Zacks Small-Cap Research

November 5, 2012
Jason Napodano, CFA
312-265-9421
jnapodano@zacks.com

scr.zacks.com
111 North Canal Street, Chicago, IL 60606

Tonix Pharmaceuticals Holding Corp. (TNXP-OTC)

TNXP: Initiating Coverage of Tonix Pharma At 'Neutral' and $1.50 Target…

Current Recommendation	**Neutral**
Prior Recommendation	N/A
Date of Last Change	07/23/2012
Current Price (11/05/12)	$0.68
Target Price	**$1.50**

INITIATION

We are initiating coverage of Tonix Pharmaceuticals with a 'Neutral' rating. The company is developing a novel cyclobenzaprine product, TNX-102-SL, that offers improved pharmacokinetics and convenient sublingual dose formulation for the treatment of fibromyalgia (FM). TNX-102-SL is being designed specifically for bedtime dosing in order to help patients improve quality (restorative) sleep and reduce the next-day pain and "fibro-fog" that is persistent with FM. We believe this is a meaningful opportunity for Tonix, mainly because currently approved FM medications, such as Pfizer's Lyrica (pregabalin) and Lilly's Cymbalta (duloxetine), do little to improve sleep quality. We see TNX-102-SL as a $300 million opportunity in the U.S. We have performed a discounted cash flow analysis and arrived at a target price for Tonix of $1.50.

SUMMARY DATA

52-Week High	**$1.50**
52-Week Low	**$0.65**
One-Year Return (%)	**N/A**
Beta	**0.02**
Average Daily Volume (sh)	**4,119**
Shares Outstanding (mil)	**34**
Market Capitalization ($mil)	**$23**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**3**
Insider Ownership (%)	**N/A**
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 2012 Estimate	**N/A**
P/E using 2013 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)
2011	0 A	0 A	0 A	0 A	0 A
2012	0 A	0 A	0 E	0 E	0 E
2013					0 E
2014					0 E

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

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2011	-$0.03 A	-$0.04 A	-$0.04 A	-$0.05 A	-$0.16 A
2012	-$0.06 A	-$0.09 A	-$0.05 E	-$0.05 E	-$0.26 E
2013					-$0.18 E
2014					-$0.17 E

© Copyright 2012, Zacks Investment Research. All Rights Reserved.

WHAT'S NEW

Initiating Coverage Of Tonix Pharmaceuticals

We are initiating coverage of Tonix Pharmaceuticals with a 'Neutral' rating. The company is developing a sublingual very low dose cyclobenzaprine product, TNX-102-SL, that offers improved pharmacokinetics and convenient sublingual dose formulation for the treatment of fibromyalgia (FM). FM is a complex medical disorder characterized by widespread musculoskeletal pain, fatigue, lack of sleep, and mood and memory issues. The National Pain Foundation estimates that 90% of all FM patients have sleep problems. A sublingual formulation of cyclobenzaprine is being designed specifically for bedtime dosing in order to help patients improve quality (restorative) sleep and reduce the next-day pain and "fibro-fog" that is persistent with FM.

We believe this is a meaningful opportunity for Tonix, mainly because currently approved FM medications, such as Pfizer's Lyrica (pregabalin) and Lilly's Cymbalta (duloxetine), do little to improve sleep quality. Plus, cyclobenzaprine is a well-known and commonly used medication already for FM. Market research conducted by Frost & Sullivan found that cyclobenzaprine was the third most commonly prescribed medication for FM behind Lyrica and Cymbalta in 2010. Decision Resources estimates that approximately 50 million cyclobenzaprine tablets were taken by FM patients, off-label, in 2011. That's 5% of the cyclobenzaprine market. TNX-102-SL is an improved, very low dose, sublingual formulation suitable for long-term dosing and designed to have fewer next-day residual effects.

We see TNX-102-SL as a potential $300 million opportunity in the U.S., and believe that, if successful in its first phase 3 trial, Tonix should be able to secure a commercialization deal in 2014. With positive phase 3 data from a first registration trial, we believe Tonix should be able to secure over $25 million upfront for TNX-102-SL, with development, regulatory, and backend sales milestones north of $250 million.

…Neutral While We Wait…

Tonix exited the second quarter (ended June 30, 2012) with approximately $1.34 million in cash. We forecast that cash at the end of the third quarter (ended September 30, 2012) stood at around $0.2 million. We believe that management is planning to raise an estimated $8 to $10 million in cash sometime in the next few weeks. The cost of the entire phase 3 program is estimated at approximately $20 million. We believe that Tonix requires at least $4 million to fund the first pivotal program and another $4 million to fund operations and then negotiate with commercialization partners.

We have conducted a discounted cash flow (DCF) analysis on Tonix Pharmaceuticals incorporating our assumptions for a partnership and peak sales with TNX-102-SL in FM and PTSD, and the upcoming financing. We see $1.50 per share as fair-value. We would be buyers following completion of the financing.

INVESTMENT OVERVIEW

Tonix Pharmaceuticals is a specialty pharmaceutical company focused on developing new pharmaceutical products for central nervous system (CNS) conditions that may be safer and more effective than currently available treatments. The company uses ongoing advances in science and medicine to search for potential therapeutic solutions among already existing prescription pharmaceutical agents that have been successfully used in patients for other conditions. The goal is to create new dose formulations for these agents with the intent to developing products that are optimized for the new therapeutic uses or indications.



Fibromyalgia Syndrome

Fibromyalgia Syndrome (FM) is a complex medical disorder characterized by widespread musculoskeletal pain, fatigue, lack of sleep, and mood and memory issues. The pain associated with FM is often described as a constant dull ache or burning sensation, typically arising from the muscles along the back, neck and shoulders. FM tender points are identified by applying pressure to specific areas of the body, including the back of the head, between the shoulders, along the neck, the upper chest, the hips, and the knees.

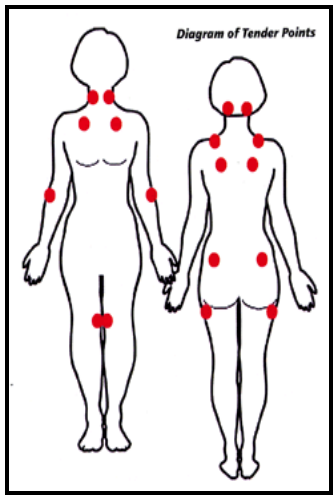


Figure 1

The FM diagnostic criteria, established by the American College of Rheumatology (ACR) in 1990, includes a history of widespread pain in all four quadrants of the body for a minimum duration of three months, and pain in at least 11 of the 18 designated tender points when a specified amount of pressure is applied (Figure 1).

Besides the dull aching pain and fatigue, patients with FM often also experience mood and psychological disorders such as anxiety and depression. Many people who have fibromyalgia also have tension headaches and temporomandibular joint disorders. The symptoms are often worse in cold or damp weather.

People with FM tend to wake up with body aches and stiffness. For some patients, pain improves during the day and gets worse at night. However, fatigue and sleep problems are common in almost all patients. The National Pain Foundation estimates that 90% of all FM patients have sleep problems. Patients with FM often report waking up tired, even after sleeping a long period of time. Others report frequent awakenings due to pain, sleep apnea, and restless leg syndrome in the middle of the night. Almost all FM patients report memory and concentration problems associated with the lack of sleep and distracting pain.

These sleep and concentration problems, referred to as “fibro-fog”, severely affect many FM patients to the point where employment is difficult to obtain and/or maintain. Approximately 20% of FM patients file some form of disability claim. Approximately 70% of FM patients report difficulty in conducting normal daily tasks, such as light housework. Chronic fatigue syndrome (CFS) has similar characteristics to FM, and patients are often diagnosed as having both FM and CFS.

…Causes…

The causes of FM are largely idiopathic, but common comorbid conditions include hypothyroidism, Lyme disease, endometriosis and irritable bowel syndrome. Physical trauma, surgery, infection, and psychological stress may bring about the onset of FM. In fact, stress is thought to play a significant role in the development of FM. There is a high correlation (approximately 42%) between the development of FM and post-traumatic stress disorder (PTSD).

…Medical & Psychiatric Comorbidity…

Medical	Prevalence		Psychiatric	Prevalence
Chronic Fatigue Syndrome	20-80%		Major Depressive Disorder	62%
Irritable Bowel Syndrome	32-80%		Bipolar Disorder	11%
Temporomandibular Disorder	75%		Panic Disorder	29%
Tension / Migraine Headaches	10-80%		Post-Traumatic Stress Disorder	21%
Chemical Sensitivities	33-35%		Social Phobias	19%
Interstitial Cystitis	13-21%		Obsessive Compulsive Disorder	7%
Chronic Pelvic Pain	18%			

Source: Aaron LA, et al. *BestPract Res Clin Rheumatol*. 2003;17:563-574; & Arnold LM, et al. *JClinPsychiatry*. 2006;67:1219-1225.

There is evidence that genetic factors may also play a role in the development of FM. Research has demonstrated that FM is potentially associated with polymorphisms of genes in the serotoninergic, dopaminergic and catecholaminergic systems. Many researchers and physicians believe that dopamine dysfunction is centrally responsible for the symptoms associated with FM. Others believe that decreased serotonin levels are involved in the pathophysiology of FM.

Increasing attention is being devoted to irregularities of the central nervous system as the underlying mechanism of FM. Patients with FM commonly have elevated corticotrophin releasing hormone (CRH) and elevated Substance P in the cerebrospinal fluid, and increased activated mast cells and chemokines (MCP-1 and IL-8) in the blood.

…Epidemiology…

The National Institutes of Health (NIH) estimates that FM affects approximately 5 million adult Americans, or roughly 2% of the general population. The American Fibromyalgia Syndrome Association (AFSA) pegs the prevalence higher, at approximately 3 to 5% of the general population. These statistics are in agreement with the National Fibromyalgia Association (NFA), which estimates approximately 10 million Americans with FM.

Diagnosis is usually made between the ages of 20 to 50 years, but the incidence of FM rises with age. In fact, by age 80, approximately 8% of adults meet the ACR classification of FM. Diagnosis is often done by a rheumatologist (~42% of the time) or general practitioner (~35% of the time).

Women outnumber men diagnosed with FM by 9 to 1. Many female FM patients report flare-ups associated with their menstrual cycle. As noted above, there is a high correlation of FM and endometriosis. FM is often seen in families, among siblings or mothers and their children as well. Risk in developing FM increased by 8.5x if a first-degree family member has been diagnosed with FM.

…Treatment Options…

FM is a relatively new diagnosis. Prior to the 1990's it was often incorrectly diagnosed as osteoarthritis or chronic fatigue syndrome. In fact, a survey conducted by Russell K. Portenoy, MD, Chairman and Gerald J. Friedman Chair in Pain Medicine and Palliative Care at the Departments of Pain Medicine and Palliative Care, Beth Israel Medical Center, New York, NY, in 2007 found that 46% of newly diagnosed FM patients (n=2,596) consulted between 3 and 6 physicians before being finally being diagnosed with FM.

There is no cure for FM. Treatment typically consists of symptom management. Beside cognitive behavioral therapy and physical therapy, data suggests that FM patients are high pharmacological treatment seekers. Over 50% of FM patients visit their treatment physician over five times a year. Nearly three-fourths spend between $100 and $500 per month on OTC medications and nearly two-thirds spend the same amount on prescription medications.

FM is a highly complex disease, with manifestation of pain, mood and psychological disorders, and sleep disturbances. The NFA notes healthcare practitioners should, "Establish a multifaceted and individualized approach…" for each specific patient depending on the severity of the symptoms in pain, mood, and sleep. There is no universally accepted standard-of-care. As such, multi-pharmacology is the norm for treating patients with FM

Lyrica

There were no FDA approved medications for FM until 2007 when the U.S. FDA approved Pfizer's Lyrica (pregabalin). Lyrica is a second-generation alpha-2-delta ligand calcium channel blocker that decreases the release of neurotransmitters including glutamate, noradrenaline, substance P and calcitonin gene-related peptide. Pfizer designed the drug as a more potent successor to gabapentin. The approval of Lyrica was a major step forward for the treatment of FM associated pain. The drug replaced the use of off-label analgesics, including gabapentin, but does little to address the mood or sleep-related issues associated with FM.

Pfizer sold $3.7 billion worth of Lyrica worldwide in 2011. U.S. sales of Lyrica totaled $1.5 billion. FDA approvals include neuropathic pain and fibromyalgia. We estimate that around 1/3rd of Lyrica prescriptions, or around 3.2 million prescriptions annually in the U.S. accounting for roughly $500 million in sales, are in FM.

Cymbalta & Savella

In 2008, the U.S. FDA approved Eli Lilly's Cymbalta (duloxetine), a serotonin-norepinephrine reuptake inhibitor (SNRI) for the treatment of FM. Cymbalta is a highly effective molecule for addressing both pain and the mood / psychological disorders associated with FM. The drug has only a modest benefit on improvement in quality (restorative) sleep. Still, however, the approval of Cymbalta facilitated the replacement of older generation and off-label use of anti-depressants for the treatment of FM.

Lilly sold $4.2 billion worth of Cymbalta worldwide in 2011. U.S. sales of Cymbalta totaled $3.2 billion. FDA approvals include major depressive disorder, diabetic peripheral neuropathic pain, general anxiety disorder, and fibromyalgia and chronic musculoskeletal pain. We estimate that around 1/5th of U.S. Cymbalta sales, or around 3.5 million tablets annually in the U.S. accounting for roughly $550 million in sales, are in FM. In 2009, the U.S. FDA approved Forest Lab's Savella (milnacipran), a serotonin-norepinephrine reuptake inhibitor (SNRI) for the treatment of FM. Savella is only indicated for the treatment of FM. Sales were approximately $100 million in 2011.

SNRI molecules carry significant side-effect risks, including nausea, headache, constipation, dizziness, insomnia, hypertension, increased heart rate and palpitations, loss of appetite, vision changes, mood swings, restlessness, sedation, sexual dysfunction, and suicidal thoughts.

Besides the above approved treatment options, many physicians and patients seek off-label medications to augment Lyrica and Cymbalta to create a more complete treatment regimen for FM.

Opioids & Tramadol

Opioid use is common for the treatment of severe pain. In fact, almost 40% of all FM patients will try opioids as a treatment option for managing the pain associated with FM. However, opioids carry significant side effects and addiction risk, so they should be used with caution. Opioids may also worsen mood (increase depression) and have little to no effectiveness in restorative sleep.

Tramadol is a centrally acting analgesic with atypical opioid and anti-depressant-like activity. The drug is moderately effective in treating FM pain. Effects on mood and restorative sleep are less predictable. Side effects included constipation, drowsiness, nausea, headache, and dizziness. In addition, long-term use of tramadol may be associated with physical dependence and withdrawal syndrome.

Naltrexone, an opioid antagonist, at very low dosage has been found to be effective in reducing fibromyalgia symptoms in a small controlled trial. Naltrexone also acts at very low dosage to inhibit microglia cells thereby reducing pro-inflammatory cytokines and neurotoxic superoxides.

Dopamine Agonists

Dopamine agonists such as Mirapex (pramipexole) and ReQuip (ropinirole) have been shown to result in some improvement in a minority of patients, but numerous side effects, including the onset of impulse control disorders have led to limited use.

Muscle Relaxants

Muscle relaxants, such as cyclobenzaprine, are wildly used for the treatment of muscle spasms and acute musculoskeletal pain. We discuss cyclobenzaprine in greater detail below.

With the approvals of Lyrica, Cymbalta, and Savella, use of off-label or experimental medications for the treatment of FM is declining. Frost & Sullivan conducted a market study on behalf of Tonix Pharmaceuticals that concluded the total prescription market for FM was approximately $1.2 billion in 2010. Frost & Sullivan concluded that the market has grown at a compound annual growth rate of 18% since 2007. Decision Resources estimates that approximately $1.1 billion of the $1.3 billion market in 2011 was on-label sales of Lyrica (~$450M), Cymbalta (~$550M), and Savella (~$100M), with the other $0.2 billion coming from off-label use of drugs like Tramadol, naltrexone, and cyclobenzaprine. We note that dollar sales of off-label cyclobenzaprine is muted by the low cost of the generic molecules. In actual prescription numbers, Tonix management estimates that cyclobenzaprine is third most commonly prescribed drug for FM.

…Limitations Of Existing Treatments…

Despite the fact that the FM market is generating $1.2+ billion in prescription sales, headlined by blockbuster drugs such as Lyrica and Cymbalta, we see a significant void for one of the main manifestations of the disease – sleep disturbance. No one molecule targets all three areas of the disease (Figure 2). As noted above, The National Pain Foundation estimates that 90% of all FM patients have sleep problems. Unfortunately, drugs indicated specifically for insomnia, such as Ambien (zolpidem) and Lunesta (eszopiclone), seem to do little to reduce the chronic fatigue and lethargy associated with FM. For most FM patients, it's not a lack of sleep; it's a lack of quality restorative sleep.

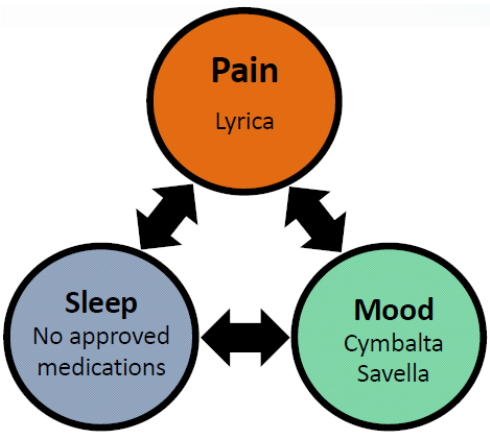


Figure 2

The combination of pain and sleep disturbance is a double-edged sword: the pain makes sleep more difficult and sleep deprivation exacerbates pain. In fact, data shows that a reduction in sleep disturbance is usually followed by improvement in pain symptoms. This also highlights the importance of healthy sleep and access to sleep specialists in treating the disease.

Accordingly, we see a meaningful opportunity for a new medication that targets this unmet area. Polypharmacy is already common in the treatment of FM, as is experience with cyclobenzaprine.

Cyclobenzaprine

Cyclobenzaprine is a muscle relaxant medication used to relieve skeletal muscle spasms and associated pain in acute musculoskeletal conditions. The drug was first synthesized by scientists at Merck in 1961. Merck received U.S. approval for 10 mg immediate-release formulation, called Flexeril, in 1977. It is also commonly used off-label for the treatment of fibromyalgia. In fact, there have been a number of well-controlled clinical studies addressing the potential use and benefit of cyclobenzaprine in treatment symptoms of FM; however, to management's knowledge, Tonix is the only company pursuing U.S. FDA approval of a cyclobenzaprine product for fibromyalgia.

In the 1990's, Merck conducted studies to support an application to market a low dose (5 mg) Flexeril tablet for the over-the-counter (OTC) market. Although Merck's studies re-affirmed the safety and efficacy of cyclobenzaprine in several large clinical trials, the OTC division of the FDA rejected the application for use without a prescription, most likely because muscle spasm was deemed a condition that required a physician to diagnose and supervise the cyclobenzaprine (or other) treatment.

Merck divested the Flexeril franchise to Alza Pharmaceuticals. Alza subsequently was acquired by Johnson & Johnson. Based largely on the Merck studies, J&J won approval of Flexeril 5 mg tablets as a prescription medicine to treat muscle spasm. J&J promoted Flexeril 5 mg tablets briefly under Hatch-Waxman. There are now several generics providers of immediate release cyclobenzaprine at 10 mg. Doses below 10mg, such as the 5 mg tablet, are available but not in particularly high demand.

Cephalon acquired the rights to a 15 and 30 mg controlled-release cyclobenzaprine product, Amrix, in 2007 from ECR Pharmaceuticals. It is now also available as a generic. We think this is important to note because applications for approval of new formulations of older generic drugs sometimes get held up at the FDA because the safety or efficacy data in the monograph are out of date. The FDA will use the 505(b)(2) application as an opportunity to update the efficacy dossier (see Cipher Pharmaceuticals application for approval of CIP-Isotretinoin) or enhance the safety database (see Transcept Pharmaceuticals application for approval of low-dose zolpidem).

We believe the FDA's files on cyclobenzaprine are relatively fresh thanks to the work done by Merck and ECR Pharma over the past decade. The drug is not a controlled substance and is widely known among physicians that treat FM. Prescription tracking services note over 223 million prescriptions written in 2010.

…Market Research In FM…

In 1991, the Department of Psychiatry at Toronto Hospital in Ontario, Canada published a paper in the Journal of Rheumatology (1991,18(3):452-4) entitled, "The effects of cyclobenzaprine on sleep physiology and symptoms in patients with fibromyalgia." The paper highlighted a double blind, placebo controlled, crossover design study examining overnight sleep physiology, pain, fatigue, and mood symptoms in 12 patients with fibromyalgia treated with cyclobenzaprine. Nine patients completed the study. Patients receiving cyclobenzaprine showed a decrease in evening fatigue ($F = 4.7$, $p<0.05$) and an increase in total sleep time ($F = 4.4$, $p<0.05$). Pain, including tender point count and dolorimetry, mood ratings, and alpha non-REM EEG sleep anomaly were unchanged by cyclobenzaprine.

Despite the fact that cyclobenzaprine did little to improve pain or mood scores, the effects on sleep physiology were intriguing. In 1993, the Rheumatology Unit at L. Sacco Hospital in Milan, Italy published a paper in the Journal of International Medical Research (1993,21(2):74-80) entitled, "A double-blind crossover study of two cyclobenzaprine regimens in primary fibromyalgia syndrome." In the study, the efficacy and tolerability of oral cyclobenzaprine were compared in 40 patients affected by primary fibromyalgia syndrome. The patients were randomly divided into two groups, each treated for 15 days with either a single dose of 10 mg/day cyclobenzaprine at bedtime or 30 mg/day cyclobenzaprine in three equal doses daily. Both regimens resulted in a significant decline in the number of tender points; significant improvements were also reported in the quality of sleep, anxiety, fatigue, irritable bowel syndrome and stiffness.

Results show there was no significant difference in efficacy between the two therapeutic regimens at any stage during the trial – i.e. higher doses of cyclobenzaprine were no more effective than lower doses. However, the frequency of reported side-effects was significantly greater ($p<0.001$) when patients received 30 mg/day cyclobenzaprine (26 patients, 84%) than when they received 10 mg/day (10 patients, 27%). Therefore, the authors concluded that a dose of 10 mg cyclobenzaprine at bedtime significantly improved the symptomatology of patients affected by primary fibromyalgia syndrome, and that the higher dose did not further reduce these symptoms but did result in a higher incidence of side-effects.

In February 2004, researchers from the Walter Reed Army Medical Center, Washington, DC and Uniformed Services University of the Health Sciences, Bethesda, MD, published a meta-analysis of previous studies conducted with cyclobenzaprine for the treatment of FM in the Journal of Arthritis & Rheumatism (Vol.51, No.1,9-13), and later presented at the American College of Rheumatology. For the paper, the authors looked at five randomized, controlled trials that included a total of 312 patients (95% were women). The studies generally included a once-daily dose of cyclobenzaprine or placebo. Dosages were generally started at 10 mg at bedtime and titrated as tolerated. If participants found the medication to be too sedating, the dosage (placebo or cyclobenzaprine) was changed to the previous dosage, with a minimum of 10 mg cyclobenzaprine or "equivalent" placebo.

Abstracted outcomes included global improvement and treatment effects on pain, fatigue, sleep, and tender points (number and/or severity). Treatment effects were extracted as continuous variables at 3 time points (4, 8, and 12 weeks). Overall, patients treated with cyclobenzaprine were more likely to report themselves to be "improved" (odds ratio [OR] 3.0, 95% confidence interval [95% CI] 1.6 –5.6) than those treated with placebo. A statistically significant improvement in sleep was noted for all time points with a standardized mean difference ranging from 0.34 to 0.50 (Figure 3). Pain was improved in the cyclobenzaprine group in week 4 only. No improvement in fatigue or tender points was noted at any time point.

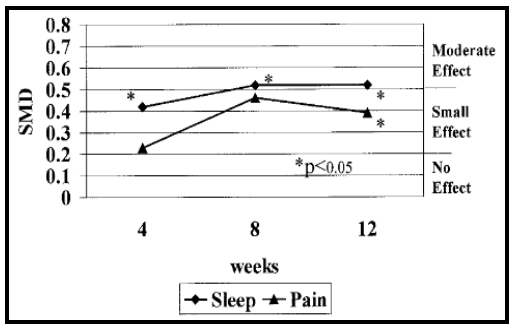


Figure 3

The authors conclude that cyclobenzaprine improves global functioning of patients with FM, with a modest improvement in sleep quality and a small improvement in pain, but no effect on fatigue or tender points. The authors suggest future studies to clarify the true benefit of cyclobenzaprine in FM.

…Limitations Of Existing Formulations…

Despite the approved uses of cyclobenzaprine in treating muscle spasm, we believe current marketed formulations of cyclobenzaprine are limited for treating FM by unpredictable absorption and significant side effects. As described in the Flexeril package insert, the amount of cyclobenzaprine absorbed into the bloodstream varies between 33-55% of the dose ingested. The variability in absorption may be due to several factors, including effects of the stomach pH on dissolution. Food in the stomach and small intestine from a recent meal contributes to variability in absorption of the oral tablet as well.

Uncertainties in absorption make it challenging for a physician contemplating a bedtime treatment for FM to ensure the intended therapeutic effect is achieved without risking side effects like next-day drowsiness, which could result if the patient has too much cyclobenzaprine remaining in the bloodstream the next day. Plus, cyclobenzaprine has a half-life of 18 hours, meaning a significant portion of the drug would remain active in the body the next morning, potentially when FM patients are driving to work. We believe that currently available generic 10 mg immediate release oral formulations of cyclobenzaprine are not well suited for a bedtime dosing.

The ideal formulation of cyclobenzaprine for FM would provide predictable absorption with rapid onset of action. Tonix believes that a very low dose (VLD) of cyclobenzaprine with improved bioavailability would be ideally suited for a bedtime dose in FM. The rapid onset means that patients are likely to receive a predictable therapeutic effect. The very low dose means that patients are less likely to experience residual side effects, including next-day drowsiness or effects on driving ability. And the sublingual dosing bypasses first-pass metabolism and variations in stomach pH and food effects.

Having witnessed the FDA's deep concern on the use of hypnotics and next-day driving, evidenced by the FDA's own insomnia workshop held in May 2011 and the Transcept Pharmaceuticals complete response letter in October 2009, we think a significant market opportunity exists for Tonix if they can gain approval for a sublingual very low dose cyclobenzaprine. We do not believe that the FDA would approve a 10 mg dose of oral cyclobenzaprine, in its existing formulation, for bedtime dosing due to the potential next-day residual effects.

Therefore, we believe that physicians, despite the availability of far cheaper generic alternatives, would consider prescribing a rationally designed dose and formulation of cyclobenzaprine specifically on improved absorption and to avoid concerns about next day residual effects and dangerous driving while cyclobenzaprine blood levels remain too high. We believe that if Tonix can demonstrate to the FDA that its sublingual VLD cyclobenzaprine, dosed at night, has acceptably safe blood levels, it would warrant market share gains upon launch.

TNX-102

Tonix Pharmaceuticals is currently developing a sublingual cyclobenzaprine product, TNX-102-SL, designed specifically for bedtime dosing in patients with FM. TNX-102-SL is a novel formulation with rapid absorption and minimal next-day somnolence.

…Phase 2a…

In December 2011, data from a phase 2a study with an oral formulation of cyclobenzaprine was published by the Sleep Disorders Clinics of the Centre for Sleep and Chronobiology, University of Toronto, Ontario, Canada (supported by Tonix Pharmaceuticals Inc.) in the Journal of Rheumatology (38(12):2499-2500). The trial was a randomized, double-blind, placebo-controlled, dose-escalating, parallel-design study in patients with FM and disrupted sleep. A total of 36 patients (1:1 VLD cyclobenzaprine vs. placebo) were treated for 8 weeks. Doses were taken between dinner and bedtime. The dosage was 1 mg for the first 7 days, after which, if clinically indicated and according to tolerability, the daily dose could be increased up to 4 mg (mean dose was 3.1 mg at week 8).

Tolerability: VLD cyclobenzaprine was well tolerated, with only 1 severe AE (headache) compared to five SAEs in the placebo group. The most common treatment related adverse events can be found in Figure 4, and was comparable between VLD cyclobenzaprine and the placebo. There were no serious adverse events in either group.

Adverse Event	VLD CBP (N = 18), n (%)	Placebo (N = 18), n (%)
Any adverse event	15 (83)	15 (83)
Headache	7 (39)	3 (17)
Dry mouth	6 (33)	1 (6)
Somnolence	4 (22)	2 (11)
Constipation	3 (17)	1 (6)
Dizziness	3 (17)	1 (6)
Nausea	2 (11)	5 (28)
Flu syndrome	2 (11)	1 (6)
Rhinitis	2 (11)	1 (6)
Pruritus	2 (11)	0

Figure 4

Pain: Musculoskeletal pain was rated on a 7-point scale (0 - 6) and showed patients on VLD cyclobenzaprine had a 26% reduction at week 8 (1.7 vs. 2.3, p=0.010) vs. no change for the placebo (p=0.044 vs. placebo).

Fatigue: Fatigue was rated on a 7-point scale (1 - 7) and showed patients on VLD cyclobenzaprine had a 14% reduction at week 8 (4.3 vs. 5.0, p=0.039) vs. a 4% (not significant) worsening for the placebo (4.9 vs. 4.7) (p=0.126 vs. placebo).

Tenderness: Application pressure was applied to specific body regions to assess tenderness. Patients on VLD cyclobenzaprine showed a 30% improvement in tenderness (18.6 vs. 14.3, p=0.006) vs. 1% (not significant) for the placebo (16.1 vs. 15.6) (p=0.029 vs. placebo).

Mood: Mood scores were assessed by the Hospital Anxiety and Depression Scale (HAD). Patients on VLD cyclobenzaprine showed a 24% reduction in HAD score (10.4 vs. 13.7, p=0.012) and 22% reduction in HAD depression (4.9 vs. 6.3, p=0.017) vs. a 4% reduction in HAD score (15.1 vs. 15.7) and 10.4% worsening in depression (7.4 vs. 6.7) for the placebo at week-8. Scores for HAD (p=0.067) and HAD depression (p=0.023) vs. placebo showed encouraging trends.

…Change In Baseline At Week-8…

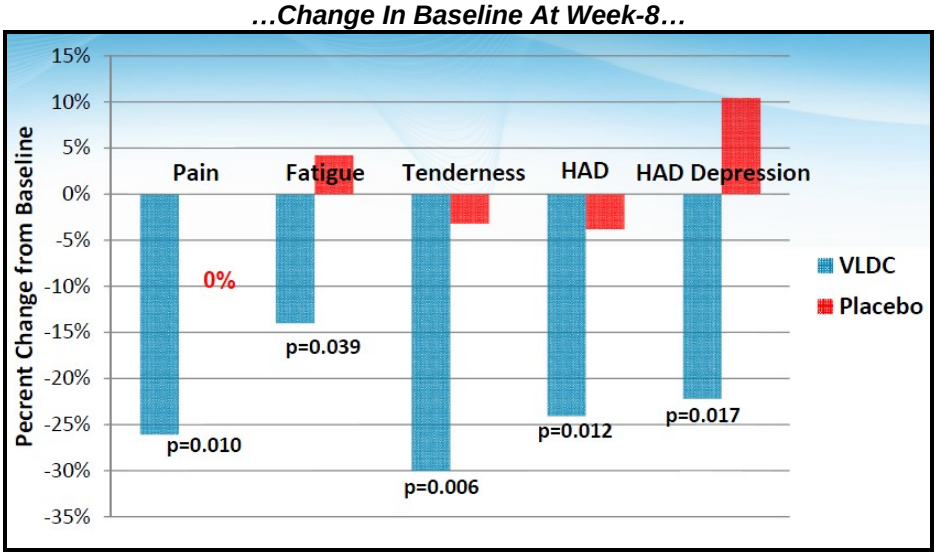


Figure 5

Subjective Ratings: The trial assessed both clinician-rated (CGIC) and patient-rated (PGIC) improvement scales for fatigue. Fatigue was evaluated using a scale of 5 ("worse") to 1 ("marked improvement"). VLD cyclobenzaprine treatment was associated with a statistically significant improvement in CGIC and PGIC in fatigue (p=0.003 and p=0.001, respectively). In contrast, placebo treatment did not result in statistically significant changes in any of these measures. However, relative to placebo, VLD cyclobenzaprine treatment did not significantly improve either measure (p=0.133 and p=0.257, respectively).

Effects On Sleep: Effects on sleep was assessed by using polysomnogram (PSG) recordings. PSG was performed at screening, at baseline, and typically at Weeks 2, 4, and 8. In the VLD cyclobenzaprine group from baseline to Week 8, total time awake decreased 38.5% (0.8 to 1.3 hrs, p=0.011), while total sleep time increased 12.3% (5.7 to 6.4 hrs, p=0.005), and sleep efficiency 15.6% (73.6% to 85.1%, p=0.023). In contrast, placebo treatment did not result in statistically significant changes in any of these measures. Compared to placebo, VLD cyclobenzaprine treatment did not significantly change total time awake, total sleep time, or sleep. Within the VLD cyclobenzaprine group from baseline to Week 8, VLD cyclobenzaprine treatment did not significantly change the percentages of Stage 1, 2, 3, or 4 or REM sleep (Figure 6).

…Effects of VLDC on Sleep…

		Last Observation Carried Forward (LOCF)						VLD CBP vs Placebo	
	Treatment	Baseline (SD)	Week 8 (SD)	Mean Change	% of Baseline	SD	LOCF p*	Treatment p**	% of Baseline
Total time awake, h	VLD CBP	1.3 (0.9)	0.8 (0.5)	–0.5	–38.5	0.74	0.011†	0.100	0.0
	Placebo	0.9 (0.7)	0.8 (0.5)	–0.1	–11.1	0.50	0.408		
Total sleep time, h	VLD CBP	5.7 (1.2)	6.4 (1.1)	0.7	12.3	0.93	0.005†	0.156	0.0
	Placebo	0.9 (0.7)	0.8 (0.5)	–0.1	–11.1	0.50	0.408		
Stage 1, %	VLD CBP	10.3 (3.7)	11.5 (3.8)	1.2	11.7	3.72	0.189	0.205	16.6
	Placebo	10.2 (5.0)	9.8 (4.6)	–0.4	–3.9	3.86	0.666		
Stage 2, %	VLD CBP	52.9 (8.1)	56.5 (10.0)	3.5	6.8	9.04	0.119	0.021†	11.1
	Placebo	53.2 (6.7)	50.6 (6.8)	–2.6	–4.9	5.87	0.077		
Stage 3, %	VLD CBP	7.4 (3.3)	8.6 (4.3)	1.2	16.2	3.52	0.166	0.166	21.9
	Placebo	7.2 (2.2)	7 (1.9)	–0.2	–2.8	2.04	0.683		
Stage 4, %	VLD CBP	10.5 (7.8)	7.5 (8.0)	–3.0	–28.6	7.64	0.114	0.029†	–55.1
	Placebo	10.9 (5.5)	13.4 (5.5)	2.5	22.9	6.81	0.138		
REM, %	VLD CBP	18.8 (5.2)	15.9 (5.1)	–2.9	–15.4	4.18	0.764	0.007†	–17.3
	Placebo	18.1 (5.1)	19.1 (4.1)	1.0	5.5	4.29	0.337		
Sleep efficiency, %	VLD CBP	73.6 (20.9)	85.1 (11.2)	11.5	15.6	19.56	0.023†	0.099	–2.3
	Placebo	83.9 (13.4)	86.9 (8.7)	3.0	3.6	8.31	0.144		

Figure 6

To conduct a more thorough analysis of sleep quality, the authors assessed cyclic alternating pattern (CAP), an objective physiological measure of electroencephalographic (EEG) activity within non-REM sleep – essentially a measure of sleep maintenance and fragmentation. CAP in sleep has been shown to reflect disturbed sleep and may give a more accurate picture of sleep quality. A CAP sequence consists of two or more CAP cycles each having an A and B phase lasting between 2 and 60 seconds. Subtype A1 may occur when the brain is trying to maintain sleep. The other two subtypes A2 and A3 may occur due to central nervous system arousal. The higher the A1 phase the better the sleep stability. The higher the A2+A3 phase, the greater the sleep disturbance. Patients with FM have been shown to demonstrate significantly higher levels of A2+A3 (*Cyclic alternating pattern: A new marker for sleep alteration in patients with fibromyalgia?* J Rheumatol 2004;31:1193-9).

The phase 2a data show that patients receiving VLD cyclobenzaprine had a meaningful and statistically significant reduction in A2+A3 phase (72% of treated patients had a reduction of 33% or more vs. only 33% for the placebo group, p=0.019) (Figure 7).

Increased levels of A2+A3 have a high correlation to other symptoms of FM, including fatigue and depression (Figure 7) (*Cyclic alternating pattern: A new marker for sleep alteration in patients with fibromyalgia?* J Rheumatol 2004;31:1193-9).

Sleep EEG	VLDC	Placebo	p
$CAP_{A2+A3(Norm)}$ ≤33%	72%	33%	0.019

	VLDC $CAP_{A2+A3(Norm)}$ Correlation	
Variable	r	p
Fatigue	0.617	0.006
HAD score	0.505	0.033
HAD depression subscore	0.556	0.017
Patient-rated change in fatigue	0.614	0.007
Clinician-rated change in fatigue	0.582	0.011

Figure 7

…Formulation Work…

In November 2011, Tonix received FDA clearance to initiate a comparative pharmacokinetic (PK) and bioavailability (BA) study of TNX-102. The comparative PK/BA study enrolled approximately 30 healthy adult volunteers who participated in a single-dose, open-label, randomized three-way-crossover study. The study compared a TNX-102 candidate gelcap (liquid filled capsule) containing a very low dose (2.4 milligrams) of cyclobenzaprine to a approved, immediate-release, 5 milligram cyclobenzaprine tablet. In addition, the effects of food on the PK of TNX-102 gelcaps were investigated in subjects who are either fasting or fed with a high-fat, high-caloric breakfast.

In April 2012, Tonix released data from the PK/BA study. The data showed both TNX-102 2.4 mg promicellar gelcaps and the cyclobenzaprine 5 mg immediate release tablet were well-tolerated. There were no serious and/or unexpected adverse events.

The gelcap formulation preserved fundamental properties of the tablet including the rate of absorption and elimination of cyclobenzaprine. Absorption was measured by the time to peak plasma concentration, or T_{max}, and elimination was measured by the half-life, or $T_{½}$. Findings show similar T_{max} and $T_{½}$ between the two formulations under fed conditions, suggesting that TNX-102 retained the therapeutic beneficial effects on FM patients observed in the phase 2a study. When compared to the generic cyclobenzaprine 5 mg immediate release tablet administered under fasting conditions, TNX-102 had a lower extent and rate of absorption, as measured by the area under the curve (AUC) of the time and concentration data and also by the maximum concentration or C_{max}.

No food effect was observed in the comparison of TNX-102 2.4 mg promicellar gelcaps between fed and fasting states, indicating this formulation provides dosing precision. Management believes the finding demonstrates that TNX-102 2.4 mg promicellar gelcap is clearly differentiated and not bioequivalent to generic cyclobenzaprine 5 mg immediate release tablet. This suggests that a commercial product based on the new formulation would be protected from substitution by pharmacists with generic cyclobenzaprine.

In late July 2012, Tonix completed another comparative bioavailability study testing a new 2.4 mg sublingual (SL) formulation of TNX-102. The phase 1b open-label trial enrolled 23 healthy volunteers looking at measures of cyclobenzaprine (and norcyclobenzaprine) in plasma and urine at various time points over a 72 hour period. Tonix also assessed the safety and tolerability of TNX-102-SL over a month long period.

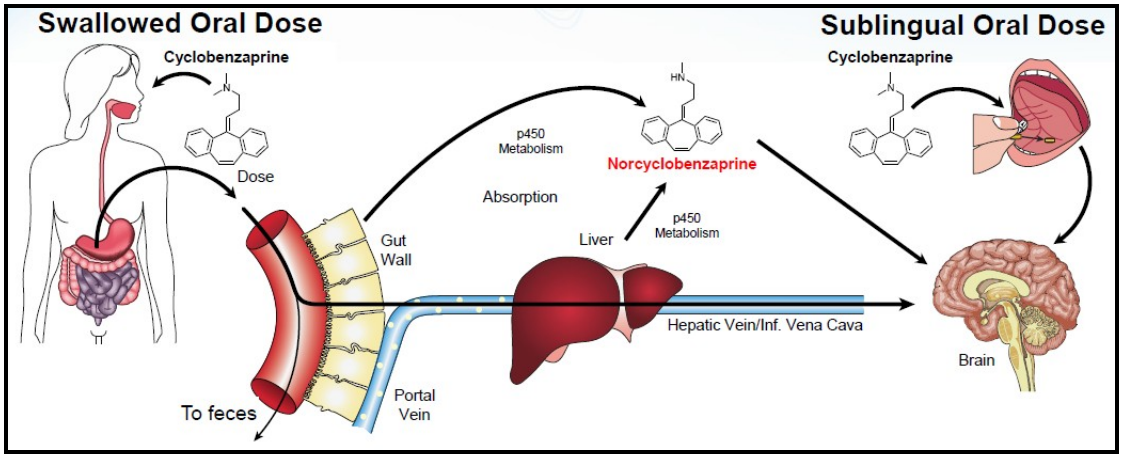
Arms	Assigned Interventions
Experimental: SL TNX-102 at pH 3.5 2.4 mg TNX-102 sublingual solution (2.4 mg/mL) in PBS at pH 3.5	Drug: SL TNX-102 2.4 mg at pH 3.5 1 dose of 2.4 mg TNX-102 sublingual solution (2.4 mg/mL) in PBS at pH 3.5, administered as 1 mL held under the tongue for 90 seconds without swallowing
Experimental: SL TNX-102 at pH 7.1 2.4 mg TNX-102 sublingual solution (2.4 mg/mL) in PBS at pH 7.1	Drug: SL TNX-102 2.4 mg at pH 7.1 1 dose of 2.4 mg TNX-102 sublingual solution (2.4 mg/mL) in PBS at pH 7.1, administered as 1 mL held under the tongue for 90 seconds without swallowing
Active Comparator: Cyclobenzaprine tablets 5 mg cyclobenzaprine tablet once	Drug: Cyclobenzaprine Tablet 1 x 5 mg cyclobenzaprine tablet, swallowed with 240 mL of room-temperature water
Active Comparator: Cyclobenzaprine IV 2.4 mg cyclobenzaprine USP in PBS (0.6 mg/mL) at pH 7.4	Drug: Cyclobenzaprine IV 1 dose of 2.4 mg cyclobenzaprine USP in PBS (0.6 mg/mL) at pH 7.4, administered intravenously as a 4 mL bolus injection over 30 seconds

Source: ClinicalTrials.gov #NCT01634412

The PK results demonstrated that the solution formulation of TNX-102-SL delivered cyclobenzaprine to the systemic circulation more efficiently than the sublingual solution of a simulated crushed tablet and faster than the ingested oral tablet. We believe this translates to more rapid effects compared with current generic cyclobenzaprine products, increased dosage precision and decreased potential for morning grogginess / residual effect.

…The Benefits of SL…

Tonix clearly now believes the path forward with TNX-102 is with the new sublingual formulation (TNX-102-SL), and we concur. The SL formulation dissolves quickly under the tongue and provides rapid absorption of cyclobenzaprine across the mucous membrane into the bloodstream. As noted above, this avoids the pH variability and food effect seen with generic oral cyclobenzaprine. It also avoids first-pass metabolism in the liver. This is very important because cyclobenzaprine, when taken orally, is absorbed into the small intestines and transported directly to the liver where it is metabolized into norcyclobenzaprine. According to the literature, norcyclobenzaprine is a long-lived, psychoactive metabolite believed to interfere with cyclobenzaprine's efficacy over time, potentially contributing to the reported decrease of benefit of oral cyclobenzaprine in fibromyalgia when taken chronically.



Source: Tonix Inc Investor Presentation (Sept. 2012)

…Pivotal Program…

Tonix has recently finalized plans to begin its pivotal studies with TNX-102-SL. We expect the company to conduct two sequential phase 3 trials, with the first to start in the first quarter 2013. This first phase 3 trial is expected to enroll 76 FM patients at 8 to 10 centers in the U.S. (1 to 1 randomization) with a primary endpoint at 12 weeks of fibromyalgia-associated pain. We expect data from this program either late 2013 or early 2014. If successful, management will move into the confirmatory phase 3 program, which is expected to be larger in both number of patients (perhaps 200-300), duration of treatment (24 weeks), and include secondary endpoints (such as fatigue, tenderness, HAD, and HAD depression). Management's goal will be to show improvement in these secondary endpoints at 24 weeks in hopes to include the language on the final label. Overall, the program is similar to what Pfizer and Eli Lilly used to gain approval for Lyrica and Cymbalta, respectively, for the treatment of FM (pain & composite endpoints).

We assume the second phase 3 program will start during the first half of 2014. However, before this program starts we expect management to seek a development and commercialization partner. The partner would help fund the costs of the second phase 3 program, and market the drug if approved. If all goes well, we could be looking at a new drug application (NDA) for TNX-102-SL under the 505(b)(2) pathway in early 2016. If approved, TNX-102 could become commercially available by the middle of 2017.

…Intellectual Property…

Intellectual property protection around TNX-102 consists of formulation technology and method of use patents. Tonix has been issued three U.S. patents to date on TNX-102:

USPTO	Name	Expiration
#6,541,523	Methods For Treating Or Preventing Fibromyalgia Using Very Low Doses Of Cyclobenzaprine.	June 27, 2021
#6,395,788	Methods And Compositions For Treating Or Preventing Sleep Disturbances And Associated Illnesses Using Very Low Doses Of Cyclobenzaprine"	August 11, 2020
#6,358,944	Methods And Compositions For Treating Generalized Anxiety Disorder	August 11, 2020

Tonix has been granted additional "Use of Composition" and "Composition and Methods" patents outside the U.S. that do not expire until August 2020 or beyond. The company has patent applications pending in the U.S. for treating fatigue using very low dose cyclobenzaprine, as well as for treating post-traumatic stress disorder and depression using very low dose cyclobenzaprine.

Tonix has obtained an exclusive worldwide option on a gelatin capsule formulation technology from Lipocine, Inc. protected by two U.S. patents (#6,294,192: "Triglyceride-free compositions and methods for improved delivery of hydrophobic therapeutic agents" and #6,451,339: "Compositions and methods for improved delivery of hydrophobic agents"). These patents expire on September 24, 2021 and September 16, 2022, respectively. However, we do not expect the company to move forward with the gelcap formulation. We expect all future clinical work will center around the new sublingual formulation.

Tonix has filed patent applications to protect the sublingual formulation of TNX-102. Management believes the new sublingual formulation supports a multi-tiered patent strategy that will provide exclusivity for TNX-102-SL to 2033. The company believes that results from preclinical and clinical pharmacokinetics and metabolic disposition studies warrant exclusivity and protection from generic alternatives. Specifically, the strategy is to obtain pharmacokinetics-based patent claims that would be difficult for generic companies to circumvent without infringement. Management does not know of any prior art that would prevent the issue of these new patents to protect TNX-102-SL.

…Sales and Commercial Potential…

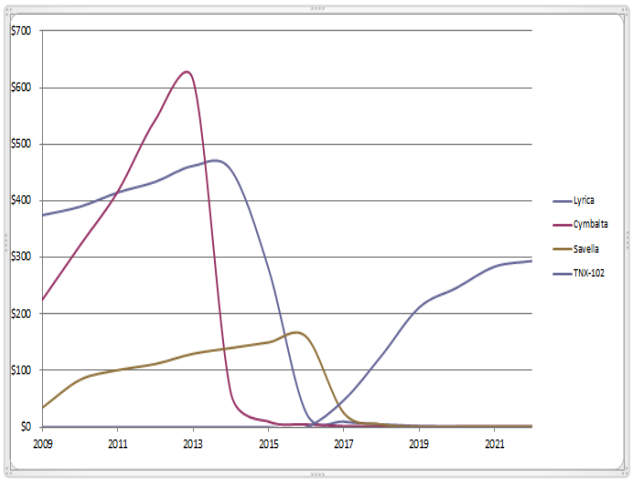
Averaging the data obtained from the NIH, AFSA, and NFA, we estimate there are approximately 8 million Americans living with FM. Over 90% of these patients have sleep problems. Approximately 70% of FM patients report difficult in conducting normal daily tasks, such as light housework due to chronic fatigue. Existing approved FM medications such as Lyrica and Cymbalta, which focus on reducing FM-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 FM.

If Tonix can gain approval for TNX-102-SL in FM using standardized pain and tenderness endpoints in its phase 3 program, while also demonstrating improvement in symptoms of fatigue and sleep quality, we believe a meaningful market opportunity exists. Frost & Sullivan estimate that 50 million tablets of cyclobenzaprine were sold specifically for FM in 2010. We believe at least a third of FM patients would actively seek out prescription therapy, either as a monotherapy or an adjunctive therapy to Lyrica or Cymbalta, with their physicians support, and try a novel sublingual formulation of VLDC. Tonix has successfully designed a superior 2.4 mg sublingual formulation of cyclobenzaprine to the readily available oral 10 mg generic. Does that mean there will be no, or even limited, generic substitution or competition once TNX-102-SL hits the market? No.

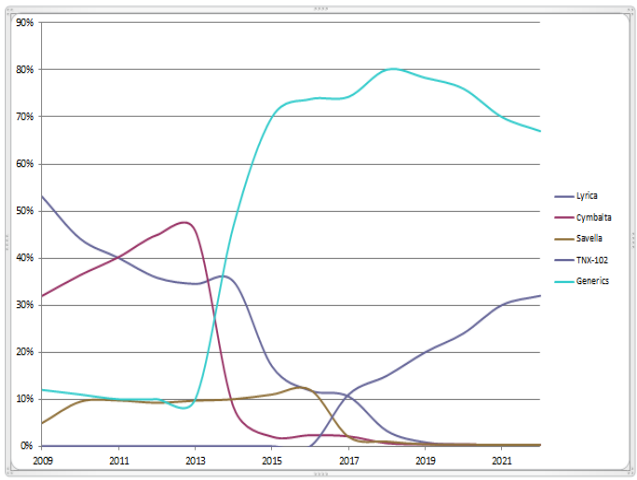
Based on the generic market, the target population for Tonix with TNX-102-SL is over 2 million patients. We think that the sublingual formulation clearly contains meaningful advantages over the generic oral formulation. These include rapid absorption and minimal next-day residual effects – ideal for a bedtime dose, and avoidance of first-pass metabolism and build-up of norcyclobenzaprine – ideal for chronic dosing.

For the purpose of our model, we assume Tonix (and its partner) can capture 5% share. That's one out of every twenty patients currently on generic oral cyclobenzaprine for FM switching to TNX-102-SL. At a cost of $6-7 per pill ($2,500 per year by 2020), with decent tier-2 and tier-3 coverage, we see TNX-102-SL as a $300 million peak drug. We expect that by 2017, both Lyrica and Cymbalta will be generic, and that Tonix' commercial partner will have one of the only (if not the only) branded prescription medications for FM available.

…Projected Sales In FM…



…Projected Market Share In FM…



Post-Traumatic Stress Disorder

Post-Traumatic Stress Disorder (PTSD) is a psychiatric disorder that can occur following the experience or witnessing of a life-threating or terrifying event or ordeal, such as military combat, natural disaster, terrorist incident, serious accident, sudden emotional loss, or physical or sexual assault in adult or childhood. People with PTSD experience persistent symptoms that include strong and unwanted memories (flashbacks) of the event, bad dreams, emotional numbness, social withdrawal, intense guilt or worry, angry outbursts, feelings of anxiety, and avoiding thoughts and situations that are reminders of the trauma.

The impact on both physical and mental health is significant. Recent research has shown people with PTSD experience clear and marked biological changes similar to that of psychiatric disorders anxiety or depression. PTSD can also change the way the body response to stress, creating imbalances in hormones and chemical neurotransmitters that last for years. These symptoms can be highly debilitating. Patients may also experience cognitive and memory impairment, which further leads to social withdrawal, occupational instability, marital problems, and family discord.

Symptoms often manifest physically in the form of sleep disturbance, feeling numb, and irritability. In fact, sleep disturbances are common symptoms of PTSD and include nightmares, nighttime anxiety attacks, and difficulty falling or staying asleep. Several lines of evidence link sleep disturbances to chronically perpetuating PTSD.

…Causes & Diagnosis…

As noted above, PTSD can be brought on by intense physical or emotional trauma. People with a history of trauma may be more apt to experience PTSD in the future. The cause of PTSD is unknown; psychological, physical, and social factors are involved. There is evidence that susceptibility to PTSD is hereditary. The traumatic events most often associated with PTSD for men are combat exposure, childhood neglect, and childhood physical abuse. The most traumatic events for women are rape, sexual molestation, physical attack, being threatened with a weapon, and childhood physical abuse.

There are no tests that can be done to diagnose PTSD, although mental health exams, physical exams, and blood tests are done to rule out other illnesses similar to PTSD like anxiety and depression. Experiencing a wide range of feelings and emotions after a traumatic event is normal, such as heightened fear and anxiety, a lack of focus, sadness, and changes in sleep or eating. But if severe disturbing thoughts and feelings persist for more than a month, or if an individual feels lack of physical and mental control, this could indicate PTSD.

The American Psychological Association (APA) suggests that only trained professionals (those who have experience with at least 10 trauma assessments) give tests to assess for PTSD. Formal diagnosis is made based on certain symptoms, and how long a time period the patient has had them, using DSM-IV and ICD-10 guidelines. In PTSD, symptoms are present for at least 30 days as opposed to a similar condition called Acute Stress Disorder (ASD), in which symptoms are present for a shorter period of time.

…Epidemiology…

According to a National Comorbidity Survey conducted by Harvard Medical School in 2005, an estimated 7.8% of Americans will experience PTSD at some point in their lives, with women (10.4%) twice as likely as men (5%) to develop PTSD. About 3.6% of U.S. adults aged 18 to 54 (5.2 million people) have PTSD during the course of a given year. This represents a small portion of those who have experienced at least one traumatic event; 60.7% of men and 51.2% of women reported at least one traumatic event.

The United States Department of Veterans Affairs estimates that 830,000 Vietnam War veterans suffered symptoms of PTSD. The National Vietnam Veterans' Readjustment Study (NVVRS) found 15.2% of male and 8.5% of female Vietnam Vets to suffer from current PTSD at the time of the study. Life-Time prevalence of PTSD was 30.9% for males and 26.9% for females. Estimates of PTSD from the Gulf War are as high as 10%. Estimates from the war in Afghanistan are between 6 and 11%. Current estimates of PTSD in military personnel who served in Iraq range from 12% to 20%.

A 2011 study from Georgia State University and San Diego State University, “The Psychological Costs of War: Military Combat and Mental Health,” concluded that for the 2.16 million U.S. troops deployed in combat zones between 2001 and 2010, the total estimated two-year costs of treatment for combat-related PTSD are between $1.54 billion and $2.69 billion.

…Treatment Options…

Modest benefits have been seen from early access to cognitive behavioral therapy (counseling). These sessions are typically three to six months, but may last up to two years. However, the ultimate benefit of post-event psychological interventions remains questionable. Some physicians feel as though multiple session or intense psychotherapy may result in worsen outcomes. Risk targeted interventions attempt to mitigate specific PTSD behavior and control anxiety.

A variety of medications has shown adjunctive benefit in reducing symptoms of PTSD, including selective serotonin reuptake inhibitors, alpha-adrenergic antagonists, anti-convulsants / mood-stabilizers, antipsychotics, beta blockers, benzodiazepines, glucocorticoids, and monoamine-oxidase inhibitors. Two SSRI molecules, Pfizer's Zoloft (sertraline) and Glaxo's Paxil (paroxetine), have been clinically shown to reduce symptoms of PTSD.

Zoloft — Pfizer gained approval for Zoloft for PTSD in December 1999. It was the first medication of its kind approved for PTSD. Data presented in the Journal of the American Medical Association (JAMA) in April 2000 (12;283(14):1837-44) showed that 53% of patients suffering from long-standing PTSD responded favorably (statistically significant reduction in Clinician-Administered PTSD Scale Part) within two weeks of treatment with the antidepressant Zoloft.

Zoloft sales peaked at $3.4 billion in 2004 before losing patent protection in December of 2005. Besides PTSD, the Zoloft label included FDA approvals for major depressive disorder, obsessive-compulsive disorder, panic attacks, social anxiety disorder, and premenstrual dysphoric disorder. We believe less than 10% of Zoloft sales are for PTSD.

Paxil — Glaxo gain approval for Paxil in PTSD in December 2001. Data presented in the American Journal of Psychiatry (158:1982-8) in 2001 showed that patients taking Paxil demonstrated a statistically significant improvement compared to placebo on all three PTSD symptom clusters (re-experiencing, avoidance / numbing, and hyperarousal), social and occupational impairment, and comorbid depression. Comorbid depression with PTSD is approximately 45%.

Paxil sales peaked at $3.1 billion in 2002 before losing patent protection in September 2003. Besides PTSD, the Paxil label included FDA approvals for major depressive disorder, obsessive-compulsive disorder, and premenstrual dysphoric disorder. Similar to Zoloft, we estimate that less than 10% of Paxil sales were for PTSD. In 2002, Glaxo gained approval for a controlled-release formulation of Paxil called Paxil-CR. Paxil-CR is not approved for use in PTSD.

Others — Many medications are used to treat PTSD off-label. Physicians may be partial to other SSRI molecules such as Prozac (fluoxetine) and Celexa (citalopram) beside Zoloft and Paxil. AstraZeneca's atypical antipsychotic, Seroquel (quetiapine), and benzodiazepines such as Valium (diazepam) and Xanax (alprazolam) are also commonly used off-label for the treatment of PTSD. The alpha-adrenergic antagonist propranolol is commonly used off-label for reducing anxiety and panic. Propranolol has modest efficacy in improvement sleep. Beta-blocker prazosin is also commonly used off-label to reduce insomnia and nightmares.

…Limitations Of Existing Treatments…

All selective serotonin reuptake inhibitors (SSRI) molecules contain a "Black Boxed" class warning for risk of suicidal ideation and potential worsening of suicidal outcomes. PTSDSupport.com notes suicide as a major risk for people suffering from PTSD. Although effective molecules for 50 to 60% of the PTSD population, prescribing a class of drugs with a known increased risk of suicide to patients with already added risk of suicide following having experienced a traumatic physical or emotional event warrants caution. Use of SSRI molecules in children and adolescents with PTSD creates even greater risk for suicidal outcome.

According to the Department of Veterans Affairs (DVA), suicide risk among military veterans is 1.6x that of the general population (37.19 per vs. 23.19 per 100,000; 2005). The DVA notes, "A body of research indicates that there is a correlation between trauma and suicidal behaviors…" and "Intensity of the combat trauma, and the number of times it occurred, may influence suicide risk in veterans." Besides the added risk of suicide, both Zoloft and Paxil contain meaningful side effects that may actually worsen symptoms of PTSD, including incidence of insomnia (21%), fatigue (12%), malaise (10%), somnolence (13%), and sexual dysfunction (14%).

…Dangerous Off-Label Pain-Killers…

In our research of the PTSD market we found significant evidence of widespread pain-killer use and abuse by patients suffering from PTSD. The Department of Veterans Affairs conducted a survey of 141,029 military veterans serving between October 2005 and December 2010, 51% were diagnosed with PTSD (32%) or another mental health problem (19%). Results were published in the January 2012 Journal of the American Medical Association (JAMA), and show that veterans are at high risk for drug abuse, specifically with prescription pain killers. In fact, these vets were two times more likely to get prescriptions for addictive painkillers than vets with only physical pain. Iraq and Afghanistan vets with PTSD who already had substance abuse problems were four times more likely to get these drugs than vets without mental health problems.

Roughly 77% of vets diagnosed with PTSD were prescribed morphine to treat the pain, compared to just 7% in the general population. The data show these soldiers are also more likely to overdose on drugs or alcohol, be involved in violence or self-harming behavior, including suicide, or have other accidents than veterans who do not use dangerous opioid pain relievers. The study also found that veterans with PTSD are 42% more likely to receive the highest doses of opioids and five times more likely to be prescribed anti-anxiety medications that can increase overdose risk when combined with opioids, compared with vets without mental disorders.

TNX-102-SL

Tonix Pharmaceuticals plans to study a very low dose cyclobenzaprine for the treatment of PTSD. PTSD is thought to be exacerbated by non-restorative sleep. In fact, many of the same criteria for FM are found in patients with PTSD. A bedtime dose of VLDC could aid in restorative sleep and improve symptoms of PTSD that manifest into pain and social withdrawal.

In PTSD, we expect that Tonix will use the same formulation of VLDC, TNX-102-SL, currently being developed for FM. Additional PK data on this novel sublingual formulation for TNX-102 is expected to be completed shortly. Tonix met with the U.S. FDA for a pre-IND meeting in October 2012. We suspect that management will look to file the IND before year end 2012, then push into a human proof-of-concept study during the first half of 2013. Any potential licensing deal for TNX-102-SL in FM may or may not include rights to PTSD.

There are an estimated 5 million Americans living with PTSD. Many of these 5 million Americans are active or retired military. We believe the Department of Defense has significant vested interest in finding suitable treatments for PTSD that do not increase risk of suicide, exacerbate side effects, or cause dangerous addiction.

PIPELINE

Beside TNX-102, Tonix has plans to develop TNX-201 for headache and TNX-301 for alcoholism. Both candidates are preclinical in nature and we do not expect human clinical studies to begin until 2014 or beyond.

Product	Indication	Status
TNX-102 SL	Fibromyalgia	• Cyclobenzaprine (CBP) in sublingual formulation and novel dose • Phase 2a successfully completed • First pivotal trial expected to begin Q1 2013
	PTSD	• Proof of concept trials in 2013 • Seeking U.S. Department of Defense partnership
TNX-201	Headache	• NDA process based on existing grandfathered (DESI) product • Potentially shortened process for FDA approval
TNX-301	Alcoholism	• US patent allowed • Potential for government funding

RISKS

We see a number of risks to the Tonix Pharmaceuticals story.

…Generics…

Generic 5 mg and 10 mg cyclobenzaprine are widely available. Tonix is working on a rapidly absorbed and convenient 2.4 mg sublingual dose for bedtime administration. The company has been granted "Use of Composition" and "Composition and Methods" patents inside the U.S. that expire in August 2020. There are additional applications granted or pending outside the U.S. Management plans to expand the intellectual property to include additional protection around the sublingual formulation, and believes that the human PK study currently underway should protect TNX-102 from generic substitution at the pharmacy. While we agree that direct generic "AB" substitution for TNX-102 seems unlikely, we suspect that many treating physicians will continue to prescribe low-dose cyclobenzaprine (5 mg or 10 mg) off-label for FM. Independent sources have pegged the current cyclobenzaprine market for FM at around 50 million tablets per year. Tonix and its commercialization partner must obtain broad formulary coverage at tier-2 or tier-3 in order to compete with cheap generic cyclobenzaprine. We expect discount cards and co-pay assistance to play a major role in TNX-102 promotion.

Additionally, by the time TNX-102 launches, we expect both Pfizer's Lyrica (ANDA's approved) and Lilly's Cymbalta (generics expected in 2013) to be available as generic molecules in the tier-1 position. This could have mixed implications for TNX-102. While the drug may benefit from being the only major promoted product for FM, pricing pressure from cheap (and effective) alternatives like pregabalin and duloxetine could make TNX-102 a second-line choice for price-conscious patients and physicians.

…Dosing & Demographics…

Cyclobenzaprine was originally approved for muscle spasms in 1977. The typical course of therapy for cyclobenzaprine in this indication is a month. For FM, it is possible that patients will be on TNX-102 for years. Cyclobenzaprine is a 'Category B' drug (no adequate well-controlled studies) for pregnancy and nursing mothers. While we do not see this as a major impediment to uptake, we remind investors that over 85% of FM patients are female. Tonix will need to submit long-term safety data on TNX-102 prior to gaining FDA approval. This includes 300 patients with six months of exposure and 100 patients with 12 months of exposure. We have yet to see this data. We are not expecting any major issues with long-term exposure to TNX-102, but until the data is in hand we cannot say with certainty that TNX-102 has no long-term safety risk that may hold up final approval.

…FDA Curve Balls…

The FDA has been known to throw curve balls. Management at Tonix is not expecting to have to conduct a highway driving study or next-day function test on patients taking TNX-102. Tonix management is also not expecting that the FDA will ask for a drug-drug interaction study testing the side-effect profile in patients taking both TNX-102 and either Lyrica or Cymbalta. Tonix is pursuing a first-line, monotherapy label for TNX-102. At this point, we do not expect either request either, but the FDA has been known to surprise.

…Cash & Financing…

Tonix exited the second quarter (ended June 30, 2012) with approximately $1.34 million in cash. We forecast that cash at the end of the third quarter (ended September 30, 2012) stood at around $0.2 million. We believe that management is planning to raise an estimated $8 to $10 million in cash sometime in the next few weeks. The cost of the entire phase 3 program is estimated at approximately $20 million. We believe that Tonix requires at least $4 million to fund the first pivotal program and another $4 million to fund operations and then negotiate with commercialization partners.

The current market capitalization based on the basic share count (34.3 million) is $23 million ($30 million based on a fully-diluted 45.2 million). Raising an estimated $8 to 10 million will be a challenge. We estimate that Tonix will need to issue 12 to 15 million shares at the current price, to raise this level of cash. This will be highly dilutive to existing stock holders. This is the biggest reason for our 'Neutral' rating. We see minimal drug development risk with TNX-102-SL. Following the completion of a major financing, we believe the risk / reward for new investors will improve dramatically.

MANAGEMENT

Seth Lederman, MD – *Co-Founder, Chief Executive Officer & Chairman*

Seth Lederman serves as the company's CEO and Chairman of the Board. Prior to founding Tonix, from 2007-2008 Dr. Lederman co-founded and was a managing partner of Konanda Pharma Partners, LLC and Konanda Pharma Fund I, LP. He co-founded and served as director and chairman of its wholly-owned operating companies Validus and Fontus Pharmaceuticals Inc., which market Equetro (carbamazepine), Marplan (isocarboxazid) and Rocaltrol (calcitriol). In 2000 Dr. Lederman founded Targent Pharmaceuticals to develop late-stage oncology drugs including pure-isomer levofolinic acid, which was sold to Spectrum Pharmaceuticals and is now FDA-approved and marketed as Fusilev for colorectal cancer. In 1998 Dr. Lederman co-founded Vela Pharmaceuticals, which developed several drugs for central nervous system disorders, including a very low dose (VLD) cyclobenzaprine.

Dr. Lederman is a member of the faculty of Columbia University's College of Physicians and Surgeons since 1985. At Columbia, he was an NIH Physician-Scientist from 1985-1990. Dr. Lederman became an Associate Professor with tenure in 1996 and Director of the Laboratory of Molecular Immunology in 1997. From 1988 to 2002, he directed basic science research at Columbia in molecular immunology, infectious diseases and the development of therapeutics for autoimmune diseases. Dr. Lederman has authored numerous scientific articles, and has been issued several patents for drug development technologies. Dr. Lederman earned an AB from Princeton in Chemistry cum laude in 1979 and an MD from Columbia University's College of Physicians and Surgeons in 1983. He trained in internal medicine and rheumatology at Columbia's Presbyterian Hospital, serving as an attending physician in its Edward Daniels Arthritis and Autoimmunity Clinic from 1988-1996.

Leland J. Gershell, MD, PhD – *Chief Financial Officer*

Leland Gershell joined Tonix Pharmaceuticals as Chief Financial Officer in April 2012. Dr. Gershell was most recently Managing Director and Senior Analyst at Madison Williams and Company, where he was responsible for research on specialty pharmaceutical and biotechnology companies. Dr. Gershell began his equity research career at Cowen and Company, and has also held analyst positions at Apothecary Capital, a pharmaceutical and biotech-focused investment fund, and at Favus Institutional Research, a boutique research firm that caters to institutional investors. Dr. Gershell's prior industry experience includes affiliations with Targent Pharmaceuticals, where he facilitated capital raising, and with Vela Pharmaceuticals, where he evaluated pharmaceutical assets for in-licensing.

He earned his M.D. and Ph.D. in Organic Chemistry from Columbia University and his B.A. magna cum laude in Chemistry and Asian Studies from Dartmouth College. Dr. Gershell is an inventor on Columbia's patents for SAHA/vorinostat, which is marketed by Merck as Zolinza and is the first histone deacetylase (HDAC) inhibitor to receive FDA approval.

Bruce L. Daugherty – *Senior Director of Drug Development*

Bruce Daugherty joined Tonix Pharmaceuticals as Senior Director, Drug Development in April 2012. Dr. Daugherty has extensive experience in drug development and basic biomedical research. For the majority of his career, Dr. Daugherty was with Merck & Co., most recently as Senior Research Fellow, where he was project leader for multiple drug discovery programs in the therapeutic areas of inflammation, immunology, respiratory, and cardiovascular diseases. Dr. Daugherty was an early pioneer in the humanization of monoclonal antibodies, and played a key role in Merck's chemokine biology program. Dr. Daugherty was a member of the team that developed nicotinic acid/laropiprant for dyslipidemia that is marketed by Merck ex-U.S. as Tredaptive. Prior to joining Merck, Dr. Daugherty was a scientist at the Roche Institute of Molecular Biology, characterizing interferon genes. Most recently, Dr. Daugherty was a consultant, where he provided drug development expertise to universities and biotechnology companies seeking to out-license their technology to large pharmaceutical companies.

Dr. Daugherty earned his MBA from Emory University's Goizueta Business School, winning the entrepreneur award. He earned his Ph.D. in Molecular Genetics from UMDNJ-Robert Wood Johnson Medical School, his M.S. in Zoology from Rutgers University and his B.A. in Biology from Washington University in St. Louis. Dr. Daugherty has authored numerous original research papers that have been published in leading scientific journals and is an inventor on three issued patents.

Donald W. Landry, MD, PhD – *Co-Founder, Director*

Dr. Landry is the Samuel Bard Professor and Chair of the Department of Medicine (tenured) at Columbia University's College of Physicians and Surgeons. Dr. Landry also serves as Director of the Division of Experimental Therapeutics. Dr. Landry was a co-founder (with Dr. Lederman, above) of Vela Pharmaceuticals, which developed several drugs for central nervous system disorders, including very low dose (VLD)-cyclobenzaprine for fibromyalgia syndrome. At Columbia, Dr. Landry developed the first artificial enzyme to degrade cocaine and his report in Science was voted one of top 25 papers in the world for 1993 by the American Chemical Society. Dr. Landry is a leader in the development and ethics of embryonic stem cell research and served as a member of the President's Council on Bioethics during the George W. Bush administration.

In 1991, he established his laboratory at Columbia University to investigate medical applications of artificial enzymes and in 1998 founded the Division of Experimental Therapeutics. The Division focuses on novel therapeutics for intractable problems such as cocaine addiction, nerve gas intoxication and vasodilatory shock. Dr. Landry graduated from Lafayette College, completed his Ph.D. in organic chemistry under Nobel laureate R.B. Woodward at Harvard University in 1979 and then obtained the M.D. degree from Columbia University's College of Physicians and Surgeons in 1983. After residency in Internal Medicine at the Massachusetts General Hospital, he returned to Columbia University as an NIH Physician-Scientist, 1985-1990.

Samuel Saks – *Director*

Dr. Saks is former CEO of Jazz Pharmaceuticals, which he co-founded in 2003. At Jazz Dr. Saks was responsible for the commercialization of Xyrem (sodium oxybate) for cataplexy and excessive daytime sleepiness associated with narcolepsy. Dr. Saks also designed and led the effort to develop sodium oxybate as a treatment for fibromyalgia. Although the program to develop sodium oxybate as a treatment for this indication was abandoned in 2011, robust efficacy in treating pain and other key symptoms was demonstrated. Sodium oxybate has also been shown to significantly improve disordered sleep, a mechanism targeted by Tonix's lead program for fibromyalgia.

Dr. Saks received his Bachelor of Science degree in biology and his Doctor of Medicine degree from the University of Illinois. From 1987 to 2000 he was Assistant Clinical Professor of Medicine in the oncology division of the Department of Medicine at the University of California, San Francisco.

Ernest Mario, PhD – *Director*

Dr. Mario is Chairman and CEO of Capnia, a private pharmaceutical company developing novel therapeutic products to treat migraine and allergic rhinitis using a proprietary gas delivery system. After working as a drugstore pharmacist and then beginning his pharmaceutical industry career as a researcher, Dr. Mario served in management at a number of drug companies before being named in 1989 Chief Executive of Glaxo, then the second-largest drug company in the world. During Dr. Mario's tenure, Glaxo brought five major new products to market and saw sales and profits increase by 15% annually. Later Dr. Mario led pioneering drug delivery technology company Alza until selling it to Johnson & Johnson in 2001. He subsequently served as Chairman and Chief Executive Officer of Reliant Pharmaceuticals, where he led the commercialization of Lovaza.

He is Chairman of the American Foundation for Pharmaceutical Education and is past Chairman of the Duke University Health System. Dr. Mario earned a BS in pharmacy at Rutgers and his MS and PhD in physical sciences at the University of Rhode Island (URI). He holds honorary doctorates from URI and Rutgers, the latter of which in 2001 renamed its pharmacy school the Ernest Mario School of Pharmacy. In 2007 he was awarded the Remington Medal by the American Pharmacists' Association, pharmacy's highest honor.

VALUATION & RECOMMENDATION

Initiating Coverage Of Tonix Pharmaceuticals

We are initiating coverage of Tonix Pharmaceuticals with a 'Neutral' rating. The company is developing a very low dose cyclobenzaprine product, TNX-102-SL, that offers improved pharmacokinetics and convenient sublingual dose formulation for the treatment of fibromyalgia (FM). FM is a complex medical disorder characterized by widespread musculoskeletal pain, fatigue, lack of sleep, and mood and memory issues. Besides the dull aching pain and fatigue, patients with FM often also experience mood and psychological disorders such as anxiety and depression. Additionally, The National Pain Foundation estimates that 90% of all FM patients have sleep problems.

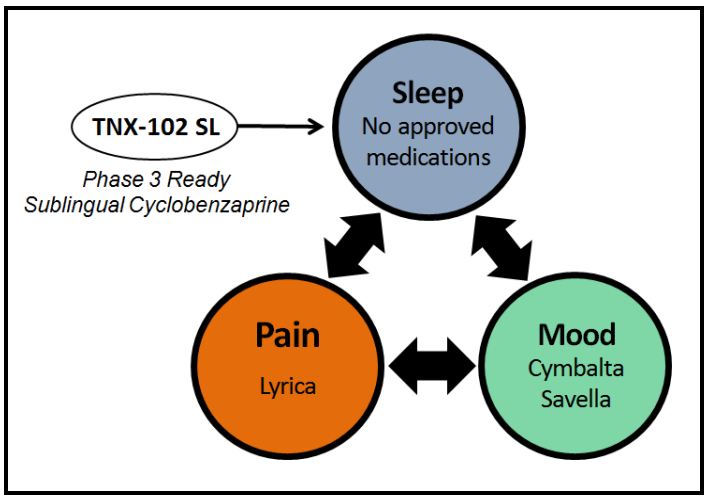
TNX-102 is being designed specifically for bedtime dosing in order to help patients improve quality (restorative) sleep and reduce the next-day pain and "fibro-fog" that is persistent with FM. We believe this is a meaningful opportunity for Tonix, mainly because currently approved FM medications, such as Pfizer's Lyrica (pregabalin) and Lilly's Cymbalta (duloxetine), do little to improve sleep quality. Plus, cyclobenzaprine is a well-known and commonly used medication for FM. Market research conducted by Frost & Sullivan found that cyclobenzaprine was the third most commonly prescribed medication for FM behind Lyrica and Cymbalta in 2010. Decision Resources estimates that approximately 50 million cyclobenzaprine tablets were taken by FM patients, off-label, in 2011. TNX-102 is an improved – very low dose – formulation of cyclobenzaprine designed to have fewer next-day residual effects.

…A Nice Opportunity…

Phase 2 proof-of-concept work sponsored by Tonix Pharmaceuticals clearly demonstrates proof-of-concept in patients with FM on validated endpoints including pain, fatigue, tenderness, and depression. The data is also suggestive of improved restorative sleep – a potential major differentiation in the treatment of FM.

Tonix is currently wrapping up formulation work on a sublingual dose of the drug, now called TNX-102-SL, and then plans to enter its first pivotal registration trial during the first half of 2013. We see little drug development or safety concerns with TNX-102-SL. Cyclobenzaprine is a well-known and understood molecule, first approved in 1977 for the treatment of muscle spasms. Since that time, the FDA has approved new low dose formulations (1990s), high-dose extended-release formulations (2007), and even entertained the idea of moving cyclobenzaprine OTC at 5 mg (ultimately deciding that the label indication of treatment for muscle spasms should remain prescription-based).

Following completion of its first pivotal phase 3 trial (data expected in 2014), we expect that Tonix will seek to secure a development and commercialization partnerships for the second phase 3 trial that includes an upfront payment, development and regulatory milestones, sales-related milestones, and royalties on sales. We see TNX-102-SL as a potential $300 million opportunity, and believe that, if successful in its first phase 3 trial, Tonix should be able to secure a commercialization deal in 2014. With positive phase 3 data from a first registration trial, we believe Tonix should be able to secure over $25 million upfront for TNX-102-SL, with development, regulatory, and backend sales milestones north of $250 million.



…Neutral While We Wait For Financing…

Tonix exited the second quarter (ended June 30, 2012) with approximately $1.34 million in cash. We forecast that cash at the end of the third quarter (ended September 30, 2012) stood at around $0.2 million. We believe that management is planning to raise an estimated $8 to $10 million in cash sometime in the next few weeks. The cost of the entire phase 3 program is estimated at approximately $20 million. We believe that Tonix requires at least $4 million to fund the first pivotal program and another $4 million to fund operations and then negotiate with commercialization partners.

We believe management is already in talks with interested partners for large private placement. We would not be surprised to see insider participation in the financing. The current market capitalization based on the basic share count is $23 million ($30 million fully-diluted). We estimate that Tonix will need to issue 10 to 15 million shares at the current price, to complete the financing. This will be highly dilutive to existing stock holders. This is the biggest reason for our 'Neutral' rating. Following the completion of a major financing, we believe the risk / reward for new investors will improve dramatically.

We have conducted a discounted cash flow (DCF) analysis on Tonix Pharmaceuticals incorporating our assumptions for a partnership and peak sales with TNX-102-SL in FM and PTSD, and the upcoming financing. We see $1.50 per share as fair-value. We would be buyers following completion of the financing.

PROJECTED FINANCIALS

Tonix Pharma
Income Statement

Tonix Pharmaceuticals	2011 A	Q1 A	Q2 A	Q3 E	Q4 E	2012 E	2013 E	2014 E	2015 E
TNX-102 (FM)	$0	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	-	-
TNX-102 (PTSD)	$0	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	-	-
Pipeline	$0	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	-	-
Research & Collaborations	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
YOY Growth	-	-	-	-	-	-	-	-	-
Total Revenues	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
YOY Growth	*100.0%*	-	-	-	-	-	-	-	-
CoGS	$0	$0	$0	$0	$0	$0	$0	$0	$0.0
Product Gross Margin	-	-	-	-	-	-	-	-	-
R&D	$1.2	$0.4	$0.8	$0.7	$0.9	$2.8	$5.0	$5.0	$5.0
% R&D	-	-	-	-	-	-	-	-	-
SG&A	$2.2	$0.8	$1.0	$0.9	$0.9	$3.6	$3.5	$3.7	$4.0
% SG&A	-	-	-	-	-	-	-	-	-
Operating Income	($3.4)	($1.2)	($1.9)	($1.6)	($1.8)	($6.4)	($8.5)	($8.7)	($9.0)
Operating Margin	*#DIV/0!*	-	-	-	-	-	-	-	-
Interest & Other Income	($0.1)	($0.9)	($1.2)	($0.1)	($0.1)	($2.3)	($1.5)	($1.2)	($1.0)
Pre-Tax Income	($3.5)	($2.0)	($3.1)	($1.7)	($1.9)	($8.7)	($10.0)	($9.9)	($10.0)
Taxes & Other	$0	$0	$0	$0	$0	$0	$0	$0	$0
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Net Income	($3.5)	($2.0)	($3.1)	($1.7)	($1.9)	($8.7)	($10.0)	($9.9)	($10.0)
Net Margin	*#DIV/0!*	-	-	-	-	-	-	-	-
Reported EPS	**($0.16)**	**($0.06)**	**($0.09)**	**($0.05)**	**($0.05)**	**($0.26)**	**($0.18)**	**($0.17)**	**($0.15)**
YOY Growth	*#REF!*	-	-	-	-	*58.6%*	*-29.2%*	*-9.3%*	*-6.8%*
Basic Shares Outstanding	21.4	31.7	34.3	34.6	34.8	33.8	55.0	60.0	65.0

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

© Copyright 2012, Zacks Investment Research. All Rights Reserved.

Tonix Pharma
DCF Model

Tonix Pharmaceuticals, Inc.	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
TNX-102 FM Royalty	**$0**	**$0**	**$0**	**$0**	**$0**	**$7.2**	**$19.0**	**$37.1**	**$43.2**	**$49.7**	**$51.4**
YoY Growth	-	-	-	-	-	-	*164%*	*67%*	*16%*	*15%*	*4%*
TNX-102 PTSD Royalty	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$3.4**	**$7.1**	**$11.0**	**$15.2**	**$15.7**
YoY Growth	-	-	-	-	-	-	-	*109%*	*55%*	*38%*	*4%*
Pipeline	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
Research Collaborations	**$0**	**$0.2**	**$20.2**	**$0.2**	**$0.0**	**$20.0**	**$0.0**	**$10.0**	**$0.0**	**$10.0**	**$0.0**
Cash Revenues (in Millions)	**$0.0**	**$0.2**	**$20.2**	**$0.2**	**$0.0**	**$27.2**	**$22.4**	**$54.2**	**$54.2**	**$74.9**	**$67.2**
CoGS	*$0*	*$0*	*$0*	*$0*	*$0*	*$0*	*$0*	*$0*	*$0*	*$0*	*$0*
R&D	*$2.8*	*$5.0*	*$5.0*	*$5.0*	*$2.5*	*$2.5*	*$2.5*	*$2.5*	*$2.5*	*$2.5*	*$2.5*
SG&A	*$3.6*	*$3.5*	*$3.7*	*$4.0*	*$4.1*	*$4.2*	*$4.3*	*$4.4*	*$4.5*	*$4.6*	*$4.7*
Other Expenses	*$0*	*$0.0*	*$0.0*	*$0.0*	*$0.0*	*$0.0*	*$0.0*	*$0.0*	*$0.0*	*$0.0*	*$0.0*
EBITDA	($6.4)	($8.3)	$11.5	($8.8)	($6.6)	$20.5	$15.6	$47.3	$47.2	$67.8	$60.0
Depreciation and amortization	*$0.1*	*$0.1*	*$0.1*	*$0.1*	*$0.1*	*$0.1*	*$0.1*	*$0.1*	*$0.1*	*$0.1*	*$0.1*
EBIT	**($6.5)**	**($8.4)**	**$11.4**	**($8.9)**	**($6.7)**	**$20.4**	**$15.5**	**$47.2**	**$47.1**	**$67.7**	**$59.9**
EBITDA margin	-	*-4200.0%*	*56.4%*	*-4450.0%*	*#DIV/0!*	*75.0%*	*69.2%*	*87.1%*	*86.9%*	*90.4%*	*89.1%*
Cash Taxes	$0	$0	$0	$0	$0	$0	($4.6)	($14.2)	($14.1)	($20.3)	($18.0)
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*30%*	*30%*	*30.0%*	*30.0%*	*30.0%*
Balance Sheet											
Capital Expenditures	$0.2	$0.2	$0.2	$0.2	$0.2	$0.2	$0.2	$0.2	$0.2	$0.2	$0.2
Working Capital	($0.2)	($0.2)	($0.2)	($0.2)	($0.2)	($0.2)	($0.2)	($0.2)	($0.2)	($0.2)	($0.2)
Non-Cash Adjustments	($0.2)	($0.2)	($0.2)	($0.2)	($0.2)	($0.2)	($0.2)	($0.2)	($0.2)	($0.2)	($0.2)
Capital Adjustments	**($0.2)**	**($0.2)**	**($0.2)**	**($0.2)**	**($0.2)**	**($0.2)**	**($0.2)**	**($0.2)**	**($0.2)**	**($0.2)**	**($0.2)**
Discounted Cash Flow											
Cash Income	($6.5)	($8.4)	$11.4	($8.9)	($6.7)	$20.4	$10.8	$33.0	$33.0	$47.4	$41.9
Depreciation and amortization	$0.1	$0.1	$0.1	$0.1	$0.1	$0.1	$0.1	$0.1	$0.1	$0.1	$0.1
Net Cash Changes	$0.2	$0.2	$0.2	$0.2	$0.2	$0.2	$0.2	$0.2	$0.2	$0.2	$0.2
Post-Tax Operating Cash Flow	**($6.2)**	**($8.1)**	**$11.7**	**($8.6)**	**($6.4)**	**$20.7**	**$11.1**	**$33.3**	**$33.3**	**$47.7**	**$42.2**
Dividends / Payments	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
Free Cash Flow	**($6.2)**	**($8.1)**	**$11.7**	**($8.6)**	**($6.4)**	**$20.7**	**$11.1**	**$33.3**	**$33.3**	**$47.7**	**$42.2**

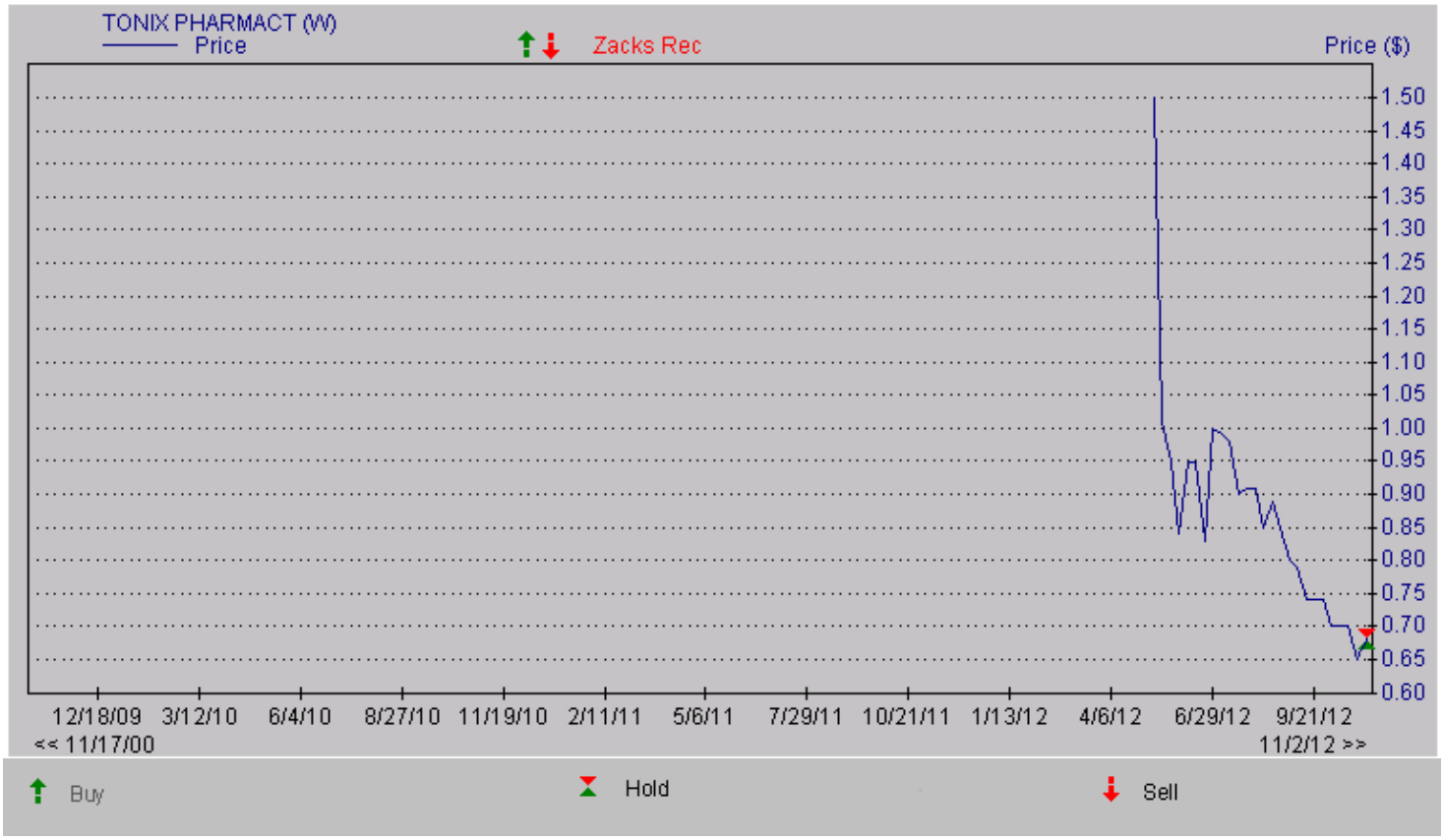
Assumptions	
Beta:	2.0
Equity Risk Premium:	7.0%
Risk Free Rate:	1.5%
Firm Risk Premium:	100%
Discount Rate:	**15.5%**

Valuation	
10-Year Model:	$40.5
Terminal Growth:	1.5%
Terminal Value:	$61.8
CA - CL + Debt:	$0.6
Firm Value:	**$102.9**

Price Target	
Basic Outstanding:	34.3
Warrants / Options:	10.9
Dilution:	22.0
Adjusted Fully Diluted:	67.2
Target Price:	**$1.53**

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

HISTORICAL ZACKS RECOMMENDATIONS



DISCLOSURES

The following disclosures relate to relationships between Zacks Investment Research ("ZIR") and Zacks Small-Cap Research ("Zacks SCR") and the issuers covered by the Zacks SCR analysts in the Small-Cap Universe.

ZIR or Zacks SCR Analysts do not hold or trade securities in the issuers which they cover. Each analyst has full discretion on the rating and price target based on their own due diligence. Analysts are paid in part based on the overall profitability of Zacks SCR. Such profitability is derived from a variety of sources and includes payments received from issuers of securities covered by Zacks SCR for non-investment banking services. No part of analyst compensation was, is or will be, directly or indirectly, related to the specific recommendations or views expressed in any report or blog.

ZIR and Zacks SCR do not make a market in any security nor do they act as dealers in securities. Zacks SCR has never received compensation for investment banking services on the small-cap universe. Zacks SCR does not expect received compensation for investment banking services on the small-cap universe. Zacks SCR has received compensation for non-investment banking services on the small-cap universe, and expects to receive additional compensation for non-investment banking services on the small-cap universe, paid by issuers of securities covered by Zacks SCR. Non-investment banking services include investor relations services and software, financial database analysis, advertising services, brokerage services, advisory services, investment research, and investment management.

Additional information is available upon request. Zacks SCR reports are based on data obtained from sources we believe to be reliable, but is not guaranteed as to accuracy and does not purport to be complete. Because of individual objectives, the report should not be construed as advice designed to meet the particular investment needs of any investor. Any opinions expressed by Zacks SCR Analysts are subject to change. Reports are not to be construed as an offer or the solicitation of an offer to buy or sell the securities herein mentioned. Zacks SCR uses the following rating system for the securities it covers. Buy/Outperform: The analyst expects that the subject company will outperform the broader U.S. equity market over the next one to two quarters. Hold/Neutral: The analyst expects that the company will perform in line with the broader U.S. equity market over the next one to two quarters. Sell/Underperform: The analyst expects the company will underperform the broader U.S. Equity market over the next one to two quarters.

The current distribution of Zacks Ratings is as follows on the 1010 companies covered: Buy/Outperform- 14.8%, Hold/Neutral- 77.6%, Sell/Underperform – 7.2%. Data is as of midnight on the business day immediately prior to this publication.

© Copyright 2012, Zacks Investment Research. All Rights Reserved.