August 16, 2024

Tonix Pharmaceuticals Provides Update on the Development of Its Single Dose Live Attenuated Virus Vaccine Candidate for Mpox, TNX-801, as WHO Declares Mpox Outbreak a Global Health Emergency

World Health Organization (WHO) has declared spread of mpox in multiple African countries a public health emergency of international concern (PHEIC) [1]

Tonix's live virus vaccine candidate, TNX-801, is designed to provide long-term protection from mpox and smallpox with one dose

TNX-801 vaccination demonstrated efficacy in protecting animals from lethal challenge with intratracheal monkeypox virus

Clade II mpox is now endemic in the U.S. with >30,000 cases reported since May 2022 [2] and Clade I mpox is endemic in the Democratic Republic of the Congo [3]

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

CHATHAM, N.J., Aug. 16, 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, has reiterated its commitment to advance development of its live attenuated virus vaccine, TNX-801 (recombinant horsepox virus), for preventing mpox (formerly known as monkeypox) and other infectious diseases. On August 14, 2024, the World Health Organization (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 1 monkeypox virus, while the 2022 outbreak was Clade 2 monkeypox virus.

TNX-801 is a live replicating attenuated vaccine candidate based on horsepox that is believed to provide immune protection with better tolerability than 20th century vaccinia viruses. The same vaccine platform upon which TNX-801 is based was selected by the U.S. National Institutes of Health (NIH) for Project NextGen for an engineered version that expresses the spike protein of SARS-CoV-2.

As previously disclosed, TNX-801 protected animals against lethal challenge with intratracheal Clade 1 monkeypox virus[4]. 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[4]. These 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.

"The recent WHO declaration underscores the urgent need for additional treatments to stop these outbreaks and save lives," said Seth Lederman, M.D., Chief Executive Officer of Tonix. "We are motivated to advance development for our mpox vaccine with urgency given the global public health emergency. Preclinical trials demonstrate that TNX-801 combines immune protection with improved tolerability and safety compared to other vaccines based on orthopoxviruses, and is administered with a single dose which has advantages over two-dose regimens. The durability of protection from 19th century live virus vaccinia vaccines suggests that our attenuated TNX-801 will not require multiple repeated doses at six-month intervals like mRNA vaccines. Also, the stability of live virus vaccines eliminates the need for ultra-cold storage which complicates the widespread use of mRNA vaccines in Africa, where they are needed most right now."

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 U.S. 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 20 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.[2,8]

Further, the Bipartisan Commission on Biodefense recently highlighted the renewed dual threats of a more virulent mpox epidemic and a smallpox re-introduction from lab accidents or bad actors[9]. The National Academies of Science, in its review of smallpox preparedness, highlighted the need for new single dose vaccines, like TNX-801 against smallpox[10].

About TNX-801* and Tonix's RPV Platform

TNX-801 (recombinant horsepox virus) is a live virus vaccine for percutaneous administration that is being developed to target smallpox, and mpox (monkeypox). TNX-801 is also the basis of the RPV platform based on a horsepox vector, which is being adapted as a COVID-19 vaccine, term TNX-1800*. Horsepox is a live replicating, attenuated virus that has been shown to be >1,000-fold more attenuated than 20th century vaccinia (VACV) strains in immunocompromised mice. Horsepox and the vaccinia vaccine viruses are closely related orthopoxviruses that are believed to share a common ancestor. Molecular analysis shows that horsepox is closer than modern vaccinia vaccines in DNA sequence to the vaccine discovered and disseminated by Dr. Edward Jenner. 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.

The current formulation is a frozen liquid, but we believe that future lyophilized versions can be stored and shipped at standard refrigeration. Horsepox-based vaccines are designed to be single dose, vial-sparing vaccines that can be administered without sterile injection, manufactured using conventional cell culture systems with the potential for mass scale production, and packaged in multi-dose vials.

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 in an Other Transaction Agreement (OTA) 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 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. 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.

[1]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)

[2]McQuiston JH, et al. *U.S. Preparedness and Response to Increasing Clade I Mpox Cases*

in the Democratic Republic of the Congo. 2024, MMWR Morb Mortal Wkly Rep: United States. p. 435-440

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

[4]Noyce RS, et al. *Viruses*. 2023 Jan 26;15(2):356. doi: 10.3390/v15020356

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

[6]Awasthi M, et al. *Viruses*. 2023 Oct 21;15(10):2131. doi: 10.3390/v15102131.

[7]Awashti M et al *Vaccines* (Basel). 2023 Nov 2;11(11):1682. doi:10.3390/vaccines11111682.

[8]World Health Organization SAGE meeting highlights on updated mpox vaccine recommendations. 2024, March

[9]Bipartisan Commission on Biofense. Box the Pox: Reducing the risk of Smallpox and Other Orthopoxviruses, Washington: 2024

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

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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