Zacks Small-Cap Research

May 12, 2016
David Bautz, PhD
312-265-9471
dbautz@zacks.com

scr.zacks.com
10 S. Riverside Plaza, Ste 1600, Chicago, IL 60606

Tonix Pharmaceuticals Holding Corp. (TNXP - NASDAQ)

TNXP: PTSD Data to be Reported in the Second Half of May 2016…

Based on our probability adjusted DCF model that takes into account potential future revenues from TNX-102 SL in fibromyalgia and PTSD, TNXP is valued at $10/share. This model is highly dependent upon continued clinical success of TNX-102 SL in both indications and will be adjusted accordingly based upon future clinical results.

Current Price (05/12/16)	$2.27
Valuation	**$10.00**

OUTLOOK

On May 9, 2016, Tonix Pharmaceuticals Holdings Corp. announced financial results for the first quarter of 2016 and provided a business update. Tonix had a net loss of $14.0 million, or $0.74 per share, in the first quarter of 2016. As of Mar. 31, 2016, the company had cash and cash equivalents of $27.5 million.

The company's main focus now is the two ongoing clinical trials with TNX-102 SL in fibromyalgia and PTSD. Data from the PTSD trial is expected in the second half of May 2016, while data from the fibromyalgia trial is expected in the third quarter of 2016. Positive data from one or both of these trials is likely to cause a significant revaluation of the company's shares.

SUMMARY DATA

52-Week High	**$10.72**
52-Week Low	**$1.85**
One-Year Return (%)	**-64.51**
Beta	**3.09**
Average Daily Volume (sh)	**171,103**
Shares Outstanding (mil)	**19**
Market Capitalization ($mil)	**$41**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**48**
Insider Ownership (%)	**10**
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 2015 Estimate	**N/A**
P/E using 2016 Estimate	**N/A**

Risk Level	**High**
Type of Stock	**Small-Growth**
Industry	**Med-Biomed/Gene**

ZACKS ESTIMATES

Revenue

(In millions of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2015	0 A	0 A	0 A	0 A	0 A
2016	0 A	0 E	0 E	0 E	0 E
2017					0 E
2018					0 E

Earnings per Share

(EPS is operating earnings before non recurring items)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2015	-$0.71 A	-$0.73 A	-$0.72 A	-$0.71 A	-$2.86 A
2016	-$0.74 A	-$0.57 E	-$0.52 E	-$0.47 E	-$2.30 E
2017					-$2.04 E
2018					-$2.00 E

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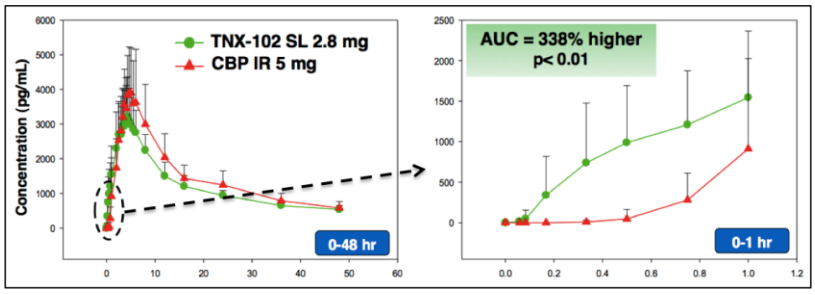
WHAT'S NEW

TNX-102 SL Update

Tonix's lead product, TNX-102 SL, is currently being tested in two clinical programs in fibromyalgia and post-traumatic stress disorder (PTSD). TNX-102 SL is a small, rapidly disintegrating tablet containing 2.8 mg of cyclobenzaprine (CBP) for sublingual administration and transmucosal absorption. CBP is the active ingredient of two products that are FDA approved in the U.S. for the treatment of muscle spasms. These products are sold as immediate-release tablets and extended-release capsules. The sublingual formulation has a differentiated pharmacokinetic profile from the oral immediate-release CBP tablet as exemplified by the following:

- TNX-102 SL rapidly delivers CBP across the mucosal membrane and into the plasma, resulting in 12X faster onset of absorption relative to the CBP immediate release tablet

- The plasma levels of CBP were 338% higher during the first hour and 83% higher during the first two hours following dosing with TNX-102 SL compared to the oral CBP tablet. The following figure shows the plasma level of CBP over 48 hours (below left) and a detailed look at the first hour after dosing showing a clear separation between TNX-102 SL and oral CBP.



Adapted from: Daugherty *et al.*, 2016

- The bioavailability of CBP is 154% higher with TNX-102 SL compared to the CBP tablet

- The most frequent adverse event reported thus far with TNX-102 SL was transient numbness in the oral cavity, which has been reported by 44% of the TNX-102 SL subjects. However, this typically resolved within 30-45 minutes.

These data clearly show how TNX-102 SL is differentiated from the currently available CBP products, which should help with physician and patient uptake upon approval of the drug.

Data from PTSD Trial Due in the Second Half of May 2016

Tonix is currently conducting a Phase 2 clinical trial (the AtEase Study) of TNX-102 SL in patients with military-related post-traumatic stress disorder (PTSD). The AtEase study is a randomized, double-blind, placebo-controlled trial to evaluate the efficacy and safety of TNX-102 SL in people with military-related PTSD and related conditions (NCT02277704). The three-arm trial enrolled over 240 participants, who were randomized to receive either 2.8 mg or 5.6 mg of TNX-102 SL or placebo taken sublingually at bedtime daily for 12 weeks. We are anticipating data in the second half of May 2016.

The rationale for developing TNX-102 SL as a treatment for PTSD is multi-faceted, and includes the following:

1) TNX-102 SL is a serotonin 2A and alpha-1 adrenergic receptor antagonist. In addition, it inhibits the reuptake of serotonin and norepinephrine. Paroxetine and sertraline, the only two compounds approved by the FDA to treat PTSD, are believed to exert their clinical benefit by blocking serotonin reuptake.

2) In the Phase 2b BESTFIT clinical trial of TNX-102 SL in fibromyalgia patients, there was a statistically significant improvement in all measures of sleep quality, including the Patient Reported Outcomes Measurement Information System (PROMIS) sleep instrument (P=0.004), the daily sleep diary (P<0.001), and the Fibromyalgia Impact Questionnaire-Revised (FIQ-R) sleep item (P<0.001). This could prove to be beneficial

for PTSD patients, as sleep disturbance is one of the most commonly cited symptoms of PTSD patients (DSM 5), sleep disturbance following a traumatic event is linked to the development of PTSD (Koren *et al*., 2002), and sleep disturbance has been linked to suicide ideation in those with PTSD (Betts *et al*., 2013).

3) CBP has potent antagonist activity against the 5-HT_{2A}, α_{1A}, and H_1 receptors (Daugherty *et al*., 2015). Trazodone, which is occasionally used off-label for sleep disturbance in PTSD (Warner *et al*., 2001), is a 5-HT_{2A} antagonist, however it's principle metabolite (mCPP) can also cause panic attacks and flashbacks in PTSD patients due to its 5-HT_{2C} agonist activity. Prazosin is a α_{1A} antagonist that is commonly used to treat nightmares and sleep disturbance in PTSD (Kung *et al*., 2012). Low-dose doxepin specifically blocks the H_1 receptor and is effective at treating insomnia, a common symptom of PTSD (Goforth *et al*., 2009).

The primary endpoint of the AtEase trial is the week twelve mean change from baseline in the total CAPS-5 (Clinician-Administered PTSD Scale) score in participants who received 2.8 mg of TNX-102 SL as compared to those who received placebo only. Safety will also be evaluated. The CAPS is a structured interview designed to make a categorical PTSD diagnosis and is considered the "gold standard" in PTSD assessment and corresponds to the DSM-5 (the latest edition of the Diagnostic and Statistical Manual of Mental Disorders) diagnosis for PTSD. The assessor combines information on frequency and intensity of an item into a single severity rating (0-4) for the 20 DSM-5 PTSD symptoms, thus patients are assigned a score with a maximum of 80 points possible. A higher score corresponds to more severe PTSD and patients are categorized as follows:

CAPS-5 Score	Category
0 – 10	asymptomatic/few symptoms
11 – 22	mild PTSD/subthreshold
23 – 34	moderate PTSD/threshold (moderate dx cutoff of 25 is a few points into the moderate range)
35 – 46	severe PTSD (stringent dx cutoff of 37 is a few points into the severe range)
47 +	extreme PTSD

Tonix's Phase 2 study is 80% powered to detect an effect size of 0.5, which translates to approximately a 10 point difference in total CAPS-5 score at the group level between subjects taking 2.8 mg TNX-102 SL and placebo.

We feel its important for investors to understand that even if the trial does not hit statistical significance that does not mean it was a failure. A trend toward significance would be incredibly important and something that would certainly justify continuing the program. The reason for this is the AtEase study could be considered a "proof-of-concept" study as there was no prior data to use in order to make the proper powering assumptions in terms of number of patients necessary to see a statistically significant difference. A trend toward significance would allow for proper powering assumptions in future studies and the opportunity to apply for accelerated approval from the FDA (only one pivotal study necessary for approval) along with breakthrough designation due to the fact there are no treatments currently available for military related PTSD. In addition to lowering CAPS-5 score, positive treatment outcomes could also be represented by moving from a more severe to less severe CAPS-5 category (i.e., from severe PTSD to moderate PTSD) and/or a loss of diagnostic status (as mentioned above, patients must have a requisite number of symptoms in each of four sets of symptom categories, thus not meeting PTSD diagnosis anymore if any category falls under that number).

Conversely, if the study does hit statistical significance it is even possible that the company could approach the FDA to request the AtEase study be the basis for approval. However, we will have to wait and see what the data shows before we know more about the next steps in the PTSD program.

Data from AFFIRM Trial of Tonmya™ in Fibromyalgia to be Reported in the Third Quarter of 2016

On June 17, 2015, Tonix announced the FDA has conditionally accepted the trade name Tonmya™ for TNX-102 SL for the treatment of fibromyalgia. Tonix is currently conducting the Phase 3 AFFIRM trial (NCT02436096). The trial is a randomized, double-blind, placebo-controlled 12-week safety and efficacy study that is expected to enroll approximately 500 fibromyalgia (FM) patients. The patients will be given either a 2.8 mg Tonmya™ tablet or placebo at bedtime in a 1:1 randomization. The trial is taking place at 35 sites in the U.S. We anticipate topline results in the third quarter of 2016.

Tonix is using a 30% responder analysis for the primary outcome measure in the AFFIRM study. The 30% responder analysis is defined as an improvement in pain, as measured by the number of subjects who achieve at

least a 30% improvement in their pain scores. A 30% improvement is considered moderate or clinically significant response. For example, if pain is rated on a numeric rating scale of 0 to 10, with 10 being the highest, a patient with a baseline pain score of 6 that is reduced to 4 at the end of the treatment period would have experienced a ~33% reduction in pain. This patient would count towards the primary endpoint. However, a patient with a baseline of 8 reduced to 6 at the end of the study would only have seen a 25% reduction in pain and thus not counted as a responder towards the primary endpoint.

Tonix elected to use the 30% responder analysis for the planned Phase 3 trial because this endpoint demonstrated a statistically significant separation from the placebo group in the Phase 2b BESTFIT study. A 30% responder analysis was a pre-specified secondary outcome measure of BESTFIT. As a reminder, in late September 2014, Tonix announced top-line results for the Phase 2b BESTFIT trial. The study did not achieve statistical significance in the primary efficacy endpoint of change in average daily pain score at week 12 (p=0.086 by mixed-effect model repeated measure analysis, p=0.172 by jump-to-control, multiple imputation analysis).

However, the study demonstrated that TNX-102 SL had a statistically significant effect on pain as measured by a 30% responder analysis of the primary pain data (*P* =0.033). The 30% response rate in the final analysis was 34.0% in the active treatment arm as compared to 20.6% in the control arm. Based on inputting the 30% responder data from BESTFIT into our powering-calculator, we believe AFFIRM is approximately 90% powered to succeed (*P*<0.05).

There is the potential, albeit very small, that with strong results from the AFFIRM trial the company can package an application to the U.S. FDA using both BESTFIT and the new data on 30% responder analysis from AFFIRM. However, we view this as unlikely. Since results from two Phase 3 clinical trials will most likely be necessary to gain approval, the company will be initiating a second Phase 3 program for Tonmya™ in FM in the second quarter of 2016.

Financial Update

On May 9, 2016, Tonix Pharmaceutical Holdings Corp. (TNXP) announced financial results for the first quarter of 2016. As expected, the company did not report any revenues. Net loss for the first quarter of 2016 was $14.0 million, or $0.74 per share, and was comprised of $10.7 million in R&D expenses and $3.3 million in G&A expenses. This also included $0.9 in non-cash, share-based compensation. Actual cash burn during the first quarter was $10.8 million.

As of Mar. 31, 2016, Tonix had cash and cash equivalents of $27.5 million. We anticipate this will be sufficient to fund operations for at least the next 12 months, as cash burn should be reduced in 2016 compared to 2015 due to the discontinuation of the TNX-201 program and the bulk manufacturing of the Phase 3 TNX-102 SL drug product completed. On April 28, 2016, the company entered into an agreement with Cowen and Company, LLC in which Tonix can sell up to $15 million worth of stock in an at-the-market offering. The agreement will remain in effect until all shares have been sold, unless it is terminated early.

Conclusion and Valuation

The U.S. PTSD population is estimated to be 8 million in size. We believe approximately 25% of these cases are associated with military service, about half of which seek medical treatment for the disease. This puts the U.S. military-associated PTSD population at around 1 million. Assuming a cost of $15 per day and 5% market penetration, we believe TNX-102 SL could have peak sales in PTSD of around $450 million in 2026. We assign a probability of 15% for approval of TNX-102 SL in PTSD based on the historic difficulty in treating PTSD patients and the earlier-stage nature of the program.

For fibromyalgia, our model estimates that an NDA will be filed in 2018 after completion of two Phase 3 studies; the AFFIRM trial and the trial that will initiate in the second quarter of 2016. This would lead to approval and first sales in 2019. Of the 5 million Americans with fibromyalgia (NIAMS/NIH, November 2014), approximately 50% are diagnosed, which represents approximately 2.5 million U.S. adults. Of those diagnosed, 85% receive treatment (Robinson *et al*., 2012), thus making the target population approximately 2.1 million individuals in 2015. We estimate peak market share of 5%, which represents approximately 125,000 patients and close to $775 million in peak sales.

Based on a probability adjusted discounted cash flow analysis, we believe the shares are worth $10. However, positive data from one or both of the ongoing clinical trials is likely to cause a significant revaluation of the shares.

PROJECTED FINANCIALS

Tonix Pharmaceuticals Holding Corp.
Income Statement

Tonix Pharmaceuticals	2015 A	Q1 A	Q2 E	Q3 E	Q4 E	2016 E	2017 E	2018 E
TNX-102 SL (FM)	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	-
TNX-102 SL (PTSD)	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	-
Research & Collaborations	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
YOY Growth	-	-	-	-	-	-	-	-
Total Revenues	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
YOY Growth	-	-	-	-	-	-	-	-
CoGS	$0	$0	$0	$0	$0	$0.0	$0.0	$0.0
Product Gross Margin	-	-	-	-	-	-	-	-
R&D	$35.5	$10.7	$8.0	$7.0	$6.0	$31.7	$34.0	$37.0
SG&A	$12.7	$3.3	$2.9	$3.0	$3.0	$12.2	$13.0	$15.0
Operating Income	($48.2)	($14.0)	($10.9)	($10.0)	($9.0)	($43.9)	($47.0)	($52.0)
Operating Margin	-	-	-	-	-	-	-	-
Interest & Other Income	$0.1	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Pre-Tax Income	($48.1)	($14.0)	($10.9)	($9.9)	($9.0)	($43.9)	($47.0)	($52.0)
Taxes & Other	$0	$0	$0	$0	$0	$0	$0	$0
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Net Income	($48.1)	($14.0)	($10.9)	($9.9)	($9.0)	($43.9)	($47.0)	($52.0)
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($2.86)**	**($0.74)**	**($0.57)**	**($0.52)**	**($0.47)**	**($2.30)**	**($2.04)**	**($2.00)**
YOY Growth	*3.5%*	-	-	-	-	*-19.8%*	*-11.0%*	*-2.1%*
Weighted Shares Outstanding	16.8	18.9	19.1	19.2	19.3	19.1	23.0	26.0

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

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WEEKLY PRICE CHART



Source: Stockcharts.com

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