UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of report (date of earliest event reported): October 19, 2023

TONIX PHARMACEUTICALS HOLDING CORP.

(Exact name of registrant as specified in its charter)

Nevada	**001-36019**	**26-1434750**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

26 Main Street, Chatham, New Jersey 07928
(Address of principal executive offices) (Zip Code)

Registrant's telephone number, including area code: (862) 904-8182

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock	TNXP	The NASDAQ Capital Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On October 19, 2023, Tonix Pharmaceuticals Holding Corp. (the "Company") announced that it presented data on its horsepox-based live virus vaccine platform in an oral presentation at the World Vaccine Congress Europe ("WVC") being held October 16 to 19, 2023.. A copy of the press release which discusses this matter is furnished hereto as Exhibit 99.01, and incorporated herein by reference. A copy of the presentation is furnished hereto as Exhibit 99.02, and incorporated herein by reference.

The information in this Item 7.01 of this Current Report on Form 8-K, including Exhibits 99.01 and 99.02 attached hereto, shall not be deemed "filed" for purposes of Section 18 of the United States Securities Exchange Act of 1934 (the "Exchange Act") or otherwise subject to the liabilities of that section, nor shall they be deemed incorporated by reference in any filing under the United States Securities Act of 1933 or the Exchange Act, except as shall be expressly set forth by specific reference in such a filing.

Item 8.01. Other Events.

On October 19, 2023, the Company announced that it presented data an on its horsepox-based live virus vaccine platform in an oral presentation at the WVC. The presentation, entitled, "A Novel Mpox Vaccine (Horsepox virus) to Enhance Preparedness and Vaccine Equity," includes recent preclinical data that indicate that the Company's TNX-801 vaccine platform is naturally attenuated and potentially safer than the vaccines utilized to eradicate smallpox. TNX-801 was found to be up to 100-fold more attenuated than modern vaccinia vaccine viruses in primary human cell lines derived from dermal and respiratory tract cells, which are the two main poxvirus routes of entry and transmission of the smallpox virus, and more than 1,000-fold attenuated relative to modern vaccinia vaccine viruses in an immunocompromised murine model with targeted knock-outs of the IFN-α and/or IFN-γ receptors. In these mice, TNX-801 did not cause any observable clinical disease, and in most measured parameters (disease score, body temperature, weight loss, and survival), the TNX-801 infected mice were indistinguishable from the uninfected mice. The Company believes that these data suggest that TNX-801 potentially should be a safer vaccine in immunocompromised populations than many vaccinia virus-based vaccines.

Forward- Looking Statements

This Current Report on Form 8-K contains certain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934 and Private Securities Litigation Reform Act, as amended, including those relating to the Company's product development, clinical trials, clinical and regulatory timelines, market opportunity, competitive position, possible or assumed future results of operations, business strategies, potential growth opportunities and other statement that are predictive in nature. These forward-looking statements are based on current expectations, estimates, forecasts and projections about the industry and markets in which we operate and management's current beliefs and assumptions.

These statements may be identified by the use of forward-looking expressions, including, but not limited to, “expect,” “anticipate,” “intend,” “plan,” “believe,” “estimate,” “potential,” “predict,” “project,” “should,” “would” and similar expressions and the negatives of those terms. These statements relate to future events or our financial performance and involve known and unknown risks, uncertainties, and other factors which may cause actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Such factors include those set forth in the Company’s filings with the SEC. Prospective investors are cautioned not to place undue reliance on such forward-looking statements, which speak only as of the date of this press release. The Company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise.

Item 9.01 Financial Statements and Exhibits.

(d)

Exhibit No.	Description.
99.01	Press release of the Company, dated October 19, 2023
99.02	A Novel Mpox Vaccine (Horsepox virus) to Enhance Preparedness and Vaccine Equity
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURE

Pursuant to the requirement of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

TONIX PHARMACEUTICALS HOLDING CORP.

Date: October 19, 2023

By: /s/ Bradley Saenger
Bradley Saenger
Chief Financial Officer

Exhibit 99.01

Tonix Pharmaceuticals Presents Data from its Horsepox-Based Vaccine Development Platform at the World Vaccine Congress Europe

Preclinical Data Demonstrate Attenuation of TNX-801 (horsepox live virus vaccine) Compared to Modern Vaccinia Vaccines

TNX-801 is in Preclinical Development as a Novel Vaccine to Protect Against Smallpox and Mpox

CHATHAM, N.J., October 19, 2023 (GLOBE NEWSWIRE) – Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP), a biopharmaceutical company with marketed products and a pipeline of development candidates, presented data on its horsepox-based live virus vaccine platform in an oral presentation at the World Vaccine Congress Europe being held in Barcelona, Spain, October 16-19, 2023. A copy of the Company's presentation is available under the Scientific Presentations tab of the Tonix website at www.tonixpharma.com.

"Tonix's horsepox-based live virus vaccine platform is designed to help protect against emerging infectious diseases by engaging T cell responses, which have the potential to provide durable protection and block forward transmission," said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals. "In addition, we believe horsepox-based vaccines can be widely deployed without the need for sterile injection or ultra-cold shipping and storage. Our lead vaccine candidate, TNX-801[1], is in development to protect against Mpox (monkeypox) and smallpox. Tonix's TNX-801 is based on the sequence of a natural field isolate.[2,3] Molecular analysis suggests that TNX-801 is closer than modern smallpox vaccines to the vaccine discovered and disseminated by Dr. Edward Jenner in 1798[4-6]. Archaic smallpox vaccines based on horsepox were used in the U.S. and Europe to successfully control smallpox in the Nineteenth Century."[4,7-9]

The presentation, titled, "*A Novel Mpox Vaccine (Horsepox virus) to Enhance Preparedness and Vaccine Equity*," includes recent preclinical data that indicate that the TNX-801 platform is naturally attenuated and potentially safer than the vaccines utilized to eradicate smallpox.

"TNX-801 was found to be up to 100-fold more attenuated than modern vaccinia vaccine viruses in primary human cell lines derived from dermal and respiratory tract cells, which are the two main poxvirus routes of entry and transmission," said Zeil Rosenberg, M.D., M.P.H., Executive Vice President, Medical. "TNX-801 was also found to be more than 1,000-fold attenuated relative to modern vaccinia vaccine viruses ("VACV") in an immunocompromised murine model with targeted knock-outs of the IFN-α and/or IFN-γ receptors. In these mice, TNX-801 did not cause any observable clinical disease, and in most measured parameters (disease score, body temperature, weight loss, and survival), the TNX-801 infected mice were indistinguishable from the uninfected mice. Together, these data suggest that TNX-801 potentially should be a safer vaccine in immunocompromised populations than many VACV-based vaccines."

Dr. Rosenberg added, "A new attenuated live-virus smallpox and Mpox vaccine has the potential to enhance vaccine equity and preparedness in the event of a global emergency.

About TNX-801

TNX-801 is a live virus vaccine based on horsepox[2,3]. Tonix is developing TNX-801 for percutaneous administration as a vaccine to protect against Mpox and smallpox. Tonix's TNX-801 is based on the sequence of the 1976 natural isolate Mongolian horsepox clone MNR-76.[2,3] Molecular analysis of DNA sequences suggests that TNX-801 is closer than modern smallpox vaccines to the vaccine discovered and disseminated by Dr. Edward Jenner in 1798[4-6]. For example, recent studies[7,8] have shown approximately 99.7% colinear identity between TNX-801 and the circa 1860 U.S. smallpox vaccine VK05.[9] The small plaque size in the culture of TNX-801 appears identical to the U.S. Centers for Disease Control publication of the natural isolate[10]. Relative to vaccinia, horsepox has substantially decreased virulence in mice[2]. Dr. Edward Jenner invented vaccination in 1798 and the procedure was called "vaccination" because 'cow' is 'vacca' in Latin and the inoculum material was initially obtained from lesions on the udders of cows affected by a mild disease known as cowpox. However, Dr. Jenner suspected that cowpox originated from horses[6]. 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'[11]. Equination and vaccination were practiced side-by-side in Europe[11,12]. Tonix received an 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 as a potential vaccine to protect against Mpox disease 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.

About the Recombinant Pox Virus (RPV) Platform

Horsepox virus and vaccines based on its use as a vector are live replicating viruses that elicit strong immune responses. Live replicating orthopoxviruses, like vaccinia or horsepox, can be engineered to express foreign genes and have been exploited 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) manufacturable at scale, and (7) ability to provide direct antigen presentation. 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. Tonix's TNX-801 and RPV vaccine candidates are administered percutaneously using a two-pronged, or "bifurcated" needle, and are amendable to microneedle technology. The major cutaneous reaction or "take" to the 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.

About Mpox and Smallpox

Mpox[13] and smallpox[14] are diseases in humans caused by the Mpox and smallpox (or variola) viruses, respectively. Mpox and variola are closely related orthopox viruses. Vaccination against smallpox with live virus vaccines based on horsepox or vaccinia protects against Mpox. After routine smallpox vaccination was stopped in about 1970, Mpox has become a growing problem in Africa. Since May of 2022, approximately 30,000 cases have been identified in the United States[15,16]. There are two distinct clades of the Mpox virus: the central African (Congo Basin) clade, and the West African clade which is associated with the recent outbreak. Historically, the Congo Basin clade has caused more severe disease than the West African clade. In recent times, the case fatality ratio for the virus is about 3–6%[17]. In November 2022, the WHO began using a new preferred term "Mpox" as a synonym for monkeypox[18]. Smallpox is considered eradicated, but there are concerns about malicious reintroduction.

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, LLC 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[19] 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 late December 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 were reported 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 early November of 2023. TNX-4300 (estianeptine) is a single isomer version of TNX-601, a 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 early December 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 fourth 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.

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

[1]TNX-801 is an investigational new drug and has not been approved for any indication.
[2]Noyce RS, et al. (2018) PLoS One. 13(1):e0188453
[3]Tulman ER, et al. (2006) J Virol. 80(18):9244-58.PMID:16940536
[4]Schrick L et al. (2017) N Engl J Med. 377:1491.
[5]Qin et al. (2015) J. Virol. 89:1809.
[6]Jenner E. "An Inquiry Into the Causes and Effects of the Variolae 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.
[7]Brinkmann A et al, Genome Biology (2020) 21:286.
[8]Duggan A et al. Genome Biology (2020) 21:175.
[9]Tonix press release. Dec 4, 2020 https://ir.tonixpharma.com/news-events/press-releases/detail/1236/vaccine-genome-researchers-report-99-7-colinear-identity
[10]Trindale GS et al. (2016) Viruses (12). Pii: E328. PMID:27973399
[11]Esparza E, et al (2017) Vaccine. 35(52):7222-7230.
[12]Esparza J et al. (2020) Vaccine.; 38(30):4773-4779.
[13]www.cdc.gov/poxvirus/monkeypox/about.html
[14]www.cdc.gov/smallpox/research/
[15]Mandavilli, A. The New York Times. May 26, 2020. "Who is protected against monkeypox"
[16]www.cdc.gov/poxvirus/monkeypox/response/2022/us-map.html - Accessed October 18, 2023
[17]https://www.who.int/news-room/fact-sheets/detail/monkeypox#:~:text=There%20are%20two%20distinct%20genetic,thought%20to%20be%20more%20transmissible – Accessed October 18, 2023
[18]https://www.who.int/news/item/28-11-2022-who-recommends-new-name-for-monkeypox-disease - Accessed October 18, 2023
[19]Tonix's product candidates in development are investigational new drugs and have not been approved for any indication

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; 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, 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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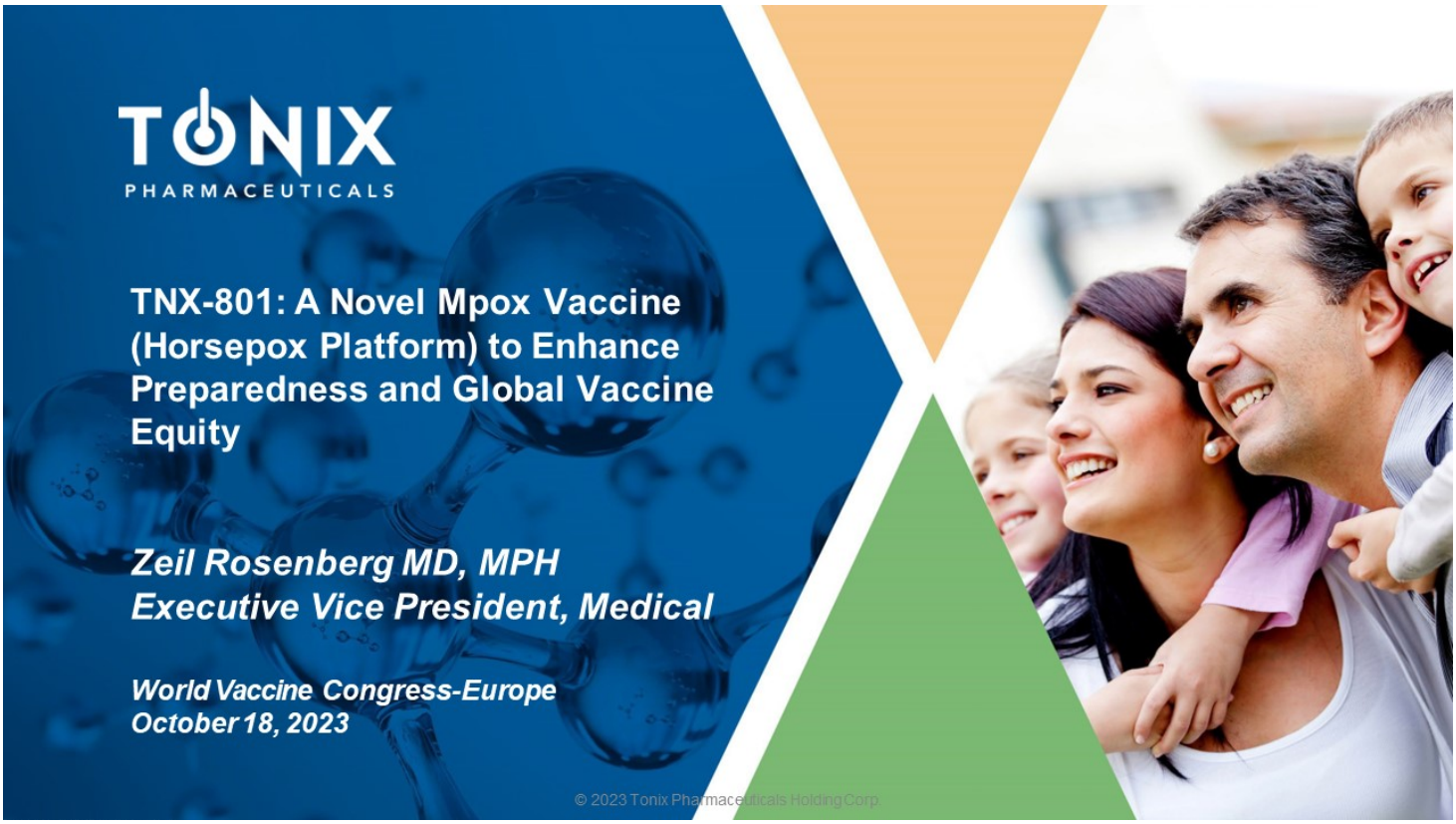
Exhibit 99.02



Cautionary Note on Forward-Looking Statements

Certain statements in this presentation regarding strategic plans, expectations and objectives for future operations or results are "forward-looking statements" as defined by 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" 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, the 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. The forward-looking statements in this presentation are made as of the date of this presentation, even if subsequently made available by Tonix on its website or otherwise. Tonix does not undertake an obligation to update or revise any forward-looking statement, except as required by law. 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 and current 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.

Tonix Pharmaceuticals

- NASDAQ traded, commercial stage biopharmaceutical company
- Focus: CNS (incl. 2 commercial), Long Covid, and Infectious Disease
- Poxvirus – based Vaccine program:
  - **Mpox/Smallpox** (TNX-801)
  - **COVID** (TNX-1800)

Infectious Disease R&D Center (RDC) – Frederick, MD
Accelerated development of vaccines and antiviral drugs
~48,000 square feet, BSL-2 and BSL-3

Advanced Development Center (ADC) – North Dartmouth, MA
Development and clinical scale manufacturing of biologics
~45,000 square feet, BSL-2

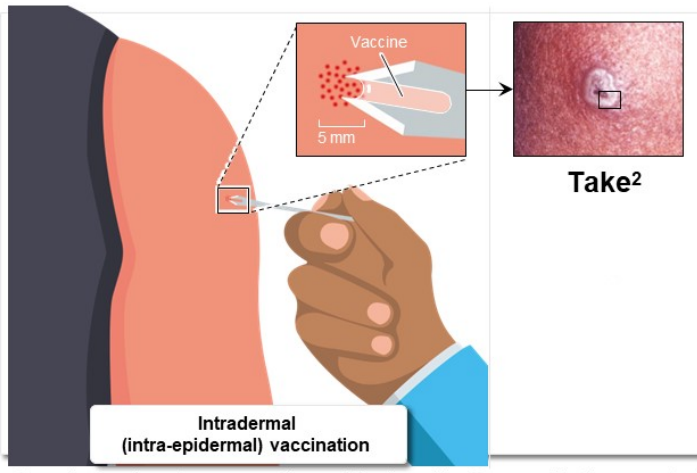
In 1796 Edward Jenner Successfully Used Vaccination to Protect Against Smallpox

- Jenner reasoned infection with illness similar to smallpox, but less deadly, could protect against smallpox
  - "Jenner "vaccinated" (*vacca*, Latin for "cow") a patient with pustule matter from "cowpox" sores on a milkmaid's hands;
  - Patient remained healthy when challenged with smallpox virus

Jenner wrote he suspected that the agent causing cowpox, which he called **vaccinia**, *actually originated in horses* and was transferred from horses to cows' udders by contaminated farm workers' hands.

The College of Physicians of Philadelphia. Accessed July 15, 2021. https://www.historyofvaccines.org

Vaccinia Induces a Skin Reaction Called "Take" Described by Dr. Edward Jenner



Take[2]

- **Biomarker of protection**
  - Smallpox was eradicated using this marker
  - Revaccination indicated for recipients without "take"
- **Measure of T cell immunity**
  - No need for blood draws or complex laboratory studies
  - No other functional T cell assay is approved or in clinical use for vaccination

*Example of major cutaneous reaction, or "take," resulting from a replication-competent live-virus vaccine with intradermal delivery, indicating successful vaccination[1,2]

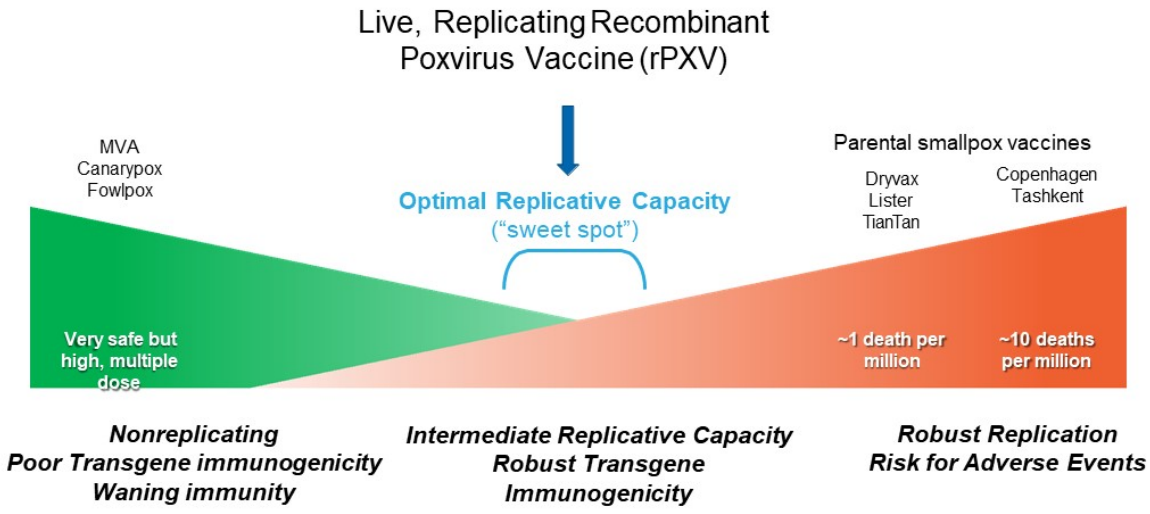
[1]Fulginiti VA, et al. *Clin Infect Dis.* 2003;37(2):241-250.
[2]Centers for Disease Control and Prevention. Accessed April 15, 2020. https://phil.cdc.gov/Details.aspx?pid=32 76

TNX-801 Development

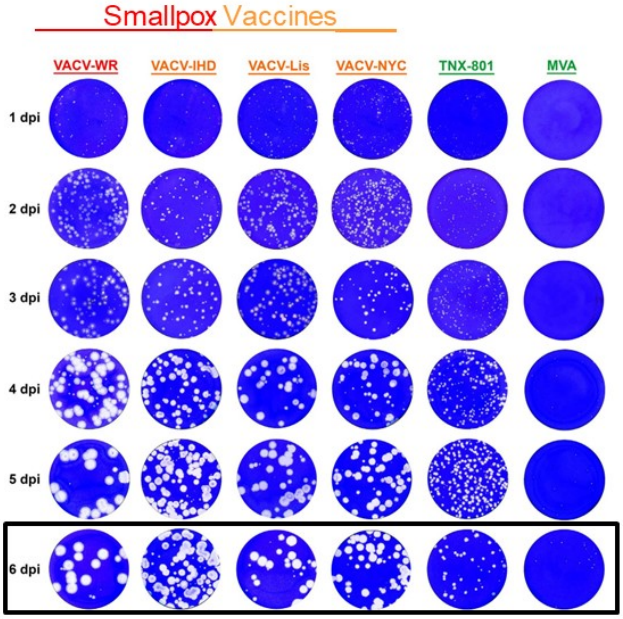
- **U.S. smallpox vaccine manufactured in 1902 (H.K. Mulford)**
  - **99.7% similar to horsepox in core viral sequence[1,2]**
- **Tonix-801 is based on a sequence of an isolated horsepox (HPXV) clone[3]**
  - Synthesized[4] in 2018 (isolate was unavailable outside of CDC)
  - No new gene elements introduced
- **Sequencing showed Tonix-801 identical to CDC publication of a 1976 horsepox isolate[5]**

[1]Tulman ER, et al. Genome of horsepox virus. *J Virol.* 2006 80(18):9244-58.PMID:16940 536
2 Schrick, L. et al An Early American Smallpox Vaccine Based on Horsepox *N Engl J Med* 2017; 377:149
3Noyce RS, et al.. Construction of an infectious horsepox virus vaccine from chemically synthesized DNA fragments. *PLoS One.* 2018 Jan 19;13(1):e0188453
4Trindade GS, et al. Serro 2 Virus Highlights the Fundamental Genomic and Biological Features of a Natural Vaccinia Virus Infecting Humans. *Viruses* 2016 Dec 10;8(12). pii: E328. PMID:27 973399
PMCID: PMC5192389 DOI: 10.3390/v8120328
5Noyce, RS, et al. Synthetic Chimeric Horsepox Virus (scHPXV) Vaccination Protects Macaques from Monkeypox* Presented as a poster at the American Society of Microbiology BioThreats Conference - January 29, 2020, Arlington, VA. (https://content.equisolve.net/tonixpharma/media/10929ac27f4fb5f5204f5cf41d59a121.pdf)

Illustrative Safety Spectrum Of Pox-based Vaccine Vectors
Optimizing Live Virus Vaccines

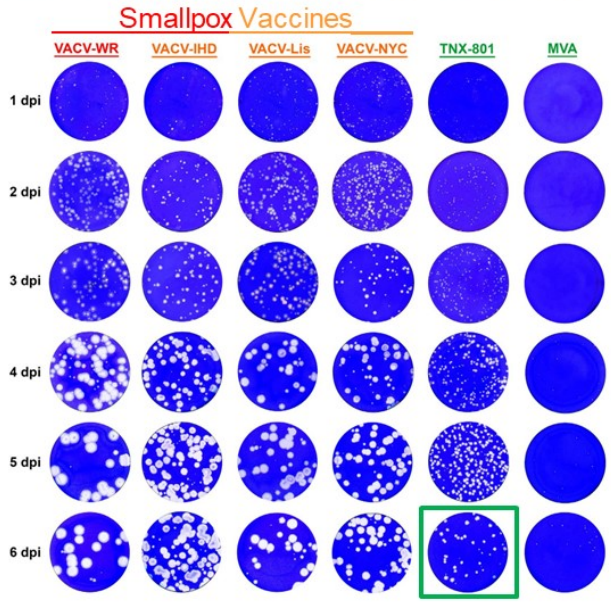


Characterization of TNX-801 Platform: Naturally Attenuated Relative to VACV Based Vaccines (Smallpox)



Plaque Size -
VACV (~3-4 mm)
TNX-801 (~1-2 mm)

Characterization of TNX-801 Platform: Naturally Attenuated Relative to VACV Based Vaccines (Smallpox)

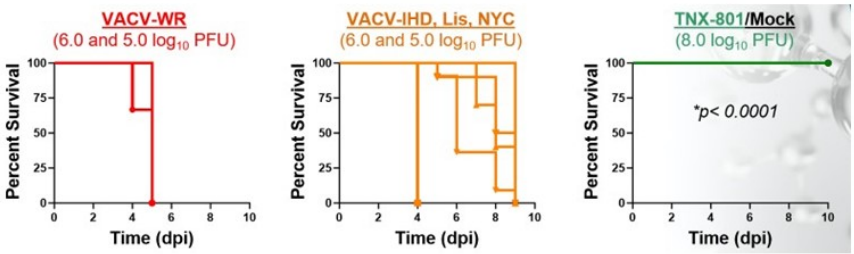


- TNX-801 is **attenuated *in vitro*** relative to all VACV (WR, IHD, Lis, NYC)
  - Immortalized NHP cell lines:
    - Up to ***119-fold***
  - Primary Human cells
    1) Dermal Track
    2) Respiratory Track
    - Up to ***28- or 112-fold***

Plaque Size -
VACV (~3-4 mm)
TNX-801 (~1-2 mm)

TONIX PHARMACEUTICALS

Characterization of TNX-801 Platform: Naturally Attenuated Relative to VACV Based Smallpox Vaccines



Murine Model :
Mpox Clade 1 Challenge

Immunocompromised mice with deficiencies in the IFN-α and/or IFN-γreceptors.

1000x more attenuated than older VACV-based vaccines

TONIX PHARMACEUTICALS

viruses

MDPI

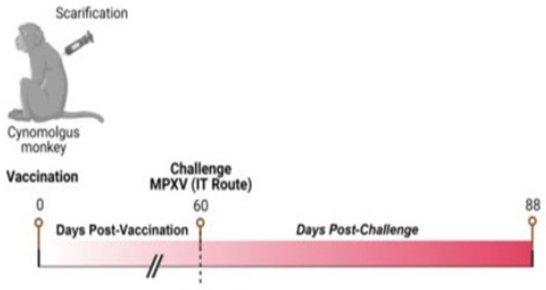
Article

Single Dose of Recombinant Chimeric Horsepox Virus (TNX-801) Vaccination Protects Macaques from Lethal Monkeypox Challenge

Ryan S. Noyce [1], Landon W. Westfall [2,†], Siobhan Fogarty [3], Karen Gilbert [2], Onesmo Mpanju [4], Helen Stillwell [3,‡], José Esparza [5], Bruce Daugherty [3], Fusataka Koide [2], David H. Evans [1] and Seth Lederman [3,*]

TNX-801 Vaccination and Lethal Challenge in Macaques

Vaccination					Challenge		
Group	Vaccine	N	Dose (Log_{10} PFU)	Route	*Virus*	*Dose (Log_{10} PFU)*	*Route*
1	TNX-801 (High Dose)	4	6.6	Scarification	*MPXV (Zaire)*	*5.0*	*IT*
2	TNX-801 (Low Dose)	4	5.7	Scarification	*MPXV (Zaire)*	*5.0*	*IT*
3	rVACV	4	5.0	Scarification	*MPXV (Zaire)*	*5.0*	*IT*
4	Mock	4	-	Scarification	*MPXV (Zaire)*	*5.0*	*IT*

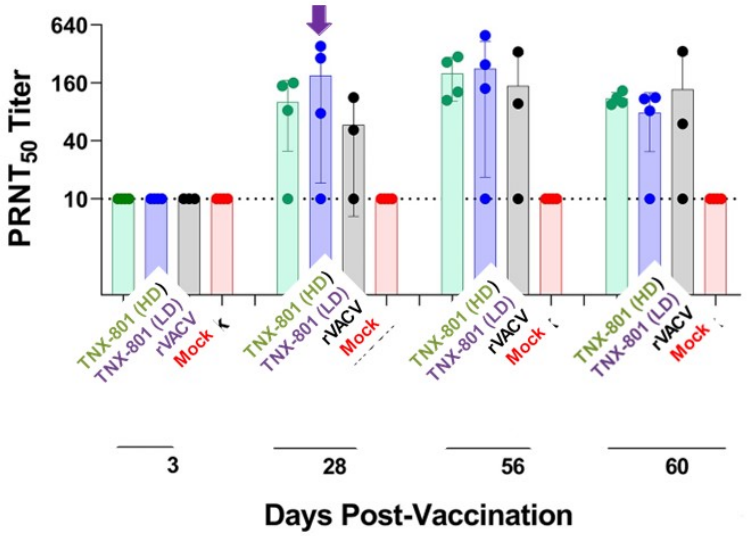


"Take" observed in all TNX-801 vaccinated NHPs except one.

- If no take by day 7 NHPs were revaccinated on day 14.

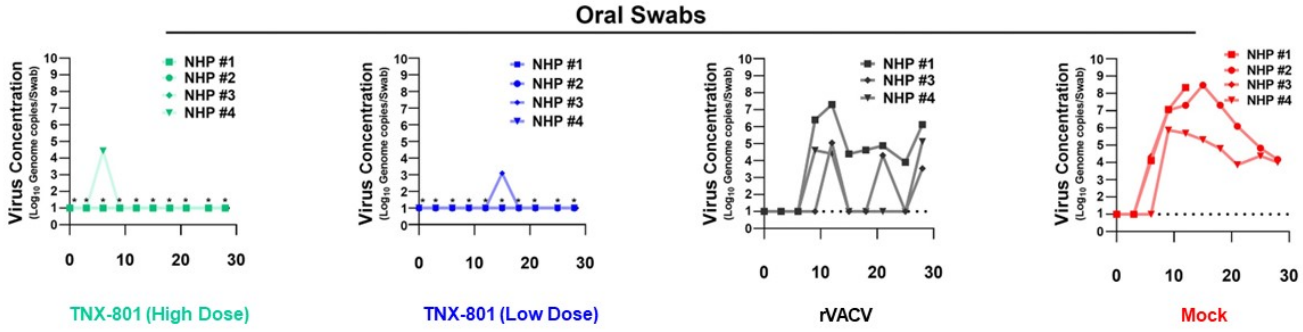
Post-vaccination, no NHP showed lesions during first 60 days

Immunogenicity: Neutralizing Antibody ($PRNT_{50}$ Assay)



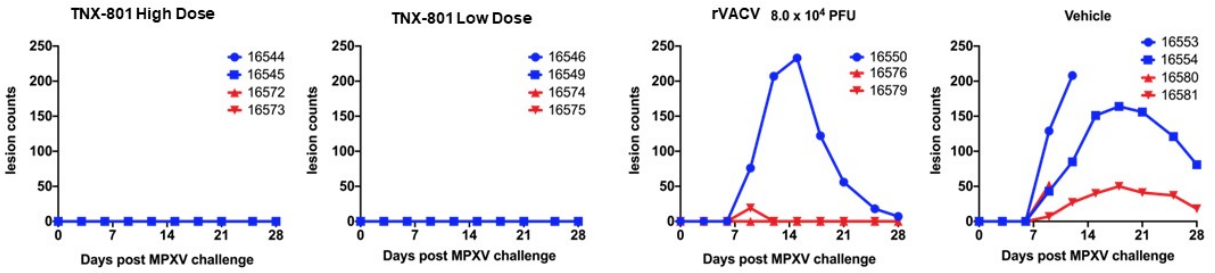
88% of TNX-801 vaccinated NHPs had neutralizing antibody responses 8- to 50-fold from baseline

Measured Virus Shedding: Oral Swabs



Minimal or no virus shedding in Tonix-801 vaccinated groups

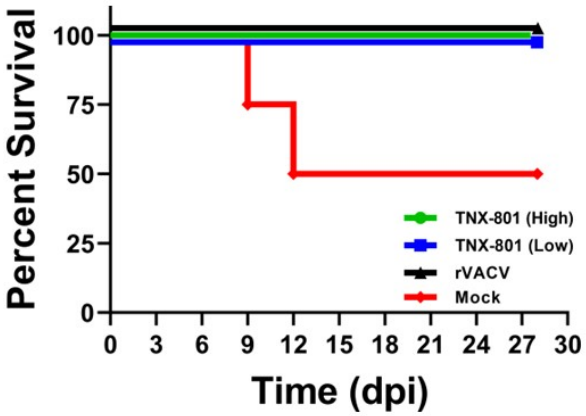
Clinical Signs After MPXV Challenge



NHPs vaccinated with Tonix-801:
No lesions observed after MPXV challenge in any of the eight animals

[1]Noyce, RS, et al. Synthetic Chimeric Horsepox Virus (scHPXV) Vaccination Protects Macaques from Monkeypox* Presented as a poster at the American Society of Microbiology BioThreats Conference - January 29, 2020, Arlington, VA. (https://content.equisolve.net/tonixpharma/media/10929ac27f4fb5f5204f5cf41d59a121.pdf)

Clinical Disease: Lethality



No deaths in Tonix-801 vaccinated groups

Study Conclusions for TNX-801 Non-Human Primate Challenge

- A single dose vaccination was well tolerated
  - No severe adverse events
- Vaccination was immunogenic
- Mpox disease (lesions) was not observed following MPXV (Zaire) challenge
- All vaccinated NHPs survived lethal challenge

Efficacy of Current Vaccines- RWE Mpox

- **Jynneos- Most recent data**
  - Earliest study had VE 86% but CI was 59%-95%[1].
  - More recent data towards bottom of CI.
  - CDC US National Study[2]
  - Epic Database : 173 million persons capturing 2193 mpox cases
  - 2 dose adjusted VE 66.0% (CI 47.4-78.1)
  - 1 dose adjusted VE 35.8% (CI 22.1-47.1)
- **ACAM2000 (EUA only; not approved by FDA for mpox)**
  - US Military Vaccine Program[3] 2.7 million former and current personnel
  - ACAM2000 Adjusted VE 75% (CI 58-85)

[1]Sagy Nature Medicine 2023
[2]Deputy et al NEJM 2023
[3]Titanji et al NEJM 2023

Do we need an additional approved Mpox vaccine?

- **Durable Immunity**
- **Attenuated for safety**
- **One dose microneedle**
  - Improve compliance
  - Reduce administrative burden in epidemic setting
- **Ring vaccination strategy**
  - Proven effective for disease eradication
  - Potential to reduce onward transmission
  - "Take" as biomarker of protection
- **Global Vaccine Equity**……

Global Vaccine Equity : TNX-801

- Epidemic continues in Africa[1]
- Distribution and Finance are significant barriers[2]
- Developed countries ordered nearly all available and future doses of mpox vaccine[3]
- Africa access to vaccines is patchy or non-existent[4]

TNX-801

- Potentially lower relative price than incumbent
  - One dose
  - Smaller dose & multi-dose packaging stretches supply
  - High scale manufacturing using existing technologies
- Competition in marketplace
  - Sustainable access
- Microneedle one-dose delivery improves accessibility
- Free up vaccine supplies to countries now without

[1]Koslov Nature Medicine 2023
[2]Ogunkola Vaccines 2023
[3]LA times May 30, 2023
[4]GAVI VaccineWorks June 21, 2023

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