

November 24, 2025



Tonix Pharmaceuticals Announces FDA IND Clearance for Phase 2 Study of TNX-102 SL for the Treatment of Major Depressive Disorder

Tonix plans to initiate potential pivotal Phase 2 HORIZON study of TNX-102 SL in adults with major depressive disorder in mid-2026

More than 21 million US adults experience a major depressive episode each year

CHATHAM, N.J., Nov. 24, 2025 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) ("Tonix" or the "Company"), a fully-integrated commercial biotechnology company, today announced the U.S. Food and Drug Administration (FDA) has cleared the Investigational New Drug (IND) application to support clinical development of TNX-102 SL (cyclobenzaprine HCl sublingual tablets) 5.6 mg for the treatment of major depressive disorder (MDD) in adults.

"There is a clear need for innovative therapies that address depression," said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals. "We believe TNX-102 SL offers a promising approach for individuals suffering from MDD. The unique pharmacological profile of TNX-102 SL is designed to target the disruptive sleep which is often associated with depression. Prior studies of TNX-102 SL in fibromyalgia and post-traumatic stress disorder (PTSD) showed promising signals for improvement of depressive symptoms on the Beck Depression Inventory-II and the Montgomery-Asberg Depression Rating Scale (MADRS), respectively. We are excited to advance TNX-102 SL and look forward to evaluating its potential as a new treatment option for those affected by depression."

The IND clearance enables Tonix to proceed with the potentially pivotal Phase 2 HORIZON study, a 6-week, randomized, double-blind, placebo-controlled study of TNX-102 SL as a first-line monotherapy in adults with MDD. About 360 patients will be enrolled at approximately 30 U.S. sites. Eligible participants are 18 years or older and currently experiencing a moderate to severe major depressive episode. The study will compare TNX-102 SL 5.6 mg, taken sublingually at bedtime to placebo, with the primary endpoint being the MADRS total score change from baseline at Week 6. Secondary endpoints include global impression scores, anxiety ratings, and measures of sleep disturbance. Tonix plans to initiate enrollment of the study in mid-year 2026.

"TNX-102 SL is designed to target the disturbed sleep of depression, which is a novel mechanism of action," said Gregory Sullivan, M.D., Chief Medical Officer of Tonix Pharmaceuticals. "TNX-102 SL has been generally well tolerated in registrational studies of

fibromyalgia patients. In the fibromyalgia studies, TNX-102 SL treatment was associated with a low incidence of side effects common with traditional antidepressants like weight gain, blood pressure changes, sexual dysfunction and cognitive issues.”

About Major Depressive Disorder

Major Depressive Disorder (MDD) is a prevalent and serious psychiatric illness that affects adults of all ages, races, and backgrounds. It is characterized by persistent feelings of sadness or loss of interest, along with symptoms such as sleep and appetite disturbances, fatigue, difficulty concentrating, and thoughts of worthlessness or suicide. These symptoms must last at least two weeks and significantly impair daily functioning. In the United States, more than 21 million adults experience a major depressive episode each year. While several antidepressant medications are available, many individuals do not achieve adequate relief or discontinue treatment due to side effects like weight gain, sleep disruption, and sexual dysfunction. MDD is associated with increased risk of suicide and substantial impairment in quality of life, underscoring the urgent need for new, first-line therapies that are both effective and well-tolerated.

About TNX-102 SL

TNX-102 SL is a patented sublingual tablet formulation of cyclobenzaprine hydrochloride that enables rapid transmucosal absorption and reduces production of the persistent active metabolite, norcyclobenzaprine, by bypassing first-pass hepatic metabolism. TNX-102 SL is a tertiary amine tricyclic (TAT) and multifunctional agent with potent binding and antagonist activities at the 5-HT_{2A} serotonergic, α_1 -adrenergic, H₁-histaminergic, and M₁-muscarinic receptors. It is currently FDA approved in the U.S. as a once-daily bedtime treatment for fibromyalgia in adults under the brand name TONMYA™ (cyclobenzaprine HCl sublingual tablets). TNX-102 SL is also in development as a daily bedtime treatment for acute stress reaction/acute stress disorder under an Investigator-initiated IND. In addition to MDD, Tonix also holds active INDs for the following indications for TNX-102 SL: Long COVID (post-acute sequelae of COVID-19), PTSD, alcohol use disorder, and agitation in Alzheimer’s disease. The United States Patent and Trademark Office issued United States Patent No. 9636408 in May 2017, Patent No. 9956188 in May 2018, Patent No. 10117936 in November 2018, Patent No. 10357465 in July 2019, and Patent No. 10736859 in August 2020. The Protectic™ protective eutectic and Angstro-Technology™ formulation claimed in the patents are important elements of Tonix’s proprietary composition. These patents are expected to provide TNX-102 SL U.S. market exclusivity until 2034. Pending patent applications related to method of use could extend exclusivity until 2044.

Tonix Pharmaceuticals Holding Corp.

Tonix Pharmaceuticals is a fully-integrated biotechnology company with marketed products and a pipeline of development candidates. Tonix markets FDA-approved TONMYA™, a first-in-class, non-opioid analgesic medicine for the treatment of fibromyalgia, a chronic pain condition that affects millions of adults. TONMYA is the first new prescription medicine approved by the FDA for fibromyalgia in more than 15 years. TONMYA was investigated as TNX-102 SL. Tonix also markets two treatments for acute migraine in adults: Zembrace® SymTouch® (sumatriptan injection) and Tosymra® (sumatriptan nasal spray). Tonix’s development portfolio* is focused on central nervous system (CNS) disorders, immunology, immuno-oncology, rare disease and infectious disease. TNX-102 SL is being developed to treat acute stress reaction and acute stress disorder under an Investigator-Initiated IND at the University of North Carolina in the OASIS study funded by the U.S.

Department of Defense (DoD). TNX-102 SL is also in development for major depressive disorder. Tonix's immunology development portfolio consists of biologics to address organ transplant rejection, autoimmunity and cancer, including TNX-1500, which is a Phase 2-ready Fc-modified humanized monoclonal antibody targeting CD40-ligand (CD40L or CD154) being developed for the prevention of allograft rejection and for the treatment of autoimmune diseases. Tonix's rare disease portfolio includes TNX-2900, intranasal oxytocin potentiated with magnesium, in development for Prader-Willi syndrome and expected to start a potential pivotal Phase 2 study in 2026. Tonix's infectious disease portfolio includes TNX-801, a vaccine in development for mpox and smallpox, as well as TNX-4800, a Phase 2-ready long-acting humanized monoclonal antibody for the seasonal prevention of Lyme disease. Finally, TNX-4200 for which Tonix has a contract with the U.S. DoD's Defense Threat Reduction Agency (DTRA) for up to \$34 million over five years, is a small molecule broad-spectrum antiviral agent targeting CD45 for the prevention or treatment of high lethality infections to improve the medical readiness of military personnel in biological threat environments. Tonix owns and operates a state-of-the art infectious disease research facility in Frederick, Md.

* 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 under development.

This press release and further information about Tonix can be found at www.tonixpharma.com.

Forward Looking Statements

Certain statements in this press release are forward-looking within the meaning of 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," "expect," 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, risks related to the failure to successfully launch and commercialize Tonmya and any of our approved products; risks related to the failure to obtain FDA clearances or approvals and noncompliance with FDA regulations; risks related to the timing and progress of clinical development of our product candidates; our need for additional financing; uncertainties of patent protection and litigation; uncertainties of government or third party payor reimbursement; limited research and development efforts and dependence upon third parties; and substantial competition. As with any pharmaceutical under development, there are significant risks in the development, regulatory approval and commercialization of new products. Tonix does not undertake an obligation to update or revise any forward-looking statement. Investors should read the risk factors set forth in the Annual Report on Form 10-K for the year ended December 31, 2024, as filed with the Securities and Exchange Commission (the "SEC") on March 18, 2025, and periodic reports filed with the SEC on or after the date thereof. 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
investor.relations@tonixpharma.com
(862) 799-8599

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

Media Contacts

Mary Ann Ondish
Tonix Pharmaceuticals
maryann.ondish@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 $\geq 2\%$ 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.

Indication and Usage

Zembrace[®] SymTouch[®] (sumatriptan succinate) injection (Zembrace) and Tosymra[®] (sumatriptan) nasal spray are prescription medicines used to treat acute migraine headaches with or without aura in adults who have been diagnosed with migraine.

Zembrace and Tosymra are not used to prevent migraines. It is not known if Zembrace or Tosymra are safe and effective in children under 18 years of age.

Important Safety Information

Zembrace and Tosymra can cause serious side effects, including heart attack and other heart problems, which may lead to death. Stop use and get emergency help if you have any signs of a heart attack:

- discomfort in the center of your chest that lasts for more than a few minutes or goes away and comes back
- severe tightness, pain, pressure, or heaviness in your chest, throat, neck, or jaw
- pain or discomfort in your arms, back, neck, jaw or stomach
- shortness of breath with or without chest discomfort
- breaking out in a cold sweat
- nausea or vomiting
- feeling lightheaded

Zembrace and Tosymra are not for people with risk factors for heart disease (high blood pressure or cholesterol, smoking, overweight, diabetes, family history of heart disease) unless a heart exam shows no problem.

Do not use Zembrace or Tosymra if you have:

- history of heart problems
- narrowing of blood vessels to your legs, arms, stomach, or kidney (peripheral vascular disease)
- uncontrolled high blood pressure
- hemiplegic or basilar migraines. If you are not sure if you have these, ask your

provider.

- had a stroke, transient ischemic attacks (TIAs), or problems with blood circulation
- severe liver problems
- taken any of the following medicines in the last 24 hours: almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, ergotamines, or dihydroergotamine. Ask your provider for a list of these medicines if you are not sure.
- are taking certain antidepressants, known as monoamine oxidase (MAO)-A inhibitors or it has been 2 weeks or less since you stopped taking a MAO-A inhibitor. Ask your provider for a list of these medicines if you are not sure.
- an allergy to sumatriptan or any of the components of Zembrace or Tosymra

Tell your provider about all of your medical conditions and medicines you take, including vitamins and supplements.

Zembrace and Tosymra can cause dizziness, weakness, or drowsiness. If so, do not drive a car, use machinery, or do anything where you need to be alert.

Zembrace and Tosymra may cause serious side effects including:

- changes in color or sensation in your fingers and toes
- sudden or severe stomach pain, stomach pain after meals, weight loss, nausea or vomiting, constipation or diarrhea, bloody diarrhea, fever
- cramping and pain in your legs or hips; feeling of heaviness or tightness in your leg muscles; burning or aching pain in your feet or toes while resting; numbness, tingling, or weakness in your legs; cold feeling or color changes in one or both legs or feet
- increased blood pressure including a sudden severe increase even if you have no history of high blood pressure
- medication overuse headaches from using migraine medicine for 10 or more days each month. If your headaches get worse, call your provider.
- serotonin syndrome, a rare but serious problem that can happen in people using Zembrace or Tosymra, especially when used with anti-depressant medicines called SSRIs or SNRIs. Call your provider right away if you have: mental changes such as seeing things that are not there (hallucinations), agitation, or coma; fast heartbeat; changes in blood pressure; high body temperature; tight muscles; or trouble walking.
- hives (itchy bumps); swelling of your tongue, mouth, or throat
- seizures even in people who have never had seizures before

The most common side effects of Zembrace and Tosymra include: pain and redness at injection site (Zembrace only); tingling or numbness in your fingers or toes; dizziness; warm, hot, burning feeling to your face (flushing); discomfort or stiffness in your neck; feeling weak, drowsy, or tired; application site (nasal) reactions (Tosymra only) and throat irritation (Tosymra only).

Tell your provider if you have any side effect that bothers you or does not go away. These are not all the possible side effects of Zembrace and Tosymra. For more information, ask your provider.

This is the most important information to know about Zembrace and Tosymra but is not comprehensive. For more information, talk to your provider and read the Patient Information and Instructions for Use. You can also visit <https://www.tonixpharma.com> or call 1-888-869-7633.

You are encouraged to report adverse effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.



Source: Tonix Pharmaceuticals Holding Corp.