December 14, 2021

Tonix Pharmaceuticals Announces IND Clearance for Skin Test (TNX-2100) to Measure SARS-CoV-2 Exposure and T Cell Immunity

First-in-Human Study Expected to be Initiated in the First Quarter of 2022

An Approved Test Would Lead to Identification of People Requiring Vaccine Boosters

CHATHAM, N.J., Dec. 14, 2021 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a clinical-stage biopharmaceutical company, today announced the U.S. Food and Drug Administration (FDA) has cleared the Investigational New Drug (IND) application to initiate a first-in-human clinical study for TNX-2100 (SARS-CoV-2 epitope peptide mixtures for intradermal administration), a 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 T cell immunity. Tonix expects to initiate the clinical study in the first quarter of 2022.

“When fully developed, our proposed skin test has the potential to provide clinicians, patients, employers and public health officials with important diagnostic, safety and predictive information, including the durability of immune responses in vaccinated, convalescent and exposed individuals,” stated Seth Lederman, M.D., President and Chief Executive Officer of Tonix. “One of the goals of clinical development of TNX-2100 will be to study the potential correlation of a positive skin test with protective immunity. A test that measures protective immunity could allow for a personalized approach to determining the need for vaccine boosters which would reduce costs as well as risks associated with unnecessary vaccinations. In contrast, a one-size-fits-all booster strategy would be relatively more expensive and likely unsustainable.”

T cell immunity to SARS-CoV-2 is believed to provide an important element of protection against serious COVID-19 illness after infection with SARS-CoV-2. T cell immunity persists longer than antibody immunity and is sometimes present in the absence of a measurable antibody response. For example, T cell immunity has been detected 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 would require 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 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.

Dr. Lederman continued, “While the pandemic continues with new waves of infection from novel variants, the surveillance of immunity to COVID-19 disease is important in managing public health. Many experts expect COVID-19 to become endemic, so the need for COVID-19 immunity and disease surveillance will be ongoing.”

In parallel to developing TNX-2100 as a potential diagnostic tool, Tonix is developing TNX-1800, a live virus vaccine for COVID-19 designed to elicit primarily T cell immunity. Tonix has completed positive immune response and challenge studies in non-human primates and expects to start a Phase 1 study in humans in the second half of 2022, based on the FDA written responses of a pre-IND meeting.

About TNX-2100

TNX-2100 is a diagnostic product candidate in the pre-Investigational New Drug (IND) stage 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 tests 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 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 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.*

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 primarily composed of immunology and central nervous system (CNS) product candidates. Tonix's immunology 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 Company'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[1] (cyclobenzaprine HCl sublingual tablets), is in mid-Phase 3 development for the management of fibromyalgia. TNX-1300[2] is a biologic designed to treat cocaine intoxication that is expected to start a Phase 2 trial before year end. Tonix's lead vaccine candidate for COVID-19, TNX-1800[3], 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 also developing TNX-2100[4], an *in vivo* diagnostic to measure the presence of functional T cell immunity to SARS-CoV-2 and intends to initiate a first-in-human clinical study in the first quarter of 2022. TNX-3500[5] (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 is a small molecule drug being developed to treat Long COVID, a chronic post-COVID condition, and is also in the pre-IND stage. Tonix expects to conduct a Phase 2 study in Long COVID in the first half of 2022. Tonix's immunology portfolio also includes biologics to address immunosuppression, cancer, and autoimmune diseases.

[1]*TNX-102 SL is an investigational new drug and has not been approved for any indication.*
[2]*TNX-1300 is an investigational new biologic at the pre-IND stage of development and has not been approved for any indication.*
[3]*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.*
[4]*TNX-2100 is an investigational new biologic and has not been approved for any indication*
[5]*TNX-3500 is an investigational new drug at the pre-IND stage of development 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, 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 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.

CONTACTS

Jessica Morris (corporate)
Tonix Pharmaceuticals
investor.relations@tonixpharma.com
(862) 904-8182

Olipriya Das, Ph.D. (media)
Russo Partners
Olipriya.Das@russopartnersllc.com
(646) 942-5588

Peter Vozzo (investors)
Westwicke, an ICR Company
peter.vozzo@westwicke.com
(443) 213-0505

Source: Tonix Pharmaceuticals Holding Corp.