September 9, 2024

Tonix Pharmaceuticals Presented Data on the Potential Mpox Vaccine TNX-801 in "Using Synthetic Biology to Battle Mpox" Talk at Immunology Symposium at the University of Alberta

TNX-801 vaccination demonstrated efficacy in protecting animals from lethal challenge with clade I monkeypox and is in development as an mpox vaccine

New data show improved tolerability in immunocompromised animals and no evidence of spreading to blood or tissues even at high doses

Tonix's synthetic horsepox vaccine platform has been selected by NIH's Project NextGen for clinical testing

CHATHAM, N.J., Sept. 09, 2024 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a fully-integrated biopharmaceutical company with marketed products and a pipeline of development candidates, today announced data presented at a symposium hosted by the Department of Medical Microbiology & Immunology and the Li Ka Shing Institute of Virology to celebrate the career and honor the retirement of Tonix's collaborator, David Evans, Ph.D., FCAHS, Emeritus Professor, Department of Cell Biology, University of Alberta. A copy of the Company's presentation is available under the Scientific Presentations tab of the Tonix website at www.tonixpharma.com.

The presentation titled, "*Using Synthetic Biology to Battle Mpox*", detailed the Company's vaccine platform, led by TNX-801 (horsepox, live virus vaccine for percutaneous administration) for preventing mpox (formerly known as monkeypox). TNX-801 is an attenuated live-virus vaccine based on synthesized horsepox that has been shown to provide single-dose immune protection against a monkeypox challenge with better tolerability than 20th century vaccinia live-virus vaccines in animals.

TNX-801 is structurally closer to 19th century live-virus vaccinia vaccines than 20th century versions.[1-3] Genomic sequencing of archaic smallpox vaccines has shown that vaccines used prior to 1900 would be called 'horsepox' today.[1-3] While effective against smallpox as single-dose vaccines, 20th century vaccines have diverged from horsepox-like progenitors to have greater virulence and toxicity than TNX-801 in animals. The U.S. Food and Drug Administration (FDA) recently approved ACAM2000® from Emergent Technologies for preventing mpox.[4] ACAM200 is a live-virus vaccine derived from a 20th Century vaccinia

vaccine. ACAM2000 carries a Black Box warning on its package insert labeling warning of tolerability issues, including myocarditis and pericarditis, encephalitis, encephalomyelitis, encephalopathy, progressive vaccinia, generalized vaccinia, severe vaccinial skin infections, erythema multiforme major, eczema vaccinatum resulting in permanent sequelae or death, and risks in certain individuals that may result in severe disability, permanent neurological sequelae and/or death.[5]

The Jynneos® vaccine from Bavarian Nordic is a non-replicating vaccinia vaccine that is FDA-approved for mpox with a two-dose regimen requiring sterile injection.[6] Single-dose TNX-801 has advantages over non-replicating vaccinia vaccines which require two doses. Percutaneous TNX-801 has advantages over vaccines which require sterile injection.

The durability of protection from 19th century live-virus vaccinia vaccines was believed to last decades or even be live-long. Consequently, single-dose TNX-801 is believed to stimulate long-lived T cell immunity. Consequently, TNX-801 will not require multiple repeated doses at six-month intervals like mRNA vaccines.[7] Also, the stability of live-virus vaccines, particularly in lyophilized form, eliminates the need for ultra-cold storage which complicates the widespread use of mRNA vaccines in Africa, where they are needed most right now.

Tonix's focus on single-dose vaccines adheres to recommendations by the Bipartisan Commission on Biodefense[8], and the U.S. National Academies of Science (NAS).[9] For example, the NAS report highlights the difficulty of a case-contact or "ring" vaccination strategy with even a two-dose regimen.[9]

In the presentation, Tonix highlighted positive preclinical efficacy data, demonstrating that TNX-801 protected animals against lethal challenge with intratracheal clade I monkeypox virus.[10] An outbreak of Clade I mpox has recently been declared a Public Health Emergency of International Concern (PHEIC) by the World Health Organization (WHO).[11,12] Starting from an outbreak in the Democratic Republic of the Congo, clade I mpox has spread to several Central African Countries and cases have been reported in Sweden, Thailand and Singapore. According to the U.S. Centers for Disease Control and Prevention (CDC), and other experts, there is a significant risk that clade I strain may appear in the U.S.[13] Clade I mpox is typically associated with higher case fatality rates than clade II mpox.

After a single dose vaccination, TNX-801 prevented clinical disease and lesions and also decreased shedding in the mouth and lungs of animals challenged with clade I monkeypox.[10] These findings are consistent with TNX-801 inducing mucosal immunity and suggest TNX-801 has the ability to block forward transmission, similar to Dr. Edward Jenner's vaccinia vaccine, descendants of which eradicated smallpox and kept mpox out of the human population.

The presentation at University of Alberta included results from Tonix scientists at the Research and Development Center (RDC) in Frederick, Md. Data from a manuscript showed that TNX-801 is highly attenuated relative to 20th century vaccinia vaccines in in immunocompromised animals.[14] New data showed TNX-801 is unable to spread in blood or tissues in these animals, even at an approximately 100-Fold higher dose than 20th century vaccinia vaccines.

In addition to characterizing TNX-801's activity and tolerability, Tonix scientists have explored the characteristics of the monkeypox virus. The prior 2022 global clade IIb mpox outbreak, affected over 90,000 persons in countries where mpox previously had not been endemic, including Europe and the US. The spread of clade IIb strain mpox in 2022 underscores the pandemic potential of mpox. Data presented show that monkeypox clade IIb from a 2022 isolate in Massachusetts is 10,000- to 100,000-fold more attenuated than clade IIa isolates from 2003. The attenuation of clade II monkeypox in the recent 2022 outbreak may have contributed to its greater dissemination. The new and more lethal clade I monkeypox has not yet been analyzed.

"We are excited to develop TNX-801 to prevent mpox and control mpox epidemics," said Seth Lederman, M.D., Chief Executive Officer of Tonix. "TNX-801 has conferred protective immunity to animals with single-dose administration. We believe TNX-801 can be manufactured at scale economically with standard shipping and storing requirements. Evidenced by the second WHO declared PHEIC involving an mpox epidemic since 2022, viral diseases are rapidly evolving and our methods to developing effective vaccines must evolve just as rapidly. Synthetic biology is an important technology for vaccine development. We believe the potential of TNX-801 is supported by real world evidence based on the success of horsepox-like vaccines prior to 1900 in protecting against smallpox and containing smallpox outbreaks. When smallpox vaccination with live-virus vaccinia vaccines was employed in Africa prior to eradication, mpox was kept out of the human population."

Dr. Lederman continued, "We recently announced a collaboration to develop GMP manufacturing processes for TNX-801 with Bilthoven Biologics (Bbio), part of the world's largest vaccine manufacturer, the Cyrus Poonawalla Group, which also includes the Serum Institute of India. In addition, TNX-801 has the potential to be used as a viral vector platform, for which recombinant versions, like TNX-1800 for COVID-19[11,12], can be developed to protect against other infectious diseases that may emerge from this ever-evolving viral landscape. We are excited for TNX-1800's inclusion into the U.S. National Institute of Health's (NIH's) Project NextGen."

About TNX-801*

TNX-801 is a live replicating attenuated vaccine based on horsepox that is believed to provide immune protection with better tolerability than 20th century vaccinia viruses. As previously disclosed, TNX-801 protected animals against lethal challenge with intratracheal clade I monkeypox virus.[10] After a single dose vaccination, TNX-801 prevented clinical disease and lesions and also decreased shedding in the mouth and lungs of non-human primates.[10] The Findings are consistent with mucosal immunity and suggest the ability to block forward transmission, similar to Dr. Edward Jenner's vaccinia vaccine, which eradicated smallpox and kept mpox out of the human population. On August 26, 2024, Tonix announced a collaboration to develop GMP manufacturing processes for its mpox vaccine with Bilthoven Biologics (Bbio), part of the world's largest vaccine manufacturer, the Cyrus Poonawalla Group, which also includes the Serum Institute of India.

On the horsepox platform, Tonix is developing TNX-1800 (horsepox expressing SARS-CoV-2 spike protein) for protecting against COVID-19. TNX-1800 is an engineered version of horsepox that expresses the spike protein of SARS-CoV-2. In preclinical studies of TNX-1800 highlighted in the presentation, TNX-1800 was tested for immunogenicity and efficacy

of TNX-1800 in nonhuman primates following a SARS CoV-2 challenge.[14,15] TNX-1800 vaccination results in a neutralizing antibody response that was associated with significant reduction in virus replication/shedding in the respiratory tract and tolerability. [11,12] TNX-1800 was selected by the NIH's, Project NextGen for inclusion in clinical trials as part of a select group of next generation COVID-19 vaccine candidates with the intent to identify promising vaccine platforms. NIH plans to conduct a Phase 1 trial of TNX-1800 and cover the full cost of the study, while Tonix provides the vaccine candidate.

About Mpox*

On August 14, 2024, the WHO determined that the upsurge of mpox in a growing number of countries in Africa constitutes a public health emergency of international concern, the second such declaration in the past two years called in response to an mpox outbreak. The current outbreak was caused by clade I monkeypox virus, while the 2022 outbreak was clade II monkeypox virus. The global mpox outbreak, which commenced in 2022 has affected over 90,000 persons in countries where mpox had previously not been endemic, including Europe and the US. The spread of clade IIb strain mpox in 2022 underscores the pandemic potential of mpox. Unlike clade IIb mpox, the clade I strain of mpox appears to be spreading to countries neighboring the Democratic Republic of the Congo. Clade I mpox is typically associated with approximately twenty times the case fatality rates than Clade IIb mpox in Africa. According to the U.S. Centers for Disease Control and Prevention (CDC), and other experts, there is a significant risk that the deadlier clade I strain may appear in the U.S.[13]

Tonix Pharmaceuticals Holding Corp.*

Tonix is a fully-integrated biopharmaceutical company focused on developing, licensing and commercializing therapeutics to treat and prevent human disease and alleviate suffering. Tonix recently announced the U.S. Department of Defense (DoD), Defense Threat Reduction Agency (DTRA) awarded it a contract for up to $34 million over five years to develop TNX-4200 small molecule broad-spectrum antiviral agents targeting CD45 for the prevention or treatment of infections to improve the medical readiness of military personnel in biological threat environments. Tonix owns and operates a state-of-the art infectious disease research facility in Frederick, MD. The company's Good Manufacturing Practice (GMP)-capable advanced manufacturing facility in Dartmouth, MA was purpose-built to manufacture TNX-801 and the GMP suites are ready to be reactivated in case of a national or international emergency. Tonix's development portfolio is focused on central nervous system (CNS) disorders. Tonix's priority is to submit a New Drug Application (NDA) to the FDA in the second half of 2024 for TNX-102 SL, a product candidate for which two statistically significant Phase 3 studies have been completed for the management of fibromyalgia. The FDA has granted Fast Track designation to TNX-102 SL for the management of fibromyalgia. TNX-102 SL is also being developed to treat acute stress reaction. Tonix's CNS portfolio includes TNX-1300 (cocaine esterase), a biologic in Phase 2 development, designed to treat cocaine intoxication that has Breakthrough Therapy designation. Tonix's immunology development portfolio consists of 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. Tonix also has product candidates in development in the areas of rare disease and infectious disease, including a vaccine for mpox, TNX-801. Tonix Medicines, our commercial

subsidiary, markets Zembrace® SymTouch® (sumatriptan injection) 3 mg and Tosymra® (sumatriptan nasal spray) 10 mg for the treatment of acute migraine with or without aura in adults.

*Tonix's product development candidates are investigational new drugs or biologics and have not been approved for any indication.

This press release and further information about Tonix can be found at www.tonixpharma.com.

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[2]Brinkmann A, et al. Genome Biol. 2020;21(1):286.

[4]August 30, 2024. Reuters. "US FDA approves Emergent's smallpox vaccine for people at high risk of mpox". https://www.msn.com/en-us/health/other/us-fda-approves-emergent-s-smallpox-vaccine-for-people-at-high-risk-of-mpox/

[5]FDA Package insert ACAM2000, https://www.fda.gov/media/75792

[6]Zaeck LM, et al. Low levels of monkeypox virus-neutralizing antibodies after MVA-BN vaccination in healthy individuals. Nat Med. 2023 Jan;29(1):270-278. doi: 10.1038/s41591-022-02090-w. Epub 2022 Oct 18. PMID: 36257333; PMCID: PMC9873555.

[7]Mucker et al., (in press) Comparison of protection against mpox following mRNA or modified vaccinia Ankara vaccination in nonhuman primates, Cell (2024), https://doi.org/10.1016/j.cell.2024.08.043

[8]Bipartisan Commission on Biodefense. Box the Pox: Reducing the risk of Smallpox and Other Ortho poxviruses, Washington:2024

[9]U.S. National Academies of Science. Future State of Smallpox Medical Countermeasures. Washington:2024

[10]Noyce RS, et al. *Viruses*. 2023 Jan 26;15(2):356. Doi: 10.3390/v15020356. PMID: 36851570; PMCID: PMC9965234

[11]WHO Press Release August 14, 2024. "WHO Director-General declares mpox outbreak a public health emergency of international concern". URL: www.who.int/news/item/14-08-2024-who-director-general-declares-mpox-outbreak-a-public-health-emergency-of-international-concern (accessed 8-15-24)

[12]McQuiston JH, et al. *U.S. Preparedness and Response to Increasing Clade I Mpox Cases in the Democratic Republic of the Congo*. 2024, MMWR Morbi Mortal Wkly Rep: United States. p. 435-440

[13]CDC. 2022-2023 Mpox: US Map and Case Count. https://www.cdc.gov/poxvirus/mpox/response/2022/us-map.html

[14]Trefry, SV et al. bioRxiv 2023.10.25.564033; doi: https://doi.org/10.1101/2023.10.25.564033

[15]Awasthi M, et al. *Viruses*. 2023 Oct 21;15(10):2131. Doi: 10.3390/v15102131. PMID: 37896908; PMCID: PMC10612059.

[16]Awasthi M et al *Vaccines* (Basel). 2023 Nov 2;11(11):1682. Doi: 10.3390/vaccines11111682.PMID: 38006014

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, 2023, as filed with the Securities and Exchange Commission (the “SEC”) on April 1, 2024, 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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