**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): March 28, 2022**

# TONIX PHARMACEUTICALS HOLDING CORP.

**(Exact name of registrant as specified in its charter)**

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

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

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

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

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

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

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

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

Emerging growth company ☐

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

**Item 7.01 Regulation FD Disclosure.**

Tonix Pharmaceuticals Holding Corp. (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 99.01 hereto and incorporated herein by reference.

The information in this Item 7.01 of this Current Report on Form 8-K, including Exhibit 99.01 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 | Corporate Presentation by the Company for March 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: March 28, 2022

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

**Exhibit 99.01**


## CAUTIONARY NOTE ON FORWARD-LOOKING STATEMENTS

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

TONIX PHARMACEUTICALS

## WHAT WE DO

### OUR MISSION

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
## CNS PORTFOLIO

| Candidates* | INDICATIONS | STATUS / NEXT MILESTONE |
|---|---|---|
| | **CNS** | |
| TNX-102 SL[1] | Fibromyalgia (FM)<br>Posttraumatic Stress Disorder (PTSD)<br>Long COVID (PASC[2]) | Mid-Phase 3<br>Phase 2, Targeted 1H 2022 Start<br>Phase 2, Targeted 1H 2022 Start[3] |
| TNX-1300[4] | Cocaine Intoxication / Overdose<br>*FDA Breakthrough Designation* | Phase 2, Targeted 1H 2022 Start |
| TNX-1900[5] | Migraine, Craniofacial Pain and Binge Eating Disorder | Phase 2, Targeted 2H 2022 Start[6] |
| TNX-2900[7] | Prader-Willi Syndrome<br>*Orphan Drug Designation* | Preclinical |
| TNX-601 CR | Depression, PTSD, Neurocognitive Dysfunction from Steroids | Phase 2, Targeted Q1 2023 Start[8] |
| TNX-1600[9] | Depression, PTSD and ADHD | Preclinical |

**All of Tonix's product candidates are investigational new drugs or biologics and have not been approved for any indication.*
[1]TNX-102 SL (cyclobenzaprine HCl sublingual tablets) is 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]Pre-IND (Investigational New Drug) meeting with FDA completed; Company plans to start Phase 2 study in subset of patients whose symptoms overlap with fibromyalgia pending IND clearance.
[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]Co-exclusive license agreement with French National Institute of Health and Medical Research (Inserm)
[8]TNX-601 CR is in the pre-IND stage in the U.S.; a Phase 1 trial for formulation development was completed outside of the U.S; Phase 2 expected to start Q1 2023
[9]Acquired from TRImaran Pharma; license agreement with Wayne State University

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



CNS PORTFOLIO

## PIPELINE
## IMMUNOLOGY & INFECTIOUS DISEASE PORTFOLIO

| CANDIDATES* | PORTFOLIO & INDICATION | STATUS / NEXT MILESTONE |
|---|---|---|
| | **Immunology & Immuno-Oncology** | |
| TNX-1500[1] | Organ Transplant Rejection/ Autoimmune Conditions | Phase 1, Targeted 2H 2022 Start |
| TNX-1700[2] | Gastric and colorectal cancers | Preclinical |
| | **BioDefense** | |
| TNX-801[3] | Smallpox and monkeypox preventing vaccine | Preclinical |
| TNX-701 | Radioprotection | Preclinical |
| | **COVID** | |
| TNX-1840/TNX-1850[4] | COVID-19 Vaccine (RPV – horsepox-based live virus vaccine) | Preclinical |
| TNX-2100[5] | SARS-CoV-2 Diagnostic for T Cell Immunity | First-in-human study initiated Q1 2022 |
| TNX-3500[6] | COVID-19 Antiviral | Preclinical |
| TNX-3600[7] | COVID-19 Therapeutic Platform (monoclonal antibodies) | Preclinical |
| TNX-3700[8] | COVID-19 Vaccine (zinc nanoparticle mRNA technology) | Preclinical |

**All of Tonix's product candidates are investigational new drugs or biologics and have not been approved for any indication.*
[1]anti-CD40L humanized monoclonal antibody
[2]Recombinant trefoil factor 2 (rTFF2) based protein; licensed from Columbia University
[3]Live attenuated vaccine based on horsepox virus
[4]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.
[5]*In vivo* diagnostic: SARS-CoV-2 peptide epitope mixtures for intradermal administration to measure delayed-type hypersensitivity to SARS-CoV-2.
[6]Sangivamycin for injection; licensed from OyaGen, Inc.
[7]Fully human monoclonal antibody generated from COVID-19 convalescent patients
[8]anti-CD40L/COVID vaccine based on mRNA in zinc nanoparticle (ZNP) formulation



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

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

Second Phase 3 study RALLY missed primary endpoint

**Next Steps:** Confirmatory Phase 3 study RESILIENT (F307) planned for 1H 2022 start

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

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## TNX-102 SL: FIBROMYALGIA
## PROGRAM UPDATE

CNS PORTFOLIO

### Phase 3 Study, RALLY (F306)

- 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

### Phase 3 Study, RESILIENT (F307)

- Anticipated start in 1H 2022
- Projecting adverse event related discontinuations to decrease towards rates in RALLY and PTSD Studies

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

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

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

TEAE = treatment-emergent adverse event

### Adverse events in RALLY

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

CNS PORTFOLIO

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

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

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

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

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

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

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

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

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

* MMRM with MI was the pre-specified primary analysis

**MMRM without MI was a pre-specified analysis

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

CNS PORTFOLIO

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## TNX-102 SL: FIBROMYALGIA PROGRAM UPDATE

CNS PORTFOLIO

**Phase 3 Study, RESILIENT (F307)**

- Anticipated start in 1H 2022
- Projecting adverse event related discontinuations to decrease towards rates in RALLY and PTSD Studies

**Similar to RALLY, RESILIENT will compare TNX-102 SL 5.6 mg and placebo**

- Parallel design, double-blind, randomized placebo-controlled study
- Primary endpoint is pain at week 14 analyzed by MMRM with MI
- All U.S. sites

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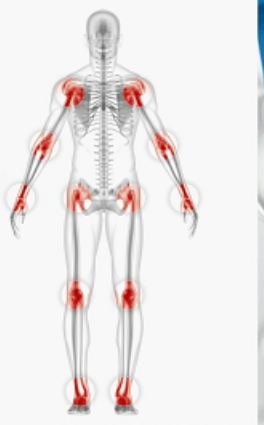
## ROLE OF INFECTIONS IN TRIGGERING FIBROMYALGIA OR CHRONIC FATIGUE (CFS)-LIKE ILLNESSES

CNS PORTFOLIO

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

CNS PORTFOLIO

- 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.



TONIX PHARMACEUTICALS



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

CNS PORTFOLIO

### PROFILE

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

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

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

***Patents Issued***

### DEVELOPMENT PROGRAM

**Market Entry**: Long COVID (PASC)

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

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

*TNX-102 SL is in the pre-IND stage of development for Long Covid and 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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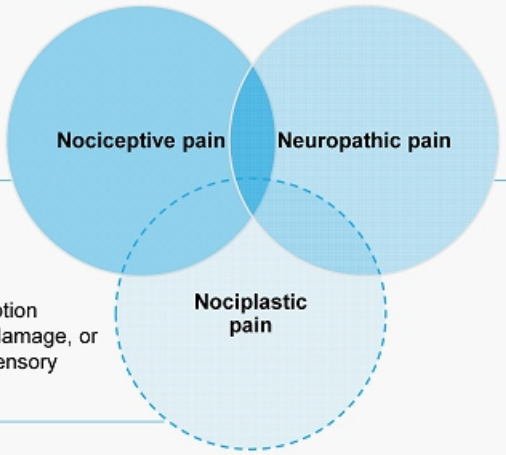
## NEW CLASSIFICATION FOR PAIN: NOCIPLASTIC

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




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

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

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







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## OPPORTUNITIES TO EXPAND TNX-102 SL TO OTHER INDICATIONS

**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*

## 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:** 1H 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;16:28.
ED = emergency department.



TONIX PHARMACEUTICALS



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## 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: PMC1135633.
[3]Meyerowitz, J.G., *et al.* The oxytocin signaling complex reveals a molecular switch for cation dependence. *Nat Struct Mol Biol* (2022). (https://doi.org/10.1038/s41594-022-00728-4)
[4]A Phase 2 trial under an investigator-initiated IND has been completed in the U.S. using TNX-1900.



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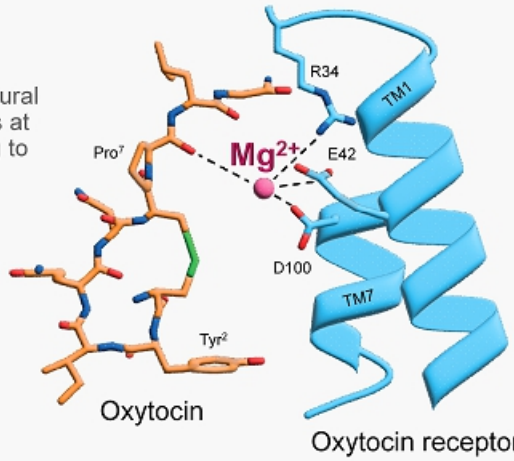
## TNX-1900* FOR MIGRAINE
## MAGNESIUM ($Mg^{2+}$) IS AT THE CORE OF OXYTOCIN BINDING[1]

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




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







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

### PROFILE

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

- Orphan disease occurring in 1 in 15,000 births

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

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

***Patents Issued***

### DEVELOPMENT PROGRAM

**Market Entry:** Prader-Willi Syndrome

**Additional Indications:** Rare, Orphan Hyperphagia Conditions

**Status:** Preclinical, granted orphan drug designation by FDA

**Next Steps:** pre-IND Meeting to seek agreement on development plans; Submit application to the FDA for Fast Track designation

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

## 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:** Q1 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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## IMMUNOLOGY: KEY CANDIDATES



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## TNX-1500 (α-CD40L mAb): PROPHYLAXIS OF TRANSPLANT REJECTION
## POTENTIAL TREATMENT FOR AUTOIMMUNE CONDITIONS

IMMUNOLOGY PORTFOLIO

**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.

TONIX PHARMACEUTICALS





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## TNX-1500
## MARKET OPPORTUNITY

IMMUNOLOGY PORTFOLIO

**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)

TONIX PHARMACEUTICALS

## 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):3295-3308.




TONIX PHARMACEUTICALS





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## NEXT GENERATION α-CD40 LIGAND (CD40L) ANTIBODY
## TNX-1500*: PREVENTION OF ALLOGRAFT REJECTION

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

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

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

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

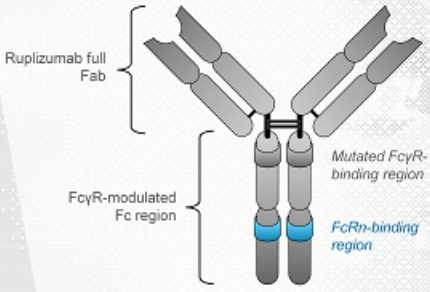
- Expected to deliver efficacy without compromising safety

**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.

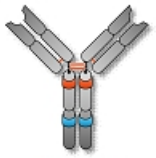


TONIX PHARMACEUTICALS

## THIRD-GENERATION anti-CD40L
## ENGINEERED TO DECREASE RISK OF THROMBOSIS



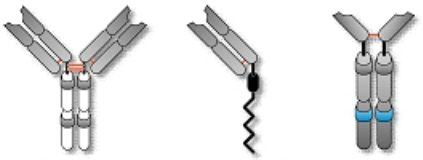
**First-generation anti-CD40L mAbs**



*Ruplizumab*

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

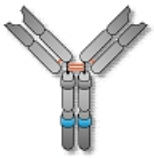
**Second-generation anti-CD40L mAbs**



*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 AT-1501 also are Fc modified


[1]Imwald 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



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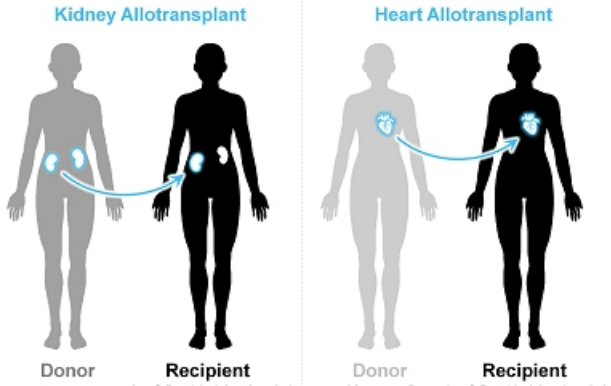
## anti-CD40L TREATMENT TO PREVENT ALLOGRAFT REJECTION



- 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.



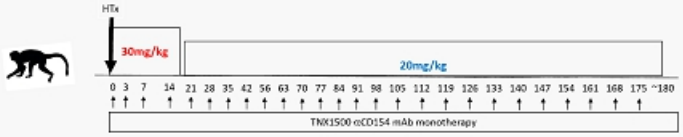

TONIX PHARMACEUTICALS

## NON-HUMAN PRIMATE HEART HETEROTOPIC ALLOGRAFT STUDY

### DR. RICHARD PIERSON, MASS GENERAL HOSPITAL

IMMUNOLOGY PORTFOLIO

- **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.



TONIX PHARMACEUTICALS



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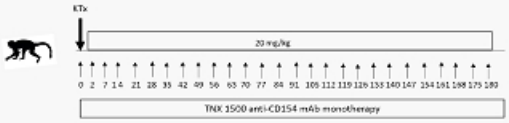
## NON-HUMAN PRIMATE KIDNEY ALLO-TRANSPLANTATION STUDY

### DR. TATSUO KAWAI, MASS GENERAL HOSPITAL

IMMUNOLOGY PORTFOLIO

- **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



TONIX PHARMACEUTICALS

# 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.







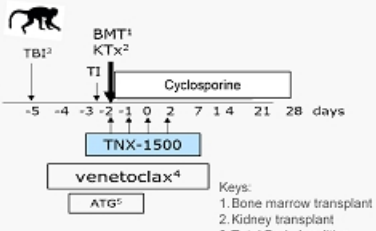
# NON-HUMAN PRIMATE COMBINED KIDNEY AND BONE MARROW TRANSPLANTATION(CKBMT) WITH TONIX-1500 INDUCED ALLOGRAFT TOLERANCE

## DR. TATSUO KAWAI, MASS GENERAL HOSPITAL

### A. CONDITIONING REGIMEN FOR BONE MARROW & KIDNEY TX

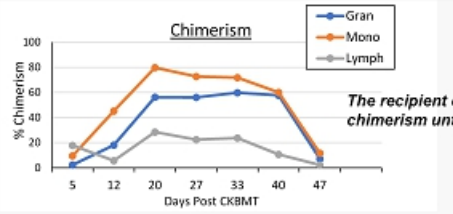
The nonhuman primate recipient received the conditioning regimen that includes low dose total body irradiation (TBI, 1.5Gy), thymic irradiation (TI, 7Gy), venetoclax and ATG. The recipients then received combined kidney and bone marrow (BM) transplantation (CKBMT), after which treated with TNX-1500 (20mg/kg 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



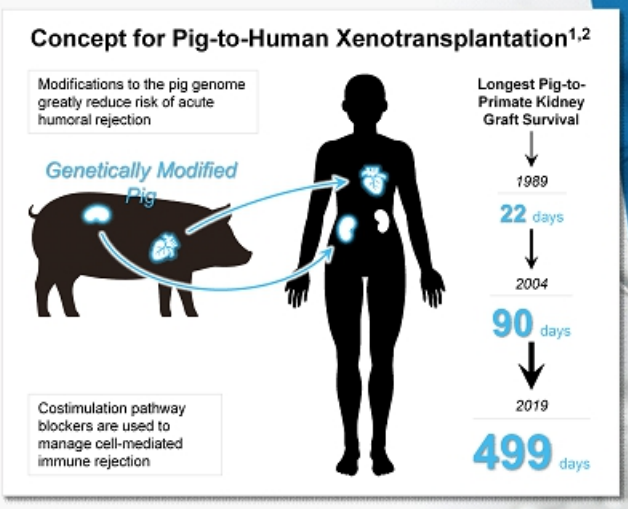

***The recipient developed multilineage chimerism until day 47***

### 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.

## anti-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)







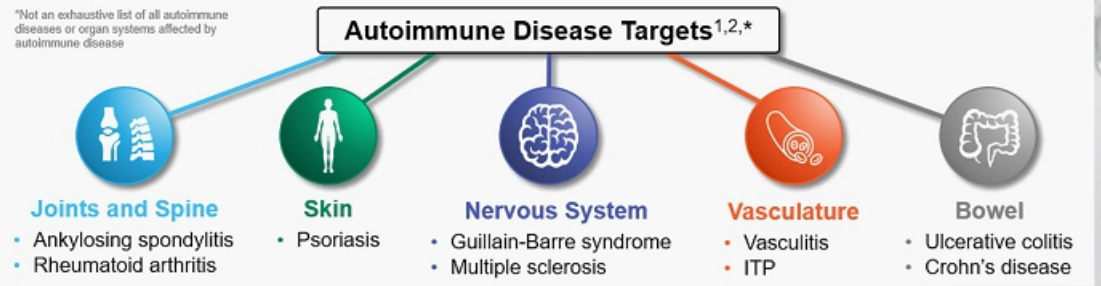
## RECENT XENOTRANSPLANT HEADLINES

| | | |
|---|---|---|
| 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* |

## anti-CD40L BEYOND ALLOGRAFTS: 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]

*Not an exhaustive list of all autoimmune diseases or organ systems affected by autoimmune disease




[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) Q2 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™ (sacituzumab 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"

**November**

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

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

**December**

**2021** — **January**

**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

[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



TONIX PHARMACEUTICALS





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## 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%20an%20increase%20of%20,1%20on%20an%20operational%20basis.



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## 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.

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# TNX-801: SMALLPOX AND MONKEYPOX VACCINE
# LIVE VIRUS PLATFORM DEVELOPMENT PROGRAM

INFECTIOUS DISEASE PORTFOLIO

## 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 Q1 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.

[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/10929ac27f4fb6f5204f5cf41d59a121.pdf)



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# LIVE VIRUS VACCINES: DEVELOPMENT RATIONALE

INFECTIOUS DISEASE PORTFOLIO

- **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



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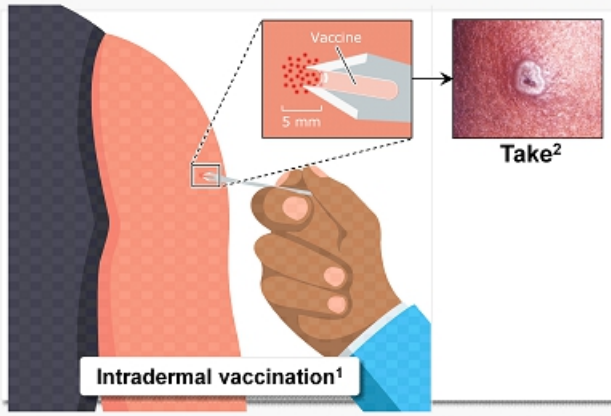
# VACCINIA INDUCES A SKIN REACTION CALLED "TAKE" – DESCRIBED BY DR. EDWARD JENNER




- **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

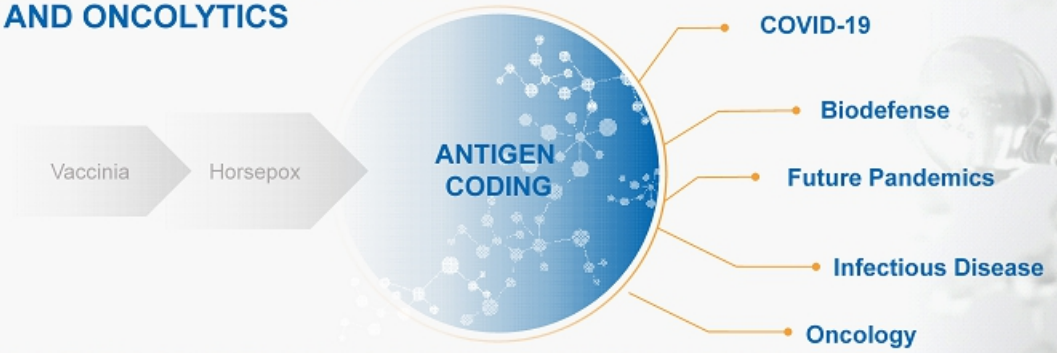
## PROGRAMMABLE VECTOR DESIGN FOR USE IN DIFFERENT DISEASE MODELS

- 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:
## NEW 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







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## 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) is considered active against the omicron variant of SARS-CoV-2;
  - Lilly's bebtelovimab, active against omicron, recently received EUA for treatment of mild or moderate COVID[2]
- **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]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?)







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## 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?

INFECTIOUS DISEASE PORTFOLIO

### 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/

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## TNX-1840 AND TNX-1850*: COVID-19 VACCINE
## LIVE VIRUS PLATFORM DEVELOPMENT PROGRAM

INFECTIOUS DISEASE PORTFOLIO

### 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 Q4 2020
- Non-human primate CoV-2 challenge testing: positive data reported in Q1 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-1800, 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/)

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## 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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## LIVE VIRUS RPV PLATFORM & COVID-19 VACCINE INTERNAL DEVELOPMENT & MANUFACTURING CAPABILITIES

### Infectious Disease R&D Center (RDC) – Frederick, MD

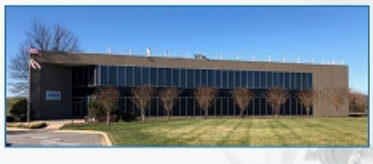
- Function: Accelerated development of vaccines and antiviral drugs against COVID-19, its variants and other infectious diseases
- Description: ~48,000 square feet; currently BSL-2 but being converted to BSL-3
- Status: Operational; acquisition completed on October 1st, 2021

### 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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## ASSESSING anti-SARS-CoV-2 PROTECTIVE IMMUNITY

### TWO TYPES OF IMMUNITY

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

### NEUTRALIZING ANTIBODIES – APPEAR TO CORRELATE WITH PROTECTION[1]

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

### FUNCTIONAL T CELL IMMUNITY

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

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

INFECTIOUS DISEASE PORTFOLIO

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



## DESIGNED TO MEASURE THE PRESENCE AND STRENGTH OF FUNCTIONAL *IN VIVO* T CELL IMMUNITY

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

## POTENTIALLY SCALABLE FOR WIDESPREAD USE

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

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



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# TNX-2100*: POTENTIAL USES AND DEVELOPMENT PLAN



## POTENTIAL BENEFITS OF TESTING FOR PROTECTIVE IMMUNITY

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

## DEVELOPMENT PLANS

- Initiated first-in-human, dose-finding clinical study in January 2022
- Topline data expected first half 2023
- Patents filed

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



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## SMALL MOLECULE COVID-19 THERAPEUTICS

INFECTIOUS DISEASE PORTFOLIO

**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 – molnupiravir, oral, - EUA[3]

**Concerns about antiviral efficacy**

- Remdesivir resistance reported[2]
- Molnupiravir 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

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## TNX-3500*: COVID-19 ANTIVIRAL TREATMENT
## SANGIVAMYCIN

INFECTIOUS DISEASE PORTFOLIO

### 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:** 1H 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.153185)

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## MONOCLONAL ANTIBODY COVID-19 THERAPEUTICS

INFECTIOUS DISEASE PORTFOLIO

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

- Vir/GSK – XEVURDY® (sotrovimab)[1] – ONLY mAb ACTIVE AGAINST OMICRON
- Lilly - bebtelovimab – EUA for treatment of mild or moderate COVID[2]
- AstraZeneca – Evusheld (Tixagevimab/cilgavimab) – EUA for long term prophylaxis

### New mAbs under development[3]

- AstraZeneca – AZD7442 – EUA request submitted[4]
- Brii Biosciences – BRII-196 and BRII-198[5]
- Adagio Therapeutics – ADG20[6]
- Many other companies[7]

### 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 against omicron*
- 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]https://investor.lilly.com/news-releases/news-release-details/lillys-bebtelovimab-receives-emergency-use-authorization
[3]Dolgin, E. *Nature Biotechnology* volume 39, pages783–785 (2021) https://doi.org/10.1038/s41587-021-00980-x
[4]https://www.cnbc.com/2021/11/18/astrazeneca-antibody-drug-83percent-effective-at-preventing-covid-trial.html
[5]https://endpts.com/brii-bio-gets-all-hands-on-deck-for-covid-19-antibody-hunt-leveraging-chinese-partners-work-with-recovered-patients/
[6]https://endpts.com/qa-tillman-gerngross-explains-why-his-covid-mab-will-have-an-edge-over-an-already-crowded-field/
[7]e.g., Centivax, Corat Therapeutics, IDBiologics, Leyden Labs, Memo Therapeutics and SpikImm



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## TNX-3600*: COVID-19 THERAPEUTIC
## FULLY HUMAN MONOCLONAL ANTIBODY PLATFORM

INFECTIOUS DISEASE PORTFOLIO

### 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; 1H 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



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## TNX-3700*: COVID-19 VACCINE
## ZINC NANOPARTICLE (ZNP) FORMULATION FOR mRNA VACCINE

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; 1H 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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## KEY DEVELOPMENT PARTNERS

Massachusetts General Hospital · Harvard Medical School

**TNX-1500:** ALLOGRAFT REJECTION

Columbia University

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

Stanford University · Université de Genève

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

University of Alberta · Southern Research

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

InsermTransfert · CHU de Toulouse · Aix*Marseille université

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





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## MILESTONES: RECENTLY COMPLETED AND UPCOMING*

- ☑ **4th Quarter 2020** **Positive topline data from TNX-102 SL Phase 3 F304/RELIEF study in fibromyalgia reported**
- ☑ **1st Quarter 2021** **Non-human primate positive efficacy data from TNX-1800 in COVID-19 models reported**
- ☑ **1st Quarter 2022** **First-in-human study of TNX-2100 initiated for skin test to detect T cell immunity to SARS-CoV-2**
- ☑ **1st Quarter 2022** **Topline data from TNX-102 SL Phase 3 F306/RALLY study in fibromyalgia**

**Expected Clinical Trial Initiations**

- ☐ 1st Half 2022 Phase 2 OL safety study start of TNX-1300 in ED setting for cocaine intoxication
- ☐ 1st Half 2022 Phase 2 study start of TNX-102 SL for the treatment of PTSD in Kenya
- ☐ 1st Half 2022 Phase 3 study start of TNX-102 SL for the management of fibromyalgia
- ☐ 1st Half 2022 Phase 2 study start of TNX-102 SL for the treatment of Long COVID
- ☐ 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.

## MANAGEMENT TEAM

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

**Gregory Sullivan, MD**
Chief Medical Officer

**Bradley Saenger, CPA**
Chief Financial Officer

**Jessica Morris**
Chief Operating Officer





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# THANK YOU



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