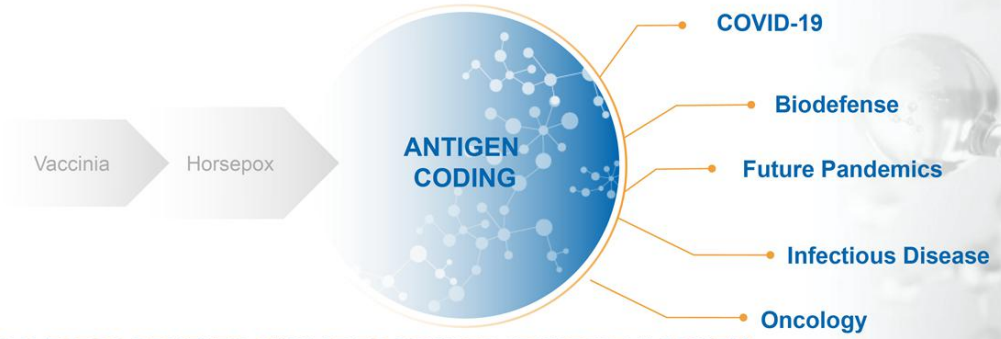
**PROGRAMMABLE VECTOR DESIGN FOR USE IN DIFFERENT DISEASE MODELS**

- Large capacity for expressing inserted genes
- 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
- Multi-dose packaging, standard cold-chain products

## 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***

[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







## COVID-19: Entering Endemic Phase in the US

- **Delta and Omicron variant waves are waning in most parts of the US**
  - Leaving a path of morbidity and mortality, including "breakthrough" infection and disease among vaccinated and convalescent
- **U.S. states are rolling back state pandemic restrictions**
  - CDC continues mask recommendation and recently increased the frequency of booster recommendations to every 3 months for individuals with weak immunity[1]
  - California plans to treat COVID as endemic by June, 2022[2]
- **Vaccines: new focus on SARS-CoV-2 variants Omicron and BA.2[3]**
  - Omicron has out-competed the original Wuhan strain, which has become rare
  - Omicron substantially evades *antibody immunity* to earlier variants, but is recognized by *T cell immunity* to earlier variants from vaccination or prior COVID[4]
  - Next generation vaccines are focusing on Omicron and its potential successor, BA.2

[1]Achenbach, J. "Americans are tired of the pandemic. But disease experts preach caution - and endure a 'kill the messenger moment'. *Washington Post* Feb 17, 2022. (www.washingtonpost.com/health/2022/02/17/mask-mandates-opposition/)
[2]Beachum L and Suliman A, "California unveils plan to become first state to treat coronavirus as 'endemic' risk." *Washington Post* Feb 18, 2022. (www.washingtonpost.com/nation/2022/02/18/california-covid-newsom-endemic-smarter-plan/)
[3]Bernstein L. "There's a new version of omicron but so far it doesn't appear to be more dangerous." *Washington Post* Jan 24, 2022 (www.washingtonpost.com/health/2022/01/24/covid-omicron-ba2/)
[4] Keeton R et al., "T cell responses to SARS-CoV02 spike cross-recognize omicron." *Nature Jan 31, 2022.* (www.nature.com/articles/s41586-022-04460-3)

## COVID-19: The Missing Pieces

- **Vaccines: early vaccines slowed pandemic, but are showing limitations**
  - Short term protection – requirement for boosters with mRNA vaccines;
  - Increasing focus on preventing hospitalization and death
- **Anti-viral drugs: Veklury® (remdesivir), Paxlovid™ (nirmatrelvir[1]), and Lagevrio® (molnupiravir) are available**
  - Pfizer's Paxlovid looks promising; Merck's Lagevrio did not show benefit in 2nd cohort[2]
- **Anti-SARS-CoV-2 monoclonal antibodies: increasing adoption; concern about variants**
  - Of the original EUA mAbs, only Vir/GSK's XEVURDY® (sotrovimab) was considered active against the omicron variant of SARS-CoV-2 but is not considered active against BA.2 and is not longer distributed in 8 US states[3]
  - Lilly's bebtelovimab, active against omicron, recently received EUA for treatment of mild or moderate COVID[4]
- **Tests: unmet need to determine COVID immunity[3]**
- **Long COVID: no approved treatment for 'Long Covid'**

[1]PAXLOVID™ (nirmatrelvir plus ritonavir)
[2]Merck Says Its Covid Pill Is Less Effective in a Final Analysis - The New York Times (nytimes.com)
[3]Brennan, Z. *Endpoints*, March 28, 2022 US halts use of GSK/Vir monoclonal in 8 states as FDA says it can't defeat new Omicron subvariant. endpts.com/us-halts-use-of-gsk-vir-monoclonal-in-8-states-as-fda-says-it-cant-defeat-new-omicron-subvariant/
[4]Redfield R and Siegel S. "A test to determine COVID immunity could reshape US policy." The Hill. Feb 17, 2022: (https://thehill.com/opinion/healthcare/594522-a-test-to-determine-covid-immunity-could-reshape-us-policy?)







## COVID-19 Vaccines: Where We Are Today

**Durability of protection**
- mRNA vaccinated people lose protection, starting at 4-6 months[1]
- High rates of "breakthrough" COVID during Delta and Omicron waves
- Booster vaccinations with mRNA vaccines recommended at 4-6 months

**Effect on forward transmission (spread of infection to others)**
- Concerns about whether vaccinated people can be infectious to others

**Detecting vaccine failure**
- Need a strategy for identifying individuals at risk after vaccination

**No recognized, clinical applicable biomarker of vaccine protection**
- Best proxy is neutralizing antibodies, which are hard to measure

**Current and future variants (e.g., Delta, Omicron variants)**
- Less protection from existing vaccines
- Unknown effectiveness for future variants

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

## COVID-19 Vaccines: Where Do We Go From Here?

### mRNA vaccines have slowed pandemic, but may not be a long-term solution

- Vaccinated people lost protection and showed high rates of "breakthrough" COVID during Delta and Omicron waves
- COVID is becoming endemic in the US; vaccination of entire world every 6 months not practical

### Operation Warp Speed (OWS) identified 4 types of vaccines:

1. RNA/DNA – Pfizer[1] and Moderna[2] are fully approved by the FDA
2. Subunit – NovaVax submitted EUA; Sanofi/GSK have announced data showing protection from hospitalization and death
3. Non-replicating – J&J has EUA; AstraZeneca widely used ex-US
4. Live Virus Vaccines – none were ultimately adopted by OWS

### Live Virus Vaccines

- Merck was developing two programs: VSV and Measles, but they were not included in OWS and were abandoned in January 2021[3]

[1]COMIRNATY is the brand name for the Pfizer-BioNTech COVID-19 vaccine
[2]https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-takes-key-action-approving-second-covid-19-vaccine
[3]https://www.merck.com/news/merck-discontinues-development-of-sars-cov-2-covid-19-vaccine-candidates-continues-development-of-two-investigational-therapeutic-candidates/







## TNX-1840 and 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 versions TNX-1840 and TNX-1850 encode spike protein from SARS-CoV-2, omicron and BA.2 strains, respectively[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-1840 (omicron) and TNX-1850 (BA.2) versions

*TNX-1840 and TNX-1850 are 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/)

## Live Virus Platform: What Makes TNX-1840 and TNX-1850 Different from mRNA Vaccines

| CRITERIA | mRNA VACCINES | TNX-1840/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-1840 and 1850 shown in table represent expectations.*

INFECTIOUS DISEASE PORTFOLIO

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## 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.

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[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

## Live Virus RPV Platform & COVID-19 Vaccine
## Internal Development & Manufacturing Capabilities

**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) – North Dartmouth, 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 partially operational in first half 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*

INFECTIOUS DISEASE PORTFOLIO

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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/-1840/-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/)

INFECTIOUS DISEASE PORTFOLIO

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## Small Molecule COVID-19 Therapeutics

**The only COVID-19 antiviral that is FDA approved is Remdesivir/Veklury®**

- Gilead – Intravenous (*i.v.*) medicine
- FDA approved for patients who are at least 12 years old and require hospitalization
- May shorten the time to recover from acute COVID-19
- World Health Organization has recommended against its use[1]
- Resistance reported[2]

**Antivirals available under Emergency Use Authorization (EUA)**

- Pfizer – PAXLOVID™ (PF-07321332; ritonavir) - oral protease C3L inhibitor - Emergency Use Authorization (EUA)
- Merck/Ridgeback – Lagevrio® (molnupiravir,) – oral polymerase inhibitor - EUA[3]

**Concerns about antiviral efficacy**

- Veklury resistance reported[2]
- Lagevrio efficacy was not repeated in second cohort of Phase 3 trial[4]

[1]*World Health Organization (2021). Therapeutics and COVID-19: living guideline, 6 July 2021 (Report).* (http://apps.who.int/iris/handle/10665/342368)
[2]https://yaledailynews.com/blog/2021/12/02/yale-scientists-identify-remdesivir-resistance-in-immunocompromised-covid-19-patient/
[3]www.merck.com/news/merck-announces-supply-agreement-with-u-s-government-for-molnupiravir-an-investigational-oral-antiviral-candidate-for-treatment-of-mild-to-moderate-covid-19
[4]www.merck.com/news/merck-announces-supply-agreement-with-u-s-government-for-molnupiravir-an-investigational-oral-antiviral-candidate-for-treatment-of-mild-to-moderate-covid-19







## TNX-3500*: COVID-19 Antiviral Treatment
## Sangivamycin

### PROFILE

**New variants heighten need for therapeutics**

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

**Potential monotherapy antiviral[1,2]**

- 65 times more potent than remdesivir in inhibiting SARS-CoV-2 as demonstrated in cell culture infectivity studies (dose to achieve $IC_{90}$)

**Potential combination therapy with remdesivir[1,2]**

- 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:** 2Q 2022 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]Bennett, RP et al. *JCI Insight*. 2021 in press preview (10.1172/jci.insight.153165)

## Monoclonal Antibody COVID-19 Therapeutics

### Monoclonal antibodies (mAbs) (EUA) – 3 with US Emergency Use Authorization[1]

- Vir/GSK – XEVURDY® (sotrovimab)[1] – ONLY mAb that was active against omicron, but now withdrawn from distribution in 8 states because of insufficient activity against BA.2[2]
- Lilly - bebtelovimab – EUA for treatment of mild or moderate COVID[3]
- AstraZeneca – Evusheld (Tixagevimab/cilgavimab) – EUA for long term prophylaxis

### New mAbs under development[4]

- AstraZeneca – AZD7442 – EUA request submitted[5]
- Brii Biosciences – BRII-196 and BRII-198[6]
- Adagio Therapeutics – ADG20[7]
- Many other companies[8]

### Concerns about efficacy of mAbs against new variants

- Regeneron/Genentech - REGEN-COV® Casirivimab/imdevimab
  - *EUA revised Jan '22 to susceptible variants – unlikely to be effective against omicron*
- Eli Lilly/AbCellera – Bamlanivimab/etesevimab
  - *EUA revised Jan '22 to susceptible variants – unlikely to be effective against omicron*
- Vir/GSK – XEVURDY® (sotrovimab)[1] – – *unlikely to be effective* against BA.2[2]
- Delta and Omicron variants have many changes in the spike protein, which is the target of current mAbs

[1]Indicated for individuals with mild-to-moderate COVID-19 who are at high risk for progression to severe disease; [11]Dec 7, 2021 Glaxo Says Its Covid-19 Antibody Drug Works Against Omicron – WSJ
[2]Brennan, Z. *Endpoints*, March 28, 2022 0US halts use of GSK/Vir monoclonal in 8 states as FDA says it can't defeat new Omicron subvariant. endpts.com/us-halts-use-of-gsk-vir-monoclonal-in-8-states-as-fda-says-it-cant-defeat-new-omicron-subvariant/
[3]https://investor.lilly.com/news-releases/news-release-details/lillys-bebtelovimab-receives-emergency-use-authorization
[4]Dolgin, E. *Nature Biotechnology* volume 39, pages783–785 (2021) https://doi.org/10.1038/s41587-021-00980-x
[5]https://www.cnbc.com/2021/11/18/astrazeneca-antibody-drug-83percent-effective-at-preventing-covid-trial.html
[6]https://endpts.com/brii-bio-gets-all-hands-on-deck-for-covid-19-antibody-hunt-leveraging-chinese-partners-work-with-recovered-patients/
[7]https://endpts.com/qa-tillman-gerngross-explains-why-his-covid-mab-will-have-an-edge-over-an-already-crowded-field/
[8]e.g., Centivax, Corat Therapeutics, IDBiologics, Leyden Labs, Memo Therapeutics and SpikImm







## 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

### 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; 2Q 2022 Initiate Animal Studies

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.

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

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

## 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; 2Q 2022 Initiate Animal Studies

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

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

RARE DISEASE PORTFOLIO

### PROFILE

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

- Rare 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 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.

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## Key Development Partners

Massachusetts General Hospital · Harvard Medical School

**TNX-1500:** ALLOGRAFT REJECTION

Stanford University · Université de Genève

**TNX-1900:** MIGRAINE & OTHER INDICATIONS

InsermTransfert · CHU de Toulouse · Aix*Marseille université

**TNX-2900:** PRADER-WILLI SYNDROME

Columbia University

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

University of Alberta · SR Southern Research

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

Kansas State University

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

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## Milestones:
## Recently Completed and Upcoming*

- ☑ 1st Quarter 2021 Non-human primate positive efficacy data from TNX-1800 in COVID-19 models reported
- ☑ 1st Quarter 2022 Topline data from Phase 3 F306/RALLY study of TNX-102 SL for the management of fibromyalgia
- ☑ 2nd Quarter 2022 Phase 3 F307/RESILIENT study start of TNX-102 SL for the management of fibromyalgia

**Expected Data**

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

**Expected Clinical Trial Initiations**

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

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

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## Management Team

**Seth Lederman, MD**
Co-Founder, CEO & Chairman

TARGENT X | Fusilev (levoleucovorin) for injection | vela pharmaceuticals

**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 SiliconValleyBank | American Capital

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# THANK YOU