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Tonix Pharmaceuticals Announces Two Publications of Data in American Journal of Transplantation Showing TNX-1500 (anti-CD40L mAb) Prolongs Nonhuman Primate Renal and Heart Allograft Survival

Research Directed by Faculty of the Center for Transplantation Sciences, Massachusetts General Hospital

CHATHAM, N.J., April 17, 2023 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP), a clinical-stage biopharmaceutical company, today announced the on-line publication of two papers[1,2] in the *American Journal of Transplantation* by faculty at the Center for Transplantation Sciences, Massachusetts General Hospital (MGH) in collaboration with Tonix Pharmaceuticals. The data involve studies of Tonix's TNX-1500 (Fc-modified anti-CD40L humanized monoclonal antibody [mAb]) product candidate in development for the prevention of organ transplant rejection. The molecular target of TNX-1500 is CD40-ligand (CD40L), which is also known as CD154, T-BAM or 5c8 antigen. The publications include data demonstrating that TNX-1500 showed activity in preventing organ rejection and was well tolerated in non-human primates. Blockade of CD40L with TNX-1500 monotherapy consistently and safely prevented pathologic alloimmunity in non-human primate models of cardiac and kidney allograft model without clinical thrombosis.

"There remains a significant need for new treatments with improved activity and tolerability to prevent organ transplant rejection," said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals. "To date, there has not been a humanized anti-CD40L antibody that can effectively prevent transplant rejections with an acceptable level of tolerability. TNX-1500 is a third generation anti-CD40L mAb that has been designed by protein engineering to decrease FcγRII binding and to reduce the potential for thrombosis. The animal studies found that TNX-1500 retains activity to prevent rejection and preserve graft function. Tonix expects to start a first-in-human Phase 1 study in the second quarter of 2023 of TNX-1500 for prophylaxis of organ rejection in adult patients receiving a kidney transplant."

Tatsuo Kawai, M.D., Ph.D., A. Benedict Cosimi Chair in Transplant Surgery, MGH and Professor of Surgery, Harvard Medical School (HMS) and senior author of the kidney transplant publication, said, "The blockade of the CD40L-CD40 pathway with anti-CD40L mAbs has been the most promising immunomodulatory approach to prevent allograft rejection. However, long-term graft and patient survival following transplantation of kidneys and other solid organs are constrained by side effects of the existing medications. Our data demonstrate a favorable safety profile associated with TNX-1500, since neither non-human

primate nor human platelet activation were observed *in-vitro* when exposed to TNX-1500-sCD40L immune complexes. The therapeutic effects of TNX-1500 to consistently inhibit rejection of mismatched kidney allografts were not associated with infectious or thromboembolic complications, suggesting that clinical studies are warranted to evaluate TNX-1500 for transplant indications."

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 at HMS and senior author of the heart transplant paper said, "Anti-CD40L therapy has a unique activity in controlling the immune response to organ transplants. There remains a significant need for new treatments with improved activity and tolerability to prevent or treat organ transplant rejection. Anti-CD40L has shown great promise to facilitate transplant tolerance in multiple preclinical transplant models. A safe, effective anti-CD40L also has potential to enable use of genetically modified or humanized pig organs to treat humans with advanced organ failure or diabetes, an emerging field known as xenotransplantation."

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), a small molecule 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 of tianeptine 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, a class of broad-spectrum small molecule oral antivirals.

*All of Tonix's product candidates are investigational new drugs or biologics and none has

been approved for any indication.

[1]Lassiter, G., et al. (2023). TNX-1500, a crystallizable fragment–modified anti-CD154 antibody, prolongs nonhuman primate renal allograft survival. *American Journal of Transplantation*. April 3, 2023. https://doi.org/10.1016/j.ajt.2023.03.022

[2]Miura, S., et al. (2023) TNX-1500, a crystallizable fragment–modified anti-CD154 antibody, prolongs nonhuman primate cardiac allograft survival. *American Journal of Transplantation*. April 6, 2023. https://doi.org/10.1016/j.ajt.2023.03.025

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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