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Tonix Pharmaceuticals Holding Corp. (TNXP-NASDAQ)

TNXP: Phase 2 Trial of TNX-601 ER Enrolling; New Treatment Concept in Depression…

Based on our probability adjusted DCF model that takes into account potential future revenues from the company's CNS, immunology, and biodefense programs, TNXP is valued at $6.50/share. This model is highly dependent upon continued clinical success of the company's assets and will be adjusted accordingly based upon future clinical results.

Current Price (05/01/23)	$0.52
Valuation	**$6.50**

OUTLOOK

On March 16, 2023, Tonix Pharmaceuticals Holding Corp. (TNXP) announced the initiation of the Phase 2 UPLIFT trial of TNX-601 ER for the treatment of major depressive disorder (MDD). TNX-601 ER (tianeptine hemioxalate extended-release tablet) is a once-daily tablet that is bioequivalent to three-times-daily tianeptine sodium immediate release, which has been available in Europe, Asia, and Latin America for >30 years. We anticipate a planned interim analysis for the trial in the fourth quarter of 2023.

Looking ahead, we anticipate topline results for the Phase 2 PREVAIL trial in the third quarter of 2023 and topline results for the Phase 3 RESILIENT study and the Phase 2 PREVENTION study in the fourth quarter of 2023.

SUMMARY DATA

52-Week High	**$4.89**
52-Week Low	**$0.29**
One-Year Return (%)	**-88.84**
Beta	**2.17**
Average Daily Volume (sh)	**664,107**
Shares Outstanding (mil)	**63**
Market Capitalization ($mil)	**$33**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**10**
Insider Ownership (%)	**2**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**N/A**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2018 Estimate	**-0.3**
P/E using 2019 Estimate	**-0.4**

Risk Level	**High**
Type of Stock	**Small-Value**
Industry	**Med-Drugs**

ZACKS ESTIMATES

Revenue
(In millions of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2022	0 A	0 A	0 A	0 A	0 A
2023	0 E	0 E	0 E	0 E	0 E
2024					0 E
2025					0 E

Earnings per Share

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2022	-$1.60 A	-$1.22 A	-$0.69 A	-$0.56 A	-$3.27 A
2023	-$0.40 E	-$0.39 E	-$0.38 E	-$0.37 E	-$1.53 E
2024					-$1.26 E
2025					-$1.10 E

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WHAT'S NEW

Business Update

Phase 2 Trial of TNX-601 ER Initiates; Planned Interim Analysis Likely in 4Q23

On March 16, 2023, Tonix Pharmaceuticals Holding Corp. (TNXP) announced the initiation of the Phase 2 UPLIFT study of TNX-601 ER (tianeptine hemioxalate extended-release tablet) for the treatment of major depressive disorder (MDD). The double blind, placebo controlled trial is expected to enroll approximately 300 participants at approximately 30 trial sites across the U.S. (NCT05686408). All participants will have a DSM-5 diagnosis of major depression and a duration for the current major depressive episode of at least 12 weeks. The primary efficacy endpoint is the mean change from baseline in the Montgomery-Asberg Depression Rating Scale (MADRS) total score at Week 6. An interim analysis is expected after 50% of enrolled patients have completed the study for the purpose of potential sample size re-estimation. We expect results from the interim analysis in the fourth quarter of 2023.

TNX-601 ER is a once-daily formulation of tianeptine that is designed to be bioequivalent to the three-times-a-day formulation of tianeptine sodium immediate release tablets that have been available in Europe, Asia, and Latin America for >30 years. The FDA has never approved a tianeptine-containing product in the U.S. and there is no once-daily tianeptine product available in any jurisdiction.

In contrast to currently available MDD treatments that are designed to modify neurotransmitter levels, tianeptine exerts direct restorative plastogenic effects on neurons and glial cells and in animal models the compound also reverses stress-induced impairments in synaptic glutamate neurotransmission while restoring hippocampal neurogenesis (McEwen *et al*., 2010). The efficacy of tianeptine sodium IR is comparable to selective serotonin reuptake inhibitors (SSRIs) or tricyclic antidepressants (Jeon *et al*., 2014; Emsley *et al*., 2018). This efficacy is accompanied with a lower overall incidence of sexual dysfunction, sedation, weight gain, or cognitive impairment compared to traditional antidepressants (Bonierbale *et al*., 2003; Costa e Silva *et al*., 1997). Lastly, since tianeptine is not metabolized via the hepatic cytochrome P450 system, TNX-601 ER likely has a reduced risk of drug-drug interactions compared to currently marketed antidepressants in the U.S.

Phase 3 RESILIENT Topline Results Expected in 4Q23

Tonix is currently conducting the Phase 3 RESILIENT trial, which is a randomized, double blind, placebo controlled potentially pivotal study of TNX-102 SL 5.6 mg for the treatment of fibromyalgia. In December 2022, the company announced that the first 50% of participants had been enrolled. Recently, Tonix announced that it is eliminating the interim analysis of the RESILIENT trial to ensure that topline data will be available in the fourth quarter of 2023. The target enrollment remains at approximately 470 participants.

In December 2020, Tonix announced positive topline results for the Phase 3 RELIEF study of TNX-102 SL 5.6 mg (primary endpoint, P=0.010). Thus, since Tonix has already conducted one positive trial in fibromyalgia, positive results from the RESILIENT study could put the company in position to file a new drug application (NDA) for TNX-102 SL 5.6 mg for the treatment of fibromyalgia.

Topline Results for Phase 2 PREVENTION Study of TNX-1900 in 4Q23

In February 2023, Tonix announced the initiation of the Phase 2 PREVENTION study of potentiated intranasal oxytocin (TNX-1900) for the prevention of migraine headaches in chronic migraineurs. It is a double blind, randomized, multicenter, placebo controlled study with three arms: two treatment regimens of TNX-1900 and one of placebo in a 1:1:1 ratio in approximately 300 patients. After a four-week run-in phase to confirm chronic migraine criteria is met, the participants will be treated for 12 weeks followed by a two-week safety follow up. The primary efficacy endpoint is the 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. We anticipate approximately 150 participants being enrolled in the trial and topline results will be available in the fourth quarter of 2023.

Phase 2 Trial of TNX-1300 to Initiate in 3Q23

We anticipate that Tonix will initiate a Phase 2 clinical trial of TNX-1300, a double mutant cocaine esterase, for the treatment of cocaine intoxication in the third quarter of 2023. Tonix licensed the asset in May 2019 from Columbia University, which has Breakthrough Therapy Designation from the U.S. FDA.

TNX-1300 is a recombinant enzyme derived from the *cocE* gene of a *Rhodococcus* species that utilizes cocaine as a sole source of carbon and nitrogen (Bresler *et al*., 2000). The CocE enzyme was tested in a rat model of cocaine toxicity to determine if it could protect the animals from cocaine-induced lethality (Cooper *et al*., 2006). Results showed that it required a 1000 mg/kg dose of cocaine to overcome the protective effects of 1 mg CocE (LD_{50} for IP dose is 70 mg/kg cocaine).

One of the issues with the native CocE enzyme is that its half-life is only a few minutes at physiological temperature (37ºC) (Cooper *et al*., 2006). Thus, a study was performed to develop thermostable variants of CocE using a computational approach along with *in vitro* and *in vivo* studies (Gao *et al*., 2009). A variant was identified with two amino acid substitutions (T172R/G173Q) that resulted in increased stability at 37ºC.

The double mutant CocE enzyme (then called RBP-8000, now TNX-1300) was evaluated in a Phase 2 clinical trial conducted by Reckitt Benckiser Pharmaceuticals, the previous licensee to the product (NCT01846481). It was a double blind, placebo controlled, randomized, four-sequence, two-period cross-over study. Subjects were non-treatment seekers with a DSM-IV diagnosis of cocaine abuse. During the study period, subjects were given an IV infusion of 50 mg of cocaine over 10 minutes followed by TNX-1300 (100 mg or 200 mg) or matching placebo one minute after completion of the cocaine infusion. Outcomes included pharmacokinetics of both cocaine and TNX-1300 along with any effect by TNX-1300 on cocaine-induced physiological changes (Nasser *et al*., 2014).

A total of 29 subjects were randomized in the trial. Safety results showed that no anti-TNX-1300 antibodies were detected in any of the subjects at any time point. In addition, there were no clinically significant abnormalities in vital signs, clinical laboratory markers, or physical examinations. A total of seven subjects reported treatment-emergent adverse events that were considered related to treatment with any study drug, with most being assessed as mild in severity. Of note, vital signs of subjects treated with TNX-1300 returned to or below baseline earlier than subjects that received placebo.

Plasma cocaine rapidly decreased following administration of TNX-1300, with a 90% drop of peak plasma cocaine concentrations within two minutes and a 95% decline in plasma cocaine exposure. The 200 mg dose of TNX-1300 produced a longer-lasting effect on cocaine pharmacokinetics compared to the 100 mg dose. These preliminary results fully support the continued develop of TNX-1300 as a treatment for cocaine intoxication.

Phase 2 PREVAIL Trial Results in 3Q23

In August 2022, Tonix announced the initiation of the PREVAIL Phase 2 clinical trial of TNX-102 SL in patients with Long COVID (NCT05472090), a heterogeneous condition that involves nociplastic pain following infection with and recovery from SARS-CoV-2, the virus that causes COVID-19 (Bierle *et al*., 2021). It is a 14-week, double blind, randomized, multicenter, placebo controlled trial to evaluate the efficacy and safety of TNX-102 SL in patients with multi-site pain associated with post-acute SARS-CoV-2 infection (PASC). The company has discontinued enrollment and the approximately 60 patients enrolled to date will be followed to completion, with topline data expected in the third quarter of 2023. The data from this study will be used to guide future development and support grant applications.

In February 2023, Tonix participated in a virtual event titled, “Long COVID: What Will it Take to Accelerate Therapeutic Progress?”. The company presented emerging research describing the role of infections in triggering fibromyalgia or chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) and other fibromyalgia-like illnesses. Symptoms of Long COVID, such as multi-site pain, fatigue, and insomnia, are the hallmarks of chronic pain syndromes like CFS/ME.

In September 2022, Tonix announced the presentation of a retrospective observational study from approximately 75 million patients from a network of inpatient and outpatient electronic medical records from 48 U.S. healthcare organizations at the 2022 World Congress on Pain. The results showed that of 1 million patients diagnosed with COVID, approximately 52,000 had Long COVID symptoms that lasted between 3 and 6 months. In addition, of the patients with Long COVID, 41% had multi-site pain. These patients took a variety of medications, including benzodiazepines, opioids, and antidepressants. The rate of opioid use was 50% for patients that had multi-site pain and insomnia, with or without fatigue. This is especially concerning since approximately 25% of patients prescribed

opioids long term will struggle with opioid addiction (U.S. Department of Labor). The results of this study clearly show that there is a large patient population suffering from Long COVID that need additional treatment options.

Phase 1 Trial of TNX-1500 to Initiate in 3Q23

TNX-1500 is a third-generation anti-CD40 ligand (CD40L) monoclonal antibody (mAb) that is being developed for the prevention of allograft rejection, xenotransplantation, and the treatment of autoimmune disease. The CD40/CD40L signaling pathway is involved in the activation of both the innate and adaptive immune response. CD40 is predominantly expressed on antigen presenting cells (APCs) and delivers intracellular activating signals. CD40L, which does not contain any signaling capacity, is found on multiple cell types, including T cells, B cells, natural killer (NK) cells, macrophages, and platelets (Schönbeck *et al*., 2001). The CD40/CD40L pathway is essential for humoral immune responses to T cell-dependent antigens (Lederman *et al*., 1992), the production of proinflammatory cytokines (Cella *et al*., 1996), and generating effective cytotoxic T cell responses (Liu *et al*., 2013).

Tonix recently announced two research collaborations to investigate TNX-1500 in preclinical studies:

- In February 2023, Tonix announced a sponsored research agreement with the University of Maryland, Baltimore (UMB) to study TNX-1500 for the prevention of rejection in heart xenograft transplantation in animals.
- In December 2022, Tonix announced a collaboration with Boston Children's Hospital to study TNX-1500 for the prevention of graft-versus-host disease (GvHD) after hematopoietic stem cell transplantation in animals.

Pending clearance of the IND, Tonix will be initiating a Phase 1 clinical trial of TNX-1500 in healthy volunteers evaluating single ascending doses of TNX-1500 and the assessment of pharmacokinetics and pharmacodynamics with a target indication of the prophylaxis of organ rejection in adult patients receiving a kidney transplant. We anticipate the trial initiating in the third quarter of 2023.

Financial Update

On March 13, 2023, Tonix announced financial results for the fourth quarter and full year 2022. As expected, the company did not report any revenues for the fourth quarter or full year 2022. Net loss available to stockholders for the fourth quarter of 2022 was $34.1 million, or $0.56 per share, compared to a net loss available to stockholders of $29.6 million, or $2.08 per share, for the fourth quarter of 2021. The weighted average common shares outstanding for the fourth quarter of 2022 were approximately 61.4 million compared to approximately 14.2 million for the fourth quarter of 2021.

R&D expenses for the fourth quarter of 2022 were $24.7 million, compared to $22.3 million for the fourth quarter of 2021. The increase was primarily due to increased employee-related, facility, and laboratory expenses. G&A expenses for the fourth quarter of 2022 were $8.1 million, compared to $7.3 million for the fourth quarter of 2021. The increase was primarily due to an increase in employee-related and financial reporting expenses.

For 2022, net loss available to stockholders was $116.9 million, or $3.27 per share, compared to a net loss available to stockholders of $92.3 million, or $8.10 per share, for 2021. The weighted average common shares outstanding for full year 2022 was approximately 35.7 million, compared to approximately 11.4 million for full year 2021. R&D expenses in 2022 were $81.9 million, compared to $68.8 million for 2021. The increase was primarily due to increased employee-related, facility, and laboratory expenses. G&A expenses for 2022 were $30.2 million, compared to $23.5 million for 2021. The increase was primarily due to increased employee-related and financial reporting expenses.

As of December 31, 2022, Tonix had approximately $120.2 million in cash and cash equivalents. As of March 13, 2023, Tonix had approximately 62.5 million shares outstanding and, when including outstanding options and warrants, a fully diluted share count of approximately 65.0 million.

Conclusion

Tonix has multiple inflection points coming up in 2023, with topline results for the Phase 2 PREVAIL trial expected in the third quarter of 2023 and topline results for the Phase 3 RESILIENT study and the Phase 2 PREVENTION study expected in the fourth quarter of 2023. In addition, we expect results from an interim analysis of the Phase 2 study of TNX-601 ER in the fourth quarter of 2023. We have advanced our model forward one year, which has resulted in a slight increase to our valuation to $6.50 per share.

PROJECTED FINANCIALS

Tonix Pharmaceuticals	2022 A	Q1 E	Q2 E	Q3 E	Q4 E	2023 E	2024 E	2025 E
TNX-102 SL (FM)	$0	$0	$0	$0	$0	$0	$0	$0
Research & Collaborations	$0	$0	$0	$0	$0	$0	$0	$0
Total Revenues	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
CoGS	$0.0	$0	$0	$0	$0	$0.0	$0.0	$0.0
Product Gross Margin	-	-	-	-	-	-	-	-
R&D	$81.9	$21.0	$22.0	$23.0	$24.0	$90.0	$95.0	$100.0
SG&A	$30.2	$8.0	$8.0	$8.0	$8.0	$32.0	$33.0	$34.0
Operating Income	($112.1)	($29.0)	($30.0)	($31.0)	($32.0)	($122.0)	($128.0)	($134.0)
Operating Margin	-	-	-	-	-	-	-	-
Interest & Other Income	$1.9	$1.0	$0.8	$0.6	$0.8	$3.2	$2.0	$2.0
Pre-Tax Income	($110.2)	($28.0)	($29.2)	($30.4)	($31.2)	($118.8)	($126.0)	($132.0)
Preferred Stock Deemed Dividend	$6.7	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Warrant Deemed Dividend	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Taxes & Other	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Net Income	($116.9)	($28.0)	($29.2)	($30.4)	($31.2)	($118.8)	($126.0)	($132.0)
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($3.27)**	**($0.40)**	**($0.39)**	**($0.38)**	**($0.37)**	**($1.53)**	**($1.26)**	**($1.10)**
YOY Growth	*56.7%*	-	-	-	-	*-81.3%*	*-84.6%*	*-31.3%*
Weighted Shares Outstanding	35.7	70.0	75.0	80.0	85.0	77.5	100.0	120.0

Source: Zacks Investment Research, Inc. *David Bautz, PhD*

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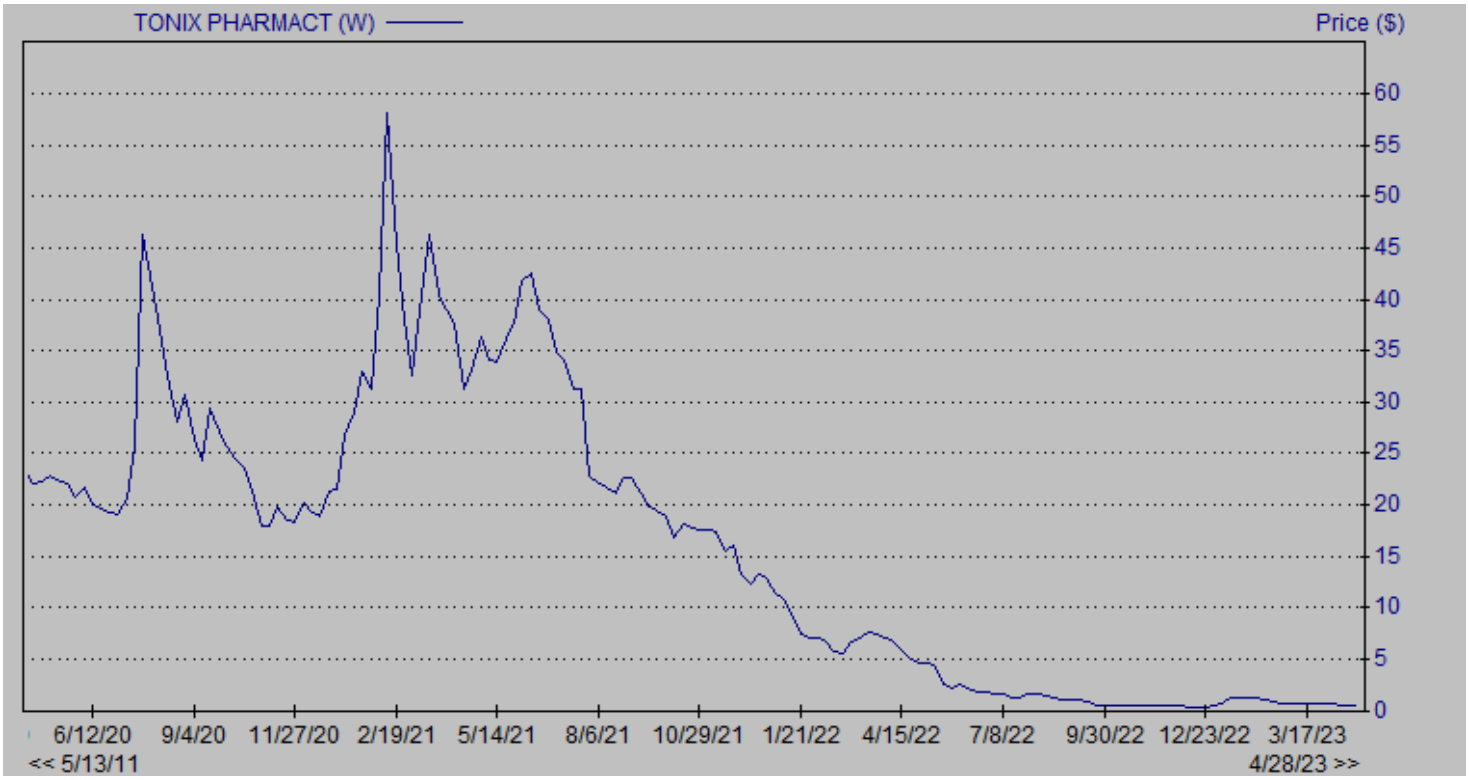
HISTORICAL STOCK PRICE



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