Certain statements in this presentation regarding strategic plans, expectations and objectives for future operations or results are “forward-looking statements” as defined by the Private Securities Litigation Reform Act of 1995. These statements may be identified by the use of forward-looking words such as “anticipate,” “believe,” “forecast,” “estimate” and “intend,” among others. These forward-looking statements are based on Tonix’s current expectations and actual results could differ materially. There are a number of factors that could cause actual events to differ materially from those indicated by such forward-looking statements. These factors include, but are not limited to, substantial competition; our ability to continue as a going concern; our need for additional financing; uncertainties of patent protection and litigation; uncertainties of government or third party payer reimbursement; limited sales and marketing efforts and dependence upon third parties; and risks related to failure to obtain U.S. Food and Drug Administration clearances or approvals and noncompliance with its regulations. As with any pharmaceutical under development, there are significant risks in the development, regulatory approval and commercialization of new products. The forward-looking statements in this presentation are made as of the date of this presentation, even if subsequently made available by the Company on its website or otherwise. Tonix does not undertake an obligation to update or revise any forward-looking statement, except as required by law. Investors should read the risk factors set forth in the amended Annual Report on Form 10-K for the year ended December 31, 2013, as filed with the Securities and Exchange Commission (the “SEC”) on March 28, 2014 and future periodic reports filed with the SEC on or after the date hereof. All of the Company’s forward-looking statements are expressly qualified by all such risk factors and other cautionary statements.
New approaches to treating CNS disorders

**First-in-class medicines for common disorders of the central nervous system (CNS)**
- Innovative treatment paradigms
- Late stage candidates
- Large unmet medical needs

**Entering 2015 with three clinical development programs**

- **Fibromyalgia**
- **Post-Traumatic Stress Disorder**
- **Episodic Tension-Type Headache**

TNX-102 SL (cyclobenzaprine HCl sublingual tablet) 2.8 mg and TNX-201 ((R)-isometheptene mucate) are Investigational New Drugs and are not approved for any indication.
Pipeline led by TNX-102 SL for fibromyalgia

<table>
<thead>
<tr>
<th>Candidate</th>
<th>Indication</th>
<th>Preclinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>NDA</th>
<th>Market</th>
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TNX-102 SL (cyclobenzaprine HCl sublingual tablet) 2.8 mg and TNX-201 ((R)-isometheptene mucate) are Investigational New Drugs and are not approved for any indication.

© Copyright 2015 Tonix Pharmaceuticals
Fibromyalgia market opportunity

Estimated to affect 5 - 15 million U.S. adults*

Three FDA approved prescription medications:

<table>
<thead>
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<th>Class</th>
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<th>Approval Year in FM</th>
</tr>
</thead>
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<tr>
<td>Membrane Stabilizer</td>
<td>Lyrica®</td>
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<td>SNRI</td>
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<td>Eli Lilly</td>
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<td>Savella®</td>
<td>Forest</td>
<td>2009</td>
</tr>
</tbody>
</table>

Tonix is pursuing a different approach:

| Sleep Quality | TNX-102 SL | Tonix |

---


**Estimates based on information from publicly-available sources

SNRI = Serotonin Norepinephrine Reuptake Inhibitor
Restorative sleep improves pain and other fibromyalgia symptoms
  >90% of fibromyalgia patients complain of poor sleep quality*
  Sleep quality improvement is not a feature of approved medications

Phase 2a study with low-dose cyclobenzaprine (CBP) capsule showed proof-of-concept**

TNX-102 SL is a sublingual tablet formulation of CBP
  Pharmacokinetic profile well-suited to bedtime administration
  Tolerability profile well-suited to chronic use

Phase 2b BESTFIT results support Phase 3 program in fibromyalgia
  Contribute to evidence of efficacy to support the planned NDA
  Phase 3 confirmatory trial to begin in 2Q 2015

** Moldofsky et al., J Rheum 2011;38:2653-63.
TNX-102 SL (cyclobenzaprine HCl sublingual tablet) 2.8 mg is an Investigational New Drug and is not approved for any indication.
BESTFIT Phase 2b trial in fibromyalgia

**BESTFIT = BEdtime Sublingual TNX-102 SL as Fibromyalgia Intervention Therapy**

Randomized, double-blind, placebo-controlled trial
2010 American College of Rheumatology diagnostic criteria for fibromyalgia
205 participants were randomized 1:1 at 17 U.S. sites
One sublingual tablet of TNX-102 SL 2.8 mg or placebo daily at bedtime for twelve weeks

**Primary efficacy endpoint**
Mean change from baseline in the daily diary pain score during week 12
11-point (0-10) Numerical Rating Scale (NRS) to assess prior 24-hour average pain intensity

First Patient – First Dose September 2013

Last Patient – Last Dose August 2014

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TNX-102 SL (cyclobenzaprine HCl sublingual tablet) 2.8 mg is an Investigational New Drug and is not approved for any indication.
## TNX-102 SL improved pain in fibromyalgia in the BESTFIT study

<table>
<thead>
<tr>
<th>Outcome Measure at Week 12</th>
<th>Intent-to-Treat Population</th>
<th>p value</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily Pain Diary, NRS</td>
<td>Mean Change**</td>
<td>0.086</td>
<td>MMRM</td>
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<tr>
<td></td>
<td></td>
<td>0.172</td>
<td>JTC-MI</td>
</tr>
<tr>
<td>Daily Pain Diary, NRS</td>
<td>Proportion Achieving 30% Improvement*</td>
<td>0.033</td>
<td>LR</td>
</tr>
<tr>
<td>Clinic NRS 7-day pain recall</td>
<td>Mean Change</td>
<td>0.029</td>
<td>MMRM</td>
</tr>
<tr>
<td>FIQ-R Pain Item</td>
<td>Mean Change</td>
<td>0.004</td>
<td>MMRM</td>
</tr>
</tbody>
</table>

NRS = Numeric Rating Scale for pain; FIQ-R = Fibromyalgia Impact Questionnaire-Revised  
MMRM = Mixed-Effect Model Repeated Measure; JTC-MI = Jump to Control-Multiple Imputation (FDA-preferred analysis); LR = Logistic Regression  
** Declared primary endpoint; was primary endpoint for FDA approvals of Lyrica and Cymbalta  
* Declared secondary endpoint; will be the primary endpoint in the upcoming Phase 3 study  
† N=205 (TNX-102 SL N=103, placebo N=102)  

Source: Phase 2b BESTFIT preliminary top line results  
TNX-102 SL (cyclobenzaprine HCl sublingual tablet) 2.8 mg is an Investigational New Drug and is not approved for any indication.
TNX-102 SL improved sleep quality in fibromyalgia in the BESTFIT study

<table>
<thead>
<tr>
<th>Outcome Measure at Week 12</th>
<th>Intent-to-Treat Population</th>
<th>p value</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily Sleep Quality Diary, NRS</td>
<td>Mean Change*</td>
<td>&lt;0.001</td>
<td>MMRM</td>
</tr>
<tr>
<td>PROMIS Sleep Disturbance</td>
<td>T-score Change*</td>
<td>0.005 0.004</td>
<td>MMRM JTC-MI</td>
</tr>
<tr>
<td>FIQ-R Sleep Quality Item</td>
<td>Mean Change</td>
<td>&lt;0.001</td>
<td>MMRM</td>
</tr>
</tbody>
</table>

**PROMIS** = Patient-Reported Outcome Measures in Sleep

* Declared secondary endpoint

Source: Phase 2b BESTFIT preliminary top line results

TNX-102 SL (cyclobenzaprine HCl sublingual tablet) 2.8 mg is an Investigational New Drug and is not approved for any indication.
TNX-102 SL broadly improved fibromyalgia symptoms in the BESTFIT study

<table>
<thead>
<tr>
<th>Outcome Measure at Week 12</th>
<th>Intent-to-Treat Population</th>
<th>p value</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Global Impression of Change</td>
<td>Responder Analysis*</td>
<td>0.025</td>
<td>LR</td>
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<tr>
<td>FIQ-R Total Score</td>
<td>Mean Change*</td>
<td>0.014</td>
<td>MMRM</td>
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<tr>
<td></td>
<td></td>
<td>0.015</td>
<td>JTC-MI</td>
</tr>
<tr>
<td>FIQ-R Symptom Domain</td>
<td>Mean Change</td>
<td>0.004</td>
<td>MMRM</td>
</tr>
<tr>
<td>FIQ-R Function Domain</td>
<td>Mean Change</td>
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<td>MMRM</td>
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<tr>
<td>FIQ-R Anxiety Item</td>
<td>Mean Change</td>
<td>0.015</td>
<td>MMRM</td>
</tr>
<tr>
<td>FIQ-R Sensitivity Item</td>
<td>Mean Change</td>
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<td>MMRM</td>
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<tr>
<td>FIQ-R Stiffness Item</td>
<td>Mean Change</td>
<td>0.039</td>
<td>MMRM</td>
</tr>
</tbody>
</table>

* Declared secondary endpoint

Source: Phase 2b BESTFIT preliminary top line results

TNX-102 SL (cyclobenzaprine HCl sublingual tablet) 2.8 mg is an Investigational New Drug and is not approved for any indication.
TNX-102 SL was well-tolerated in the BESTFIT Study

No serious adverse events (SAE) reported

<table>
<thead>
<tr>
<th>Systemic adverse events reported by at least 3.0% of the total study population</th>
<th>TNX-102 SL (N=103)</th>
<th>Placebo (N=101)</th>
<th>Total (N=204)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Somnolence</td>
<td>1.9</td>
<td>6.9</td>
<td>4.4</td>
</tr>
<tr>
<td>Dry Mouth</td>
<td>3.9</td>
<td>4.0</td>
<td>3.9</td>
</tr>
<tr>
<td>Back Pain</td>
<td>4.9</td>
<td>3.0</td>
<td>3.9</td>
</tr>
</tbody>
</table>

Most frequent local adverse events were administration site reactions
Previously reported in TNX-102 SL Phase 1 studies; no detectable bias on efficacy results
Transient tongue numbness (42% TNX-102 SL vs. 1% placebo)
Abnormal taste (8% TNX-102 SL vs. 0% placebo)

Trial completion rates of 86% with TNX-102 SL vs. 83% with placebo

Source: Phase 2b BESTFIT preliminary top line results
TNX-102 SL (cyclobenzaprine HCl sublingual tablet) 2.8 mg is an Investigational New Drug and is not approved for any indication.
Phase 2b BESTFIT study confirmed activity and tolerability
Statistically-significant improvements across key fibromyalgia symptoms were observed
Systemic tolerability similar to placebo
2.8 mg daily dose confirmed for future development

Phase 3 program to commence in 2Q 2015
Randomized, double-blind, parallel-group, placebo-controlled
N=500; 30-35 U.S. sites; 1:1 randomization
12-week study similar to the BESTFIT design
One sublingual tablet of TNX-102 SL 2.8 mg or placebo daily at bedtime

30% responder analysis at 12 weeks* – primary efficacy endpoint based on FDA written acceptance

*TNX-102 SL demonstrated $p=0.03$ in BESTFIT 30% responder analysis (pre-specified secondary endpoint)

TNX-102 SL (cyclobenzaprine HCl sublingual tablet) 2.8 mg is an Investigational New Drug and is not approved for any indication.
Study measuring pain reduction for two hypothetical drugs

30% improvement is considered moderate or clinically significant response

Pain rated from 0–10 least to worst

Baseline (10 Subjects)
Mean 6.0

30% response (moderate/clinically significant)
Non-responder

Drug 1
4 responders
Mean 3.6
40% responder rate
A few strong responders

Placebo
Mean 5.6

Drug 2
5 responders
Mean 5.0
50% responder rate
Several significant responders

30% Responder Rate (RR) indicates how many patients have \( \geq 30\% \) (clinically meaningful) improvement in pain score

**Drug 1**
- A few strong responders
- Mean pain \( \Delta \) is significant
- 30% RR is not significant

**Drug 2**
- Several significant responders
- 30% RR is significant
- Mean pain \( \Delta \) is not significant


Both change in mean pain and 30% responder analysis are FDA-acceptable primary endpoints for FM trials.
TNX-102 SL had a significant effect on 30% response rate but not mean pain in BESTFIT

Week 12 Change from Baseline in Mean Pain NRS (pre-specified primary)

<table>
<thead>
<tr>
<th></th>
<th>Placebo (n=102)</th>
<th>TNX-102 SL (n=103)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change from Baseline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-2</td>
<td>Placebo</td>
<td>TNX-102 SL</td>
</tr>
<tr>
<td>-1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
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<tr>
<td>1</td>
<td></td>
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<tr>
<td>2</td>
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</tbody>
</table>

JTC-I = Jump-to-Control, Multiple Imputation; MMRM = Mixed-Effects Model Repeated Measures; NRS = Numeric Rating Scale
Chronic pain conditions lead to the development of central pain conditions

Reversal of the central pain syndrome may reveal the original cause

Back pain

Fibromyalgia

Back pain remains

Pain centralization

Fibromyalgia treated

Time
Central sensitization contributes to hyperalgesia and allodynia

- Nociception and touch pathways are normally separate
- Central sensitization amplifies response to pain and reduces inhibition of pain

Conditioning of the peripheral and visceral nerves can lead to central sensitization and dermatome hypersensitivity

Stimulation of viscera (eg, acid reflux in esophagus) leads to
- central sensitization
- visceral hypersensitivity
- referred pain on chest wall

Referred pain

Sustained stimulation of myofascial trigger points induces central sensitization and referred pain

Prolonged muscle pain induces
- central sensitization
- referred pain in related muscles
Review of fibromyalgia endpoints reflects dissatisfaction with current treatments

- Fibromyalgia is one of 16 conditions chosen by FDA’s Patient-Focused Drug Development program
  - Solicit patient input to determine meaningful clinical endpoints

http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm347317.htm
Phase 2 trial of TNX-102 SL for PTSD is recruiting

<table>
<thead>
<tr>
<th>Candidate</th>
<th>Indication</th>
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<td>Episodic Tension-Type Headache</td>
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* Recruitment begin in December 2014.

TNX-102 SL (cyclobenzaprine HCl sublingual tablet) 2.8 mg and TNX-201 ((R)-isomehtepene mucate) are Investigational New Drugs and are not approved for any indication.
Post-traumatic stress disorder is a chronic, debilitating condition
High incidence among soldiers and veterans, but experiencing any trauma can lead to PTSD
Associated with suicide and unpredictable, violent behaviors
Patients desperate despite two FDA approved drugs; no new treatment in >10 years

Among 8.5 million U.S. patients, approximately half are receiving medical treatment*

FDA approved prescription medications:

<table>
<thead>
<tr>
<th>Class</th>
<th>Product</th>
<th>Company</th>
<th>Approval Year in PTSD</th>
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<tbody>
<tr>
<td>SSRI</td>
<td>Paxil®</td>
<td>Glaxo</td>
<td>2001</td>
</tr>
<tr>
<td></td>
<td>Zoloft®</td>
<td>Pfizer</td>
<td>1999</td>
</tr>
</tbody>
</table>

**Tonix is pursuing a different approach:**

| Sleep Quality | TNX-102 SL | Tonix   | 2019E               |


SSRI = Selective Serotonin Reuptake Inhibitor
Rationale for developing TNX-102 SL for PTSD

Overlap between PTSD and fibromyalgia

~50% of fibromyalgia or PTSD patients meet criteria for the other disorder

Patients experience disturbed sleep

Widespread pain is considered “co-morbid” with PTSD

Opioid, benzodiazepine, other sedative-hypnotic drug misuse common

TNX-102 SL (cyclobenzaprine HCl sublingual tablet) 2.8 mg is an Investigational New Drug and is not approved for any indication.
Sleep quality is a new target for PTSD therapy

Poor sleep quality after trauma is linked to onset of PTSD

PTSD patients complain of poor sleep quality as a core symptom
  Distressing dreams (nightmares) are part of “re-experiencing”
  Restless sleep is part of “hyper-arousal”
  Correlated with depression, substance abuse and suicide

Military-related PTSD is an unmet need
  Evidence suggests that SSRIs may be ineffective in military-related PTSD

Response of PTSD in men to SSRIs has not been adequately studied

TNX-102 SL targets mechanisms associated with treating disturbed sleep in PTSD

TNX-102 SL (cyclobenzaprine HCl sublingual tablet) 2.8 mg is an Investigational New Drug and is not approved for any indication.
TNX-102 SL acts on neurotransmitter systems intrinsic to sleep physiology

Serotonin and Norepinephrine Antagonist and Reuptake Inhibitor (SNARI)
Blocks serotonin and norepinephrine reuptake
Selectively blocks serotonin 2A and α-1 adrenergic receptors

TNX-102 SL (cyclobenzaprine HCl sublingual tablet) 2.8 mg is an Investigational New Drug and is not approved for any indication.
Mechanistic relationship of TNX-102 SL with trazodone and prazosin

**Trazodone** blocks serotonin reuptake and 2A receptors

**Prazosin** blocks α-1 adrenergic receptors

---

TNX-102 SL (cyclobenzaprine HCl sublingual tablet) 2.8 mg is an Investigational New Drug and is not approved for any indication.
PTSD program with TNX-102 SL

Fibromyalgia program informs development of TNX-102 SL in PTSD
Safety data from fibromyalgia studies are potentially supportive for PTSD program

Efficacy data support potential for activity in PTSD
Improvements in several outcomes analyses of BESTFIT that relate to PTSD core symptoms:
sleep; FIQ-R sensitivity; and FIQ-R anxiety

2.8 mg dose supported by BESTFIT study results

Phase 2 study of TNX-102 SL in military-related PTSD ("AtEase") is recruiting

TNX-102 SL (cyclobenzaprine HCl sublingual tablet) 2.8 mg is an Investigational New Drug and is not approved for any indication.
"AtEase" Phase 2 trial of TNX-102 SL in PTSD

Randomized, double-blind, placebo-controlled trial in military-related PTSD

N=220; approximately 25 U.S. clinical sites

Primary efficacy endpoint:
Difference in Clinician-Administered PTSD Scale (CAPS) score between TNX-102 SL 2.8 mg and placebo

**TNX-102 SL at bedtime once-daily**
- 2.8 mg, N = 88
- 5.6 mg, N = 44

**Placebo at bedtime once-daily**
- N = 88

12 weeks

open-label extension

TNX-102 SL (cyclobenzaprine HCl sublingual tablet) 2.8 mg is an Investigational New Drug and is not approved for any indication.
### TNX-201 in development for episodic tension-type headache

<table>
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<tr>
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<th>Phase 2</th>
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TNX-102 SL (cyclobenzaprine HCl sublingual tablet) 2.8 mg and TNX-201 ((R)-isomeptene mucate) are Investigational New Drugs and are not approved for any indication.
Episodic tension-type headache (ETTH)

75 million adults in the U.S. experience frequent episodic tension-type headaches*

Constant band of pressure on the back/sides of head; “squeezed in a vice” feeling
“Frequent” = one to 15 headaches per month over a three-month period
Approximately 60% receive treatment**

All of the FDA approved prescription medications contain barbiturates

Over-the-counter medications are inadequate for many
No new medications introduced for >40 years

<table>
<thead>
<tr>
<th>Class</th>
<th>Product</th>
<th>Company</th>
<th>Regulatory Status</th>
<th>Approval Year in ETTH</th>
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<tr>
<td>Barbiturate</td>
<td>Fiorinal®</td>
<td>Actavis</td>
<td>Approved NDA</td>
<td>1976</td>
</tr>
<tr>
<td></td>
<td>Fioricet®</td>
<td>Actavis</td>
<td>Approved NDA</td>
<td>1992</td>
</tr>
<tr>
<td>Barbiturate + Opiate</td>
<td>Fiorinal with Codeine®</td>
<td>Actavis</td>
<td>Approved NDA</td>
<td>1990</td>
</tr>
</tbody>
</table>

** Scher et al, Cephalalgia 2010;30:321-328; company analysis of public literature.
TNX-201 in clinical development for ETTH

**TNX-201 is (R)-isomethyptene mucate**
Tonix is developing TNX-201 for ETTH
Phase 2 study to begin in 2Q 2015

**Racemic isomethyptene mucate is a mixture of (R) and (S) isomers**
Had been widely prescribed for many decades in the U.S. as:
- a single-agent medicine (pre-1962)
- a component of combination drug products
  - Midrin® – NDA withdrawn
  - Prodrin® – marketed under “unapproved drug category”

*No product containing isomethyptene mucate is currently FDA-approved for any indication*

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TNX-201 ((R)-isomethyptene mucate) is an Investigational New Drug and is not approved for any indication.
Phase 1 study in healthy volunteers

Single ascending dose study (N=45) – three cohorts of 15 subjects
Randomized to TNX-201, racemic isometheptene mucate, or placebo (3:1:1 ratio, resp.)

<table>
<thead>
<tr>
<th></th>
<th>TNX-201 35 mg (N=9)</th>
<th>TNX-201 70 mg (N=9)</th>
<th>TNX-201 140 mg (N=9)</th>
<th>Rac. Isometh. 70 mg (N=9)</th>
<th>Placebo (N=9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects reporting ≥1 adverse event, %</td>
<td>22</td>
<td>11</td>
<td>0</td>
<td>11</td>
<td>33</td>
</tr>
</tbody>
</table>

Adverse events reported by TNX-201 subjects all rated as “mild” and most are not study drug-related
No subject discontinued due to treatment-emergent adverse events
Dose-related increase in TNX-201 plasma levels (Cmax, AUC)
No evidence of isomer interconversion

Results support the advancement of TNX-201 into Phase 2 development

TNX-201 ((R)-isometheptene mucate) is an Investigational New Drug and is not approved for any indication.
Phase 2 trial of TNX-201 in ETTH to begin in 2Q15

Randomized, double-blind, placebo-controlled trial in episodic tension-type headache

N=150; approximately 10 U.S. clinical sites

**Primary efficacy endpoint:**

Number of subjects who report “pain free” at two hours following one dose of study medication (upon first ETTH episode experienced)

To report top-line results by YE 2015

TNX-201 ((R)-isometheptene mucate) is an Investigational New Drug and is not approved for any indication.
What is episodic tension-type headache?

International Classification of Headache Disorders, 3rd edition

Primary headaches

1) Migraine
   - Lasts 4 hours to 3 days
   - Localized to left or right
   - Pulsating quality
   - Aggravated by routine activity
   - Nausea and light/sound sensitivity
   - May or may not be accompanied by aura

2) Episodic Tension-Type Headache (ETTH)
   - Lasts 30 minutes to 7 days
   - Both left and right side
   - Pressing/tightening quality
   - Not aggravated by routine activity
   - No nausea or light/sound sensitivity

ETTH category
1. Infrequent 10-11
2. Frequent 12-179
3. Chronic ≥180

3) Trigeminal autonomic cephalalgia
4) Other

Secondary headaches

Due to other causes
5) Trauma or injury
6) Vascular disorder
7) Non-vascular disorder
8) Substance use

8.2) Medication overuse headaches
9) Infection
10) Homeostatic disorder
11) Disorder of various structures of the head/neck
12) Psychiatric disorder

Other
13) Cranial neuropathy
14) Other


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ETTH is the most common type of headache

Global prevalence of ETTH

A review of 107 publications on the epidemiology of headache
- Regional differences exist (higher in Europe, lower in Asia)

One-Year Prevalence for Global Population

- All Headaches: 47%
- ETTH: 38%
- Migraine: 10%
- Chronic: 3%


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ETTH is the most common type of headache

US Prevalence of ETTH

Episodic tension-type headaches account for approximately:
- 63% of all headaches
- 80% of all non-migraine headaches
  - “Non-migraine” consists primarily of ETTH; >70% female

One-Year Prevalence for U.S. Adult Population (18-65)

<table>
<thead>
<tr>
<th>Headache Type</th>
<th>Prevalence Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Headaches</td>
<td>60%</td>
</tr>
<tr>
<td>ETTH</td>
<td>38%</td>
</tr>
<tr>
<td>Migraine</td>
<td>13%</td>
</tr>
<tr>
<td>Chronic</td>
<td>2%</td>
</tr>
</tbody>
</table>

Estimated number of adults (18-65, 2013 census)
- ~119 M
- ~75 M
- ~26 M
- ~4.4 M

1) Schwartz et al., JAMA, 1998; 279:381-383
Non-migraine headaches lead to 9.2 million emergency room or office visits

Patients with non-migraine headache (primarily ETTH) seek medical attention

Care-Seeking For Non-Migraine Headache

<table>
<thead>
<tr>
<th></th>
<th>Number of Patients in Millions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emergency Room¹</td>
<td>1.7</td>
</tr>
<tr>
<td></td>
<td>4.5</td>
</tr>
<tr>
<td>Office Visits²</td>
<td>7.6</td>
</tr>
<tr>
<td></td>
<td>4.7</td>
</tr>
</tbody>
</table>

¹ Heath Care Utilization Project data, 2011
² IMS National Disease and Therapeutic Index™ 2013
Butalbital combinations are the only prescription medications approved for ETTH.

Butalbital combinations are used extensively to treat headaches.

Total of 8.2 Million Butalbital Combination Prescriptions
3.5 Million for Non-Migraine Headache

Source: IMS Health, IMS National Prescription Audit™, 08/2013 – 07/2014 and IMS National Disease and Therapeutic Index™, Q3 2008 – Q3 2014
Current treatment pattern for non-migraine

OTC products dominate but prescription market is still sizable (~10 M TRx)

### Treatment Patterns From Two Perspectives

#### Patient Survey: ¹
(captures OTC & Rx)

#### Drug Mentions in Office Visits²
(captures Rx)

<table>
<thead>
<tr>
<th>Treatment Pattern</th>
<th>Relative Usage/Mention (%)</th>
<th>Estimated TRx</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSAIDs/Acetaminophen</td>
<td>90%</td>
<td>~9 M TRx</td>
</tr>
<tr>
<td>Butalbital Combos</td>
<td>5%</td>
<td>~3.5 M TRx</td>
</tr>
<tr>
<td>Opioids and Triptans (estimated)</td>
<td>5%</td>
<td>6.5 M TRx</td>
</tr>
<tr>
<td>Opioids</td>
<td>1%</td>
<td>~5 M TRx</td>
</tr>
<tr>
<td>Triptans</td>
<td>1%</td>
<td>~5 M TRx</td>
</tr>
<tr>
<td>Others</td>
<td>1%</td>
<td>~5 M TRx</td>
</tr>
</tbody>
</table>

2) Based on independent study conducted by Trinity Partners using IMS National Prescription Audit (8/2013 – 7/142014) and IMS National Disease and Therapeutic Index™ Q3 2008 – Q3 2014
Annual cost of health care for migraine and headache in the U.S. exceeds $4B

Costs for different treatment settings in 2010 dollars\(^1\)

**Annual Health Care Cost by Setting**

- **Outpatient**: $3200
- **ER**: $700
- **Inpatient**: $375

- Prescription costs are not included in these amounts

Better pharmacological treatment **reduced overall annual healthcare costs** by almost **$19K/patient** in an HMO setting\(^2\)

---

Public health attention to headache has increased in the past decade

- **2004**
  - Lifting the Burden initiated
    - The global campaign against headache involving WHO and 3 international headache NGOs

- **2007**
  - Eurolight Project initiated
    - European Union–level health agency initiative on treatment of headache disorders to systematically fill gaps in knowledge

- **2010**
  - Updated guidelines for clinical trials for ETTH

- **2012**
  - Migraine ranked 7th leading cause of disability by WHO’s Global Burden of Disease 2010

- **2013**
  - 3rd edition of the International Classification of Headache Disorders

- **2014**
  - Principal results of Eurolight project published
    - Significant global impact of headache on family and work life, and need for additional research in ETTH and medication-overuse headache

**NGO = Non-governmental organization**


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All of the FDA-approved medications for ETTH contain butalbital

Butalbital is a DEA schedule III substance due to its abuse potential and its extended use is not recommended.

<table>
<thead>
<tr>
<th>% of Butalbital TRx</th>
<th>Butalbital combination</th>
<th>Trade name</th>
</tr>
</thead>
<tbody>
<tr>
<td>77%</td>
<td>Acetaminophen/ butalbital/caffeine</td>
<td>Fioricet</td>
</tr>
<tr>
<td>6%</td>
<td>Acetaminophen/ butalbital/caffeine/codeine</td>
<td>Fioricet with codeine</td>
</tr>
<tr>
<td>3%</td>
<td>Acetaminophen/ butalbital</td>
<td>Axocet</td>
</tr>
<tr>
<td>9%</td>
<td>Acetylsalicylic acid/ butalbital/caffeine</td>
<td>Fiorinal</td>
</tr>
<tr>
<td>5%</td>
<td>Acetylsalicylic acid/ butalbital/caffeine/codeine</td>
<td>Fiorinal with codeine</td>
</tr>
<tr>
<td>&lt;1%</td>
<td>Butalbital</td>
<td></td>
</tr>
</tbody>
</table>

Warning in product label
Butalbital is habit-forming and potentially abusable. Consequently, the extended use of this product is not recommended.

Certain prescription products exempted from DEA enforcement in most states.

Source: IMS Health, IMS National Prescription Audit™, 08/2013 – 07/2014
DEA = Drug Enforcement Agency
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Racemic isomethetepine combination (RIC) prescriptions had been commonly written.

Number of RIC prescriptions peaked at 2.5 million.

Usage of RIC Prescriptions for All Diagnoses

IMS Health, IMS National Disease and Therapeutic Index™, 01/1995 – 12/2000, extracted 8/2014

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Migraine and ETTH can exist together in mixed headache syndrome

Distinct from each other in pathophysiology and clinical presentation

**Migraine**
- Spectrum of presentations
- Milder attacks are similar to ETTH
- Episodic migraine has features distinct from ETTH (aura, light and noise sensitivity, GI disturbance)

**ETTH**
- Can involve central sensitization but does not lead to migraine symptoms
- No migraine features


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Pathophysiology of migraine and ETTH

Migraine

Three branches of trigeminal nerve

Vasodilation leads to reflex activation of trigeminal nerve

Trigeminal nerve

Migraine symptoms
Nausea, aura, light and sound sensitivity

Cranial vessels

Spinal tract

ETTH

• May be a mild form of migraine or have distinct etiology
• Believed to involve vasodilation


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The vascular theory of headache pathogenesis and treatment


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Sympathomimetic control of vasoconstriction has historically been the focus of a considerable amount of drug development.
Targets in the treatment of headache and pain

- Sodium channel, \(^1\) Na(V)\(_{1.7/1.8}\)
- Nerve growth factor\(^2\)
- Calcium channel alpha-2-delta (“gabapentinoids”)\(^3\)
- Serotonin receptors, 5-HT\(_{1B/D/F}\)\(^4\) (“triptans”)
- Prostanoid receptors (EP\(_2/EP_4\)) \(^4\)
- Calcitonin gene-related peptide (CGRP) receptor\(^4\)
- NO receptor\(^4\)
- Cannabinoid receptors (“cannabinoids”)\(^5\)
- Opioid receptors (naltrexone, low dose)\(^6\)
- NMDA receptor (ketamine)\(^7\)

Racemic isomethoheptene (IMH) has a long track record of use

- **1930s**
  - IMH introduced for GI conditions

- **1960s**
  - Drug Efficacy Study Implementation (DESI) recommends IMH for tension and vascular headache, and possibly migraine

- **1970s**
  - Research showed effects in migraine
  - Sympathomimetic activity similar to ergotamines

- **2011**
  - Discontinued from the market (marketed under “unapproved drug category”)

- **2013**
  - Tonix discovers TNX-201 (R-isomer of IMH) and begins development
  - Developing science around TNX-201

---

1) MigraTen Prescribing Information; Pharmelle; Gilbert AZ, 2004.

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Racemic IMH is a sympathomimetic amine

Sympathomimetic activity presumed to account for activity in headache

• Sympathomimetic action leads to vasoconstriction in cranial vessels
  – Common therapeutic strategy for vascular headaches
• New proprietary data points to a different mechanism

IMH isomers have different pharmacological activities

- Previously marketed isomethetepene drugs were a mixture of two chemically distinct, mirror-image isomers

**R-isomer**
- Analgesic
- Binds to imidazoline-1 receptor
- Inactive on adrenergic receptors

**S-isomer**
- Sympathomimetic
R-IMH binds to the imidazoline-1 receptor

Binding of isomethetene isomers and racemic mixture to I\textsubscript{1}-R

\[ \text{Clonidine, } \% \text{ Initial Bound} \]

- (S)-Isomethetene, \( K_i = 1100 \text{ nM} \)
- (R)-Isomethetene, \( K_i = 18 \text{ nM} \)
- Racemic Isomethetene, \( K_i = 42 \text{ nM} \)

R-IMH has reduced effects on blood pressure compared to S-IMH and racemic IMH

Comparison of the effects of isometheptene mucate (IMH), (R)-IMH, and (S)-IMH on blood pressure following IV administration in anesthetized rats at doses ranging from 0.03 to 10 mg/kg

Diastolic arterial blood pressure, change in mmHg

Discovery of the imidazoline receptor

- Clonidine has been in clinical use for 40 years\(^1\)
  - High blood pressure, migraine, pain, psychiatric disorders
  - Use in pain limited by side effects
  - Primary activity—\(\alpha_2\) adrenergic agonist

- Imidazoline receptor hypothesized in ‘80s when \(\alpha_2\) activity could not fully explain pharmacologic action\(^2\)

---

The imidazoline-1 receptor is a novel target for the treatment of pain

**Imidazoline I₁ Receptor (I₁-R)**

**Characteristics**¹

- Transmembrane receptor
- Distinct from α₂AR and MAO receptor subtypes
- No sequence similarity to GPCRs or ATP-sensitive K⁺ channels
- Shares similarities to ryanodine and cytokine receptors

**Mouse Studies**²

- I₁-R null mice show no difference in systolic blood pressure or heart rate compared to wild type
- I₁-R null mice show a reduction in pain threshold compared to wild type in both the hot plate and tail flick tests

---


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The imidazoline-1 receptor is a novel target for the treatment of pain

Imidazoline I₁ Receptor (I₁-R)

Drugs with I₁-R Affinity¹

<table>
<thead>
<tr>
<th>Drug</th>
<th>I₁ agonist</th>
<th>α₁/α₂ agonist</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clonidine</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Rilmenidene</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Moxonidine</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Dexmedetomidine</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Isomethptene</td>
<td>✓</td>
<td>✗</td>
</tr>
</tbody>
</table>

Isomethptene is a non-imidazoline, selective imidazoline-1 receptor (NISIR) agonist

Initial physician response to TNX-201

• Based on the established use of racemic isomethoephtene, the single isomer, TNX-201, should have a superior safety profile* with similar efficacy compared to NSAIDs and Fioricet

• The likelihood of a non-habit forming nature and a low rebound risk, judging from the racemate, differentiate TNX-201 from other tension-type headache therapies

• Familiarity and experience with racemic isomethoephtene translates to physician comfort using TNX-201

* Preliminary Phase 1 results showed that TNX-201 is well tolerated at all doses studied. The adverse event profile is similar to placebo.
Future opportunities for TNX-201

• There are currently a limited number of MOAs used in treating headache pain

• The MOA of TNX-201 on headache pain is novel, with the imidazole $I_1$ receptor representing a strong candidate
All IP wholly-owned by Tonix without obligations to others

**TNX-102 SL**
Fibromyalgia, PTSD

- **Composition-of-matter (eutectic)**
  - Patents filed
  - Protection expected to 2034

- **Pharmacokinetics (PK)**
  - Patents filed
  - Protection expected to 2033

- **Method-of-use**
  - Fibromyalgia: patents issued, 3Q 2020 expiry
  - PTSD: patents filed

**TNX-201**
Headache

- **Composition-of-matter (isomer)**
  - Patents filed
  - Protection expected to 2033

---

TNX-102 SL (cyclobenzaprine HCl sublingual tablet) 2.8 mg and TNX-201 ((R)-isometheptene mucate) are Investigational New Drugs and are not approved for any indication.
# Financial summary

<table>
<thead>
<tr>
<th>NASDAQ: TNXP</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cash reported at September 30, 2014</td>
<td>$46.2 million</td>
</tr>
<tr>
<td>Net cash used in operations in 3Q14</td>
<td>$4.9 million</td>
</tr>
<tr>
<td>Shares outstanding†</td>
<td>10.8 million</td>
</tr>
</tbody>
</table>

† As of January 9, 2015
Management team

Seth Lederman, MD
Chief Executive Officer

Leland Gershell, MD, PhD
Chief Financial Officer

Bruce Daugherty, PhD
Chief Scientific Officer

Don Kellerman, PharmD
SVP, Clinical Development & Regulatory Affairs
Milestones – recent and upcoming

**TNX-102 SL – Fibromyalgia**
- September 2014 – Reported top line results from Phase 2b BESTFIT study
- January 2015 – Reported on FDA acceptance of 30% responder analysis as primary endpoint
- 2Q 2015 – Begin Phase 3 program

**TNX-102 SL – Post-Traumatic Stress Disorder**
- June 2014 – Received IND clearance in PTSD
- December 2014 – Began recruiting Phase 2 AtEase study in military-related PTSD

**TNX-201 – Episodic Tension-Type Headache**
- October 2014 – Received IND clearance in ETTH
- December 2014 – Completed clinical pharmacology study
- 2Q 2015 – Begin Phase 2 study in ETTH

TNX-102 SL (cyclobenzaprine HCl sublingual tablet) 2.8 mg and TNX-201 ((R)-isomeptene mucate) are Investigational New Drugs and are not approved for any indication.
BACKUP SLIDES
Headache costs U.S. employers approximately $20B annually

- Headache is the most common pain condition causing lost productive time, costing employers $19.6B annually (2002 US $)\(^1\)
- ETTH contributes the majority of the disability burden (>58\%)\(^3\)

Lost productivity* in days/year\(^2\)

19.55

Annual loss to employers per patient* (2000 US $)\(^2\)

$3309

*Due to migraine only

Medications used for treatment of ETTH

A vast majority of people with episodic headache are treated with analgesics

Current and Past Pain Medication Used for ETTH

Listed in decreasing order of usage:
- Acetaminophen
- Ibuprofen
- OTC/Caf/Combo
- Aspirin
- Naproxen
- Total Rx

Rx medications used for treatment of ETTH

Existing prescription therapies have low market penetration

**Current and Past Pain Medication Used for ETTH**

<table>
<thead>
<tr>
<th>Medication Preference (%)</th>
<th>1st Choice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triptan</td>
<td>3.4%</td>
</tr>
<tr>
<td>Butalbital compounds</td>
<td>1.6%</td>
</tr>
<tr>
<td>Opioid compounds</td>
<td>1.1%</td>
</tr>
</tbody>
</table>

0% 4%

Isomethetepine prescriptions previously were commonly written

Number of Isomethetepine prescriptions peaked at 2.5 million

Usage of Isomethetepine Combinations for all Diagnoses

![Bar chart showing the usage of Isomethetepine combinations for all diagnoses from 1995 to 2014. The chart indicates the number of prescriptions in millions, with the categories of Other, Non-Migraine, and Migraine. The combination of Isomethetepine/dichloralphenazine/acetaminophen was discontinued in 2002. Source: IMS Health, National Prescription Audit, 01/1995 – 7/2014- extracted 8/2014. IMS Health, IMS National Disease and Therapeutic Index™, 01/1995 – 12/2000, extracted 8/2014.]