at a glance™

TONIX PHARMACEUTICALS

Upcoming: ***Interim analysis of TNX-102 SL Phase 3 study in fibromyalgia expected in September with topline data due before year end; key data from preclinical trial of lead T cell eliciting Covid-19 vaccine candidate due 4Q20, including results of challenge study in non-human primates. Cash at June 30 was $55 million – additional $12 raised after the quarter's close.***

Key Considerations

- **Tonix's two lead candidates are TNX-102 SL* for the treatment of fibromyalgia and TNX-1800*, a live attenuated virus vaccine for Covid-19.**
- **TNX-102 SL is a non-opioid, centrally acting 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.**
- **It is currently in a pivotal Phase 3 registration trial in fibromyalgia. An interim analysis is scheduled to be performed in September. Topline data is expected 4Q20.**
- **Tonix's previous clinical trials with TNX-102 SL served to optimize the dose, patient enrollment criteria, and endpoints for the current Phase 3 study in fibromyalgia - *see TNX-102 SL Clinical Strategy*.**
- **The company's Covid-19 vaccine candidate, TNX-1800, is designed to potentially elicit a strong T cell response to confer long-term immunity against SARS-CoV-2, the virus that causes Covid-19. Non-human primate data from a trial at Southern Research is expected 4Q20.**
- **TNX-1800's design differs from most of the other announced Covid-19 vaccine programs which utilize vaccine technologies designed mainly to confer temporary immunity – their biggest advantage being a much quicker path to approval.**
- **Tonix reported $55 million cash and cash equivalents as of June 30, 2020. An additional $12 million was raised after the close of the quarter.**

Tonix Pharmaceuticals Holding Corp.
(Nasdaq: TNXP)

Recent Price:	**$0.84**
Shares O/S:	**130 Million**
Approx. Mkt Cap:	**$109 Million**
Fiscal Year Ends:	**Dec. 31**

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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 a high affinity for three brain receptors associated with sleep quality.

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 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 and aligning the bioavailability 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 extends 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. As such they will provide only temporary immunity (generally 6 to 9 months). They will require multiple doses for extended coverage, and they have not been shown to prevent contagion. The good news: they potentially can be approved and available relatively quickly.

Vaccines designed to produce single dose long term immunity require different technology. They need to elicit predominately T cells which are known for their long-term memories. They 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.

Accomplished & Upcoming

-4Q19 – Initiated Phase 3 study in fibromyalgia

-4Q19 – Expanded pipeline to include major depressive disorder and alcohol use disorder

-2H20 – Expanded pipeline with acquisition of migraine and pain programs

-3Q20 – Interim results Phase 3 fibromyalgia (Sept)

-4Q20 – Topline Phase 3 in fibromyalgia anticipated

-4Q20 – Preclinical data expected on lead Covid-19 vaccine

T cell eliciting vaccines for other diseases have been proven to prevent contagion, or forward expression, which is mandatory 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 in being used by Tonix in all five of its Covid-19 vaccine candidates and by one other US company – Merck, a world leader in vaccines.

TNX-102 SL Clinical Strategy

Tonix conducted two earlier Phase 3 clinical trials of TNX-102 SL in fibromyalgia and PTSD. Neither met their primary endpoints but both showed strong activity on the primary analyses as well as multiple key secondary endpoints.

The failed outcome in fibromyalgia is believed to be due to the selection of a low dose and a surprising imbalance in patient dropouts.

The prior Phase 3 trial narrowly missed the 30 percent responder primary endpoint analysis at Week 12 ($p = 0.095$), one of several primary endpoints that could have been selected.

A retrospective analysis, however, showed that patients experienced a nominal benefit ($p = .005$) as measured by average pain improvement at Week 12 using the numerical rating scale (NRS), as analyzed by the statistical method MMRM with MI (Mixed Model Repeated Measures-with Multiple Imputation). This type of analysis is believed to be equally acceptable to the FDA, had it been prespecified. In this Phase 3 trial TNX-102 SL was studied at a single 2.8 mg tablet, which is a low dose.

In the currently on-going fibromyalgia Phase 3 study, the TNX-102 SL dose has been doubled to 5.6 mg (two 2.8 mg tablets daily at bedtime), and the primary endpoint was changed to average pain improvement after 12 weeks of treatment using the NRS, as analyzed by MMRM with MI.

The registration of TNX-102 SL 5.6 mg for the fibromyalgia indication is expected to be supported by the long-term safety exposure from the PTSD program for TNX-102 SL 5.6 mg.

Tonix's lead candidate, TNX-1800, utilizes live attenuated horsepox virus technology that is very similar to what Edward Jenner used more than 200 years ago to develop the smallpox vaccine. It can be easily manufactured at scale on conventional cell culturing systems

Preclinical trials of TNX-1800 are being conducted at Southern Research under a multi-phase collaborative agreement. Topline data in small animal and non-human primates (including a virus-challenged cohort) is expected 4Q20, potentially setting the stage for human trials in 2021.

Tonix has taken a lead in sponsoring research at several prominent organizations (Southern Research, Kansas State University, 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 to be more effective.

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.

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 Phase 3 in Fibromyalgia

On December 10, 2019, Tonix enrolled the first patient in the Phase 3 RELIEF study of TNX-102 SL for the management of fibromyalgia.

In July, Tonix completed enrollment of RELIEF with approximately 470 patients randomized 1:1 to TNX- 102 SL or placebo at roughly 40 US sites.

Patients in the TNX-102 SL arm are treated with two 2.8 mg tablets (5.6 mg total) daily at bedtime, which is twice the dose studied in the earlier Phase 3 study.

An interim analysis of RELIEF by an Independent Data Monitoring Committee (IDMC) is expected to be completed this September based on unblinded results from approximately 50 percent of enrolled patients. The four possible IDMC recommendations are: (1) stop the study for success; (2) continue the study as planned; (3) continue to enroll with a specified increase in the total number of participants in the full study; or (4) stop the study for futility. Topline results from the full study are anticipated in 4Q20.

The primary endpoint is weekly average daily diary pain severity score change from baseline after 12 weeks of treatment using the 5.6 mg dose, analyzed by MMRM with MI.

Other Pipeline Candidates*

TNX-102 SL for agitation associated with 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 for depression, **TNX-1300** for cocaine intoxication/overdose (Breakthrough Therapy designation), **TNX-1600** for daytime treatment of PTSD, **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.

** All of Tonix's product candidates are investigational new drugs or biologics and have not been approved for any indication.*

Summary

- **Three key events are expected before year end 2020: (1) interim analysis of Ph 3 study of TNX-102 SL in fibromyalgia in September; (2) topline results from the same Ph 3 study in 4Q; and (3) pre-clinical results in 4Q of TNX-1800 Covid-19 vaccine in small animals and non-human primates, including SARS-CoV-2 challenged non-human primates.**
- **Tonix-sponsored research at Southern Research, Columbia University, and Kansas State University is expected to yield critical information for guiding the design of Covid-19 vaccines and therapeutics.**
- **At June 30, 2020, cash and cash equivalents stood at $55 million. $12 million was raised after the quarter close.**

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