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Tonix Pharmaceuticals Initiates Enrollment in Clinical Trial of TNX-2100, a Diagnostic Skin Test to Measure Functional T Cell Immunity to SARS-CoV-2

Potential Uses Include: Biomarker of Immunity to SARS-CoV-2; Personalized Approach to Timing COVID-19 Vaccine Boosters; Public Health Surveillance; and Serving as an Endpoint for COVID-19 Vaccine Trials

Topline Data Expected in First Half 2022

CHATHAM, N.J., Jan. 11, 2022 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a clinical-stage biopharmaceutical company, today announced that the first participant was enrolled in a dose-finding study for TNX-2100 (SARS-CoV-2 epitope peptide mixtures for intradermal administration), an *in vivo* skin test to measure delayed-type hypersensitivity (DTH) to SARS-CoV-2 (CoV-2), the virus that causes COVID-19. DTH is a measure of functional T cell immunity.

“The SARS-CoV-2 skin test is designed to measure T cell immunity,” said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals. “In other infectious diseases, T cell immunity prevents serious disease and blocks forward transmission. Because antibodies are easier to measure, there has been more discussion about antibodies rather than T cells as a biomarker of immunity to SARS-CoV-2. However, T cells, not antibodies, are the body’s major defense against viruses. The skin test has the potential to serve as: 1) a biomarker for T cell protective immunity and durability of vaccine protection; 2) a personalized approach for vaccine boosters; 3) a method to stratify participants in COVID-19 vaccine trials with a more complete picture of immune status; 4) an endpoint in COVID-19 vaccine trials for vaccines that elicit T cell immunity, and 5) public health surveillance. We believe the TNX-2100 skin test has the potential to address the unmet need for a rapid, sensitive, and specific test that may indicate current or past infection with SARS-CoV-2 and potentially predict protective immunity. We also believe the skin test has the potential to inform strategies to protect individuals and communities from COVID-19.”

T cell immunity to SARS-CoV-2 is believed to provide an important element of protective immunity against serious COVID-19 illness after infection with SARS-CoV-2. T cell immunity to several viruses is known to persist substantially longer than antibody immunity, often present when there is no measurable antibody response, and in many cases provides a more durable protective immunity that may last for years to decades. For example, T cell immunity has been detected to SARS-CoV-2 in some individuals who do not make antibody responses and in others after their antibody responses have waned and become

undetectable over time. A complete picture of a patient's immune status requires assessment of both antibody titers and T cell immunity.

Skin tests that elicit DTH responses are well-established methods for the detection of antigen-specific T cell responses. Tests of this kind are known as *in vivo* diagnostics because they require injection of small representative peptides into the skin. A positive result is evidenced by a skin reaction surrounding the site of the injection produced by local infiltration of functional antigen-specific T cells. This reaction, also called "induration", has been shown to be dependent on the presence of memory T cells. Both the CD4+ and CD8+ fractions of T cells participate in this response.

Herbert Harris, M.D., Ph.D., Executive Vice President of Translational Medicine at Tonix said, "There is continued uncertainty about the durability of protection provided by mRNA vaccines for COVID-19 and the number and frequency of boosters required to maintain protective immunity. This skin test, with its potential to allow for measurement of functional T cell immunity to SARS-CoV-2, could provide a personalized approach to determining the need for a booster. A personalized approach to boosters has advantages over the lock-step boosters-for-everyone strategy, which is expensive, exposes people to unknown risks and is unlikely to be sustainable."

This dose finding, multi-cohort study is designed to evaluate the safety and efficacy of intradermally-injectedTNX-2100, synthesized SARS-CoV-2 peptide antigens and assess the presence and magnitude of DTH reactions.

The study is expected to be conducted in the U.S. in approximately 90 healthy adult subjects (30 subjects per cohort) who are either uninfected/unexposed healthy individuals (Cohort 1), who are confirmed to have recovered from SARS-CoV-2 infection, independent of vaccination status (Cohort 2), or who have received a complete SARS-CoV-2 vaccine course with no known history of natural infection (Cohort 3). The study schedule will consist of a baseline/skin test administration at visit 1 (Day 1) at which time baseline assessments are to be completed, the skin test is performed, and appropriate test samples are collected. Follow-up visits to monitor safety and evaluate the presence or absence of DTH reactions will be conducted at visit 1 (Day 1), visit 2 (Day 2), visit 3 (Day 3), visit 4 (Day 4), and visit 5 (Day 5). Safety monitoring will continue through visit 6 (Day 30) and visit 7 (Day 180).

An interim analysis is expected to be conducted after all subjects have completed their Day 5 visit (or early terminated prior to Day 5). The purpose of the interim analysis will be to assess the presence of DTH reactions in response to intradermal injection of TNX-2100, synthesized SARS-CoV-2 peptide antigens, and to assess safety up to 96 hours post-administration. A full database lock will occur after all subjects have completed their visit 7 (or early terminated prior to visit 7).

About TNX-2100

TNX-2100 is a diagnostic product candidate and has not been approved for any indication. TNX-2100 is a test comprising three different mixtures of synthetic peptides (TNX-2110, -2120 and -2130), which are designed to represent different protein components of the SARS-CoV-2 virus. TNX-2110 (SARS-CoV-2 multi-antigen peptides) represents epitopes of multiple proteins from SARS-CoV-2. TNX-2120 (SARS-CoV-2 spike peptides) represents only the spike protein. TNX-2130 (SARS-CoV-2 non-spike peptides) represents non-spike

proteins. Each of these three synthetic peptide mixtures is expected to be administered as part of the same procedure, at separate locations on the forearm, and each is expected to elicit a DTH response after approximately 48 hours in individuals with pre-existing T cell immunity to peptides in that mixture. Individuals who have been infected by or exposed to SARS-CoV-2 would be expected to respond to all three mixtures. In contrast, a successfully vaccinated individual who has not been exposed or infected by SARS-CoV-2 would be expected to respond only to TNX-2120 (SARS-CoV-2 spike peptides), since the currently available vaccines only encode spike protein. In the planned clinical protocol for testing TNX-2100, positive skin test controls will be used to confirm that study participants have intact T cell immunity and are not immunodeficient.

The test is designed to be administered in the same manner as skin tests for tuberculosis, or TB, sold as Tubersol® or Aplisol® or generically as the Mantoux tuberculin purified protein derivative (PPD) test. A thin gauge needle is used to apply each of the three separate TNX-2100 peptide mixtures into the skin, or intradermally, on the inner surface of the forearm between the wrist and the elbow. In a typical positive test, the skin surrounding the injection site is expected to become red, raised and hardened, or “indurated”, after approximately 48 hours. Induration above a threshold level would signify a positive result and the diameter of the induration would indicate the amount of T cell immunity to the test peptides. DTH skin test responses are believed to reflect functional *in vivo* immunity. Clinical trials are expected to correlate skin test results with clinical history and laboratory findings. to inform estimates about the sensitivity and specificity of the test as a marker of T cell immunity in individuals who are pre- and post-COVID-19 vaccination, recovered from COVID-19; or exposed but asymptomatic.

Discovered in 1882 by Robert Koch, the DTH reaction has been used for more than a century as a clinical test for T cell-mediated immune reactions[1]. In the 1940s, Landsteiner and Chase demonstrated that the reaction was mediated by the cellular and not the antibody arm of the immune system[2]. The DTH reaction has been shown to be dependent on the presence of memory T cells. Both the CD4+ and CD8+ T cells have been shown to participate in this response. DTH skin tests have been commonly used to detect T cell responses to tuberculosis, fungal pathogens, and mumps virus.

[1]*Black CA. Delayed type hypersensitivity: current theories with an historic perspective. Dermatol Online J. 1999;5:7.*

[2]*Landsteiner K, Chase MW. Studies on the sensitization of animals with simple chemical compounds: vii. Skin sensitization by intraperitoneal injections. J Exp Med. 1940;71:237.*

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Aplisol® is a trademark of Par Pharmaceutical, Inc.

About Tonix Pharmaceuticals Holding Corp.

Tonix is a clinical-stage biopharmaceutical company focused on discovering, licensing, acquiring and developing therapeutics and diagnostics to treat and prevent human disease and alleviate suffering. Tonix’s portfolio is composed of infectious diseases, central nervous system (CNS) and immunology product candidates. Tonix’s infectious disease portfolio

includes COVID-19-related product candidates to prevent and treat COVID-19, to treat Long COVID as well as to detect functional T cell immunity to SARS-CoV-2. The portfolio also includes a vaccine in development to prevent smallpox. The Company's CNS portfolio includes both small molecules and biologics to treat pain, neurologic, psychiatric and addiction conditions. The immunology portfolio includes biologics to address immunosuppression, cancer, and autoimmune diseases. Tonix's lead vaccine candidate for COVID-19, TNX-1800[1], is a live replicating vaccine based on Tonix's recombinant pox vaccine (RPV) platform to protect against COVID-19, primarily by eliciting a T cell response. Tonix expects to start a Phase 1 study in humans in the second half of 2022. Tonix is developing TNX-2100[2], an *in vivo* diagnostic to measure the presence of functional T cell immunity to SARS-CoV-2 and initiated a first-in-human clinical study in the first quarter of 2022. TNX-3500[3] (sangivamycin, *i.v.* solution) is a small molecule antiviral drug to treat acute COVID-19 and is in the pre-IND stage of development. Finally, TNX-102 SL[4] (cyclobenzaprine HCl sublingual tablets), is a small molecule drug being developed to treat Long COVID, a chronic post-COVID condition. Tonix expects to initiate a Phase 2 study in Long COVID in the first half of 2022. Tonix's lead CNS candidate, TNX-102 SL, is in mid-Phase 3 development for the management of fibromyalgia with a new Phase 3 study expected to start in the first half of 2022. TNX-1300[5] is a biologic designed to treat cocaine intoxication that is expected to start a Phase 2 trial in the first quarter of 2022.

[1]TNX-1800 is an investigational new biologic and has not been approved for any indication. TNX-1800 is based on TNX-801, live horsepox virus vaccine for percutaneous administration, which is in development to protect against smallpox and monkeypox. TNX-801 is an investigational new biologic and has not been approved for any indication.

[2]TNX-2100 is an investigational new biologic and has not been approved for any indication

[3]TNX-3500 is an investigational new drug at the pre-IND stage of development and has not been approved for any indication.

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

[5]TNX-1300 is an investigational new biologic and 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 development of TNX-2100; 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, 2020, as filed with the Securities and Exchange Commission (the "SEC") on March 15, 2021, 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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