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Tonix Pharmaceuticals Presents New Preclinical Data at Seventh International Cancer Immunotherapy Conference 2023

mTNX-1700 (mTFF2-MSA) suppresses tumor growth and increases survival rates in preclinical colorectal cancer models

mTNX-1700 shows single agent activity and additive effects in combination with anti-PD-1

mTNX-1700 targets myeloid-derived suppressor cells (MDSCs) in a novel mechanism to treat cancer

CHATHAM, N.J., Sept. 21, 2023 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP), a biopharmaceutical company with marketed products and a pipeline of development candidates, today announced a poster presentation showing research results for mTNX-1700 (murine trefoil factor family member 2- murine serum albumin, or mTFF2-MSA) at the Seventh International Cancer Immunotherapy Conference 2023 (CICON23): Translating Science into Survival, being held September 20-23, 2023, in Milan, Italy. The poster is available under the [Scientific Presentations](#) tab of the Tonix website at www.tonixpharma.com.

The poster presentation, titled, "*mTFF2-MSA (mTNX-1700) Suppresses Tumor Growth and Increases Survival in Anti-PD-1 Treated CT26.WT Subcutaneous and CT26-Luciferase Orthotopic Syngeneic Colorectal Cancer Models by Targeting MDSCs in BALB/C Mice*," includes data demonstrating that the novel fusion protein, mTNX-1700 has single agent activity and can improve on the therapeutic effects of anti-PD-1 in treating syngeneic mouse models of advanced colorectal cancer. In two models, mTNX-1700 increases survival rates and suppresses tumor growth. Additive tumor growth suppression effects were observed when mTNX-1700 and anti-PD-1 were used in combination.

"mTNX-1700 is a novel fusion protein that has single agent activity and augments PD-1 blockade therapy in combination therapy in advanced and metastatic syngeneic mouse models of colorectal and gastric cancer," said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals. "Certain cancers are unresponsive to anti-PD-1 therapy. Despite the significance of PD-1 checkpoint blockade in treating many types of cancer, there's a need to better understand why some cancers don't respond and how to make them responsive. We believe these data show the potential of TNX-1700 in treating cancer both as a single agent and in combination with other immuno-oncology drugs, particularly anti-PD-1, and highlight how mTNX-1700 targets MDSCs as a novel mechanism to treat cancer."

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.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.

¹Dubeykovskaya ZA *et al*, *Nat Commun* 2016

²Kim W *et al*, *Gastroenterology* 2021

Tonix Pharmaceuticals Holding Corp.*

Tonix is a biopharmaceutical company focused on commercializing, developing, discovering and licensing therapeutics to treat and prevent human disease and alleviate suffering. Tonix Medicines, our commercial subsidiary, markets Zembrace[®] SymTouch[®] (sumatriptan injection) 3 mg and Tosymra[®] (sumatriptan nasal spray) 10 mg under a transition services agreement with Upsher-Smith Laboratories, LLC from whom the products were acquired on June 30, 2023. Zembrace SymTouch and Tosymra are each indicated for the treatment of acute migraine with or without aura in adults. Tonix's development portfolio is composed of central nervous system (CNS), rare disease, immunology and infectious disease product candidates. Tonix's CNS development portfolio includes both small molecules and biologics to treat pain, neurologic, psychiatric and addiction conditions. Tonix's lead development CNS candidate, TNX-102 SL (cyclobenzaprine HCl sublingual tablet), is in mid-Phase 3 development for the management of fibromyalgia, having completed enrollment of a potentially confirmatory Phase 3 study in the third quarter of 2023, with topline data expected in the fourth quarter of 2023. TNX-102 SL is also being developed to treat fibromyalgia-type Long COVID, a chronic post-acute COVID-19 condition. Enrollment in a

Phase 2 proof-of-concept study has been completed, and topline results were reported in the third quarter of 2023. TNX-601 ER (tianeptine hemioxalate extended-release tablets) is a once-daily oral formulation being developed as a treatment for major depressive disorder (MDD), that completed enrollment in a Phase 2 proof-of-concept study in the third quarter of 2023, with topline results expected in the fourth quarter of 2023. TNX-4300 (estianeptine) is a single isomer version of TNX-601, small molecule oral therapeutic in preclinical development to treat MDD, Alzheimer's disease and Parkinson's disease. Relative to tianeptine, estianeptine lacks activity on the μ -opioid receptor while maintaining activity in the rat Novel Object Recognition test in vivo and the ability to activate PPAR- β/δ and neuroplasticity in tissue culture. TNX-1900 (intranasal potentiated oxytocin), is in development for preventing headaches in chronic migraine, and has completed enrollment in a Phase 2 proof-of-concept study with topline data expected in the fourth quarter of 2023. TNX-1900 is also being studied in binge eating disorder, pediatric obesity and social anxiety disorder by academic collaborators under investigator-initiated INDs. 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 fourth quarter of 2023. Tonix's rare disease development 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 development 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 rejection and for the treatment of autoimmune diseases. A Phase 1 study of TNX-1500 was initiated in the third quarter of 2023. Tonix's infectious disease pipeline includes TNX-801, a vaccine in development to prevent smallpox and mpox. TNX-801 also serves as the live virus vaccine platform or recombinant pox vaccine platform for other infectious diseases. The infectious disease development portfolio also includes TNX-3900 and TNX-4000, which are classes of broad-spectrum small molecule oral antivirals.

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

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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; 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, 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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