November 2, 2023

Tonix Pharmaceuticals' Vaccine Candidate, TNX-1800, Selected by NIH/NIAID Project NextGen for Inclusion in Clinical Trials

NIAID is conducting early phase clinical trials on select next generation COVID-19 vaccine candidates with the intent to identify promising vaccine candidates

TNX-1800, a live virus percutaneous vaccine candidate, is based on Tonix's recombinant pox virus (RPV) platform

Phase 1 clinical trial of TNX-1800 expected to start in the second half of 2024

NIAID will cover the full cost of the clinical trial; Tonix will supply the vaccine candidate

CHATHAM, N.J., Nov. 02, 2023 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP), a biopharmaceutical company with marketed products and a pipeline of development candidates, today announced that the National Institute of Allergy and Infectious Diseases (NIAID), a part of the National Institutes of Health (NIH), will conduct a Phase 1 clinical trial with TNX-1800 (recombinant horsepox virus, live vaccine),[1] Tonix Pharmaceuticals' vaccine candidate to protect against COVID-19.

Tonix is developing a novel vaccine platform initially targeting COVID-19, smallpox and mpox (monkeypox). The intent is to provide durable protection against severe disease and prevent forward transmission, primarily by eliciting a T-cell immune response. TNX-1800 expresses the spike protein of SARS-CoV-2, was immunogenic, well tolerated[2] and showed promise in protecting animals from challenge with SARS-CoV-2 delivered directly into the lungs.[3] A related horsepox-based vaccine, TNX-801[1], protected animals against challenge with monkeypox virus delivered directly into the lungs.[4] TNX-801 is also the vector on which TNX-1800 is based and has been shown to be >1,000-fold more attenuated than modern vaccinia virus vaccine (VACV) strains in immunocompromised mice.[5] The Phase 1 trial of TNX-1800 is expected to start in the second half of 2024. NIAID will study TNX-1800 by percutaneous administration.

"We believe our novel vaccine platform technology has the potential to provide durable protection from respiratory pathogens and slow their spread," said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals. "TNX-1800 will be the first vaccine candidate using our live virus recombinant pox virus (RPV) platform technology to enter clinical trials. We hope to expand the portfolio of RPV-based vaccines to address several other known respiratory threats including smallpox, mpox and tuberculosis. We are

committed to supporting NIAID in assembling a variety of vaccine platform options to ensure the availability of effective vaccines in the face of known and emerging threats. We look forward to participating in the Project NextGen initiative."

"Project NextGen," is an initiative by the U.S. Department of Health and Human Services (HHS) to advance a pipeline of new, innovative vaccines and therapeutics for COVID-19. NIAID will be conducting clinical trials to evaluate several early-stage vaccine candidates. The Phase 1 study involving TNX-1800 is designed to assess safety and immunogenicity in approximately 60 healthy adult volunteers. Upon completion of the trial, NIAID and Tonix Pharmaceuticals will assess the results and determine the next steps for the development of TNX-1800.

NIAID will cover the full cost of the clinical trial, including operations and related analysis. Tonix will be responsible for providing clinical trial materials, and upon completion will have the right to rely on the findings in regulatory filings with the U.S. Food and Drug Administration (FDA) to support the approval of its COVID-19 vaccine and other vaccines based on the RPV platform.

About Project NextGen

Project NextGen is a $5 billion initiative to develop the next generation of vaccines and therapeutics to combat COVID-19. Based at the HHS and led by the Administration for Strategic Preparedness and Response's Biomedical Advanced Research and Development Authority and the NIH's NIAID, Project NextGen will coordinate across the federal government and the private sector to advance the pipeline of new, innovative vaccines and therapeutics into clinical trials and potential review by the U.S. Food and Drug Administration (FDA) for authorization or approval, and commercial availability for the American people. The program will focus on several areas, including mucosal vaccines, vaccines that provide broader protection against variants of concern and a longer duration of protection, pan-coronavirus vaccines, and new and more durable monoclonal antibodies.

About TNX-1800*
TNX-1800 (recombinant horsepox virus) is a live virus vaccine for percutaneous administration that is designed to express the spike protein of the SARS-CoV-2 virus and to elicit a predominant T cell response. The RPV platform is based on a horsepox vector, which is a live replicating, attenuated virus that has been shown to be >1,000-fold more attenuated than modern VACV strains in immunocompromised mice.[5] Horsepox and the vaccinia vaccine viruses are closely related orthopoxviruses that are believed to share a common ancestor. Molecular analysis shows that horsepox is closer than modern vaccinia vaccines in DNA sequence to the vaccine discovered and disseminated by Dr. Edward Jenner. [6-9] Live replicating orthopoxviruses, like vaccinia or horsepox, can be engineered to express foreign genes and have been explored as platforms for vaccine development because they possess; (1) large packaging capacity for exogenous DNA inserts, (2) precise virus-specific control of exogenous gene insert expression, (3) lack of persistence or genomic integration in the host, (4) strong immunogenicity as a vaccine, (5) ability to rapidly generate vector/insert constructs, (6) readily manufacturable at scale, and (7) ability to provide direct antigen presentation. Relative to vaccinia, horsepox has substantially decreased virulence in mice.[4,6] The current formulation is a frozen liquid, but we believe that future lyophilized versions can be stored and shipped at standard refrigeration. Horsepox-based vaccines are

designed to be single dose, vial-sparing vaccines that can be administered without sterile injection, manufactured using conventional cell culture systems with the potential for mass scale production, and packaged in multi-dose vials. Moreover, we believe the low dose of TNX-1800 makes this technology amenable for future implementation in microneedle delivery systems.

About TNX-801*

TNX-801 (recombinant horsepox virus) is a live virus vaccine based on horsepox[4-7] in pre-clinical development to prevent smallpox and mpox. Tonix reported positive preclinical efficacy data, demonstrating that TNX-801 vaccination protected non-human primates against lethal challenge with monkeypox.[4] Tonix has received official written response from a Type B pre-Investigational New Drug Application (IND) meeting with the U.S. Food and Drug Administration (FDA) to develop TNX-801 as a potential vaccine to protect against mpox disease and smallpox.[10] Tonix believes the FDA feedback provides a path to agreement on the design of a Phase 1 /2 study and the overall clinical development plan. The Phase 1/2 clinical trial will assess the safety, tolerability, and immunogenicity of TNX-801, following the submission and clearance of an IND. More than 30,000 people have contracted mpox in the U.S. so far during the 2022-23 epidemic,[11] The recent cluster of mpox in Chicago revealed breakthrough cases of mpox in individuals who had been vaccinated with the currently authorized non-replicating vaccine, which is administered in two doses.[12] In contrast, TNX-801 is delivered percutaneously with only one dose and therefore may achieve higher rates of community protection by eliminating drop-out between doses and limiting forward transmission. Moreover, relying on only one approved mpox vaccine at present is a risk for the global supply chain that has already led to insufficient availability of vaccines to meet global health needs, especially in Africa. TNX-801 has the potential to make a global impact on mpox and the risk of smallpox because of its durable T-cell immune response, the potential to manufacture at scale, and the use of a lower dose than non-replicating vaccines.

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 late December 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-1900 (intranasal potentiated oxytocin), is in development as a preventive

treatment for chronic migraine, and enrollment has been completed in a Phase 2 proof-of-concept study with topline data expected in early December 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, including TNX-1800, in development as a vaccine to protect against COVID-19. 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.

[1] TNX-1800 and TNX-801 are experimental new vaccines and have not been approved for any indication.

[2] Awasthi, M. et al. *Viruses*. 2023. 15(10):2131.

[3] Awasthi, M. et al. *BioRxiv*. 2023.

[4] Trefry S, et al. *BioRxiv*. 2023.

[5] Noyce RS, et al. *Viruses*. 2023. 15(2):356.

[6] Jenner E. "An Inquiry Into the Causes and Effects of the Variole Vaccinae, a Disease Discovered in Some of the Western Counties of England, Particularly Gloucestershire and Known by the Name of the cow-pox." London: Sampson Low, 1798.

[7] Noyce RS, et al. *PloS One.* 2018. 13(1):e0188453.

[8] Schrick L et al. *N Engl J Med.* 2017. 377:1491-1492.

[9] Tulman ER, et al. *J Virol*. 2006. 80(18):9244-58.

[10] TNX-801 PR pre-IND meeting August 20, 2023: https://ir.tonixpharma.com/news-events/press-releases/detail/1417/tonix-pharmaceuticals-announces-results-of-pre-ind-meeting

[11] McQuiston JH, et al. *MMWR Morb Mortal Wkly Rep.* 2023. 72:547–552.

[12] Centers for Disease Control. *MMWR Morb Mortal Wkly Rep.* 2023. 72(25);696-698.

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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