TONIX PHARMACEUTICALS

TNX-801: A Novel Mpox Vaccine: Live, Replicating, Attenuated Orthopoxvirus (Horsepox) Vaccine

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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.

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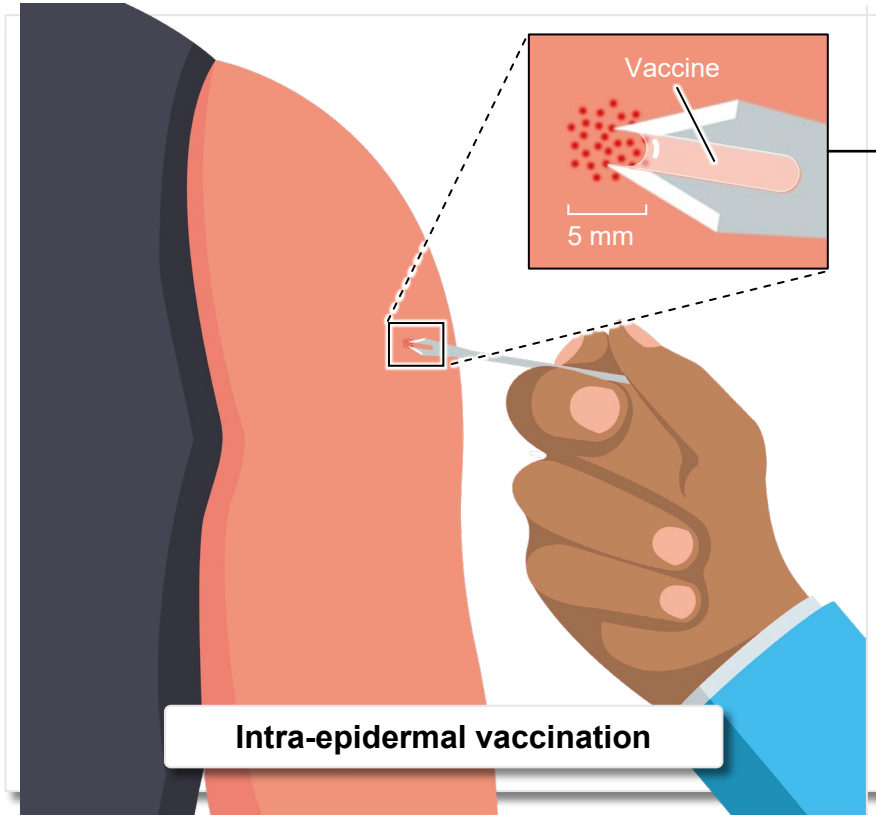
In 1796 Edward Jenner Successfully Used Vaccination to Protect Against Smallpox

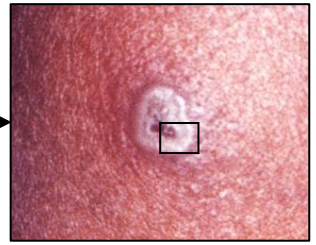
- Jenner reasoned infection with illness similar to smallpox, but less deadly, could protect against smallpox
  - "Jenner "vaccinated" (*vacca*, Latin for "cow") a patient with pustule matter from "cowpox" sores on a milkmaid's hands;
  - Patient remained healthy when challenged with smallpox virus

- 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=3276

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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:16940536
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: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)

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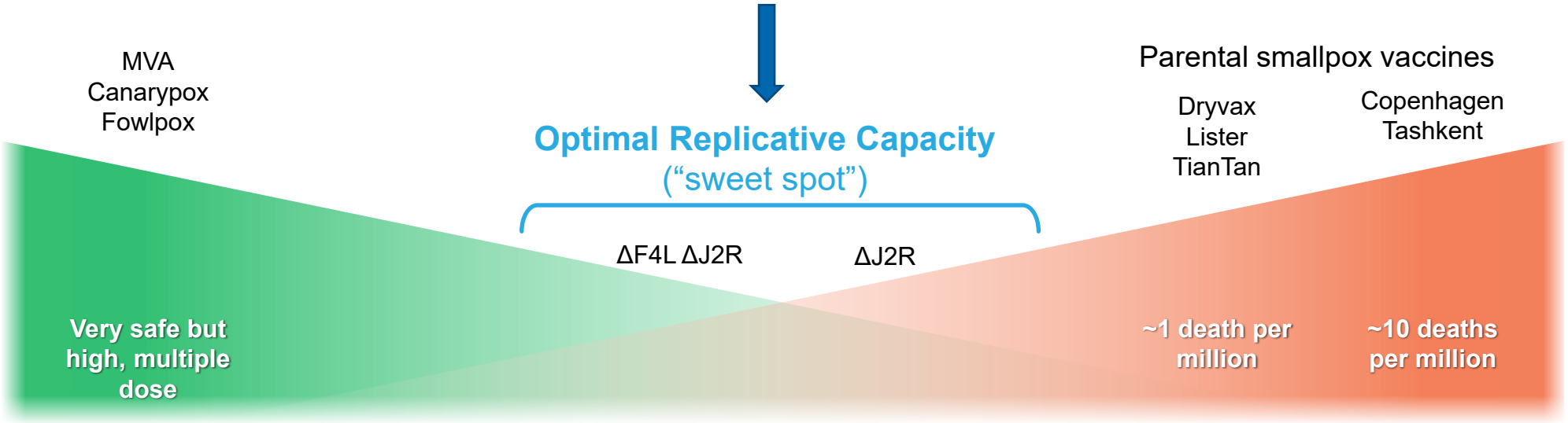
Illustrative Safety Spectrum Of Pox-based Vaccine Vectors

Optimizing Live Virus Vaccines

New Live Recombinant Poxvirus Vaccine
(rPXV)



Nonreplicating
Poor Transgene immunogenicity
Waning immunity

Intermediate Replicative Capacity
Robust Transgene Immunogenicity

Robust Replication
Risk for Adverse Events

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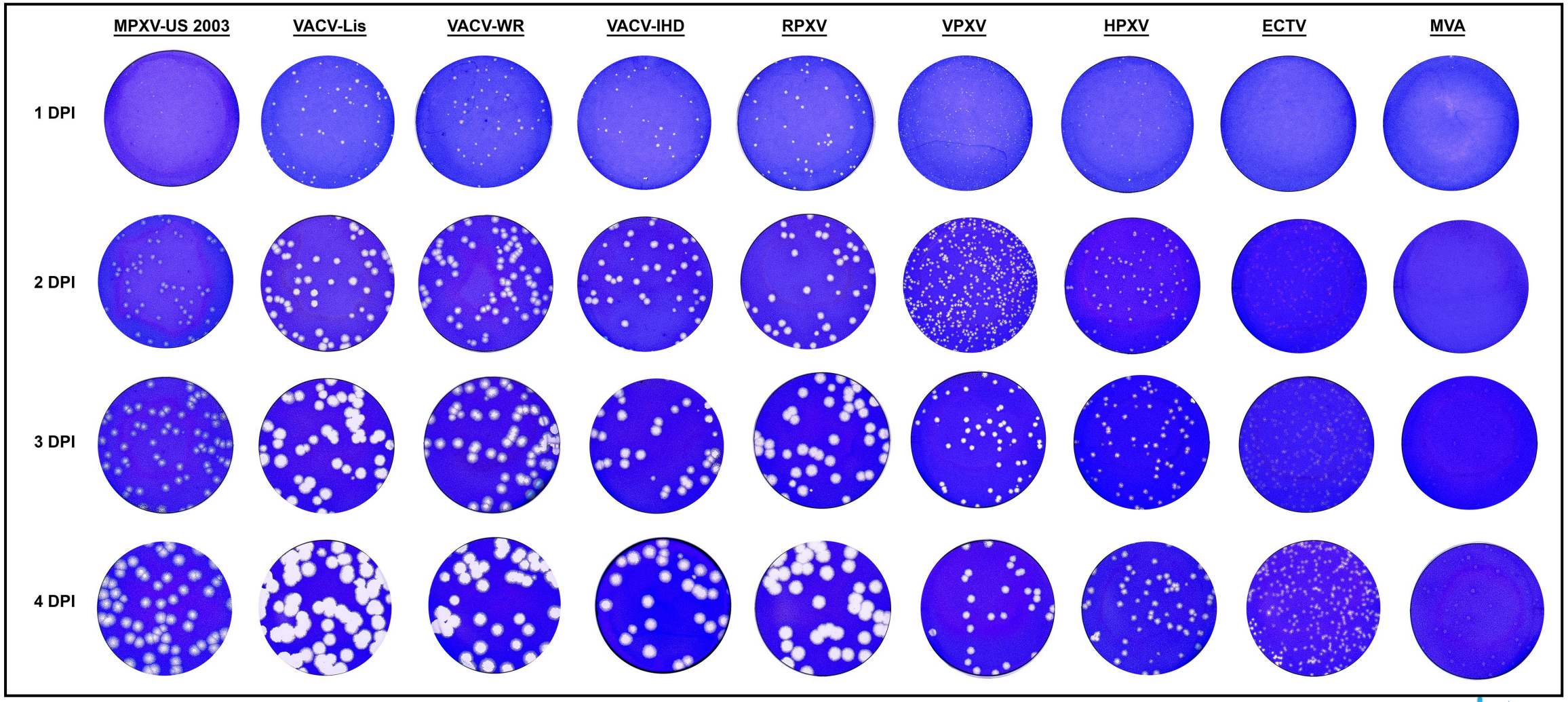
Orthopoxvirus Virulence as Visualized by Plaque Assay



viruses

MDPI

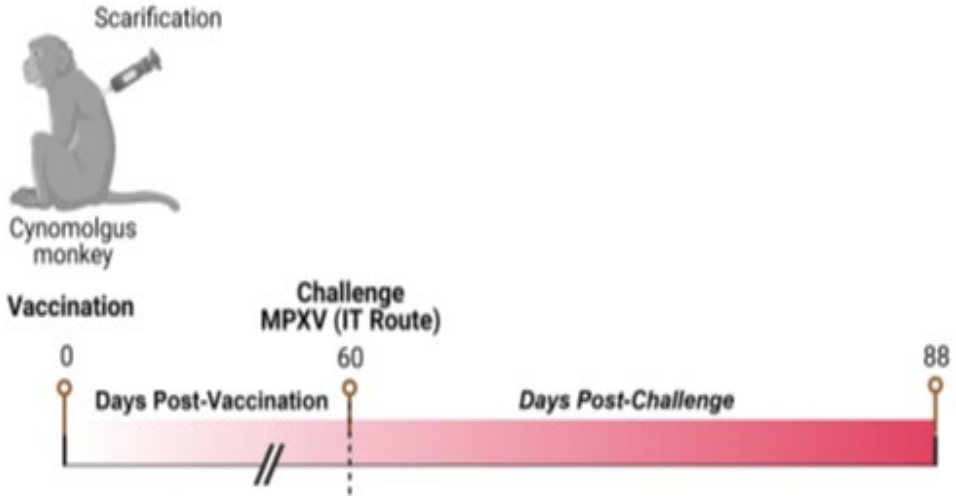
Article

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 were revaccinated on day 14.

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

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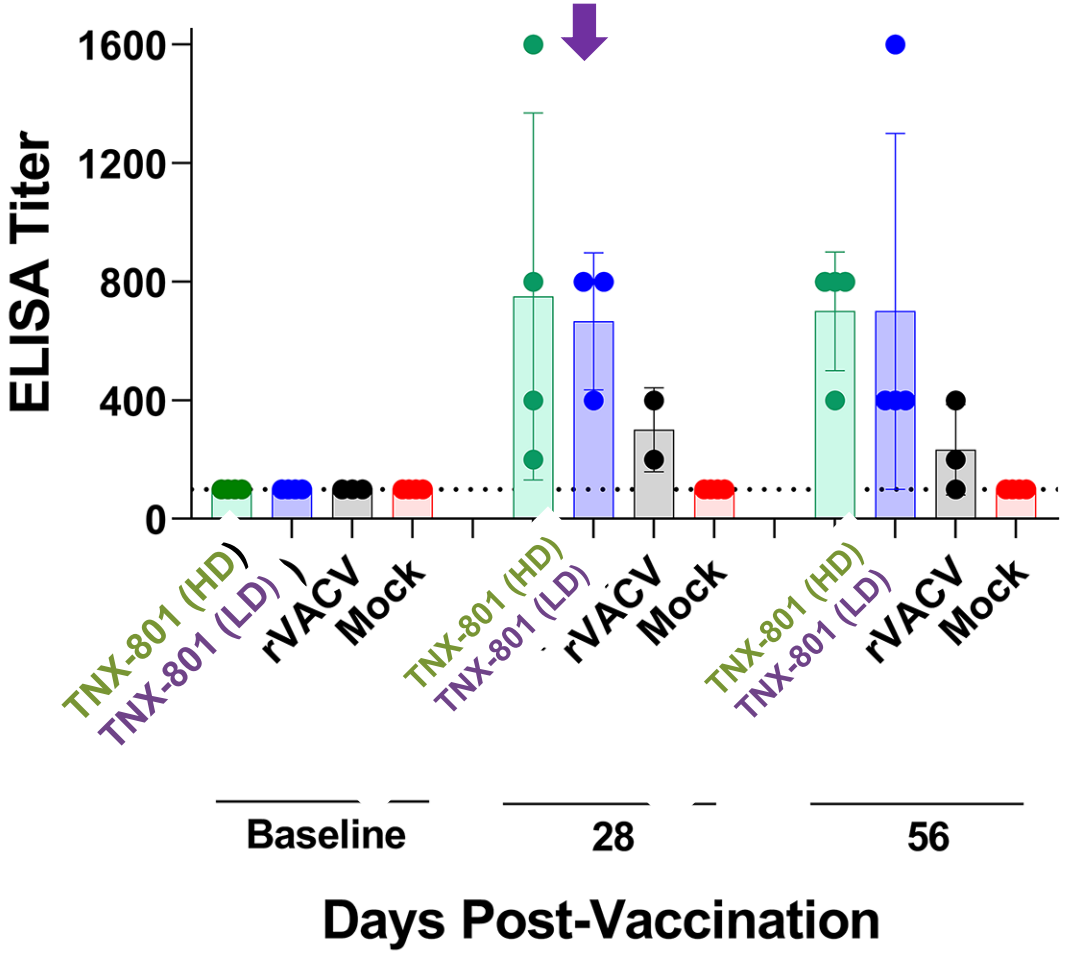
Immunogenicity: Total IgG (ELISA)



100% seroconversion in Tonix-801 vaccinated groups with antibody titers 2- to 16-fold higher than baseline by day 28 and 4-to 8–fold higher at day 56.

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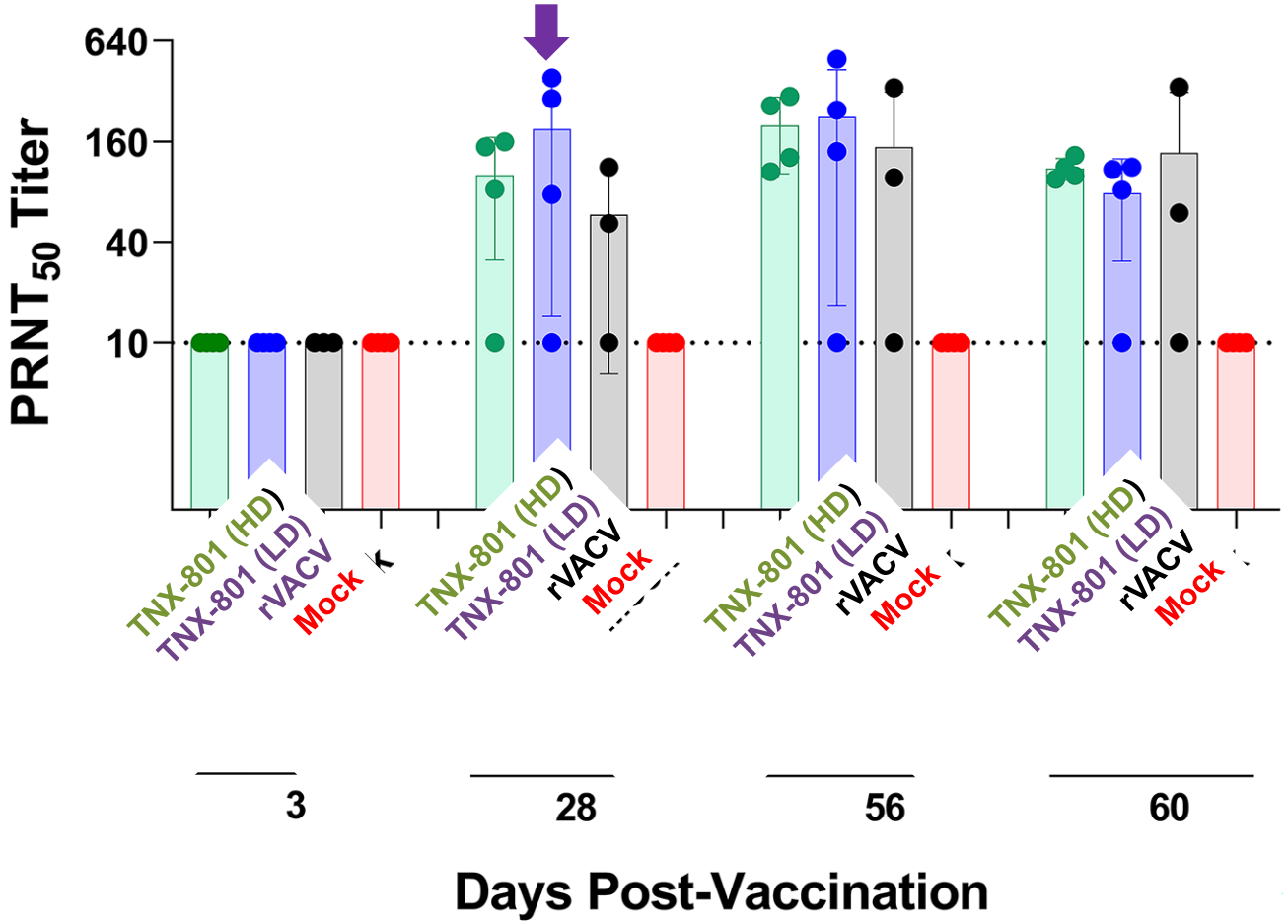
Immunogenicity: Neutralizing Antibody ($PRNT_{50}$ Assay)



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

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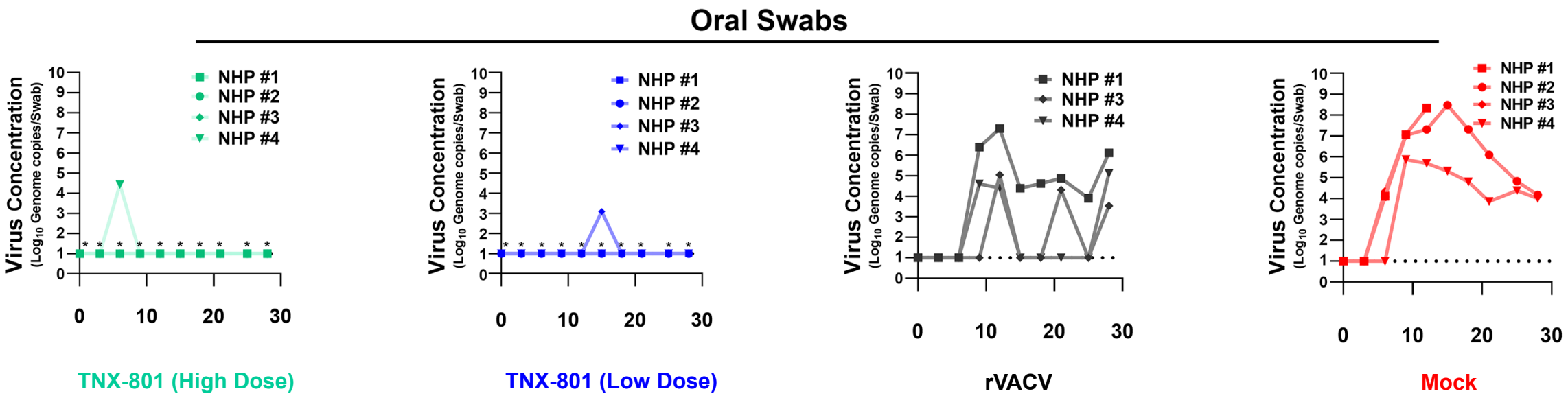
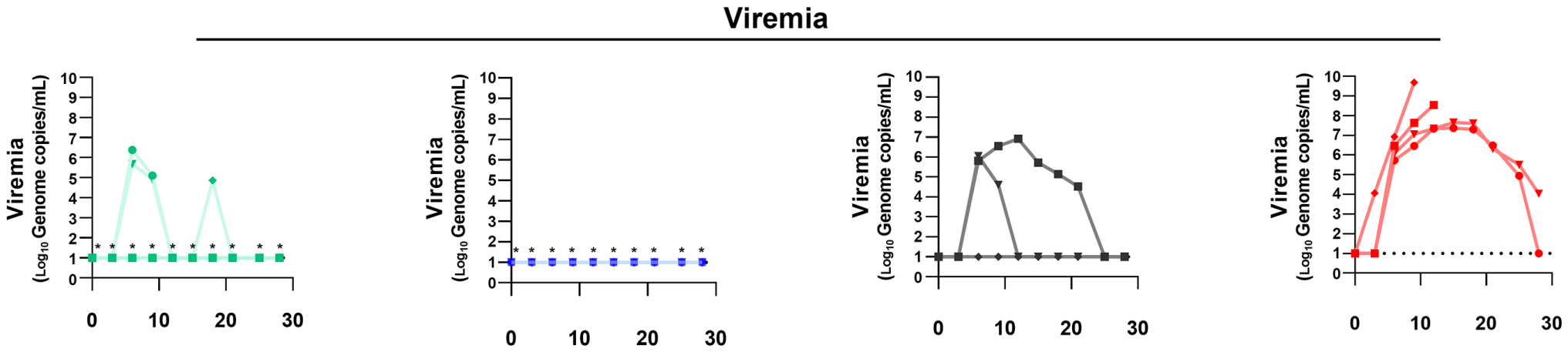
Measured Virus Shedding: Oral Swabs



Minimal or no virus shedding in Tonix-801 vaccinated groups

Measured Viremia



TNX-801 (High Dose)

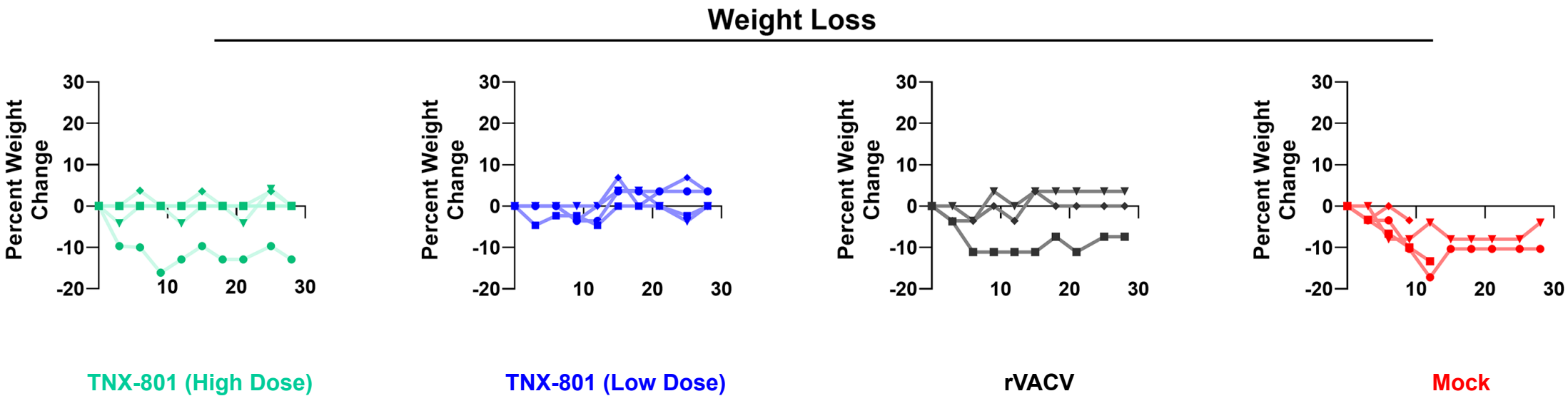
TNX-801 (Low Dose)

rVACV

Mock

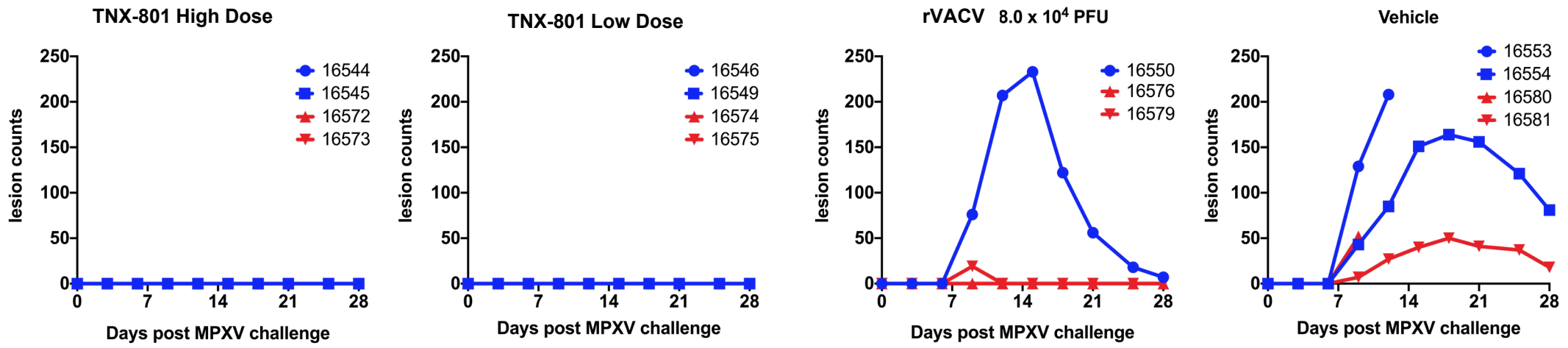
Minimal sporadic or no viremia in Tonix-801 vaccinated groups

Clinical Disease: Weight Loss



Minimal or no weight loss 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)

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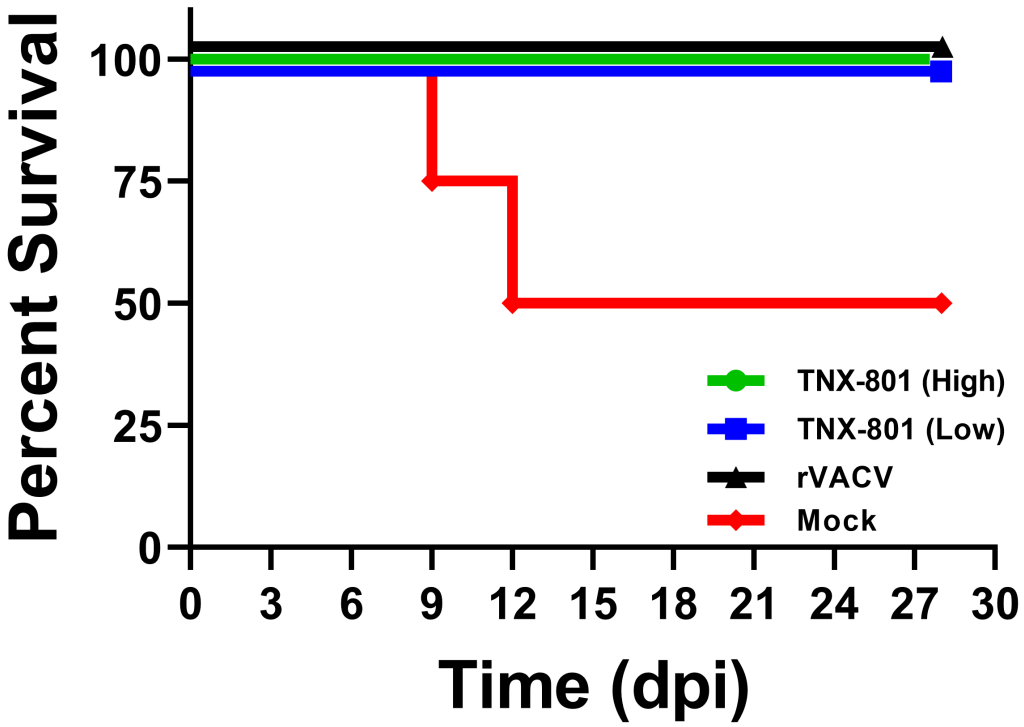
Clinical Disease: Lethality



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

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Live Recombinant Poxvirus (rPXV) Vaccine Platform Profile

POTENTIALLY LONGER DURABILITY DUE TO POX-ENGINEERED ARCHITECTURE

- Live virus vaccines present unique “danger signals” (PAMPs)
- Results in strong immune response

PROGRAMMABLE VECTOR DESIGN FOR USE IN DIFFERENT DISEASES

- Large capacity for expressing inserted genes
- Wide range of clinical applications: pandemic, biodefense, infectious disease, smallpox, oncology

LIVE VIRUS-BASED SCIENCE IS WELL ESTABLISHED

- Streamlined development
- Ability to vertically integrate development and manufacturing
- Standard cold-chain requirements

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Approved Recombinant Poxvirus-Based Commercial Products[1-3]

Product	Application / disease	Location	Poxvirus vector	Host restricted?	Doses released to environment
TROVAC-AIV H5N1 *Boehringer Ingelheim*	Agriculture/avian influenza	Mexico, Central America	TROVAC-AIV H5N1	**No** ***Replication competent***	**2 billion** (as of 2006)
Purevax FeLV *Boehringer Ingelheim*	Companion animals (cats)/FeLV	US, others	ALVAC-FeLV Gag/Pol	Yes *Replication incompetent*	Unknown
Purevax Rabies *Boehringer Ingelheim*	Companion animals (cats)/rabies	US, others	ALVAC-RG	Yes *Replication incompetent*	Unknown
Recombitek *Boehringer Ingelheim*	Companion animals (dogs)/canine distemper	US, others	ALVAC-HA, F	Yes *Replication incompetent*	Unknown
Raboral V-RG **Rabisin** *Boehringer Ingelheim*	Wildlife control of rabies	US, Europe, Israel	Vaccinia Copenhagen RG	**No** ***Replication competent***	**250 million doses** *5 million doses/year*

[1]Boehringer Ingelheim. Accessed July 15, 2021. https://www.boehringer-ingelheim.com/animal-health/products
[2]Bublot M, Pritchard N, Swayne DE, et al. Development and use of fowlpox vectored vaccines for avian influenza. *Ann N Y Acad Sci*. 2006;1081:193-201.
[3]Maki J, Guiot AL, Aubert M, et al. Oral vaccination of wildlife using a vaccinia-rabies-glycoprotein recombinant virus vaccine (RABORAL V-RG®): a global review. *Vet Res*. 2017;48(1):57.

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Emerging Infectious Disease R&D and Manufacturing Capability

R&D Center –Frederick, MD

Advanced Development, MA

Commercial Manufacturing, MT(Planned)

American Pandemic Preparedness Plan (AP3) White House OSTP

AP3 Plan Element	Tonix rPXV Vaccine Platform Potential
Rapid Design, Testing Review <100 days	4-6 mo. Design-to-FIH trial
Rapid Production Scale Up	Large scale production <130 days possible
Distribution	Stable Traditional cold-chain
Administration	Intraepidermal : BFN or skin patch Non-Sterile No syringes
Adaptation	rPXV platform can express large inserts
Public Health Strategy	Potential to reduce onward transmission 1 dose only Ideal for Ring Vaccination Strategy

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Investigators and Collaborators

Tonix

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Current Addresses

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THANK YOU