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Tonix Pharmaceuticals Reports Positive Immune Response Results from COVID-19 Vaccine Candidate TNX-1800, Following Vaccination of Non-Human Primates

Anti-SARS-CoV-2 Neutralizing Antibodies Elicited in All Eight TNX-1800 Vaccinated Animals

Skin Reaction or "Take," a Validated Biomarker of Functional T cell Immunity, Elicited in All Eight TNX-1800 Vaccinated Animals

CHATHAM, N.J., Nov. 16, 2020 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a clinical-stage biopharmaceutical company, today announced preliminary results following vaccination of non-human primates with TNX-1800 (modified horsepox virus, live vaccine), a live attenuated COVID-19 vaccine candidate engineered to express the SARS-CoV-2 (CoV-2) spike protein after vaccination. The research is part of an ongoing collaboration between Southern Research Institute, the University of Alberta and Tonix.

"We are pleased that all eight animals vaccinated with TNX-1800 manifested "takes", a skin reaction which is a validated biomarker of functional T cell immunity, and that vaccination was associated with neutralizing antibodies in each case," said Seth Lederman, M.D., President and Chief Executive Officer of Tonix Pharmaceuticals. "'Take' has a long history as a validated biomarker for T cell immunity. 'Take' is important because it is otherwise difficult and costly to measure the T cell response to a vaccine. Vaccines that elicit a strong T cell response, like horsepox and closely related vaccinia, have been established to provide long-term, durable immunity and to block forward transmission. Single dose horsepox and vaccinia vaccination led to the eradication of smallpox, which, like CoV-2, is transmitted by the respiratory route. In the successful campaign to eradicate smallpox, 'take' was used as a biomarker for protective immunity."

Dr. Lederman continued, "Our hope and our goal is to produce a vaccine that will provide long term immunity with a single dose using a proven technology that can be readily scaled up for manufacturing and that does not require a costly and cumbersome cold chain for distribution and storage. These results encourage us to advance TNX-1800 to human Phase 1 trials in 2021, when we expect to have Good Manufacturing Practice, or cGMP, quality TNX-1800 available. We have previously announced that our manufacturing partner is FUJIFILM Diosynth Biotechnologies."

Key features and results:

- **STUDY DESIGN**: This on-going study of non-human primates compares TNX-1800 (modified horsepox virus encoding CoV-2 spike protein) to TNX-801 (horsepox virus, live vaccine) at two doses. A control group received a placebo. Each of these five groups (TNX-1800 high and low dose; TNX-801 high and low dose and placebo) includes four animals.
- **NEUTRALIZING ANTI-CoV-2 ANTIBODIES**: At day 14 after a single vaccination, all eight of the TNX-1800 vaccinated animals made anti-CoV-2 neutralizing antibodies (≥1:40 titer) and, as expected, none of the eight TNX-801 vaccinated control animals, or any of the four animals in the placebo group, made anti-CoV-2 neutralizing antibodies (≤1:10 titer). The level of neutralizing anti-CoV-2 antibody production was similar between the low and high dose TNX-1800 groups ((1 x 10^6 Plaque Forming Units [PFU]) and 3 x 10^6 PFU, respectively).
- **TOLERABILITY**:TNX-1800 and TNX-801 were well tolerated at both doses.
- **SKIN *TAKE* BIOMARKER**: Further, as an expected additional outcome, all 16 animals vaccinated with either dose of TNX-1800 or the control TNX-801 manifested a “take”, or cutaneous response, signaling that the horsepox vector elicited a strong T cell immune response.
- **DOSE:** These results support the expectation that TNX-1800 at the low dose of 1 x 10^6 PFU is an appropriate dose for a one-shot vaccine in humans, and indicate that 100 doses per vial is the target format for commercialization, which is suited to manufacturing and distribution at large scale.
- **CONCLUSIONS**: Together, these data show that TNX-1800 induces a strong immune response to CoV-2 in non-human primates. These data confirm that “take” is a biomarker of a strong immunological response to TNX-1800’s vector, horsepox virus vaccine, and also indicate that “take” is predictive of a neutralizing antibody response to TNX-1800’s cargo COVID-19 antigen, which is the CoV-2 spike protein.
- **NEXT PHASE**: In the second phase of the study, the TNX-1800 vaccinated and control animals will be challenged with CoV-2. Results are expected in the first quarter of 2021.

About TNX-1800

TNX-1800 is a live modified horsepox 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. Horsepox and vaccinia are closely related orthopoxviruses that are believed to share a common ancestor. Tonix’s TNX-1800 vaccine candidate is administered percutaneously using a two-pronged, or “bifurcated” needle. TNX-1800 is based on a horsepox vector, which is a live replicating, attenuated virus that elicits a strong immune response. The major cutaneous reaction or “take” to vaccinia vaccine was described by Dr. Edward Jenner in 1796 and has been used since then as a biomarker for protective immunity to smallpox, including in the World Health Organization’s (WHO) accelerated smallpox eradication program that successfully eradicated smallpox in the 1960’s. The “take” is a measure of functional T cell immunity validated by the eradication of smallpox, a respiratory-transmitted disease caused by variola. Tonix’s proprietary horsepox vector is believed to be more closely related to Jenner’s vaccinia vaccine than modern vaccinia vaccines, which appear to have evolved by deletions and mutations to a phenotype of larger

plaque size in tissue culture and greater virulence in mice. 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[1]. Horsepox-based vaccines are designed to be single dose, vial-sparing vaccines, that can be manufactured using conventional cell culture systems, with the potential for mass scale production and packaging in multi-dose vials.

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

About Southern Research

Founded in 1941, Southern Research (SR) is an independent, 501(c)(3) nonprofit, scientific research organization with more than 400 scientists and engineers working across three divisions: Drug Discovery, Drug Development, and Engineering. SR has supported the pharmaceutical, biotechnology, defense, aerospace, environmental, and energy industries. SR works on behalf of the National Institutes of Health, the U.S. Department of Defense, the U.S. Department of Energy, NASA and other major aerospace firms, utility companies, and other external academic, industry and government agencies. SR pursues entrepreneurial and collaborative initiatives to develop and maintain a pipeline of intellectual property and innovative technologies that positively impact real-world problems. SR has numerous ongoing drug discovery programs, which encompass drug discovery programs to combat various forms of cancer, Alzheimer's, schizophrenia, opioid use disorder, human immunodeficiency virus, disease, Parkinson's, tuberculosis, influenza, and others. SR's strong history, which includes over 75 years of successful collaborations to solve complex problems, has led to the discovery of seven FDA-approved cancer drugs—a number rivaling any other U.S. research institute. Furthermore, experts at SR are well-equipped to assist with the challenging landscapes of drug design and development technologies and market viability. SR is headquartered in Birmingham, Alabama with additional laboratories and offices in Frederick, Maryland.

Further information about SR can be found at https://southernresearch.org/

About Tonix Pharmaceuticals Holding Corp.

Tonix is a clinical-stage biopharmaceutical company focused on discovering, licensing, acquiring and developing small molecules and biologics to treat and prevent human disease and alleviate suffering. Tonix's portfolio is primarily composed of central nervous system (CNS) and immunology product candidates. The immunology portfolio includes vaccines to prevent infectious diseases and biologics to address immunosuppression, cancer and autoimmune diseases. The CNS portfolio includes both small molecules and biologics to treat pain, neurologic, psychiatric and addiction conditions. Tonix's lead vaccine candidate, TNX-1800*, is a live replicating vaccine based on the horsepox viral vector platform to protect against COVID-19, primarily by eliciting a T cell response. Tonix expects data from animal studies of TNX-1800 in the fourth quarter of this year and the first quarter of 2021. TNX-801*, live horsepox virus vaccine for percutaneous administration, is in development to

protect against smallpox and monkeypox.. Tonix is also developing TNX-2300* and TNX-2600*, live replicating vaccine candidates for the prevention of COVID-19 but using bovine parainfluenza as the vector. Tonix's lead CNS candidate, TNX-102 SL**, is in Phase 3 development for the management of fibromyalgia. The Company expects topline data in the Phase 3 RELIEF study in the fourth quarter of 2020. Tonix is also currently enrolling participants in the Phase 3 RALLY study for the management of fibromyalgia using TNX-102 SL, and the results are expected in second half of 2021. TNX-102 SL is also in development for PTSD, agitation in Alzheimer's disease (AAD) and alcohol use disorder (AUD). The PTSD program is in Phase 3 development, while AAD and AUD are Phase 2 ready The AAD program has FDA Fast Track designation. Tonix's programs for treating addiction conditions also include TNX-1300* (T172R/G173Q double-mutant cocaine esterase 200 mg, i.v. solution), which is in Phase 2 development for the treatment of life-threatening cocaine intoxication and has FDA Breakthrough Therapy designation. TNX-601 CR** (tianeptine oxalate controlled-release tablets) is another CNS program, currently in Phase 1 development as a daytime treatment for depression while TNX-1900**, intranasal oxytocin, is in development as a non-addictive treatment for migraine and cranio-facial pain. Tonix's preclinical pipeline includes TNX-1600** (triple reuptake inhibitor), a new molecular entity being developed as a treatment for PTSD; TNX-1500* (anti-CD154), a monoclonal antibody being developed to prevent and treat organ transplant rejection and autoimmune conditions; and TNX-1700* (rTFF2), a biologic being developed to treat gastric and pancreatic cancers.

*TNX-1800, TNX-801, TNX-2300, TNX-2600, TNX-1300, TNX-1500 and TNX-1700 are investigational new biologics and have not been approved for any indication.

**TNX-102 SL, TNX-601 CR, TNX-1600 and TNX-1900 are investigational new drugs and have 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 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, 2019, as filed with the Securities and Exchange Commission (the "SEC") on March 24, 2020, 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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