



TNX-801: A Novel Mpox Vaccine (Horsepox Platform) to Enhance Preparedness and Global Vaccine Equity

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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

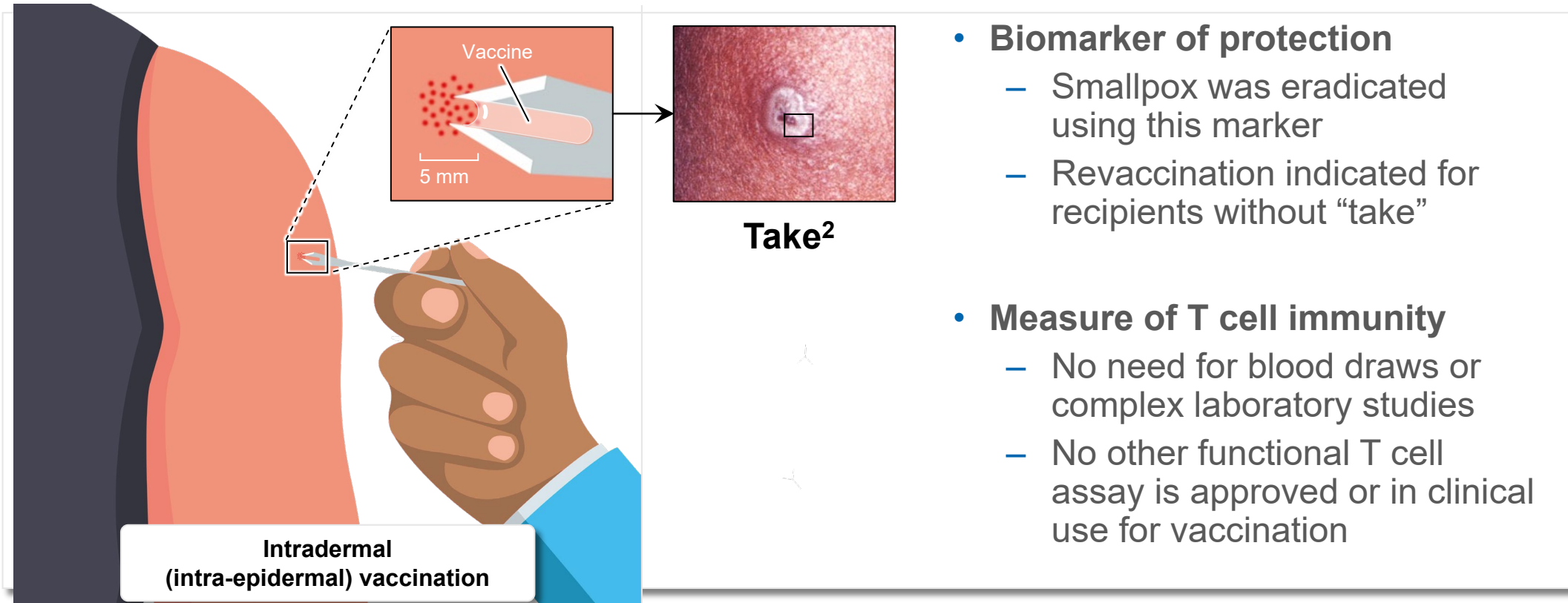
Development and clinical scale manufacturing of biologics
~45,000 square feet, BSL-2

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.



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



*Example of major cutaneous reaction, or “take,” resulting from a replication-competent live-virus vaccine with intradermal delivery, indicating successful vaccination^{1,2}

¹Fulginiti VA, et al. *Clin Infect Dis*. 2003;37(2):241-250.

²Centers for Disease Control and Prevention. Accessed April 15, 2020. <https://phil.cdc.gov/Details.aspx?pid=3276>

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) clone³**
 - Synthesized⁴ 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 isolate⁵**

¹Tulman ER, et al. [Genome of horsepox virus](#). *J Virol*. 2006 80(18):9244-58.PMID:16940536

²Schrick, L. et al [An Early American Smallpox Vaccine Based on Horsepox](#) *N Engl J Med* 2017; 377:149

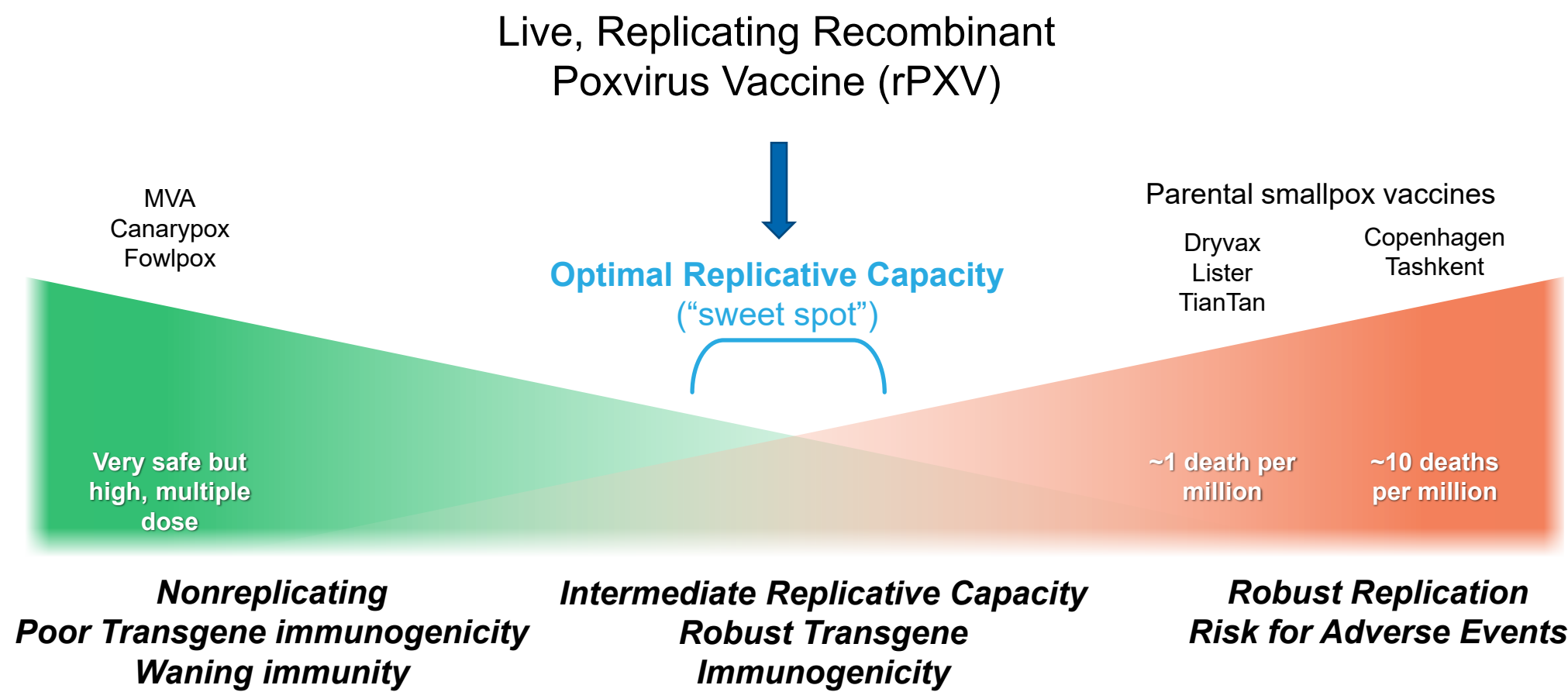
³Noyce RS, et al.. [Construction of an infectious horsepox virus vaccine from chemically synthesized DNA fragments](#). *PLoS One*. 2018 Jan 19;13(1):e0188453

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:27973399
PMCID: [PMC5192389](#) DOI: [10.3390/v8120328](#)

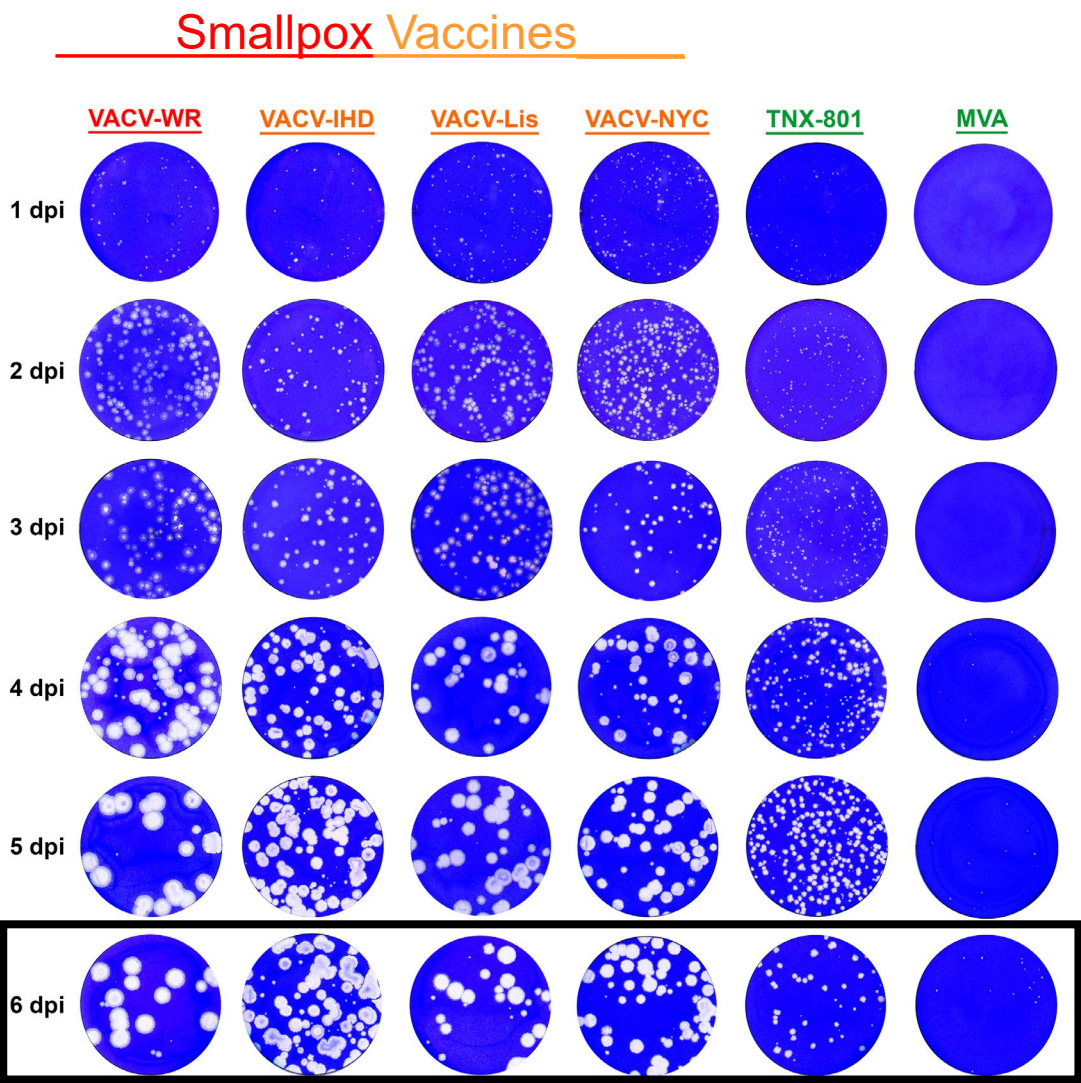
⁵Noyce, RS, et al. Synthetic Chimeric Horsepox Virus (scHPXV) Vaccination Protects Macaques from Monkeypox* Presented as a poster at the American Society of Microbiology BioThreats Conference - January 29, 2020, Arlington, VA. (<https://content.equisolve.net/tonixpharma/media/10929ac27f4fb5f5204f5cf41d59a121.pdf>)

Illustrative Safety Spectrum Of Pox-based Vaccine Vectors

Optimizing Live Virus Vaccines

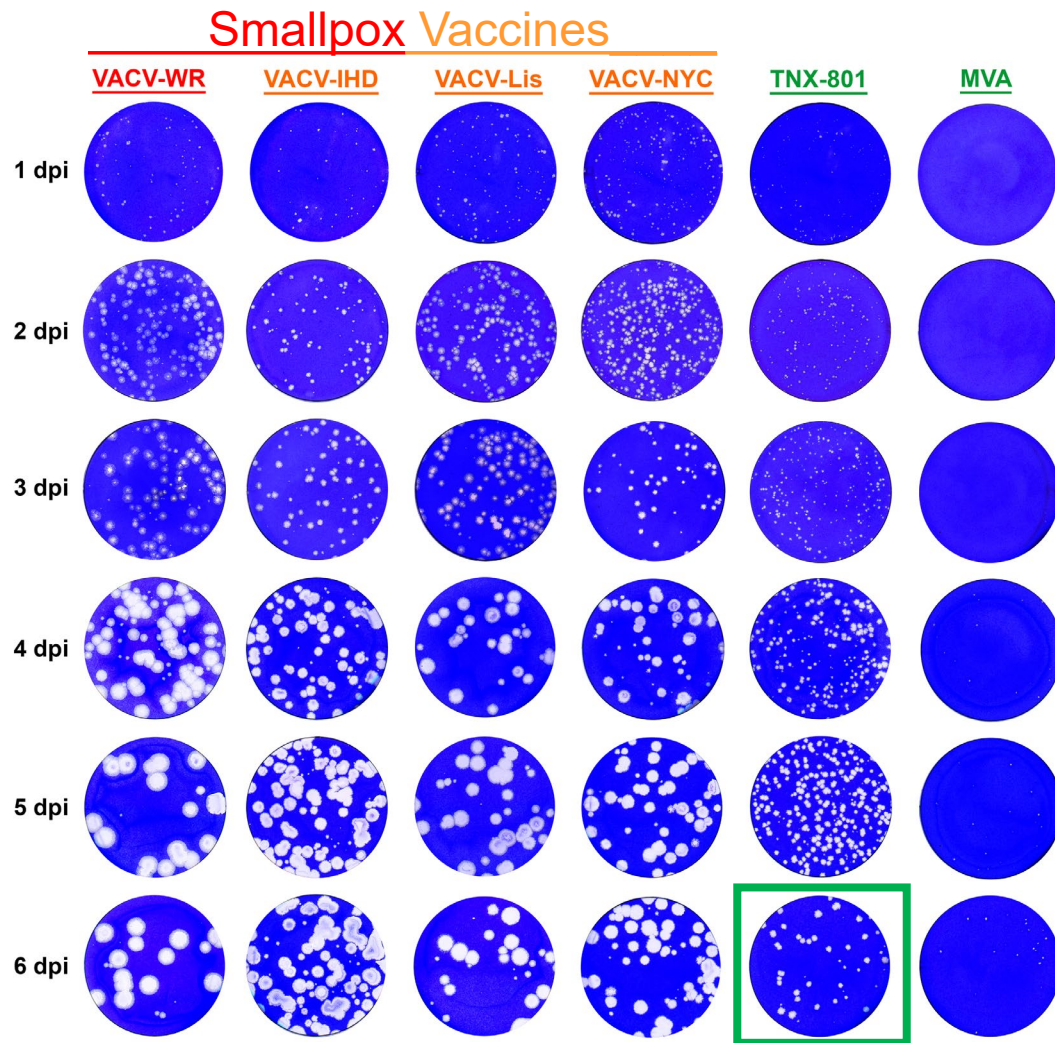


Characterization of TNX-801 Platform: Naturally Attenuated Relative to VACV Based Vaccines (Smallpox)



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

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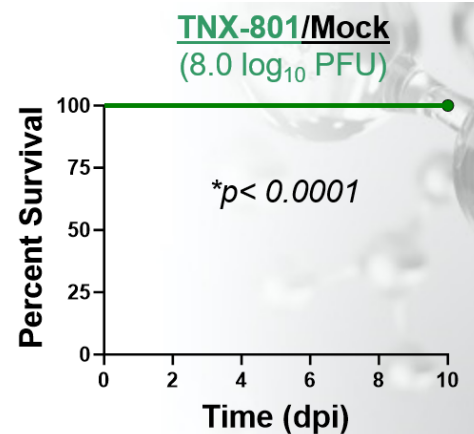
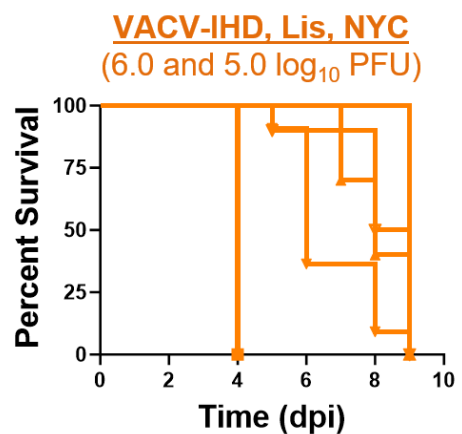
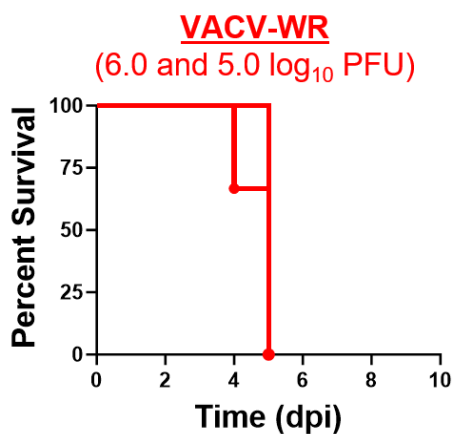
➤ TNX-801 is **attenuated *in vitro*** relative to all VACV (WR, IHD, Lis, NYC)

- 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)

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

Survival: 100% Immunized







Murine Model : Mpox Clade 1 Challenge

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

1000x more attenuated than
older VACV-based vaccines

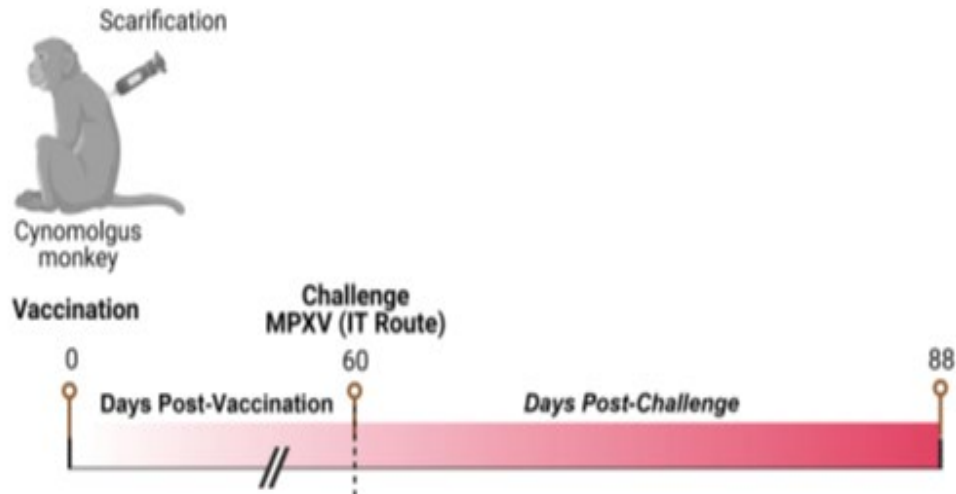
Article

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

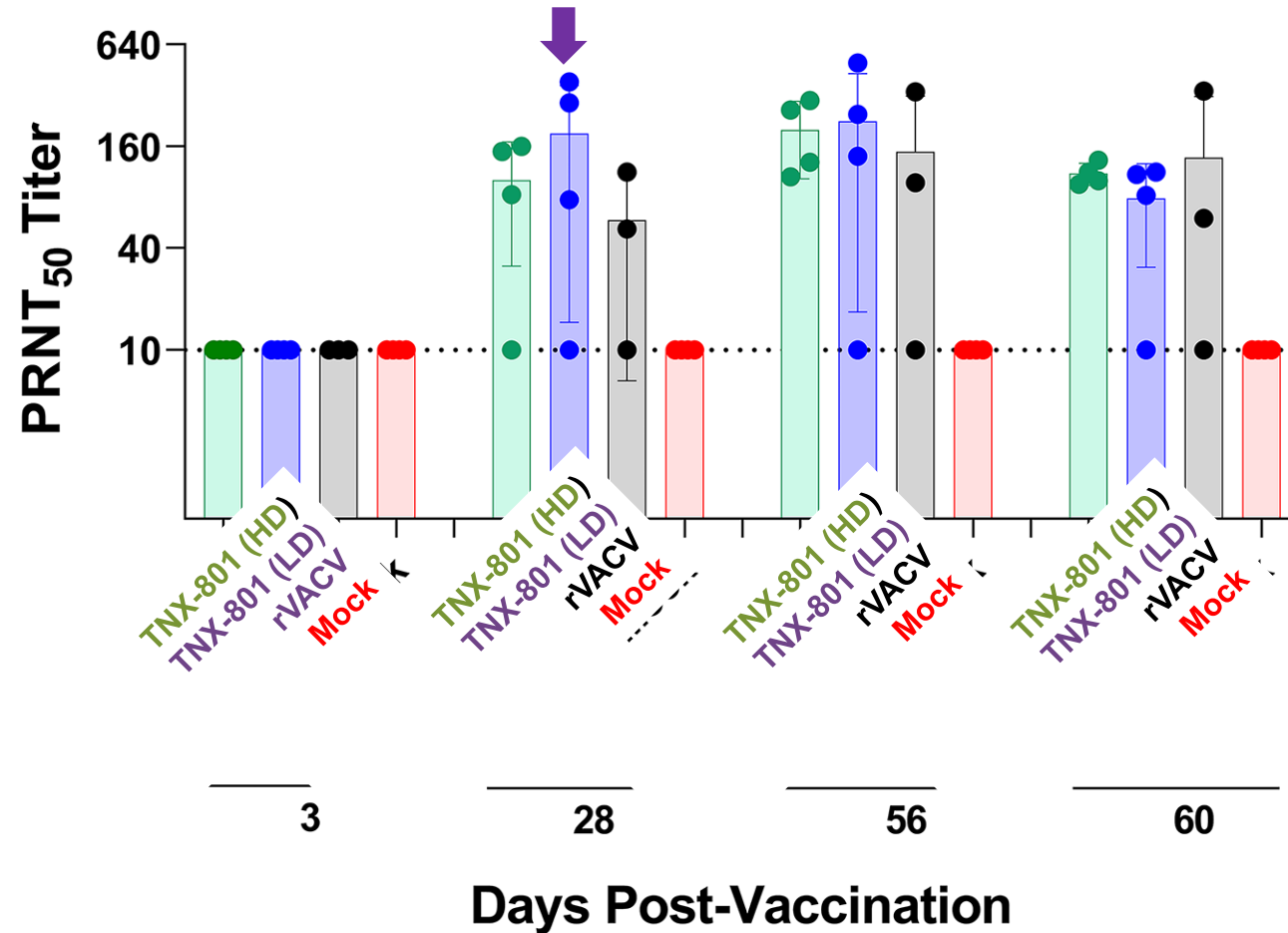


“Take” observed in all TNX-801 vaccinated NHPs except one.

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

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

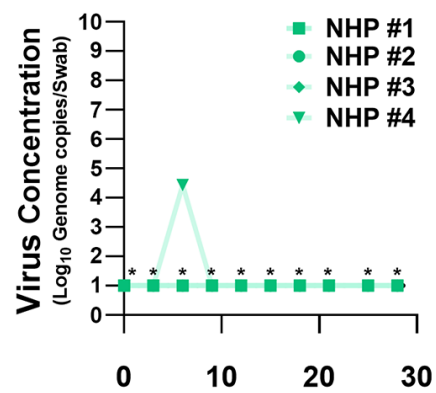
Immunogenicity: Neutralizing Antibody (PRNT₅₀ Assay)



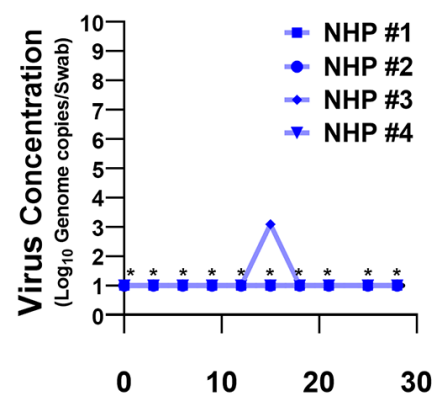
**88% of TNX-801 vaccinated NHPs had neutralizing antibody responses
8- to 50-fold from baseline**

Measured Virus Shedding: Oral Swabs

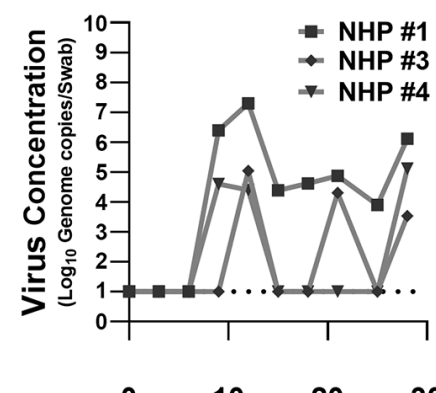
Oral Swabs



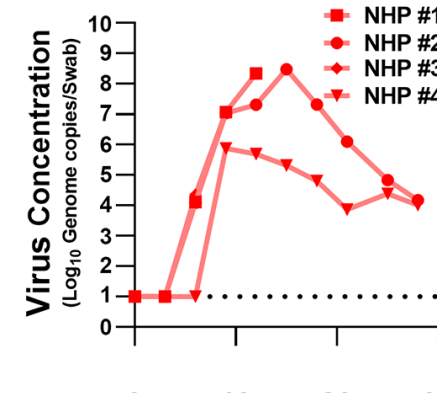
TNX-801 (High Dose)



TNX-801 (Low Dose)



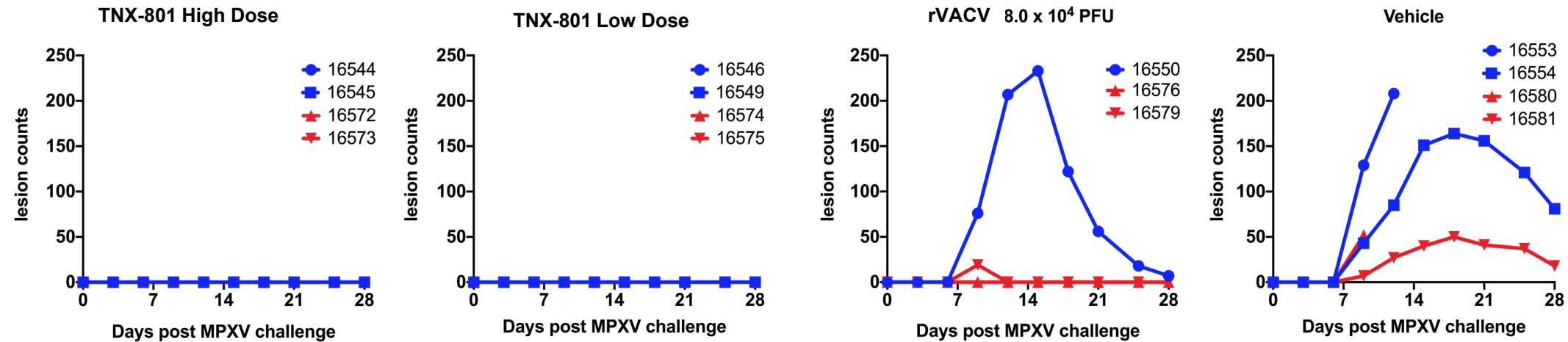
rVACV



Mock

Minimal or no virus shedding in Tonix-801 vaccinated groups

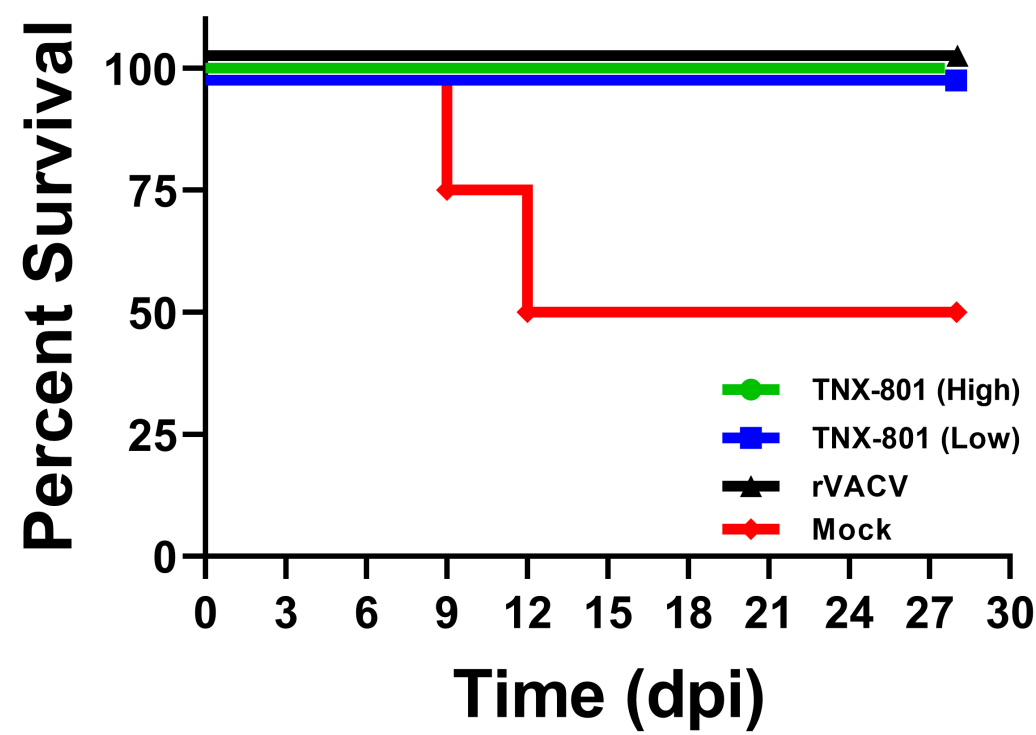
Clinical Signs After MPXV Challenge



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

¹Noyce, RS, et al. Synthetic Chimeric Horsepox Virus (schHPXV) 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)

¹Sagy Nature Medicine 2023

²Deputy et al NEJM 2023

³Titanji 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 Africa¹
- Distribution and Finance are significant barriers²
- Developed countries ordered nearly all available and future doses of mpox vaccine³
- Africa access to vaccines is patchy or non-existent⁴

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

¹Koslov Nature Medicine 2023

²Ogunkola Vaccines 2023

³LA times May 30, 2023

⁴GAVI VaccineWorks June 21, 2023

Investigators and Collaborators

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- Siobhan Fogarty
- Sina Bavari
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- David Evans

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Univ. of Maryland – Institute of Human Virology

- José Esparza

Southern Research

- Fusataka Koide
- Landon Westfall²
- Karen Gilbert³

LINQ Pharma Consulting

- Onesmo Mpanju



THANK YOU

