Zacks Small-Cap Research

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Tonix Pharmaceuticals

(TNXP-NASDAQ)

TNXP: TNX-102 SL Misses Primary Efficacy Endpoint in BESTFIT Trial…

Current Recommendation	**Hold**
Prior Recommendation	Buy
Date of Last Change	09/29/14
Current Price (09/29/14)	$6.95
Target Price	**$8.00**

On September 29, 2014, Tonix released top-line data from the BESTFIT trial of TNX-102 SL in patients with fibromyalgia. The study did not achieve statistical significance in the primary efficacy endpoint in change in average daily pain score at week 12.

While the study did not meet the primary efficacy endpoint, the results showed a statistically significant effect on pain by a 30 percent responder analysis as well as on measures of sleep quality.

The company is planning to meet with the FDA as soon as possible to obtain guidance toward a Phase 3 program. However, with so much uncertainty regarding the future of the compound in the treatment of fibromyalgia we have lowered our rating to 'Neutral' with a $8 price target.

SUMMARY DATA

52-Week High	**$18.67**
52-Week Low	**$3.10**
One-Year Return (%)	**73.85**
Beta	**2.13**
Average Daily Volume (sh)	**87,641**
Shares Outstanding (mil)	**10**
Market Capitalization ($mil)	**$112**
Short Interest Ratio (days)	**1.52**
Institutional Ownership (%)	**31**
Insider Ownership (%)	**12**
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 2014 Estimate	**N/A**
P/E using 2015 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)
2013	0 A	0 A	0 A	0 A	0 A
2014	0 A	0 A	0 E	0 E	0 E
2015					0 E
2016					0 E

Earnings per Share

(EPS is operating earnings before non recurring items)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2013	-$0.93 A	-$0.95 A	-$0.87 A	-$0.74 A	-$3.37 A
2014	-$0.59 A	-$0.61 A	-$0.72 E	-$0.79 E	-$2.73 E
2015					-$2.67 E
2016					-$2.06 E

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WHAT'S NEW

Update

Tonix reports results from the Phase 2b/3 BESTFIT trial

On September 29, 2014, Tonix Pharmaceuticals announced top line results for the Phase 2b/3 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, there was a statistically significant effect on pain when examining the percentage of patients achieving a 30% or greater improvement (p=0.030).

Below we will briefly review the BESTFIT trial, take a deeper look at the additional efficacy results that were obtained during the trial, and go over potential next steps for the company.

…Brief review of the BESTFIT trial…

BESTFIT was a randomized, double-blind, placebo-controlled 12-week safety and efficacy study in fibromyalgia patients who were given either a TNX-102 SL (cyclobenzaprine HCl 2.8 mg) tablet or placebo at bedtime. A total of 205 patients were enrolled at 17 centers in the U.S. with trial participants randomized to either TNX-102 SL (n=103) or placebo (n=102).

The primary endpoint of the trial was the change in pain from baseline to week 12 as measured by the Numeric Rating Scale (NRS). The company also collected information on secondary endpoints, including NRS scores at other time points during the 12-week study, the Fibromyalgia Impact Questionnaire (FIQ), and the Patient Global Impression of Change (PGIC).

…BESTFIT trial does meet primary efficacy endpoint…

The company conducted two statistical tests to analyze the primary efficacy endpoint, which was the change in average daily pain score. The mixed-effect model repeated measure analysis (MMRM) and the jump-to-control (JTC) multiple-imputation analysis both showed no statistically significant change in pain at week 12 (MMRM p=0.086; JTC p=0.172). While the MMRM analysis would be considered a standard statistical test, the JTC analysis is quite conservative, as it relies on imputed calculations for missing data. Thus, while it could be argued that the data was trending toward significance using the MMRM analysis, the same was not true with the JTC analysis.

The primary endpoint chosen for the BESTFIT trial was the same that was utilized by Pfizer and Eli Lilly to gain approval for Lyrica and Cymbalta, respectively, for the treatment of fibromyalgia syndrome. Thus, investors had hoped to see a significant improvement in change in pain just as those two drugs had shown. Failure to reach significance in this endpoint was viewed quite negatively, as the stock dropped by approximately 50% following release of the data.

The drug was well tolerated in the study, with 86.4% and 83.3% of subjects randomized to TNX-102 SL and placebo, respectively, finishing the trial. There were no reports of serious adverse events during the trial. As was expected based on the Phase 1 study results, the rate of tongue numbness (41.7% vs. 1.0%) and abnormal taste (7.8% vs. 0.0%) were higher in the active treatment group. The company reported that tongue numbness was a local effect related to dose administration and was transient in almost all cases. There were only three systemic adverse effects that occurred at a rate of 3.0% or greater in the overall trial population, which are indicated below.

Systemic	TNX-102 SL (N=103)		Placebo (N=101)		Total (N=204)	
Adverse Event	N	%	N	%	N	%
Somnolence	2	1.9	7	6.9	9	4.4
Dry Mouth	4	3.9	4	4.0	8	3.9
Back Pain	5	4.9	3	3.0	8	3.9

Source: Tonix Pharmaceuticals, Inc.

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…Secondary analyses show significant clinical activity…

While TNX-102 SL did not show statistically significant activity in the primary endpoint, there were a number of secondary analyses performed where the compound did show statistical significance. These included outcomes in relation to pain, sleep, and fibromyalgia-related symptoms. The table below provides a summary of these analyses.

Outcome Measure at Week 12	Intent-to-Treat Analysis	P value (1)
Pain		
Daily Pain Diary, NRS	Mean Change (2)	0.086 / 0.172 (JTC)
Daily Pain Diary, NRS	Proportion of Patients Achieving 30% Improvement (3)	0.030* (LR)
Clinic NRS 7-day pain recall	Mean Change	0.029*
FIQ-R Pain Item	Mean Change	0.004*
Sleep		
Daily Sleep Quality Diary, NRS	Mean Change	<0.001*
PROMIS Sleep Disturbance	T-score Change	0.003* / 0.004* (JTC)
FIQ-R Sleep Quality Item	Mean Change	<0.001*
Fibromyalgia-Related		
Patient Global Impression of Change	Responder Analysis	0.025* (LR)
FIQ-R Total Score	Mean Change	0.014* / 0.015* (JTC)
FIQ-R Symptom Domain	Mean Change	0.004*
FIQ-R Function Domain	Mean Change	0.060
FIQ-R Anxiety Item	Mean Change	0.015*
FIQ-R Sensitivity Item	Mean Change	0.017*
FIQ-R Stiffness Item	Mean Change	0.039*

JTC = Jump to Control, Multiple Imputation; LR = Logistic Regression; NRS = Numeric Rating Scale

** p < 0.05*

(1) Analysis by Mixed-Effect Model Repeated Measure unless otherwise indicated.

(2) Primary endpoint for FDA approvals of Lyrica® and Cymbalta® in fibromyalgia.

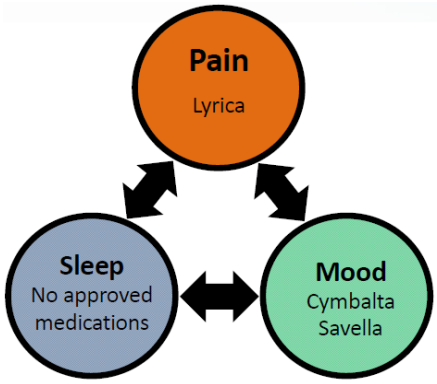
(3) Primary endpoint for FDA approval of Savella® in fibromyalgia.

Source: Tonix Pharmaceuticals, Inc.

The fact that so many different efficacy results showed a statistically significant improvement is encouraging, albeit less so with the primary endpoint failing to reach significance. The company has indicated that they will be presenting the full data from the study at an upcoming medical conference, but will not release any more details about the data before that time. Thus, it is quite difficult to gain any further insight into why so many different outcome measurements yielded statistically significant results while the primary endpoint did not reach statistical significance.

One of the more important analyses from the chart above has to do with the effect of TNX-102 SL on sleep and sleep quality. TNX-102 SL showed a statistically significant improvement in the Daily Sleep Quality Diary score, the PROMIS Sleep Disturbance Instrument, and the FIQ-R Sleep Quality Item.

The National Pain Foundation estimates that 90% of all FM patients have sleep problems. For most FM patients, it's not a lack of sleep; it's a lack of quality restorative sleep. Current treatment options for fibromyalgia continue to leave many patients dissatisfied, particularly in regards to sleep related symptoms. The reason for this is that existing approved fibromyalgia medications such as Lyrica and Cymbalta, which focus on reducing fibromyalgia-associated pain and mood disorder, respectively, do little to improve sleep quality. Insomnia medications such as Ambien and Lunesta improve total sleep time, but do little to improve the chronic fatigue associated with fibromyalgia. The results from the BESTFIT trial show that TNX-102 SL significantly improved sleep related outcomes, thus representing a potential niche in the fibromyalgia market for the compound.



Another important outcome noted in the chart above is the statistical significance seen in the proportion of patients achieving a 30% improvement in pain score (p=0.030). Of interest, this outcome was utilized by Forest Laboratories to gain approval for Savella in 2009 and thus could be one path forward as the company looks ahead to developing a Phase 3 program.

…The path forward is now much less clear…

The company is planning on meeting with the FDA as quickly as possible to discuss the results from the BESTFIT trial and to prepare for a Phase 3 program. We anticipate this meeting occurring in the first quarter of 2015. There are a number of positives that the company will be able to present to the agency, including the statistically significant improvements noted in multiple aspects of the FIQ-R, which looks at a broad range of symptoms associated with fibromyalgia, along with a statistically significant improvement in the Patient Improvement of Change score. While these measures are important to showing that the compound does have clinical activity, management stopped short of suggesting how the FDA may advise the company to move forward.

Clearly, TNX-102 SL shows clinical activity in regards to improving sleep and sleep related symptoms along with certain other pain and fibromyalgia related outcomes in fibromyalgia patients. However, the fact that the change in pain did not show statistical significance is a large hindrance, and makes it quite difficult to forecast the clinical development path from this point forward before the conclusion of the meeting with the FDA.

…Conclusion and Recommendation…

We were disappointed to see that the BESTFIT trial did not meet statistical significance in the primary efficacy outcome. With the stock price down approximately 50% on the news, Tonix currently has a market cap of approximately $82 million on a fully diluted basis. The company reported almost $44 million in cash at the end of the second quarter of 2014. Thus, the company currently has an enterprise value of only $38 million.

We will be quite interested to hear what the FDA has to say in regards to a potential Phase 3 program for TNX-102 SL in fibromyalgia along with what primary outcomes would be acceptable to the agency as part of a path to approval. Based upon the BESTFIT results, we are downgrading the stock to 'Hold' and adjusting our price target to $8/share as the path forward to approval for TNX-102 SL for the treatment of fibromyalgia is not currently clear.

PROJECTED FINANCIALS

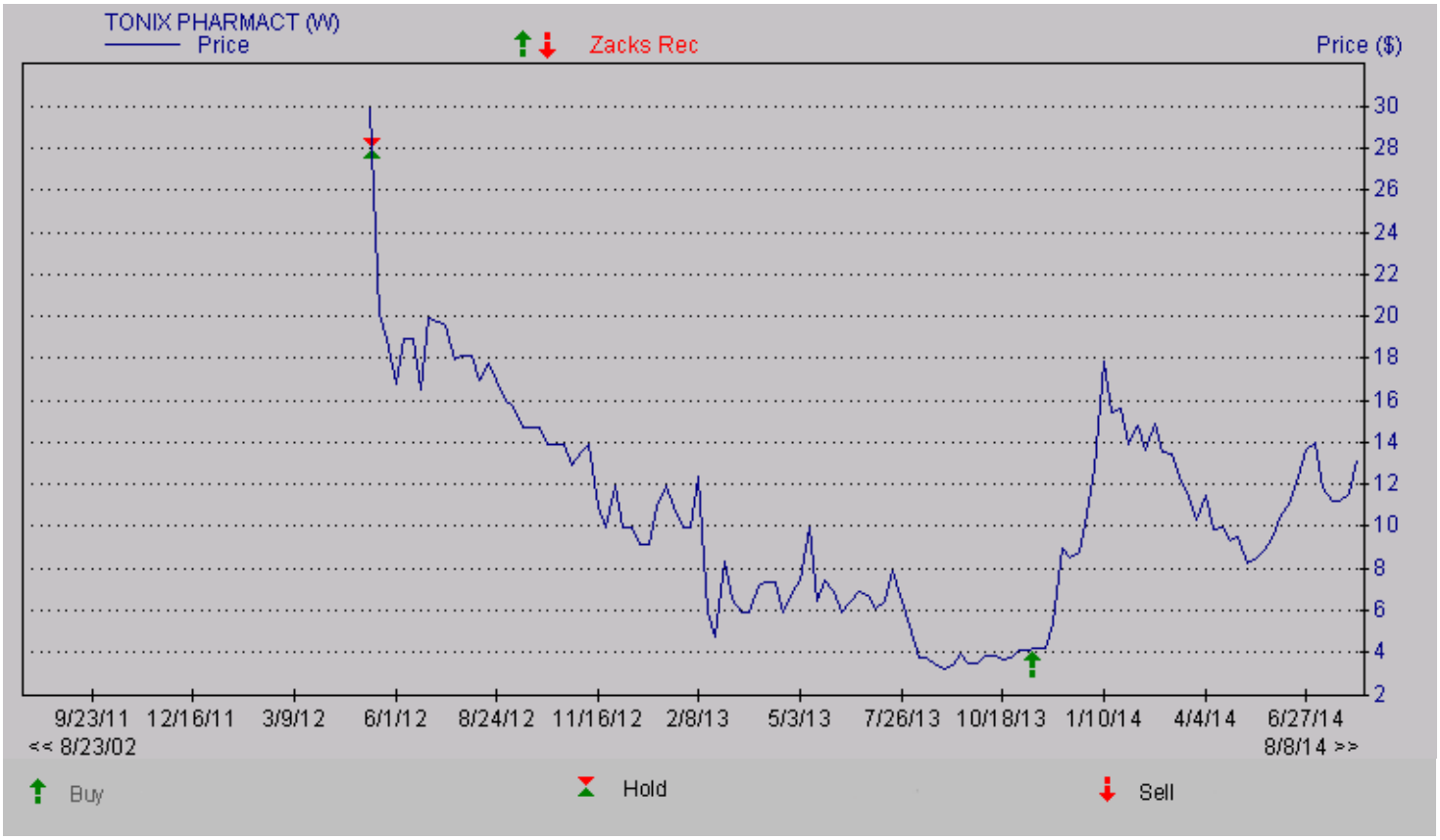
Tonix Pharma
Income Statement

Tonix Pharmaceuticals	2013 A	Q1 A	Q2 A	Q3 E	Q4 E	2014 E	2015 E	2016 E
TNX-102SL (FM)	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	-
TNX-102SL (PTSD)	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	-
TNX-201 (ETTH)	$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
Product Gross Margin	-	-	-	-	-	-	-	-
R&D	$4.7	$3.6	$4.1	$5.5	$6.5	$19.6	$25.0	$22.0
% R&D	-	-	-	-	-	-	-	-
SG&A	$6.2	$1.6	$2.0	$2.1	$2.1	$7.8	$8.5	$9.0
% SG&A	-	-	-	-	-	-	-	-
Operating Income	($10.9)	($5.2)	($6.0)	($7.6)	($8.6)	($27.4)	($33.5)	($31.0)
Operating Margin	-	-	-	-	-	-	-	-
Interest & Other Income	$0.0	$0.0	$0.0	$0.0	$0.1	$0.1	$0.1	$0.1
Pre-Tax Income	($10.9)	($5.2)	($6.0)	($7.6)	($8.5)	($27.3)	($33.4)	($30.9)
Taxes & Other	$0	$0	$0	$0	$0	$0	$0	$0
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Net Income	($10.9)	($5.2)	($6.0)	($7.6)	($8.5)	($27.3)	($33.4)	($30.9)
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($3.37)**	**($0.59)**	**($0.61)**	**($0.72)**	**($0.79)**	**($2.73)**	**($2.67)**	**($2.06)**
YOY Growth	*-39.6%*	-	-	-	-	*-18.8%*	*-2.3%*	*-22.9%*
Weighted Shares Outstanding	3.2	8.7	9.9	10.6	10.7	10.0	12.5	15.0

Source: Zacks Investment Research, Inc. *Jason Napodano, CFA*

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