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Tonix Pharmaceuticals Announces Results of Pre-IND Meeting with FDA for TNX-801 as a Potential Vaccine to Prevent Mpox and Smallpox

Phase 1/2 Clinical Trial of TNX-801 for the Prevention of Mpox and Smallpox to Commence Following Submission of an IND

TNX-801 is Based on a Proprietary Live Virus Vaccine Platform Designed to Stimulate Durable T-Cell Immunity

TNX-801 Vaccination Protected Animals from a Lethal Challenge with Monkeypox in Preclinical Testing

CHATHAM, N.J., Aug. 21, 2023 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a biopharmaceutical company with marketed products and a pipeline of development candidates, today announced that it received the 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[1] (recombinant horsepox virus, live vaccine) as a potential vaccine to protect against mpox disease (formerly known as monkeypox) and smallpox. 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.

“The FDA’s response to the pre-IND meeting marks an important milestone in the development of TNX-801 since we have FDA concurrence on the proposed manufacturing, toxicology studies, and the Phase 1/2 clinical design,” said Seth Lederman, M.D., President and Chief Executive Officer of Tonix. “TNX-801 is believed to be closely related to Edward Jenner’s original smallpox vaccine.[2-10] Jenner’s live virus smallpox vaccine – the first vaccine - remains one of the most effective vaccines in history, since it typically provided lifetime immunity with a single dose, prevented forward transmission of the smallpox virus, and ultimately eradicated the disease. TNX-801 has an attenuated phenotype relative to modern vaccinia viruses, which comprise a group of vaccine viruses that evolved from Jenner’s vaccine during passage in man and animals for over 100 years. When live virus vaccinia vaccination was routinely practiced in Africa, mpox was kept out of the human population.”[2,11]

TNX-801 is a live replicating attenuated vaccine based on horsepox that is believed to protect against smallpox and mpox, primarily by eliciting a T-cell response evidenced by the

“take”. The “take” is a functional measure of protective T-cell immunity validated by the eradication of smallpox. TNX-801 is administered with a single dose, can be readily scaled up for manufacturing using proven technology and can be distributed and stored without requiring a costly and cumbersome ultra-cold supply chain. Live replicating vaccines have the potential to induce durable T-cell immunity, prevent serious illness after infection and block forward transmission. Tonix reported positive preclinical efficacy data, demonstrating that TNX-801 vaccination protected non-human primates against lethal challenge with mpox.[12]

“More than 30,000 people have contracted mpox in the U.S. so far during the 2022-23 epidemic,”[13] said Dr. Zeil Rosenberg, Executive Vice President, Medical at Tonix. “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.[14] In contrast, TNX-801 is delivered intradermally 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 vaccine to meet global health needs, especially in Africa.”

Dr. Rosenberg added, “We believe TNX-801 could make a global impact on mpox and the risk of smallpox because of its potential durable T-cell immune response, the ability to manufacture at scale, to use a lower dose than non-replicating vaccines. The current formulation is a frozen liquid, but we believe that future lyophilized versions can be stored and shipped at standard refrigeration. Moreover, we believe the low dose of TNX-801 makes this technology amenable for future implementation in microneedle delivery systems.”

Dr. Lederman concluded, “In addition to its potential use as a vaccine, TNX-801 also has the potential as a viral vector platform, for which versions can be developed to protect against a host of infectious diseases beyond smallpox and mpox, including COVID-19. In light of the recent resurgence in COVID cases across the country with the new EG.5 “Eris” variant, we believe that the horsepox recombinant pox virus platform may provide next generation vaccines to prevent future outbreaks.”

About TNX-801*

TNX-801 is a live virus vaccine based on horsepox[2,11]. Horsepox and vaccinia are closely related orthopoxviruses that are believed to share a common ancestor. TNX-801 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. Molecular analysis shows that horsepox is closer than modern vaccinia vaccines in DNA sequence to the vaccine discovered and disseminated by Dr. Edward Jenner.[2-10] Vaccine genome researchers have recently shown the contemporaneous use of horsepox and horsepox-related viruses in the United States as smallpox vaccines in the 1860’s[9,10]. Additionally they found a remarkable degree of identity with the circa 1860 U.S. smallpox vaccine VK05 and the 1976 Mongolian horsepox isolate called MNR-76, upon which Tonix’s TNX-801 is based.[3,5] These recent discoveries are further steps in establishing that what is called ’horsepox‘ today was used to vaccinate against smallpox in the 19th century. Dr. Edward Jenner invented vaccination in 1798 and the procedure was called “vaccination” because the inoculum material was initially obtained

from lesions on the udders of cows affected by a mild disease known as cowpox[2]. 'Cow' is 'vacca' in Latin. However, Dr. Jenner suspected that cowpox originated from horsepox.[2] Subsequently, Dr. Jenner and others immunized against smallpox using material directly obtained from horses. The use of vaccines from horses was sometimes called 'equination' from the Latin 'equus' which means 'horse'. Equination and vaccination were practiced side-by-side in Europe[6]. The small plaque size in culture of TNX-801 appears identical to the U.S. Centers for Disease Control publication of the natural isolate[12]. Relative to vaccinia, horsepox has substantially decreased virulence in mice[3]. Tonix's TNX-801 vaccine candidate is administered intradermally. 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.

1. TNX-801 is in the pre-IND stage and has not been approved for any indication.

2. 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.
3. Noyce RS, et al. (2018) *PLoS One*. 13(1):e0188453
4. Schrick L, et al. (2017) *N Engl J Med* 377:1491-1492
5. Tulman ER, et al. (2006) J Virol. 80(18):9244-58.
6. Esparza J, et al. (2017) *Vaccine*. 35(52):7222-7230.
7. Esparza J, et al. (2020) *Vaccine*. 38(30):4773-4779.
8. Qin L, et al. (2015) *J Virol*. 89(3):1809-24.
9. Brinkmann A, et al, (2020) *Genome Biology* 21:286
10. Duggan A, et al. (2020) *Genome Biology* 21:175 https://doi.org/10.1186/s13059-020-02079-z
11. Noyce RS, et al., (2023) *Viruses.* 15(2):356.
12. Trindade GS, et al. (2016) *Viruses.* 8(12):328.
13. McQuiston JH, et al. (2023) The CDC Domestic Mpox Response — United States, 2022–2023. *MMWR Morb Mortal Wkly Rep.* 72(20):547–552
14. Faherty EAG, et al.(2023) Emergence of an mpox cluster primarily affecting persons previously vaccinated against mpox-Chicago, Illinois, March 18-June 12, 2023. *MMWR Morb Mortal Wkly Rep.* , 72(25);696-698.

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 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 the fourth quarter of 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 are expected in the third quarter of 2023. TNX-601 ER (tianeptine hemioxalate extended-release tablets) is a once-daily oral formulation being developed as a treatment for major depressive disorder (MDD), that completed enrollment in a Phase 2 proof-of-concept study in the third quarter of 2023, with topline results expected in the fourth quarter of 2023. TNX-4300 (estianeptine) is a single isomer version of TNX-601, small molecule oral therapeutic in preclinical development to treat MDD, Alzheimer's disease and Parkinson's disease. Relative to tianeptine, estianeptine lacks activity on the μ-opioid receptor while maintaining activity in the rat Novel Object Recognition test *in vivo* and the ability to activate PPAR-β/δ and neuroplasticity in tissue culture. TNX-1900 (intranasal potentiated oxytocin), is in development for preventing headaches in chronic migraine, and has completed enrollment in a Phase 2 proof-of-concept study with topline data expected in the fourth quarter of 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 third 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. 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.

Tonix Medicines has contracted to acquire the Zembrace SymTouch and Tosymra registered trademarks. Intravail is a registered trademark of Aegis Therapeutics, LLC, a wholly owned subsidiary of Neurelis, Inc.

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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