at a glance™

TONIX PHARMACEUTICALS

Notable: ***A rich pipeline of recent and upcoming clinical activity puts Tonix in a position of realizing several potential milestones in 2023, starting with the interim analysis of a potentially registration-enabling Phase 3 trial in fibromyalgia, a large market rife with dissatisfied patients that hasn't seen a new FDA drug approval in more than a dozen years. Cash and cash equivalents totaled approximately $120 million at December 31, 2022.***

Key Considerations

- **A potentially pivotal and confirmatory Phase 3 trial of TNX-102 SL is underway in fibromyalgia and, if successful, will be the second of two adequate and well-controlled Phase 3 trials required for filing for FDA approval.**
- **The results of an interim analysis are expected 2Q23 and could set the stage for a major inflection point in the company's valuation.**
- **Weeks ago, Tonix initiated enrollment in a Phase 2 clinical trial of TNX-1900 in chronic migraine sufferers. Tonix has also initiated enrollment in a Phase 2 clinical trial of TNX-102 SL in fibromyalgia-type Long COVID.**
- **Tonix guides that it will initiate enrollment in a Phase 2 clinical trial of TNX-601 ER in depression this quarter.**
- **The balance of 2023's clinical calendar includes the expected start of a Phase 2 trial in cocaine intoxication.**
- **Two additional clinical trials starting in 2023 include Phase 1 trials of a novel monoclonal antibody to prevent organ transplant rejection, TNX-1500, and a vaccine candidate for smallpox/mpox, TNX-801.**
- **The company is expanding its internal research and development capabilities to accelerate infectious disease programs and for future pandemic responses under guidelines set forth by the American Pandemic Preparedness Plan, or AP3, created by the White House Office of Science and Technology Policy.**
- **Tonix's Research and Development Center (RDC) in Fredrick, MD and its Advanced Development Center (ADC) in Dartmouth, MA are now fully operational.**

Tonix Pharmaceuticals Holding Corp.
(Nasdaq: TNXP)

Recent Price:	**$0.74**
Shares O/S (1/24/23):	**60.9 Million**
Approx. Mkt Cap:	**$45 Million**
Avg. Daily Volume:	**7.2 Million**
Fiscal Year Ends:	**Dec. 31**

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TNX-102 SL - Phase 3 Fibromyalgia

TNX-102 SL is a non-opioid, centrally acting analgesic formulated as a sublingual tablet for treatment of several chronic CNS disorders in which poor sleep quality is believed to be a major component of the disease process. Cyclobenzaprine – its active ingredient – has no recognized addiction or dependency risk.

In 2Q22, Tonix initiated RESILIENT, a pivotal Phase 3 trial of TNX-102 SL in fibromyalgia. Results of an interim analysis are expected to be available in 2Q23, after approximately 50 percent of the 470 planned participants have completed the 14-week trial.

Fibromyalgia affects between six to 12 million adults in the US according to the American Chronic Pain Association. Approximately 90 percent of patients are women.

Fibromyalgia is devastating and expensive for individuals and society. Approximately 70 percent of patients indicate they have difficulty with routine daily activities and an estimated 20 percent of patients file claims for disability insurance.

Patients and care givers alike report dissatisfaction with currently approved drugs for fibromyalgia. The market is characterized by patients switching back and forth between the three approved brands – Cymbalta®, Lyrica®, and Savella® -- and their generics, as well as use of off-label drugs, including opiates.

The current RESILIENT trial is Tonix's third Phase 3 trial of TNX-102 SL 5.6 mg in fibromyalgia.

The first, named RELIEF, successfully met its primary endpoint (p=0.010). The second Phase 3 trial, RALLY, did not (p=0.115) and was early terminated for futility on the recommendation of the Independent Data Monitoring Committee, after a pre-specified review of the unblinded results of approximately 50 percent of anticipated study participants.

The trial experienced abnormally high (compared to the earlier RELIEF trial) adverse event related discontinuations in both the drug treatment and placebo groups (79 percent and 77 percent respectively). The company notes the trial was conducted during a peak phase of the COVID-19 pandemic in the U.S. when many Americans were getting vaccinated.

If the current RESILIENT trial is successful, it will be the second of two adequate and well-controlled Phase 3 trials required by the FDA for the filing of a New Drug Application (NDA) for marketing approval.

The company is studying TNX-102 SL in

Recent & Anticipated Milestones

-1Q23 – Initiated Ph. 2 of TNX-1900 in chronic migraine

-1Q23 – Initiate Ph. 2 study of TNX-601-ER in depression

-2Q23 – Initiate Ph. 2 study of TNX-1300 in cocaine intoxication

-2Q23 – Interim results from Ph. 3 study of TNX-102 SL in fibromyalgia

-2Q23 – Initiate Ph. 1 study of TNX-1500 for prevention of rejection in kidney transplants

-2H23 – Initiate Ph. 1 study of TNX-801 vaccine candidate in smallpox/mpox

an additional indication, fibromyalgia-type Long COVID.

TNX-102 SL - Phase 2 Fibromyalgia-Type Long COVID

About 40 percent of Long COVID patients have a constellation of symptoms including multi-site pain, sleep disturbance, fatigue, insomnia, and brain fog, which together seem very similar to fibromyalgia, which Tonix calls fibromyalgia-type Long COVID.

The prevalence of fibromyalgia-type symptoms in the Long COVID population led Tonix to file an Investigational New Drug (IND) application.

The IND received FDA clearance to initiate a Phase 2 study of TNX- 102 SL in Long COVID sufferers whose symptoms are similar to those of fibromyalgia and who experience multi-site pain, in particular.

The double-blind, placebo-controlled study expects to enroll approximately 470 patients at 30 sites.

A retrospective observational database study conducted for Tonix of more than 50,000 patients with Long COVID showed that more than 40 percent had fibromyalgia-type persistent multi-site pain, which is the specific population Tonix is currently recruiting for the PREVAIL study, a potentially pivotal Phase 2 study.

The study's most alarming finding revealed that approximately 35 percent of the fibromyalgia-type Long COVID sufferers with multi-site pain had turned to opioids for symptom relief – and the number on opioids grew to 50 percent if they also experienced sleep problems.

The findings point to an urgent need for treatments with no known addictive properties, such as TNX-102 SL. The US Department of Labor estimates that 25 percent of patients prescribed opioids long term will struggle with lifelong opioid addiction, adding to an already growing health crisis.

Infectious Diseases

The company's infectious disease and biodefense portfolio includes vaccines to protect against smallpox/mpox, and COVID-19. Note that monkeypox is now called, "mpox".

All of the company's principal vaccine candidates hold the potential to offer long term T cell immunity with a single dose, prevent forward transmission, minimize cold chain requirements, and allow high density, glass sparing packaging.

Tonix previously reported positive efficacy data from a SARS-CoV-2 challenge study in non-human primates with the live virus vaccine expressing the Wuhan spike protein. The predominately T cell eliciting vaccine technology is being updated into a new version to express the spike protein of the BA.2 variant.

The company is expanding its internal research and development capabilities to accelerate infectious disease programs and for future pandemic responses under guidelines set forth by the American Pandemic Preparedness Plan, or AP3.

TNX-1900 - Migraine Headache

In 1Q23, Tonix initiated the Phase 2 PREVENTION clinical trial of TNX-1900 (intranasal oxytocin) for the prevention of migraine headache in chronic suffers.

The double blinded, placebo-controlled trial has a target enrollment of 300 participants at approximately 25 sites across the U.S.

The candidate's mechanism is reported to be multimodal, giving it the ability to inhibit the release of calcitonin gene-related peptide in the brain and brain stem, and suppress signaling in pain neurons.

Tonix's formulation of oxytocin contains magnesium which has been shown in animal models to potentiate oxytocin at oxytocin receptors to improve the consistency of treatment.

Results of a planned interim analysis are expected 4Q23.

TNX-601 ER - MDD

Tonix expects to initiate enrollment in UPLIFT, a Phase 2 double-blind, placebo-controlled clinical trial of TNX-601 ER (tianeptine hemioxalate extended release tablets) in approximately 300 adults with major depressive disorder (MDD) in 1Q23.

Earlier versions of tianeptine have been prescribed outside the U.S. for more than three decades, since being introduced in France in 1989.

Tonix's once daily formulation has imbued the native compound with distinctive mechanisms that reportedly help refresh the brain's neuronal system, instead of simply altering the levels of serotonin, norepinephrine, and dopamine, which is the principal mechanism of traditional drugs in this category.

The company believes TNX-601 ER enhances the brain's neuroplasticity and its ability to cause mature neurons to sprout new connections and may provide long term benefit to MDD patients.

Results from an interim analysis are planned for 4Q23.

TNX-1300 – Cocaine Overdose

TNX-1300, a synthetically engineered version of an enzyme from coco scavenging bacteria, is expected to enter a potentially pivotal Phase 2 clinical trial in 2Q23 to treat cocaine intoxication.

The compound was licensed from Columbia University and is intended to be an emergency room treatment to quickly degrade cocaine in human blood, reversing the effects of cocaine overdose.

An earlier Phase 2a study conducted by Columbia University, showed that TNX-1300 dropped plasma exposure to cocaine by 90 percent in two minutes and reversed the physiological effects of cocaine.

Common symptoms of cocaine intoxication include tachyarrhythmias and elevated blood pressure, either of which can be life-threatening.

Narcan® is available for opioid overdoses, but there is no FDA-approved product for cocaine overdose. TNX-1300 was granted Breakthrough Therapy designation by the FDA.

Other Key Pipeline Candidates[1]

TNX-2900 for treating Prader-Willi Syndrome (Orphan Drug designation) and, **TNX-1500** for prevention of organ transplant rejection and treatment of autoimmune diseases.

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

Summary

- **A potentially pivotal Phase 3 trial of TNX-102 SL is underway in fibromyalgia with results of an interim analysis due 2Q23.**
- **If topline results, expected in 4Q23, are positive it will be the second of two adequate and well-controlled Phase 3 trials required for filing for FDA approval.**
- **A Phase 2 trial of TNX-102 SL in fibromyalgia-type Long COVID is underway. If the trial is successful, it holds the hope of providing an alternative therapy for those who are increasingly turning to addictive opioids for relief in the absence of another solution.**
- **A Phase 2 trial of TNX-1900 in chronic migraine suffers is expected to report interim results in 4Q23.**
- **Two additional CNS programs (depression and cocaine intoxication) are expected to enter Phase 2 trials in 1Q23 and 2Q23, respectively.**
- **Work in infectious diseases continues in high gear, with a Phase 1 trial of a vaccine to protect against smallpox/mpox expected to begin in 2H23.**
- **At December 31, 2022 cash and cash equivalents stood at approximately $120 million.**

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