



NASDAQ: TNXP

January 2015

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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

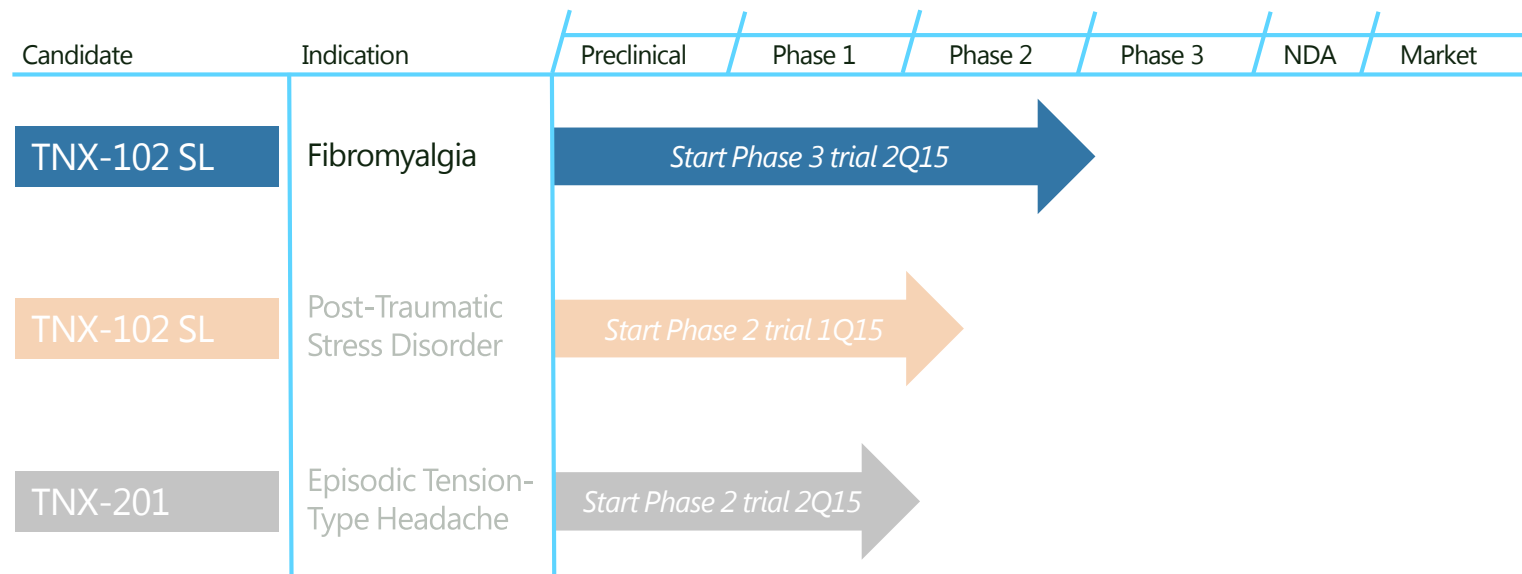
Episodic Tension-Type Headache

TNX-102 SL

TNX-201

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



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.

Fibromyalgia market opportunity

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

Three FDA approved prescription medications:

Class	Product	Company	Approval Year in FM
Membrane Stabilizer	Lyrica®	Pfizer	2007
SNRI	Cymbalta®	Eli Lilly	2008
	Savella®	Forest	2009

Tonix is pursuing a different approach:

Sleep Quality	TNX-102 SL	Tonix
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* Lawrence et al, *Arthritis Rheum* 2008;58:26-35; Vincent et al, *Arthritis Care Res* 2013;65:786-792.

** Estimates based on information from publicly-available sources

SNRI = Serotonin Norepinephrine Reuptake Inhibitor

Sleep quality is a new target for fibromyalgia therapy

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

* Swick, *Ther Adv Musculoskel Dis* 2011;3:167-178.

** 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

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

Outcome Measure at Week 12	Intent-to-Treat Population [†]	<i>p</i> value	Method
Daily Pain Diary, NRS	Mean Change ^{**}	0.086	MMRM
		0.172	JTC-MI
Daily Pain Diary, NRS	Proportion Achieving 30% Improvement [*]	0.033	LR
Clinic NRS 7-day pain recall	Mean Change	0.029	MMRM
FIQ-R Pain Item	Mean Change	0.004	MMRM

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)

$p < 0.05 \rightarrow$ achieved statistical significance

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

Outcome Measure at Week 12	Intent-to-Treat Population	p value	Method
Daily Sleep Quality Diary, NRS	Mean Change*	<0.001	MMRM
PROMIS Sleep Disturbance	T-score Change*	0.005 0.004	MMRM JTC-MI
FIQ-R Sleep Quality Item	Mean Change	<0.001	MMRM

PROMIS = Patient-Reported Outcome Measures in Sleep

* Declared secondary endpoint

p < 0.05 → achieved statistical significance

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

Outcome Measure at Week 12	Intent-to-Treat Population	p value	Method
Patient Global Impression of Change	Responder Analysis*	0.025	LR
FIQ-R Total Score	Mean Change*	0.014	MMRM
		0.015	JTC-MI
FIQ-R Symptom Domain	Mean Change	0.004	MMRM
FIQ-R Function Domain	Mean Change	0.060	MMRM
FIQ-R Anxiety Item	Mean Change	0.015	MMRM
FIQ-R Sensitivity Item	Mean Change	0.017	MMRM
FIQ-R Stiffness Item	Mean Change	0.039	MMRM

* Declared secondary endpoint

p < 0.05 → achieved statistical significance

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

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

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.

Registration program for TNX-102 SL in fibromyalgia

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

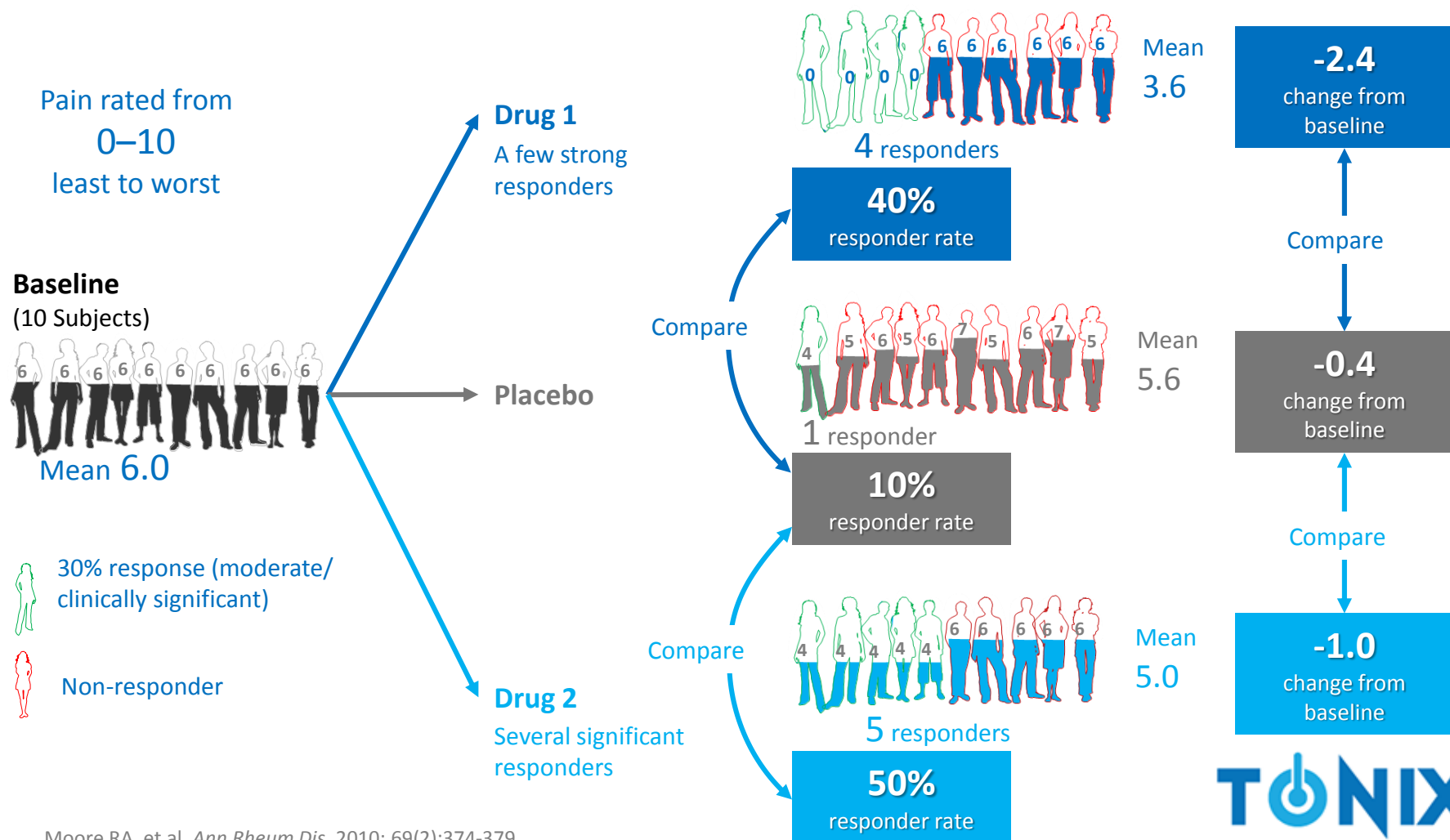
30% responder analysis at 12 weeks* – primary efficacy endpoint based on FDA written acceptance

**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



Moore RA, et al. *Ann Rheum Dis*. 2010; 69(2):374-379.

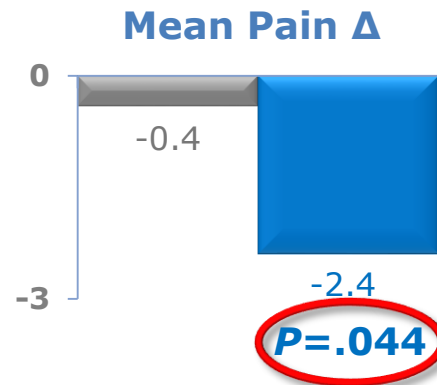
Illustration of mean pain vs. responder analyses with hypothetical drugs 1 and 2

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

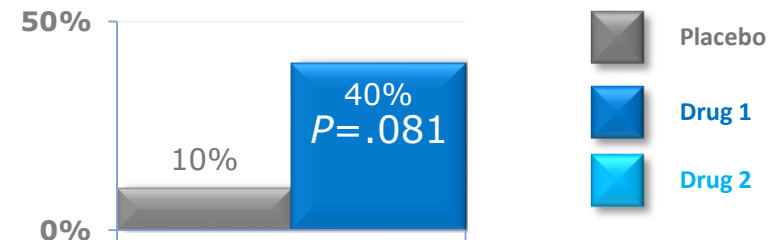
Drug 1

A few strong responders

- Mean pain Δ is significant
- 30% RR is not



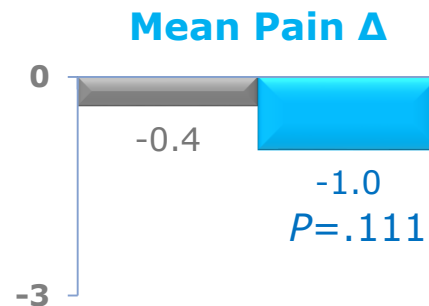
30% RR



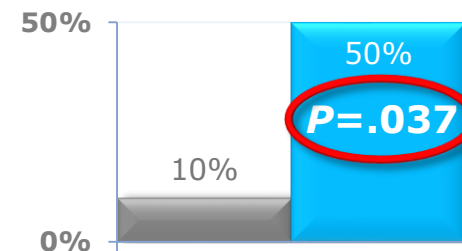
Drug 2

Several significant responders

- 30% RR is significant
- Mean pain Δ is not



30% RR

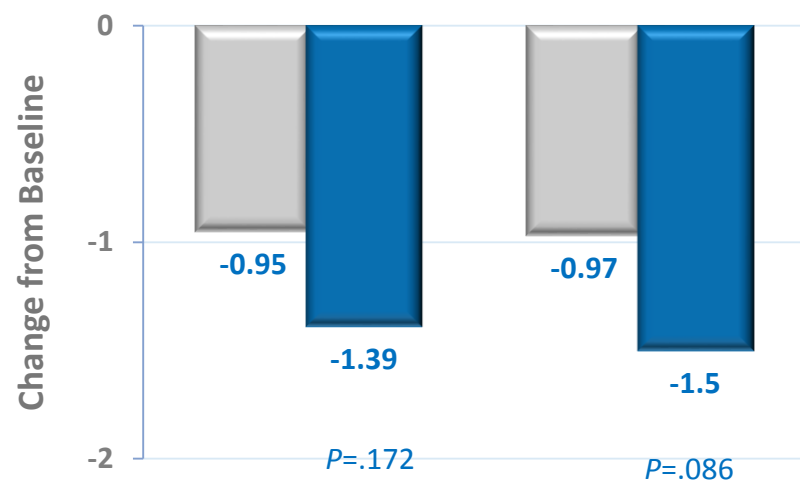


Farrar JT, et al. *Pain*. 2001; 94(2):149-158.

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

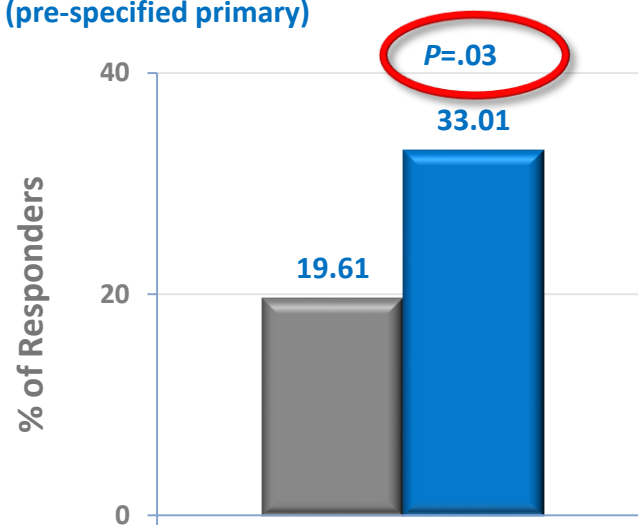
Week 12 Change from Baseline in Mean Pain NRS
(pre-specified primary)



Placebo
(n=102)

TNX-102 SL
(n=103)

30% Responder Rate Based on Pain NRS
(pre-specified primary)

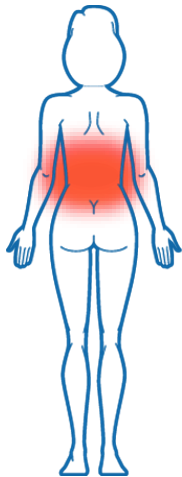


JTC-I = Jump-to-Control, Multiple Imputation; MMRM = Mixed-Effects Model Repeated Measures; NRS = Numeric Rating Scale

Chronic pain conditions lead to the development of central pain conditions

Reversal of the central pain syndrome may reveal the original cause

Back pain



Pain centralization

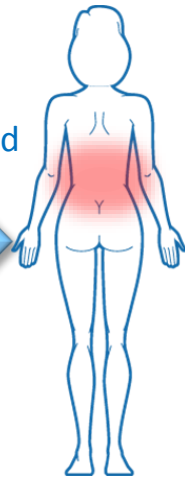
Fibromyalgia



Fibromyalgia treated



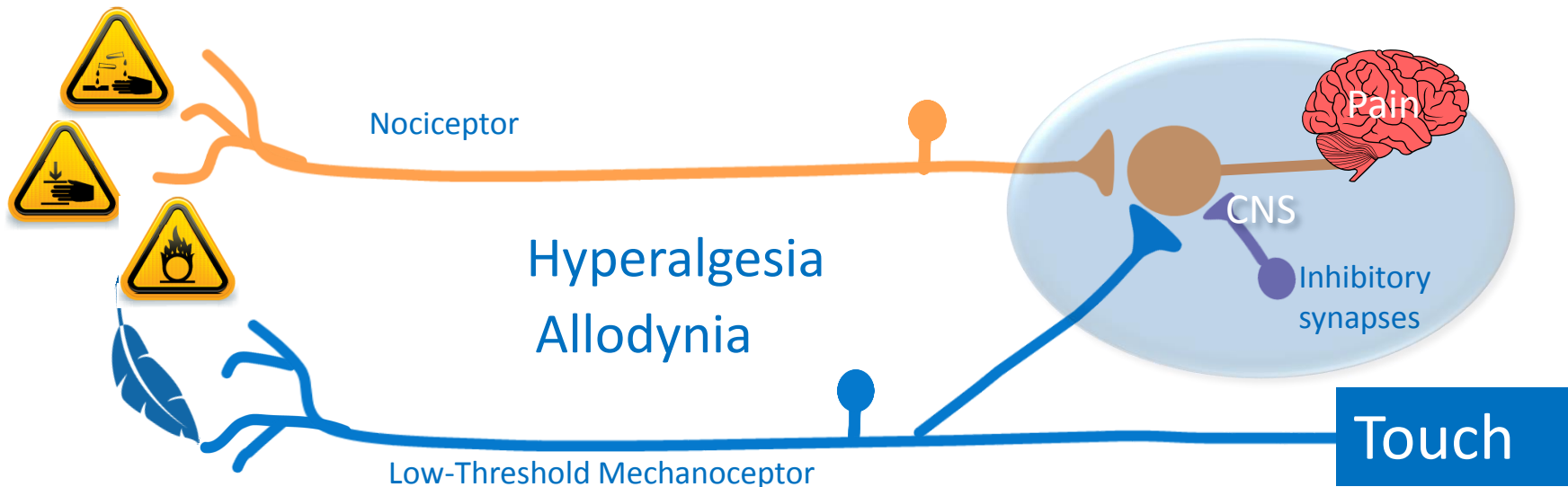
Back pain remains



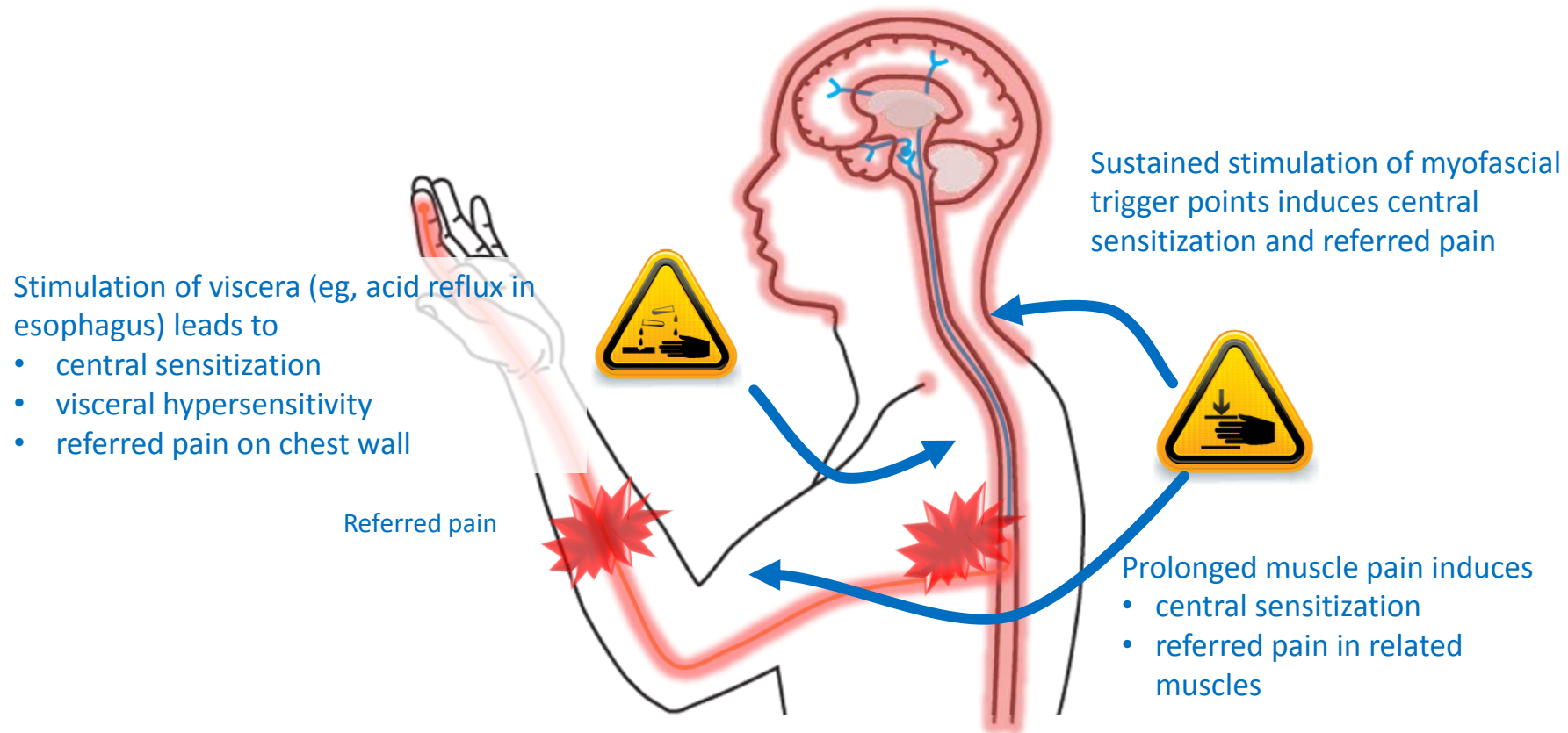
Time

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

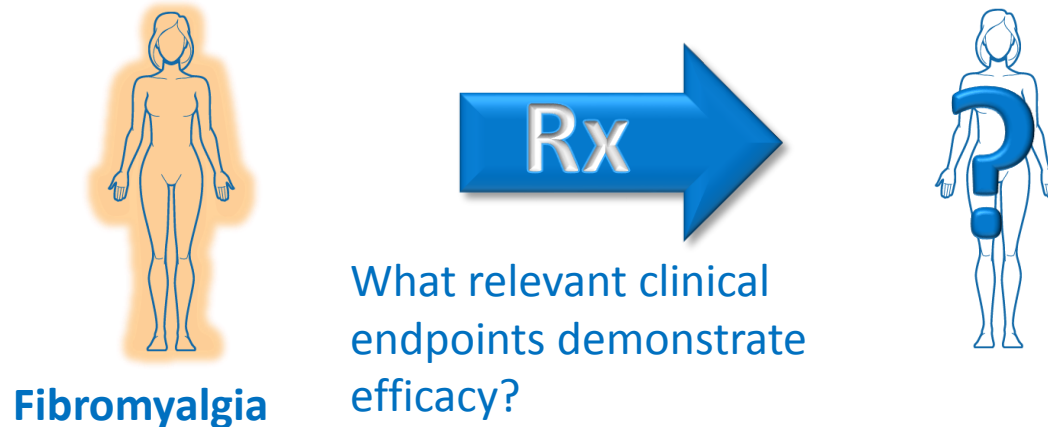


Conditioning of the peripheral and visceral nerves can lead to central sensitization and dermatome hypersensitivity

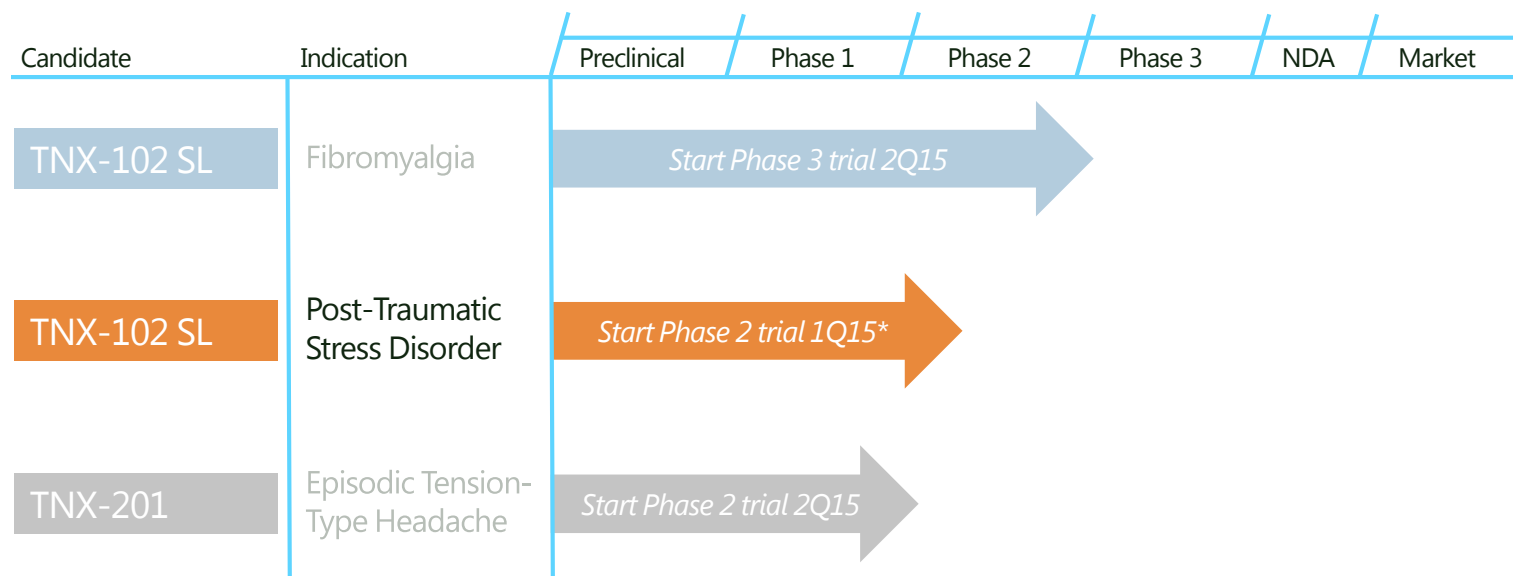


Review of fibromyalgia endpoints reflects dissatisfaction with current treatments

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



Phase 2 trial of TNX-102 SL for PTSD is recruiting



* Recruitment begin in December 2014.

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.

PTSD: A significant and growing public health problem

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:

Class	Product	Company	Approval Year in PTSD
SSRI	Paxil®	Glaxo	2001
	Zoloft®	Pfizer	1999

Tonix is pursuing a different approach:

Sleep Quality	TNX-102 SL	Tonix	2019E
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* Kessler et al, Arch Gen Psych 2005;62:617-627; Wang et al, Arch Gen Psych 2005;62:629-640.

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

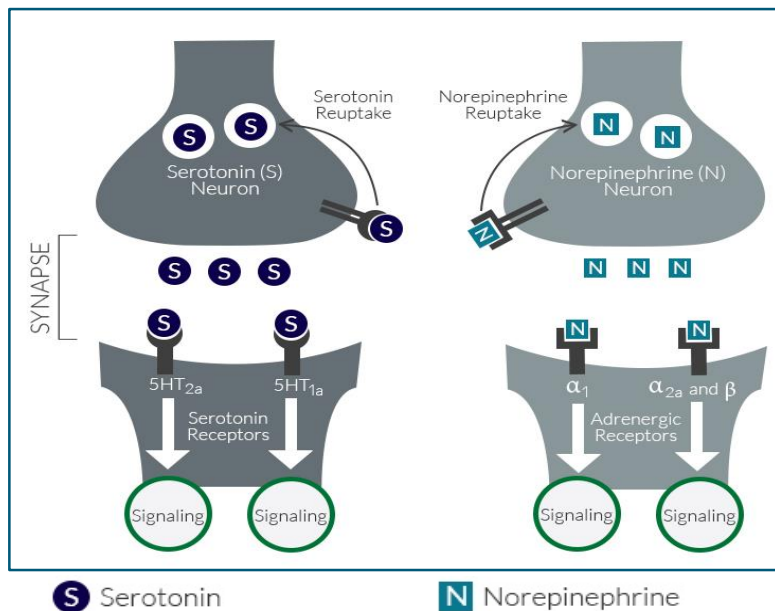
TNX-102 SL (cyclobenzaprine HCl sublingual tablet) 2.8 mg is an Investigational New Drug and is not approved for any indication.

TNX-102 SL acts on neurotransmitter systems intrinsic to sleep physiology

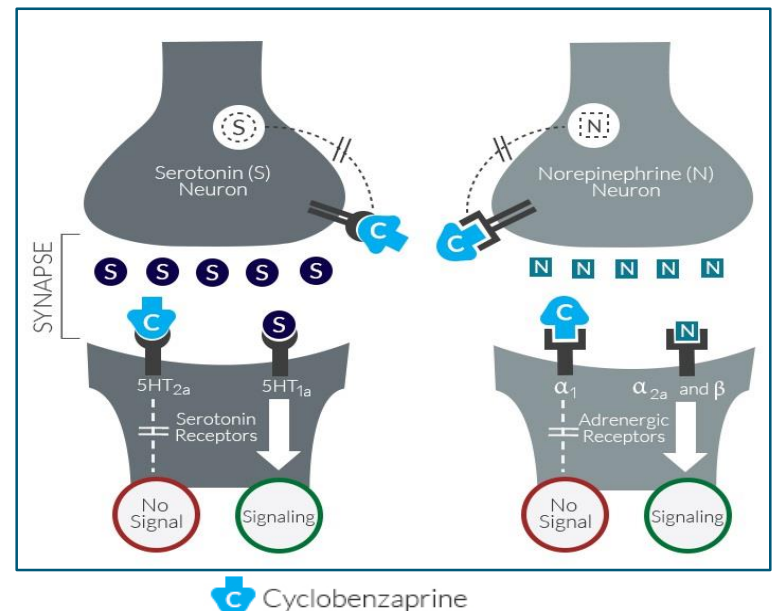
Serotonin and Norepinephrine Antagonist and Reuptake Inhibitor (SNARI)

Blocks serotonin and norepinephrine reuptake

Selectively blocks serotonin 2A and α -1 adrenergic receptors



TNX-102 SL

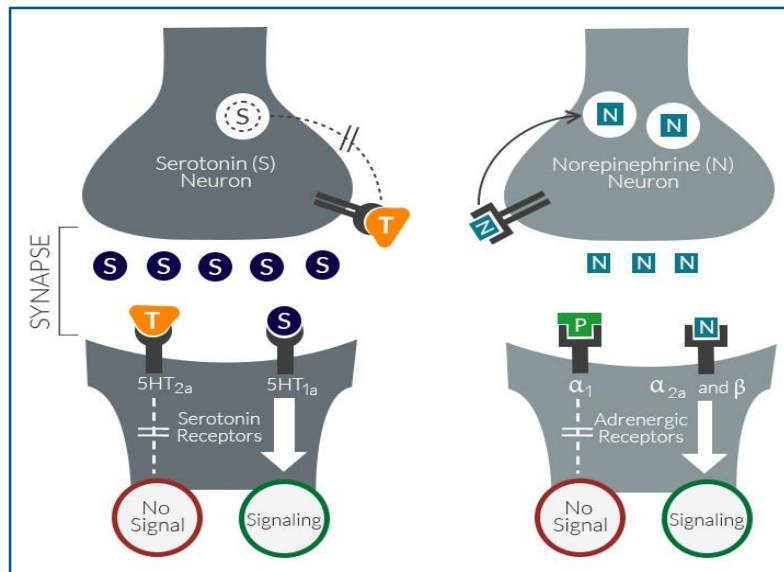


TNX-102 SL (cyclobenzaprine HCl sublingual tablet) 2.8 mg is an Investigational New Drug and is not approved for any indication.

Mechanistic relationship of TNX-102 SL with trazodone and prazosin

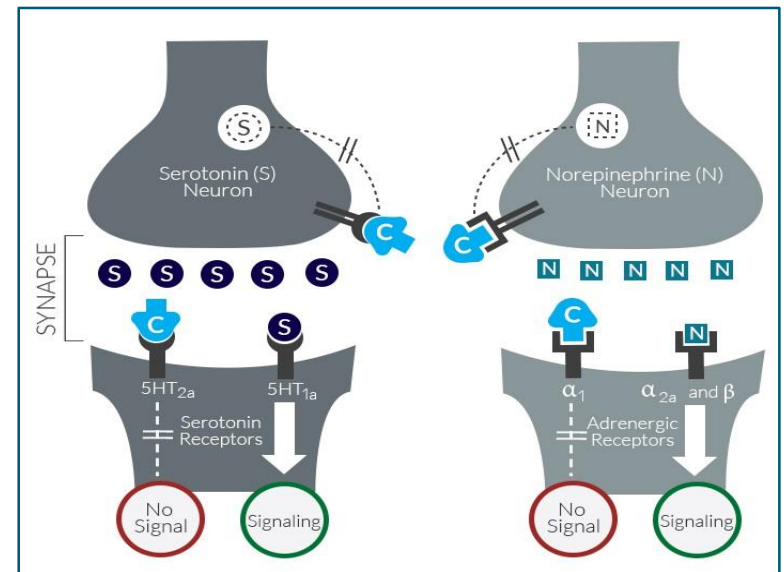
Trazodone blocks serotonin reuptake and 2A receptors

Prazosin blocks α -1 adrenergic receptors



T Trazodone
P Prazosin

TNX-102 SL



S Serotonin
N Norepinephrine
C Cyclobenzaprine

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

TNX-102 SL at bedtime once-daily

2.8 mg

N = 88

TNX-102 SL at bedtime once-daily

5.6 mg

N = 44

Placebo at bedtime once-daily

N = 88

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

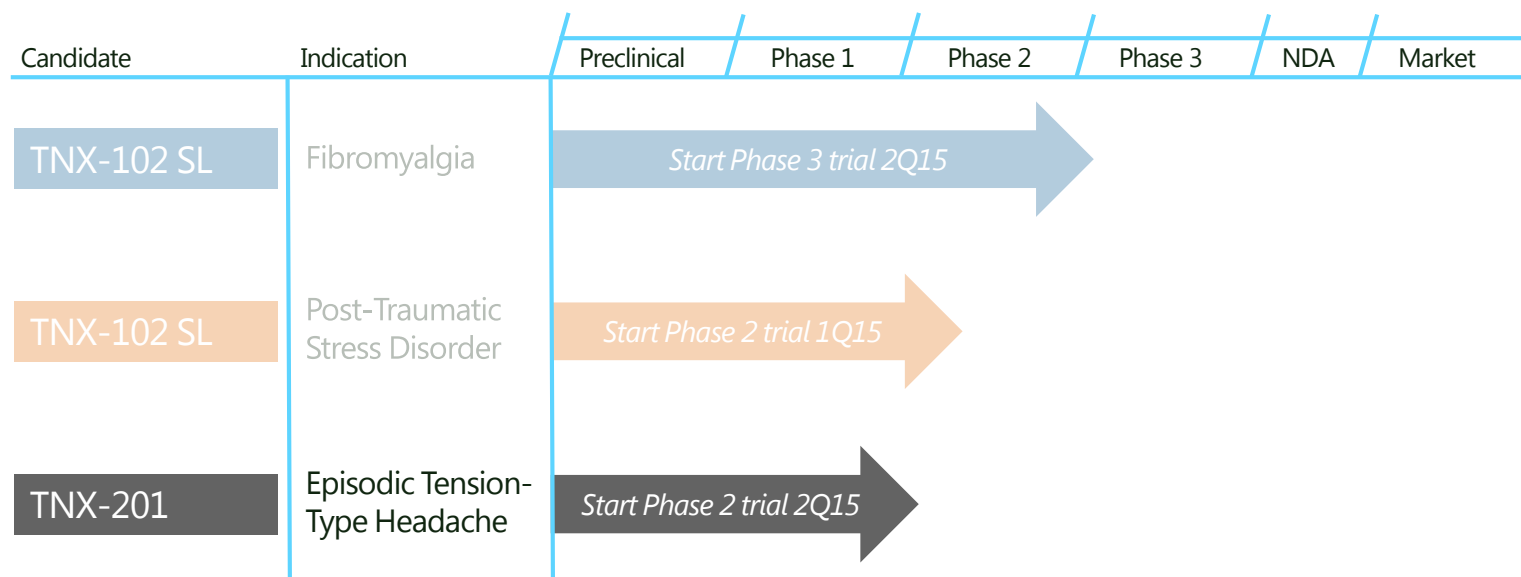
N=220; approximately 25 U.S. clinical sites

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



TNX-102 SL (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



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.

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

Class	Product	Company	Regulatory Status	Approval Year in ETTH
Barbiturate	Fiorinal®	Actavis	Approved NDA	1976
	Fioricet®	Actavis	Approved NDA	1992
Barbiturate + Opiate	Fiorinal with Codeine®	Actavis	Approved NDA	1990

* Schwartz et al, JAMA 1998;279:381-383; Chowdhury, Ann Ind Acad Neurol 2012;15:83-88; company analysis of public literature.

** Scher et al, Cephalalgia 2010;30:321-328; company analysis of public literature.

TNX-201 in clinical development for ETTH

TNX-201 is (R)-isometheptene mucate

Tonix is developing TNX-201 for ETTH
Phase 2 study to begin in 2Q 2015

Racemic isometheptene 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 isometheptene mucate is currently FDA-approved for any indication

TNX-201 ((R)-isometheptene mucate) is an Investigational New Drug and is not approved for any indication.

Phase 1 study of TNX-201 completed

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.)

	TNX-201 35 mg (N=9)	TNX-201 70 mg (N=9)	TNX-201 140 mg (N=9)	Rac. Isometh. 70 mg (N=9)	Placebo (N=9)
Subjects reporting ≥1 adverse event, %	22	11	0	11	33

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 (C_{max}, 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

TNX-201

140 mg

N = 75

Placebo

N = 75

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	Headaches/year
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

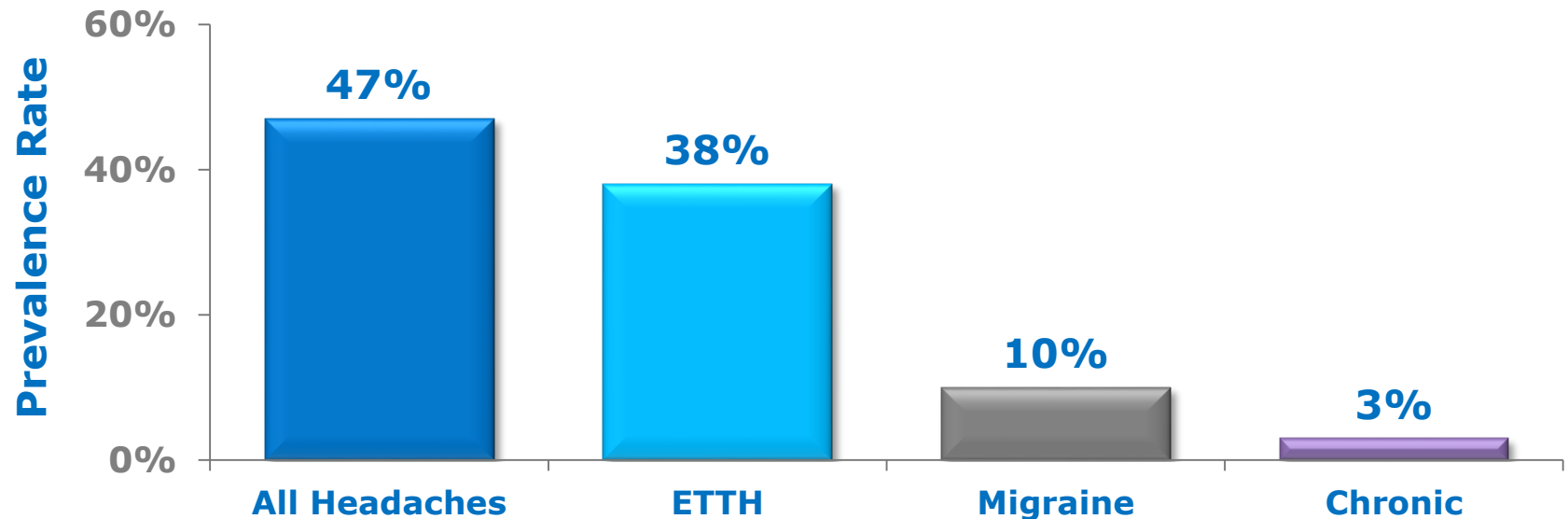
ETTH is the most common type of headache

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



Stovner L, et al. *Cephalalgia*. 2007; 27(3):193-210.

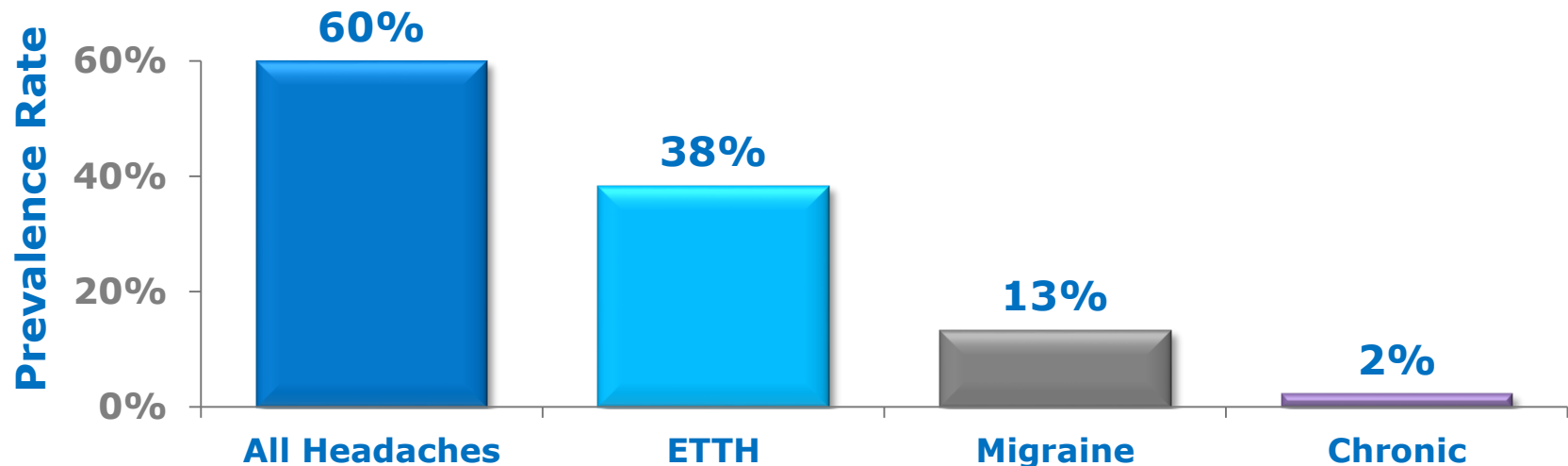
ETTH is the most common type of headache

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)



Estimated number
of adults (18-65,
2013 census)

~119 M

~75 M

~26 M

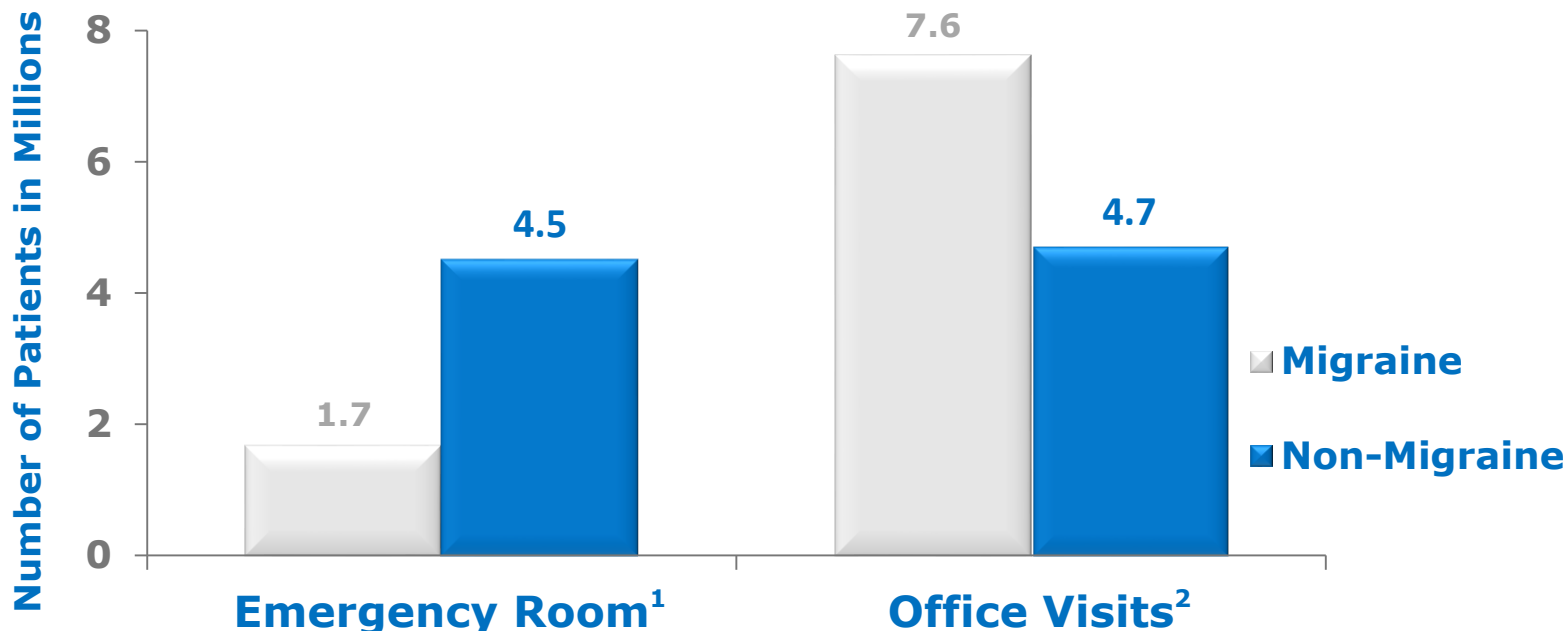
~4.4 M

- 1) Schwartz et al., JAMA, 1998; 279:381-383
- 2) Stovner L, et al. *Cephalalgia*. 2007; 27(3):193-210

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

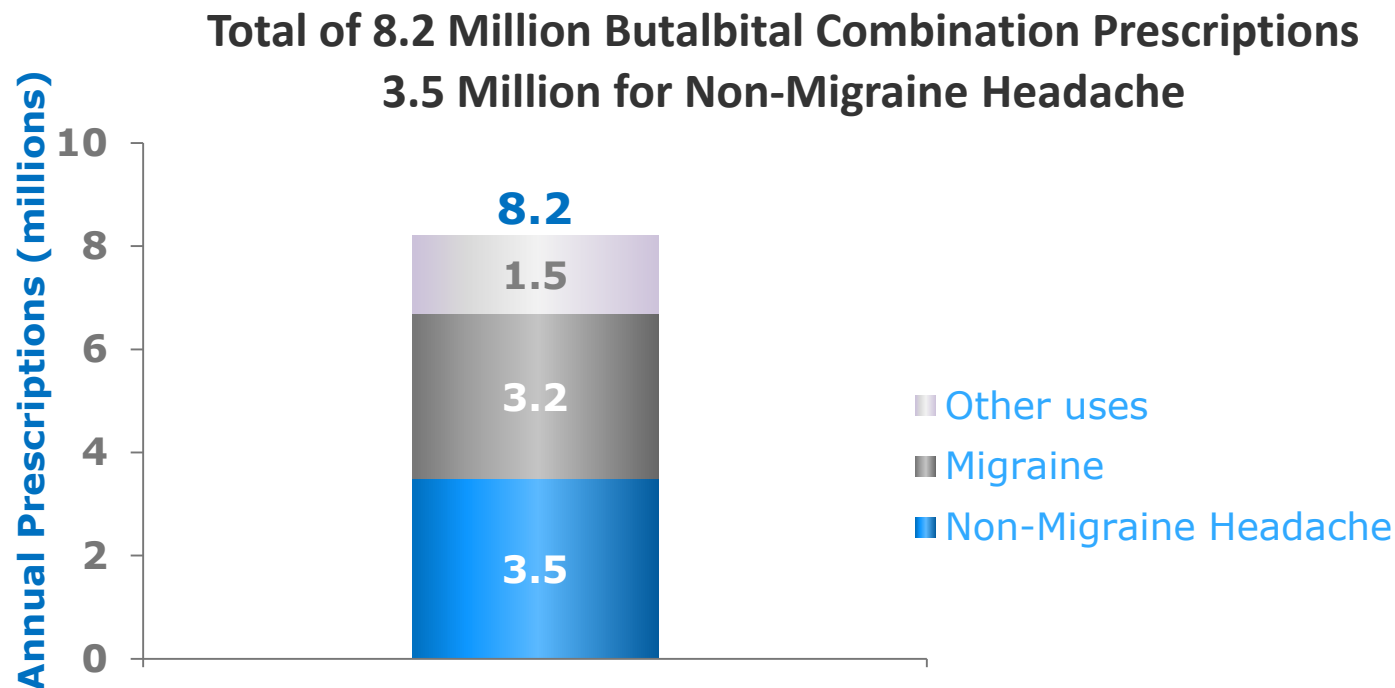


1) Heath Care Utilization Project data, 2011

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

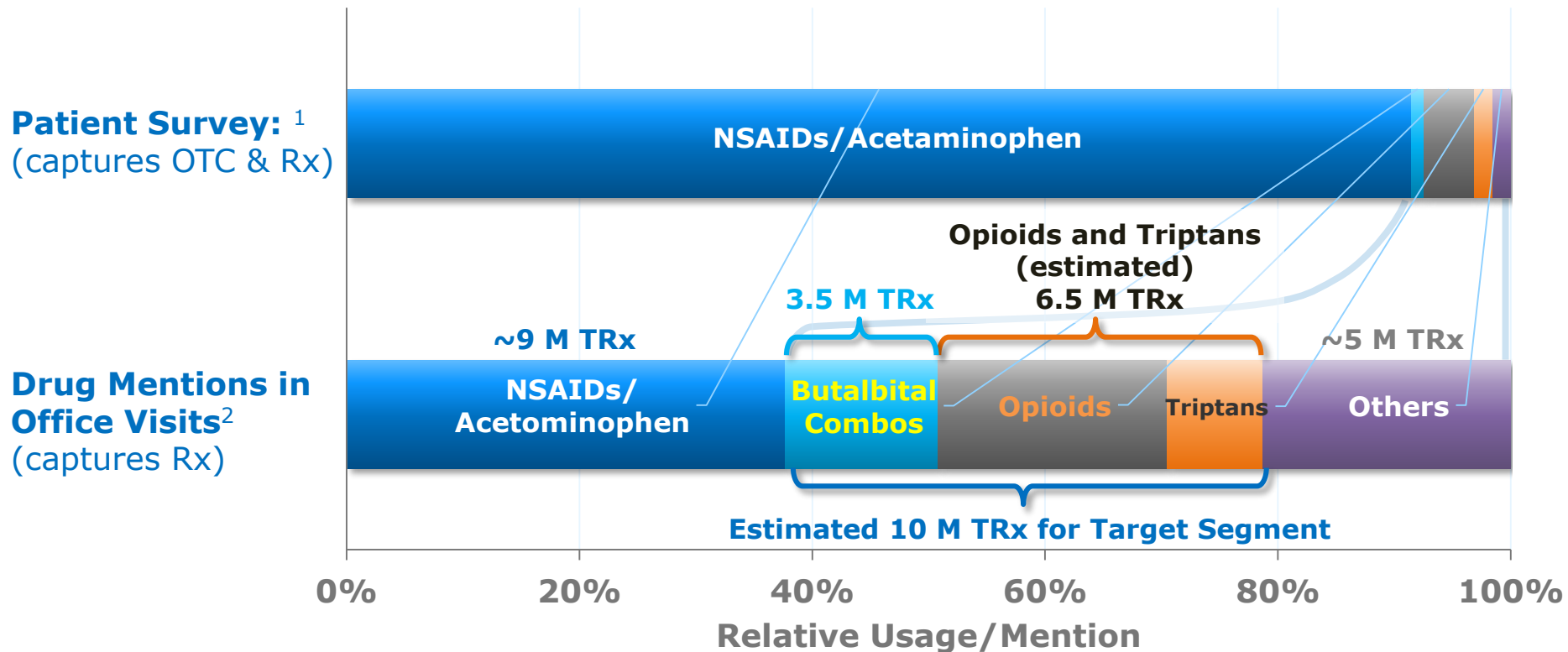


Source: IMS Health, IMS National Prescription Audit™, 08/2013 – 07/2014 and
IMS National Disease and Therapeutic Index™, Q3 2008 – Q3 2014

Current treatment pattern for non-migraine

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

Treatment Patterns From Two Perspectives

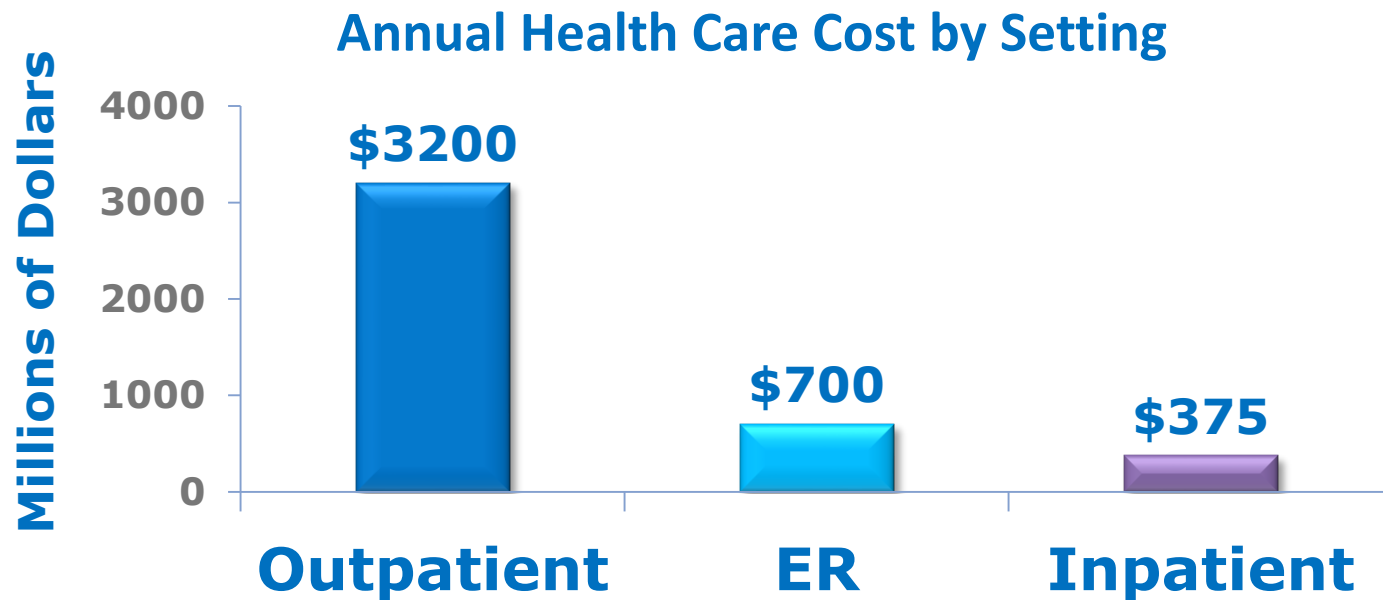


1) Scher AI, et al. *Cephalalgia*. 2010; 30(3):321-328.

2) Based on independent study conducted by Trinity Partners using IMS National Prescription Audit (8/2013 – 7/14/2014) 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 dollars¹



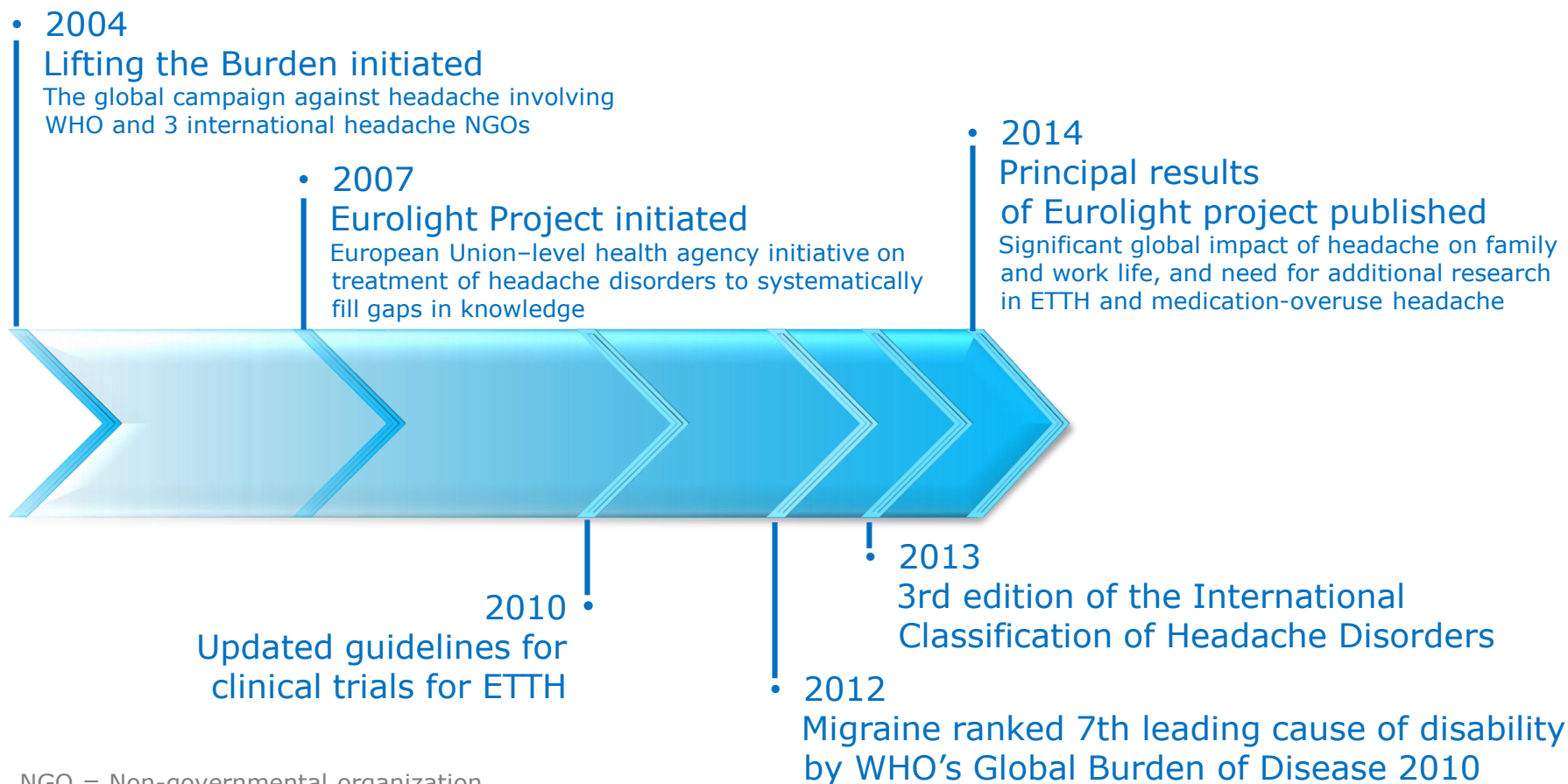
- Prescription costs are not included in these amounts

Better pharmacological treatment **reduced overall annual healthcare costs** by almost **\$19K/patient** in an HMO setting²

1) Insinga RP, et al. *Cephalalgia*. 2011; 31(15):1570-1575.

2) Maizels M, et al. *Headache*. 2003; 43(6):621-627.

Public health attention to headache has increased in the past decade

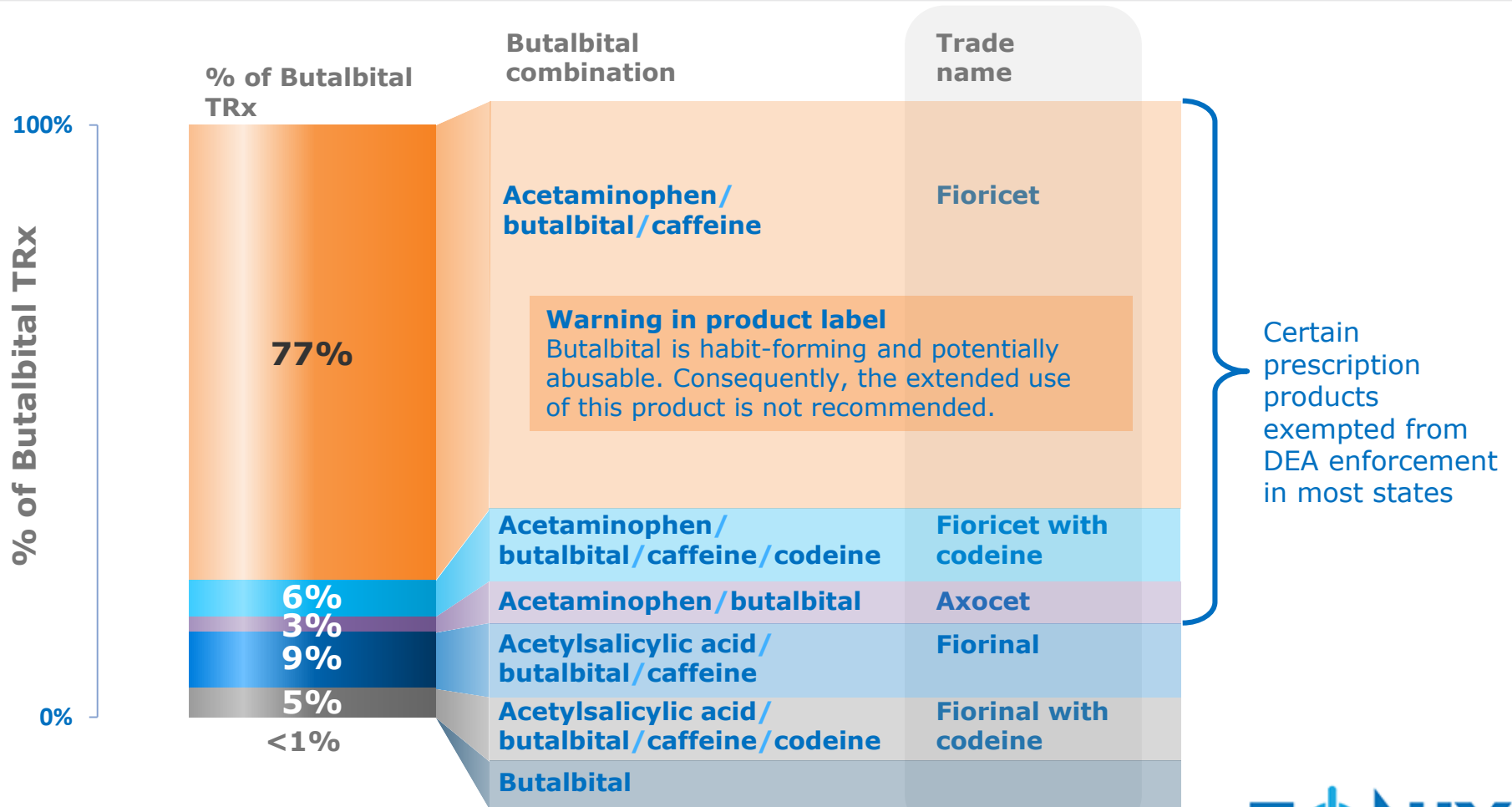


NGO = Non-governmental organization

- 1) Bendtsen L, et al. *Cephalalgia*. 2010; 30(1):1-16.
- 2) Steiner TJ. *Lancet Neurol*. 2004; 3(4):204-205.
- 3) Vos T, et al. *Lancet*. 2012; 380(9859):2163-2196.
- 4) *Cephalalgia*. 2013; 33(9):629-808.

All of the FDA-approved medications for ETT^H contain butalbital

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



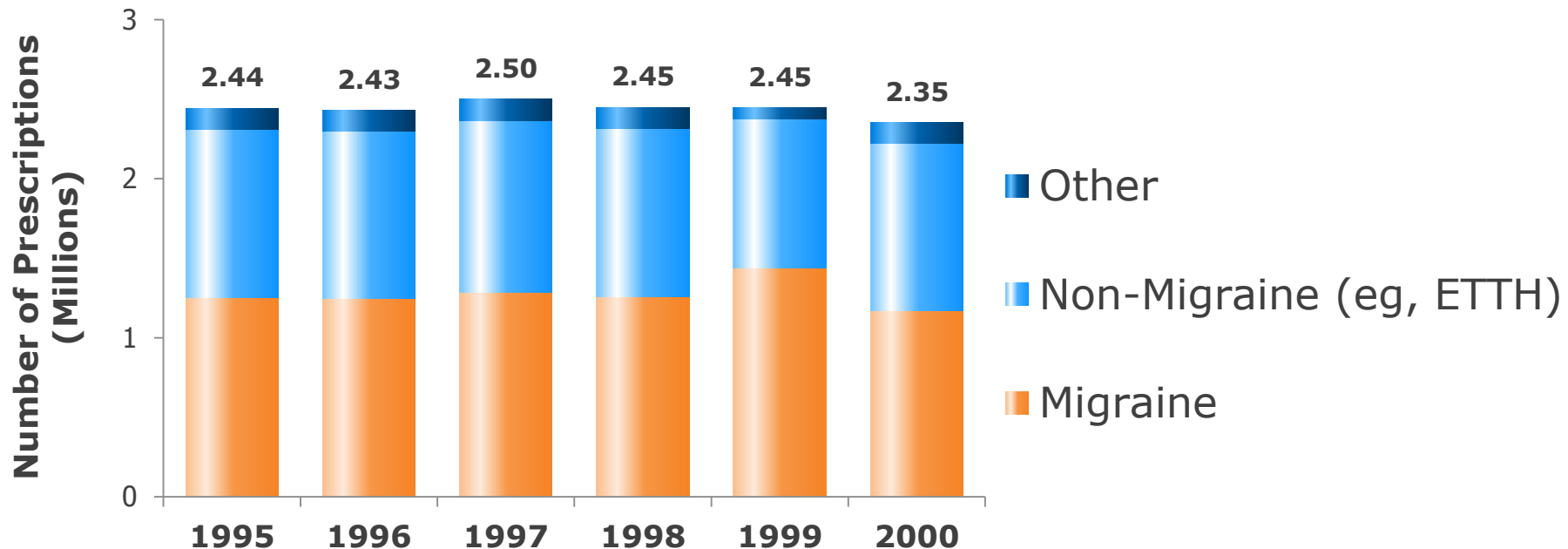
Source: IMS Health, IMS National Prescription Audit™, 08/2013 – 07/2014
Fioricet Prescribing Information. Actavis Pharma, Inc: Parsippany, NJ; 2014.

DEA = Drug Enforcement Agency

Racemic isometheptene combination (RIC) prescriptions had been commonly written

Number of RIC prescriptions peaked at 2.5 million

Usage of RIC Prescriptions for All Diagnoses



Source: IMS Health, National Prescription Audit, 01/1995 – 12/2000- extracted 8/2014
IMS Health, IMS National Disease and Therapeutic Index™, 01/1995 – 12/2000, extracted 8/2014

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

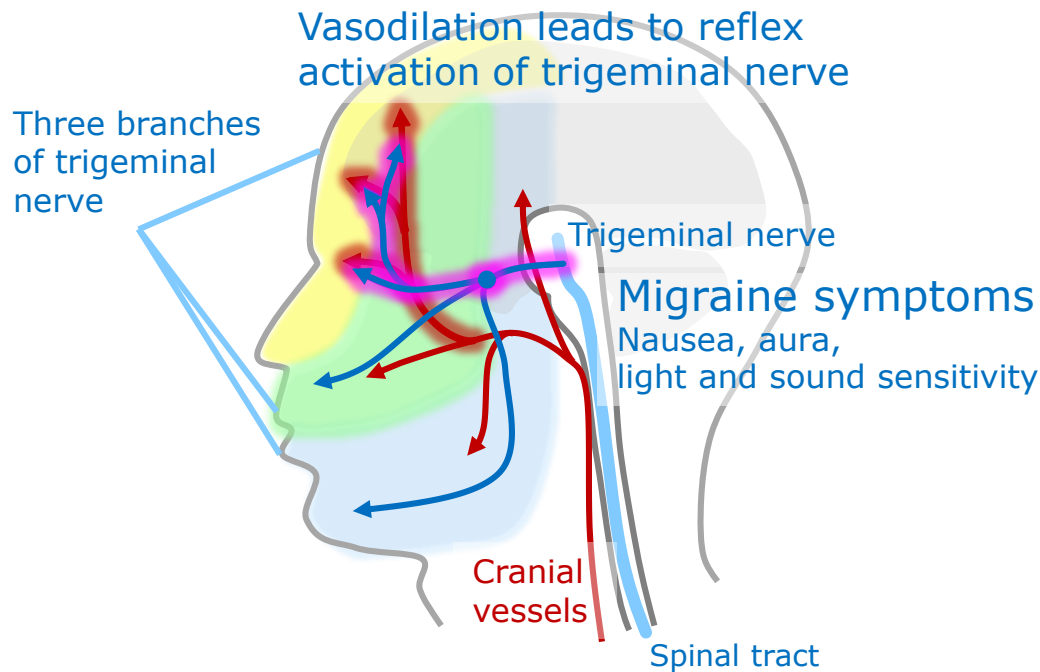


Mixed
headache
syndrome

The diagram illustrates the relationship between Migraine and ETTH in the context of Mixed headache syndrome. Two boxes at the top, 'Migraine' (dark blue) and 'ETTH' (light blue), each have a list of characteristics. From the bottom of the 'Migraine' box, a blue line extends downwards and to the right. From the bottom of the 'ETTH' box, a blue line extends downwards and to the left. These two lines cross each other and then merge into a single blue arrow that points down to an oval labeled 'Mixed headache syndrome'.

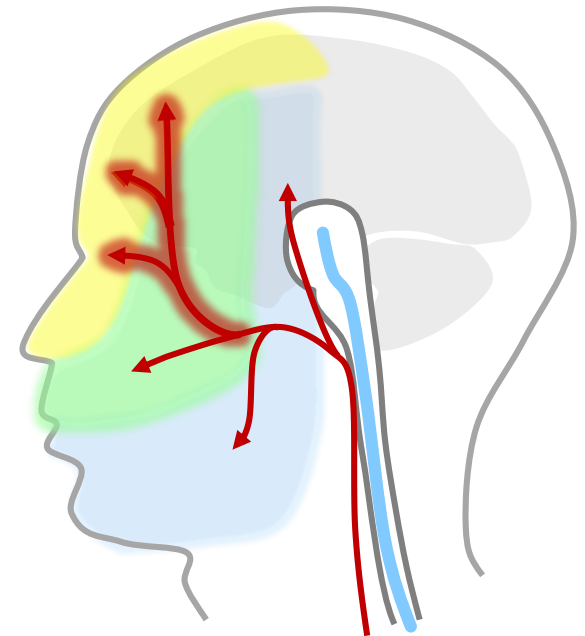
Pathophysiology of migraine and ETTH

Migraine



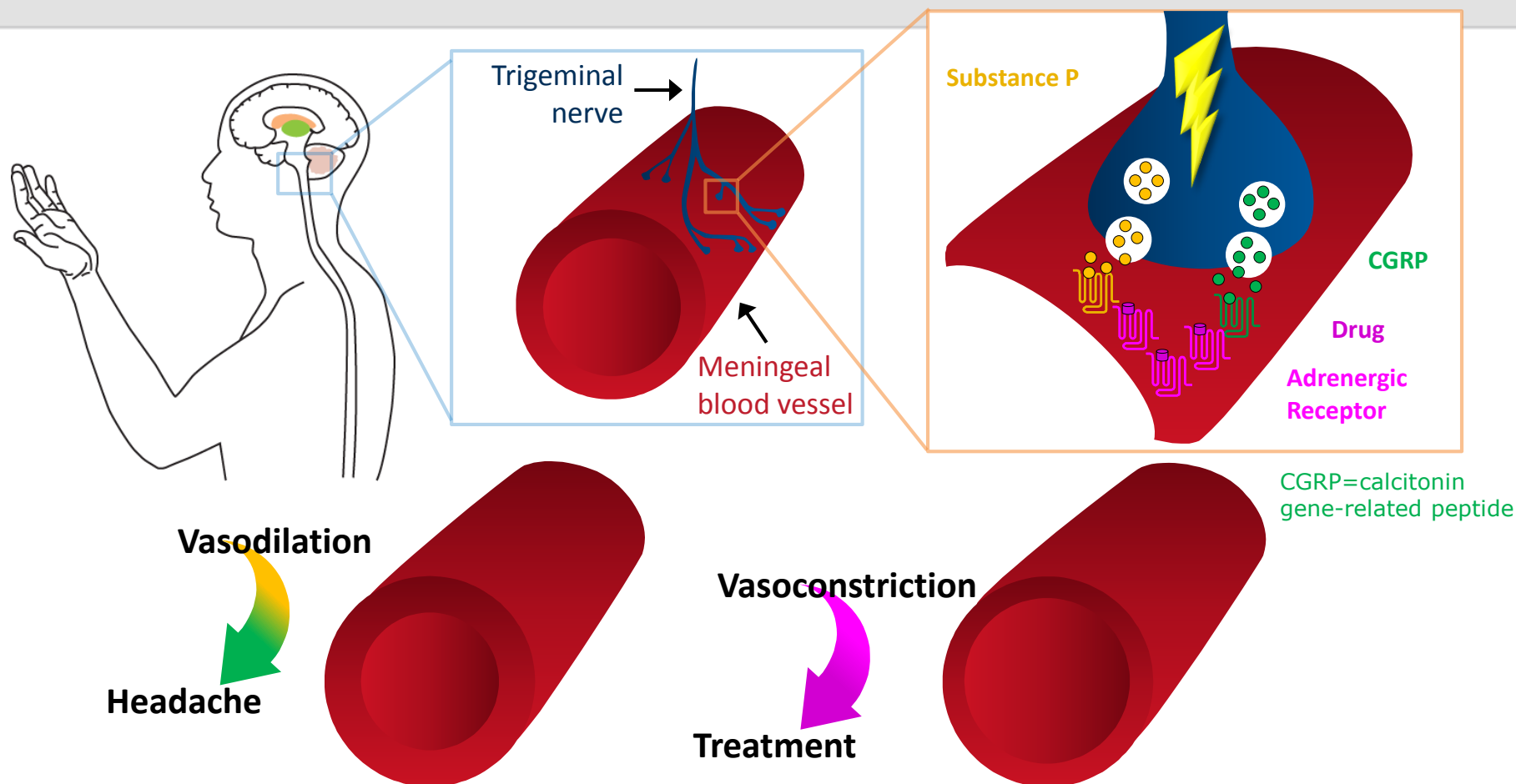
ETTH

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



Solomon GD. *Semin Pediatr Neurol.* 1995; 2(2):165-177.

The vascular theory of headache pathogenesis and treatment



Sympathomimetic control of vasoconstriction has historically been the focus of a considerable amount of drug development

Solomon GD. *Semin Pediatr Neurol*. 1995; 2(2):165-177.

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TONIX
PHARMACEUTICALS

Targets in the treatment of headache and pain

- Sodium channel,¹ Na(V)_{1.7/1.8}
- Nerve growth factor²
- Calcium channel alpha-2-delta (“gabapentinoids”)³
- Serotonin receptors, 5-HT_{1B/D/F}⁴ (“triptans”)
- Prostanoid receptors (EP₂/EP₄)⁴
- Calcitonin gene-related peptide (CGRP) receptor⁴
- NO receptor⁴
- Cannabinoid receptors (“cannabinoids”)⁵
- Opioid receptors (naltrexone, low dose)⁶
- NMDA receptor (ketamine)⁷

1) Dib-Hajj SD, et al. *Pain Med.* 2009; 10(7):1260-1269.

2) Ossipov MH. *Curr Pain Headache Rep.* 2011; 15(3):185-192.

3) Hauser W, Pain.2009;145(1-2):69-81.

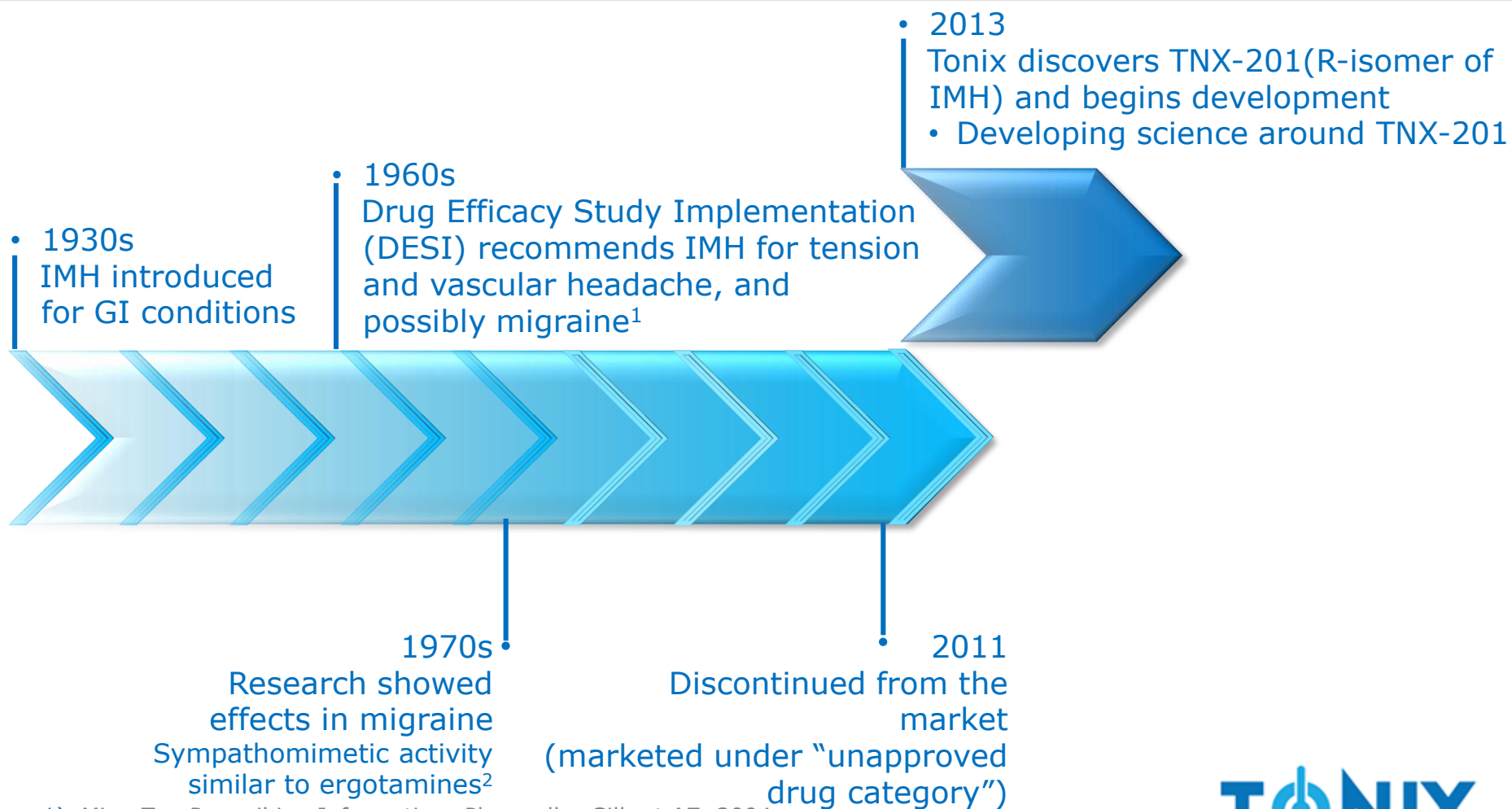
4) Nagy AJ, et al. *Neurol Sci.* 2013; 34 Suppl 1:S101-108.

5) Lynch ME, et al. *Br J Clin Pharmacol.*2011;72(5):735-744.

6) Younger J, et al. *Arthritis Rheum.* 2013;65(2):529-538.

7) Staahl C, et al. *Br J Clin Pharmacol* 2009;68:322-41.

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



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

2) Diamond S, et al. *Headache*. 1975; 15(3):211-213.

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

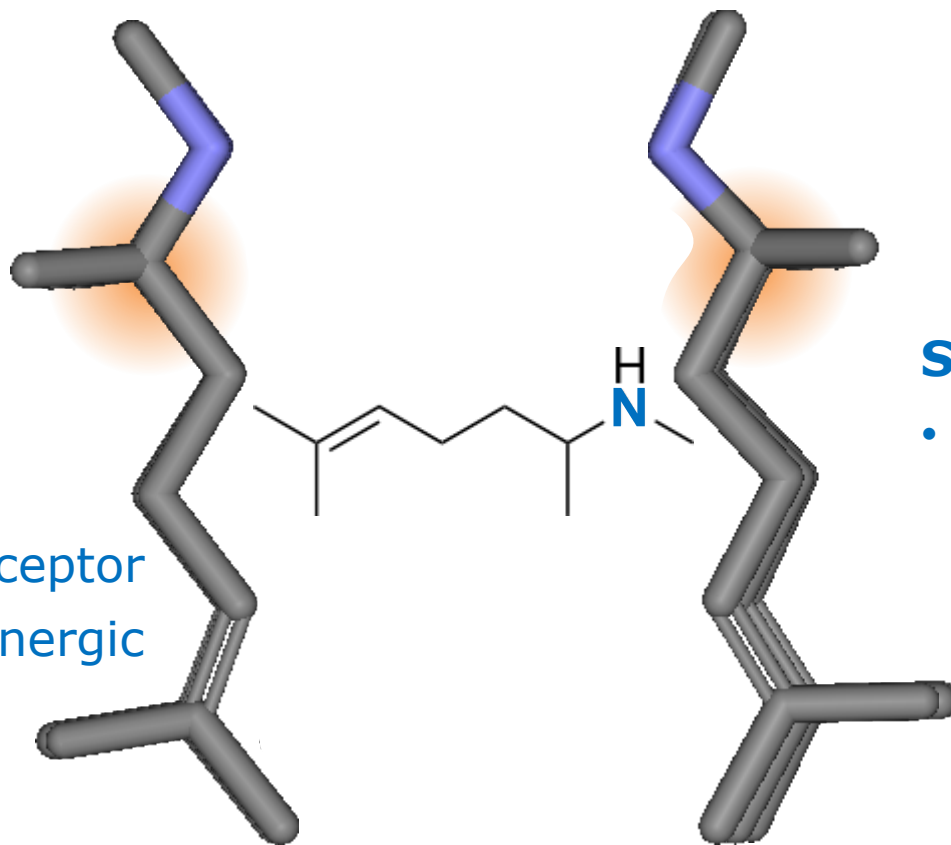
Willems EW, et al. *Naunyn Schmiedebergs Arch Pharmacol.* 2001; 364(1):27-32.

IMH isomers have different pharmacological activities

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

R-isomer

- Analgesic
- Binds to imidazoline-1 receptor
- Inactive on adrenergic receptors

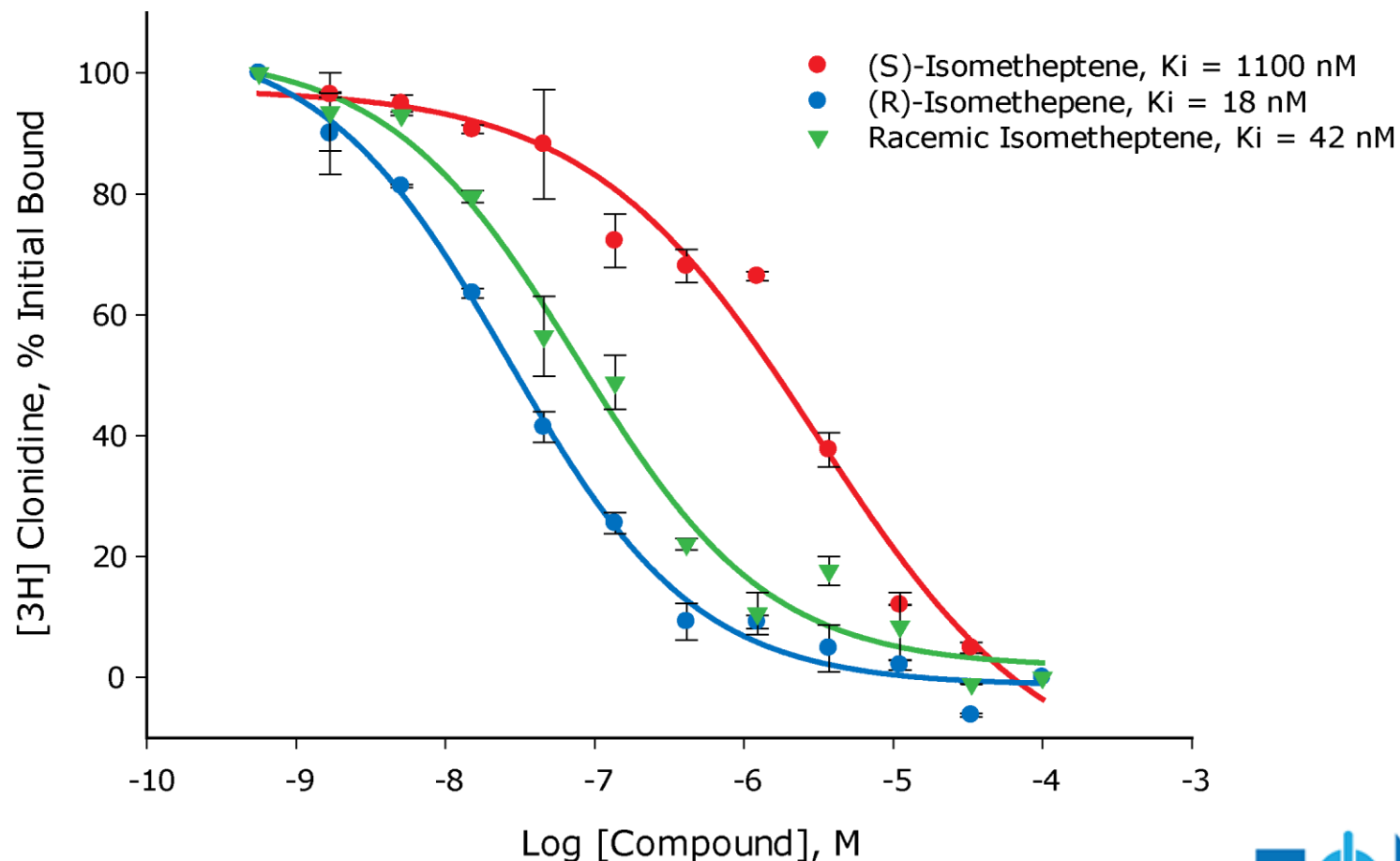


S-isomer

- Sympathomimetic

R-IMH binds to the imidazoline-1 receptor

Binding of isometheptene isomers and racemic mixture to I₁-R

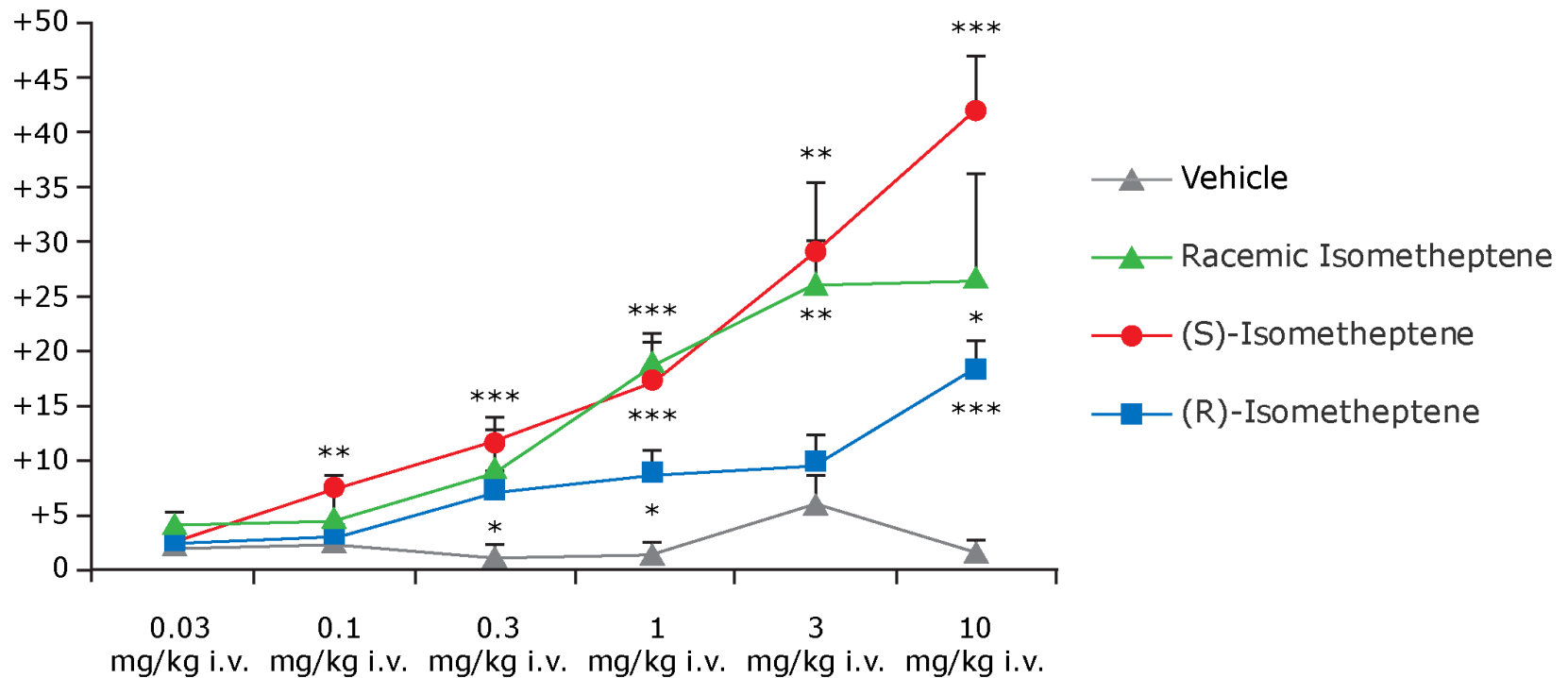


Data on file. Tonix Pharmaceuticals, 2015.

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

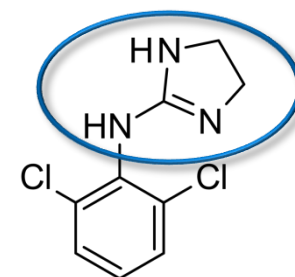


Data on file. Tonix Pharmaceuticals, 2015.

Discovery of the imidazoline receptor

- Clonidine has been in clinical use for 40 years¹
 - High blood pressure, migraine, pain, psychiatric disorders
 - Use in pain limited by side effects
 - Primary activity— α_2 adrenergic agonist
- Imidazoline receptor hypothesized in '80s when α_2 activity could not fully explain pharmacologic action²

Imidazoline



Clonidine

1) Neil MJ. *Curr Clin Pharmacol*. 2011; 6(4):280-287.

2) Bousquet P, et al. *J Pharmacol Exp Ther*. 1984; 230(1):232-236.

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

Imidazoline I₁ Receptor (I₁-R)

Characteristics¹

- Transmembrane receptor
- Distinct from α_2 AR and MAO receptor subtypes
- No sequence similarity to GPCRs or ATP-sensitive K⁺ channels
- Shares similarities to ryanodine and cytokine receptors

Mouse Studies²

- 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



Hot Plate Test

1) Piletz JE et al. DNA and Cell Biology. 2000; 19(6):319-329.

2) Zhang L et al. CNS Neurosci Ther. 2013; 19(12):978-981.

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

Imidazoline I₁ Receptor (I₁-R)

Drugs with I₁-R Affinity¹

Drug	I ₁ agonist	α_1/α_2 agonist
Clonidine	✓	✓
Rilmenidine	✓	✓
Moxonidine	✓	✓
Dexmedetomidine	✓	✓
Isometheptene	✓	✗

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

1) Khan ZP et al. *Anaesthesia*. 1999;54:146-165.

Initial physician response to TNX-201

- Based on the established use of racemic isometheptene, 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 isometheptene 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.

Data on file. Tonix Pharmaceuticals, 2015.

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

Intellectual property

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

NASDAQ: TNXP

Cash reported at September 30, 2014	\$ 46.2 million
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Net cash used in operations in 3Q14	\$ 4.9 million
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Shares outstanding [†]	10.8 million
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[†] As of January 9, 2015

Management team

Seth Lederman, MD

Chief Executive Officer

TARGET
X

Fusilev[®]
(levoleucovorin) for injection

vela
PHARM
VELA PHARMACEUTICALS INC.

Leland Gershell, MD, PhD

Chief Financial Officer

COWEN
AND COMPANY

ATON[™]
PHARMA

Zolinza
[vorinostat] capsules

Bruce Daugherty, PhD

Chief Scientific Officer

 **MERCK**

Roche

Don Kellerman, PharmD

SVP, Clinical Development
& Regulatory Affairs

 **MAP**
PHARMACEUTICALS, INC.

GlaxoWellcome

INSPIRE
PHARMACEUTICALS, INC.

 **SEPRACOR**

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)-isometheptene mucate) are Investigational New Drugs and are not approved for any indication.



NASDAQ: TNXP

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BACKUP SLIDES

Headache costs U.S. employers approximately \$20B annually

Costs due to missed work time and reduced performance while at work

- Headache is the most common pain condition causing lost productive time, costing employers \$19.6B annually(2002 US \$)¹

19.55

Lost productivity*
in days/year²

\$3309

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

- ETTH contributes the majority of the disability burden (>58%)³

*Due to migraine only

1) Stewart WF, et al. *JAMA*. 2003; 290(18):2443-2454.

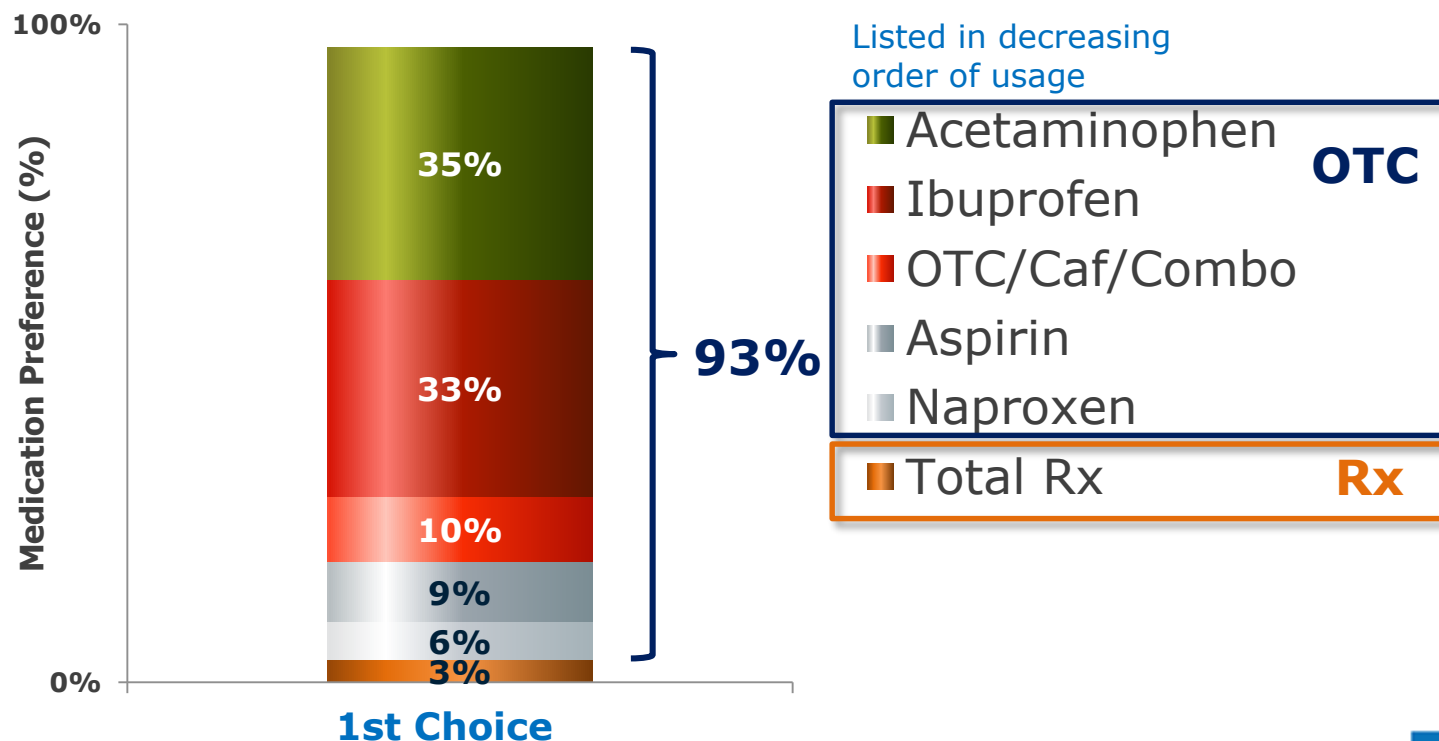
2) Gerth WC, et al. *Pharmacoeconomics*. 2001; 19(2):197-206.

3) Stovner L, et al. *Cephalalgia*. 2007; 27(3):193-210.

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

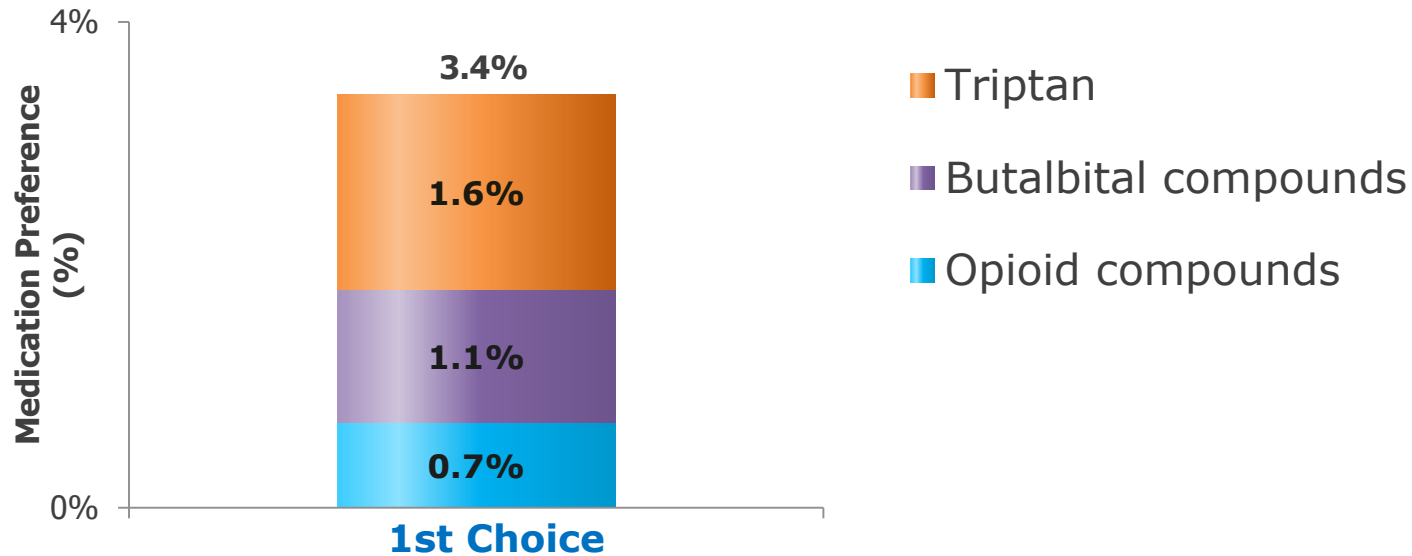


Scher AI, et al. *Cephalalgia*. 2010; 30(3):321-328.

Rx medications used for treatment of ETTH

Existing prescription therapies have low market penetration

Current and Past Pain Medication Used for ETTH

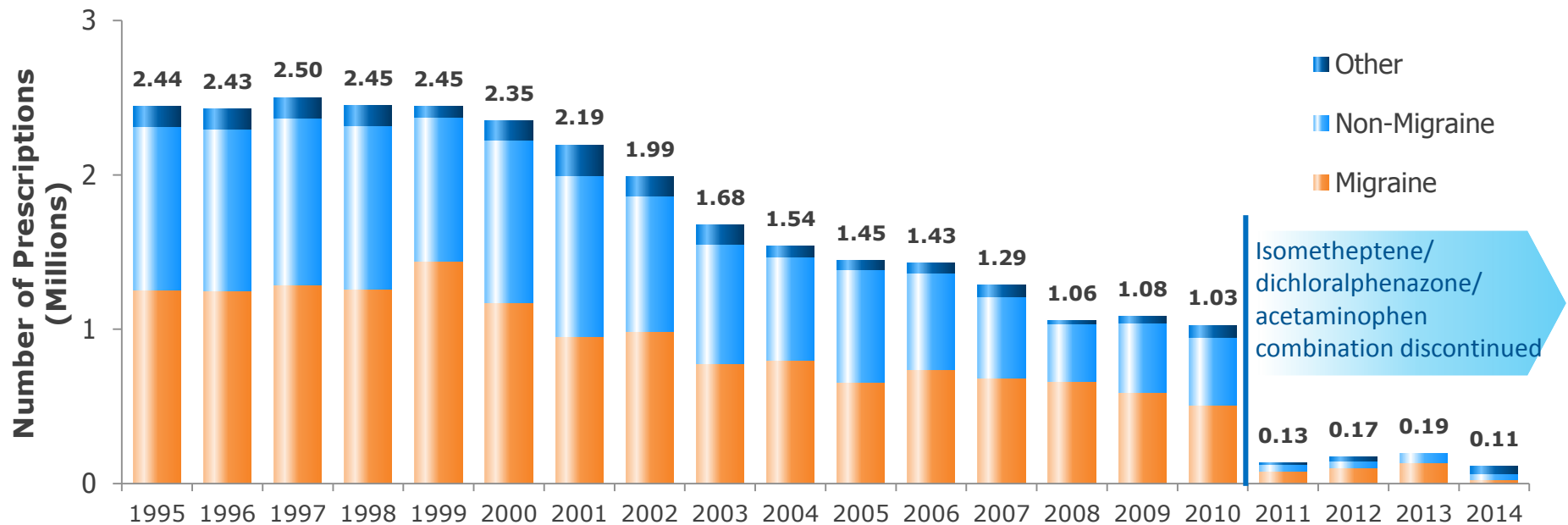


Scher AI, et al. *Cephalalgia*. 2010; 30(3):321-328.

Isometheptene prescriptions previously were commonly written

Number of Isometheptene prescriptions peaked at 2.5 million

Usage of Isometheptene Combinations for all Diagnoses



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