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# Tonix Pharmaceuticals Reports Positive COVID-19 Vaccine Efficacy Results in Non-Human Primates Vaccinated with TNX-1800 and Challenged with Live SARS-CoV-2

***Vaccine Candidate TNX-1800 Protected Both Upper and Lower Airways After Challenge with SARS-CoV-2, Suggesting an Ability to Block Forward Transmission***

***TNX-1800 is Based on a Proprietary Vaccine Platform Designed to Stimulate Long Term T cell Immunity***

CHATHAM, N.J., March 17, 2021 (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. Immunogenicity and protective efficacy of single-dose TNX-1800 were assessed at two dose levels (n=4 per group). At Day 41 after the vaccination, animals were challenged with live SARS-CoV-2 through intra-nasal and intra-tracheal routes. Protection was assessed at Day 47, six days after challenge. The research is part of an ongoing collaboration between Southern Research, the University of Alberta and Tonix.

“We are pleased that all eight animals vaccinated with TNX-1800 had undetectable SARS-CoV-2 in their upper and lower airways 6 days after challenge with SARS-CoV-2,” said Seth Lederman, M.D., President and Chief Executive Officer of Tonix Pharmaceuticals. “Today’s results are from the second phase of a study in which TNX-1800 vaccinated and control animals were challenged with SARS-CoV-2. Last Fall, we reported that all eight of animals vaccinated manifested ‘takes’, a skin reaction to horsepox vaccination which is a validated biomarker of functional T cell immunity, and that vaccination was associated with neutralizing antibodies in each case. The positive results of the protection from live CoV-2 challenge that we are reporting today validate the capacity for TNX-1800 to protect against COVID-19, and also validate the ‘take’ after TNX-1800 vaccination as a biomarker for functional T cell immunity.”

Dr. Lederman continued, “ ’Take‘ is considered 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. We believe the absence of detectable CoV-2 in the upper or lower airways shows the potential for TNX-1800 to decrease shedding of virus and is consistent with decreased transmission.”

“Although many successful vaccines have been put into use around the world, much remains unknown about COVID-19, its emerging variants, and the durability of current vaccines,” Dr. Lederman continued “We designed TNX-1800 as a single dose vaccine using a vector known to provide long term T cell immunity. This was originally demonstrated by the vector’s use as the backbone of Edward Jenner’s smallpox vaccine which typically provided lifetime immunity with a single dose. Moreover, by preventing forward transmission of the smallpox virus, it became a defining force in establishing herd immunity.Like Jenner’s smallpox vaccine, TNX-1800 can be scaled up for manufacturing and will not require a costly and cumbersome cold chain for distribution and storage. It will also be glass-sparing, with 100 doses filled per vial. These features, coupled with the results announced today, encourage us to advance TNX-1800 to human Phase 1 trials in the second half of 2021 when we expect to have Good Manufacturing Practice, or cGMP, quality TNX-1800 available.”

The Company believes the findings also demonstrate the flexibility of the horsepox vaccine platform and its capability to be tailored to other diseases of interest in military and civilian populations.

Key features and results:

- **STUDY DESIGN**: This study of non-human primates compared TNX-1800 (modified horsepox virus encoding CoV-2 spike protein) to TNX-801 (horsepox virus, live vaccine) at two doses. Also 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) included four animals.
- **CoV-2 CHALLENGE**: At day 41 after vaccination (or placebo), each animal was exposed to SARS-COV-2 by intra-tracheal ($1 \times 10^6$ $TCID_{50}$) and intra-nasal ($1 \times 10^6$ $TCID_{50}$) administration.
- **DETECTION OF SARS-COV-2 in Upper and Lower Airway**: Upper airway virus was studied by oropharyngeal swabs and lower airway virus by tracheal lavage using qRT-PCR to determine the number of genome copies of SARS-CoV-2 present in the samples. Six days after challenge, no (0/8) samples taken from animals vaccinated with TNX-1800 showed infection (more than 1,000 genome copies of SARS CoV-2) in either upper or lower airway samples. In contrast, all (8/8) animals vaccinated with the control vaccine TNX-801 showed infection in either the upper or lower airway samples as did all (4/4) monkeys vaccinated with vehicle control.
- **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). At 6 days after CoV-2 challenge, TNX-1800 vaccinated animals showed neutralizing antibody titers of (≥1:1280 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). For unvaccinated animals challenged with SARS-CoV-2, neutralizing antibodies were measurable after vaccination (≥1:40 titer) that were lower and appeared later than neutralizing antibodies in TNX-1800 vaccinated animals.

- **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 elicits 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 well suited to manufacturing and distribution at large scale.
- **CONCLUSIONS**: Together, these data show that TNX-1800 induces protection against SARS-COV-2 infection in non-human primates. These data confirm that "take" is a biomarker of protection of upper and lower airways from SARS-CoV-2 challenge, and a biomarker of immunological response to TNX-1800's cargo COVID-19 antigen, which is the CoV-2 spike protein.
- **NEXT PHASE**: Phase 1 human study targeted to start in the second half of 2021, following Investigational New Drug (IND) clearance by the U.S. Food and Drug Administration (FDA) and the production of GMP material.

Anthony Macaluso, Ph.D., Executive Vice President, Strategic Development at Tonix said, "In addition to their impact on the development of a COVID-19 vaccine, these data also demonstrate the utility of horsepox as a vaccine platform that can be used to address many other diseases of interest to the military and the general public. The horsepox platform has the following attributes favorable for vaccine development: strong induction of both B and T cell immunity; amenability to genetic modification; and the ability to express multiple genes, either alone or in combination. In addition, the horsepox vaccine platform allows for rapid scalability of manufacturing, which is a key advantage of the horsepox virus over other platforms such as non-replicating viruses, DNA/RNA, or protein subunit vaccines."

**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 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 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], is in mid-Phase 3 development for the management of fibromyalgia, and positive data on the RELIEF Phase 3 trial were recently reported. The Company expects interim data from a second Phase 3 study, RALLY, in the third quarter of 2021[2] and topline data in the fourth quarter of 2021. The immunology portfolio includes vaccines to prevent infectious diseases and biologics to address immunosuppression, cancer, and autoimmune diseases. Tonix's lead vaccine candidate, TNX-1800[3], 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 reported positive efficacy data from animal studies of TNX-1800 in the first quarter of 2021. TNX-801[3], live horsepox virus vaccine for percutaneous administration, is in development to protect against smallpox and monkeypox.

[1]TNX-102 SL is an investigational new drug and has not been approved for any indication.
[2]Pending submission and agreement from FDA on statistical analysis plan.
[3]TNX-1800 and TNX-801 are investigational new biologics 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, 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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