Zacks Small-Cap Research

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Tonix Pharmaceuticals Holding Corp. (TNXP-NASDAQ)

TNXP: Topline Results From AFFIRM Study in Fibromyalgia in September 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 $12/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 (08/23/16)	$2.72
Valuation	**$10.00**

OUTLOOK

On August 8, 2016, Tonix Pharmaceuticals Holding Corp. (TNXP) announced financial results for the second quarter of 2016. Net loss for the quarter was $9.8 million, or $0.50 per share, compared to $11.8 million, or $0.73 per share, for the second quarter of 2015. The company exited the quarter with $31.2 million in cash, cash equivalents, and marketable securities, which we believe is enough to fund operations for at least the next 12 months.

The company will be reporting topline results from the AFFIRM study of TNX-102 SL in fibromyalgia patients in September 2016. A second Phase 3 study of TNX-102 SL in fibromyalgia patients was recently initiated. A Phase 3 study of TNX-102 SL in patients with post-traumatic stress disorder (PTSD) is likely to get underway in the first quarter of 2017.

SUMMARY DATA

52-Week High	**$7.79**
52-Week Low	**$1.94**
One-Year Return (%)	**-56.13**
Beta	**2.65**
Average Daily Volume (sh)	**378,303**
Shares Outstanding (mil)	**26**
Market Capitalization ($mil)	**$70**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**34**
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 2016 Estimate	**N/A**
P/E using 2017 Estimate	**N/A**

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)
2015	0 A	0 A	0 A	0 A	0 A
2016	0 A	0 A	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	-$0.50 A	-$0.39 E	-$0.35 E	-$1.89 E
2017					-$1.68 E
2018					-$1.73 E

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WHAT'S NEW

Financial Update

On August 8, 2016, Tonix Pharmaceutical Holdings Corp. (TNXP) announced financial results for the second quarter of 2016. As expected, the company did not report any revenues. Net loss for the first quarter of 2016 was $9.8 million, or $0.50 per share, and was comprised of $7.5 million in R&D expenses and $2.3 million in G&A expenses. Actual cash burn during the first quarter was $5.3 million.

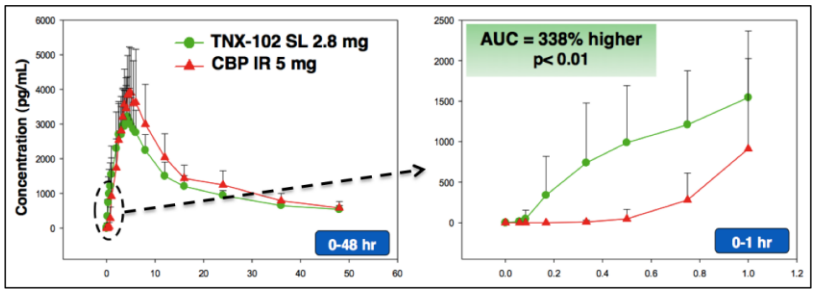
As of June 30, 2016, Tonix had cash and cash equivalents of $31.2 million. On June 20, 2016, the company announced the closing of a $10 million public offering of 5 million shares of common stock sold at $2.00 per share. The financing was led by healthcare focused institutional investors. We anticipate this will be sufficient to fund operations for at least the next 12 months, as cash burn should continue to 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 is completed.

TNX-102 SL Update

Tonix's lead product, TNX-102 SL, is currently being developed for the treatment of two conditions: 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 50% of the TNX-102 SL subjects. However, this 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 AFFIRM Trial of Tonmya™ in Fibromyalgia to be Reported in September 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 recently completed the clinical phase of the Phase 3 AFFIRM trial (NCT02436096) and we anticipate topline results from the study to be announced in September. The trial is a

randomized, double-blind, placebo-controlled 12-week safety and efficacy study that enrolled approximately 500 fibromyalgia patients. The patients were given either a 2.8 mg Tonmya™ tablet or placebo at bedtime in a 1:1 randomization.

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 initiated a second Phase 3 program for Tonmya™ in fibromyalgia in July 2016. The RE-AFFIRM trial is a randomized, double blind, placebo controlled study similar in design to the AFFIRM trial and is expected to also enroll approximately 500 fibromyalgia patients (NCT02829814).

Positive Results Reported for TNX-102 SL in PTSD

In addition to fibromyalgia, Tonix is also developing TNX-102 SL as a treatment for PTSD. The AtEase study was a Phase 2 randomized, double blind, placebo controlled trial of TNX-102 SL in patients with military-related PTSD (NCT02277704). The three-arm trial enrolled 231 participants, who were randomized to receive either 2.8 mg of TNX-102 SL (n=90), 5.6 mg of TNX-102 SL (n=49), or placebo (n=92) taken sublingually at bedtime daily for 12 weeks. The primary endpoint of the trial was the week twelve mean change from baseline in the total CAPS-5 (Clinician-Administered PTSD Scale) score in participants who received TNX-102 SL as compared to those who received placebo. Safety was also evaluated. The CAPS is a structured interview designed to make a categorical PTSD diagnosis and provide a total PTSD symptom severity score, and is considered the “gold standard” in PTSD assessment and corresponds to the DSM-5 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

The following table gives results for various parameters of the AtEase study. The results showed that the 5.6 mg dose had a statistically significant effect on total CAPS-5 by two statistical analyses, mixed model repeated measures (MMRM) with multiple imputation (*P*=0.031) and ANCOVA (*P*=0.038). In addition, there was a statistically significant effect for various items that go into the CAPS-5 score, including the Sleep E6 item (*P*=0.010), the

Arousal and Reactivity criteria cluster (*P*=0.048), and Startle E4 item (*P*=0.015). The fact that the Arousal and Reactivity criteria cluster was significant is very important, as this set of symptoms has been notoriously difficult to treat in PTSD patients. The 5.6 mg dose was also statistically significant for the Clinician Global Impression-Improvement (CGI-I; *P*=0.041) and the Patient Global Impression of Change (PGIC; P=0.035). Lastly, the percentage of those who finished the trial were 73% on placebo, 79% on 2.8 mg of TNX-102 SL, and 84% on 5.6 mg of TNX-102 SL. The fact that the highest retention rate was in the 5.6 mg dosage group potentially alludes to the clinical efficacy seen with that dose and the fact that the drug was well tolerated. In addition, attaining statistically significant results with a patient population of only 49 individuals means there was a substantial effect size for TNX-102 SL at the 5.6 mg dose. Thus, fewer patients will be required for properly powering Phase 3 studies than would have been necessary had there been a smaller effect size.

Assessment	Domain	Analysis	p Values 2.8 mg (N=90)	p Values 5.6 mg (N=49)
CAPS-5	Total	MMRM[1] with Multiple Imputation	0.211	0.031*
	Total	ANCOVA	0.090	0.038*
	Arousal and Reactivity	MMRM	0.141	0.048*
	Sleep E6 Item	MMRM	0.185	0.010*
	Startle E4 Item	MMRM	0.336	0.015*
CGI-I[2]		Responder	0.240	0.041*
PGIC[3]		MMRM	0.075	0.035*
Sheehan Disability Scale	Total	MMRM	0.174	0.079
	Work/school Item	MMRM	0.123	0.050*
	Social/leisure Item	MMRM	0.198	0.031*
	Family life/home responsibilities Item	MMRM	0.375	0.524

[1]MMRM = Mixed Model Repeated Measures
[2]CGI-I = Clinician Global Impression-Improvement
[3]PGIC = Patient Global Impression of Change
*$p \leq 0.05$

Source: Tonix Pharmaceuticals Holding Corp.

Side effects reported during the trial were generally mild. Patients who took TNX-102 SL experienced a higher degree of tongue numbness than those on placebo. However, this side effect has been seen previously in clinical trials involving TNX-102 SL, is usually transient, and often resolves within 30-45 minutes after administration. The following table lists adverse events that were reported by >5% of subjects in any treatment arm.

	Placebo (N=94)	TNX-102 SL 2.8 mg (N=93)	5.6 mg (N=50)	Total TNX-102 SL (N=143)
Local Administration Site Conditions				
Hypoaesthesia oral	2 (2.1%)	36 (38.7%)	18 (36.0%)	54 (37.8%)
Paraesthesia oral	3 (3.2%)	15 (16.1%)	2 (4.0%)	17 (11.9%)
Glossodynia	1 (1.1%)	3 (3.2%)	3 (6.0%)	6 (4.2%)
Systemic Adverse Events				
Somnolence	6 (6.4%)	11 (11.8%)	8 (16.0%)	19 (13.3%)
Dry mouth	10 (10.6%)	4 (4.3%)	8 (16.0%)	12 (8.4%)
Headache	4 (4.3%)	5 (5.4%)	6 (12.0%)	11 (7.7%)
Insomnia	8 (8.5%)	7 (7.5%)	3 (6.0%)	10 (7.0%)
Sedation	1 (1.1%)	2 (2.2%)	6 (12.0%)	8 (5.6%)
Upper respiratory infection	5 (5.3%)	3 (3.2%)	2 (4.0%)	5 (3.5%)
Abnormal dreams	5 (5.3%)	1 (1.1%)	1 (2.0%)	2 (1.4%)
Weight increased	5 (5.3%)	1 (1.1%)	1 (2.0%)	2 (1.4%)

Source: Tonix Pharmaceuticals Holding Corp.

Next Steps in PTSD

The company is currently developing a Phase 3 program for the 5.6 mg dose of TNX-102 SL in PTSD. It will likely involve two clinical trials. The first clinical trial will be in military-related PTSD and be similar to the AtEase study. The trial is likely to begin in the first quarter of 2017 and we anticipate enrollment of approximately twice as many patients as the AtEase study. Now that Tonix knows how to recruit for a study such as that, we expect enrollment to take approximately one year, with topline data under this scenario being available in the first half of 2018.

The second Phase 3 study would likely involve individuals with any type of PTSD, not just military-related. The reason for this is because recruiting for two studies in military-related PTSD would likely prove difficult, as there are many more civilian patients with PTSD than military-related. In addition, civilians with PTSD are more amenable to being treated for PTSD and are an easier patient population to treat. For example, the FDA approved sertraline for the treatment of PTSD based on studies involving only civilians. However, a clinical trial of sertraline for military-

related PTSD was unsuccessful. It is unclear at this point whether this second trial would be run concurrently with the first trial or not.

Based on the fact that PTSD is such a serious issue, particularly in the military, as exemplified by the fact that the suicide rate among military veterans is quite high, with as many as five to eight thousand suicides a year (2012 VA Suicide Data Report), it is conceivable that strong results in one Phase 3 clinical trial in PTSD could form the basis for a regulatory filing along with the data from the AtEase trial. This would be entirely dependent upon the Phase 3 results being highly statistically significant, and at this point we only mention it as a possibility.

Conclusion and Valuation

We are looking forward to the topline results from the AFFIRM trial in September 2016 and will deliver an analysis of those data when they are announced. Our model estimates that an NDA will be filed in 2018 after completion of the AFFIRM and RE-AFFIRM trials. 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.

The positive results for the Phase 2 AtEase trial was welcome news for the company, but especially for patients who suffer from PTSD, particularly military veterans afflicted with the condition. Up to this point, there was essentially no effective pharmacological treatment option for these patients, and the AtEase results could be looked at as a real scientific breakthrough. In terms of timeline, we anticipate the first Phase 3 trial for PTSD initiating in the first quarter of 2017, with results from that trial most likely by the first half of 2018. We will await further guidance on whether the second Phase 3 trial will be run concurrently with the first Phase 3 trial or not. We are modeling for peak sales in PTSD of approximately $650 million, but this number is highly contingent upon successful results in a Phase 3 program in both a military and civilian population.

The company recently completed a public offering of five million shares of common stock for $2.00 per share. The increased number of shares outstanding has resulted in our valuation decreasing slightly to $10/share, however the stock continues to trade at a significant discount to this valuation. A run up in the stock price is possible leading up to the announcement of the AFFIRM results in September 2016, and positive results are likely to lead to a significant revaluation of the shares.

PROJECTED FINANCIALS

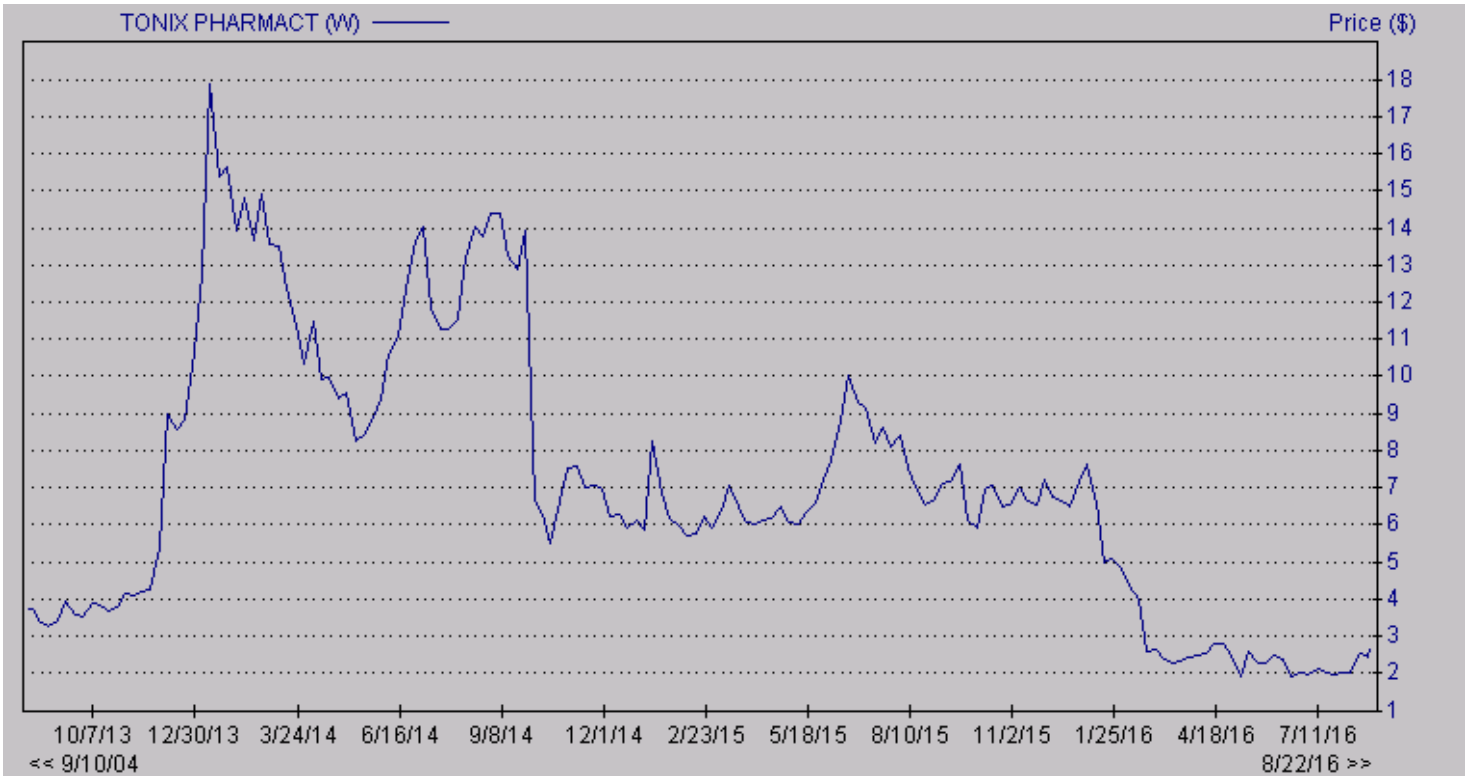
Tonix Pharmaceuticals Holding Corp.
Income Statement

Tonix Pharmaceuticals	2015 A	Q1 A	Q2 A	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	$7.5	$7.0	$6.0	$31.2	$34.0	$37.0
SG&A	$12.7	$3.3	$2.3	$3.0	$3.0	$11.6	$13.0	$15.0
Operating Income	($48.2)	($14.0)	($9.8)	($10.0)	($9.0)	($42.8)	($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)	($9.8)	($9.9)	($9.0)	($42.8)	($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)	($9.8)	($9.9)	($9.0)	($42.8)	($47.0)	($52.0)
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($2.86)**	**($0.74)**	**($0.50)**	**($0.39)**	**($0.35)**	**($1.89)**	**($1.68)**	**($1.73)**
YOY Growth	*3.5%*	-	-	-	-	*-33.8%*	*-11.4%*	*3.3%*
Weighted Shares Outstanding	16.8	18.9	19.7	25.8	26.0	22.6	28.0	30.0

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

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