



Corporate Presentation

November 2023

NASDAQ: TNXP



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; risks related to the failure to successfully market any of our products; 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, 2022, as filed with the Securities and Exchange Commission (the “SEC”) on March 13, 2023, 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.

Who We Are

Tonix is committed to developing and marketing therapeutics to treat pain, neurologic, psychiatric and addiction conditions through our ***central nervous system portfolio*** and within other areas of ***high unmet need***, including immunology, infectious disease, and rare disease

CNS-Focused Biopharma with Preclinical to Commercial Stage Products

Robust Development Pipeline

Topline data for two late-stage CNS programs expected by end of 2023

Internal Facilities

For R&D and clinical-scale manufacturing

Marketed Products

For the treatment of acute migraine

Strategic Partnerships

With world-class academic & research organizations to bring innovative therapeutics to market faster

Late-Stage Clinical Portfolio

Molecule*	Indication	Phase 1	Phase 2	Phase 3	NDA Submission
TNX-102 SL Cyclobenzaprine Protectic® Sublingual Tablets	Fibromyalgia (FM)		Phase 3 Topline Results Expected 4Q'23 (Late December)		
	FM-Type Long COVID		Phase 2 Topline Results Reported 3Q'23		
TNX-1900 Intranasal Potentiated Oxytocin with Magnesium	Chronic Migraine		Phase 2 Topline Results Expected 4Q'23 (Early December)		
TNX-1300 Cocaine Esterase	Cocaine Intoxication		Phase 2 Study Start Expected 4Q'23		

*All of Tonix's product candidates are investigational new drugs or biologics and none has been approved for any indication.



TONIX MEDICINES: MARKETED PRODUCTS



Two Marketed Proprietary Migraine Drugs

Non-oral Formulations of Sumatriptan

Zembrace® SymTouch® (sumatriptan injection) 3 mg¹



- Each indicated for the **treatment of acute migraine with or without aura in adults**
- Sumatriptan remains the acute migraine ‘gold standard’ treatment for many patients and continues to represent the largest segment of the market in terms of unit sales³
- Each may provide migraine **pain relief in as few as 10 minutes** for some patients^{1,2,4,5}
- Patents to 2036 (Zembrace) and 2031 (Tosymra)

Tosymra® (sumatriptan nasal spray) 10 mg²



Acquired from Upsher-Smith Laboratories which has managed care contracts covering ~200 M lives

- Contract includes a transition period during which Tonix expects to secure its own contracts

Retail Product Sales for the 12 months ended December 31st 2022

- Retail sales: ~\$23 M (Zembrace ~\$19.6 M and Tosymra ~\$3.5 M)⁴

Tonix is prepared to meet potential increased demand for Tosymra following GSK’s planned discontinuation of Imitrex® (sumatriptan) nasal spray after January 2024

¹Zembrace SymTouch [package insert]. Maple Grove, MN: Upsher-Smith Laboratories, LLC: February 2021 - For more information, talk to your provider and read the [Patient Information](#) and [Instructions for Use](#). – Important Safety Information is provided in the appendix

²Tosymra [package insert]. Maple Grove, MN: Upsher-Smith Laboratories, LLC: Feb 2021.

For more information, talk to your provider and read the [Patient Information](#) and [Instructions for Use](#). – Important Safety Information is provided in the appendix

³Upsher-Smith Laboratories, LLC; Data On File, 2023

⁴Mathew NT, et al. Dose ranging efficacy and safety of subcutaneous sumatriptan in the acute treatment of migraine. US Sumatriptan Research Group. Arch Neurol. 1992;49(12):1271-1276.

⁵Wendt J, et al. A randomized, double-blind, placebo-controlled trial of the efficacy and tolerability of a 4-mg dose of subcutaneous sumatriptan for the treatment of acute migraine attacks in adults. Clinical Therapeutics. 2006;28(4):517-526.

Tonix has contracted to acquire the Zembrace, SymTouch and Tosymra trademarks. Intravail is a registered trademark of Aegis Therapeutics, LLC, a wholly owned subsidiary of Neurelis, Inc.



Zembrace and Tosymra Bypass the GI Tract

Bypassing gastrointestinal (GI) tract is *potential advantage for treating acute migraine*

- GI absorption may be inconsistent in migraineurs due to gastric stasis (also called “gastroparesis”)¹⁻⁴
- Nausea and vomiting are symptoms of migraine⁵ which can complicate oral treatment

Existing intranasal products

- Imitrex® nasal spray (sumatriptan)
- Migranal® (dihydroergotamine) nasal spray – developed by Novartis, sold by Bausch Health

New intranasal products bringing attention to non-oral route

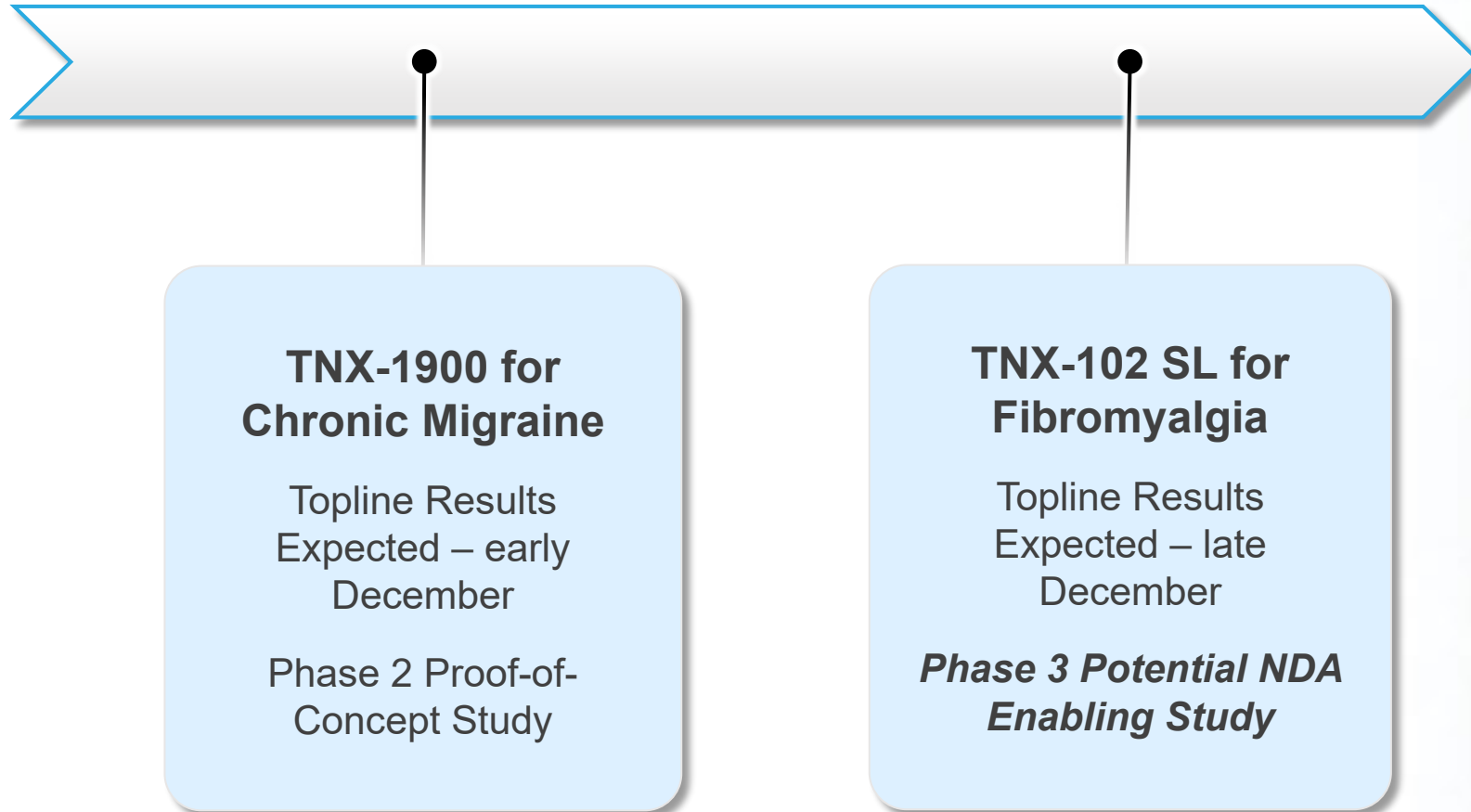
- Pfizer’s Zavzpret® (zavegepant), FDA approved in March, 2023¹ is the first intranasal gepant
- Impel NeuroPharma’s Trudhesa® (dihydroergotamine) FDA approved 2021²

¹Pfizer Press Release March 10, 2023. – <https://www.pfizer.com/news/press-release/press-release-detail/pfizers-zavzprettm-zavegepant-migraine-nasal-spray>

²Impel Press Release September 3, 2021 - <https://impelpharma.com/2021/09/03/impel-neuropharma-announces-u-s-fda-approval-of-trudhesa-dihydroergotamine-mesylate-nasal-spray-for-the-acute-treatment-of-migraine/>

Upcoming Expected Topline Results

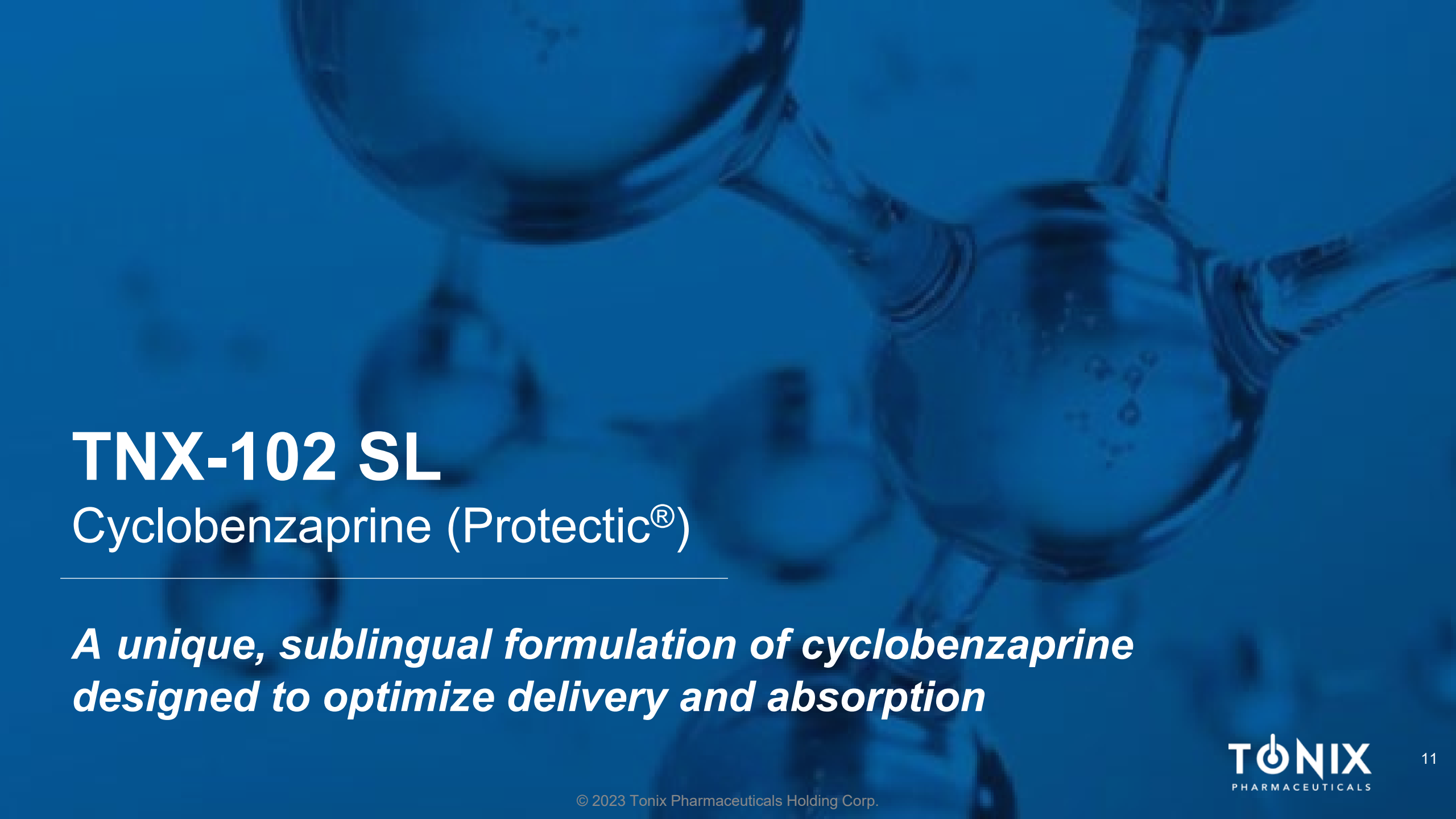
Fourth Quarter **2023**





TONIX
PHARMACEUTICALS

**CNS:
KEY DEVELOPMENT
CANDIDATES**



TNX-102 SL

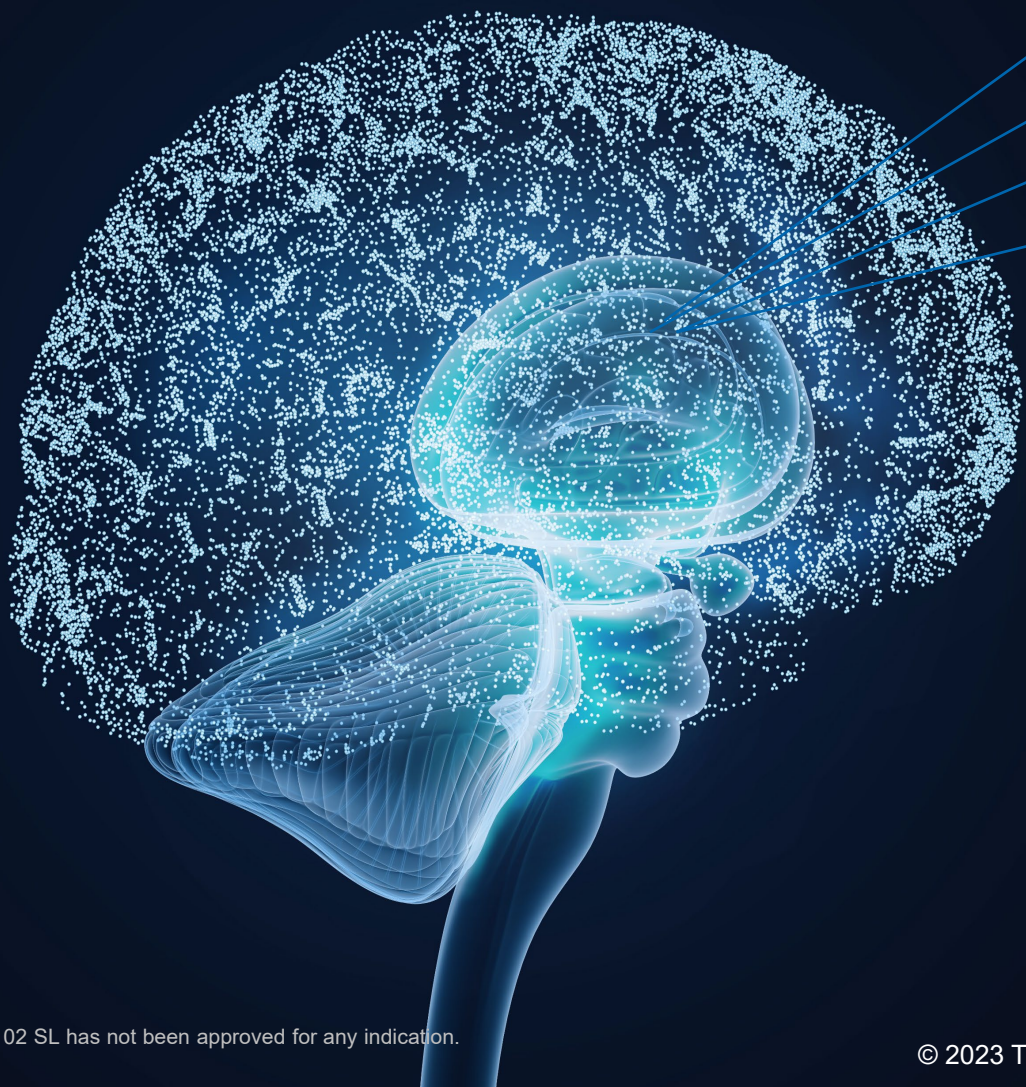
Cyclobenzaprine (Protectic[®])

A unique, sublingual formulation of cyclobenzaprine designed to optimize delivery and absorption

TNX-102 SL: Unique MOA Facilitates Restorative Sleep

Centrally Acting Analgesic

Potent binding and antagonist activities at four key receptors facilitate *restorative sleep*



- *serotonergic-5-HT_{2A}*
- *adrenergic- α ₁*
- *histaminergic-H₁*
- *muscarinic-M₁*

Key Differentiators

Relative to Oral Cyclobenzaprine

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

Relative to Standard of Care

- Potential for better tolerability while maintaining efficacy
- Not scheduled nor with recognized abuse potential



About Fibromyalgia

*Fibromyalgia (FM) is a **chronic pain disorder** resulting from amplified sensory and pain signaling within the CNS. Symptoms include chronic widespread pain, **nonrestorative sleep**, fatigue, and cognitive dysfunction*

6-12
million adults

Fibromyalgia afflicts an estimated 6-12 million adults in the US, predominantly women¹

Large unmet need:

- Patients struggle with daily activities, have impaired quality of life, and frequently are disabled
- Physicians and patients report common dissatisfaction with currently marketed products
 - Average patient has 20 physician office visits per year²

Current standard of care:

- FDA-approved products include Lyrica, Cymbalta, and Savella
- Fewer than half of those treated for fibromyalgia receive sustained benefit from the approved drugs³
 - Majority (60%) fail therapy due to lack of a response (25%) or poor tolerability (35%)⁴
 - Opioid usage is not uncommon

¹American Chronic Pain Association (www.theacpa.org, 2019)

²Robinson et al, Pain Medicine 2013;14:1400

³The three drugs with FDA approval for the treatment of fibromyalgia: Pregabalin (Lyrica); Duloxetine (Cymbalta); Milnacipran (Savella)

⁴Market research by Frost & Sullivan, commissioned by Tonix



Fibromyalgia Program Status

TNX-102 SL

Cyclobenzaprine Protectic®
Sublingual Tablets

Fibromyalgia

Phase 3 Topline Results Expected 4Q'23
(Late December)

FM-Type Long
COVID

Phase 2 Topline Results Reported 3Q'23

- 1) One **positive Phase 3 study (RELIEF) completed**¹
- 2) Second Phase 3 study (RALLY) missed primary endpoint
 - Unexpected increase in adverse event-related discontinuations in both drug and placebo arms, potentially due to recruiting during COVID-19
- 3) Confirmatory Phase 3 study (RESILIENT) **enrollment complete**
 - Clinical stage complete as of November 15, 2023

Next Steps: *Potentially confirmatory topline results expected 4Q 2023 (Late December)*

*TNX-102 SL has not been approved for any indication.
¹Lederman et al., (2023) *Arthritis Care & Research* "Efficacy and Safety of TNX-102 SL (Sublingual Cyclobenzaprine) for the Treatment of Fibromyalgia: Results From the RELIEF Trial", doi: 10.1002/acr.25142. Epub ahead of print. PMID: 37165930.
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TNX-102 SL: Phase 3 RESILIENT Study Design

General study characteristics:

- Randomized, double-blind, placebo-controlled study in fibromyalgia
- U.S. sites only, **completed enrollment of 457 patients**
- Clinical stage complete as of November 15, 2023
- Preliminary unaudited rate of adverse-event related discontinuations was 4.8%
 - Compares favorably with prior FM studies RELIEF, 6.0% and RALLY, 10.7%

Primary Endpoint:

- Daily diary pain severity score change from baseline to Week 14 (TNX-102 SL vs. placebo)
 - Weekly averages of the daily numerical rating scale scores
- Threshold for potential NDA-enabling study is $p < 0.05$

Key Secondary Endpoints:

- Patient Global Impression of Change responder analysis
- Fibromyalgia Impact Questionnaire - Revised (FIQ-R) Symptom Domain score
- FIQ-R Function Domain score
- PROMIS Sleep Disturbance instrument
- PROMIS Fatigue instrument
- Weekly average of the daily diary assessment of sleep quality

TNX-102 SL once-daily at bedtime
5.6 mg (2 x 2.8 mg tablets)*

Placebo once-daily at bedtime

14 weeks

*Two week run in at 2.8 mg dose at bedtime, followed by 12 weeks at 5.6 mg dose

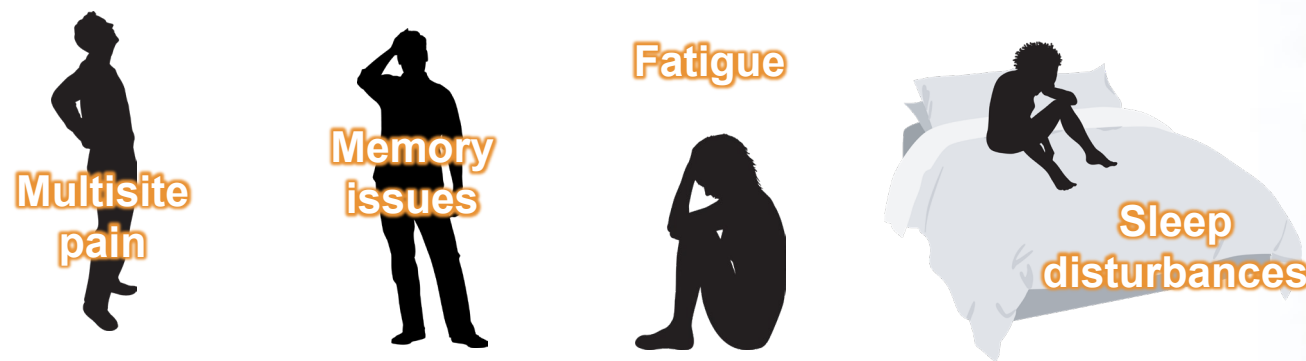
ClinicalTrials.gov Identifier: NCT05273749

A Phase 3 Study to Evaluate the Efficacy and Safety of TNX-102 SL
Taken Daily in Patients With Fibromyalgia (RESILIENT)



About Fibromyalgia-Type Long COVID

Long COVID is broadly defined as signs, symptoms, and conditions that continue or develop after acute COVID-19 infection¹



Many Long-COVID symptoms overlap with core symptoms of fibromyalgia and are hallmarks of other chronic pain syndromes like myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS)

- 19% Long COVID occurs in approximately 19% of recovered COVID-19 patients²
- 40% As many as 40% of Long COVID patients experience multi-site pain^{3,4}

¹CDC - <https://www.cdc.gov/coronavirus/2019-ncov/long-term-effects/index.html#:~:text=Some%20people%20who%20have%20been,after%20acute%20COVID%2D19%20infection.>
²CDC Press Release, June 22, 2022 - https://www.cdc.gov/nchs/pressroom/nchs_press_releases/2022/20220622.htm
³Harris, H, et al. Tonix data on file. 2022
⁴TriNetX Analytics



TNX-102 SL: Phase 2 PREVAIL Study Design



PREVAIL Study

Study characteristics:

- Randomized, double-blind, placebo-controlled study of TNX-102 SL in fibromyalgia-type Long COVID
- U.S. sites only, **completed enrollment of 63 patients**

Primary Endpoint:

- Daily diary pain severity score change from baseline to Week 14 (TNX-102 SL vs. placebo)
 - Weekly averages of the daily numerical rating scale scores

TNX-102 SL once-daily at bedtime
5.6 mg (2 x 2.8 mg tablets)*

*Two week run in at 2.8 mg dose at bedtime, followed by 12 weeks at 5.6 mg dose

Placebo once-daily at bedtime

ClinicalTrials.gov Identifier: NCT05472090
“A Phase 2 Study to Evaluate the Efficacy and Safety of TNX-102 SL in Patients With Multi-Site Pain Associated With Post-Acute Sequelae of SARS-CoV-2 Infection (PREVAIL)”

————— **14 weeks** —————>

Next Steps: *End of Phase 2 Meeting with FDA 1Q 2024*



TNX-102 SL: Phase 2 PREVAIL Topline Results¹

Did not meet the primary endpoint of multi-site pain reduction at Week 14

However, findings fulfill the objectives of proof-of-concept study, supporting the decision to advance the program based on a proposed primary endpoint using the PROMIS Fatigue scale

- TNX-102 SL showed robust effect size in improving fatigue and consistent activity across secondary measures of sleep quality, cognitive function, disability and Patient Global Impression of Change (PGIC)
- Was generally well tolerated with an adverse event (AE) profile comparable to prior studies with TNX-102 SL:
 - AE-related discontinuations were similar in drug and placebo arms
 - No new safety signals were observed

Fatigue is the signature symptom of Long COVID and has been identified as the dominant symptom contributing to disability²

- We observed numerical improvement in the PROMIS fatigue score (in RELIEF $p=0.007$ MMRM and in RALLY $p=0.007$ MMRM) in both prior Phase 3 studies of TNX-102 SL in fibromyalgia,
- We believe the results of PREVAIL, together with extensive data from studies in other chronic conditions³⁻⁵, makes PROMIS Fatigue a solid candidate for the primary endpoint of future Long COVID registrational studies

¹Tonix Press Release, September 5, 2023 - <https://bit.ly/3Z6FQHQ>

²Walker S, et al. *BMJ Open* 2023;13:e069217. doi:10.1136/bmjopen-2022-069217

³Cook, K.F., et al. 2016. *Journal of Clinical Epidemiology*, 73, 89- 102

⁴Cella, D., et al. 2016. *Journal of Clinical Epidemiology*, 73, 128-134

⁵Lai, J.S., et al. 2011. *Archives of Physical Medicine and Rehabilitation*, 92(10 Supplement), S20-S27.



Acute Stress Reaction (ASR)/ Acute Stress Disorder (ASD)

ASR/ASD are acute stress conditions resulting from trauma which can affect both civilian and military populations.

Large unmet need:

- According to National Center for PTSD, about 60% of men and 50% of women in the US are exposed least one traumatic experience in their lives¹
- In the US alone, one-third of emergency department visits (40-50 million patients per year) are for evaluation after trauma exposures²

Current standard of care:

- No medications are currently available at or near the point of care to treat patients suffering from acute traumatic events and support long-term health

¹National Center for PTSD. How Common is PTSD in Adults? https://www.ptsd.va.gov/understand/common/common_adults.asp

²Wisco et al. *J Clin Psychiatry*. 2014;75(12):1338-46



ASR/ASD Program Status

Status: Expect to start Phase 2 in 1Q 2024

Phase 2 Trial Funded by DoD grant to University of North Carolina (UNC)

- UNC Institute for Trauma Recovery awarded a \$3M grant from the Department of Defense (DoD)
- OASIS trial will build upon infrastructure developed through the UNC-led, \$40M AURORA initiative
 - AURORA study is a major national research initiative to improve the understanding, prevention, and recovery of individuals who have experienced a traumatic event
 - Supported in part by funding from the National Institutes of Health (NIH) and the health care arm of Google's parent company Alphabet
- Opportunity to investigate the correlation between motor vehicle collisions and the emergence of ASD and PTSD
- Supported by multiple clinical trials:
 - Phase 2 trial in military-related PTSD (AtEase or NCT02277704)
 - Phase 3 trial in military-related PTSD (HONOR or NCT03062540)
 - Phase 3 trial in primarily civilian PTSD (RECOVERY or NCT03841773)
- In each of these studies, early and sustained improvements in sleep were associated with TNX-102 SL treatment by the PROMIS sleep disturbance (SD) scale and the Clinician Administered PTSD Scale (CAPS-5) "sleep disturbance" item.

Together these studies provide preliminary evidence that TNX-102 SL is well-tolerated and may promote recovery from PTSD via a pharmacodynamic facilitation of sleep-dependent emotional memory processing



TNX-102 SL: Phase 2 OASIS Study Design

General study characteristics:

- Randomized, double-blind, placebo-controlled study in Acute Stress Reaction (ASR) / Acute Stress Disorder (ASD)
- The proposed Optimizing Acute Stress reaction Interventions with TNX-102 SL (OASIS) trial will examine the safety and efficacy of TNX-102 SL to reduce adverse posttraumatic neuropsychiatric sequelae among patients presenting to the emergency department after a motor vehicle collision (MVC)
- The trial will enroll approximately 180 individuals who acutely experienced trauma at study sites across the US
- Participants will be randomized in the emergency department to receive a two-week course of either TNX-102 SL or placebo
- Investigator-initiated IND

Objective:

- Investigate the potential of Tonix's TNX-102 SL (cyclobenzaprine HCl sublingual tablets) to reduce the frequency and severity of the adverse effects of traumatic exposure, including acute stress reaction (ASR), acute stress disorder (ASD), and posttraumatic stress disorder (PTSD).
- ASR refers to the body's immediate response to trauma, whereas ASD is the short-term effects of trauma (within 1 month), and PTSD is the long-term effects of trauma (beyond 1 month)

TNX-102 SL once-daily at bedtime
5.6 mg (2 x 2.8 mg tablets)*

Placebo once-daily at bedtime

————— **2 weeks** —————→

*First dose of TNX-102 SL 5.6 mg versus placebo taken in the emergency department, and then daily at bedtime to finish 2 weeks of treatment

A Phase 2 Study to Evaluate the Efficacy and Safety of TNX-102 SL Taken Daily in Patients With ASR/ ASD (OASIS)

- Primary outcome measure: Acute Stress Disorder Scale (ASDS) assessed at 7 and 21 days post MVC
- Posttraumatic stress symptom severity assessed at 6 and 12 weeks post MVC using the PTSD Checklist for DSM-5 (PCL-5)
- Standardized survey instruments of sleep disturbances, anxiety and depression symptoms, general physical and mental health, and clinical global improvement also employed
- Detailed and brief neurocognitive assessments are performed from baseline to 12 weeks after MVC at specific timepoints throughout study participation period



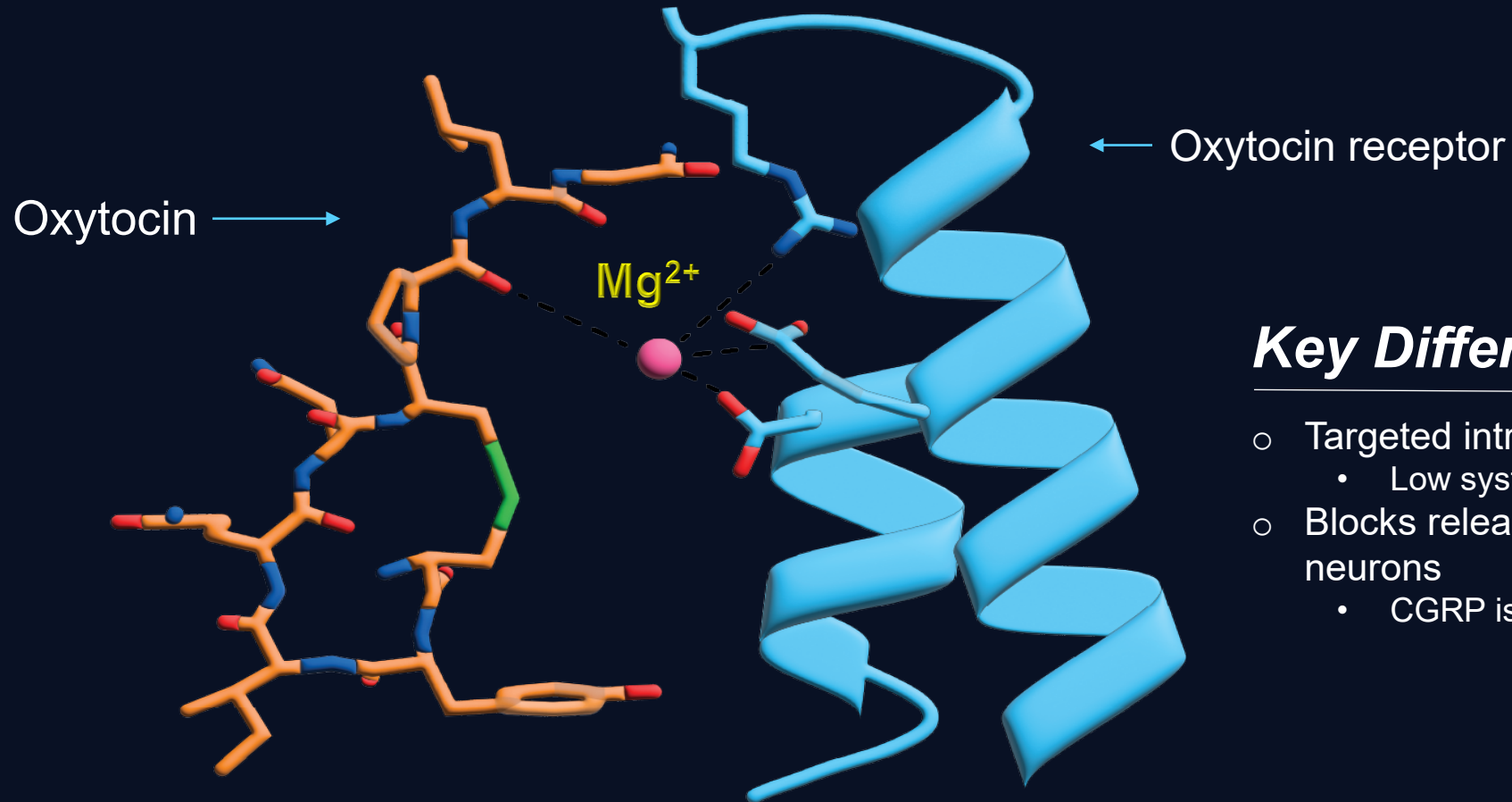
TNX-1900 and TNX-2900

Intranasal Potentiated Oxytocin with Magnesium

A novel, non-CGRP antagonist approach to treatment

TNX-1900 & TNX-2900: Novel Formulation of Intranasal Oxytocin (OT) Potentiated with Magnesium

*Magnesium is known to **potentiate** the binding of OT to its receptor^{1,2}*



Key Differentiators

- Targeted intranasal delivery
 - Low systemic exposure
- Blocks release of CGRP from trigeminal ganglia neurons
 - CGRP is a key peptide in the pathogenesis of migraine

¹Antoni et al., 1989. *Biochem J.* 257(2):611-4

²Meyerowitz et al., 2022. *Nat Struct Mol Biol.* (3):274-281

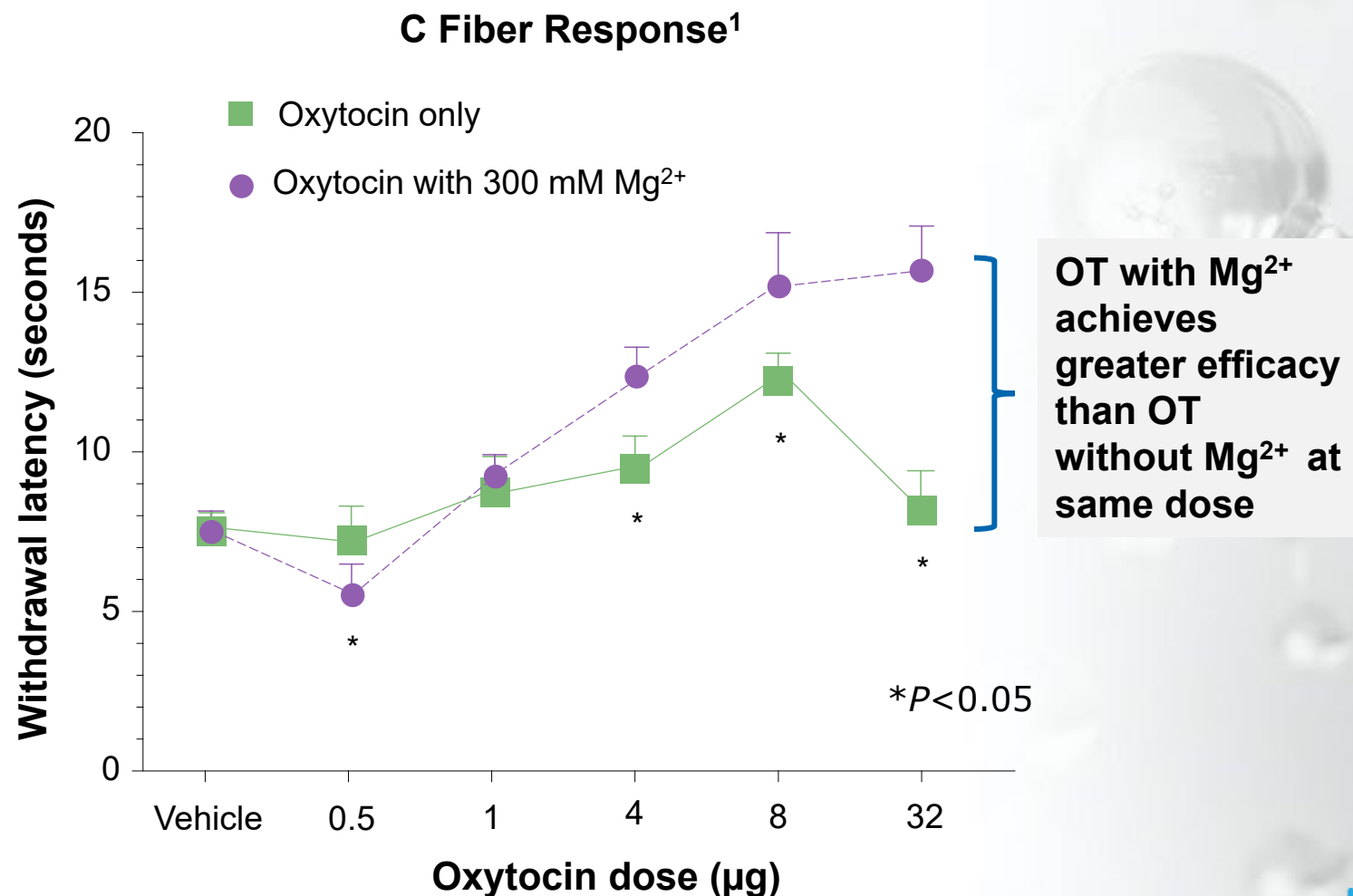
*TNX-1900 and TNX-2900 have not been approved for any indication.



Oxytocin Effects – Addressing the “Inverted U” Dose Response

Addition of Mg^{2+} Augments Oxytocin-Induced Analgesia in Animal Model

- A **nonlinear dose response** decreases efficacy at higher doses
- Addition of **Mg^{2+} rescues the efficacy** of oxytocin at high doses



¹Adapted from: Bharadwaj VN, et al. *Pharmaceutics*. 2022;14(5):1105.



About Chronic Migraine

*Chronic migraine involves frequent (>15 days per month) or long-lasting episodes of headaches and migraines over the course of at least 3 months. Migraines can occur with or without an aura and are often **debilitating for patients**.*

3-7
million adults

Chronic migraine afflicts 3-7 million adults in the US¹

Current standard of care:

- Anti-CGRP antibodies and Botox® (onabotulinumtoxinA) are specifically approved to prevent headaches in chronic migraine
- Nurtec® (Rimegepant), a gepant, is approved for both prevention of migraine and acute treatment

Large unmet need:

- Anti-CGRP antibodies and oral gepants involve systemic exposure
- Long term safety concerns with prolonged systemic blockade of CGRP receptor²

¹Natoli et al., Global prevalence of chronic migraine: a systematic review, Cephalgia, 2010, 30:599-609

²Robbins, At Stake: The Possible Long-Term Side Effects of CGRP Antagonists, <https://www.practicalpainmanagement.com/pain/headache/stake-possible-long-term-side-effects-cgrp-antagonists>, accessed November 8, 2020.



TNX-1900: Phase 2 PREVENTION Study Design

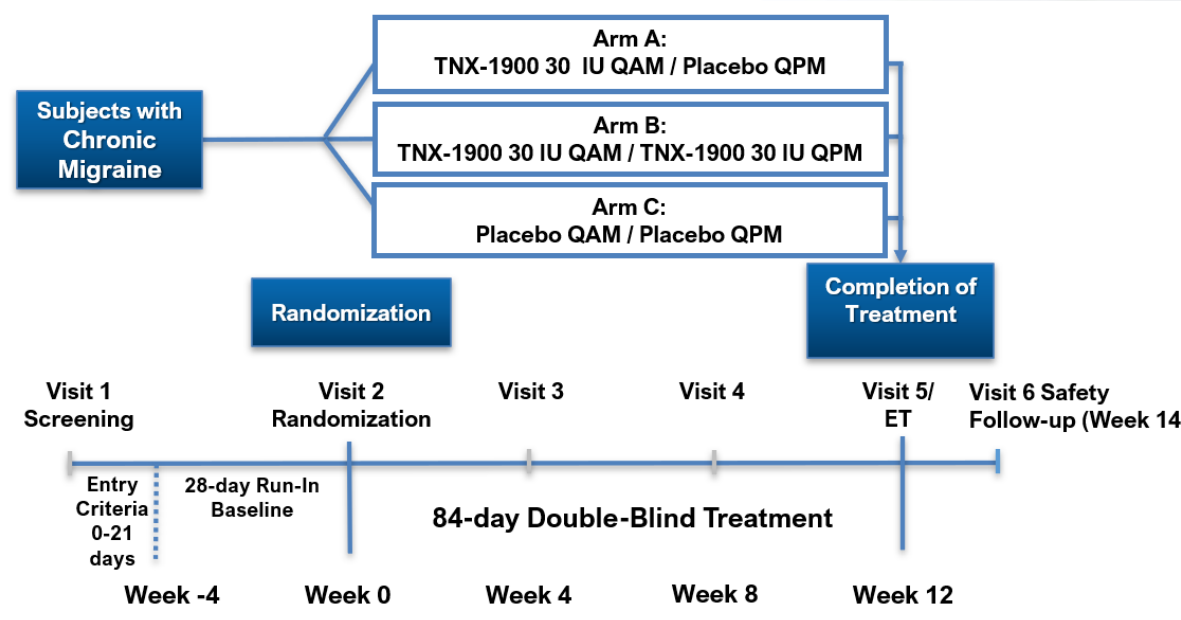


General study characteristics:

- Randomized, double-blind, placebo-controlled study (three arms— two treatment regimens and one placebo) in chronic migraine
- U.S. sites only, **completed enrollment with 88 patients**
- Clinical stage complete as of October 26, 2023

Primary Endpoint:

- Mean change in the number of migraine headache days between the 28-day Run-In phase and the last 28-days of the Treatment phase (TNX-1900 vs. placebo)
- Threshold for achieving positive proof-of-concept is Effect Size (ES) > 0.2



ClinicalTrials.gov Identifier: NCT05679908
A Study to Evaluate the Efficacy and Safety of TNX-1900 in Patients With Chronic Migraine (PREVENTION)

Next Steps: *Topline results expected 4Q 2023 (Early December)*

Potential Applications of TNX-1900 & TNX-2900: Investigator Led Studies

Pain Conditions

Migraine
Craniofacial Pain

Phase 2 Study in Prevention of Headache in Chronic Migraine

- Topline results expected 4Q 2023

Phase 2 Biomarker Study



Eating Behavior and Weight Disorders

Adolescent Obesity
Binge Eating Dis.

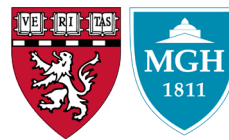
Phase 2 Study Enrolling

- Investigator-Initiated IND



Phase 2 Study Enrolling

- Investigator-Initiated IND



Social Functioning Disorders

PWS*

Autism

Social Anxiety Disorder

Phase 2 Study initiated

- Investigator-Initiated IND



Phase 2 Study initiated

- Investigator-Initiated IND



*Prader-Willi Syndrome



TNX-1900 – Other Studies in Collaboration with Academic Investigators

Pharmacodynamic biomarker study related to headache¹

- Testing TNX-1900 effects on capsaicin- or electrical stimulation-induced forehead dermal blood flow in healthy female human volunteers
- Forehead dermal blood flow is considered a trigeminovascular biomarker for antimigraine drugs.
 - Both a CGRP inhibitor and a triptan have been successfully tested in the model and have been found to inhibit the forehead dermal blood flow response to capsaicin in migraineurs and healthy volunteers, respectively.^{2,3}
- Erasmus University Medical Center, Dr. Antoinette Maassen van den Brink, Principal Investigator (P.I.)

Pediatric Obesity⁴

- Phase 2 double-blind ‘POWER’ study testing TNX-1900 as a novel therapeutic agent to induce weight loss and improve indicators of cardiometabolic risk in adolescent patients with obesity
- Massachusetts General Hospital (MGH), Dr. Elizabeth Lawson, P.I.

Social Anxiety⁵

- Study effects of TNX-1900 on social safety learning in social anxiety disorder (SAD)
- Univ. of Washington, Dr. Angela Fang, P.I.

Binge Eating Disorder⁶

- Phase 2 double-blind STROBE’ study testing TNX-1900 as a novel therapeutic agent to study effects of TNX-1900 on social safety learning in Binge Eating ‘STROBE’ study
- Massachusetts General Hospital (MGH), Dr. Elizabeth Lawson, P.I.

¹Tonix Press Release May 22, 2023: <https://ir.tonixpharma.com/news-events/press-releases/detail/1391/tonix-pharmaceuticals-announces-clinical-proof-of-concept>

²de Vries Lentsch S, et al. 2022 “CGRP-mediated trigeminovascular reactivity in migraine patients treated with erenumab.” *J Neurol Neurosurg Psychiatry*. Aug;93(8):911-912.

³Ibrahimi K, et al. 2017 “A human trigeminovascular biomarker for antimigraine drugs: A randomized double-blind, placebo-controlled, crossover trial with sumatriptan.” *Cephalalgia*. Jan;37(1):94-98.

⁴Tonix Press Release July 10 2023 – <https://ir.tonixpharma.com/news-events/press-releases/detail/1404/tonix-pharmaceuticals-announces-initiation-of-enrollment-in>

⁵Tonix Press Release July 17, 2023 – <https://ir.tonixpharma.com/news-events/press-releases/detail/1405/tonix-pharmaceuticals-announces-agreement-and-initiation-o>

⁶Tonix Press Release July 31, 2023 – <https://ir.tonixpharma.com/news-events/press-releases/detail/1410/tonix-pharmaceuticals-announces-enrollment-initiated-in-the>



TNX-1900 for Pediatric Autism

- Children with Autism Spectrum Disorder (ASD) are at risk for low bone density
- Preliminary data suggest that administration of oxytocin may favorably impact bone formation and strength
- Recent meta-analysis reported that plasma oxytocin levels tend to be lower in children with Autism Spectrum Disorder than controls¹

“BOX” Investigator-Initiated Study in Pediatric Autism at MGH

- Randomized, placebo-controlled study to evaluate the effects of twice daily administration of TNX-1900 on bone measures in children with ASD
- Study subjects, ages six to 18 years old, will be randomized 1:1 to receive TNX-1900 twice per day or placebo for 12 months in the double-blind phase, followed by a six-month open label phase during which all study subjects will receive TNX-1900 twice daily
- Primary endpoint: difference between TNX-1900 compared to placebo groups in 12-month change in whole body less head bone mineral density Z-scores
 - Z-score compares one's bone density to the average bone density of age and gender matched controls

¹John S and Jaeggi, AV. *Autism*. 2021. 25:2152-2161

TNX-2900 for Prader-Willi Syndrome

*Prader-Willi Syndrome (PWS) is the most common genetic cause of life-threatening childhood obesity. PWS causes unhealthy behaviors around food¹⁻⁴, consequences such as **obesity, type 2 diabetes, and cardiovascular disease**¹⁻⁵, and creates significant caretaker burden¹⁻⁴*

10-20 Rare genetic disease that afflicts 10-20 thousand individuals in the US
thousand individuals

Current standard of care:

- Human growth hormone treatment is FDA-approved for growth failure in PWS children

Large unmet need:

- Currently no cure, and no treatment for PWS-related hyperphagia
- Consequences can be life threatening - obesity and cardiovascular disease are leading cause of death

****TNX-2900 has been granted FDA Orphan Drug Designation***

¹Miller et al., 2011. *Am J Med Genet A*. 155A(5):1040-1049

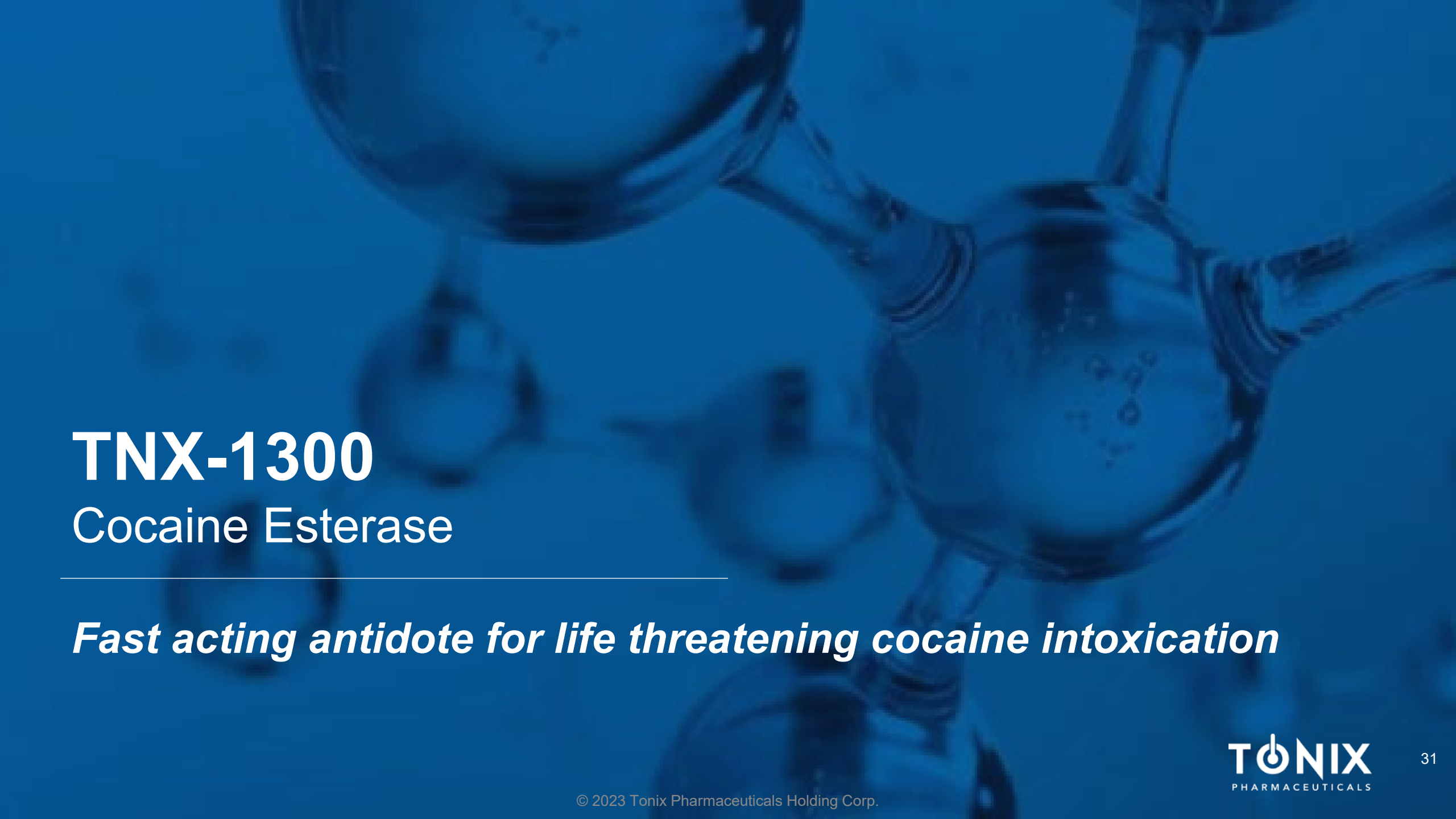
²Butler et al., 2017. *Genet Med*. 19(6):635-642

³Butler MG. NORD. Updated 2018. Accessed May 25, 2022. <https://rarediseases.org/rare-diseases/prader-willi-syndrome/>

⁴Prader-Willi Syndrome Association USA. Accessed May 25, 2022. <https://www.pwsausa.org/what-is-prader-willi-syndrome/>

⁵Muscogiuri et al., 2021. *J Endocrinol Invest*. 44(10):2057-2070





TNX-1300

Cocaine Esterase

Fast acting antidote for life threatening cocaine intoxication

TNX-1300: Recombinant Protein Rapidly Degrades Cocaine in the Bloodstream

Drops plasma exposure by 90% in 2 minutes



Key Differentiators

- Rapidly metabolizes cocaine within matter of minutes
- No other product currently on the market for this indication



About Cocaine Intoxication

Over 5 million Americans reported current cocaine use in 2020, which is almost 2% of the population¹. In 2021, more than 24,900 individuals in the US died from drug overdose deaths involving cocaine²

500k Over 500,000 emergency department visits for cocaine, annually^{3,4}

Current standard of care:

- Patients are currently managed only by supportive care for the adverse effects of cocaine intoxication on the cardiovascular and central nervous systems

Large unmet need:

- No other product currently on the market for this indication
- TNX-1300 could significantly reduce the time and resources required for other detox services
- Potentially reduces the risk of morbidity and mortality

¹Substance Abuse and Mental Health Services Administration. (2021). Results from the 2020 National Survey on Drug Use and Health: Detailed Tables: Prevalence Estimates, Standard Errors, and Sample Sizes.

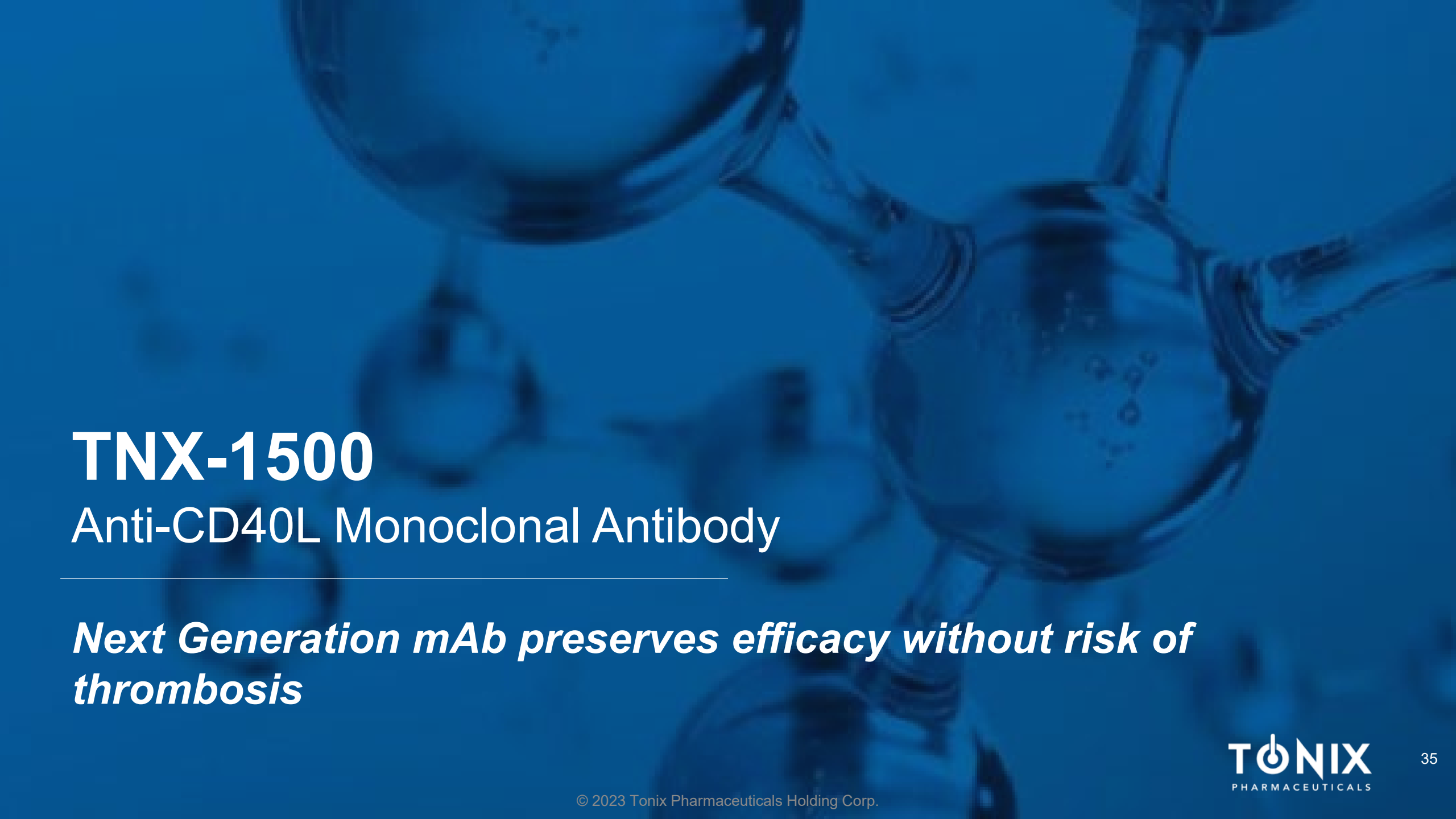
²Centers for Disease Control and Prevention (CDC) - <https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm>

³Substance Mental Health Services Administration, Drug Abuse Warning Network, 2011: National Estimates of Drug-Related Emergency Department Visits. HHS Publication No. (SMA) 13-4760, DAWN Series D-39. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2013.

⁴Drug Abuse Warning Network, 2011: Selected Tables of National Estimates of Drug-Related Emergency Department Visits. Rockville, MD: Center for Behavioral Health Statistics and Quality, SAMHSA, 2013.



IMMUNOLOGY: KEY CANDIDATES



TNX-1500

Anti-CD40L Monoclonal Antibody

Next Generation mAb preserves efficacy without risk of thrombosis

TNX-1500: Next Generation anti-CD40L mAb

Re-engineered to better modulate the binding of FcγR and mitigate risk of thrombosis

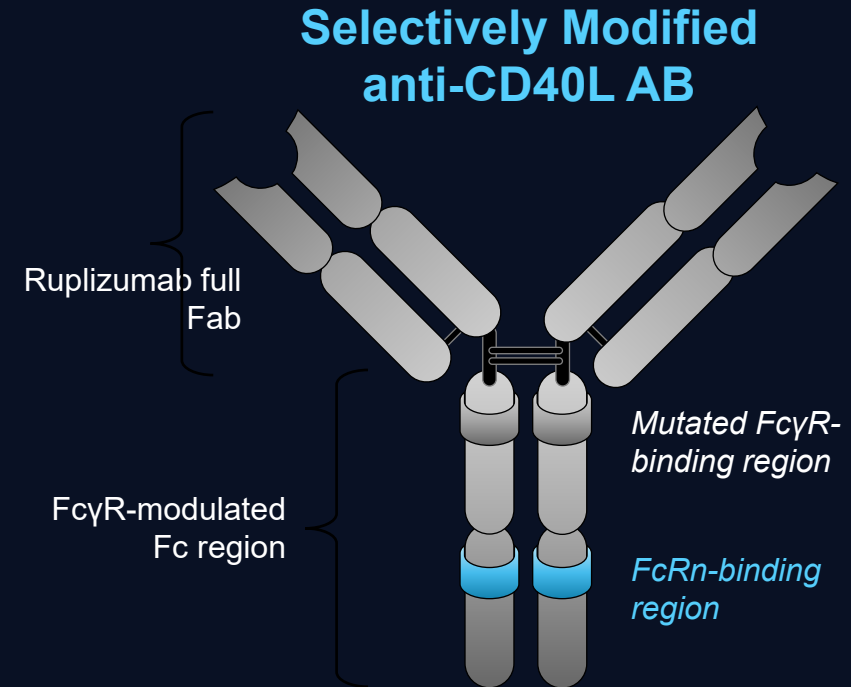
Key Differentiators

Expected to deliver efficacy without compromising safety

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.



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



TNX-1500 Strategy and Status

1 Proposed Initial Indication: Prevention of Allograft Rejection

Status: *Phase 1 currently enrolling*

- Collaborations ongoing with Mass General Hospital on heart and kidney transplantation in non-human primates
- Collaboration with Boston Children's on bone marrow transplantation in non-human primates

Next Steps: Initiate Phase 2 study in Kidney Transplant Recipients

2 Second Indication: Hematopoietic Cell Transplant (Bone Marrow Transplant)

- Potential to reduce GvHD

3 Third Indication (and beyond): Autoimmune Diseases (e.g., Multiple Sclerosis, Sjögren's Syndrome, Systemic Lupus Erythematosus)

- These indications require large studies, but represent large target markets

Actively exploring strategic partnerships and out-licensing opportunities



TNX-1500 Preclinical Data and Publications

Non-human Primate Kidney Allo-Transplantation

- TNX-1500 monotherapy consistently prevents kidney transplant rejection with no thrombosis observed
- April 2023 Publication: Lassiter, G., et al. (2023). TNX-1500, an Fc-modified Anti-CD154 Antibody, Prolongs Nonhuman Primate Renal Allograft Survival. *American Journal of Transplantation*. www.sciencedirect.com/science/article/pii/S1600613523003714

Non-human Primate Heart Heterotopic Allo-Transplantation

- TNX-1500 monotherapy consistently prevents heart transplant rejection. Similar activity to chimeric hu5c8² during treatment phase in prior studies
- April 2023 Publication: Miura, S., et al. (2023) TNX-1500, an Fc-modified Anti-CD154 Antibody, Prolongs Nonhuman Primate Cardiac Allograft Survival. *American Journal of Transplantation*. www.sciencedirect.com/science/article/pii/S1600613523003969

Non-Human Primate Kidney Xenograft Transplantation

- TNX-1500 therapy is part of a regiment to prevent rejection in kidney xenograft transplants
 - Anand, R.P., Layer, J.V., Heja, D. et al. (2023). Design and testing of a humanized porcine donor for xenotransplantation. *Nature*. <https://www.nature.com/articles/s41586-023-06594-4>
 - Kozlov, M. (2023). Monkey survives two years after gene-edited pig-kidney transplant. *Nature*. <https://www.nature.com/articles/d41586-023-03176-2>
 - Mohiuddin, M. (2023). Pig-to-primate organ transplants require genetic modifications of donor. *Nature*. <https://www.nature.com/articles/d41586-023-02817-w>

TNX-1700

Recombinant Trefoil Factor Family Member 2 (rTFF2-HSA)
Fusion Protein

Targeting the toxic tumor micro-environment

TNX-1700: Fighting Cancer by Targeting the Tumor Micro-Environment

Suppresses myeloid-derived suppressor cells (MDSCs) and activates anti-cancer CD8+ T cells



Key Differentiators

- Different MOA than checkpoint inhibitors
- ***Potential synergy with anti-PD-1 or anti-PD-L1 monoclonal antibodies***

Preclinical Evidence

- mTNX-1700 (mTFF2-MSA fusion protein) and anti-PD-1 monotherapy each was able to evoke anti-tumor immunity in the MC38 model of colorectal cancer¹
- mTNX-1700 augmented the anti-tumor efficacy of anti-PD-1 therapy in both the MC38 and the CT26.wt models¹

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

¹Daugherty, B. et al. March 6, 2023 Keystone Poster, <https://bit.ly/48nIRHM>



About Gastric and Colorectal Cancer

Gastric and colorectal cancer are both leading cancers in the US. Colorectal cancer is the 3rd leading cause of cancer-related deaths in both men and women.¹

>1.3M People living with colorectal cancer in the US²

>125k People living with gastric cancer in the US³

Current standard of care:

- PD-1 blockade
 - However, gastric and colorectal cancer are relatively unresponsive

Large unmet need:

- Gastric and colorectal cancer have a relative 5-year survival rate of 35.7% and 65%, respectively
 - Despite advances in the field, patients are still in need of life saving treatment

¹American Cancer Society, accessed September 2023 - <https://www.cancer.org/cancer/types/colon-rectal-cancer/about/key-statistics.html>
²NIH, accessed September 2023 - <https://seer.cancer.gov/statfacts/html/colorect.html>
³NIH, accessed September 2023 - <https://seer.cancer.gov/statfacts/html/stomach.html> © 2023 Tonix Pharmaceuticals Holding Corp.



INFECTIOUS DISEASE: KEY CANDIDATES



Internal Development & Manufacturing Capabilities



R&D Center (RDC): Frederick, MD

- Research advancing CNS and immunology drugs
- Accelerated development of vaccines and antiviral drugs against infectious diseases
- ~48,000 square feet, BSL-2 with some areas designated BSL-3



Advanced Development Center (ADC): North Dartmouth, MA

- Development and clinical scale manufacturing of biologics
- ~45,000 square feet, BSL-2



Broad-Spectrum Antiviral Discovery Programs

Host-directed antiviral discovery programs

CD45 targeted therapeutics

- Small molecule therapeutics that reduce endogenous levels of CD45, a protein tyrosine phosphatase
- Reduction in CD45 protects against many viruses including the Ebola virus

Cathepsin inhibitors

- Small molecule therapeutics that inhibit **essential cathepsins** which are required by viruses such as coronaviruses and filoviruses to infect cells
- Activity as monotherapy and in combination with other antivirals

Virus-directed antivirals discovery program

Viral glycan-targeted engineered biologics

- Bind to viral densely branched high-mannose (DBH) glycans
- **Neutralize circulating virus** and stop the entry of the progeny virus into cells
- Antiviral activity against a broad range of RNA viruses
- Activity as monotherapy and in combination with other antivirals



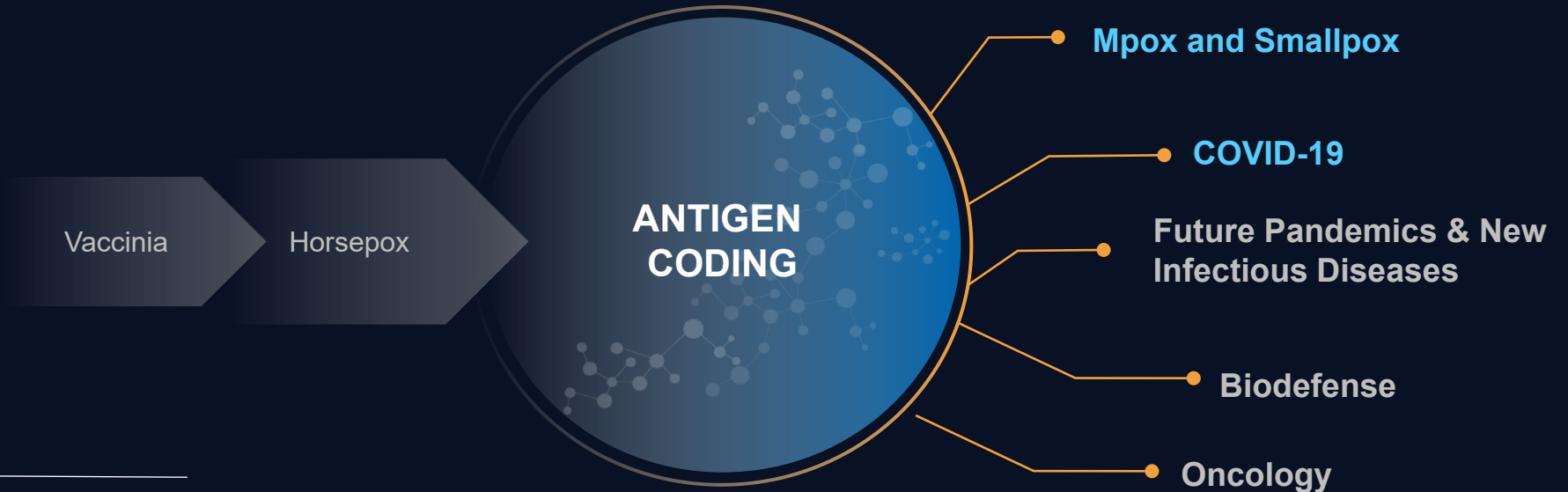
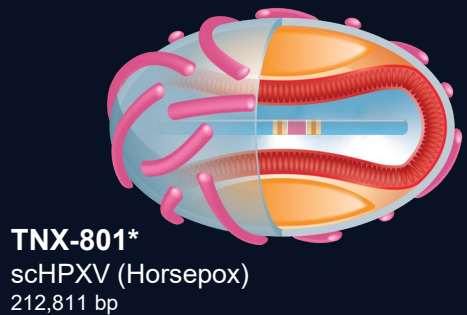
TNX-801

Live Virus Vaccine

Live virus vaccine platform with multitude of potential applications

TNX-801: Recombinant Pox Vaccine (RPV) Platform Using Live Virus Technology

Cloned version of horsepox¹ purified from cell culture



Key Differentiators

Live virus vaccines are the most established vaccine technology

- Prevents forward transmission
- Effective in eliciting durable or long-term immunity

Economical to manufacture at scale

- Low dose because replication amplifies dose *in vivo*
- Single administration

Standard refrigeration for shipping and storage



TNX-1800: Designed to Express the SARs-CoV-2 Spike Protein

TNX-1800 (recombinant horsepox virus) is a live virus vaccine based on Tonix's TNX-801 that is designed to express the spike protein of the SARS-CoV-2 virus and to elicit a predominant T cell response

- Immunogenic and well tolerated¹
- Showed promise in protecting animals from challenge with SARS-CoV-2 delivered directly into the lungs¹

Status: *National Institute of Allergy and Infectious Diseases (NIAID) will conduct a Phase 1 clinical trial with TNX-1800*

- Expected to start in 2H 2024
- First vaccine candidate using Tonix's live virus recombinant pox virus (RPV) platform technology to enter clinical trials
- "Project NextGen" is an initiative by the U.S. Department of Health and Human Services (HHS) to advance a pipeline of new, innovative vaccines and therapeutics for COVID-19. NIAID will be conducting clinical trials to evaluate several early-stage vaccine candidates, including TNX-1800
- Phase 1 study is designed to assess safety and immunogenicity in approximately 60 healthy adult volunteers
- Upon completion of the trial, NIAID and Tonix will assess the results and determine the next steps for the development of TNX-1800

¹Awasthi, M. et al. *Viruses*. 2023. 15(10):2131.

²Awasthi, M. et al. *BioRxiv*. 2023.



TONIX
PHARMACEUTICALS

**TEAM,
NETWORK, &
UPCOMING
MILESTONES**



Key Development Partners

TNX-1500: ALLOGRAFT REJECTION



TNX-1900: MIGRAINE & OTHER INDICATIONS



TNX-1300: COCAINE INTOXICATION TNX-1700: GASTRIC AND COLORECTAL CANCERS



TNX-801: SMALLPOX AND MONKEYPOX VACCINE



TNX-2900: PRADER-WILLI SYNDROME



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



Summary of Upcoming Milestones

Clinical Trial Initiations

- Phase 2 study of TNX-1300 for the treatment of cocaine intoxication – expected 4Q 2023
- Phase 1 study of TNX-1800 with NIAID – expected 2H 2024

4th Quarter 2023 Data Readouts

- Phase 2 PREVENTION study of TNX-1900 for chronic migraine – topline early December 2023
 - Affects approximately 3-7 M adults in the U.S¹
- Phase 3 RESILIENT study of TNX-102 SL for fibromyalgia – topline late December 2023
 - Affects approximately 6-12 M adults in the U.S²

¹Natoli et al., Global prevalence of chronic migraine: a systematic review, Cephalgia, 2010, 30:599-609

²American Chronic Pain Association (www.theacpa.org, 2019)



THANK YOU



Zembrace® Important Safety Information (1 of 2)

Zembrace SymTouch (Zembrace) can cause serious side effects, including heart attack and other heart problems, which may lead to death. Stop use and get emergency help if you have any signs of a heart attack:

- Discomfort in the center of your chest that lasts for more than a few minutes or goes away and comes back; severe tightness, pain, pressure, or heaviness in your chest, throat, neck, or jaw; pain or discomfort in your arms, back, neck, jaw or stomach; shortness of breath with or without chest discomfort; breaking out in a cold sweat; nausea or vomiting; feeling lightheaded

Zembrace is not for people with risk factors for heart disease (high blood pressure or cholesterol, smoking, overweight, diabetes, family history of heart disease) unless a heart exam shows no problem.

Do not use Zembrace if you have:

- History of heart problems; narrowing of blood vessels to your legs, arms, stomach, or kidney (peripheral vascular disease); uncontrolled high blood pressure; hemiplegic or basilar migraines. If you are not sure if you have these, ask your provider.
- Had a stroke, transient ischemic attacks (TIAs), or problems with blood circulation; severe liver problems; taken any of the following medicines in the last 24 hours: almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, ergotamines, dihydroergotamine; are taking certain antidepressants, known as monoamine oxidase (MAO)-A inhibitors or it has been 2 weeks or less since you stopped taking a MAO-A inhibitor. Ask your provider for a list of these medicines if you are not sure.
- An allergy to sumatriptan or any of the components of Zembrace

Tell your provider about all of your medical conditions and medicines you take, including vitamins and supplements.

Zembrace can cause dizziness, weakness, or drowsiness. If so, do not drive a car, use machinery, or do anything where you need to be alert.



Zembrace® Important Safety Information (2 of 2)

Zembrace may cause serious side effects including:

- Changes in color or sensation in your fingers and toes; sudden or severe stomach pain, stomach pain after meals, weight loss, nausea or vomiting, constipation or diarrhea, bloody diarrhea, fever; cramping and pain in your legs or hips; feeling of heaviness or tightness in your leg muscles; burning or aching pain in your feet or toes while resting; numbness, tingling, or weakness in your legs; cold feeling or color changes in one or both legs or feet; increased blood pressure including a sudden severe increase even if you have no history of high blood pressure; medication overuse headaches from using migraine medicine for 10 or more days each month. If your headaches get worse, call your provider.
- Serotonin syndrome, a rare but serious problem that can happen in people using Zembrace, especially when used with anti-depressant medicines called SSRIs or SNRIs. Call your provider right away if you have: mental changes such as seeing things that are not there (hallucinations), agitation, or coma; fast heartbeat; changes in blood pressure; high body temperature; tight muscles; or trouble walking.
- Hives (itchy bumps); swelling of your tongue, mouth, or throat
- Seizures even in people who have never had seizures before

The most common side effects of Zembrace include: pain and redness at injection site; tingling or numbness in your fingers or toes; dizziness; warm, hot, burning feeling to your face (flushing); discomfort or stiffness in your neck; feeling weak, drowsy, or tired.

Tell your provider if you have any side effect that bothers you or does not go away. These are not all the possible side effects of Zembrace. For more information, ask your provider.

This is the most important information to know about Zembrace but is not comprehensive. For more information, talk to your provider and read the [Patient Information](#) and [Instructions for Use](#). You can also visit www.upsher-smith.com or call 1-888-650-3789. For full Prescribing Information, visit: <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=6e5b104f-2b9e-416e-92fb-ef1bdaea867d>

You are encouraged to report adverse effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Zembrace is a prescription medicine used to treat acute migraine headaches with or without aura in adults who have been diagnosed with migraine.

Zembrace is not used to prevent migraines. It is not known if it is safe and effective in children under 18 years of age.



Tosymra® Important Safety Information (1 of 2)

Tosymra® can cause serious side effects, including heart attack and other heart problems, which may lead to death. Stop Tosymra and get emergency medical help if you have any signs of heart attack:

- Discomfort in the center of your chest that lasts for more than a few minutes or goes away and comes back; severe tightness, pain, pressure, or heaviness in your chest, throat, neck, or jaw; pain or discomfort in your arms, back, neck, jaw, or stomach; shortness of breath with or without chest discomfort; breaking out in a cold sweat; nausea or vomiting; feeling lightheaded

Tosymra is not for people with risk factors for heart disease (high blood pressure or cholesterol, smoking, overweight, diabetes, family history of heart disease) unless a heart exam is done and shows no problem.

Do not use Tosymra if you have:

- History of heart problems; narrowing of blood vessels to your legs, arms, stomach, or kidney (peripheral vascular disease); uncontrolled high blood pressure; severe liver problems; hemiplegic or basilar migraines. If you are not sure if you have these, ask your healthcare provider.
- Had a stroke, transient ischemic attacks (TIAs), or problems with blood circulation; taken any of the following medicines in the last 24 hours: almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, ergotamines, or dihydroergotamine. Ask your provider if you are not sure if your medicine is listed above
- are taking certain antidepressants, known as monoamine oxidase (MAO)-A inhibitors or it has been 2 weeks or less since you stopped taking a MAO-A inhibitor. Ask your provider for a list of these medicines if you are not sure
- An allergy to sumatriptan or any ingredient in Tosymra

Tell your provider about all of your medical conditions and medicines you take, including vitamins and supplements. Tosymra can cause dizziness, weakness, or drowsiness. If so, do not drive a car, use machinery, or do anything where you need to be alert.



Tosymra® Important Safety Information (2 of 2)

Tosymra may cause serious side effects including:

- Changes in color or sensation in your fingers and toes; sudden or severe stomach pain, stomach pain after meals, weight loss, nausea or vomiting, constipation or diarrhea, bloody diarrhea, fever; cramping and pain in your legs or hips, feeling of heaviness or tightness in your leg muscles, burning or aching pain in your feet or toes while resting, numbness, tingling, or weakness in your legs, cold feeling or color changes in one or both legs or feet; increased blood pressure including a sudden severe increase even if you have no history of high blood pressure; medication overuse headaches from using migraine medicine for 10 or more days each month. **If your headaches get worse, call your provider.**
- Serotonin syndrome, a rare but serious problem that can happen in people using Tosymra, especially when used with anti-depressant medicines called SSRIs or SNRIs. **Call your provider right away if you have:** mental changes such as seeing things that are not there (hallucinations), agitation, or coma; fast heartbeat; changes in blood pressure; high body temperature; tight muscles; or trouble walking.
- Seizures even in people who have never had seizures before

The most common side effects of Tosymra include: tingling, dizziness, feeling warm or hot, burning feeling, feeling of heaviness, feeling of pressure, flushing, feeling of tightness, numbness, application site (nasal) reactions, abnormal taste, and throat irritation.

Tell your provider if you have any side effect that bothers you or does not go away. These are not all the possible side effects of Tosymra. For more information, ask your provider.

This is the most important information to know about Tosymra but is not comprehensive. For more information, talk to your provider and read the [Patient Information and Instructions for Use](#). You can also visit www.upsher-smith.com or call 1-888-650-3789. For full Prescribing Information, visit: <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=015a5cf9-f246-48bc-b91e-cd730a53d8aa>

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Tosymra is a prescription medicine used to treat acute migraine headaches with or without aura in adults.

Tosymra is not used to treat other types of headaches such as hemiplegic or basilar migraines or cluster headaches.

Tosymra is not used to prevent migraines. It is not known if Tosymra is safe and effective in children under 18 years of age.