Investor Presentation
NASDAQ:TNXP

TONIX PHARMACEUTICALS

March 2021

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Tonix Pharmaceuticals

Who We Are – Mission And Purpose

Clinical-stage biopharmaceutical company that invents and develops medicines to help patients manage the central nervous system (CNS) and immunology diseases.

"Advancing science to improve patient care and public health"

Our Pipeline – CNS Portfolio

	CANDIDATES	INDICATION	STATUS
CNS Portfolio	**TNX-102 SL**[1]	**Fibromyalgia (FM) - Lead Program**	**Mid-Phase 3 – ongoing**
		PTSD	Phase 3 ready
		Agitation in Alzheimer's	Phase 2 ready
		Alcohol Use Disorder	Phase 2 ready
	TNX-1300[2]	Cocaine Intoxication / Overdose	Phase 2
	TNX-1900[3]	Migraine and Craniofacial Pain	Clinical – pre-IND[4]
	TNX-2900[5]	Prader-Willi Syndrome	Clinical – pre-IND
	TNX-601 CR	Depression, PTSD, Neurocognitive Dysfunction from Corticosteroids	Clinical – pre-IND[6]
	TNX-1600[7]	Depression, PTSD and ADHD	Preclinical

[1]TNX-102 SL (cyclobenzaprine HCl sublingual tablets) is an investigational new drug and has not been approved for any indication.
[2]TNX-1300 (T172R/G173Q double-mutant cocaine esterase 200 mg, i.v. solution) is an investigational new biologic and has not been approved for any indication; licensed from Columbia University.
[3]Acquired from Trigemina; license agreement with Stanford University
[4]A Phase 2 trial under an investigator-initiated IND has been completed in the U.S. using TNX-1900
[5]Co-exclustive license agreement with French National Institute of Health and Medical Research (Inserm)
[6]TNX-601 CR is in the pre-IND stage in the U.S.; a Phase 1 trial for formulation development was recently completed outside of the U.S.
[7]Acquired from TRImaran Pharma; license agreement with Wayne State University

Our Pipeline – Immunology & Biodefense Portfolio

	CANDIDATES	INDICATION	STATUS
Immunology Portfolio	**TNX-1800**	**Covid-19 vaccine – Prioritized Program[1]**	**Preclinical**
	TNX-2100	SARS-CoV-2 skin test for T cell immunity[2]	Pre-IND
	TNX-2300	Covid-19 vaccine[3]	Preclinical
	TNX-801	Smallpox and monkeypox preventing vaccine[4]	Preclinical
	TNX-1500	Organ Transplant Rejection/Autoimmune Conditions[5]	Preclinical
	TNX-1700	Gastric and pancreatic cancers[6]	Preclinical
	TNX-701	Radioprotection	Preclinical

[1]Live attenuated vaccine based on horsepox virus vector
[2]*In vivo* diagnostic: SARS-CoV-2 peptide epitope mixtures for intradermal administration to measure delayed-type hypersensitivity to SARS-CoV-2
[3]Live attenuated vaccine based on bovine parainfluenza virus vector; option for license with Kansas State University
[4]Live attenuated vaccine based on horsepox virus
[5]anti-CD40L humanized monoclonal antibody
[6]recombinant trefoil factor 2 (TFF2) based protein; licensed from Columbia University

TNX-102 SL FM Lead Program
Background on Fibromyalgia

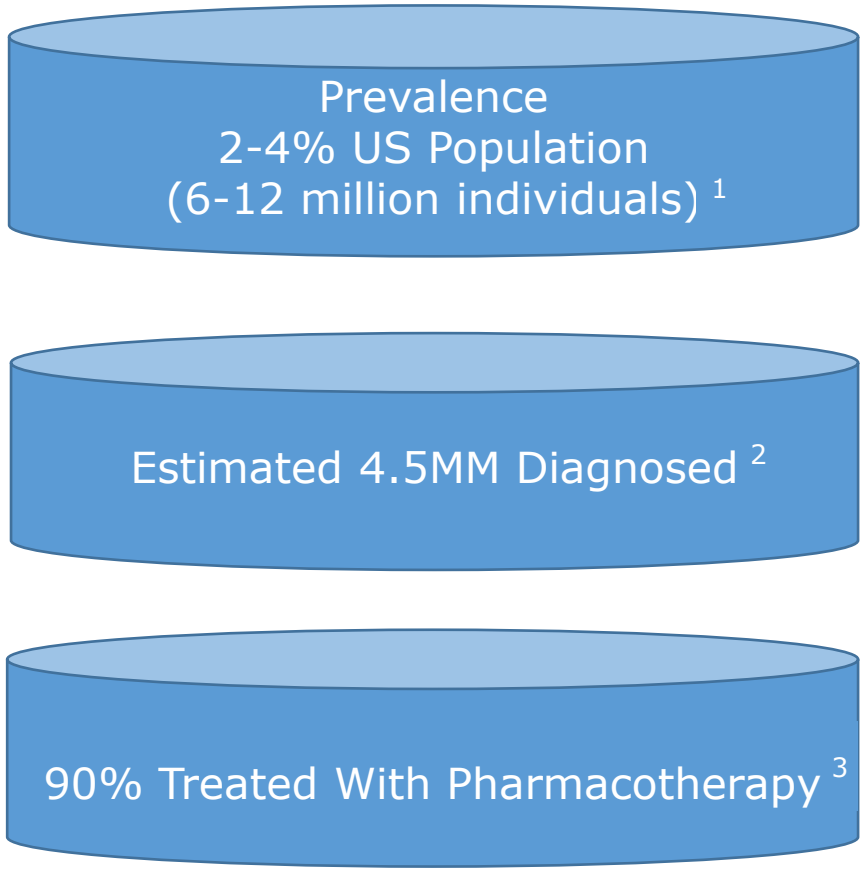
Fibromyalgia (FM):

A chronic condition

Core symptoms:
- widespread pain
- sleep disturbance
- fatigue
- cognitive symptoms.

Significant disabilities (impaired daily function).

Course of disease can last decades



1 American Chronic Pain Association (www.theacpa.org, 2019)
2 .Walitt, B., Nahin, R.L., Katz, R.S., Bergman, M.J., Wolfe, F. (2015). The Prevalence and Characteristics of Fibromyalgia in the 2012 National Health Interview Survey. *PLoS One;* 10(9): e0138024.
3. Decision Resources, Fibromyalgia, 2012

Challenges with Current Pharmacotherapy

Limitations of Current Therapies

Fewer than half of those treated for fibromyalgia receive relief from the three FDA-approved drugs[1]

- Lack of overall response leading to discontinuation or augmentation
- Lack of tolerability leading to discontinuation or reduction in dose (underdosing)

Current Treatment Patterns As A Result of Limitations

Switch Rates/Rotation/Discontinuation

- Over 50% of patient starting an FDA approved therapy for FM switch or discontinue therapy after 12 months[2]

Polypharmacy

- Average patient is using 2.6 drugs for treating their fibromyalgia, 50% of patients take 3 or more medications concomitantly[3]

Opioid usage is not uncommon

Market Dissatisfaction

Only 43% of patients indicated that they are satisfied with their medication for FM[5]

1. Frost and Sullivan, 2010
2. Liu et al., 2016
3. Robinson et al., 2012; prospective observational study with 1,700 participants with fibromyalgia.
4. Sarmento et al., J Opioid Manag 2019; 15(6):460-77 – prescription opioid usage among diagnosed FM patients at one site
5. Robinson et al., 2013; prospective observational study with 1,700 participants with fibromyalgia

Fibromyalgia Unmet Need and Ideal Treatment Profile

Unmet Medical Need:

Current treatment patterns indicate that new, more effective, and better-tolerated treatments are necessary for management of FM[1]

Ideal Treatment Profile:

Treats FM as a syndrome

Relief from major symptoms (pain, sleep disturbances, fatigue)

Reduces disability and improves daily living (global function)

Well tolerated with low discontinuation

- Low systemic side-effects
- No daytime somnolence
- No weight gain or impact on sexual function

Suitable for chronic use

- Not scheduled
- Non opioid
- Non abuse potential

Source: 1. Yang, et al, 2016

TNX-102 SL: Engineered to Treat FM

This unique formulation of cyclobenzaprine has been designed to optimize delivery and absorption, while minimizing the potential residual effects of oral formulations of cyclobenzaprine.

Innovative and proprietary Protectic® delivery technology

- Overcomes mucosal absorption barrier
- Allows sublingual (SL) administration to achieves relevant systemic drug exposure
- Stable SL tablet formulation

- **Benefits of sublingual delivery**
  - Rapid drug exposure following nighttime administration
  - Lower daytime exposure
  - Avoids first-pass metabolism
    - Reduces risk of pharmacological interference from major metabolite

No recognized abuse or dependency concerns

Phase 3 F304/RELIEF Study: Design

General study characteristics:

- Randomized, double-blind, placebo-controlled study in fibromyalgia
- Adaptive Design: one unblinded interim analysis based on 50% of randomized participants

TNX-102 SL once-daily at bedtime
5.6 mg (2 x 2.8 mg tablets)[1] *N= 248*

Placebo once-daily at bedtime
N= 255

14 weeks

Primary endpoint (Week 14):

- Daily diary pain severity score change from baseline

Key Secondary endpoints (Week 14):

Symptom Relief
- PROMIS Sleep Disturbance instrument T-score
- PROMIS Fatigue instrument T-score
- FIQ-R Symptom Domain score

Global function
- PGIC responder analysis
- FIQ-R Function Domain score

Pivotal efficacy study to support NDA approval

[1]Two week run in at 2.8 mg dose at bedtime, followed by 12 weeks at 5.6 mg dose

F304/RELIEF Study Topline Primary Efficacy Endpoint

Positive outcome for primary endpoint (daily pain) at Week 14

Primary Outcome Measure at Week 14	Placebo (N=255)	TNX-102 SL[2] (N=248)	Treatment Difference	P value
LS Mean Change from Baseline (SE)	-1.5 (0.12)	-1.9 (0.12)	-0.4 (0.16)	**0.010***

Statistical Method: Mixed Model Repeated Measures analysis with Multiple Imputation
*p<0.0452 (requisite p-value hurdle for full study after Interim Analysis)
[1] Same primary endpoint analysis for FDA approvals of Cymbalta® and Lyrica® in fibromyalgia
Abbreviations: LS = least squares; NRS = numeric rating scale; SE = standard error

[2] TNX-102 SL is in clinical stage of development and not approved for any indication

Pain Relief Responder Analysis

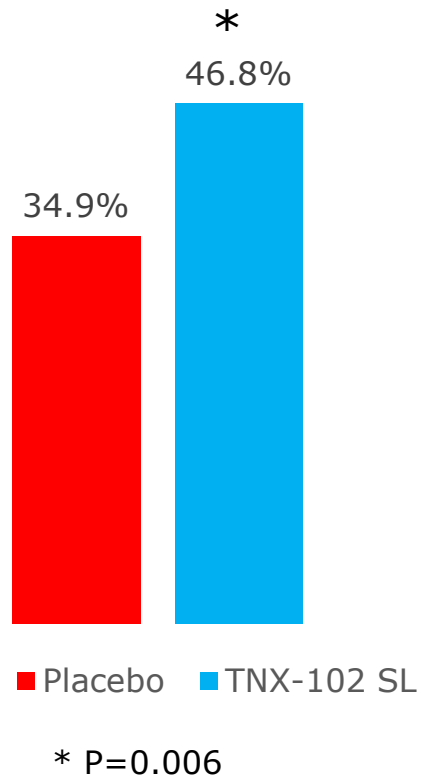
A ≥30% reduction in pain is considered clinically meaningful in pain studies

Primary efficacy analysis supported by 30% responder analysis of daily diary pain

- 47% of patients treated with TNX-102 SL versus 35% on placebo achieved a 30 percent or greater reduction in pain at Week 14

  (logistic regression; odds ratio [95% CI]: 1.67 [1.16, 2.40]; p=0.006)

Comparable to numeric values published for other drugs approved for FM[1,2,3,4]



1. Arnold et al., 2005
2. Russell et al., 2008
3. Mease et al., 2008
4. Arnold et al., 2008

F304/RELIEF Study: Key Secondary Efficacy Endpoints

Outcome Measure at Week 14	Intent-to-Treat Analysis[1]	*P*-value
Non-Specific		
Patient Global Impression of Change	Responder Analysis: Proportion "Much Improved" or "Very Much Improved"	0.058
Fibromyalgia Syndrome-Related		
FIQ-R Symptom Domain	Mean Change from Baseline	0.007[#]
FIQ-R Function Domain	Mean Change from Baseline	0.009[#]
PROMIS Fatigue	Mean Change from Baseline	0.018[#]
Daily Sleep Quality Diary, NRS	Mean Change from Baseline	<0.001[#]
PROMIS Sleep Disturbance	Mean Change from Baseline	<0.001[#]

[#] nominally significant at $p<0.0452$

[1] Combined periods (pre- and post-interim analysis); responder analysis is by Logistic Regression (missing = non-responder); the five mean change analyses are by Mixed Model Repeated Measures with Multiple Imputation

Abbreviations: FIQ-R = Fibromyalgia Impact Questionnaire – Revised; NRS = numeric rating scale; PROMIS = Patient-Reported Outcomes Measurement Information System

*TNX-102 SL is in clinical stage of development and not approved for any indication

Adverse Events*(AEs) in F304/RELIEF Study

Those AEs reported at rate of greater than 5% in either treatment arm

Systemic Adverse Events	Placebo N=255	TNX-102 SL 5.6 mg N=248
Somnolence/Sedation	1.2%	5.6%
Local Administration Site Reactions		
Tongue/mouth numbness	0.8%	17.3%
Tongue/mouth pain/discomfort	2.0%	11.7%
Taste impairment	0.4%	6.5%
Tongue/mouth tingling	0.4%	5.6%

* Table reports only AEs at rate of greater than 5% in either treatment arm

Discontinuation rate due to adverse events: 8.9% TNX-102 SL compared to 3.9% for placebo

No serious and unexpected AEs in RELIEF related to TNX-102 SL

- Systemic AEs comparable with prior studies
- Oral AEs similar to prior studies with TNX-102 SL, although tongue/mouth numbness at about half the rate in RELIEF

Approved Fibromyalgia Pharmacotherapies

Pfizer

- Drug: Lyrica® or pregabalin (U.S. patent expired in 2018)
- Approved: 2004
- Mechanism: modulates nerve impulses involved in the transmission of pain through selective binding to the alpha2-delta protein of the voltage-gated calcium channels in CNS tissues
- Peak Sales: Approximately $5 billion (including all approved indications)

Lilly

- Drug: Cymbalta® or duloxetine (U.S. patent expired 2014)
- Approved: 2004
- Mechanism: serotonin and norepinephrine reuptake inhibitor (SNRI)
- Peak Sales: Approximately $5 billion (including all approved indications)

Abbvie (developed by Forest Laboratories)

- Drug: Savella® or milnacipran (on patent)
- Approved: 2009
- Mechanism: serotonin and norepinephrine reuptake inhibitor (SNRI)
- Peak Sales: Approximately $130 million (approved for fibromyalgia indication only)

TNX-102 SL for FM: Next Steps

2nd Phase 3 study, RALLY (F306)

- Same protocol design as RELIEF study but with 200 more patients[1]
- Enrollment began in September 2020
- Interim analysis results expected in 3rd quarter 2021[2]
- Topline results expected in 4th quarter of 2021

Following positive results from RALLY, an NDA could potentially be filed in 2022

- Long term safety exposure studies completed
- GMP manufacturing processes mature and 36-month stability established

[1]Pending agreement from FDA on protocol amendment
[2]Pending submission and agreement from FDA on statistical analysis plan

TNX-102 SL Intellectual Property – U.S. Protection expected until 2035

Composition of matter (eutectic):

Protection expected to 2034/2035

- United States Patent and Trademark Office (USPTO) issued United States Patent No. 9636408 in May 2017, Patent No. 9956188 in May 2018, Patent No. 10117936 in November 2018, and Patent No. 10864175 on December 2020
- European Patent Office (EPO) issued European Patent No. 2968992 in December 2019 (validated in 37 countries). Opposition filed in October 2020 by Hexal AG
- China National Intellectual Property Administration issued Chinese Patent No. ZL 201480024011.1 in April 2019
- Japanese Patent Office (JPO) issued Japanese Patent No. 6310542 in March 2018
- 8 granted patents (Indonesia, Saudi Arabia, New Zealand, Australia, Mexico, Taiwan, Israel, South Africa)
- 11 patent applications pending (1 being allowed in Canada)

Composition of matter (sublingual):

Protection expected to 2033

- NZIPO issued New Zealand Patent No. 631144 in March 2017 and Patent No. 726488 in January 2019
- Taiwanese Intellectual Property Office issued Taiwanese Patent No. I590820 in July 2017, Patent No. I642429 in December 2018 and Patent No. I683660 in February 2020
- Australian Patent Office issued Australian Patent No. 2013274003 in October 2018 and Patent No. 2018241128 in September 2020
- JPO issued Japanese Patent No. 6259452 in December 2017
- 20 patent applications pending (1 being allowed in Mexico)

COVID-19 Vaccines: Still Uncertainty

Durability of protection

- Are vaccinated people protected one year later?
- Durable protection is associated with T cell response

Protection against forward transmission

- Highly contagious nature of CoV-2 is a major problem driving pandemic

No biomarker of protection

- No test to establish protection from vaccination

Current and future variants

- Unknown effectiveness of existing vaccines

Potential for need to have annual vaccinations

- High capacity and low costs become critical

TNX-1800[1]: a COVID-19 Vaccine Candidate

- **Utilizes Tonix's proprietary horsepox virus as a vector**
  - Encodes a protein from SARS-CoV-2, the cause of COVID-19
  - Developed in collaboration with University of Alberta, Canada
- **Animal testing with Southern Research Institute**
  - Non-human primate immune response positive results reported in 4th quarter 2020
  - Non-human primate CoV-2 challenge testing data expected in 1st quarter 2021
- **Manufacturing agreement with FUJIFILM Diosynth**
  - Development for Good Manufacturing Practice (GMP) manufacturing for human trials
  - GMP[2] clinical supply expected to be ready for human trials in 2nd half of 2021[3]

[1]TNX-1800 (horsepox/Cov-2 spike live vaccine) is at the pre-IND stage of development
[2] Good Manufacturing Practice = GMP
[3] We cannot predict whether the global COVID-19 pandemic will impact the timing of these milestones

TNX-2100[1]: Potential Skin Test to Measure SARS-CoV-2 Exposure and T Cell Immunity

TNX-2100 (SARS-CoV-2 epitope peptide mixtures for intradermal administration)

- Designed to elicit delayed-type hypersensitivity (DTH) in individuals who have been exposed to SARS-CoV-2 or who have been successfully vaccinated
- Potential to measure the presence and strength of functional *in vivo* T cell immunity

Potentially scalable test for widespread use

- Adaptive Biotech's T Detect™ COVID received FDA EUA – based on genetic analysis of T cell receptors
- Other tests[2] for T cell immunity to SARS-CoV-2 require specialized laboratories and are not amenable to standardization

Development plans

- 2nd quarter 2021: Plan to submit IND based on FDA feedback
- 2nd half 2021: Plan to initiate clinical testing pending approval of IND

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

TNX-1900 (Intranasal Potentiated Oxytocin) for the Treatment of Migraine

Intranasal oxytocin(OT) has potential utility in treating migraine[1]

- Intranasal (*i.n.*) OT reaches the trigeminal ganglion
- Preclinical evidence of OT blocking CGRP release and suppressing pain transmission
- CGRP antagonists and antibodies approved for the treatment of migraine
- Association of low oxytocin levels during and preceding migraine episodes

TNX-1900 is an intranasal formulation of magnesium and OT

- Magnesium is known to potentiate the binding of oxytocin to its receptor[2]

Submission of IND application in 2nd quarter 2021 and initiation of Phase 2 study for treatment of chronic migraine anticipated in 3rd quarter 2021

1. Tzabazis et al., 22017
2. Antoni and Chadio, 1989

TNX-2900 (*i.n.* Potentiated OT) for the Treatment of Prader-Willi Syndrome

Prader-Willi syndrome is the most common genetic cause of life-threatening childhood obesity[1]

- Results in lack of suckling in infants and, in children and adults, severe hyperphagia, an overriding physiological drive to eat, leading to severe obesity and other complications associated with significant mortality
- No approved treatment for either the suckling deficit in babies or the obesity and hyperphagia in older children associated with Prader-Willi syndrome.
- Orphan disease occurring in approximately one in 15,000 births

Intranasal OT has been shown to improve suckling in newborn animals but also suppresses feeding behaviors in adult animal models

- Tonix's patented potentiated oxytocin formulation is believed to increase specificity for OT receptors relative to vasopressin receptors

Tonix intends to submit an application to the FDA for Orphan Drug and Fast Track designations for TNX-2900

[1]Foundation for Prader-Willi Research (fpwr.org).

TNX-1300: Cocaine Esterase (CocE)

CocE is the most potent known catalyst for cocaine degradation

- Natural bacterial CocE is unstable at body temperature

Thermostable bacterial CocE (active for ~6 hours at body temperature)

- Targeted mutations stabilize CocE
- Natural bacterial CocE is unstable at body temperature

Phase 2 open-label safety study of TNX-1300 in emergency department setting for cocaine intoxication)

- Initiation of enrollment anticipated 2nd quarter 2021

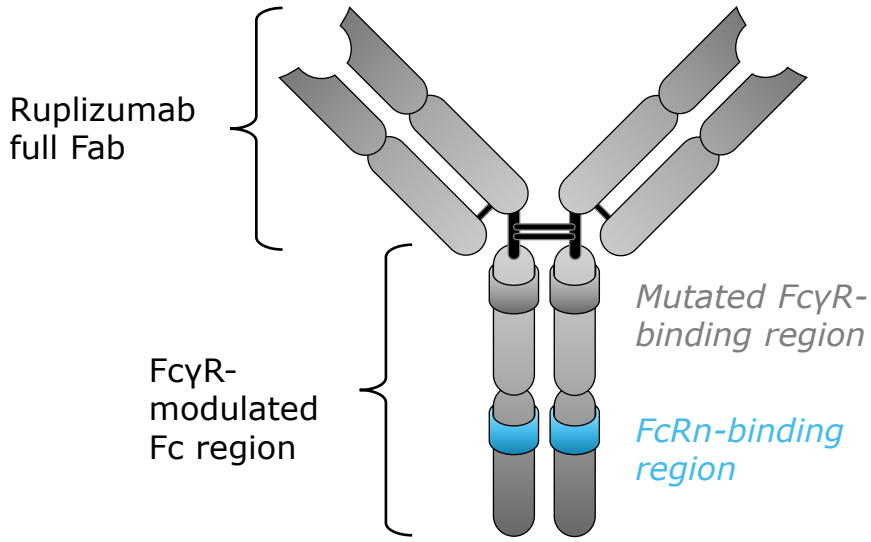
TNX 1500, a New CD40 Ligand (CD40L) Antibody, for the Prevention of Allograft Rejection

The CD40-CD40L pathway is a pivotal immune system modulator and is a well-established and very promising treatment target to more safely prevent allograft rejection[1]

- **First Generation:** Development *halted due to thromboembolic complications (TE) – blood clots*. TE complications traced to Fc gamma receptor
- **Second Generation:** Eliminated the Fc gamma receptor (TE complication) but *potency and half life reduced which limited utility*
- **TNX-1500 Third Generation**: Re-engineered based on greater understanding of the Fc gamma receptor. Modulated the binding of FcγR while preserving FcRn function
  - Expected to deliver efficacy without compromising safety

Tonix expects to have GMP product ready in the 3rd quarter of 2021 for TNX-1500

Selectively Modified Anti-CD40L Ab



TNX-1500 contains the full ruplizumab Fab and the engineered Fc region that modulates FcγR-binding, while preserving FcRn function.

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

Milestones – Recently Completed and Upcoming[1]

✓ 4th Quarter 2020	Non-human primate immune response positive results reported
✓ 4th Quarter 2020	Positive topline data from TNX-102 SL Phase 3 F304/RELIEF study in fibromyalgia reported
❑ **1st Quarter 2021**	**Non-human primate efficacy data from TNX-1800 in COVID-19 models expected**
❑ **2ND Quarter 2021**	**Initiation of Phase 2 open-label safety study of TNX-1300 in ED setting for cocaine intoxication**
❑ **2nd Quarter 2021**	**Submission of IND application for TNX-2100 for SARS-CoV-2 skin test**
❑ **2nd Quarter 2021**	**Submission of IND application for TNX-1900 for the treatment of migraine**
❑ **3rd Quarter 2021**	**Initiation of Phase 2 study of TNX-1900 for the treatment of migraine**
❑ **3rd Quarter 2021**	**Interim analysis of TNX-102 SL Phase 3 F306/RALLY study in fibromyalgia expected**
❑ **4th Quarter 2021**	**Topline data from TNX-102 SL Phase 3 F306/RALLY study in fibromyalgia expected**
❑ **2nd Half 2021**	**Initiation of Phase 1 safety study of TNX-1800 for COVID-19 expected**
❑ **2nd Half 2021**	**Initiation of clinical trials for TNX-2100 SARS-CoV-2 skin test expected**

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

Management Team

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President & CEO

TARGENT | Fusilev (levoleucovorin) for injection | vela PHARM

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Thank You!