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): June 7, 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 June 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: June 7, 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.

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) Posttraumatic Stress Disorder (PTSD) Long COVID (PASC[2])	Mid-Phase 3 Phase 2, Targeted 2Q 2022 Start Phase 2, Targeted 2Q 2022 Start[3]
TNX-1300[4]	Cocaine Intoxication / Overdose *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

CNS PORTFOLIO

*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
Rare Disease Portfolio

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

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

Pipeline
Immunology and Immuno-Oncology portfolio

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

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

RARE DISEASE & IMMUNOLOGY PORTFOLIOS

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

**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]COVID vaccine based on mRNA in zinc nanoparticle (ZNP) formulation with CD40L molecular trigger

INFECTIOUS DISEASE PORTFOLIO

TONIX PHARMACEUTICALS

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

CNS PORTFOLIO

PROFILE

A unique formulation of cyclobenzaprine designed to optimize delivery and absorption

Innovative and proprietary PROTECTIC® Rapid drug exposure following nighttime administration

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

Clinical trial program designed to examine treatment of core Fibromyalgia symptoms

Patents Issued

DEVELOPMENT PROGRAM

Market Entry: Fibromyalgia

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

Status: One Positive Phase 3 study RELIEF Completed

Second Phase 3 study RALLY missed primary endpoint

Confirmatory Phase 3 study RESILIENT is currently enrolling

Next Steps: Interim analysis results expected 1Q 2023

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

TONIX PHARMACEUTICALS

8

TNX-102 SL: Fibromyalgia
Program Update

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

CNS PORTFOLIO

TONIX PHARMACEUTICALS

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)

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

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.

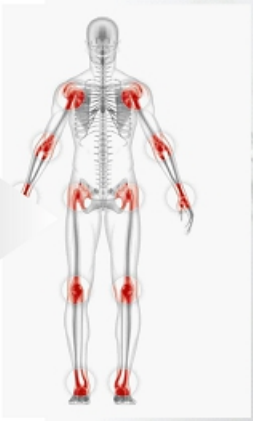
CNS PORTFOLIO

TONIX PHARMACEUTICALS

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)

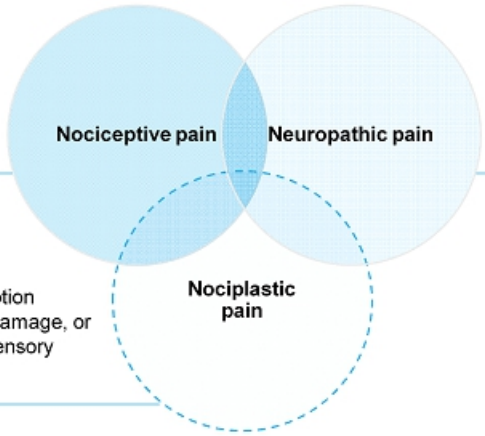
- Long COVID is a heterogeneous condition that displays elements of nociplastic pain in many individuals, who experience otherwise unexplained[1-2]:

- 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

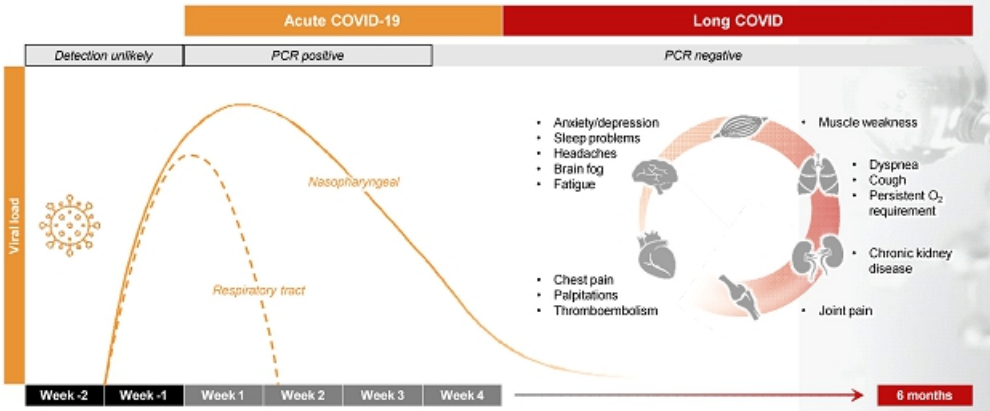


Pain caused by a lesion or disease of the somatosensory nervous system

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

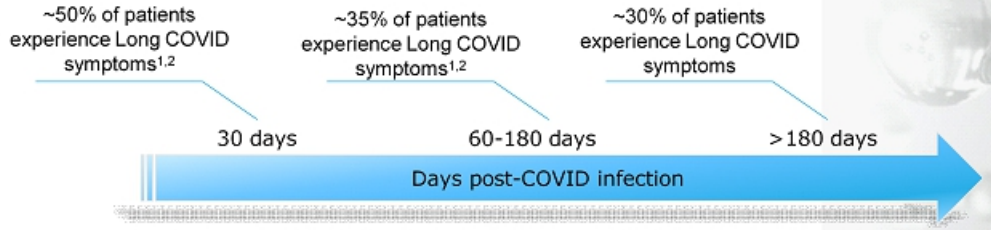
[1]Trouvin AP, et al. *Best Pract Res Clin Rheumatol*. 2019;33(3):101415.

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.

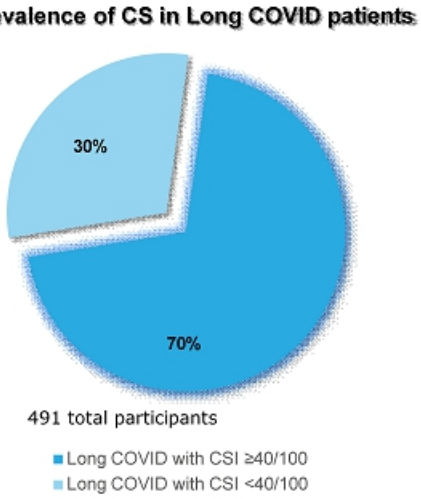
CNS PORTFOLIO

TONIX PHARMACEUTICALS

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

CNS PORTFOLIO

TONIX PHARMACEUTICALS

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

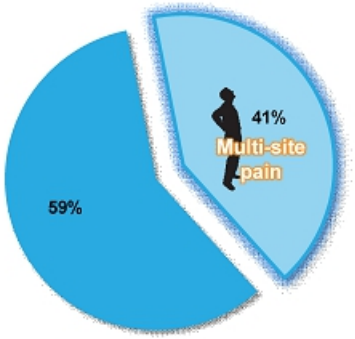
[1]Harris, H, et al. Tonix data on file. 2022.
[2]TriNetX Analytics
[3]Topaloglu, U, and Palchuk, MB. *JCO clinical cancer informatics*. 2018;2:1-10.

CNS PORTFOLIO

TONIX PHARMACEUTICALS

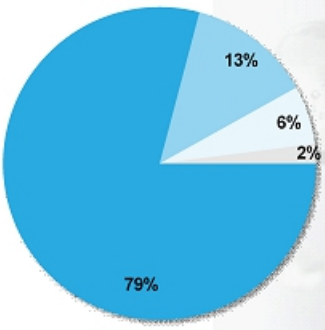
Long COVID Patients in TriNetX study[1]
Fibromyalgia-like Symptoms (Multi-Site Pain) in Over 40% of Patients[1,2]

52,322 total Long COVID patients



Multi-site pain
No multi-site pain

21,694 total FM-like Long COVID patients



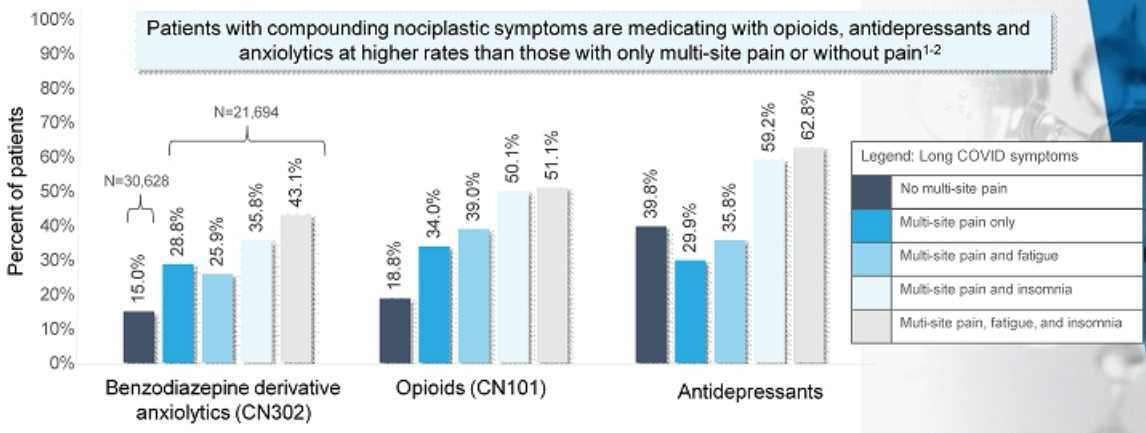
Multi-site pain only
Multi-site pain and fatigue
Multi-site pain and insomnia
Multi-site pain, fatigue, and insomnia

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

CNS PORTFOLIO

TONIX PHARMACEUTICALS

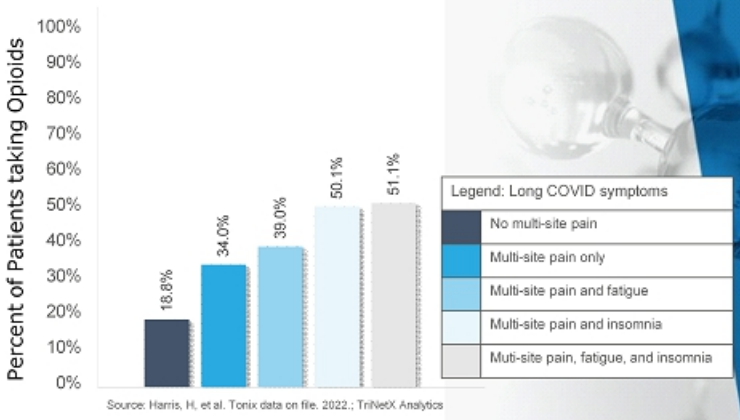
Long COVID Patients in TriNetX Study[1]
Recorded Medication Use, Days 91-180



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

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

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]

CNS PORTFOLIO

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

TONIX PHARMACEUTICALS

Opportunities to Expand TNX-102 SL to Other Indications

CNS PORTFOLIO

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*

TONIX PHARMACEUTICALS

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

CNS PORTFOLIO

PROFILE

PTSD is a serious chronic psychiatric illness

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

Affects approximately 12 million Americans adults[1,2]

Large unmet clinical need and limited effective therapies available

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

Patents Issued

DEVELOPMENT PROGRAM

Market Entry: PTSD

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

Status: One Phase 2 study (AtEase) completed

Two Phase 3 studies (HONOR, RECOVERY) conducted

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

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

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

TONIX PHARMACEUTICALS

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

CNS PORTFOLIO

PROFILE

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

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

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

CocE is a recombinant protein that degrades cocaine in the bloodstream

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

Patents Issued

DEVELOPMENT PROGRAM

Market Entry: Cocaine Intoxication

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;9:177-195.
[3]Maceira AM et al. *J Cardiovasc Magn Reson*. 2014;16:26.
ED = emergency department.

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

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

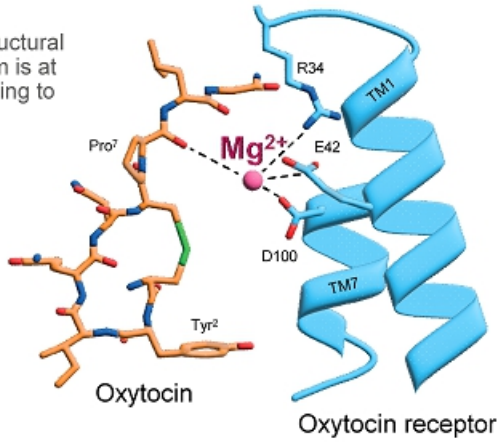
*TNX-1900 has not been approved for any indication.
CGRP = calcitonin gene-related peptide.

[1]Tzabazis A, et al. Oxytocin and Migraine Headache. Headache. 2017 May;57 Suppl 2:84-75. 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: PMC1135627.
[3]Meyerowitz, J.G., *et al.* The oxytocin signaling complex reveals a molecular switch for cation dependence. *Nat Struct Mol Biol* (2022). (https://doi.org/10.1038/s41594-022-00728-4)
[4]A Phase 2 trial under an investigator-initiated IND has been completed in the U.S. using TNX-1900.

TONIX PHARMACEUTICALS

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

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



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

TONIX PHARMACEUTICALS

TONIX PHARMACEUTICALS

RARE DISEASE: KEY CANDIDATES

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.

TONIX PHARMACEUTICALS

TONIX PHARMACEUTICALS

IMMUNOLOGY: KEY CANDIDATES

TNX-1500 (αα-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

TNX-1500 (αα-CD40 Ligand)
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-For-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(8):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 αCD40 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 (FcγγR)

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

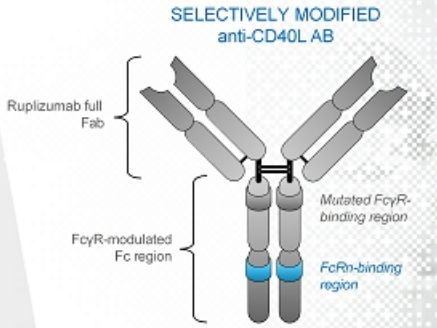
Third Generation (TNX-1500): Re-engineered to better modulate the binding of FcγγR while preserving FcRn function

- 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



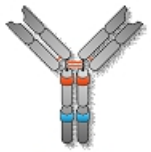
Contains the full ruplizumab Fab and the engineered Fc region that modulates FcγR-binding, while preserving FcRn function.

*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

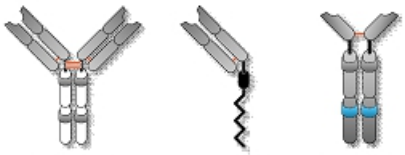
First-generation
anti-CD40L mAbs



Ruplizumab

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

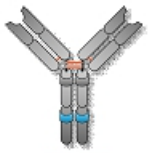
Second-generation
anti-CD40L mAbs



Aglycosyl Ruplizumab *Dapirolizumab* *Letolizumab*

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

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]

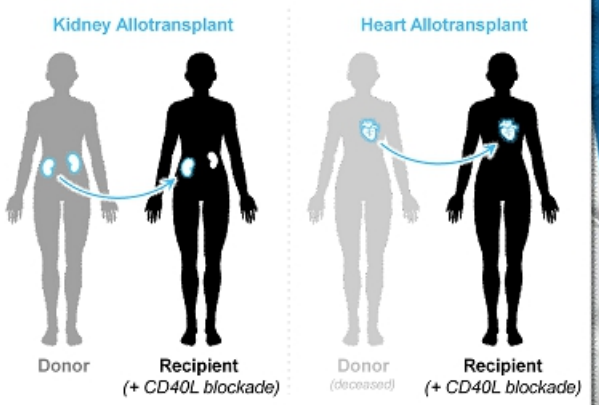
*Sanofi's SAR441344 and Eledon's tegoprubart (f.k.a., AT-1501) also are F_c-modified

[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.

αCD40L 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]

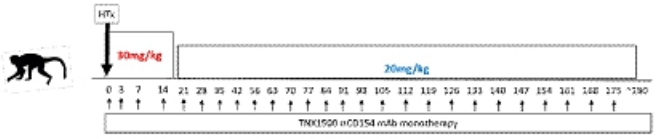


[1]Enderby C, et al. *Am J Manag Care.* 2015;21(1 Suppl):s12-s23.
[2]Camilleri B, et al. *Exp Clin Transplant.* 2016;14(5):471-483.
[3]Naesens M, et al. *Clin J Am Soc Nephrol.* 2009;4(2):481-508.
[4]Nankivell BJ, et al. *N Engl J Med.* 2003;349(24):2326-2333.
[5]Cooper DKC, et al. *Blood Purif.* 2018;45(1-3):254-259.

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)



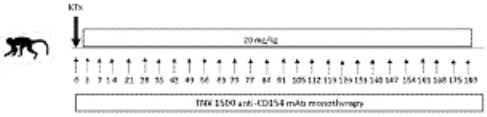
- **Similar activity to chimeric hu5c8[4] during treatment phase in prior studies[5]**
  - Last dose of hu5c8 was day 84
- **No thrombosis observed**
  - Thrombosis was observed with hu5c8 in prior studies

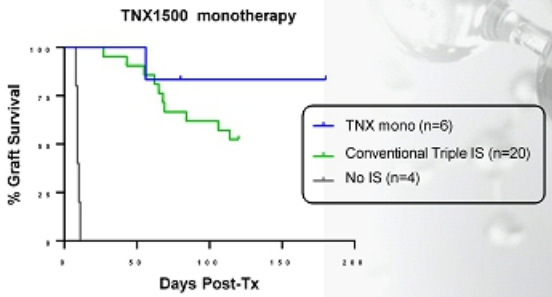
[1]TNX-1500 dosed at 30 mg/kg twice weekly on days 0, 3, 7, and 14; 20 mg/kg weekly from days 21 to 175
[2]H&E staining
[3]C4d immunohistochemistry
[4]Mouse-human IgG1κ chimeric anti-CD154
[5]TNX-1500 dosed at 30 mg/kg twice weekly on days 0, 3, 7, and 14; 10 mg/kg weekly on days 21, 28, 35 and 42; 20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

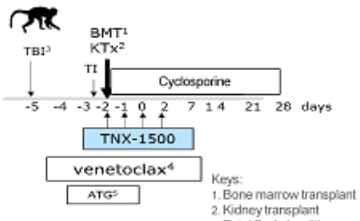
Non-Human Primate Combined Kidney and Bone marrow Transplantation (CKBMT) with TNX-1500 induced allograft tolerance

Dr. Tatsuo Kawai, Mass General Hospital

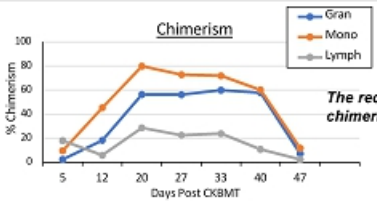
A. CONDITIONING REGIMEN FOR BONE MARROW & KIDNEY TX

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

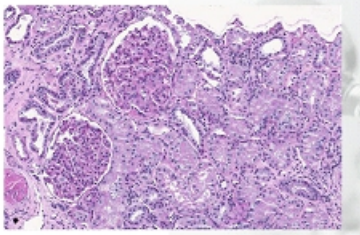


B. DONOR BLOOD CELLS TRANSIENTLY EXPANDED AFTER TRANSPLANT



The recipient developed multilineage chimerism until day 47

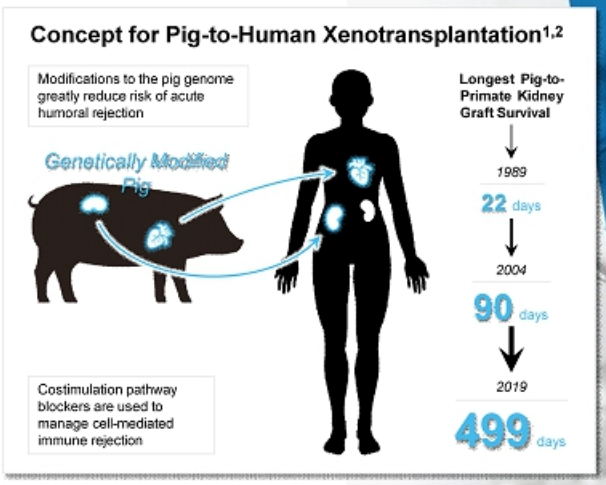
C. KIDNEY BIOPSY AT ONE YEAR SHOWING NO REJECTION



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)

IMMUNOLOGY PORTFOLIO

TONIX PHARMACEUTICALS

Recent Xenotransplant Headlines

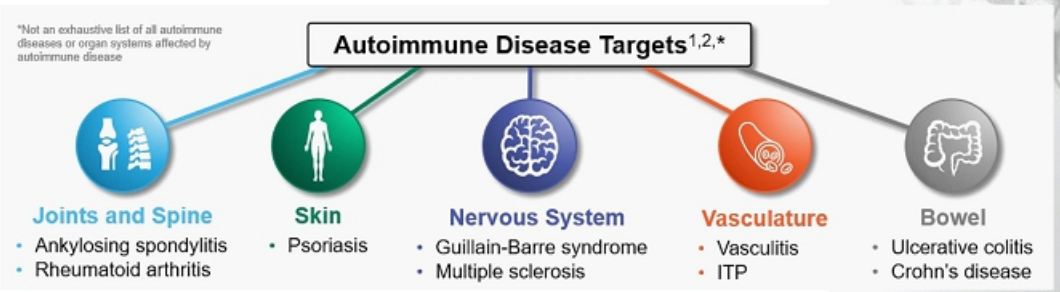
The New York Times **"In a First, Surgeons Attached a Pig Kidney to a Human, and It Worked"** Roni Caryn Rabin *October 19, 2021*	THE WALL STREET JOURNAL. **"Saved by a Pig's Heart"** The Editorial Board *January 12, 2022*	THE WALL STREET JOURNAL. **"Pig Kidneys Transplanted Into Brain-Dead Man as Patients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

IMMUNOLOGY PORTFOLIO

TONIX PHARMACEUTICALS

αCD40L 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]Tocolan 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) 3Q 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

TONIX PHARMACEUTICALS

TNFαα 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.

TONIX PHARMACEUTICALS

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

2020 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-odon) 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/

TONIX PHARMACEUTICALS

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%2[illegible]t%20on%20an%20operational%20basis.

TONIX PHARMACEUTICALS

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

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

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-801 WITH SOUTHERN RESEARCH INSTITUTE

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

DEVELOPED IN COLLABORATION WITH UNIVERSITY OF ALBERTA

- Proprietary synthetic biology approach and vector system

Patents Filed

DEVELOPMENT PROGRAM

Market Entry: Smallpox and Monkeypox Vaccine

Status: Preclinical, Pre-IND

Next Steps: Developing GMP manufacturing for TNX-801 (horsepox); initiate Phase 1 Trial, 2H 2023

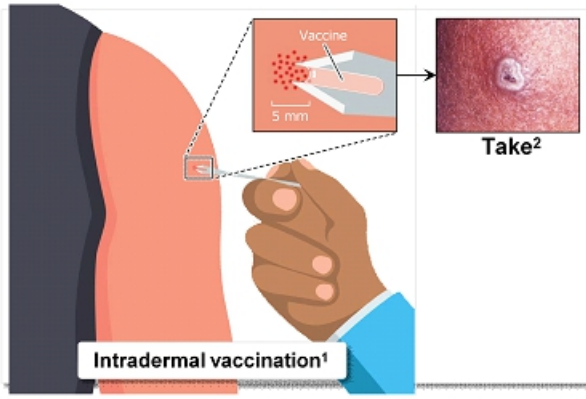
*TNX-801 is in the pre-IND stage of development and has not been approved for any indication.

[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/10929ac27f4fb5f5204f5cf41d58a121.pdf)

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

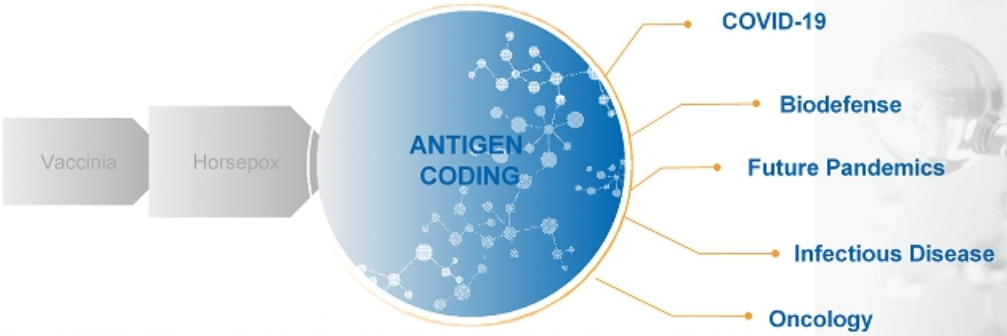
PROGRAMMABLE VECTOR DESIGN FOR USE IN DIFFERENT DISEASE MODELS

- 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; 377:1481-1492. 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

INFECTIOUS DISEASE PORTFOLIO

TONIX PHARMACEUTICALS

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)

INFECTIOUS DISEASE PORTFOLIO

TONIX PHARMACEUTICALS

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?)

TONIX PHARMACEUTICALS

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

TONIX PHARMACEUTICALS

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/

INFECTIOUS DISEASE PORTFOLIO

TONIX PHARMACEUTICALS

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; initiate Phase 1 Trial, 2H 2023

*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/)

INFECTIOUS DISEASE PORTFOLIO

TONIX PHARMACEUTICALS

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

TONIX PHARMACEUTICALS

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

LIVE VIRUS VACCINE[1-5]

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

ANIMAL TESTING OF TNX-2300 ONGOING

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

DEVELOPED IN COLLABORATION WITH KANSAS STATE UNIVERSITY (KSU)

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

Patents Filed

DEVELOPMENT PROGRAM

Market Entry: COVID-19 Vaccine

Additional Indications: Future Pandemic, Infectious Diseases

Status: Preclinical

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

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

[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

INFECTIOUS DISEASE PORTFOLIO

TONIX PHARMACEUTICALS

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

TONIX PHARMACEUTICALS

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

TONIX PHARMACEUTICALS

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/10665/342388)
[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

INFECTIOUS DISEASE PORTFOLIO

TONIX PHARMACEUTICALS

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)

INFECTIOUS DISEASE PORTFOLIO

TONIX PHARMACEUTICALS

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; [1]Dec 7, 2021 Glaxo Says Its Covid-19 Antibody Drug Works Against Omicron – WSJ
[2]Brennan, Z. *Endpoints*, March 28, 2022 GUS 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-5lman-gemgross-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.

TONIX PHARMACEUTICALS

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Key Development Partners

Massachusetts General Hospital · Harvard Medical School · Columbia University

TNX-1500: ALLOGRAFT REJECTION

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

Stanford University · Université de Genève

University of Alberta · SR Southern Research

TNX-1900: MIGRAINE & OTHER INDICATIONS

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

Inserm Transfert · CHU de Toulouse · Aix Marseille université

Kansas State University

TNX-2900: PRADER-WILLI SYNDROME

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

TONIX PHARMACEUTICALS

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.

TONIX PHARMACEUTICALS

Management Team

Seth Lederman, MD
Co-Founder, CEO & Chairman

TARGENT · Fusilev (levoleucovorin) for injection · vela

Gregory Sullivan, MD
Chief Medical Officer

Columbia University Department of Psychiatry · New York State Psychiatric Institute

Bradley Saenger, CPA
Chief Financial Officer

Shire · VERTEX · Steward · pwc

Jessica Morris
Chief Operating Officer

Deutsche Bank · svb Silicon Valley Bank · American Capital

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THANK YOU