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Tonix Pharmaceuticals Announces Publication of Clinical Pharmacokinetic Studies of TONMYA™ and Prototype Formulations in the Journal Clinical Pharmacology in Drug Development

Commercially launched in the U.S. in November 2025, TONMYA (cyclobenzaprine HCl sublingual tablets) for long-term daily dosing at bedtime is the first new FDA-approved treatment for fibromyalgia in adults in more than 15 years

The sublingual TONMYA tablet containing a basifying agent achieved the design objectives of rapid transmucosal absorption and bypassing first-pass liver metabolism

TONMYA was designed to decrease production of the active metabolite norcyclobenzaprine, which is believed to improve the durability of analgesic response in fibromyalgia relative to the transient (~1 month) effects of oral, swallowed cyclobenzaprine

BERKELEY HEIGHTS, N.J., March 05, 2026 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) ("Tonix" or the "Company"), a fully integrated, commercial biotechnology company, today announced the publication of a paper, "Single-Dose Pharmacokinetic Assessment of TNX-102 SL (Cyclobenzaprine HCl Sublingual Tablets): Results From Randomized, Open-Label Studies in Healthy Volunteers," in *Clinical Pharmacology in Drug Development*, the peer-reviewed journal of the American College of Clinical Pharmacology (ACCP). TONMYA™ was investigated as TNX-102 SL (cyclobenzaprine HCl sublingual tablets) and approved by the U.S. Food and Drug Administration (FDA) on August 15, 2025, for the treatment of fibromyalgia in adults. The manuscript can be accessed at: https://accp1.onlinelibrary.wiley.com/doi/10.1002/cpdd.70034.

"These data demonstrate the importance of the proprietary basifying agent in TONMYA's sublingual formulation," said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals. "An earlier study conducted by Tonix showed that transmucosal delivery cannot be achieved by simply applying a liquid cyclobenzaprine HCl formulation under the tongue. Due to the basifying agent ingredient, sublingual TONMYA achieves rapid transmucosal absorption that bypasses first-pass hepatic metabolism. This pharmacokinetic profile underpins TONMYA's unique sublingual formulation, which is designed to increase parent drug exposure during sleep while reducing exposure and side effects to the long half-life, active metabolite."

Dr. Lederman continued, "Bedtime oral swallowed cyclobenzaprine was one of the first drugs

studied as a treatment for fibromyalgia, but it failed because the benefits were only transient (~1 month) and fibromyalgia is a chronic condition requiring durable responses.[1] Our design objective for TONMYA was to improve the durability of cyclobenzaprine's treatment effect by decreasing liver production of the major active metabolite norcyclobenzaprine, which we believe counteracted the benefits of swallowed cyclobenzaprine over time. We believe the clinical pharmacology studies published in *Clinical Pharmacology in Drug Development*, show that TONMYA achieved this design objective. Later studies[2,3] confirmed that TONMYA as a daily bedtime medicine provides a durable analgesic benefit to fibromyalgia patients and is generally well tolerated."

The publication reports findings from two Phase 1 single-dose, open-label studies conducted in healthy adult volunteers.

In Study 1 (n=24), three sublingual formulations of cyclobenzaprine HCl 2.8 mg, each containing a different basifying agent, were compared with oral immediate-release (IR) cyclobenzaprine HCl 5 mg under fasting conditions. All sublingual formulations showed rapid absorption and increased relative bioavailability compared with oral IR cyclobenzaprine HCl. The potassium phosphate dibasic formulation (designated TNX-102 SL) demonstrated the most favorable pharmacokinetic profile, with a 154% relative bioavailability compared to oral IR, an absorption lag of approximately 3 minutes versus approximately 37 minutes for oral IR, and a 783% higher dose-normalized AUC during the first hour post-dose. Based on these results, the potassium phosphate dibasic formulation was selected for further clinical development.

In Study 2 (n=16), TNX-102 SL 2.8 mg and 5.6 mg were evaluated in a crossover design under fasting and fed conditions. The formulation exhibited dose proportionality between the two dose levels, and pharmacokinetic parameters were not affected by a high-calorie, high-fat meal, confirming the absence of a food effect. This study also provided a full clinical characterization of the active metabolite norcyclobenzaprine, demonstrating an elimination half-life of approximately 60 hours. Reduced exposure to norcyclobenzaprine following sublingual administration, as compared with oral delivery, is believed to contribute to the improved durability of efficacy and favorable tolerability profile observed with TONMYA in Phase 3 fibromyalgia studies.[2,3]

Across both studies, single-dose sublingual cyclobenzaprine HCl was generally well tolerated. All treatment-emergent adverse events were mild or moderate in severity. The most commonly reported adverse events were oral hypoesthesia and abnormal taste. No serious adverse events were reported, and no clinically meaningful changes were observed in laboratory parameters, vital signs, or electrocardiogram findings.

Citations

[1]Carette S, et al. *Arthritis Rheum*. 1994. 37(1):32-40. doi: 10.1002/art.1780370106.
[2]Lederman S, et al. *Arthritis Care Res* (Hoboken). 2023. 75(11):2359-2368. doi: 10.1002/acr.25142.
[3]Lederman S, et al. *Pain Med.* 2026. 27(1):86-94. doi: 10.1093/pm/pnaf089.

About Fibromyalgia

Fibromyalgia is a chronic pain disorder that is understood to result from amplified sensory and pain signaling within the central nervous system. Fibromyalgia afflicts an estimated 6-12 million adults in the U.S., approximately 90% of whom are women. Symptoms of fibromyalgia include chronic widespread pain, nonrestorative sleep, fatigue, and morning stiffness. Other associated symptoms include cognitive dysfunction and mood disturbances, including anxiety and depression. Individuals suffering from fibromyalgia struggle with their daily activities, have impaired quality of life, and frequently are disabled. Physicians and patients report common dissatisfaction with currently marketed products.

About TONMYA™ (cyclobenzaprine HCl sublingual tablets)

TONMYA (cyclobenzaprine HCl sublingual tablets) is a patented sublingual tablet formulation of cyclobenzaprine hydrochloride which provides rapid transmucosal absorption and reduced production of a long half-life active metabolite, norcyclobenzaprine, due to bypass of first-pass hepatic metabolism. As a multifunctional agent with potent binding and antagonist activities at the 5-HT_{2A} serotonergic, α_1-adrenergic, H_1-histaminergic, and M_1-muscarinic receptors, TONMYA was approved on August 15, 2025, by the FDA for the treatment of fibromyalgia in adults. TONMYA is the first new prescription medicine approved for fibromyalgia in more than 15 years. TONMYA was investigated as TNX-102 SL. TNX-102 SL is also being developed to treat acute stress reaction (ASR)/acute stress disorder (ASD), and major depressive disorder (MDD). The United States Patent and Trademark Office (USPTO) issued United States Patent No. 9636408 in May 2017, Patent No. 9956188 in May 2018, Patent No. 10117936 in November 2018, Patent No. 10,357,465 in July 2019, and Patent No. 10736859 in August 2020. The Protectic™ protective eutectic and Angstro-Technology™ formulation claimed in the patent are important elements of Tonix's proprietary TONMYA composition. These patents are expected to provide TONMYA with U.S. market exclusivity until 2034/2035.

Tonix Pharmaceuticals Holding Corp.*

Tonix Pharmaceuticals is a fully-integrated, commercial-stage biotechnology company focused on central nervous system (CNS) and immunology treatments in areas of high unmet medical need. TONMYA™ (cyclobenzaprine HCl sublingual tablets 2.8mg), the Company's recently approved flagship medicine, is the first new treatment for fibromyalgia in more than 15 years. Tonix's CNS commercial infrastructure supports its marketed products, including its acute migraine products, Zembrace® SymTouch® and Tosymra®. Tonix is maximizing the science behind TNX-102 SL in Phase 2 clinical trials to evaluate its potential in major depressive disorder and acute stress disorder. In addition, the company's CNS portfolio includes TNX-2900, which is Phase 2 ready for the treatment of Prader-Willi syndrome, a rare disease. Tonix is also advancing a pipeline of immunology programs, including monoclonal antibody TNX-4800 for Lyme disease prophylaxis and TNX-1500, a third-generation CD40 ligand inhibitor for the prevention of kidney transplant rejection. To learn more, visit www.tonixpharma.com and follow the Company on LinkedIn and X.

* Tonix's product development candidates are investigational new drugs or biologics; their efficacy and safety have not been established and have not been approved for any indication.

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Forward Looking Statements

Certain statements in this press release are forward-looking within the meaning of the Private Securities Litigation Reform Act of 1995 including those relating to the completion of the offering, the satisfaction of customary closing conditions, the intended use of proceeds from the offering and other statements that are predictive in nature. These statements may be identified by the use of forward-looking words such as “anticipate,” “believe,” “forecast,” “estimate,” “expect,” and “intend,” among others. These forward-looking statements are based on Tonix’s current expectations and actual results could differ materially as a result of a number of factors, including the ability of the Company to satisfy the conditions to the closing of the offering and the timing thereof, as well as those described in the Company’s Annual Report on Form 10-K for the year ended December 31, 2024, as filed with the SEC on March 18, 2025, and periodic reports filed with the SEC on or after the date thereof. Tonix does not undertake an obligation to update or revise any forward-looking statement. All of Tonix’s forward-looking statements are expressly qualified by all such risk factors and other cautionary statements. The information set forth herein speaks only as of the date thereof.

Investor Contacts
Jessica Morris
Tonix Pharmaceuticals
(862) 799-8599
investor.relations@tonixpharma.com

Brian Korb
astr partners
(917) 653-5122
brian.korb@astrpartners.com

Media Contacts
Deborah Elson
Tonix Pharmaceuticals
deborah.elson@tonixpharma.com

Ray Jordan
Putnam Insights
ray@putnaminsights.com

INDICATION
TONMYA is indicated for the treatment of fibromyalgia in adults.

CONTRAINDICATIONS
TONMYA is contraindicated:
In patients with hypersensitivity to cyclobenzaprine or any inactive ingredient in TONMYA. Hypersensitivity reactions may manifest as an anaphylactic reaction, urticaria, facial and/or tongue swelling, or pruritus. Discontinue TONMYA if a hypersensitivity reaction is suspected. With concomitant use of monoamine oxidase (MAO) inhibitors or within 14 days after discontinuation of an MAO inhibitor. Hyperpyretic crisis seizures and deaths have occurred

in patients who received cyclobenzaprine (or structurally similar tricyclic antidepressants) concomitantly with MAO inhibitors drugs.
During the acute recovery phase of myocardial infarction, and in patients with arrhythmias, heart block or conduction disturbances, or congestive heart failure. In patients with hyperthyroidism.

WARNINGS AND PRECAUTIONS
Embryofetal toxicity: Based on animal data, TONMYA may cause neural tube defects when used two weeks prior to conception and during the first trimester of pregnancy. Advise females of reproductive potential of the potential risk and to use effective contraception during treatment and for two weeks after the final dose. Perform a pregnancy test prior to initiation of treatment with TONMYA to exclude use of TONMYA during the first trimester of pregnancy.

Serotonin syndrome: Concomitant use of TONMYA with selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants, tramadol, bupropion, meperidine, verapamil, or MAO inhibitors increases the risk of serotonin syndrome, a potentially life-threatening condition. Serotonin syndrome symptoms may include mental status changes, autonomic instability, neuromuscular abnormalities, and/or gastrointestinal symptoms. Treatment with TONMYA and any concomitant serotonergic agent should be discontinued immediately if serotonin syndrome symptoms occur and supportive **symptomatic treatment should be initiated.** If concomitant treatment with TONMYA and other serotonergic drugs is clinically warranted, careful observation is advised, particularly during treatment initiation or dosage increases.

Tricyclic antidepressant-like adverse reactions: Cyclobenzaprine is structurally related to TCAs. TCAs have been reported to produce arrhythmias, sinus tachycardia, prolongation of the conduction time leading to myocardial infarction and stroke. If clinically significant central nervous system (CNS) symptoms develop, consider discontinuation of TONMYA. Caution should be used when TCAs are given to patients with a history of seizure disorder, because TCAs may lower the seizure threshold. Patients with a history of seizures should be monitored during TCA use to identify recurrence of seizures or an increase in the frequency of seizures.

Atropine-like effects: Use with caution in patients with a history of urinary retention, angle-closure glaucoma, increased intraocular pressure, and in patients taking anticholinergic drugs.

CNS depression and risk of operating a motor vehicle or hazardous machinery: TONMYA monotherapy may cause CNS depression. Concomitant use of TONMYA with alcohol, barbiturates, or other CNS depressants may increase the risk of CNS depression. Advise patients not to operate a motor vehicle or dangerous machinery until they are reasonably certain that TONMYA therapy will not adversely affect their ability to engage in such activities. Oral mucosal adverse reactions: In clinical studies with TONMYA, oral mucosal adverse reactions occurred more frequently in patients treated with TONMYA compared to placebo. Advise patients to moisten the mouth with sips of water before administration of TONMYA to reduce the risk of oral sensory changes (hypoesthesia). Consider discontinuation of TONMYA if severe reactions occur.

ADVERSE REACTIONS

The most common adverse reactions (incidence ≥2% and at a higher incidence in TONMYA-treated patients compared to placebo-treated patients) were oral hypoesthesia, oral discomfort, abnormal product taste, somnolence, oral paresthesia, oral pain, fatigue, dry mouth, and aphthous ulcer.

DRUG INTERACTIONS

MAO inhibitors: Life-threatening interactions may occur.

Other serotonergic drugs: Serotonin syndrome has been reported.

CNS depressants: CNS depressant effects of alcohol, barbiturates, and other CNS depressants may be enhanced.

Tramadol: Seizure risk may be enhanced.
Guanethidine or other similar acting drugs: The antihypertensive action of these drugs may be blocked.

USE IN SPECIFIC POPULATIONS

Pregnancy: Based on animal data, TONMYA may cause fetal harm when administered to a pregnant woman. The limited amount of available observational data on oral cyclobenzaprine use in pregnancy is of insufficient quality to inform a TONMYA-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. Advise pregnant women about the potential risk to the fetus with maternal exposure to TONMYA and to avoid use of TONMYA two weeks prior to conception and through the first trimester of pregnancy. Report pregnancies to the Tonix Medicines, Inc., adverse-event reporting line at 1-888-869-7633 (1-888-TNXPMED).

Lactation: A small number of published cases report the transfer of cyclobenzaprine into human milk in low amounts, but these data cannot be confirmed. There are no data on the effects of cyclobenzaprine on a breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for TONMYA and any potential adverse effects on the breastfed child from TONMYA or from the underlying maternal condition.

Pediatric use: The safety and effectiveness of TONMYA have not been established.

Geriatric patients: Of the total number of TONMYA-treated patients in the clinical trials in adult patients with fibromyalgia, none were 65 years of age and older. Clinical trials of TONMYA did not include sufficient numbers of patients 65 years of age and older to determine whether they respond differently from younger adult patients.

Hepatic impairment: The recommended dosage of TONMYA in patients with mild hepatic impairment (HI) (Child Pugh A) is 2.8 mg once daily at bedtime, lower than the recommended dosage in patients with normal hepatic function. The use of TONMYA is not recommended in patients with moderate HI (Child Pugh B) or severe HI (Child Pugh C). Cyclobenzaprine exposure (AUC) was increased in patients with mild HI and moderate HI compared to subjects with normal hepatic function, which may increase the risk of TONMYA-associated adverse reactions.

Please see additional safety information in the full Prescribing Information.

To report suspected adverse reactions, contact Tonix Medicines, Inc. at 1-888-869-7633, or the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Source: Tonix Pharmaceuticals Holding Corp.