

April 29, 2025



# **Tonix Pharmaceuticals Presented Preclinical Data on Gastric Cancer Models at the American Association for Cancer Research (AACR) 2025 Annual Meeting**

*Combination treatment of TFF2 with anti-PD1 antibody was associated with the activation of cancer-killing CD8+ T Cells and limiting immune evasion by tumor cells*

*TNX-1700 is in preclinical development for gastric and colorectal cancers*

CHATHAM, N.J., April 29, 2025 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a fully-integrated biopharmaceutical company with marketed products and a pipeline of development candidates, presented data in a poster presentation at the American Association for Cancer Research (AACR) 2025 Annual Meeting, held April 25-30, 2025, in Chicago, IL. A copy of the Company's presentation is available under the [Scientific Presentations](#) tab of the Tonix website at [www.tonixpharma.com](http://www.tonixpharma.com). The presentation titled, "TFF2-mediated CXCR4 partial agonism outperforms CXCR4 antagonism in reducing murine gastric cancer by suppressing PMN-MDSC generation," demonstrated positive data in gastric cancer animal models. In the AACR presentation, a fusion protein of murine trefoil factor family member 2- murine serum albumin (mTFF2-MSA) was studied. Tonix is developing human TFF2-human serum albumin (hTFF2-HAS) as TNX-1700.

"The combination therapy of mTFF2-MSA with anti-PD1 treatment shows promise in reducing immunosuppression in the tumor microenvironment (TME) in animal models," said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals. "We are excited to develop TNX-1700 (TFF2-HAS) as the lead program in our immuno-oncology pipeline, by testing potential dosing strategies, and establishing potential clinical biomarkers through preclinical models."

Immunosuppressive neutrophils, also known as polymorphonuclear myeloid-derived suppressor cells (PMN-MDSCs), are a major component in solid tumors that significantly hinder anti-tumor activity<sup>1,2</sup>. Despite being short-lived, their continuous replenishment from the bone marrow sustains their potent immunosuppression in the TME<sup>3</sup>. Stromal cells in the TME promote immunosuppression by recruiting MDSCs via secretion of CXCL12. Trefoil Factor 2 (TFF2), a secreted peptide of the trefoil factor family, has displayed activity as a partial agonist of CXCR4<sup>4,5</sup>. Data presented in the poster demonstrated that TFF2-MSA selectively reduces immunosuppressive neutrophils and cancer-driven granulopoiesis. Treatment with TFF2-MSA, in combination with an anti-PD1 antibody, induced robust anti-tumoral CD8+ T cell responses, inhibiting tumor invasion. TFF2 reduction correlated with

elevated PMN-MDSCs in gastric cancer patients, highlighting the potential negative correlation between TFF2 and PMN-MDSCs levels.

### **About Trefoil Factor Family Member 2 (TFF2)**

Human TFF2 is a secreted protein, encoded by the TFF2 gene in humans, that is expressed in gastrointestinal mucosa where it functions to protect and repair mucosa. TFF2 is also expressed at low levels in splenic immune cells and is now appreciated to have intravascular roles in the spleen and in the tumor microenvironment. In gastric cancer, TFF2 is epigenetically silenced, and TFF2 is suggested to be protective against cancer development through several mechanisms. Tonix is developing TNX-1700 (rTFF2-HSA) for the treatment of gastric and colon cancers under a license from Columbia University. The inventor of the core technology at Columbia is Dr. Timothy Wang, who is an expert in the molecular mechanisms of carcinogenesis whose research has focused on the carcinogenic role of inflammation in modulating stem cell functions. Dr. Wang demonstrated that knocking out the mTFF2 gene in mice leads to faster tumor growth and that overexpression of TFF2 markedly suppresses tumor growth by curtailing the homing, differentiation, and expansion of MDSCs to allow activation of cancer-killing CD8+ T cells. He went on to show that a novel engineered form of recombinant murine TFF2 (mTFF2-CTP) had an extended half-life *in vivo* and was able to suppress MDSCs and tumor growth in an animal model of colorectal cancer. Later, he showed in gastric cancer models that suppressing MDSCs using chemotherapy enhances the effectiveness of anti-PD1 therapy and significantly reduces tumor growth. Dr. Wang proposed the concept of employing rTFF2 in combination with other therapies in cancer prevention and early treatment.

<sup>1</sup>Kim W, et al. PD-1 Signaling Promotes Tumor-Infiltrating Myeloid-Derived Suppressor Cells and Gastric Tumorigenesis in Mice. *Gastroenterology*. 2021 Feb;160(3):781-796

<sup>2</sup>Veglia F, et al. Analysis of classical neutrophils and polymorphonuclear myeloid-derived suppressor cells in cancer patients and tumor-bearing mice. *J Exp Med*. 2021 Apr 5;218(4):e20201803.

<sup>3</sup>Colligan SH, et al. Inhibiting the biogenesis of myeloid-derived suppressor cells enhances immunotherapy efficacy against mammary tumor progression. *J Clin Invest*. 2022 Dec1;132(23):e158661.

<sup>4</sup>Dubeykovskaya Z, et al. Secreted trefoil factor 2 activates the CXCR4 receptor in epithelial and lymphocytic cancer cell lines. *J Biol Chem*. 2009 Feb 6;284(6):3650-62.

<sup>5</sup>Dubeykovskaya Z, et al. Neural innervation stimulates splenic TFF2 to arrest myeloid cell expansion and cancer. *Nat Commun*. 2016 Feb 4;7:10517.

### **Tonix Pharmaceuticals Holding Corp.\***

Tonix is a fully-integrated biopharmaceutical company focused on transforming therapies for pain management and vaccines for public health challenges. Tonix's development portfolio is focused on central nervous system (CNS) disorders. Tonix's priority is to advance TNX-102 SL, a product candidate for the management of fibromyalgia, for which an NDA was submitted based on two statistically significant Phase 3 studies for the management of fibromyalgia and for which a PDUFA (Prescription Drug User Fee act) goal date of August 15, 2025 has been assigned for a decision on marketing authorization. The FDA has also granted Fast Track designation to TNX-102 SL for the management of fibromyalgia. TNX-102 SL is also 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). Tonix's immunology development portfolio consists of biologics to address organ transplant rejection, autoimmunity and cancer, including TNX-1500, which is an 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 also has product candidates in development in infectious disease, including a vaccine for mpox, TNX-801. Tonix recently announced a contract with the U.S. DoD's Defense Threat Reduction Agency (DTRA) for up to \$34 million over five years to develop TNX-4200, small molecule broad-spectrum antiviral agents 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 Medicines, our commercial subsidiary, markets Zembrace<sup>®</sup> SymTouch<sup>®</sup> (sumatriptan injection) 3 mg and Tosymra<sup>®</sup> (sumatriptan nasal spray) 10 mg for the treatment of acute migraine with or without aura in adults.

\* 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.

Zembrace SymTouch and Tosymra are registered trademarks of Tonix Medicines. All other marks are property of their respective owners.

This press release and further information about Tonix can be found at [www.tonixpharma.com](http://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 obtain FDA clearances or approvals and noncompliance with FDA regulations; risks related to the failure to successfully market any of our products; 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, 2023, as filed with the Securities and Exchange Commission (the "SEC") on April 1, 2024, 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 and Usage

Zembrace<sup>®</sup> SymTouch<sup>®</sup> (sumatriptan succinate) injection (Zembrace) and Tosymra<sup>®</sup> (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](http://www.fda.gov/medwatch), or call 1-800-FDA-1088.



Source: Tonix Pharmaceuticals Holding Corp.