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): April 23, 2025

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 April 23, 2025, Tonix Pharmaceuticals Holding Corp. (the "Company") presented data in an oral presentation at the World Vaccine Congress Washington 2025, held April 21-24, 2025 (the "World Vaccine Congress"). 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 Exhibit 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 April 23, 2025, the Company presented data in an oral presentation at the World Vaccine Congress titled "*A Novel Single-Dose, Attenuated Live, Minimally Replicative Mpox Vaccine*" which highlighted positive preclinical efficacy data, demonstrating that the Company's TNX-801 vaccine candidate to protect against mpox and small pox protected animals from mpox and rabbitpox and was well tolerated, even in immunocompromised animals.

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, April 24, 2025
99.02	A Novel Single-Dose, Attenuated Live, Minimally Replicative Mpox Vaccine
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: April 24, 2025

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

Exhibit 99.01

Tonix Pharmaceuticals Presented Data on Potential Mpox Vaccine TNX-801 at World Vaccine Congress Washington 2025

TNX-801 is a single-dose, live virus vaccine in development to protect against mpox and smallpox

TNX-801 protects immunocompromised animals from a lethal challenge with clade IIa monkeypox virus

Durability of TNX-801 vaccination shown by six-month protection of animals from a lethal challenge with rabbitpox

Tolerability of TNX-801 demonstrated in immunocompromised animals by no spreading to blood or tissues, even at high doses

CHATHAM, N.J., April 24, 2025 – Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a fully-integrated biopharmaceutical company with marketed products and a pipeline of development candidates, presented data in an oral presentation at the World Vaccine Congress Washington 2025, held April 21-24, 2025, in Washington, D.C. The presentation titled, "*A Novel Single-Dose, Attenuated Live, Minimally Replicative Mpox Vaccine*", highlighted positive preclinical efficacy data, demonstrating that TNX-801 protected animals from mpox and rabbitpox and was well tolerated, even in immunocompromised animals. A copy of the Company's presentation is available under the Scientific Presentations tab of the Tonix website at www.tonixpharma.com.

"TNX-801 shows promise as a potential mpox and smallpox vaccine by providing protective immunity to animals with a single-dose," said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals. "TNX-801 was generally well tolerated, even in immunocompromised animals. The new data show durable six-month protection against a lethal challenge with rabbitpox virus and protection of immunocompromised animals against a lethal challenge with monkeypox clade IIa virus. These new data build upon prior studies showing protection of animals against a lethal challenge with intratracheal clade Ia mpox virus. In all of these studies, after a single dose vaccination, TNX-801 prevented both clinical disease and formation of lesions."

Dr. Lederman continued, "The ongoing clade IIb mpox epidemic that started in 2022, and the more recent and ongoing clade Ib mpox epidemic, highlight the need for additional vaccine options, particularly single-dose options. Both the 2022 clade IIb and the 2024 clade Ib mpox epidemics have been declared by the World Health Organization (WHO) to be Public Health Emergencies of International Concern (PHEICs). We believe TNX-801 has the potential to make an impact towards preventing mpox and controlling future mpox epidemics."

TNX-801 is a minimally replicative, 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. In September 2024, Tonix announced that the WHO's preferred target product profile (TPP), released at the WHO sponsored Mpox Research and Innovation Scientific Conference, aligns with the characteristics of TNX-801. Key elements of the WHO draft TPP include single-dose, durable protection, administration without special equipment, and stability at ambient temperature. Other potential beneficial characteristics include the ability to limit forward transmission, use in case-contact vaccination strategies and suitability for use in immunocompromised individuals.

About TNX-801*

TNX-801 (recombinant horsepox virus) is a single-dose, attenuated, minimally replicative, live virus vaccine based on horsepox in pre-clinical development to prevent mpox and smallpox. Tonix reported positive preclinical efficacy data, demonstrating that TNX-801 vaccination protected non-human primates against lethal challenge with monkeypox. After a single dose vaccination, TNX-801 prevented clinical disease and lesions and decreased shedding in the mouth and lungs of non-human primates. The findings are consistent with mucosal immunity and suggest the ability to block forward transmission, similar to Dr. Edward Jenner's vaccine, which eradicated smallpox and kept mpox out of the human population. TNX-801 is based on synthesized horsepox which is believed to be more closely related to Dr. Jenner's vaccine than 20th century vaccinia viruses.[6] Smallpox vaccines descended from Jenner's vaccine used prior to 1900 would be called horsepox by modern nomenclature. TNX-801 is delivered percutaneously with only one dose and therefore may achieve higher rates of community protection than two-dose vaccines by eliminating drop-out between doses and limiting forward transmission. Tonix has received 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 has announced a collaboration with the Kenya Medical Research Institute (KEMRI) to design, plan and seek regulatory approval for a Phase I clinical study of TNX-801 in Kenya. The Company believes TNX-801 has the potential to make a global impact on mpox and the risk of smallpox because of its durable T-cell immune response, the potential to manufacture at scale, and the use of a lower dose than non-replicating vaccines. The FDA-approved non-replicating mpox vaccine Jynneos® requires two doses and provides a relatively short duration of protection. FDA also recently approved ACAM2000, a live, replicating vaccinia vaccine for prevention of mpox. ACAM200 is a clone from DryVax®, a 20th century vaccinia vaccine derived from the NYCBH strain. Pre-clinical results from an mRNA vaccine recently showed some protection from a Clade I monkeypox challenge, but with multiple break-through lesions in vaccinated animals.

About Tonix Pharmaceuticals Holding Corp.*

Tonix is a fully integrated biopharmaceutical company focused on transforming therapies for pain management and vaccines for public health challenges. Tonix's development portfolio is focused on central nervous system (CNS) disorders. Tonix's priority is to advance TNX-102 SL, a product candidate for the management of fibromyalgia, for which an NDA was submitted based on two statistically significant Phase 3 studies for the management of fibromyalgia and for which a PDUFA (Prescription Drug User Fee act) goal date of August 15, 2025 has been assigned for a decision on marketing authorization. The FDA has also 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 and acute stress disorder under a Physician-Initiated IND at the University of North Carolina in the OASIS study funded by the U.S. Department of Defense (DoD). Tonix's CNS portfolio includes TNX-1300 (cocaine esterase), a biologic in Phase 2 development designed to treat cocaine intoxication that has FDA Breakthrough Therapy designation, and its development is supported by a grant from the National Institute on Drug Abuse. Tonix's immunology development portfolio consists of biologics to address organ transplant rejection, autoimmunity and cancer, including TNX-1500, which is an Fc-modified 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's infectious disease portfolio includes TNX-801, a vaccine in development for mpox and smallpox, as well as TNX-4200 for which Tonix has a contract with the U.S. Department of Defense's (DoD's) Defense Threat Reduction Agency (DTRA) for up to $34 million over five years. TNX-4200 is a small molecule broad-spectrum antiviral agent 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. 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. Their efficacy and safety have not been established and have not been approved for any indication.

Zembrace SymTouch and Tosymra are registered trademarks of Tonix Medicines. All other marks are property of their respective owners.

This press release and further information about Tonix can be found atwww.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, 2024, as filed with the Securities and Exchange Commission (the “SEC”) on March 18, 2025, 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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Indication and Usage

Zembrace® SymTouch® (sumatriptan succinate) injection (Zembrace) and Tosymra® (sumatriptan) nasal spray are prescription medicines used to treat acute migraine headaches with or without aura in adults who have been diagnosed with migraine.

Zembrace and Tosymra are not used to prevent migraines. It is not known if Zembrace or Tosymra are safe and effective in children under 18 years of age.

Important Safety Information

Zembrace and Tosymra can cause serious side effects, including heart attack and other heart problems, which may lead to death. Stop use and get emergency help if you have any signs of a heart attack:

- discomfort in the center of your chest that lasts for more than a few minutes or goes away and comes back
- severe tightness, pain, pressure, or heaviness in your chest, throat, neck, or jaw
- pain or discomfort in your arms, back, neck, jaw or stomach
- shortness of breath with or without chest discomfort
- breaking out in a cold sweat
- nausea or vomiting
- feeling lightheaded

Zembrace and Tosymra are not for people with risk factors for heart disease (high blood pressure or cholesterol, smoking, overweight, diabetes, family history of heart disease) unless a heart exam shows no problem.

Do not use Zembrace or Tosymra if you have:

- history of heart problems
- narrowing of blood vessels to your legs, arms, stomach, or kidney (peripheral vascular disease)

- uncontrolled high blood pressure
- hemiplegic or basilar migraines. If you are not sure if you have these, ask your provider.
- had a stroke, transient ischemic attacks (TIAs), or problems with blood circulation
- severe liver problems
- taken any of the following medicines in the last 24 hours: almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, ergotamines, or dihydroergotamine. Ask your provider for a list of these medicines if you are not sure.
- are taking certain antidepressants, known as monoamine oxidase (MAO)-A inhibitors or it has been 2 weeks or less since you stopped taking a MAO-A inhibitor. Ask your provider for a list of these medicines if you are not sure.
- an allergy to sumatriptan or any of the components of Zembrace or Tosymra

Tell your provider about all of your medical conditions and medicines you take, including vitamins and supplements.

Zembrace and Tosymra can cause dizziness, weakness, or drowsiness. If so, do not drive a car, use machinery, or do anything where you need to be alert.

Zembrace and Tosymra may cause serious side effects including:

- changes in color or sensation in your fingers and toes
- sudden or severe stomach pain, stomach pain after meals, weight loss, nausea or vomiting, constipation or diarrhea, bloody diarrhea, fever
- cramping and pain in your legs or hips; feeling of heaviness or tightness in your leg muscles; burning or aching pain in your feet or toes while resting; numbness, tingling, or weakness in your legs; cold feeling or color changes in one or both legs or feet
- increased blood pressure including a sudden severe increase even if you have no history of high blood pressure
- medication overuse headaches from using migraine medicine for 10 or more days each month. If your headaches get worse, call your provider.
- serotonin syndrome, a rare but serious problem that can happen in people using Zembrace or Tosymra, especially when used with anti-depressant medicines called SSRIs or SNRIs. Call your provider right away if you have: mental changes such as seeing things that are not there (hallucinations), agitation, or coma; fast heartbeat; changes in blood pressure; high body temperature; tight muscles; or trouble walking.
- hives (itchy bumps); swelling of your tongue, mouth, or throat
- seizures even in people who have never had seizures before

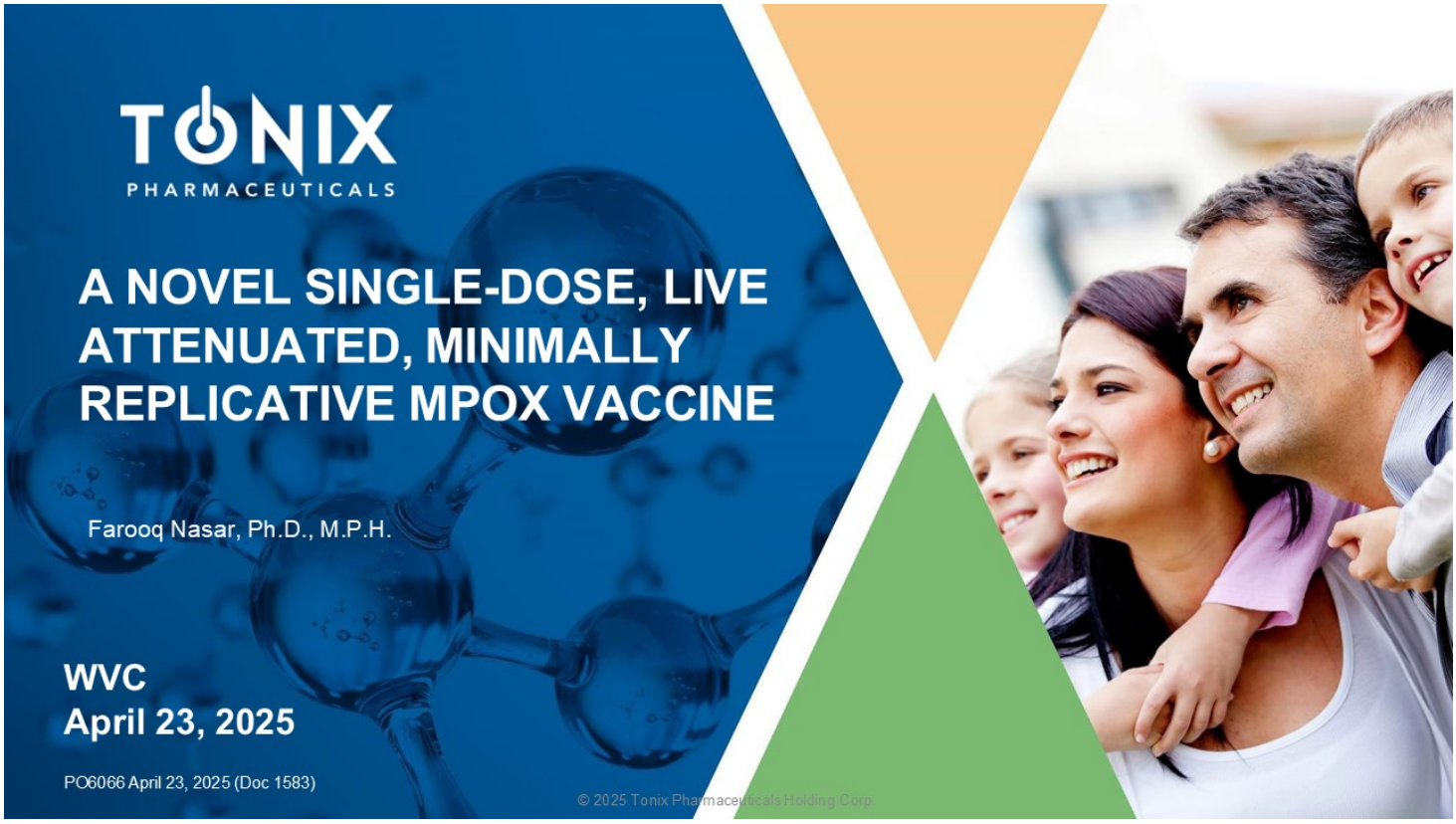
The most common side effects of Zembrace and Tosymra include: pain and redness at injection site (Zembrace only); tingling or numbness in your fingers or toes; dizziness; warm, hot, burning feeling to your face (flushing); discomfort or stiffness in your neck; feeling weak, drowsy, or tired; application site (nasal) reactions (Tosymra only) and throat irritation (Tosymra only).

Tell your provider if you have any side effect that bothers you or does not go away. These are not all the possible side effects of Zembrace and Tosymra. For more information, ask your provider.

This is the most important information to know about Zembrace and Tosymra but is not comprehensive. For more information, talk to your provider and read the Patient Information and Instructions for Use. You can also visit https://www.tonixpharma.com or call 1-888-869-7633.

You are encouraged to report adverse effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

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; 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. 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, 2024, as filed with the Securities and Exchange Commission (the "SEC") on March 18, 2025, 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.

TALK OVERVIEW

1) **Background**

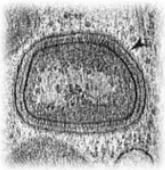
2) **TNX-801 attenuation *in vitro* and *in vivo***

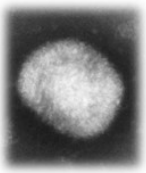
3) **TNX-801 immunogenicity and efficacy in animal models**

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

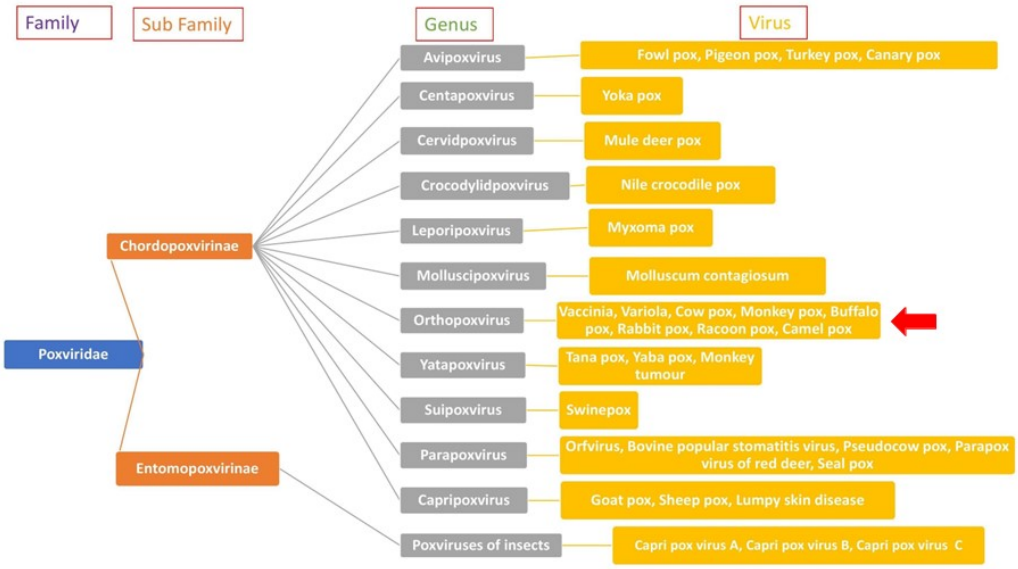
POXVIRUSES

- **Double stranded DNA, ~128-456 kb size**
- **Virions: enveloped, brick-shaped**
- **Size: ~220 to 450 nm long × 140 to 260 nm wide × 140 to 260 nm thick**
- **Infect vertebrate or invertebrate hosts**
- **Genus *Orthopoxvirus*:**
  - **Human Pathogens:**
    - **VARV: Case fatality rate ~30 to 50%**
    - **MPXV: Case fatality rate ~ 0.1 to 11%**
  - **Vaccines:**
    - **Vaccinia, Cowpox, Horsepox**
    - **Horsepox virus: ***TNX-801***</u>**

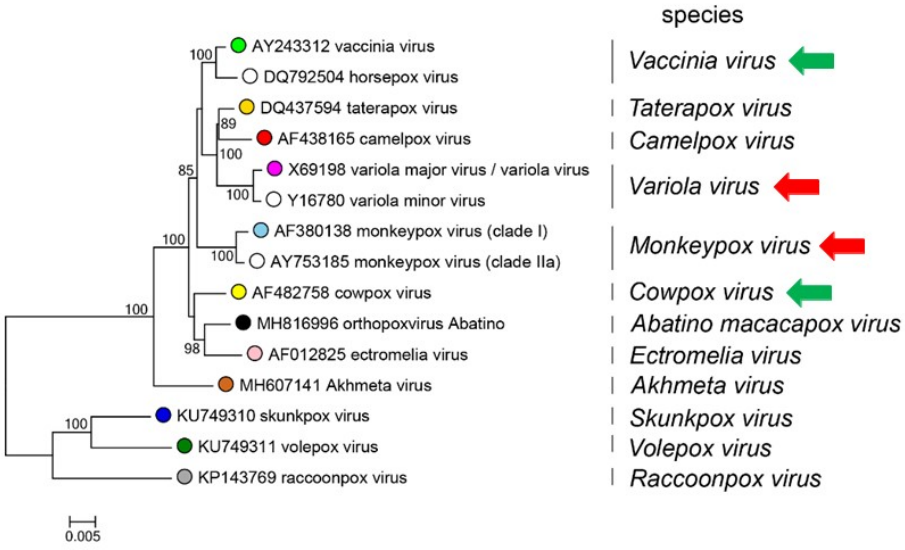




POXVIRUSES: UBIQUITOUS IN THE ENVIRONMENT



GENUS *ORTHOPOXVIRUS*



MONKEYPOX VIRUS (MPOX)

- **Endemic in Central and West Africa**
- **Two Clades:**
  1) Clade I (DRC)
  2) Clade IIa (West Africa) and IIb (Nigeria)
- **Human Case Fatality Rate:**
  - Clade I – ~11%
  - Clade IIa – ~3%
  - Clade IIb – ~<0.1%
- **Clade IIb – 2022 Outbreak**
  - 122 Countries
  - ~100,000 Confirmed Cases

VARIOLA VIRUS (SMALLPOX)

- **Oldest written record – ~3,500 years**
- **Oldest sequences – ~1,400 years**
- **Human Case Fatality Rate: ~30%**
- **20th century – ~250 to 500 million deaths**
- **Eradication: 1980**

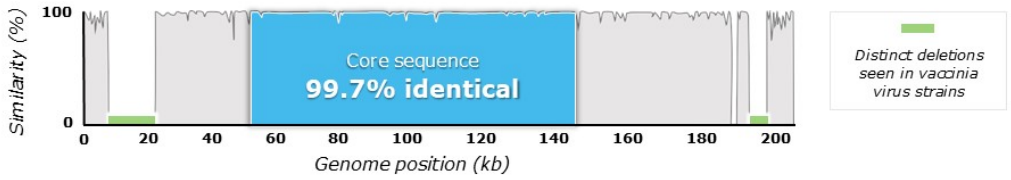
EDWARD JENNER- SMALLPOX VACCINE (1796)

- **Jenner observed milkmaids were protected from smallpox, reasoned that infection with an illness similar to smallpox but less deadly could protect one against smallpox**
  - **"Cowpox" was the name of a disease in cows that could transfer to humans and cause sores**
  - **Jenner "vaccinated" (from *vacca*, Latin for "cow") a patient with pustule matter from "cowpox" sores on a milkmaid's hands; that patient remained healthy when challenged with smallpox virus**
- **Jenner suspected that the agent causing cowpox, which he called vaccinia originated in horses and had been transferred from horses to cows' udders by dirty hands**

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

EQUINATION- SMALLPOX VACCINES FROM HORSES

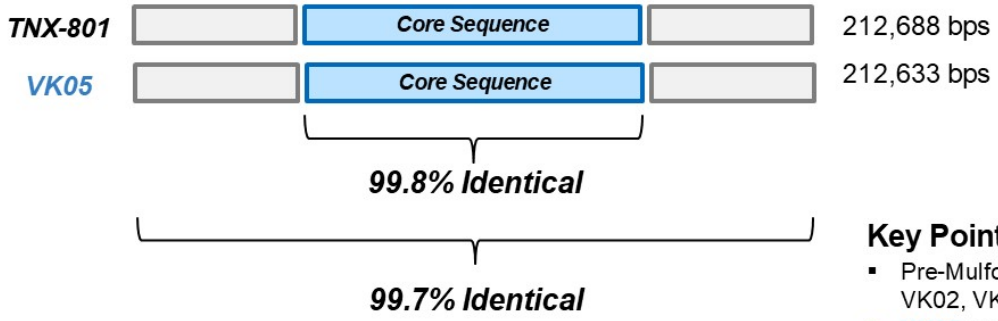
- **Equination, the use of vaccines from horses (*equus* in Latin), was successfully used in parallel with vaccination in Europe[1]**
- **Vaccine producers may have propagated stocks by periodically supplementing or refreshing them with horsepox[2]**
  - A 1902 smallpox vaccine (**Mulford**) – 99.7% identical to core viral sequence
  - **Sequence Identity for the 1902 Mulford Vaccine Compared to HPVX[3]**



1. Esparza J, et al. *Vaccine*. 2017;35(52):7222-7230.
2. Esparza J, et al. *Vaccine*. 2020;38(30):4773-4779.
3. Schrick L, et al. *N Engl J Med*. 2017;377(15):1491-1492.

HPXV WAS USED AS CIVIL WAR-ERA VACCINE

VK05 has the highest identity to HPXV across the whole genome and represents a true HSPV strain



Key Points

- Pre-Mulford vaccines: VK05, VK12, VK02, VK08, and VK01
- **VK05** and **TNX-801** (HPXV) have colinear structural identity across their whole genome

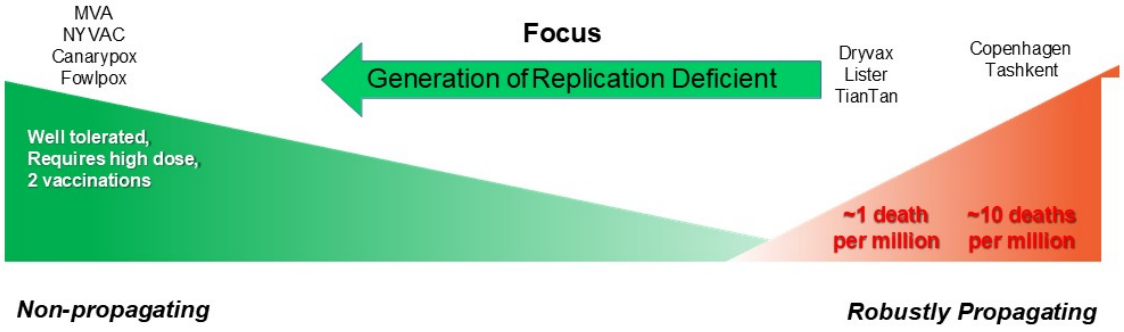
Brinkmann A, et al. *Genome Biol.* 2020;21(1):286.

SMALLPOX VACCINES

- **Vaccine: Cowpox origin**
- **Serial passaging: Humans, cows, and horses (143 years)**
- **Vaccine: Vaccinia Virus (1939) closely related to cowpox but serologically distinct[1]**
- **Multiple Vaccinia virus-based vaccines developed**
- **Smallpox eradication**

[1]Downie AW. 1939. *Br J Exp Pathol* 20:158–176.

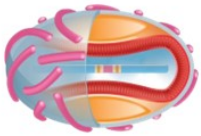
BALANCE OF TOLERABILITY AND REACTOGENICITY FOR POX-BASED VACCINES



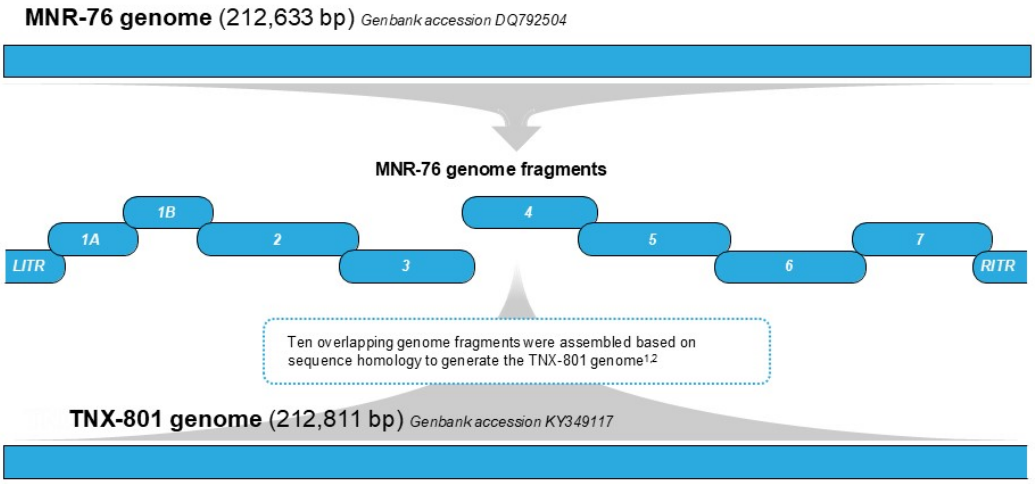
BALANCE OF TOLERABILITY AND REACTOGENICITY FOR POX-BASED VACCINES

BALANCE OF TOLERABILITY AND REACTOGENICITY FOR POX-BASED VACCINES

The core genome of TNX-801 is identical to MNR-76[1]



TNX-801
scHPXV (Horsepox)
212,811 bp



1. Noyce RS, et al. *PLoS One*. 2018;13(1):e0188453.
2. Schrick L, et al. *N Eng J Med*. 2017;377(15):1491-1492.

4 PRONG APPROACH TO MPOX/SMALLPOX VACCINE (TNX-801)

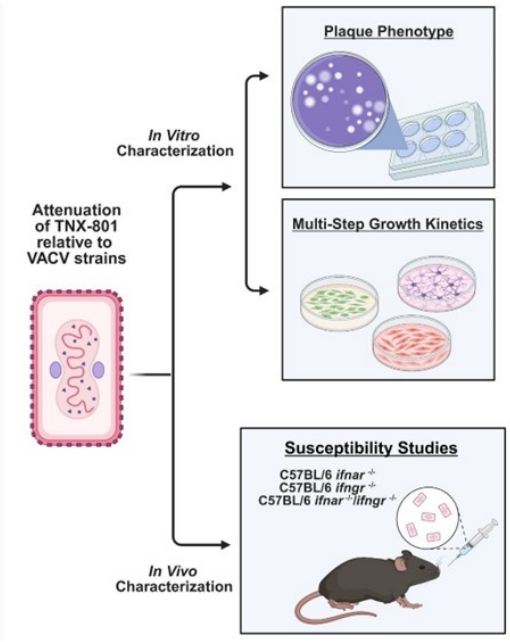
1) **Well-tolerated**

2) **Single dose**

3) **Durable**

4) **Protection against mpox disease (lesions)**

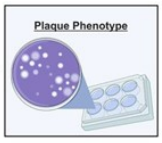
TNX-801 ATTENUATION *IN VITRO* AND *IN VIVO*

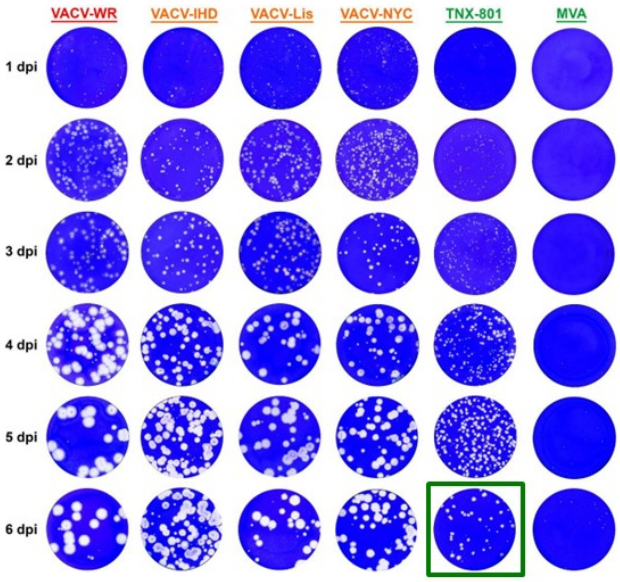


IN VITRO ATTENUATION OF TNX-801

- **Investigate attenuation of TNX-801 *in vitro* relative to VACV strains**
  - Positive Control: VACV-Western Reserve (WR), VACV-International Health Department (IHD)
  - Older vaccines used in smallpox eradication:
    1) VACV-Lister (Lis)
    2) VACV-New York City Board of Health (NYCBH)
  - New Vaccine: TNX-801
  - Non-replicating control: MVA
- ***In vitro* Assays:**
  1) **Plaque phenotype – BSC-40 and Vero-E6**
  2) **Replication Kinetics**
     - Immortalized non-human primate cell lines
     - Human primary cells from two main route of poxvirus transmission
       - Dermal and respiratory tracts

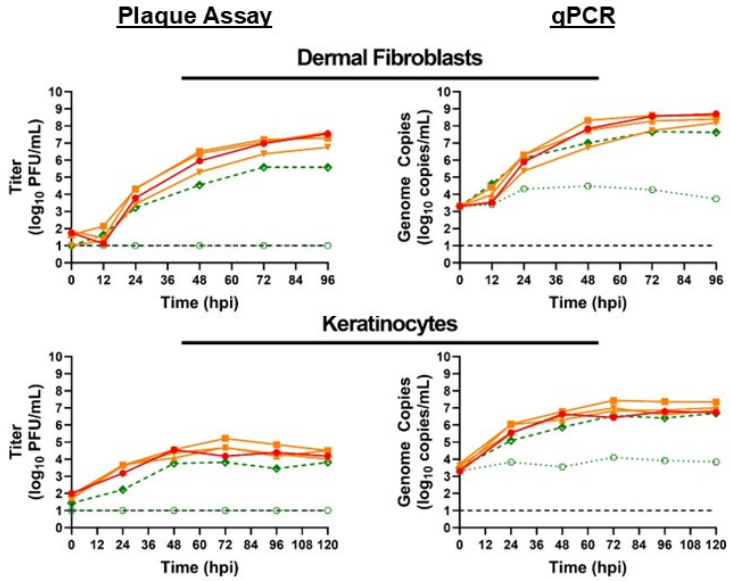
TNX-801 DISPLAYS SMALL PLAQUE PHENOTYPE VACCINA VIRUSES

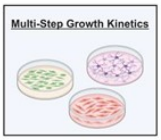




VACV-Western Reserve (WR)
VACV-International Health Department (IHD)
VACV-Lister (Lis)
VACV-New York City Board of Health (NYCBH)
TNX-801
MVA

TNX-801: REPLICATION IN PRIMARY HUMAN CELLS (DERMAL TRACT)

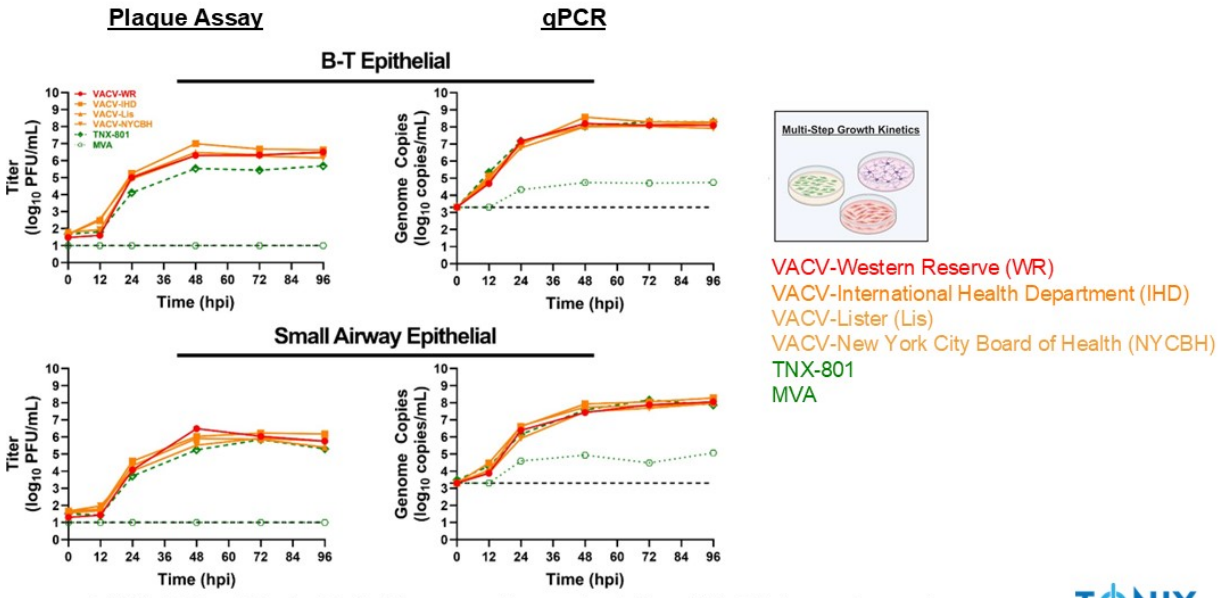




VACV-Western Reserve (WR)
VACV-International Health Department (IHD)
VACV-Lister (Lis)
VACV-New York City Board of Health (NYCBH)
TNX-801
MVA

TNX-801: *~27- to 119-fold* more attenuated than VACV based vaccines

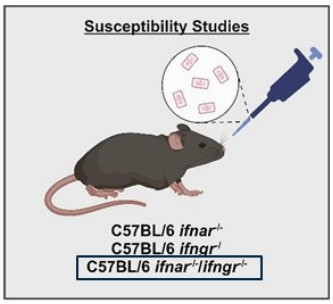
TNX-801: REPLICATION IN PRIMARY HUMAN CELLS (RESPIRATORY TRACT)



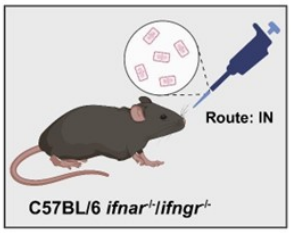
TNX-801: *~20- to 30-fold* more attenuated than VACV based vaccines

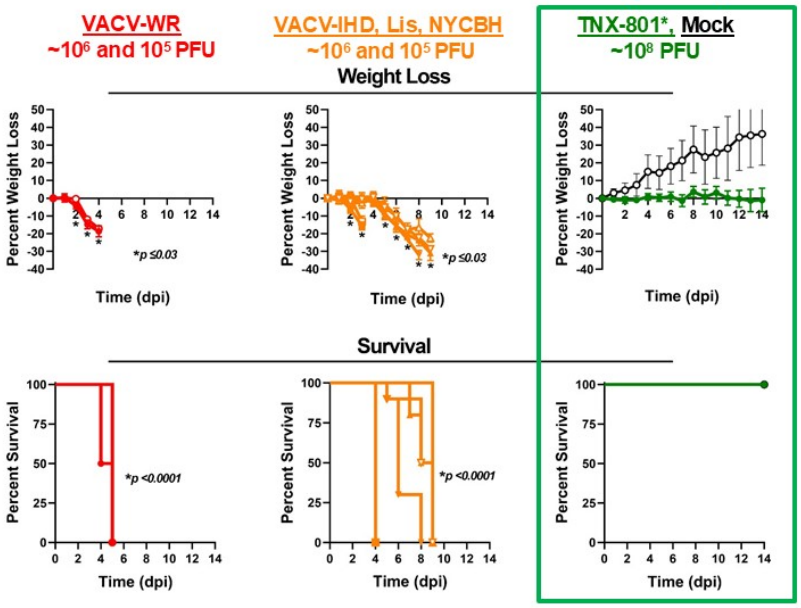
IN VIVO ATTENUATION OF TNX-801

- **Investigate attenuation of TNX-801 *in vivo* relative to VACV based vaccines**
  - Immunocompromised Mice (C57BL/6 *ifnar*$^{-/-}$, C57BL/6 *ifngr*$^{-/-}$, C57BL/6 *ifnar*$^{-/-}$/*ifngr*$^{-/-}$)
    - Interferon receptor knockout model
    - Sensitive to virus infection
  - **Positive Control:** VACV-WR, VACV-IHD
  - **Older vaccines:** VACV-Lis, VACV-NYCBH
  - TNX-801
  - **Route:** Intranasal
- **Parameters measured:**
  1) Disease Score
  2) Temperature
  3) ***Weight loss***
  4) ***Survival***



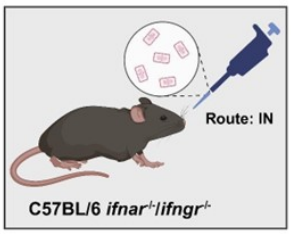
TNX-801 LACKS LETHALITY ASSOCIATED WITH OLDER SMALLPOX VACCINE STRAINS (LIS, NYCBH)

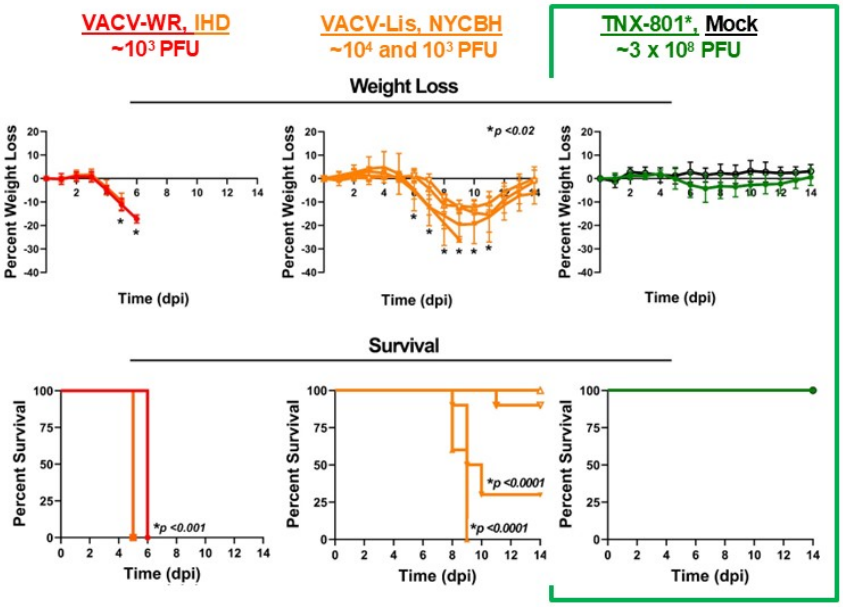




TNX-801 is 1,000-fold more attenuated

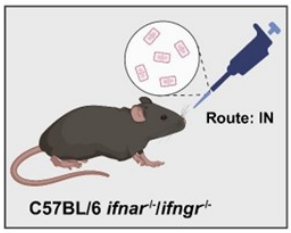
TNX-801 LACKS LETHALITY ASSOCIATED WITH OLDER SMALLPOX VACCINE STRAINS (LIS, NYCBH)





TNX-801 is up to 100,000-fold more attenuated

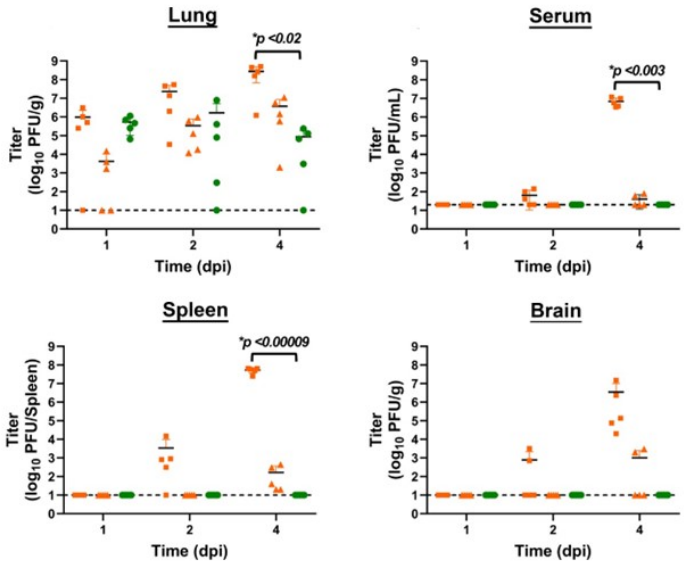
TNX-801 INFECTION DISPLAYS LIMITED REPLICATION



VACV-IHD ~10^6 PFU (■)

VACV-NYCBH ~10^6 PFU (▲)

TNX-801 ~10^8 PFU (●)



TNX-801 IS HIGHLY ATTENUATED WITH IMPROVED SAFETY PROFILES COMPARED TO OTHER VACCINA-BASED VACCINES

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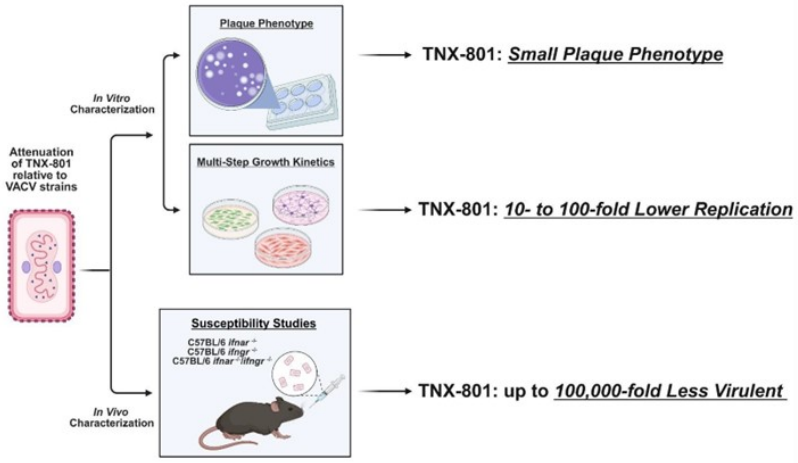
Editor's Pick | Biotechnology | Research Article

Recombinant chimeric Horsepox virus (TNX-801) is attenuated relative to Vaccinia virus strains in both *in vitro* and *in vivo* models

Stephanie V. Trefry,[1] Mayanka Awasthi,[1] Christy N. Raney,[1] Amy L. Cregger,[1] Chase A. Gonzales,[1] Brittney L. Layton,[1] Robert N. Enamorado,[1] Nelson A. Martinez,[1] Deborah S. Gohegan,[1] Masoudeh Masoud-Bahnamiri,[1] Jennifer Y. Cho,[1] Dawn M. Myscofski,[1] Tinoush Moulaei,[1] Natasza E. Ziółkowska,[1] Scott J. Goebel,[1] Seth Lederman,[1] Sina Bavari,[1] Farooq Nasar[1]

AUTHOR AFFILIATION See affiliation list on p. 23.



TNX-801 IMMUNOGENICITY AND EFFICACY IN ANIMAL MODELS

1)  → MPXV Clade Ia

2)  → RPXV

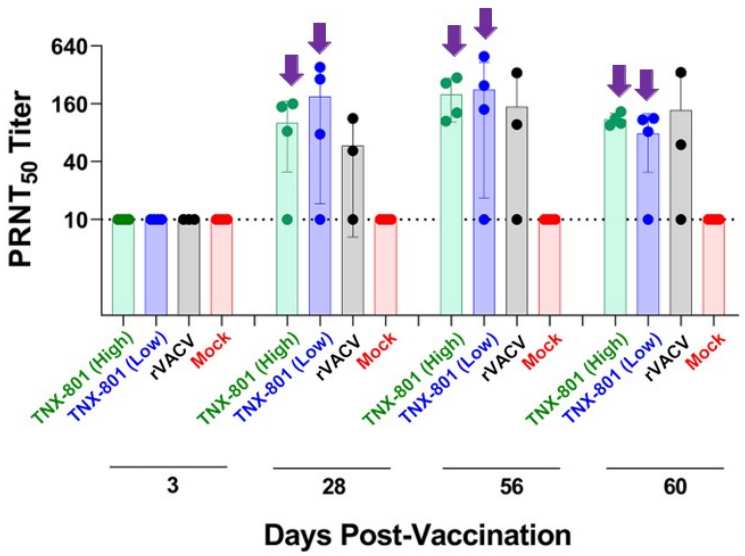
3)  → MPXV Clade IIa

NHP IMMUNOGENICITY AND EFFICACY STUDY DESIGN

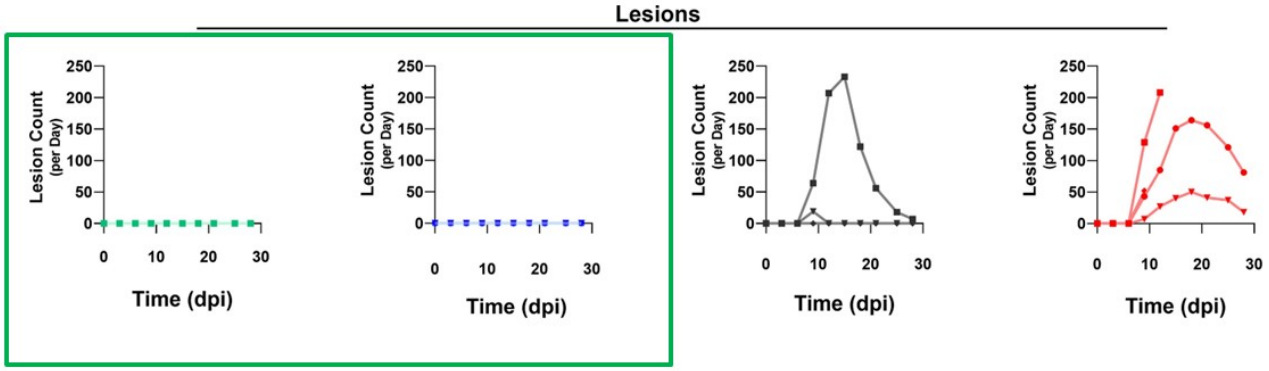
Vaccination					Challenge		
Group	Treatment	n	Dose (PFU)	Route	*Virus*	*Dose (PFU)*	*Route*
1	TNX-801 (High)	4	4×10^6	PERCUT	*MPXV (Zaire)*	10^5	*IT*
2	TNX-801 (Low)	4	5×10^5	PERCUT	*MPXV (Zaire)*	10^5	*IT*
3	rVACV	4	1×10^5	PERCUT	*MPXV (Zaire)*	10^5	*IT*
4	Mock	4	-	PERCUT	*MPXV (Zaire)*	10^5	*IT*

rVACV = synthesized vaccinia similar to ACAM2000 (Approved Vaccine)

NHP IMMUNOGENICITY: NEUTRALIZING ANTIBODY RESPONSE

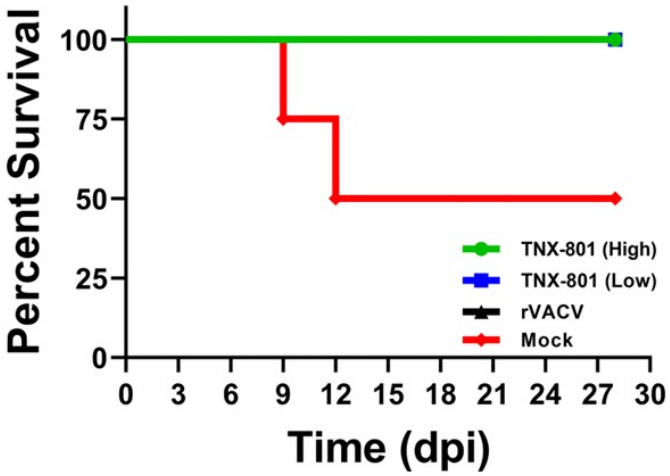


TNX-801 PROVIDES PROTECTION AGAINST MPOX DISEASE



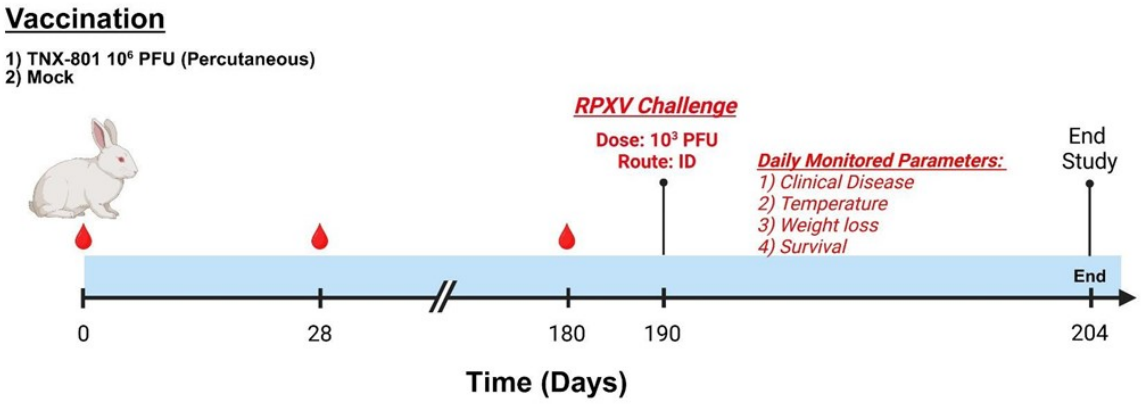
NO LESIONS in TNX-801 vaccinated groups

TNX-801 PROVIDES PROTECTION AGAINST LETHAL MONKEYPOX CLADE I CHALLENGE



NO LETHALITY in TNX-801 vaccinated groups

TNX-801 PROVIDES DURABLE PROTECTION AGAINST LETHAL RABBITPOX CHALLENGE: 6 MONTHS



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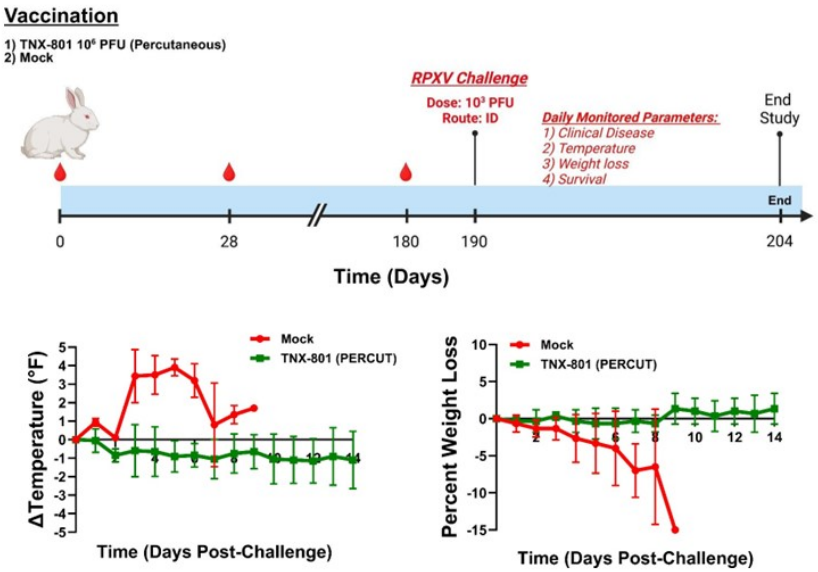

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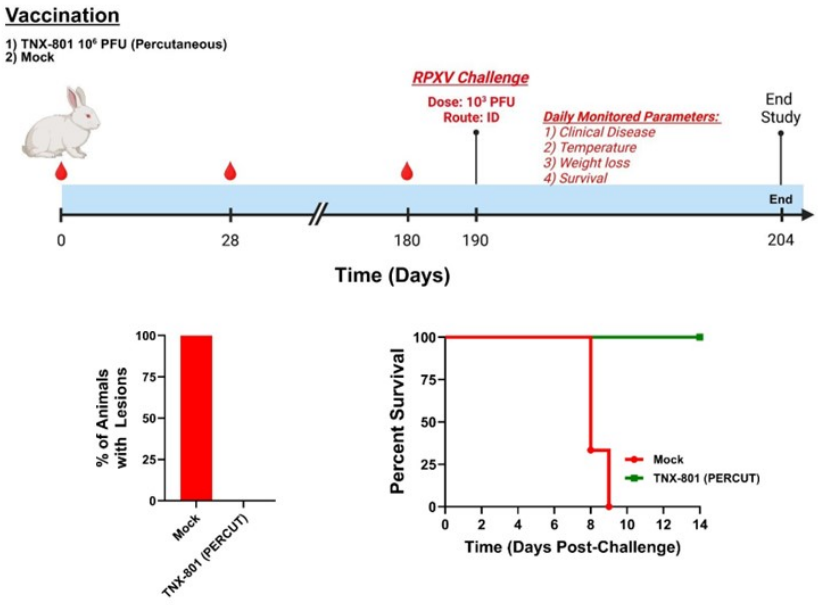
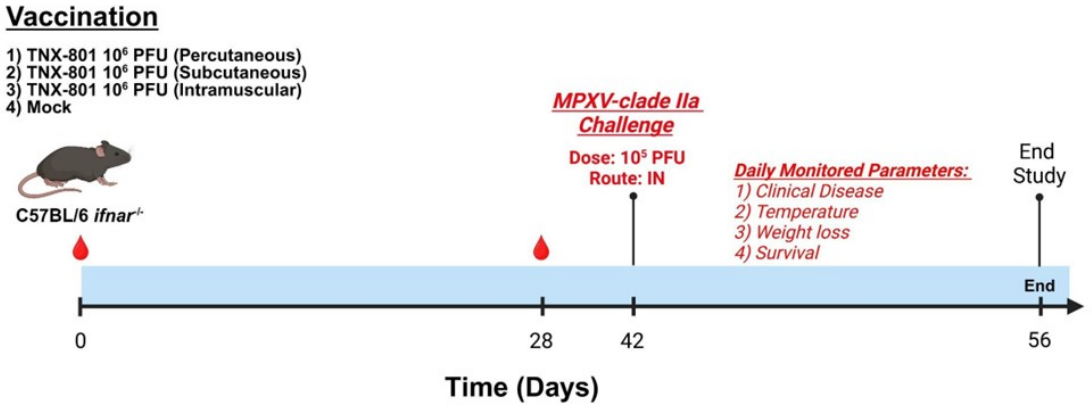
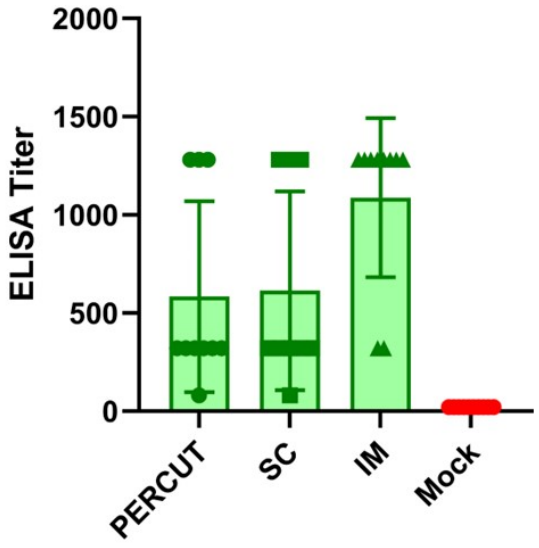


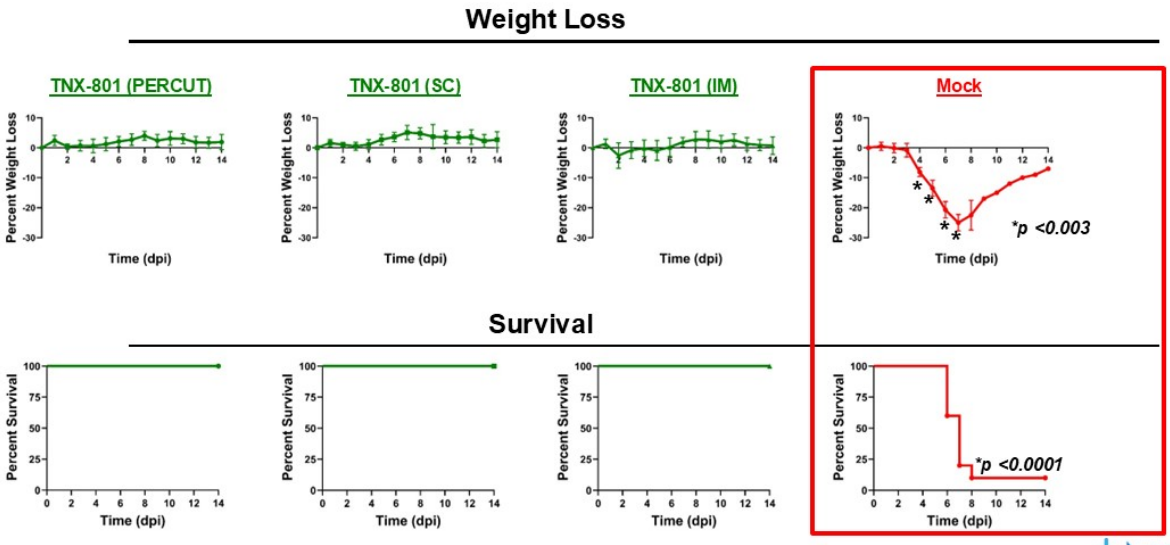
TNX-801 PROVIDES PROTECTION AGAINST LETHAL MONKEYPOX CLADE IIA CHALLENGE: ALTERNATIVE ROUTES



TNX-801 ELICITS HUMORAL IMMUNE RESPONSES: ANTI-VACV IGG TITERS (28 DAYS POST-VACCINATION)



TNX-801 PROVIDES PROTECTION AGAINST LETHAL MONKEYPOX CLADE IIA CHALLENGE: ALTERNATIVE ROUTES



TNX-801 SAFETY

- ***In vitro***:
  - Small plaque phenotype
  - Up to 100-fold lower replication than VACV strains
  - Primary cells from dermal and respiratory tracts
- ***In vivo***:
  - Well tolerated in mice, rabbits, hamsters, and NHPs
  - Minimal or no disease in immunocompromised murine models
  - up to 100,000-fold more attenuated than VACV-based vaccines
  - Minimally replicates at site of delivery

TNX-801 IMMUNOGENICITY AND EFFICACY (SINGLE DOSE)

- Evaluated in multiple animal models
  - Mouse, Rabbits, and NHPs
- Elicits IgG and/or neutralizing responses
  - Various route percutaneous, subcutaneous, intramuscular
  - Microneedle delivery
- Provides 100% protection against lesions
  - Rabbit and NHP models
- Provides 100% protection against lethal challenge
  - Models: Mouse, Rabbit, and NHP
  - Viruses: VACV, RPXV, MPXV clade Ia and IIa

4 PRONG APPROACH TO MPOX/SMALLPOX VACCINE (TNX-801)

1) Well-tolerated
2) Single dose
3) Durable
4) Protection against mpox disease (lesions)

ACKNOWLEDGEMENTS

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  - Scott Goebel
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  - Natasza Ziółkowska
  - Siobhan Fogarty
  - Helen Stillwell
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  - Ryan Noyce
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- **Southern Research**