at a glance™

TONIX PHARMACEUTICALS

Recent &Upcoming: ***Positive data from preclinical challenge trial in non-human primates of T cell eliciting Covid-19 vaccine reported March 17; interim analysis of second TNX-102 SL Phase 3 study in fibromyalgia expected 3Q21 with topline data due before year end. Cash at December 31 was $77.1 million; $110 million raised in two 1Q21 financings.***

Key Considerations

•Tonix's two lead candidates are TNX-102 SL[1] for the treatment of fibromyalgia and TNX-1800[1], a live attenuated virus vaccine for Covid-19.

•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 -- its active ingredient, cyclobenzaprine, has no recognized addiction or dependency risk.

•In December 2020 Tonix reported that TNX-102 SL 5.6 mg successfully met its primary endpoint, significantly reducing fibromyalgia daily pain compared to placebo (p=0.01) in the RELIEF study, the first of two Phase 3 trials of TNX-102 SL 5.6 mg in fibromyalgia.

•A second Phase 3 trial, RALLY, (two are required for FDA registration) is currently enrolling with 50 percent of the planned number of participants having been randomized as of March 15, 2021. An interim analysis is scheduled to be performed in 3Q21. Topline data is expected 4Q21.

•The company's Covid-19 vaccine candidate, TNX-1800, is designed to elicit a T cell response to confer long-term immunity against SARS-CoV-2, the virus that causes Covid-19.

•Positive efficacy data from a CoV-2 challenge study in non-human primates was reported March 17, 2021.

•TNX-1800 is a second generation Covid-19 vaccine utilizing live virus technology. It holds the potential to offer long term T cell immunity with a single dose, prevent forward transmission, minimize cold chain requirements, and allow high density packaging (100 does per vial).

•In February Tonix announced plans to develop TNX-2100 which is expected to be a test to detect T cell immunity to the SARS-CoV-2 virus -- a potentially significant advance in monitoring public health and evaluating Covid-19 vaccine trial results. Tonix expects to initiate clinical trials in the second half of 2021, pending IND clearance from the FDA.

Tonix Pharmaceuticals Holding Corp.

(Nasdaq: TNXP)

Recent Price:	**$1.03**
Shares O/S:	**324 Million**
Approx. Mkt Cap:	**$334 Million**
Avg. Daily Volume:	**31.2 Million**
Fiscal Year Ends:	**Dec. 31**

Published: April 2021

About TNX-102 SL

TNX-102 SL is being developed by Tonix to treat chronic central nervous system (CNS) disorders in which poor sleep quality is a core symptom and believed to be involved in the disease process.

Its active ingredient is cyclobenzaprine, which is known to have high affinity binding and antagonist activity at four neuroreceptors associated with sleep regulation (5-HT2A, α1-adrenergic, H1-histaminergic, and M1-muscarinic acetylcholine receptors).

TNX-102 SL sublingual tablets contain 2.8 mg of cyclobenzaprine each. Two tablets for a total dose of 5.6 mg are being investigated for once-daily dosing at bedtime.

The pharmacokinetic profile of TNX-102 SL and its active metabolite is uniquely suitable for bedtime use and is different from the FDA-approved orally ingested cyclobenzaprine formulations. The two tablets are placed under the tongue, allowing the active ingredient to be transported through the oral mucosa directly into the blood stream, avoiding GI absorption and first-pass liver metabolism, thereby aligning the bioavailability and pharmacodynamic effects of the drug with the sleep cycle.

Tonix owns all the intellectual property rights to TNX-102 SL - no license fees or royalties are due to any third party. US patent protection is expected to extend through 2035.

Covid-19 Vaccines

With all the popular press publicity about Covid-19 vaccines, it may be hard for the average person to sort out who's on first, and why there are so many programs underway (more than 150+ at last count) to develop a Covid-19 vaccine.

The truth is, vaccine experts believe we will need more than one vaccine –in fact, many vaccines.

Most of the vaccine candidates currently in clinical trials share a common feature. Their main function is to elicit antibodies to fight the virus, but antibodies represent only a part of the immune response. As such they may provide only temporary immunity (generally 6 to 9 months). They may require multiple doses or booster shots for extended coverage, and they have not been shown to prevent contagion (forward transmission). Currently, three vaccines are approved under Emergency Use Authorization.

Accomplished & Upcoming

-3Q20 – Initiated second Ph. 3 study in fibromyalgia

-4Q20 – Reported positive Ph. 3 study results in fibromyalgia

-1Q21 – Positive topline non-human primate challenge study of Covid-19 vaccine reported

-3Q21 – Interim analysis second Ph. 3 study results in fibromyalgia

-2H21 – Initiate Ph. 1 study of TNX-1800 Covid-19 vaccine

-4Q21 – Topline data from Ph. 3 study in fibromyalgia

Vaccines designed to produce single dose long term immunity may require different technology. They need to engage the other part of the immune response – T cells. T cells attack virus-infected cells, and they are

known for their long-term memory. T cells remember what invading pathogens look like long after an initial encounter – often for years and in some cases a lifetime, as has been demonstrated with the T cell eliciting vaccines against measles, smallpox, and several other lethal pathogens.

T cell eliciting vaccines for other diseases have been proven to prevent contagion, or forward transmission, which is essential to prevent the on-going spread of any virus.

The time-tested way to elicit a predominately T cell response is with live attenuated virus technology. This technology is being used by Tonix in its Covid-19 vaccine candidates.

Tonix's lead candidate, TNX-1800, utilizes live attenuated horsepox virus technology that is very similar to that which Edward Jenner used more than 200 years ago to develop the smallpox vaccine. It can be made in large quantities on conventional vaccine manufacturing equipment.

Tonix has taken a lead in sponsoring research at prominent organizations (Southern Research and Columbia University) to better understand how the immune systems of naturally infected people respond to SARS-CoV-2, the virus that causes Covid-19. These studies will help blueprint the immune response and inform vaccine design.

The work at Columbia is intended to identify biomarkers that will enable the use of precision medicine techniques to customize vaccines to individuals for the most robust immune responses possible to SARS-CoV-2.

Preclinical trials of TNX-1800 are being conducted at Southern Research under a multi-phase collaborative agreement.

Positive topline data from a study of non-human primates challenged with live SAR-CoV-2 showed TNX-1800 protected upper and lower airways, suggesting an ability to block forward transmission. Human trials expected to start 2H21.

About Fibromyalgia

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.

Among those diagnosed, more than one-third have used prescription opioids as a means of fibromyalgia symptom management, despite opioids not having demonstrated efficacy as a treatment. TNX-102 SL is a non-opioid, centrally acting analgesic that could provide a new therapeutic option for fibromyalgia patients. There is no known cure for fibromyalgia.

Cymbalta® from Lilly and Lyrica® from Pfizer were the two blockbuster drugs, which through massive ad campaigns, became most instrumental in building the market for fibromyalgia drugs. Both are now off patent.

Patients continue to report dissatisfaction with available treatments which suggests a favorable market opportunity for new FDA-approved entries.

TNX-102 SL Ph. 3 in Fibromyalgia

On December 7, 2020, Tonix announced that TNX-102 SL successfully met its primary endpoint, significantly reducing fibromyalgia pain compared to placebo (p=0.01) in RELIEF, the first of two Phase 3 studies.

RELIEF was a 14-week randomized, double-blind, placebo-controlled trial of TNX-102-SL 5.6 mg (2 x 2.8 mg tablets) in which 503 patients with fibromyalgia were randomized in a 1:1 ratio across 39 US sites.

All participants received TNX-102 SL 2.8 mg or placebo for the first two weeks, which was increased to TNX-102 SL 5.6 mg or placebo for the remaining 12 weeks.

The study achieved statistical significance on the primary efficacy endpoint: change from baseline in the weekly average of daily diary pain severity numeric rating scale for TNX-102 SL 5.6 mg, analyzed by mixed model repeated measures with multiple imputation.

In making the announcement, Seth Lederman, MD, CEO of Tonix, said, "These results support the proposed mechanism in which TNX-102 SL targets disturbed sleep in fibromyalgia and that improved sleep quality leads to improvement of fibromyalgia at the syndromal level.

"TNX-102 SL has the potential to be a new non-addictive, non-opiate analgesic for the management of fibromyalgia which is particularly important given that fibromyalgia is a chronic pain condition. Approximately one-third of fibromyalgia patients resort to opiates in desperation and because of dissatisfaction with available therapies.

"Cyclobenzaprine, the active ingredient of TNX-102 SL has no recognized potential for addiction. Based on our discussions with the FDA, we expect to submit an NDA without further addiction liability studies."

In 3Q20, Tonix began enrolling participants in RALLY, the second of two planned trails required by the FDA for the filing of a New Drug Application (NDA) for marketing approval. The study design is very similar to the first Phase 3 study with the exception of targeting to enroll 200 more participants. Interim analysis* results of RALLY are expected 3Q21, with final topline data anticipated 4Q21. Based on long term safety exposure data already collected, the mature stage of TNX-102 SL's GMP manufacturing processes and the established product stability at 36 months, the company expects, assuming positive results from the currently enrolling RALLY study, to be able to submit an NDA for TNX-102 SL for fibromyalgia to the FDA in 2022.

**Pending submission and agreement from FDA on statistical analysis plan.*

Other Pipeline Candidates[1]

TNX-102 SL for PTSD, for agitation in Alzheimer's disease (granted Fast Track designation by FDA) and for alcohol use disorder, **TNX-801** for prevention of smallpox, **TNX-2300** for prevention of Covid-19, **TNX-601 CR** for depression, **TNX-1300** for cocaine intoxication/overdose (Breakthrough Therapy designation), **TNX-1600** for daytime treatment of PTSD, depression and ADHD, **TNX-1500** for prevention of organ transplant rejection and treatment of autoimmune diseases, **TNX-1700** for treatment of gastric and pancreatic cancers, **TNX-1900** for migraine and craniofacial pain, and **TNX-701** for protection from radiation injury.

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

Summary

- **Two key events are expected before year end 2021: (1) interim analysis of the RALLY second Ph. 3 study of TNX-102 SL in fibromyalgia in 3Q21 – first Ph. 3 study (RELIEF) met its primary endpoint (p=0.01); and (2) topline results from RALLY Ph. 3 study in 4Q21.**
- **Positive topline results of TNX-1800 Covid-19 vaccine in non-human primates challenged with live SARS-CoV-2 were reported March 17. Ph. 1 human trials expected to start 2H21.**
- **Tonix-sponsored research at Southern Research and Columbia University is expected to yield critical information for guiding the design of Covid-19 vaccines and therapeutics.**
- **At December 31, 2020, cash and cash equivalents stood at $77.1 million. Two 1Q21 common stock offerings raised gross proceeds of $110 million.**

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