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Tonix Pharmaceuticals Announces Presentations of Pre-Clinical Data on TNX-1700 in Syngeneic Models of Colorectal and Gastric Cancer at the American Association for Cancer Research Annual Meeting 2023

CHATHAM, N.J., April 19, 2023 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP), a clinical-stage biopharmaceutical company, today announced the presentation of two posters with research results on TNX-1700 (recombinant TFF2 – albumin fusion peptide) at the American Association for Cancer Research (AACR) Annual Meeting, held April 14-19, 2023, in Orlando, Fla. Copies of the Company's posters are available under the [Scientific Presentations](#) tab of the Tonix website at www.tonixpharma.com.

The poster presentation, titled, *"MDSC-targeted TFF2-MSA suppresses tumor growth and increases survival in anti-PD-1 treated MC38 and CT26.wt murine colorectal cancer models,"* includes data demonstrating that targeting myeloid-derived suppressor cells (MDSCs) using murine TNX-1700, or mTNX-1700 (TFF2-MSA fusion protein) synergizes with PD-1 blockade therapy in advanced syngeneic mouse models of colorectal cancer. The data show that mTNX-1700 and anti-PD-1 monotherapy each were able to evoke anti-tumor immunity in the MC38 and CT26.wt models of colorectal cancer, and that mTNX-1700 augmented the anti-tumor efficacy of anti-PD-1 therapy in both of these colorectal cancer models.

The poster presentation, titled, *"MDSC-targeted TFF2-MSA synergizes with PD-1 blockade therapy in diffuse-type gastric cancer,"* includes data showing that targeting MDSCs using mTNX-1700 synergizes with PD-1 blockade therapy in advanced and metastatic syngeneic mouse models of diffuse-type gastric cancer, suggesting combination therapy of mTNX-1700 and PD-1 blockade may also be applicable to gastric cancer.

"We believe these data demonstrate that targeting MDSCs using mTNX-1700 provides additive benefits to PD-1 blockade therapy in advanced and metastatic syngeneic mouse models of colorectal and gastric cancer," said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals.

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 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.¹ 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.² Dr. Wang proposed the concept of employing rTFF2 in combination with other therapies in cancer prevention and early treatment. Dr. Wang presented data at the American Association for Cancer Research (AACR) conference as a collaboration between Tonix and Columbia University in 2020 that includes data from a preclinical study which investigated the role of PD-L1 in colorectal tumorigenesis and evaluated the utility of targeting myeloid-derived suppressor cells (MDSCs) in combination with PD-1 blockade in mouse models of colorectal cancer. The data show that anti-PD-1 monotherapy was unable to evoke anti-tumor immunity in this model of colorectal cancer, but mTFF2-CTP augmented the efficacy of anti-PD-1 therapy. Anti-PD-1 in combination with TFF2-CTP showed greater anti-tumor activity in PD-L1-overexpressing mice.

Tonix Pharmaceuticals Holding Corp.*

Tonix is a clinical-stage biopharmaceutical company focused on discovering, licensing, acquiring and developing therapeutics to treat and prevent human disease and alleviate suffering. Tonix's portfolio is composed of central nervous system (CNS), rare disease, immunology and infectious disease product candidates. Tonix's CNS portfolio includes both small molecules and biologics to treat pain, neurologic, psychiatric and addiction conditions. Tonix's lead CNS candidate, TNX-102 SL (cyclobenzaprine HCl sublingual tablet), is in mid-Phase 3 development for the management of fibromyalgia with topline data expected in the fourth quarter of 2023. TNX-102 SL is also being developed to treat Long COVID, a chronic post-acute COVID-19 condition. Enrollment in a Phase 2 study has been completed, and topline results are expected in the third quarter of 2023. TNX-1900 (intranasal potentiated oxytocin), in development for chronic migraine, is currently enrolling with topline data expected in the fourth quarter of 2023. TNX-601 ER (tianeptine hemioxalate extended-release tablets), a once-daily formulation being developed as a treatment for major depressive disorder (MDD), is also currently enrolling with interim data expected in the fourth quarter of 2023. TNX-1300 (cocaine esterase) is a biologic designed to treat cocaine intoxication and has been granted Breakthrough Therapy designation by the FDA. A Phase 2 study of TNX-1300 is expected to be initiated in the second quarter of 2023. Tonix's rare disease portfolio includes TNX-2900 (intranasal potentiated oxytocin) for the treatment of Prader-Willi syndrome. TNX-2900 has been granted Orphan Drug designation by the FDA. Tonix's immunology portfolio includes biologics to address organ transplant rejection,

autoimmunity and cancer, including TNX-1500, which is a humanized monoclonal antibody targeting CD40-ligand (CD40L or CD154) being developed for the prevention of allograft and xenograft rejection and for the treatment of autoimmune diseases. A Phase 1 study of TNX-1500 is expected to be initiated in the second quarter of 2023. Tonix's infectious disease pipeline includes TNX-801, a vaccine in development to prevent smallpox and mpox, for which a Phase 1 study is expected to be initiated in the second half of 2023. TNX-801 also serves as the live virus vaccine platform or recombinant pox vaccine platform for other infectious diseases. The infectious disease portfolio also includes TNX-3900 and TNX-4000, classes of broad-spectrum small molecule oral antivirals.

**All of Tonix's product candidates are investigational new drugs or biologics and have not been approved for any indication.*

¹Dubeykovskaya ZA et al, *Nat Commun* 2016

²Kim W et al, *Gastroenterology* 2021

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 obtain FDA clearances or approvals and noncompliance with FDA regulations; delays and uncertainties caused by the global COVID-19 pandemic; 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, 2022, as filed with the Securities and Exchange Commission (the "SEC") on March 13, 2023, 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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