TONIX PHARMACEUTICALS

A NOVEL SINGLE-DOSE, LIVE ATTENUATED, MINIMALLY REPLICATIVE MPOX VACCINE

Farooq Nasar, Ph.D., M.P.H.

WVC
April 23, 2025

PO6066 April 23, 2025 (Doc 1583)

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.

TONIX PHARMACEUTICALS

TALK OVERVIEW

1) **Background**

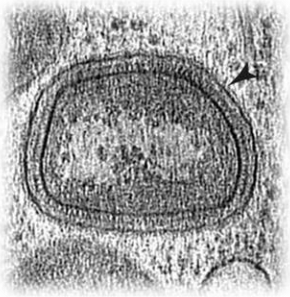
2) **TNX-801 attenuation *in vitro* and *in vivo***

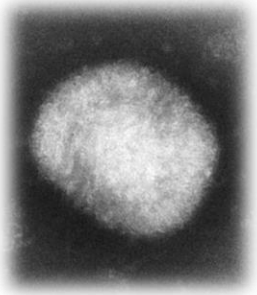
3) **TNX-801 immunogenicity and efficacy in animal models**

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

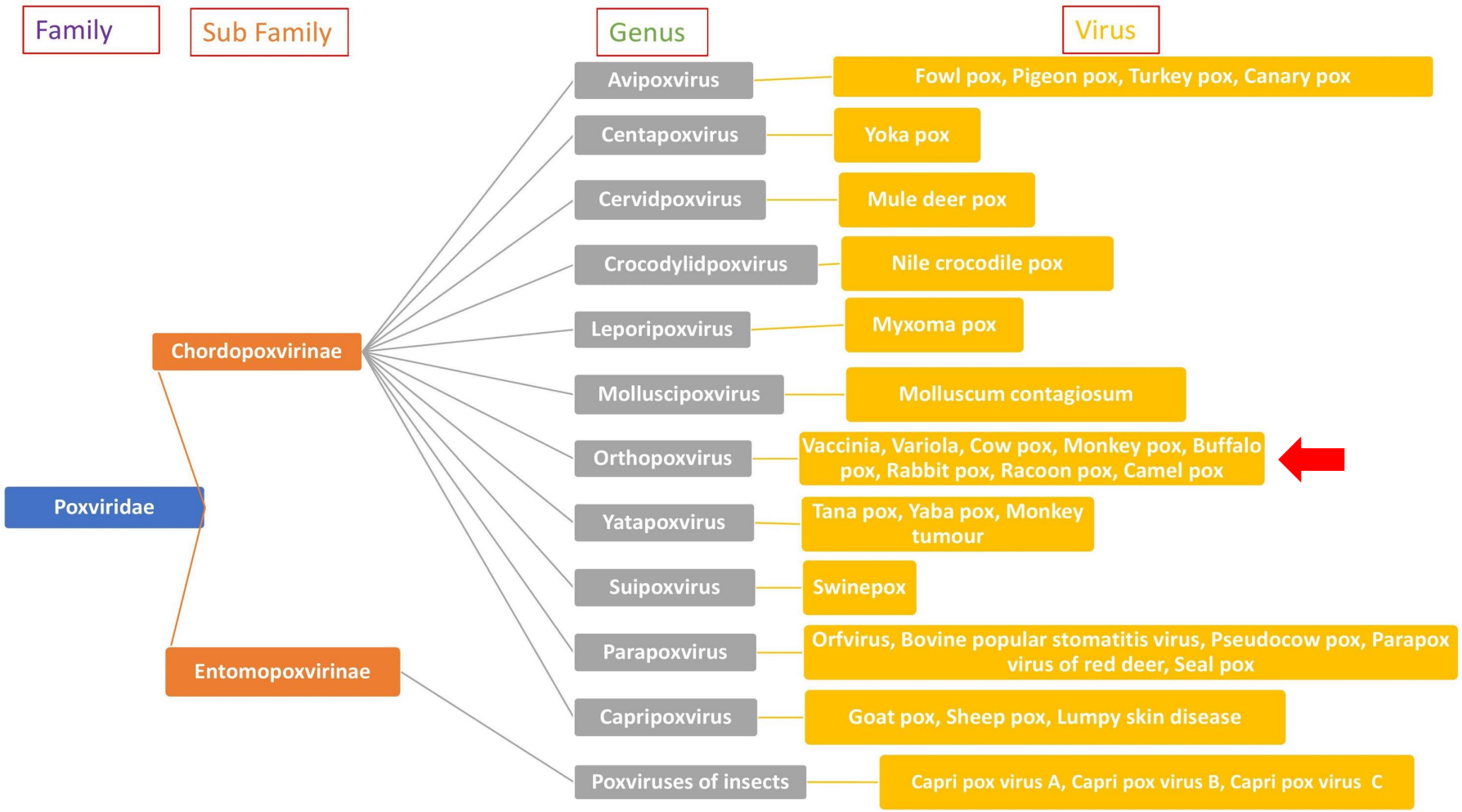
POXVIRUSES

- **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>**

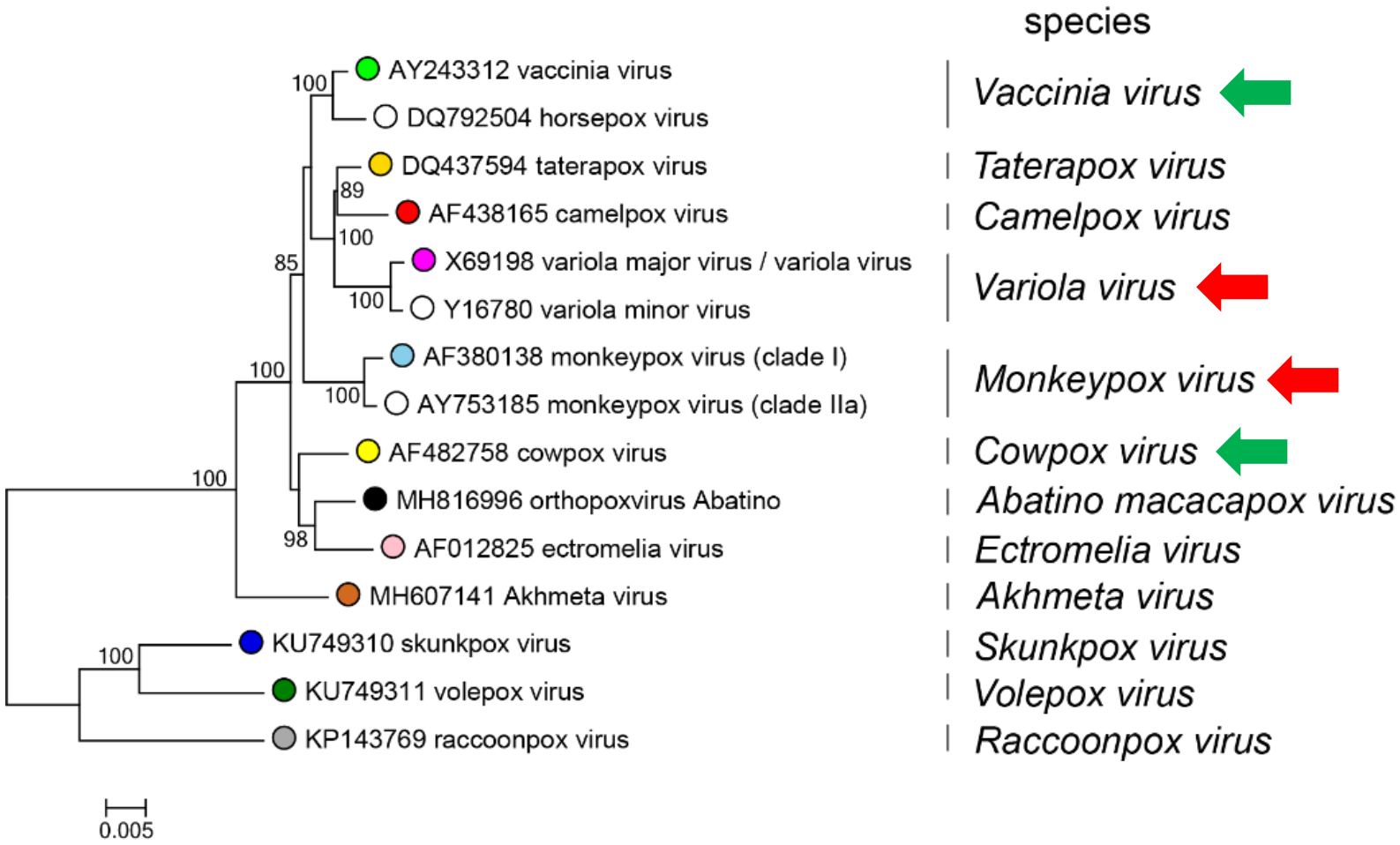




POXVIRUSES: UBIQUITOUS IN THE ENVIRONMENT



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

TONIX PHARMACEUTICALS

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)

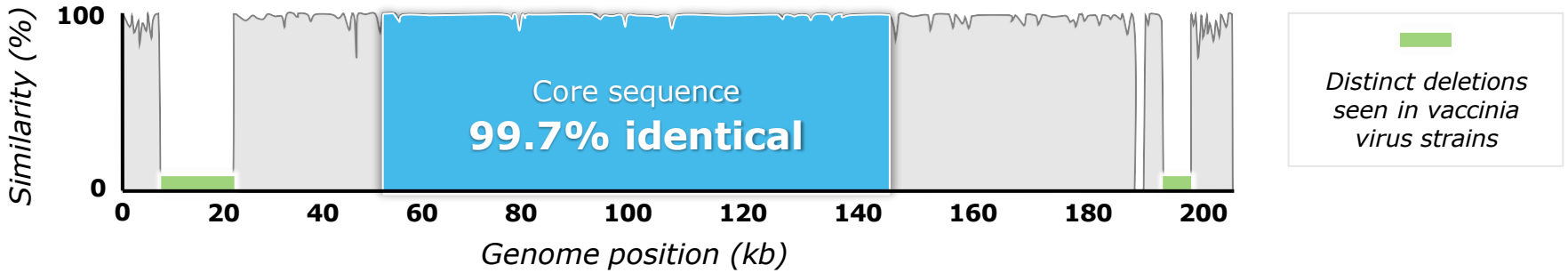
- **Jenner observed milkmaids were protected from smallpox, reasoned that infection with an illness similar to smallpox but less deadly could protect one against smallpox**
  - **“Cowpox” was the name of a disease in cows that could transfer to humans and cause sores**
  - **Jenner “vaccinated” (from *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]**

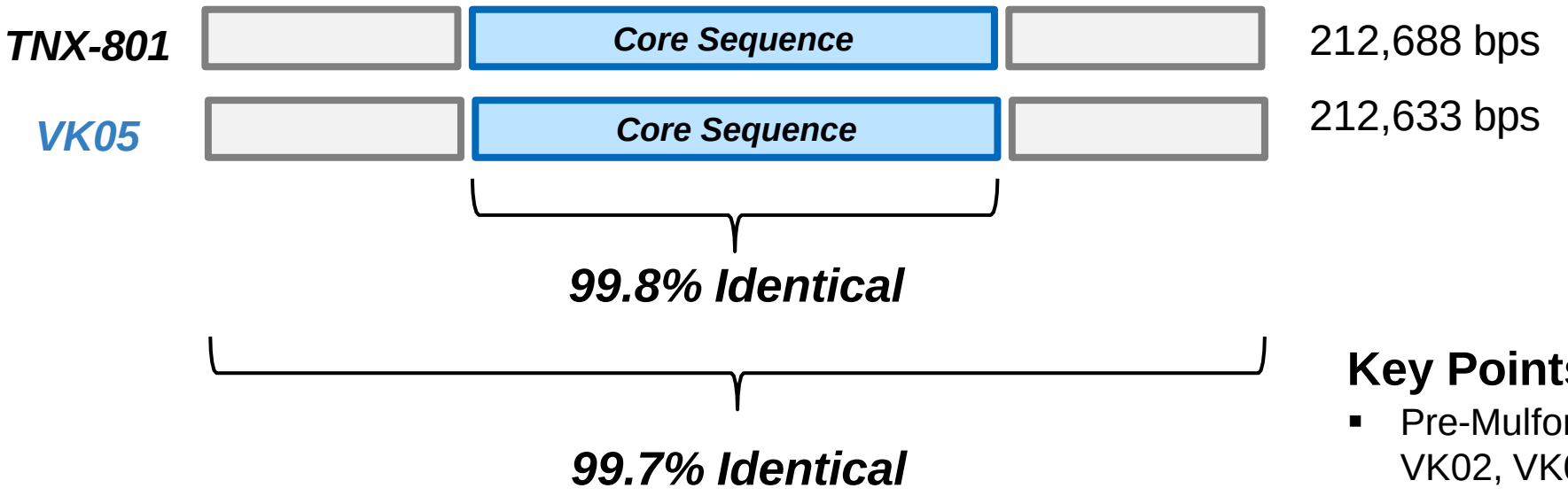
- **Vaccine producers may have propagated stocks by periodically supplementing or refreshing them with horsepox[2]**
  - A 1902 smallpox vaccine (**Mulford**) – 99.7% identical to core viral sequence
  - **Sequence Identity for the 1902 Mulford Vaccine Compared to HPVX[3]**



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

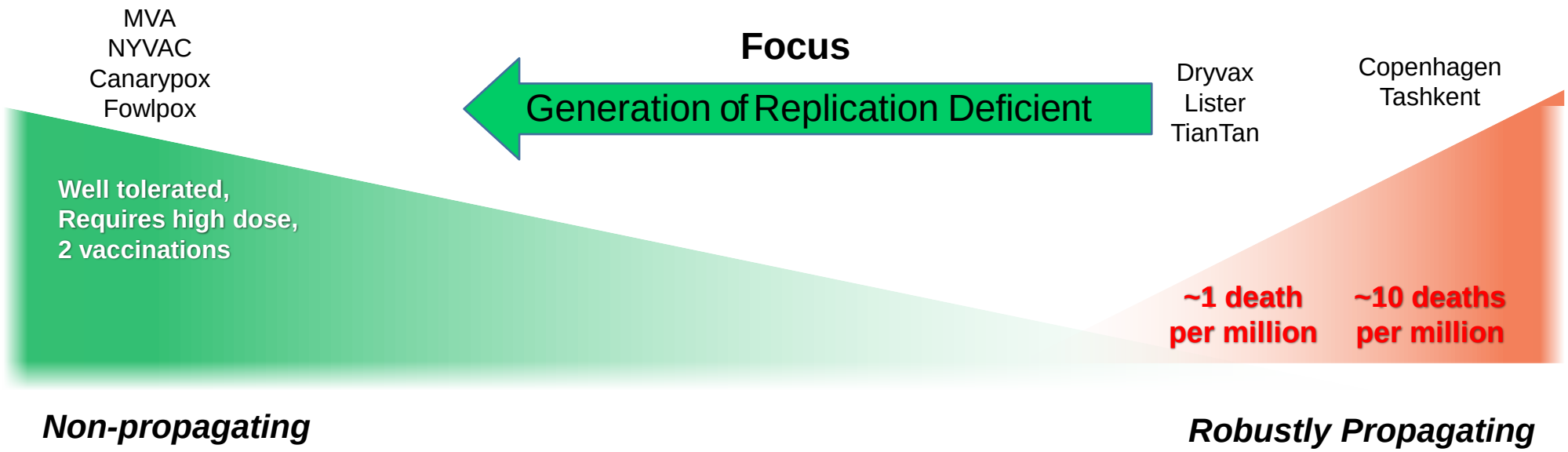
Brinkmann A, et al. *Genome Biol*. 2020;21(1):286.

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.

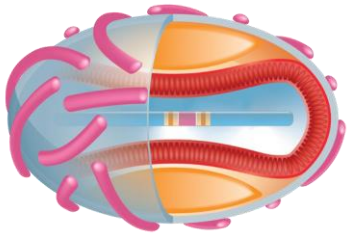
BALANCE OF TOLERABILITY AND REACTOGENICITY FOR POX-BASED VACCINES



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

MNR-76 genome (212,633 bp) *Genbank accession DQ792504*

MNR-76 genome fragments

LITR | 1A | 1B | 2 | 3 | 4 | 5 | 6 | 7 | RITR

Ten overlapping genome fragments were assembled based on sequence homology to generate the TNX-801 genome[1,2]

TNX-801 genome (212,811 bp) *Genbank accession KY349117*

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.

TONIX PHARMACEUTICALS

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

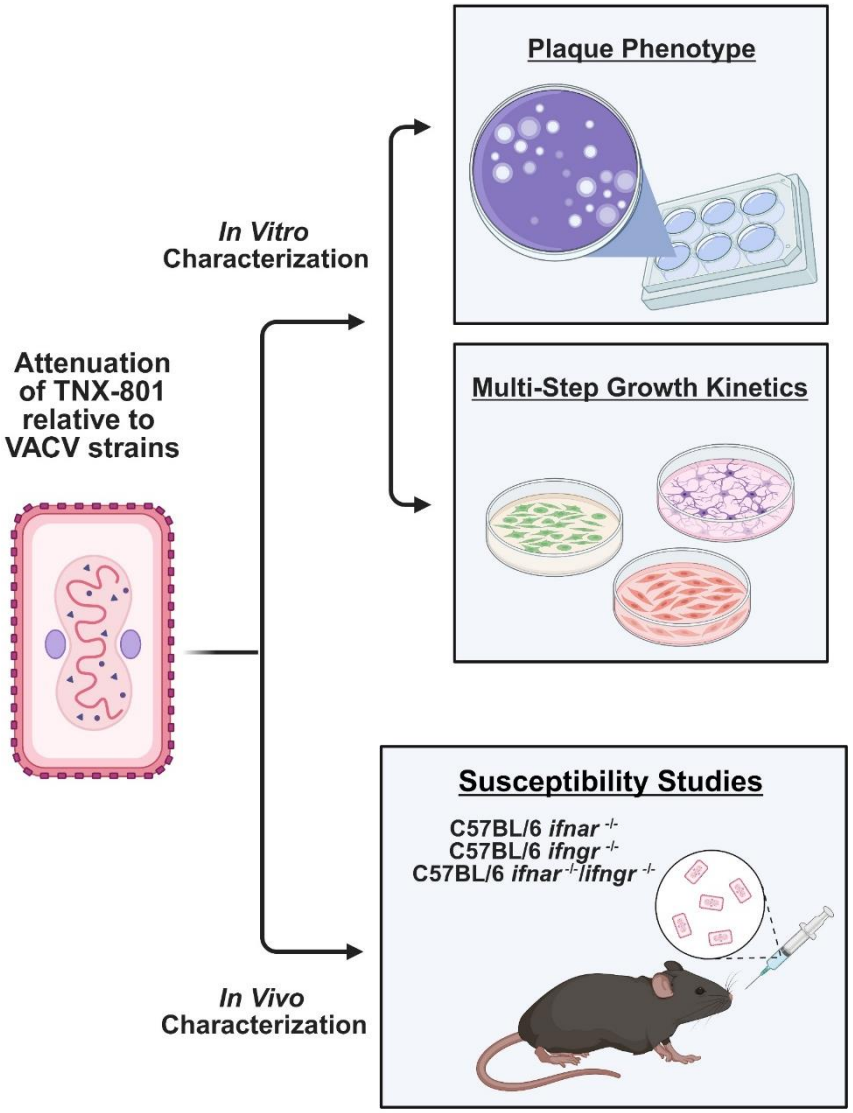
1) **Well-tolerated**

2) **Single dose**

3) **Durable**

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

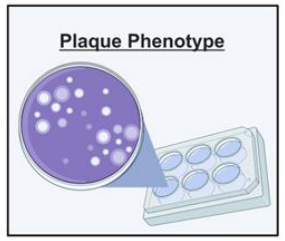
TNX-801 ATTENUATION *IN VITRO* AND *IN VIVO*

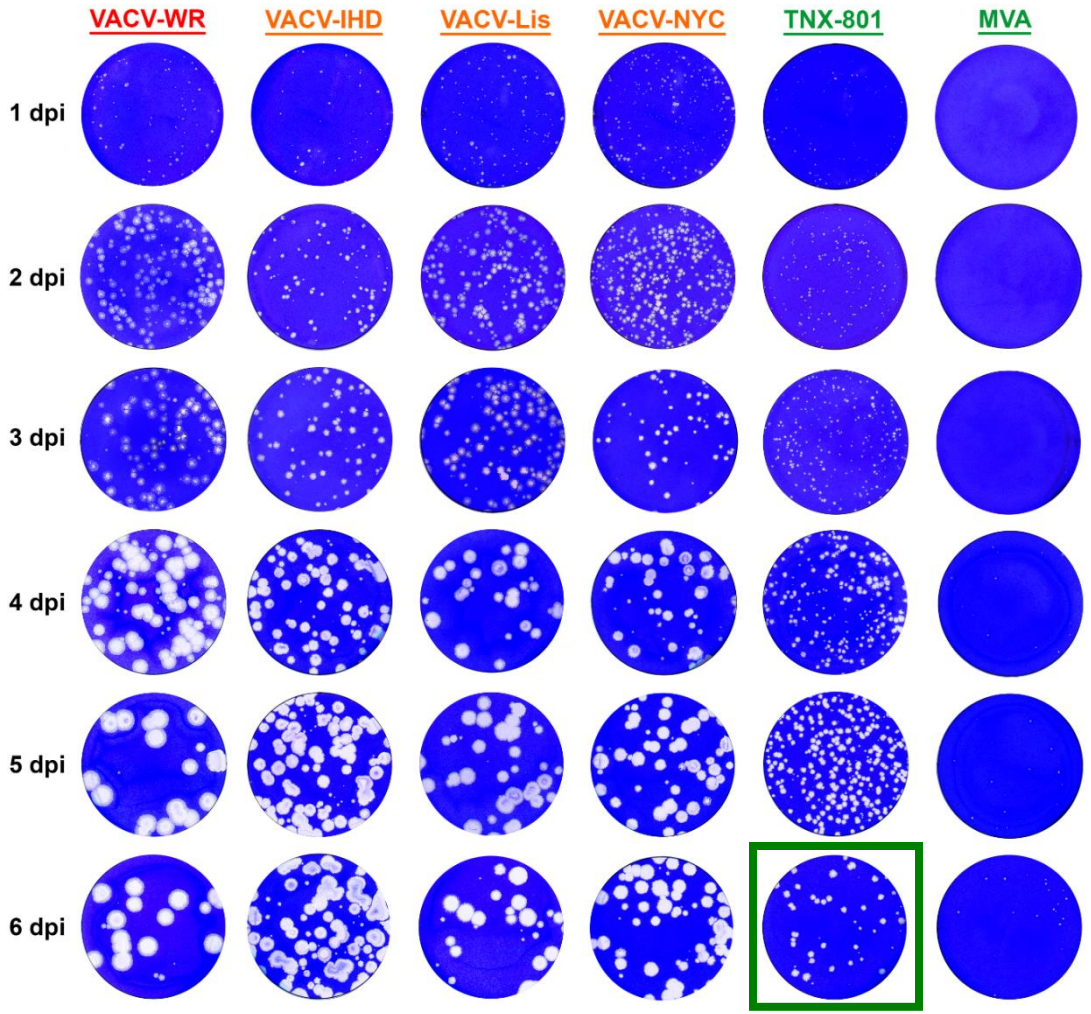


IN VITRO ATTENUATION OF TNX-801

- **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

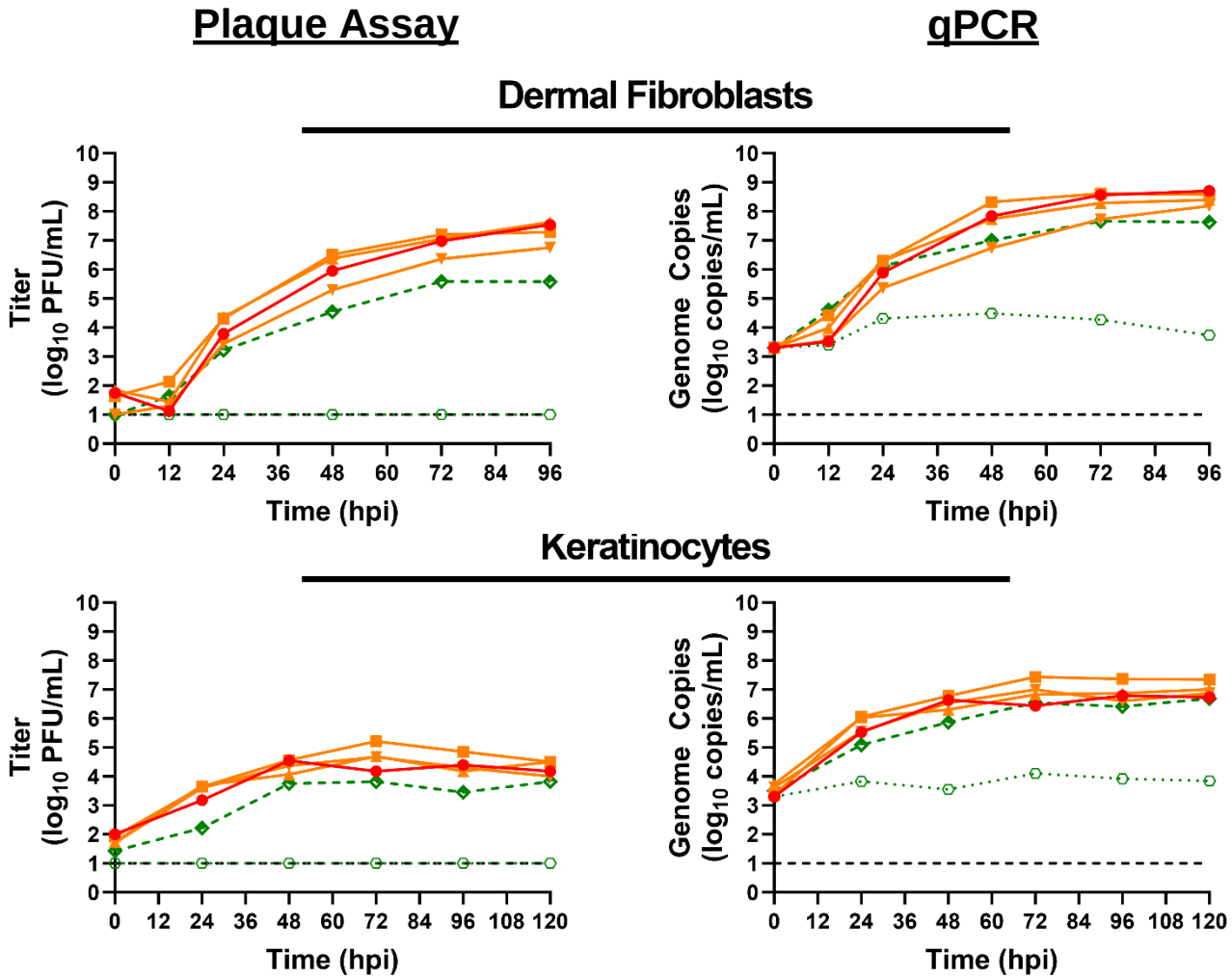
TNX-801 DISPLAYS SMALL PLAQUE PHENOTYPE VACCINA VIRUSES

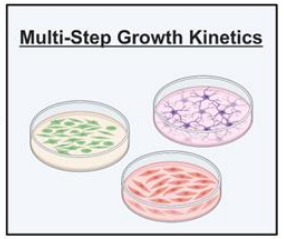




VACV-Western Reserve (WR)
VACV-International Health Department (IHD)
VACV-Lister (Lis)
VACV-New York City Board of Health (NYCBH)
TNX-801
MVA

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





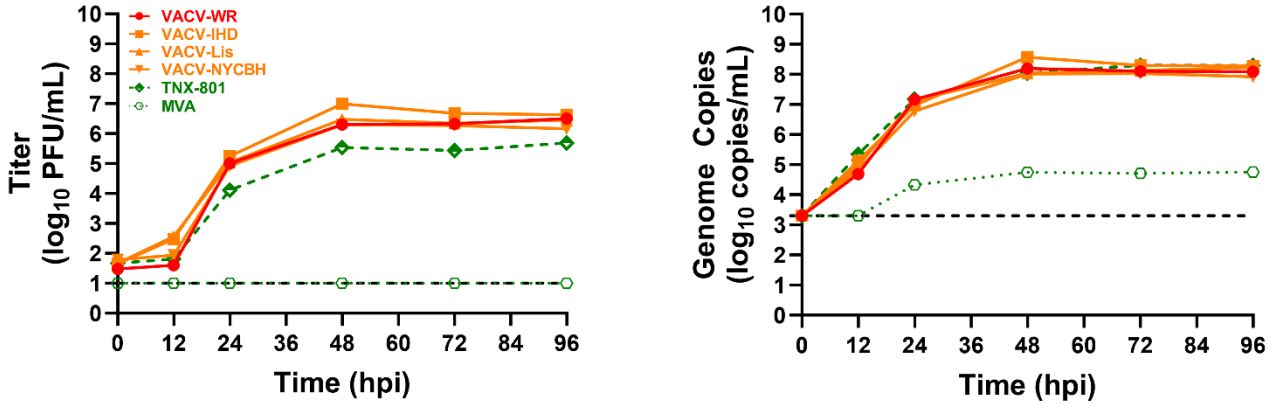
VACV-Western Reserve (WR)
VACV-International Health Department (IHD)
VACV-Lister (Lis)
VACV-New York City Board of Health (NYCBH)
TNX-801
MVA

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

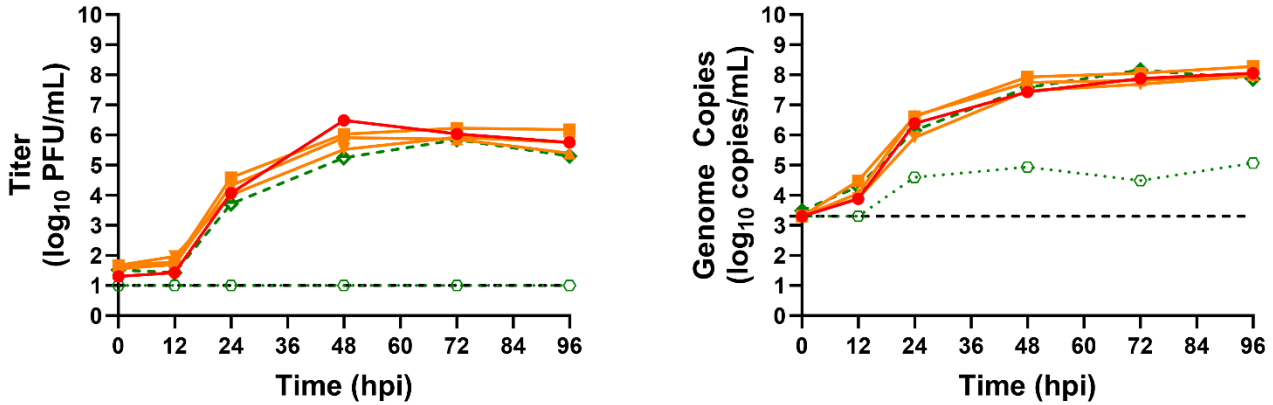
TNX-801: REPLICATION IN PRIMARY HUMAN CELLS (RESPIRATORY TRACT)

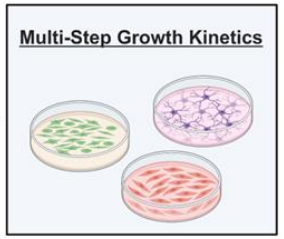
Plaque Assay **qPCR**

B-T Epithelial



Small Airway Epithelial





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

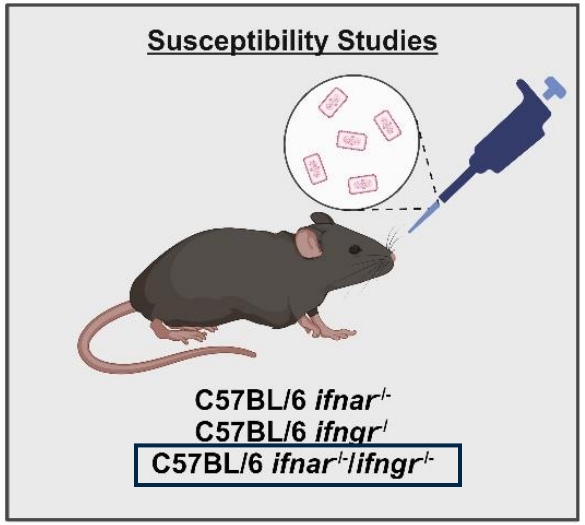
TNX-801: *~20- to 30-fold* more attenuated than VACV based vaccines

IN VIVO ATTENUATION OF TNX-801

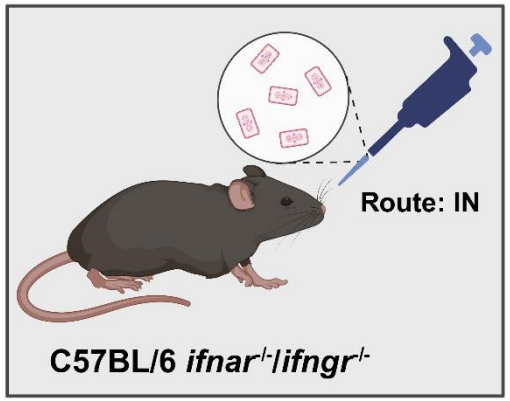
- **Investigate attenuation of TNX-801 *in vivo* relative to VACV based vaccines**
  - Immunocompromised Mice (C57BL/6 *ifnar*$^{-/-}$, C57BL/6 *ifngr*$^{-/-}$, C57BL/6 *ifnar*$^{-/-}$/*ifngr*$^{-/-}$)
    - Interferon receptor knockout model
    - Sensitive to virus infection

  - **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***



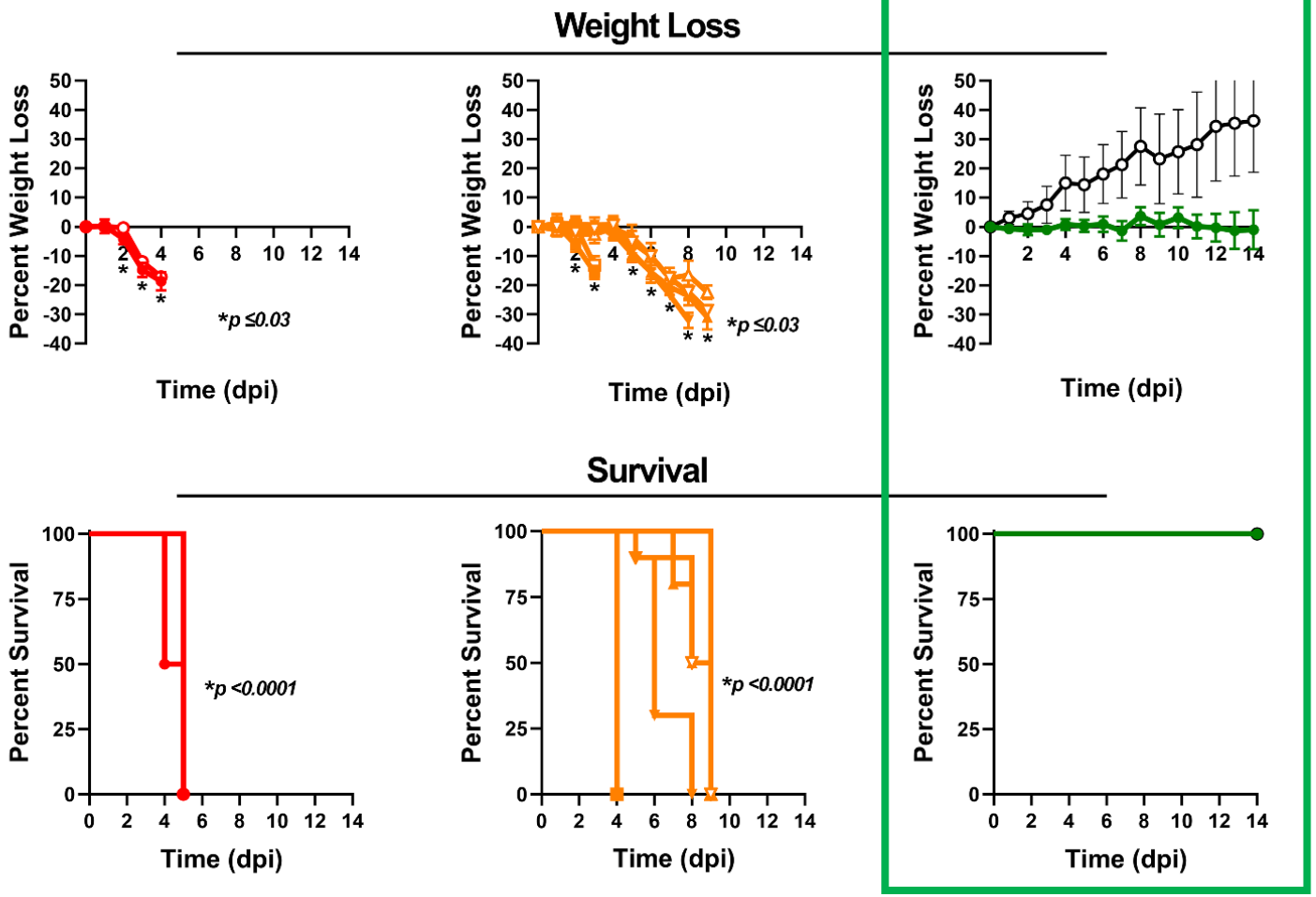
TNX-801 LACKS LETHALITY ASSOCIATED WITH OLDER SMALLPOX VACCINE STRAINS (LIS, NYCBH)



VACV-WR
~10^6 and 10^5 PFU

VACV-IHD, Lis, NYCBH
~10^6 and 10^5 PFU

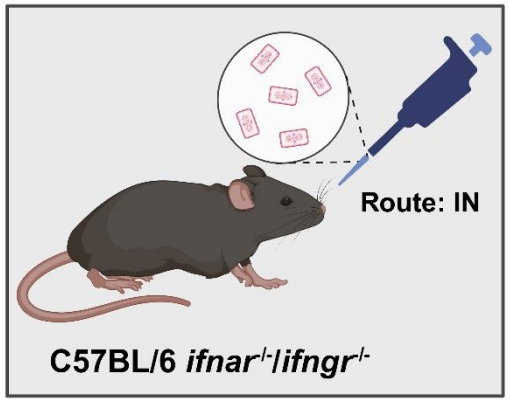
TNX-801*, Mock
~10^8 PFU



TNX-801 is 1,000-fold more attenuated

TONIX PHARMACEUTICALS

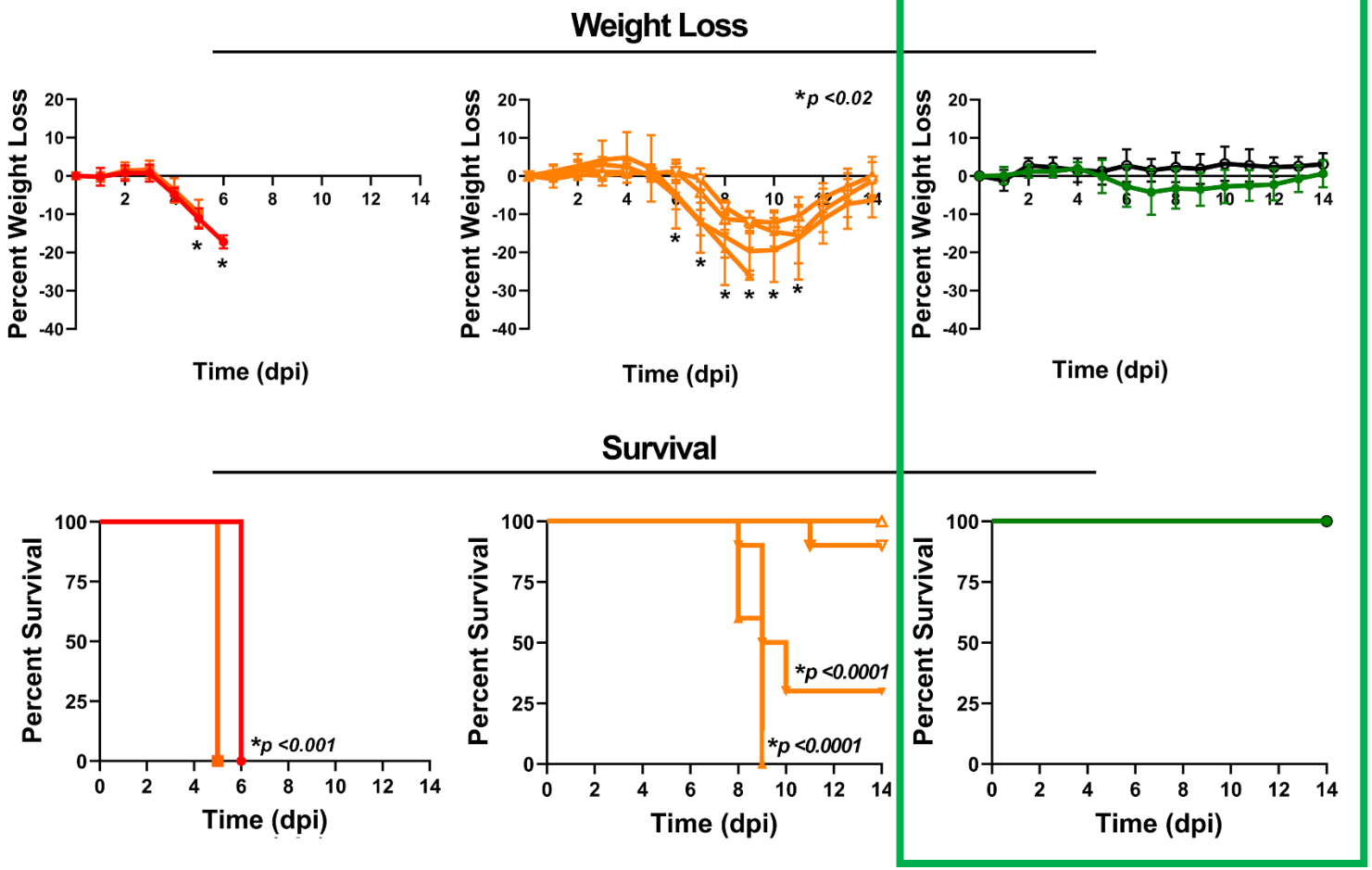
TNX-801 LACKS LETHALITY ASSOCIATED WITH OLDER SMALLPOX VACCINE STRAINS (LIS, NYCBH)



VACV-WR, IHD
~10^3 PFU

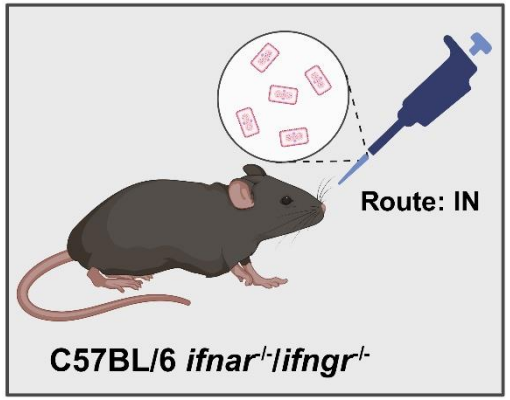
VACV-Lis, NYCBH
~10^4 and 10^3 PFU

TNX-801*, Mock
~3 x 10^8 PFU



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

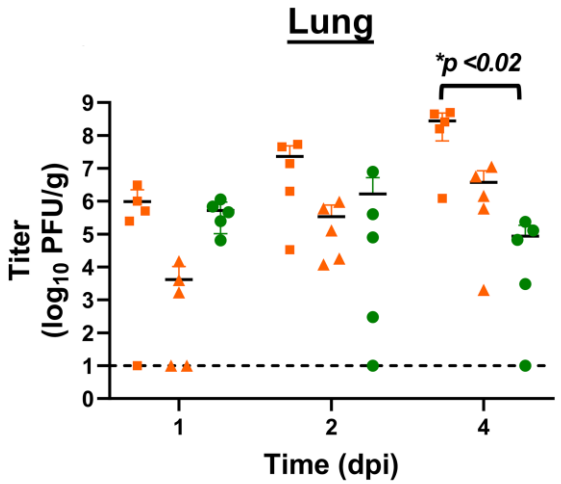
TNX-801 INFECTION DISPLAYS LIMITED REPLICATION

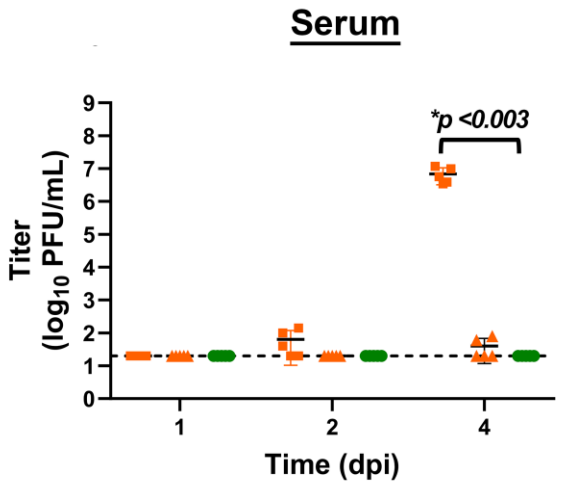


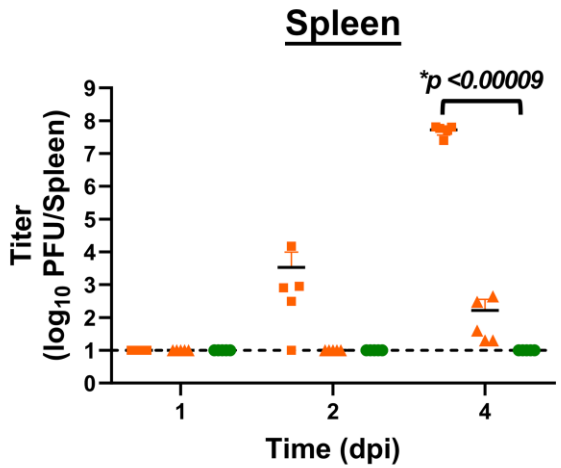
VACV-IHD ~10^6 PFU (■)

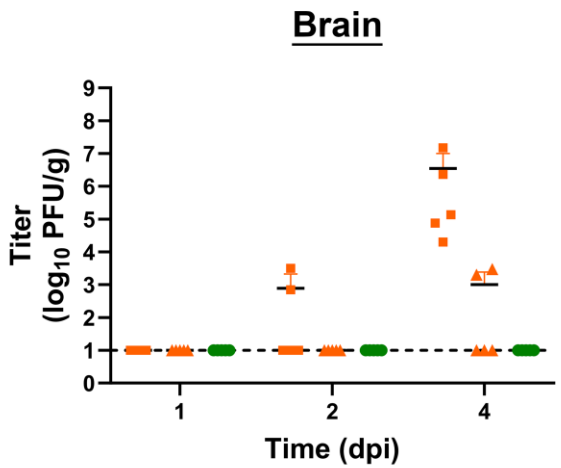
VACV-NYCBH ~10^6 PFU (▲)

TNX-801 ~10^8 PFU (●)

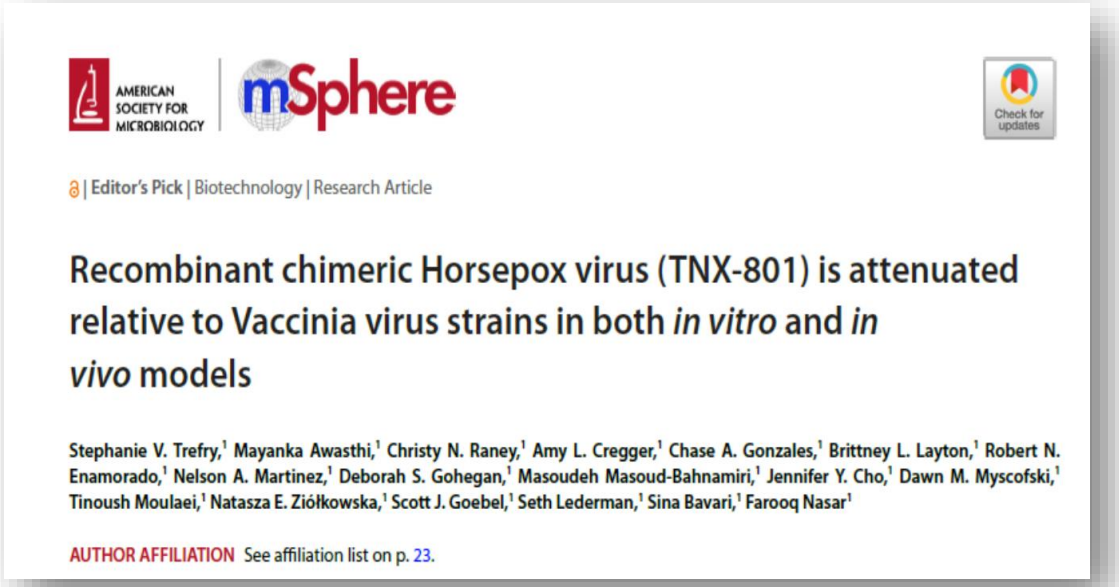








TNX-801 IS HIGHLY ATTENUATED WITH IMPROVED SAFETY PROFILES COMPARED TO OTHER VACCINA-BASED VACCINES



AMERICAN SOCIETY FOR MICROBIOLOGY | mSphere

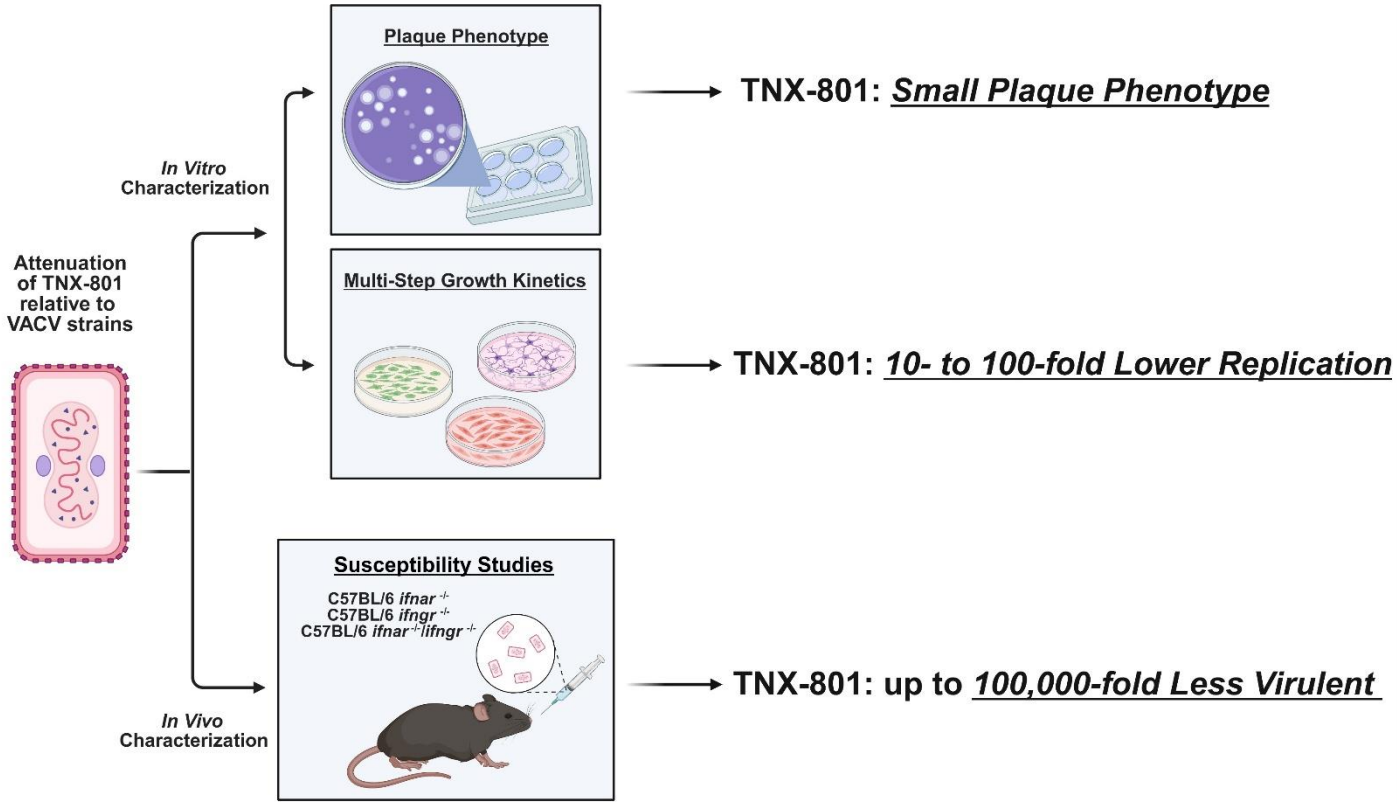
Check for updates

| 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]

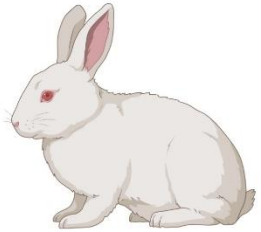
AUTHOR AFFILIATION See affiliation list on p. 23.



TONIX PHARMACEUTICALS

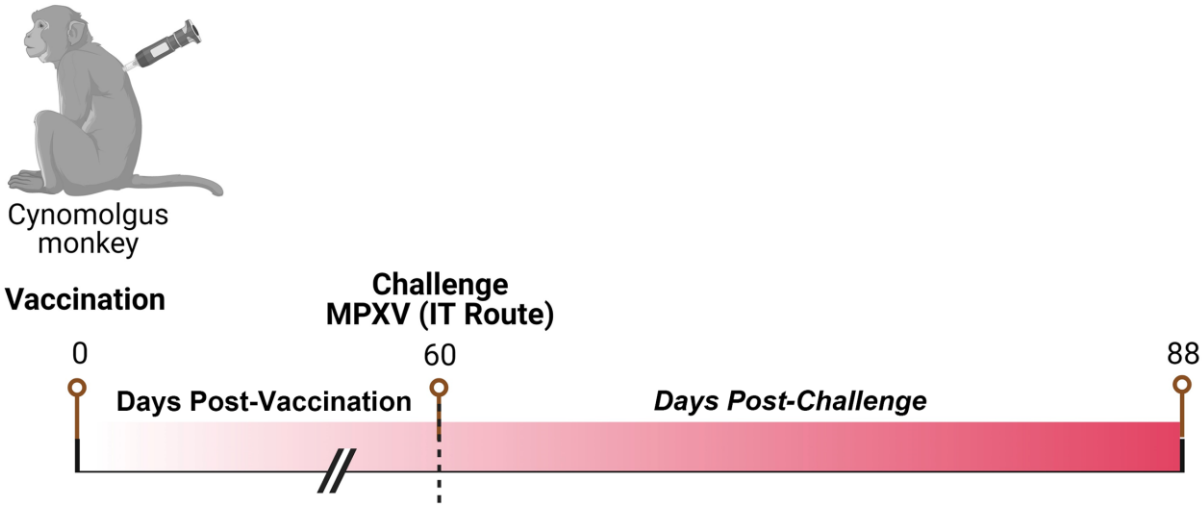
TNX-801 IMMUNOGENICITY AND EFFICACY IN ANIMAL MODELS

1)  → MPXV Clade Ia

2)  → RPXV

3)  → MPXV Clade IIa

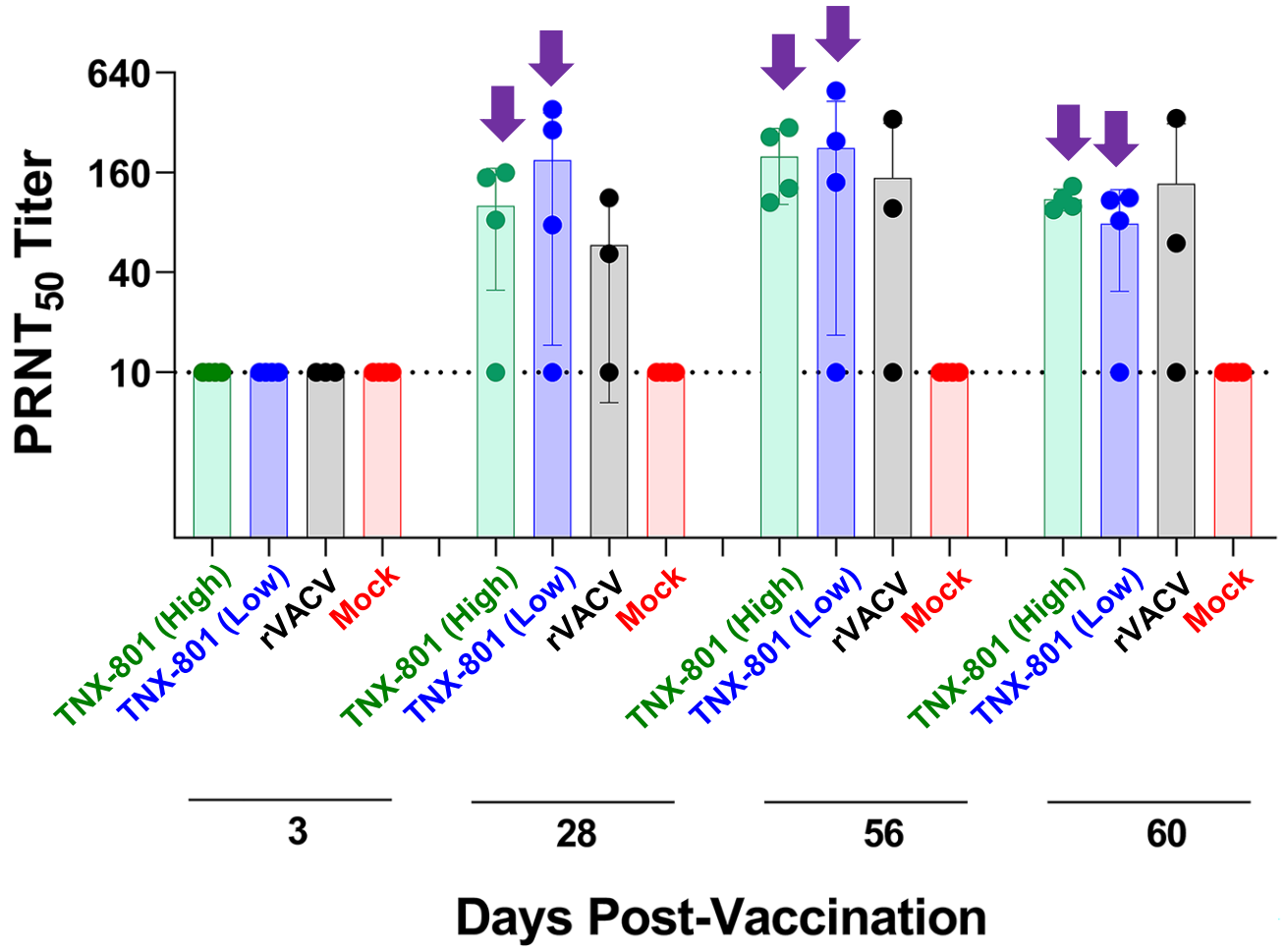
NHP IMMUNOGENICITY AND EFFICACY STUDY DESIGN



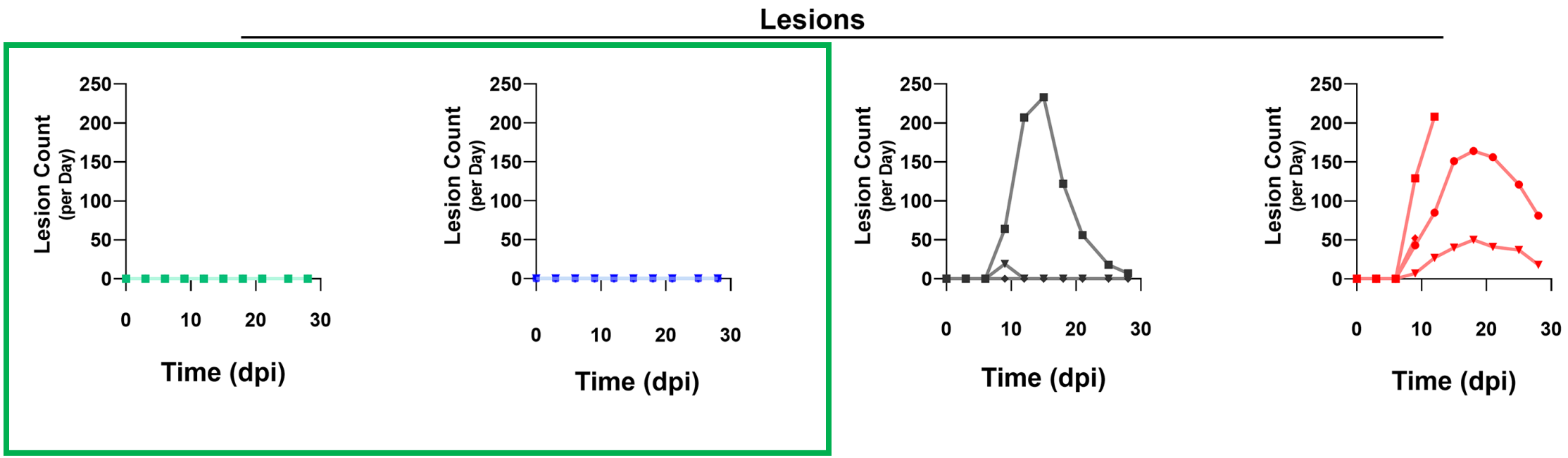
Vaccination					Challenge		
Group	Treatment	n	Dose (PFU)	Route	*Virus*	*Dose (PFU)*	*Route*
1	TNX-801 (High)	4	4×10^6	PERCUT	*MPXV (Zaire)*	10^5	*IT*
2	TNX-801 (Low)	4	5×10^5	PERCUT	*MPXV (Zaire)*	10^5	*IT*
3	rVACV	4	1×10^5	PERCUT	*MPXV (Zaire)*	10^5	*IT*
4	Mock	4	-	PERCUT	*MPXV (Zaire)*	10^5	*IT*

rVACV = synthesized vaccinia similar to ACAM2000 (Approved Vaccine)

NHP IMMUNOGENICITY: NEUTRALIZING ANTIBODY RESPONSE

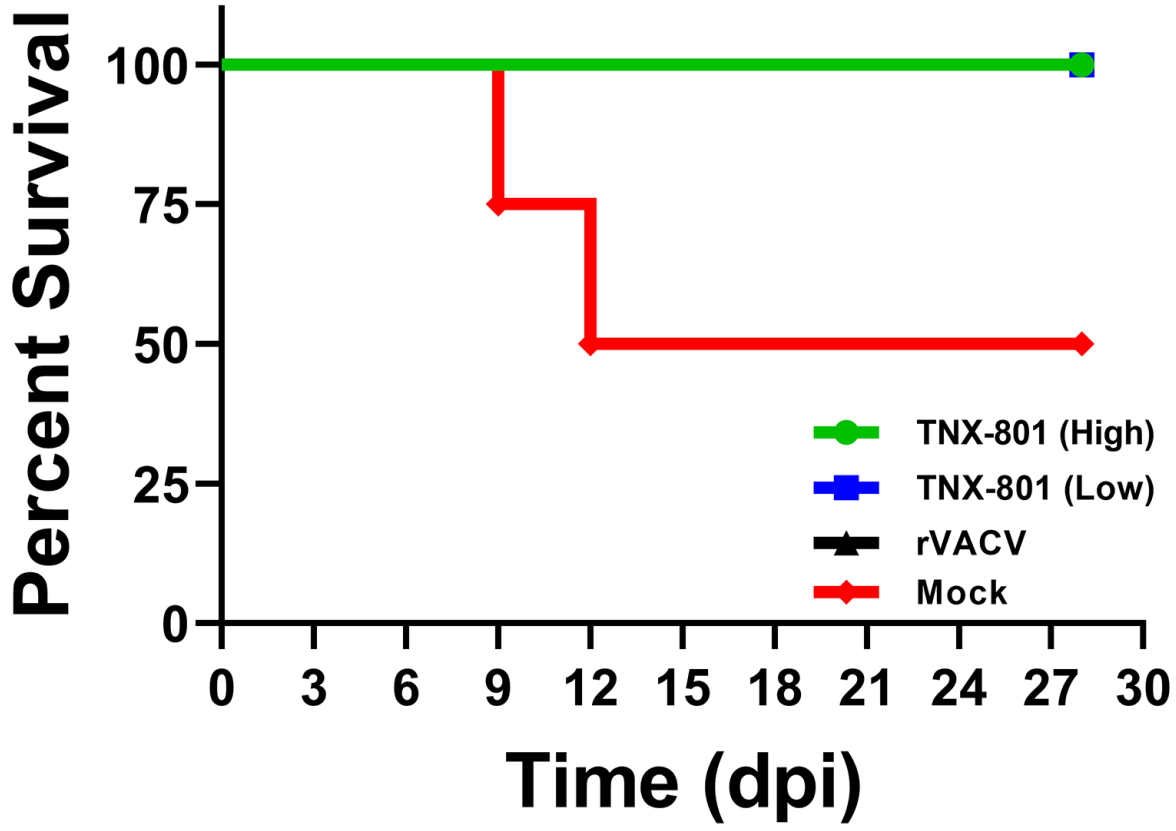


TNX-801 PROVIDES PROTECTION AGAINST MPOX DISEASE



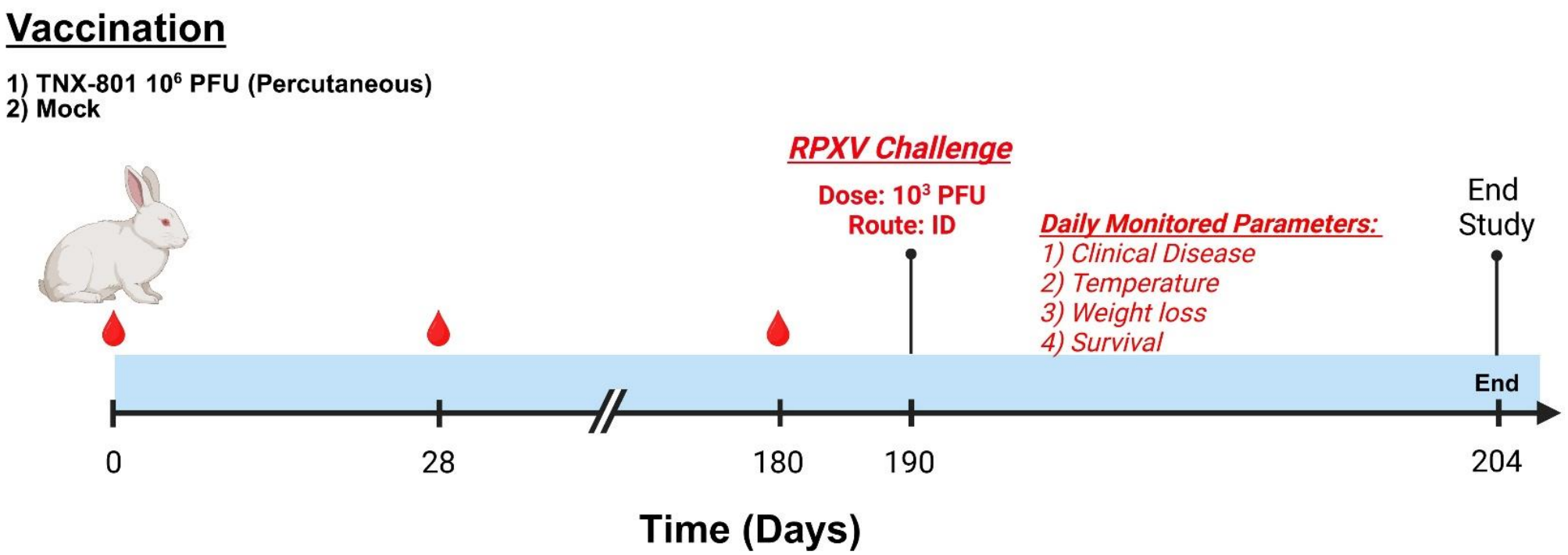
NO LESIONS in TNX-801 vaccinated groups

TNX-801 PROVIDES PROTECTION AGAINST LETHAL MONKEYPOX CLADE I CHALLENGE

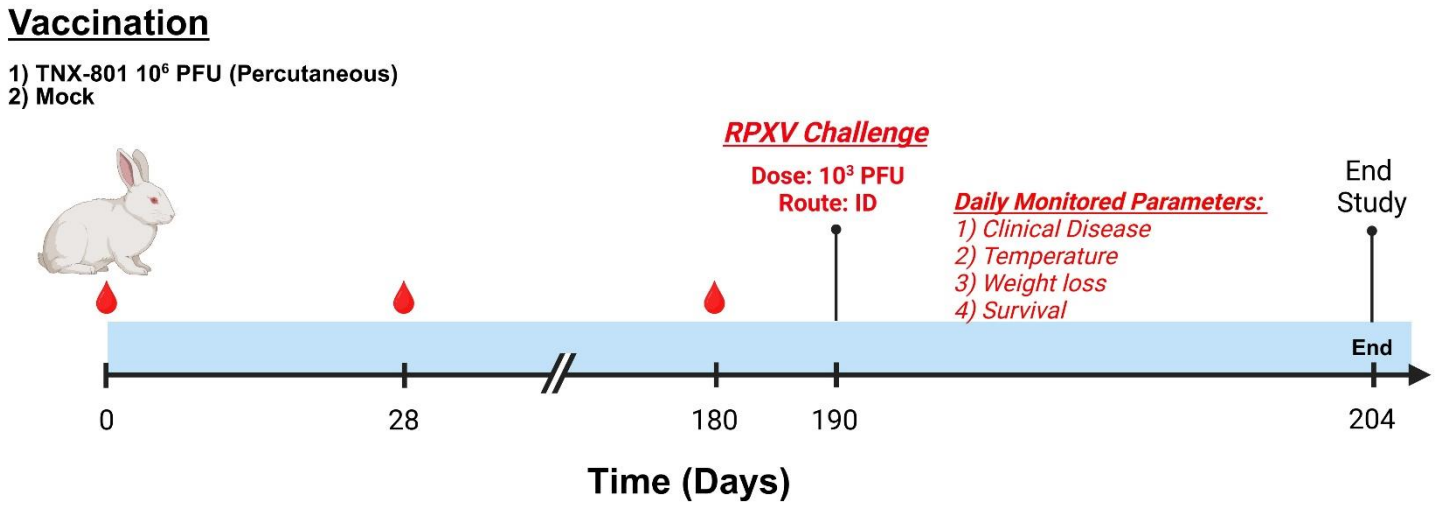


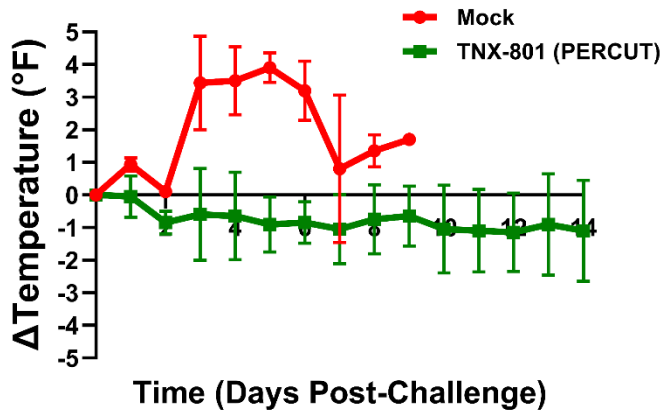
NO LETHALITY in TNX-801 vaccinated groups

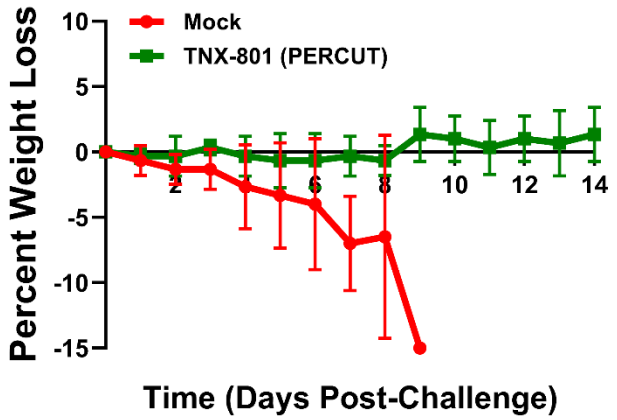
TNX-801 PROVIDES DURABLE PROTECTION AGAINST LETHAL RABBITPOX CHALLENGE: 6 MONTHS



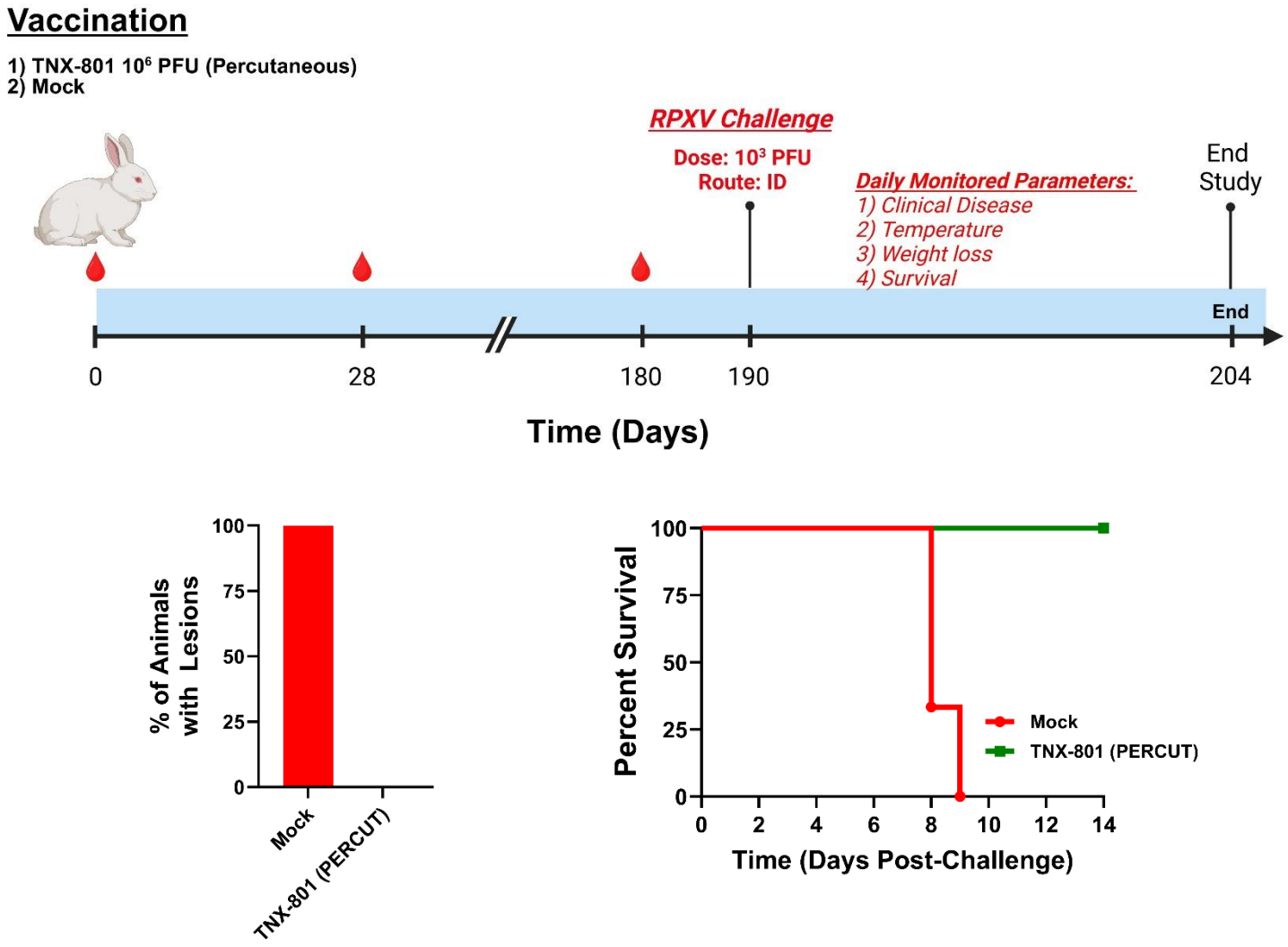
TNX-801 PROVIDES DURABLE PROTECTION AGAINST LETHAL RABBITPOX CHALLENGE: 6 MONTHS



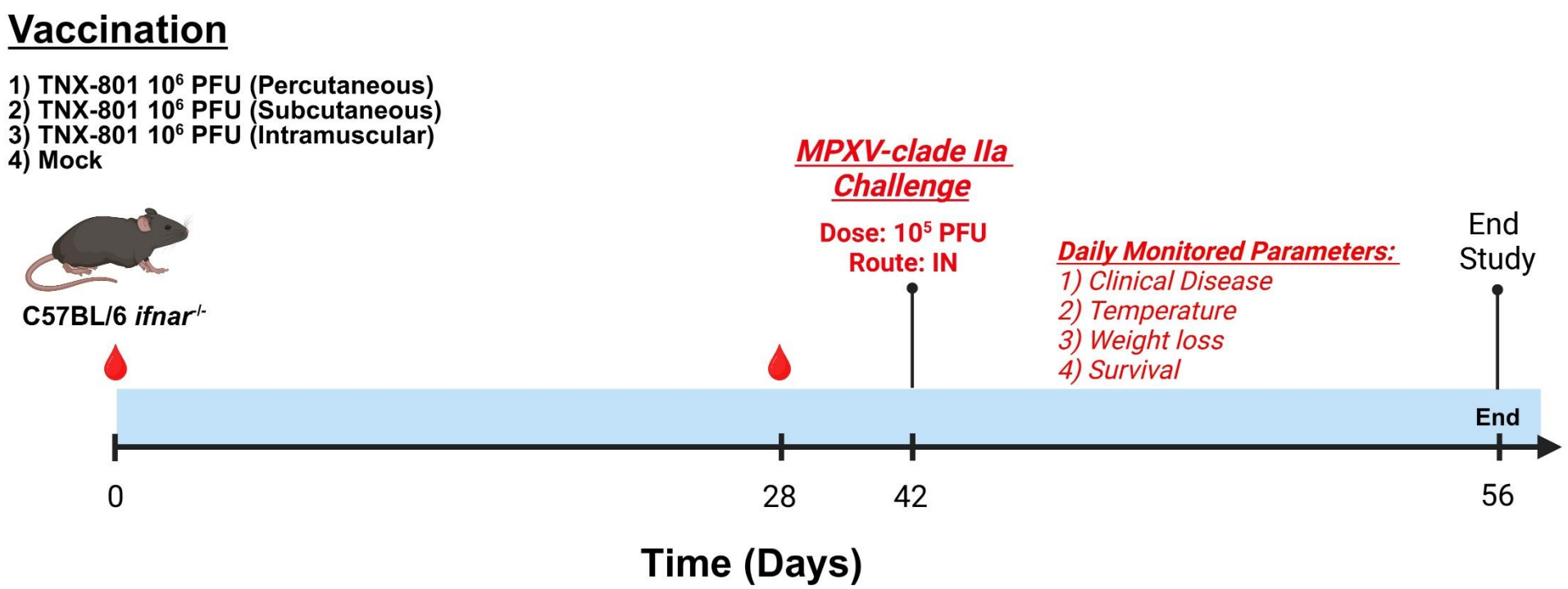




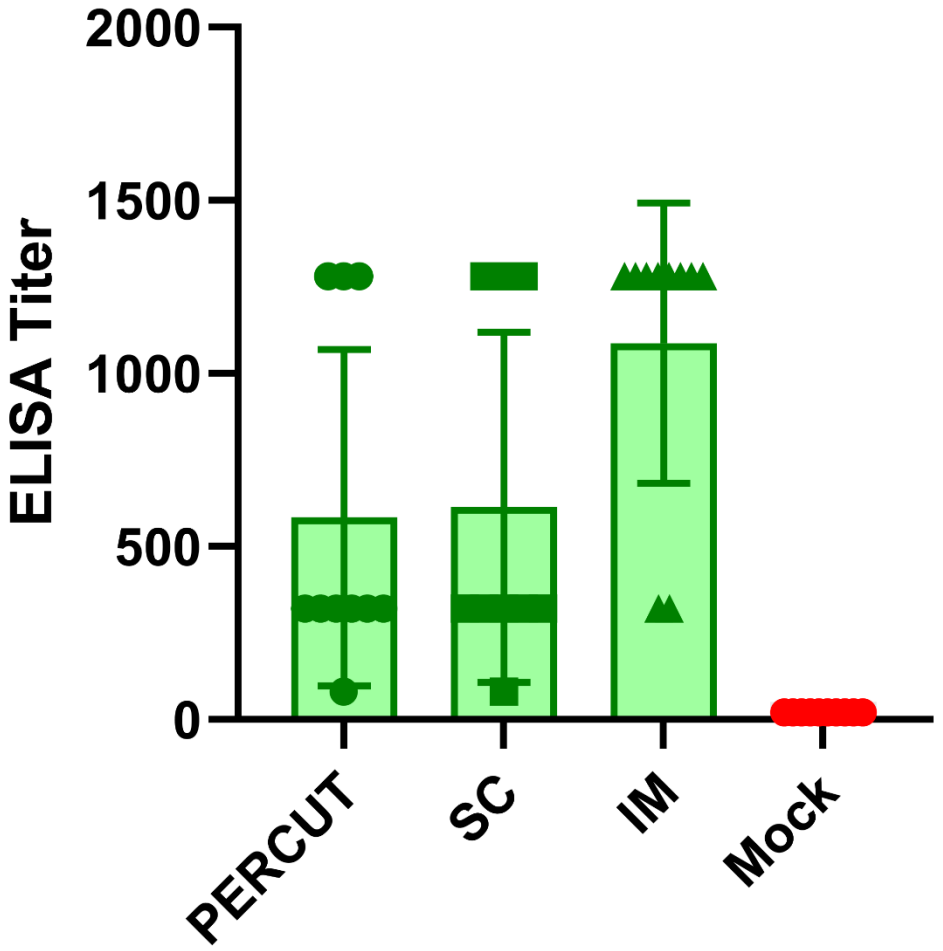
TNX-801 PROVIDES DURABLE PROTECTION AGAINST LETHAL RABBITPOX CHALLENGE: 6 MONTHS



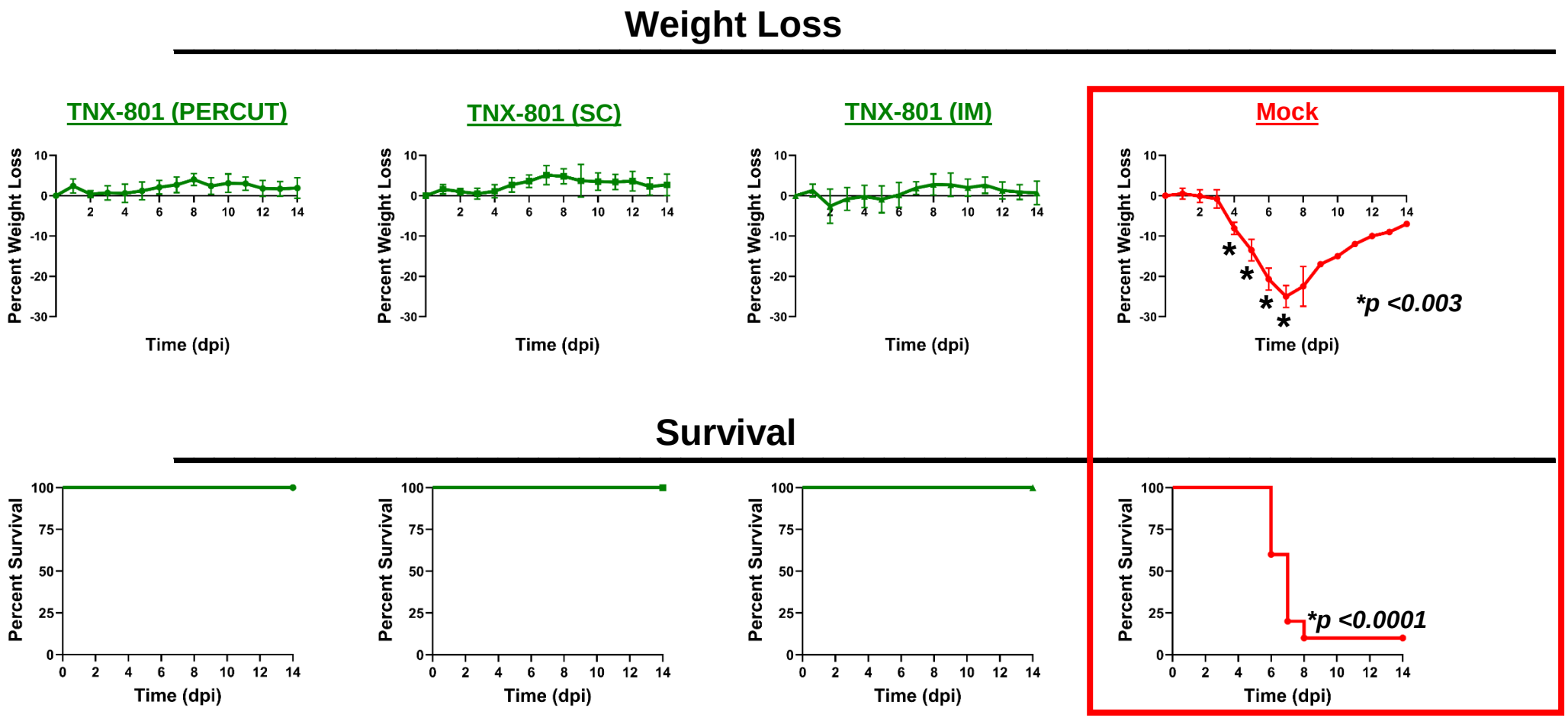
TNX-801 PROVIDES PROTECTION AGAINST LETHAL MONKEYPOX CLADE IIA CHALLENGE: ALTERNATIVE ROUTES



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**

TONIX PHARMACEUTICALS

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**

TONIX PHARMACEUTICALS

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

1) **Well-tolerated**

2) **Single dose**

3) **Durable**

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

ACKNOWLEDGEMENTS

- **Tonix Pharmaceuticals**
  - Stephanie Trefry
  - Mayanka Awasthi
  - Christy Raney
  - Amy Cregger
  - Robert Enamorado
  - Nelson Martinez
  - Deborah Gohegan
  - Zeil Rosenberg
- **Tonix Pharmaceuticals**
  - Scott Goebel
  - Tinoush Moulaei
  - Natasza Ziółkowska
  - Siobhan Fogarty
  - Helen Stillwell
  - Bruce Daugherty
  - Sina Bavari
  - Seth Lederman
- **University of Alberta**
  - Ryan Noyce
  - David Evans
- **Southern Research**