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Tonix Pharmaceuticals and Massachusetts General Hospital Enter into Research Collaboration to Develop Tonix's Third Generation Anti-CD154 Monoclonal Antibody, TNX-1500, for the Treatment and Prevention of Organ Transplant Rejection

NEW YORK, Aug. 21, 2019 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a clinical-stage biopharmaceutical company, today announced the signing of a 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 CD154 for the prevention and treatment of organ transplant rejection. TNX-1500 is another step in the strategic broadening of Tonix's portfolio of high-value programs, whose risk is mitigated by previous clinical data and extensive preclinical science. Although transplantation is the first targeted indication for TNX-1500, it is also a potential treatment for autoimmune conditions including systemic lupus erythematosus, rheumatoid arthritis and multiple sclerosis.

Tonix and MGH have agreed to work jointly under a research agreement which will bring together Tonix's internally developed, proprietary anti-CD154 mAb, TNX-1500, with transplantation experts from MGH, led by 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 Harvard Medical School (HMS). The goal of the collaboration is to advance TNX-1500 as a potential first-in-class therapeutic for 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.

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 CD154 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-CD154 therapy, first generation anti-CD154 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-CD154 mAbs had dramatically reduced binding to FcγRII, but had other issues, including decreased efficacy.[1-3] TNX-1500 is a third generation anti-CD154 mAb that has been designed by protein engineering to target CD154 therapeutically, while decreasing FcγRII binding and the potential for thrombosis."

Dr. Pierson of MGH and HMS said, “Anti-CD154 therapy has a unique activity in controlling the immune response to organ transplants.[4,5] There remains a significant need for new treatments with improved activity and tolerability to prevent or treat organ transplant rejection. Anti-CD154 has shown great promise to facilitate ‘transplant tolerance’ in multiple preclinical transplant models. A safe, effective anti-CD154 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.’” [6,7]

Dr. Lederman added, “Nearly 30 years ago, the laboratory that I directed as an Assistant Professor at Columbia University, discovered and characterized CD154, generated the first anti-CD154 monoclonal antibody, 5c8, and elucidated the molecular basis of T cell helper function.[8] It is exciting to return to the anti-CD154 field and to bring forth a third generation anti-CD154 mAb potential biologic therapeutic for treating and preventing organ transplant rejection that stands on the shoulders of previous work. We believe that TNX-1500 has the potential to maintain therapeutic activity of first generation anti-CD154 mAbs, but with reduced risk of thrombosis. We believe that the combined expertise of Tonix and MGH will be strongly synergistic. Preventing and treating organ rejection remains the greatest obstacles to long term survival in transplantation.”

[1] Waters J, *Biocentury*; October 26, (2018)

[2] NCT02273960; *ClinicalTrials.gov*; “Study to Evaluate Safety and Efficacy in Adult Subjects with ITP (ITP)”; results posted April 1, 2019, accessed July 29, 2019)

[3] Ferrant JL et al., *International Immunol.* (11):1583 (2004)

[4] O’Neill NA, et al. *Transplantation.* 101(9): 2038 (2017)

[5] Zhang T, et al. *Immunotherapy*. 7(8):899 (2015)

[6] Längin M, et al. *Nature.* 564(7736):430 (2018)

[7]Pierson RN 3rd. *J Thorac Cardiovasc Surg.* Jun 13. pii: S0022-5223(19)31024-4. doi: 10.1016/j.jtcvs.2019.04.087. (2019)

[8] Lederman, S. & al. *J. Exp. Med.* 175:1091-1101 (1992)

About CD154

CD154 is a protein expressed on the surface of activated T lymphocytes that mediates T cell helper function. CD154 is also known as the CD40-ligand (CD40-L), the T cell-B cell activating molecule (T-BAM), TRAP or gp39. CD154 is a member of the Tumor Necrosis Factor (TNF) Super Family. No mAb against CD154 has been licensed anywhere in the world. 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.

Tonix Pharmaceuticals Holding Corp.

Tonix is a clinical-stage biopharmaceutical company focused on discovering and developing small molecules and biologics to treat psychiatric, pain and addiction conditions, to improve biodefense through potential medical counter-measures and to prevent and treat organ transplant rejection. Tonix's lead program is for the development of Tonmya* (TNX-102 SL), which is in Phase 3 development as a bedtime treatment for PTSD. Tonix is also developing TNX-102 SL as a bedtime treatment for fibromyalgia, agitation in Alzheimer's disease and alcohol use disorder, to be developed under separate Investigational New Drug applications (INDs) to support potential pivotal efficacy studies. The fibromyalgia program is in Phase 3 development, the agitation in Alzheimer's program is Phase 2 ready and the alcohol use disorder program is in the pre-IND application stage. TNX-1300** (double-mutant cocaine esterase) is being developed under an IND and is in Phase 2 development for the treatment of cocaine intoxication. Tonix has two other programs in the pre-IND application stage of development for PTSD, but with different mechanisms than TNX-102 SL and designed for daytime dosing: TNX-601 (tianeptine oxalate) and TNX-1600***, a triple reuptake inhibitor. TNX-601 is also in development for a potential indication - neurocognitive dysfunction associated with corticosteroid use. Data is expected in the second half of 2019 for a Phase 1 clinical formulation selection pharmacokinetic study of TNX-601 that is being conducted outside of the U.S. TNX-801 (live virus vaccine for percutaneous (scarification) administration) is a potential smallpox-preventing vaccine based on a live synthetic version of horsepox virus, currently in the pre-IND application stage. Finally, TNX-1500 is being developed to prevent and treat organ transplant rejection, as well as to treat autoimmune conditions, and is in the pre-IND application stage.

**Tonmya has been conditionally accepted by the U.S. Food and Drug Administration (FDA) as the proposed trade name for TNX-102 SL for the treatment of PTSD. TNX-102 SL (cyclobenzaprine HCl sublingual tablets) is an investigational new drug and has not been approved for any indication.*

***TNX-1300 (T172R/G173Q double-mutant cocaine esterase 200 mg, i.v. solution) is an investigational new biologic and has not been approved for any indication.*

****TNX-1600* ((2*S*,4*R*,5*R*)-5-(((2-aminobenzo[*d*]thiazol-6-yl)methyl)amino)-2-(bis(4-fluorophenyl)methyl)tetrahydro-2*H*-pyran-4-ol) is an inhibitor of reuptake of three monoamine neurotransmitters (serotonin, norepinephrine and dopamine), or a "triple reuptake" inhibitor.

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; 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, 2018, as filed with the Securities and Exchange Commission (the "SEC") on March 18, 2019, and periodic reports on Form 10-Q filed with the SEC on or after the date thereof. Tonix does not undertake any obligation to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

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