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Tonix Pharmaceuticals Announces Collaboration with Massachusetts General Hospital to Advance Phase 2 Clinical Trial of Dimeric Fc-modified anti-CD40L mAb, TNX-1500, to Prevent Kidney Transplant Organ Rejection

Planning to initiate an open-label Phase 2 study of TNX-1500 under an investigator-initiated IND to evaluate safety and activity in the first half of 2026

Novel immunomodulatory regimen designed to reduce calcineurin inhibitor exposure and improve outcomes

Dimeric Fc-modified mAb TNX-1500 selectively targets cell-associated CD40L with once-monthly dosing

CHATHAM, N.J., Nov. 04, 2025 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) ("Tonix" or the "Company"), a fully-integrated, commercial biotechnology company, today announced a collaboration with Massachusetts General Hospital (MGH), a founding member of Mass General Brigham (MGB) to conduct a Phase 2 clinical trial evaluating monoclonal antibody (mAb) TNX-1500 in kidney transplant recipients. The investigator-initiated study will be led by Ayman Al Jurdi, M.D., at MGH and is designed to assess the safety, tolerability and activity of Fc-modified anti-CD40L mAb TNX-1500 in preventing kidney transplant rejection while significantly minimizing the dose of conventional immunosuppressive drugs, which are associated with infection, cancer, cardiovascular side effects and various metabolic derangements. The CD40 ligand (CD40L) is also known as CD154. Study initiation is contingent on institutional review board (IRB) approval and FDA clearance of an investigator-initiated investigational new drug application (IND).

"TNX-1500 represents a differentiated approach that is designed to block the function of cell-associated CD40L," said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals. "Collaborating with MGH, one of the nation's leading transplant research centers, allows us to advance this promising candidate in patients who need safer therapies with better long-term outcomes. The Fc-modified TNX-1500 has shown activity and has been well tolerated in animals[1,2] and in a Phase 1 pharmacodynamic (PD) and pharmacokinetic (PK) study that supports monthly dosing. Ultimately, our goal is to establish TNX-1500 as a monotherapy, with the potential to transform the landscape of organ transplant management."

“The ability to modulate the immune system without the toxicities associated with prolonged standard dose CNIs is one of the most pressing unmet needs in transplantation,” said Ayman Al Jurdi, M.D., Principal Investigator at MGH. “Studying TNX-1500 in this Phase II trial will allow us to explore its potential to improve long-term outcomes for kidney transplant recipients.”

Pending IRB approval and IND clearance, the open-label, single-center study will enroll five adult kidney transplant recipients at MGH. Patients will receive induction therapy with anti-thymocyte globulin, TNX-1500, tacrolimus, and corticosteroids. The corticosteroids will be tapered and discontinued by Day 33 post-transplant. TNX-1500 will be continued for 12 months (to the primary endpoint) with an option to continue treatment beyond 12 months. Tacrolimus at standard dose will be continued for six months, at which point tacrolimus will be decreased to low dose with the expectation of discontinuing tacrolimus after 12 months. The primary endpoint is the incidence of adverse and serious adverse events at 12 months. Secondary endpoints include graft survival, renal function, biopsy-proven acute rejection, and incidence of donor-specific antibodies. The study is expected to be initiated in the first half of 2026.

About TNX-1500

TNX-1500 (Fc-modified humanized anti-CD40L mAb) is a humanized monoclonal antibody that interacts with the CD40-ligand (CD40L), also known as CD154. TNX-1500 is being developed for the prevention of allograft and xenograft rejection, for the prevention of graft-versus-host disease (GvHD) after hematopoietic stem cell transplantation (HCT) and for the treatment of autoimmune diseases. The first-in-human Phase 1 PD/PK study of TNX-1500 was completed and topline reported in first quarter 2025 to support dosing in a planned Phase 2 trial in kidney transplant recipients. The primary objective of the Phase 1 trial was to assess the safety, tolerability, PD and PK of single-dose intravenous (i.v.) TNX-1500 at 3 mg/kg, 10 mg/kg, and 30 mg/kg. Two published articles in the peer-reviewed American Journal of Transplantation demonstrate TNX-1500 prevents rejection, prolongs survival and preserves graft function as a single agent or in combination with other drugs in animal renal and heart allografts.[1,2]

[1]Lassiter G, et al. *Am J Transplant.* 2023;23(8):1171-1181.
[2]Miura S, et al. *Am J Transplant*. 2023;23(8):1182-1193.

Tonix Pharmaceuticals Holding Corp.

Tonix Pharmaceuticals is a fully-integrated commercial biotechnology company with marketed products and a pipeline of development candidates. Tonix has received FDA approval for Tonmya™ (cyclobenzaprine HCl sublingual tablets), a first-in-class, non-opioid analgesic medicine for the treatment of fibromyalgia, a chronic pain condition that affects millions of adults. This marks the first approval for a new prescription medicine for fibromyalgia in more than 15 years. Tonix also markets two treatments for acute migraine in adults. Tonix’s development portfolio is focused on central nervous system (CNS) disorders, immunology, immuno-oncology, rare disease and infectious disease. TNX-102 SL (cyclobenzaprine HCl sublingual tablets) is being developed to treat acute stress reaction and acute stress disorder under a Physician-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 rare disease portfolio includes TNX-2900, intranasal potentiated oxytocin with magnesium, in development for Prader-Willi syndrome. Tonix's infectious disease portfolio includes TNX-801, a vaccine in development for mpox and smallpox, as well as TNX-4800, a 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 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.

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.

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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.