January 5, 2021

Tonix Pharmaceuticals and Massachusetts General Hospital (MGH) Enter into Research Collaboration on Tonix's Third Generation anti-CD40-Ligand Monoclonal Antibody, TNX-1500, for the Treatment and Prevention of Kidney Transplant Rejection

Expands Ongoing Research Collaboration Between Tonix and MGH Studying TNX-1500 in Heart Transplantation

TNX-1500 May Hold Potential in Treating Autoimmune Diseases Including Systemic Lupus Erythematosus, Rheumatoid Arthritis and Multiple Sclerosis

CHATHAM, N.J., Jan. 05, 2021 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a clinical-stage biopharmaceutical company, today announced the signing of a second research collaboration agreement with Massachusetts General Hospital (MGH), a teaching hospital of Harvard Medical School, to develop TNX-1500, a humanized monoclonal antibody (mAb) that targets the CD40-ligand (also known as CD154, T-BAM or 5c8 antigen[1]) for the prevention and treatment of organ transplant rejection. Transplant organ rejection occurs when the immune system of the organ recipient attacks the new organ as if it was an infection or tumor. The new collaboration will focus on kidney transplantation, while an earlier collaboration with MGH is focused on heart transplantation.

Transplantation experts led by Tatsuo Kawai, M.D., Ph.D., Surgical Director of the Living Donor Transplantation and Dialysis Access Program at MGH and Professor of Surgery at Harvard Medical School (HMS) will study TNX-1500 in kidney transplantation in a variety of models including non-human primates. The goal of the collaboration is to advance TNX-1500 as a potential first-in-class therapeutic to prevent and treat kidney transplant rejection.

Dr. Kawai said, "Anti-CD40-ligand therapy has a unique activity in controlling the immune response to organ transplants.[2] There remains a significant need for new treatments to reduce the toxicity of current treatments by more selectively suppressing immune responses or inducing specific tolerance to the transplanted organ. Anti-CD40-ligand has shown promise not only to effectively suppress rejection but also to facilitate 'transplant tolerance' in multiple preclinical transplant models.[6]"

The study of TNX-1500 in heart transplantation at MGH began last year under the direction

of Richard N. Pierson III, M.D., scientific director of the Center for Transplantation Sciences in the Department of Surgery at MGH and Professor of Surgery HMS.

Key Advances in Anti-CD40-Ligand Antibody Engineering Led to TNX-1500

Tonix's President and Chief Executive Officer, Seth Lederman, M.D. said, "A substantial body of evidence in humans and animals indicates that mAbs targeting CD40-ligand have the potential to be an important therapeutic option for preventing or treating transplant organ rejection and as a treatment for autoimmune disorders. Despite the recognized promise of anti-CD40-ligand therapy, first generation anti-CD40- ligand mAbs were limited because their constant fragment (Fc) domain interacted with a receptor called FcγRII, which raised concerns over an increased risk of thrombosis. Second generation anti-CD40- ligand mAbs had dramatically reduced binding to FcγRII, but had other issues, including decreased efficacy[5-7]. TNX-1500 is a third generation anti-CD40- ligand mAb that has been designed by protein engineering to target CD40-ligand therapeutically, while potentially decreasing FcγRII binding and the potential for thrombosis."

[1] Lederman, S. & al. *J. Exp. Med.* 175:1091-1101 (1992)
[2] Kawai T, et al. Am J Transplant. 4(9):1391 (2004)
[3] O'Neill NA, et al. *Transplantation.* 101(9): 2038 (2017)
[4] Zhang T, et al. *Immunotherapy*. 7(8):899 (2015)
[5] Waters J, *Biocentury*; October 26, (2018)
[6] NCT02273960; *ClinicalTrials.gov*; "Study to Evaluate Safety and Efficacy in Adult Subjects With ITP (ITP)"; results posted April 1, 2019, accessed July 29, 2019)
[7] Ferrant JL et al., *International Immunol.* (11):1583 (2004)

About CD40-Ligand

CD40-ligand is a protein expressed on the surface of activated T lymphocytes that mediates T cell helper function. CD40-ligand is also known as CD154, the T cell-B cell activating molecule (T-BAM), TRAP or gp39. CD40-ligand is a member of the Tumor Necrosis Factor (TNF) Super Family. Other TNF Super Family members have proven to be targets for antagonist mAbs. Licensed mAbs against TNFα include: infliximab (Remicade®), adalimumab (Humira®), certolizumab pegol (Cimzia®), and golimumab (Simponi®) for the treatment of certain autoimmune conditions. Also, etanercept (Enbrel®) is a TNFα antagonist receptor fusion protein. A licensed mAb against RANKL (CD254) is denosumab (Prolia® or Xgeva®) for the treatment of osteoporosis, treatment-induced bone loss, metastases to bone, and giant cell tumor of bone.

Remicade® and Simponi® are trademarks of Janssen; Humira® is a trademark of AbbVie Inc.; Cimzia® is a trademark of UCB S. A.; Enbrel®, Prolia® and Xgeva® are trademarks of Amgen Inc.

Tonix Pharmaceuticals Holding Corp.

Tonix is a clinical-stage biopharmaceutical company focused on discovering, licensing, acquiring and developing small molecules and biologics to treat and prevent human disease and alleviate suffering. Tonix's portfolio is primarily composed of central nervous system (CNS) and immunology product candidates. The CNS portfolio includes both small

molecules and biologics to treat pain, neurologic, psychiatric and addiction conditions. Tonix's lead CNS candidate, TNX-102 SL*, is in mid-Phase 3 development for the management of fibromyalgia since positive data on the RELIEF Phase 3 trial were recently reported. The Company expects topline data in the Phase 3 RALLY study in the fourth quarter of 2021. The immunology portfolio includes vaccines to prevent infectious diseases and biologics to address immunosuppression, cancer, and autoimmune diseases. Tonix's lead vaccine candidate, TNX-1800**, is a live replicating vaccine based on the horsepox viral vector platform to protect against COVID-19, primarily by eliciting a T cell response. Tonix expects efficacy data from animal studies of TNX-1800 in the first quarter of 2021. TNX-801**, live horsepox virus vaccine for percutaneous administration, is in development to protect against smallpox and monkeypox.

*TNX-102 SL is an investigational new drug and has not been approved for any indication.

**TNX-1800 and TNX-801 are investigational new biologics 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 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, 2019, as filed with the Securities and Exchange Commission (the "SEC") on March 24, 2020, and periodic reports filed with the SEC on or after the date thereof. All 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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Source: Tonix Pharmaceuticals Holding Corp.