March 5, 2024

Tonix Pharmaceuticals Announces Translation of Preclinical Pharmacokinetic Parameters of TNX-1500 (Fc-modified humanized anti-CD40L mAb) Supports Monthly i.v. Dosing in Humans

TNX-1500, a third generation anti-CD40L mAb, was Fc-modified to preserve the activity and bioavailability of first generation mAbs while addressing their thrombosis risk

Sanofi projects its Fc-modified humanized anti-CD40L mAb frexalimab will exceed€5B per year in peak sales[1] based on Phase 2 multiple sclerosis data recently published in the New England Journal of Medicine[2]

Topline results of TNX-1500 Phase 1 trial expected in the third quarter of 2024; clinical stage completed last month

TNX-1500 has multiple potential indications including solid organ and bone marrow transplantation and the treatment of autoimmune diseases: potential 'pipeline in a product'

CHATHAM, N.J., March 05, 2024 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP), a biopharmaceutical company with marketed products and a pipeline of development candidates, today announced the results of modeling key human pharmacokinetic (PK) properties for TNX-1500 (Fc-modified humanized anti-CD40L monoclonal antibody, or mAb)* from animal studies. TNX-1500 is in development for the prevention of rejection in solid organ and bone marrow transplantation and for the treatment of autoimmune disorders.

"For more than 30 years, anti-CD40L therapy has shown promise in transplantation and the treatment of autoimmunity, but first-generation humanized mAbs were associated with an increased risk of thrombosis and second-generation agents had poor PK properties or reduced activity," said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals. "Preclinical studies in non-human primates have shown that TNX-1500 maintains the activity of first generation mAbs, with reduced risk of thrombotic complications.[3-5] Today we are announcing that modeling studies from animal PK data[3], predict that a half-life of approximately three weeks for TNX-1500 in humans[6,7], which supports monthly dosing. This PK analysis together with TNX-1500's activity and tolerability in animals, suggests that the protein engineering of TNX-1500's Fc region has achieved its design goals."

Dr. Lederman continued, “Recently, positive clinical data have been reported by Sanofi, with its Fc-modified humanized anti-CD40L mAb frexalimab in treating relapsing multiple sclerosis with monthly *i.v.* or biweekly *s.c.* dosing regimens.[2] Based on its results in multiple sclerosis, Sanofi projects that frexalimab will exceed €5B per year in peak sales[1]. TNX-1500 was designed to reduce binding to the Fc-receptor for IgG type 2a, or FcγR2a, which has been shown to play a role in the thrombosis associated with first-generation anti-CD40L mAbs, similar to frexalimab. In addition, Eledon Pharmaceuticals is in Phase 2 development for the prevention of rejection of kidney transplants with tegoprubart, a non-covalent dimer antibody with no heavy-light or heavy-heavy interchain disulfide bridges for the prevention of rejection of kidney transplants.”[8]

“Anti-CD40L therapy has multiple possible indications in addition to solid organ and bone marrow transplantation, including autoimmune diseases,” Dr. Lederman stated, “We look forward to the results of our Phase 1 PK and pharmacodynamic trial in the third quarter of 2024 and to advancing TNX-1500 as a promising candidate for prevention of organ and bone marrow transplant rejection and for treating autoimmune conditions.”

About the Translation of Human Pharmacokinetic Parameters from Animal Data

Results of a single dose PK study in animals were analyzed to predict human PK parameters. The PK study was conducted in six healthy cynomolgus monkeys at 30, 100 and 300 mg/kg and revealed linear PK across those doses, consistent with an antibody with no target mediated drug disposition.[6,7] The half-life in cynomolgus monkeys is approximately 14 days. Human half-life prediction for TNX-1500 was based on allometric scaling for mAbs with linear PK.[6] Clearance in cynomolgus animals was 6.24 ml/day (26.6% C.V.) and the predicted clearance in humans was 141 mL/day (C.V. 22.9%).[6,7] The predicted human half-life for TNX 1500 is 23.8 days (range of 18.3 to 27.6 days) which supports monthly dosing.[6,7]

About TNX-1500

TNX-1500 (Fc-modified humanized anti-CD40L mAb) is a humanized monoclonal antibody that binds and blocks the CD40-ligand (CD40L), also known as CD154. TNX-1500 is being developed for the prevention of allograft and xenograft rejection, for the prevention of graft-versus-host disease (GvHD) after hematopoietic stem cell transplantation (HCT) and for the treatment of autoimmune diseases. A first-in-human Phase 1 trial of TNX-1500 has completed the clinical phase. Topline results are expected in the third quarter of 2024. The primary objective of the Phase 1 trial is to assess the safety, tolerability, PK, and pharmacodynamics of intravenous (*i.v.*) TNX-1500. Eligible participants enrolled in the Phase 1 trial were distributed across three dosing cohorts (3 mg/kg, 10 mg/kg, and 30 mg/kg, respectively) and evaluated regularly over a 120-day period after dosing. The Phase 1 trial is intended to support dosing in a planned Phase 2 trial in kidney transplant recipients. Two published articles in the *American Journal of Transplantation* demonstrate TNX-1500 prevents rejection, prolongs survival and preserves graft function as a single agent or in combination with other drugs in non-human primate renal and heart allografts.[3,4]

About anti-CD40L Therapeutics in Development

No anti-CD40L mAb has been approved in any jurisdiction. In addition to TNX-1500,

frexalimab and tegoprubart, tn03 fusion protein dazodalibep is being developed by Amgen (formerly Horizon Therapeutics Public Limited Company) for the treatment of Sjögren's Syndrome.[9,10] Dapirolizumab pegol, an anti-CD40L pegylated Fab, is being developed by UCB for the treatment of systemic lupus erythematosus.[11]

*TNX-1500 is an investigational new biologic and is not approved for any indication

1. Dunn, A. Endpoints. December 7, 2023. “Sanofi CEO Paul Hudson pitches 12 blockbusters in a bid to convince investors on boosting R&D spend”. https://endpts.com/sanofi-rd-day-ceo-paul-hudson-touts-12-blockbusters-ups-rd-spend/
2. Vermersch P., et al. *N Engl J Med*. 2024. 390(7):589-600 https://doi.org/10.1056/nejmoa2309439
3. Lassiter G., et al. *Am J Transplantation*. 2023. https://doi.org/10.1016/j.ajt.2023.03.022
4. Miura S., et al. *Am J Transplantation*. 2023. https://doi.org/10.1016/j.ajt.2023.03.025
5. Anand, R.P., et al *Nature.* 622, 393–401 (2023). https://doi.org/10.1038/s41586-023-06594-4
6. Deng R., et al. *Mabs*. 2011. https://doi.org/10.4161/mabs.3.1.13799
7. Tonix Pharmaceuticals – Data on File
8. Eledon press release. November 2, 2023. https://ir.eledon.com/news-releases/news-release-details/eledon-reports-updated-data-ongoing-phase-1b-trial-evaluating (accessed February 2024)
9. BioSpace. September 12, 2022. https://www.biospace.com/article/releases/horizon-therapeutics-plc-announces-phase-2-trial-evaluating-dazodalibep-for-the-treatment-of-sjoegren-s-syndrome-meets-primary-endpoint (accessed February 2024)
10. BioSpace. January 18, 2023. https://www.biospace.com/article/horizon-bags-second-phase-ii-win-in-sjoegren-s-syndrome (accessed February 2024)
11. https://www.ucb.com/our-science/pipeline (accessed August 2023)

Tonix Pharmaceuticals Holding Corp.*

Tonix is a biopharmaceutical company focused on developing, licensing and commercializing therapeutics to treat and prevent human disease and alleviate suffering. Tonix’s development portfolio is focused on central nervous system (CNS) disorders. Tonix’s priority is to submit a New Drug Application (NDA) to the FDA in the second half of 2024 for Tonmya[1], a product candidate for which two positive Phase 3 studies have been completed for the management of fibromyalgia. TNX-102 SL is also being developed to treat acute stress reaction as well as fibromyalgia-type Long COVID. Tonix’s CNS portfolio includes TNX-1300 (cocaine esterase) a biologic designed to treat cocaine intoxication with Breakthrough Therapy designation. Tonix’s immunology development portfolio consists of 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. Tonix also has product candidates in development in the areas of rare disease and infectious disease. Tonix Medicines, our commercial subsidiary, markets Zembrace® SymTouch® (sumatriptan injection) 3 mg and Tosymra® (sumatriptan nasal spray) 10 mg for the treatment of acute migraine with or without aura in adults.

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

[1]Tonmya™ is conditionally accepted by the U.S. Food and Drug Administration (FDA) as the tradename for TNX-102 SL for the management of fibromyalgia. Tonmya has 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 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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