Zacks Small-Cap Research

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Tonix Pharmaceuticals (TNXP-NASDAQ)

TNXP: Plenty of Cash to Propel Current Clinical Programs Forward…

Current Recommendation	**Buy**
Prior Recommendation	Neutral
Date of Last Change	03/02/15
Current Price (08/10/15)	$7.27
Target Price	**$14.00**

Tonix Pharmaceuticals recently filed form 10-Q with financial results for the second quarter of 2015. The company exited the quarter with $48.7 million in cash and then raised gross proceeds of $20.1 million in July 2015.

The company currently has three programs in clinical trials: TNX-102SL in a Phase 3 trial for fibromyalgia; TNX-102SL in a Phase 2 trial for post traumatic stress disorder; and TNX-201 in a Phase 2 trial for treatment of episodic tension type headache. Each of these trials should report data during 2016.

We feel Tonix shares are currently undervalued and see them as providing the opportunity for nice returns as clinical progress is likely to drive the shares higher.

SUMMARY DATA

52-Week High	**$14.76**
52-Week Low	**$5.41**
One-Year Return (%)	**-42.93**
Beta	**2.14**
Average Daily Volume (sh)	**438,783**
Shares Outstanding (mil)	**18**
Market Capitalization ($mil)	**$140**
Short Interest Ratio (days)	**1.93**
Institutional Ownership (%)	**38**
Insider Ownership (%)	**9**
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)
2014	0 A	0 A	0 A	0 A	0 A
2015	0 A	0 A	0 E	0 E	0 E
2016					0 E
2017					0 E

Earnings per Share
(EPS is operating earnings before non recurring items)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2014	-$0.59 A	-$0.61 A	-$0.71 A	-$0.83 A	-$2.77 A
2015	-$0.71 A	-$0.73 A	-$0.53 E	-$0.56 E	-$2.50 E
2016					-$2.10 E
2017					-$1.91 E

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WHAT'S NEW

Financial Update

On August 7, 2015, Tonix filed form 10-Q with financial results for the second quarter of 2015 that ended June 30, 2015. As expected, the company did not report any revenues. Net loss for the quarter was $11.8 million, or $0.73 per share, and was comprised of $8.9 million in R&D and $2.9 million in G&A expenses. Net cash burn for the quarter was $9.2 million. The company exited the second quarter of 2015 with approximately $48.7 million in cash and cash equivalents. In July 2015, the company closed a public offering of 2.325 million shares sold at $7.50 per share that generated gross proceeds of $20.1 million, thus we estimate that the company will exit the third quarter of 2015 with approximately $57 million. Based on an average cash burn of approximately $10 million per quarter, we estimate the company now has enough cash to last into the first half of 2017.

Update on TNX-201

In June 2015, Tonix Pharmaceuticals (TNXP) announced the initiation of a Phase 2 clinical trial of TNX-201 for the treatment of episodic tension-type headache (ETTH). Later in the month the company announced the presentation of preclinical data for TNX-201 showing efficacy in rat pain models. Below we go further into the recently presented data for TNX-201 and what it means for the compound's potential.

Tension type headaches

Tension type headaches (TTH) are the most common type of headaches among adults and are also known as "stress headaches". These headaches were previously known by a number of terms, however the term "tension-type headache" was chosen by the International Classification Headache Diagnosis I (ICHD) in 1988 and later retained by ICHD II in 2004. The terms "tension" and "type" refer to the unknown nature of the underlying etiology, however a number of clinical studies have been performed that underscore their neurobiological basis.

ICHD II classified tension type headaches as either episodic (ETTH) or chronic (CTTH). ETTH are further subdivided into infrequent (occurring less than 12 days per year) or frequent (more than 12 days per year but less than 180 days per year). CTTH are characterized by an occurrence of more than 180 days per year. The clinical symptoms for the three types of headache are similar and are only differentiated based on their frequency.

The pain associated with TTH is typically described as a dull pressure with the feeling of wearing a tight fitting band around the head. Clinical diagnosis of TTH is based on negative features (i.e., the absence of symptoms that characterize other headaches). Physical activity has no bearing on the intensity of the headache, which distinguishes TTH from migraine headaches where any type of physical activity worsens the pain. Nausea and vomiting, if present, precludes the diagnosis of TTH, while photophobia or phonophobia may be present but not concurrently.

Despite numerous clinical studies, the exact cause of TTH remains elusive, however there appear to be certain triggers including: stress and anxiety, squinting, poor posture, dehydration, noise, bright sunlight, tiredness, and certain smells. TTH are known as primary headaches, which means that there is no underlying condition that causes them (such as a tumor or hemorrhage). Other types of primary headaches include migraines and cluster headaches.

ETTH Market Analysis

A study in Denmark showed that the incidence of TTH increased significantly between 1989 and 2005, from 29% to 37% of interviewed patients (Lyngberg *et al.*, 2005). This corroborated an earlier study conducted in Baltimore, MD from 1992-1994 that surveyed 13,345 subjects and found an overall prevalence of ETTH of 38.3% (Schwartz *et al.*, 1998). Extrapolated to the adult U.S. population means that approximately 75 million Americans experience ETTH. Data from IMS Health points to an average of 9.2 million physician's office or emergency room visits with a primary code of non-migraine headaches per year between 2008 and 2014. This led to approximately 10 million prescriptions per year to treat ETTH.

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Women have a higher prevalence of ETTH than men in all age, race, and educational level subgroups with the peak of incidence occurring in the 30-39 year old age group. There appears to be a strong association between the prevalence of ETTH and education, as prevalence increases steadily with higher education levels and peaks with almost 50% of men and women with graduate school education experiencing ETTH (Schwartz *et al*., 1998).

Current Treatment Options for ETTH

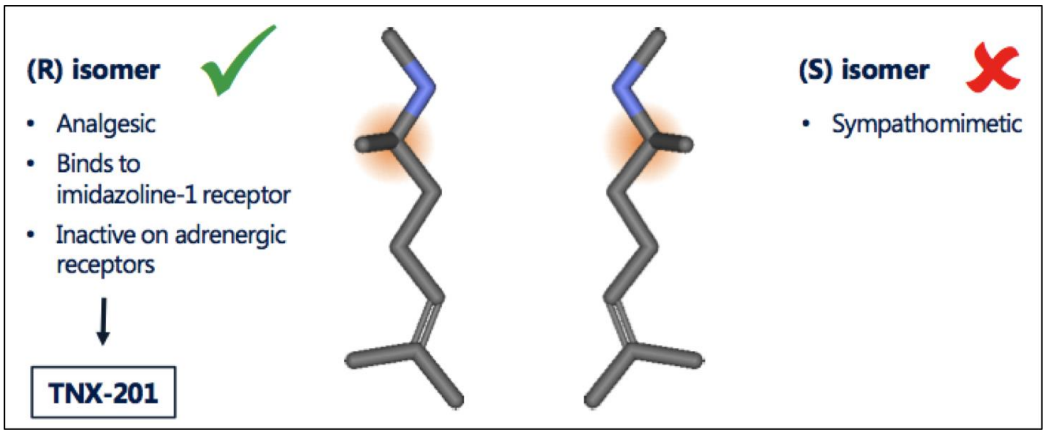
Current treatment options for ETTH include over-the-counter analgesics such as ibuprofen, acetaminophen, and aspirin, all of which have been shown to be more effective than placebo in controlled trials. Studies have shown that non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen and naproxen are most likely more effective than aspirin or acetaminophen, but these results are not unequivocal. Caffeine, codeine, sedatives, or tranquilizers are often combined with NSAIDs to increase their efficacy, however this can lead to the risk for dependency, abuse, and chronification of the headache.

The only currently FDA approved medications for the treatment of ETTH are Fioricet and Fiorinal, both of which contain butalbital, which is a barbiturate that can lead to dependency and is classified Schedule III by the DEA. According to IMS Health, butalbital combination products accounted for approximately 3.5 million prescriptions in 2013. The U.S. FDA has placed a warning on butalbital products noting the risk of potential abuse and addiction. As a result, long-term use of these products is discouraged. Combination butalbital and opioid products also exist but market share is low due to the compounded potential for abuse and addiction.

Butalbital containing compounds have also been linked to Medication Overuse Headaches (MOH), also known as rebound headaches. These headaches occur through the overuse of pain medications to relieve primary headaches. They can occur frequently, can be very painful, and are the third most common cause of headache. Regular use of over-the-counter medications such as ibuprofen and acetaminophen have also been linked to MOH, thus doctors typically advise limiting their use to not more than two days weekly. In addition to MOH, the overuse of acetaminophen has been linked to liver damage while the overuse of NSAID can cause gastrointestinal bleeding.

TNX-201 For the Treatment of ETTH

TNX-201 (dexisometheptene mucate) is an improved formulation of isometheptene (6-methylamino-2-methylheptene, IMH), which has been utilized to treat headaches for greater than 50 years. IMH is composed of two isomers, (R)-IMH and (S)-IMH), with one believed to provide efficacy while the other only contributes to side-effects. TNX-201 is the (R) isomer with no (S) isomer present. Isomers are molecules with the same molecular formula but that differ in their chemical structure. The two types of isomers are structural isomers, where the atoms of two isomers are joined together in different ways, and stereoisomers, where the molecules are identical in atomic constitution and bonding, but differ in the three-dimensional arrangement of the atoms, of which IMH is an example.



Source: Tonix Pharmaceuticals

There have been five controlled clinical trials with IMH either alone or in combination with dichlorophenazone and acetaminophen for the treatment of migraines and TTH (Diener, 2000). In two trials, the IMH combination was found to be superior to placebo. In one of those trials, IMH alone was also found to be superior to placebo and in another study was comparable to the IMH combination. Two studies examined the clinical efficacy of IMH combination in comparison with acetaminophen or IMH alone and found no significant advantage to the combination product. The fact that the combination product is not superior to IMH alone supports the development of TNX-201 as a stand-alone product.

Tonix has developed a method for purifying a single isomer of IMH that could potentially reduce the toxicity associated with the racemic mixture (a mixture of the two isomeric forms). Historically, most drugs were developed as racemates (i.e., compounds with 50:50 proportions of enantiomers). There are many examples available where both members of an enantiomer pair are active (e.g., ibuprofen), where one member is active while the other is inactive (e.g., β-lactam antibiotics), and where one member is active while the other member has toxic effects (e.g., Thalidomide). IMH falls under the category of drugs where one isomer is believed to confer the anti-headache effect while the other isomer is responsible for the unwanted side effects.

IMH History and Regulatory Pathway

IMH was sold for a number of years as a combination medication with dichloralphenazone and acetaminophen under the brand names Midrin®, Duradrin®, and Epidrine® for the treatment of migraine headaches. However, these medications never went through the proper FDA approval process, as they were originally marketed before the 1962 amendment to the 1938 Food, Drug and Cosmetic Act. This amendment required manufacturers to show that their medications were both safe and effective, while the 1938 Food, Drug and Cosmetic Act had only required a safety requirement for selling pharmaceuticals.

To comply with the new law, in 1966 the FDA established the Drug Efficacy Study Implementation (DESI) list to test all compounds approved for sale between 1938 and 1962 and classify them as effective, ineffective, or further study required. Regardless of classification, in order to continue marketing any DESI drug the FDA requires clinical trials and a proper NDA filing. Thus far, no companies manufacturing compounds containing IMH have filed an NDA for their approval by the FDA. Thus, all products containing IMH are marketed as unapproved products in the U.S. and a marketing withdrawal has been sanctioned by the FDA since 2010. Since the FDA has never approved IMH, Tonix will have to pursue the traditional 505(b)(1) NDA requirements, which includes the full complement of safety and efficacy studies in order to gain approval for TNX-201.

Preclinical Data Elucidates TNX-201 Mechanism of Action

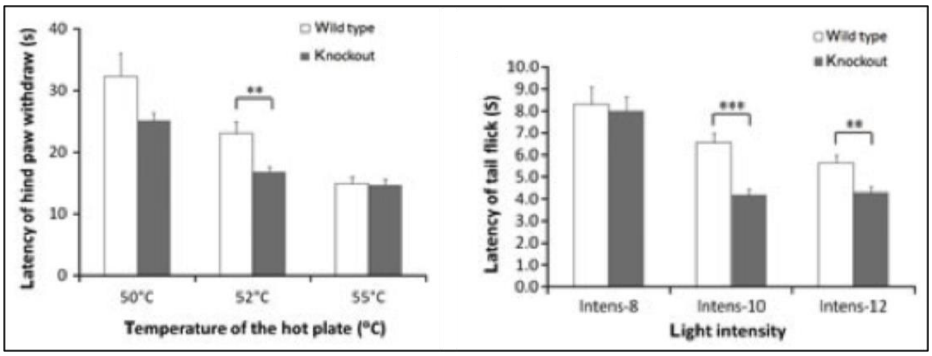
Tonix scientists screened racemic IMH against a large panel of enzymes, receptors, ion channels, and transporters to elucidate the binding target of each of the racemates. The following table shows the binding affinities of both (R)-IMH and (S)-IMH to select receptors expressed in the central nervous system. The data shows that the target of (R)-IMH is the imidazoline-1-receptor (I_1-R). In the following table, the lower the value means the greater the binding affinity between the isomer and the target protein.

	K_i(nM)				
Compound	**I_1R**	**I_2R**	**α_{2B}**	**Sigma-1 Receptor**	**Sigma-2 Receptor**
(R)-Isometheptene	18	62	50000	1900	5600
(S)-Isometheptene	1100	180	55000	2100	5200

Source: Daugherty *et al*., 2015

I_1-R is a member of a family of cell surface receptors that bind imidazolines, which are a class of heterocyclic compounds that are capable of lowering blood pressure. Most of the imidazolines, such as clonidine, bind to both the α2-adrenergic receptor and I_1-R (Ernsberger *et al*., 1987) resulting in unwanted side effects, particularly drowsiness, dry mouth, and hypotension. The data in the table above shows that (R)-IMH does not bind to the α2-adrenergic receptor with affinity that would be physiologically relevant, meaning that it may not produce some of the aforementioned side effects.

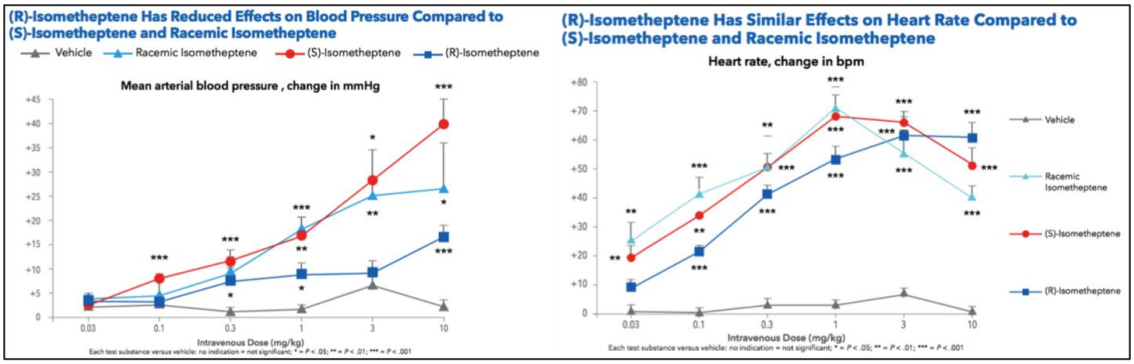
I_1-R is found in the brain, kidney, pancreas, and on platelets. It was first cloned in 2000 (Piletz *et al*., 2000), and a I_1-R knockout mouse was recently characterized (Zhang *et al*., 2013). Important observations of the I_1-R knockout mice were that the mice did not differ from wild-type mice in spontaneous locomotion, grip strength, motor coordination, spatial learning, and memory. In addition, there was no difference detected in systolic blood pressure or in the heart rate of conscious mice. Lastly, the pain threshold of I_1-R knockout mice was significantly lower than that of wild-type mice using both the hot-plate test and tail-flick test, as shown below.



Source: Zhang *et al.*, 2013

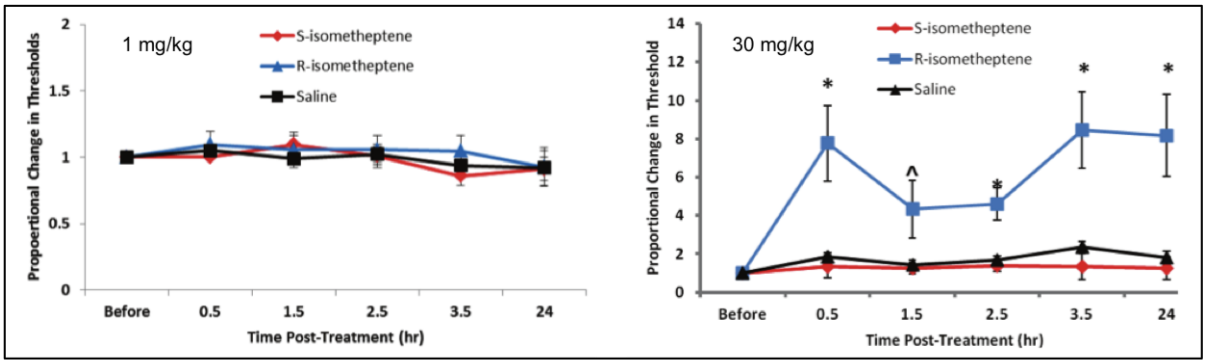
What these data indicate is that I_1-R is involved in the sensation of pain. Removing the receptor (such as in the knock-out mice) lowers the pain threshold compared to mice that express I_1-R. Thus, since the presence of the receptor is necessary for increased pain tolerance, activation of the receptor (through an agonist such as (R)-IMH) may further increase pain tolerance and create an analgesic effect. Since IMH is already known to provide relief from headaches, the identification of (R)-IMH binding to I_1-R coupled with the data showing I_1-R is involved in pain perception provides the necessary justification for testing (R)-IMH for the treatment of pain.

One of the adverse side effects of racemic IMH is a rise in blood pressure. To test which of the racemates of IMH caused this effect, increasing amounts of (R)-IMH, (S)-IMH, and the racemic mixture were administered to rats. Results showed that (S)-IMH and the racemic mixture, but not (R)-IMH, caused an increase in blood pressure. Interestingly, all of the compounds caused an increased heart rate, which based on an average 330-480 bpm for rats was approximately 12-17% for (R)-IMH.



Source: Daugherty *et al.*, 2015

Additional efficacy studies were undertaken in two rat pain models, the chronic migraine model (Oshinsky *et al.*, 2007) and the spontaneous trigeminal allodynia model, which uses rats that are genetically predisposed to episodic pain threshold decreases that respond to pain medications (Oshinsky *et al.*, 2012). In both models, administration of 30 mg/kg (R)-IMH, but not 1 mg/kg (R)-IMH or 30 mg/kg (S)-IMH, resulted in decreased trigeminal sensitivity, with results from the chronic migraine model shown below.



Source: Fried *et al.*, 2015

In summary, (R)-IMH is a potent agonist of I_1-R, a receptor shown to be associated with pain threshold, thus representing a potential mechanism of action for the analgesic activity of IMH. In addition, the data generated thus far appears to support the notion that binding of (R)-IMH generates the specific downstream mechanisms associated with reduction of pain while (S)-IMH is mostly responsible for the increase in blood pressure. These data provide strong support for testing (R)-IMH as a therapeutic for alleviating ETTH.

TNX-201 Enters the Clinic

Earlier in the year, Tonix announced that they had completed the Phase 1 safety, tolerability, and pharmacokinetic study of TNX-201 with encouraging results. Data from the 45-patient study showed a dose-related increase in TNX-201 plasma levels (C_{max}, AUC), with no evidence of isomer inter-conversion and only mild adverse events, none of which were considered drug-related or serious enough to discontinue treatment.

In June 2015, Tonix announced the initiation of a randomized, double blind, placebo controlled, proof-of-concept Phase 2 clinical study of TNX-201 in ETTH (NCT02423408). The study is expected to enroll approximately 200 patients at nine clinical centers in the U.S. Study subjects will be administered 140 mg TNX-201 (4 x 35 mg capsules) or placebo for the treatment of a single TTH. The primary efficacy endpoint is the proportion of subjects pain free at 2 hours post-dose (as recommended by the U.S. Food and Drug Administration). Pain will be assessed utilizing a four-point Numeric Rating Scale, Visual Analog Scale, and binary questionnaire for self-reporting pain. Additional endpoints include the proportion of patients that are pain-free at various time intervals post-dose up to 24 hours, the proportion of patients who utilize rescue medication during the 24-hour post-dose period, and the change from baseline in pain severity at several time intervals post-dose. We anticipate topline results from the study in the first quarter of 2016.

Robust Intellectual Property Portfolio for TNX-201

Tonix has an extensive patent portfolio for TNX-201. The intellectual property relates to IMH isomers and includes patent applications directed to a purified isomer of IMH, pharmaceutical compositions containing IMH, IMH formulations, methods for modulating headache, and other CNS conditions and treating CNS conditions utilizing IMH isomers, and methods of manufacturing IMH isomers. The IMH technology patent portfolio includes U.S. Patent Application No. 14/158,735 as well as U.S. Provisional Patent Application No. 61/953,715. If U.S. and non-U.S. patents claiming priority from those applications issue, those patents would expire in 2034, excluding any patent term adjustments or extensions.

Valuing TNX-201

As stated above, the potential market for TNX-201 is quite large as approximately 75 million Americans suffer from TTH each year. We believe the majority can be treated with OTC medications, however there were still close to 10 million prescriptions for headache medications in the U.S in 2013. We estimate that approximately 70% of these are for ETTH. The 3.5 million prescriptions for butalbital combination products is the initial low-hanging fruit for Tonix, with opportunity to take away market from prescription NSAIDs and Triptan products offering significant upside. At peak, 2.5 million prescriptions were written for IMH containing products in the late 1990s.

If we assume the average headache sufferer has about one episode per week (50/year), and we price TNX-201 comparable to migraine drugs Cambia® ($35 per pill) and Treximet® ($40 per pill), with 10% market share of the active prescription seekers, we estimate TNX-201 will have peak sales of approximately $440 million. Data from the current Phase 2 study should be available in the fourth quarter of 2015 and we estimate two registration programs will take place in 2016 and 2017 with an NDA filing in 2019 and approval in 2020. We assume peak sales in 2025. The net present value of the franchise is $67 million based on a 20% probability of approval and 65% operating margins.

TNX-102SL Update in Fibromyalgia

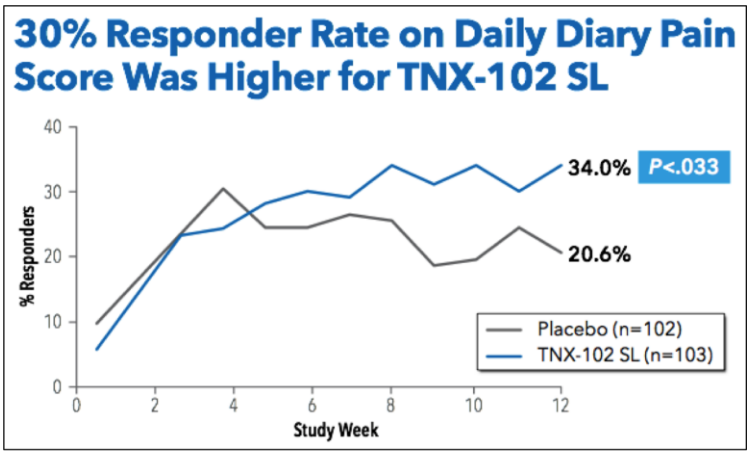
On June 17, 2015, Tonix announced the FDA has conditionally accepted the trade name Tonmya™ for TNX-102SL for the treatment of fibromyalgia.

In June 2015, Tonix presented additional data from the Phase 2b BESTFIT clinical trial at the European League Against Rheumatism Annual Congress (EULAR 2015). As a reminder, the BESTFIT study was designed to evaluate the safety and efficacy of Tonmya™, 2.8 mg, taken once daily at bedtime, in improving pain, sleep quality,

function, and other clinical measures in patients with fibromyalgia. The study enrolled 205 patients randomized 1:1 to Tonmya™ (n=103) or placebo (n=102).

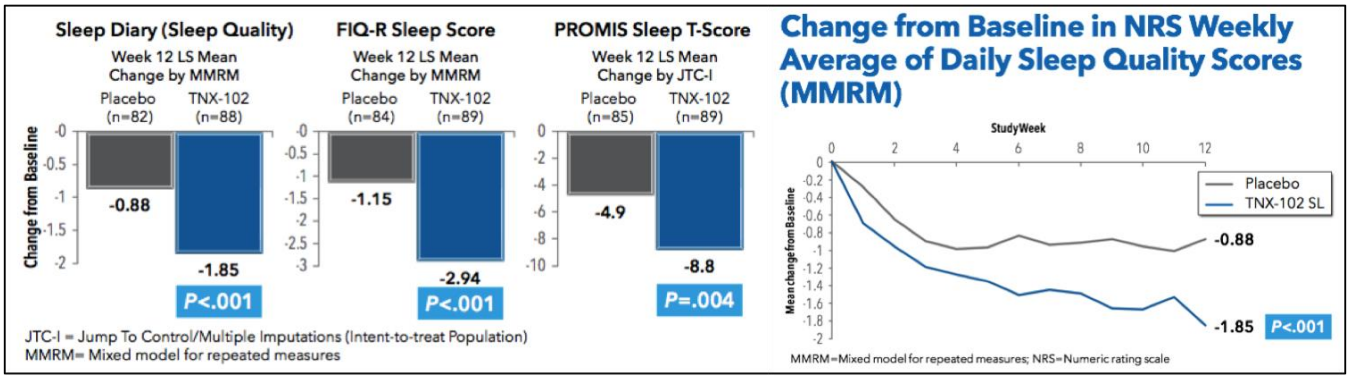
While the study did not hit the primary endpoint of statistical significance in change in average daily pain score at week 12 (*P*=0.086 by mixed-effect model repeated measure analysis, *P*=0.172 by jump-to-control, multiple imputation analysis), additional data from BESTFIT showed that Tonmya™ treatment led to significant improvements across a range of symptoms suffered by fibromyalgia patients.

30% Responder Analysis: Analysis of patients who reported a 30% improvement in their pain scores showed that Tonmya™ had a statistically significant effect on pain compared to placebo (34.0% vs. 20.6%; *P* = 0.033). What this data means is that 34% of patients taking Tonmya™ and 20.6% of patients taking placebo reported at least a 30% in improvement in pain score. As an 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. The following figure shows that the 30% responder rate began to separate between active and placebo-treated patients around week 6, with the separation continuing through the end of the 12-week treatment period.



Source: Lederman *et al.*, 2015

Sleep Quality: Treatment with Tonmya™ resulted in significant improvements 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). Importantly, the improvements in sleep quality were observed early after initiating Tonmya™ treatment, and generally preceded improvements in other outcome measures.



Source: Lederman *et al*., 2015

Additional Outcomes: Treatment with Tonmya™ led to a statistically significant improvement in the Patient Global Impression of Change (PGIC) response rate at week 12 (30.1% vs. 16.7%; *P*=0.025). A "PGIC Responder" is defined as the patient rating their overall fibromyalgia "Much Improved" or "Very Much Improved". The PGIC is a patient rating of overall improvement and is a standard assessment in pain treatment trials, including fibromyalgia.

Tonmya™ therapy also led to a statistically significant improvement from baseline in the FIQ-R Total Score (-15.6 vs. -9.1; *P*=0.014). The FIQ-R measures the impact of fibromyalgia on patients' daily lives and is a standard assessment in fibromyalgia clinical trials.

Adverse Events: Tonmya™ was very well tolerated in the BESTFIT trial, with all reported systemic adverse events occurring in less than 5% of patients. The most common adverse event for those taking Tonmya™ was intermittent tongue or mouth numbness, which occurred in 42% of study subjects. This phenomenon was previously observed in pharmacokinetic studies of healthy volunteers and in those studies it was reported to be transient and typically resolve within 45 minutes of Tonmya™ administration. Of the patients randomized to Tonmya™, 86% completed the 12-week study compared with 83% of placebo-treated patients.

AFFIRM Gets Underway

On May 13, 2015, Tonix announced the initiation of 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 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. Enrollment is expected to take 12 to 14 months and the entire trial should cost approximately $12 million to run. Enrollment should complete by the summer of 2016 and we anticipate topline results in the second half of 2016.

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. As a point of reference, Cypress Bio conducted two Phase 3 studies with milnacipran HCl using a 30% responder analysis. The placebo groups in the first and second study came in at ~16% and ~19%, respectively. The milnacipran HCl groups came in at ~25% and ~27%, respectively. We believe TNX-102SL compares favorably to Savella®, a drug that posted sales of approximately $105 million in 2014.

Based on inputting the 30% responder data from BESTFIT (~34% for TNX-102SL and 21% for the placebo) 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 in early 2017. However, we will have to wait for the data to be sure. At this time the company is planning to initiate a second confirmatory Phase 3 program in the second quarter of 2016, thus for modeling purposes we are assuming that data from both Phase 3 studies will be necessary for filing the NDA.

We remind investors that Tonix is also conducting a long-term safety study with Tonmya™. This is an open-label extension study from BESTFIT, dubbed F203. Data from this study will give Tonix the prerequisite six and 12-month safety analysis required to seek approval of Tonmya™ in fibromyalgia. In June 2015, the company provided an update that of the 174 patients who completed BESTFIT, 158 (91%) enrolled in F203. Of the 158, 108 (68%) completed at least six months in F203. Data from this study is expected in August 2015.

Additional data to be generated in 2015 or 2016 for the preparation of the NDA includes a prospective multi-dose pharmacokinetic study, a safety and tolerability study comparing Tonmya™ to cyclobenzaprine, and standard non-clinical toxicology work. We believe the most likely scenario is filing an NDA in 2018, after successful completion of two Phase 3 clinical trials, and approval in 2019. Tonix has filed patent applications around Tonmya™ that aim to protect the drug to 2034.

Valuing Tonmya™ in Fibromyalgia

Based on the generic market, the target population for Tonix with Tonmya™ is over 2 million patients. There were some 50 million prescriptions for cyclobenzaprine in 2013. We think that the sublingual formulation clearly contains meaningful advantages over the generic oral formulation of low dose cyclobenzaprine. These include rapid absorption and minimal next-day residual effects ideal for a bedtime dose, and avoidance of first pass metabolism and build-up of norcyclobenzaprine ideal for chronic dosing.

For valuation purposes, our model conservatively 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. With an 18% discount rate, a 40% probability of approval, 65% operating margin, and 30% tax rate, the net present value of Tonmya™ for fibromyalgia is approximately $169 million.

TNX-102SL Update in Military-Related PTSD

On January 15, 2015, Tonix announced the Phase 2 AtEase study had enrolled its first patient. The AtEase study is a Phase 2 randomized, double-blind, placebo-controlled trial to evaluate the efficacy and safety of TNX-102SL in people with military-related PTSD and related conditions. The three-arm trial is expected to enroll approximately 220 participants, who will be randomized to receive either 2.8 mg or 5.6 mg of TNX-102SL or placebo taken sublingually at bedtime daily for 12 weeks. More information on AtEase can be found on the study's website or on ClinicalTrials.gov (NCT02277704).

The primary endpoint of the trial is the week eight 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 trial will be conducted at approximately 25 U.S. sites. Management plans to use print and radio media to spark military interest in the study, and then hope peer-networking speeds enrollment throughout 2015. We are anticipating data in the first half of 2016.

There is enormous overlap between fibromyalgia and PTSD. According to Tonix, 50% of the FM or PTSD patient population meets the criteria for the other disorder. Plus, the manifestations and treatment paradigms are similar, and include disturbed sleep and painkiller abuse and addition. Roughly 3.5% of the U.S. adult population suffers from PTSD. The numbers are shockingly high for U.S. military service personnel, a population with high incidence of suicide and opioid addiction. It's a sad and growing problem, and there have been no new approved medications for PTSD in over a decade.

Tonix' Phase 2 program will focus specifically on PTSD associated with military / combat service. Although management has narrowed the PTSD population, eliminating things like car accidents and sexual assault, the homogenous population should lead to improved data collection. Plus, the growing attention of the U.S. government in this area should eventually lead to grants or additional funding in the future. It's an astute development plan in our view. If the AtEase trial is successful, we believe Tonix will move forward with two Phase 3 registration programs in 2016.

The U.S. PTSD population is estimated at 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 similar pricing ($15 per day) and market penetration (roughly 5%) as noted above for fibromyalgia, we believe TNX-102SL peak sales in PTSD are around $450 million in 2026.

The biggest change between our fibromyalgia model and our PTSD model is our probability of approval. We are using only 15% for this indication given the historic difficulty in treating PTSD patients and the earlier-stage nature of the program. After all, the BESTFIT data give us a very good look at what to expect from AFFIRM. With AtEase, Tonix is still attempting to generate this type of proof-of-concept data that will help design registration programs for TNX-102SL in PTSD. The historical success rate of a Phase 2 program in this type of indication is approximately 15%. We do not believe it is prudent to assume any better at this stage. As such, we believe the current value for TNX-102SL in PTSD is $60 million.

Valuation and Conclusion

For Tonmya™ in fibromyalgia, we assume approval and launch in 2019, with the drug costing approximately $15 per day. We are assuming Tonix (or its partner) can capture 5% of the market by 2023, with peak sales of close to $775 million. If we apply an 18% discount rate and 40% probability of success to the asset, we arrive at a net present value (NPV) for Tonmya™ in fibromyalgia of approximately $169 million.

For PTSD, a slightly smaller peak sales opportunity of $450 million exists. We believe approval of TNX-102SL in PTSD is approximately one year behind the timelines noted above for fibromyalgia. Thus, our NPV analysis for TNX-102SL in PTSD yields a fair value valuation of approximately $60 million. We believe there is potential for Tonix to receive partial funding of the AtEase study from the U.S. Department of Defense (DOD) not currently factored into our model. Nevertheless, together, we believe TNX-102SL in PTSD and fibromyalgia are worth roughly

$230 million in NPV. We remind investors that TNX-102SL is protected by a pharmacokinetic patent that does not expire until 2033 and a composition-of-matter patent that does not expire until 2034.

For TNX-201, we believe the drug has a 20% probability of success and based on peak sales of over $400 million in 2025 its NPV is $67 million. Once we have a look at data from the current Phase 2 study, we will get a better sense of the drug's efficacy in patients, which will help to refine both our outlook on peak sales and probability of approval.

Summing up our NPV calculations we arrive at a total firm value of approximately $296 million. Tonix exited the second quarter 2015 with $48.7 million in the bank and the company raised gross proceeds of $20.1 million from a public offering in July 2014, thus we estimate the company currently has approximately $66 million in cash and will probably exit the third quarter of 2015 with approximately $57 million. That is enough to fund operations into 2017. We believe the company will require approximately $125 million to fund operations to cash flow positive in 2020. Thus, even with the recent raise we know that Tonix will need to raise additional cash through public offerings or partnering its drugs in 2016. Based on our sum-of-parts NPV analysis, we believe the stock is worth approximately $18 per share today. We believe there are several catalysts on the horizon that can lead to a dramatically higher stock price ahead of that expected need for additional cash in 2017. For example, between now and then, Tonix should report:

- ✓ F203 Long-term safety study analysis from BESTFIT in August 2015
- ✓ Phase 2 data with TNX-201 in the Q1-2016
- ✓ Phase 2 data from AtEase in PTSD with TNX-102SL in the first half of 2016
- ✓ Phase 3 data from AFFIRM in fibromyalgia with Tonmya™ in Q4-2016

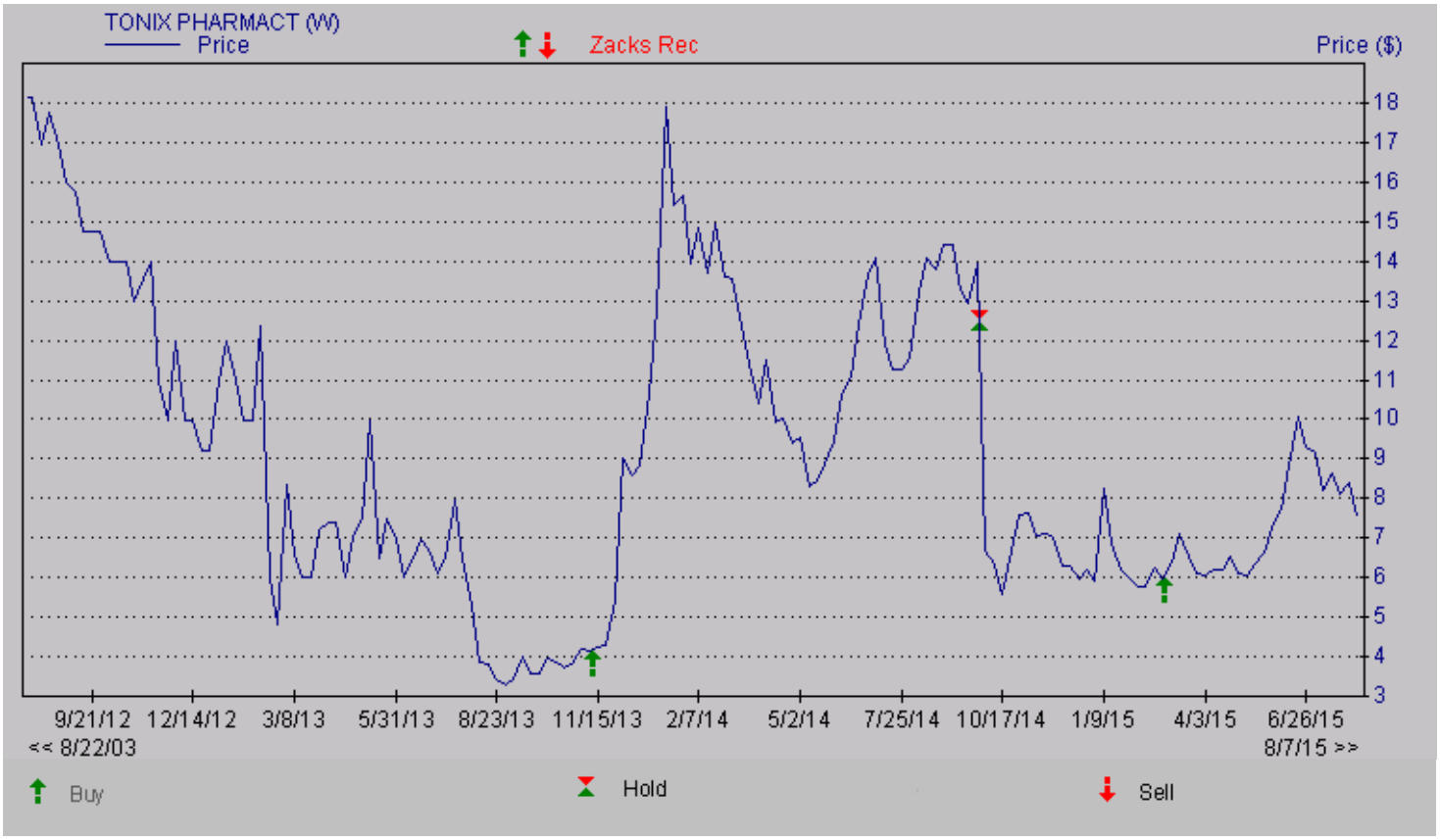
If the company can raise this $60 million in additional cash at prices in the $10-15 per share range, then the new dilution will be minimal – approximately 5 million shares. Based on the diluted share count of approximately 19.7 million today (assumes only exercisable stock options and warrants in-the-money), we see fair-value at $18 per share. However, if we add in approximately 5 million shares for expected financing activities in 2017 and 2018, we arrive at a more reasonable fair-value target of $14 per share. As such, investors with a longer time horizon can buy Tonix today and see nice returns as we expect clinical progress to drive the shares higher.

Tonix Pharma
Income Statement

Tonix Pharmaceuticals	2014 A	Q1 A	Q2 A	Q3 E	Q4 E	2015 E	2016 E	2017 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	$18.6	$6.8	$8.9	$7.0	$7.5	$30.2	$30.0	$30.0
SG&A	$9.0	$2.9	$2.9	$2.8	$3.0	$11.6	$12.0	$13.0
Operating Income	($27.7)	($9.7)	($11.8)	($9.8)	($10.5)	($41.8)	($42.0)	($43.0)
Operating Margin	-	-	-	-	-	-	-	-
Interest & Other Income	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Pre-Tax Income	($27.6)	($9.7)	($11.8)	($9.8)	($10.5)	($41.8)	($42.0)	($43.0)
Taxes & Other	$0	$0	$0	$0	$0	$0	$0	$0
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Net Income	($27.6)	($9.7)	($11.8)	($9.8)	($10.5)	($41.8)	($42.0)	($43.0)
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($2.77)**	**($0.71)**	**($0.73)**	**($0.53)**	**($0.56)**	**($2.50)**	**($2.10)**	**($1.91)**
YOY Growth	*-17.9%*	-	-	-	-	*-9.6%*	*-16.0%*	*-9.0%*
Weighted Shares Outstanding	10.0	13.7	16.1	18.4	18.6	16.7	20.0	22.5

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

HISTORICAL ZACKS RECOMMENDATIONS



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