

# Ending the HIV Epidemic – Challenges and Progress

**Carl W. Dieffenbach, Ph.D.**  
**Director, Division of AIDS**

**May 5, 2021**



National Institute of  
Allergy and  
Infectious Diseases

CENTERS FOR DISEASE CONTROL

**MMWR™**

MORBIDITY AND MORTALITY WEEKLY REPORT

---

June 5, 1981

---

***Pneumocystis Pneumonia –  
Los Angeles***

July 4, 1981

---

***Kaposi's Sarcoma and  
Pneumocystis Pneumonia Among  
Homosexual Men –  
New York City and California***

This is the 40<sup>th</sup> anniversary  
Of the first MMWR reports  
That changed the world for  
So many of us.

# Without Reliable Tools, We Are Lost

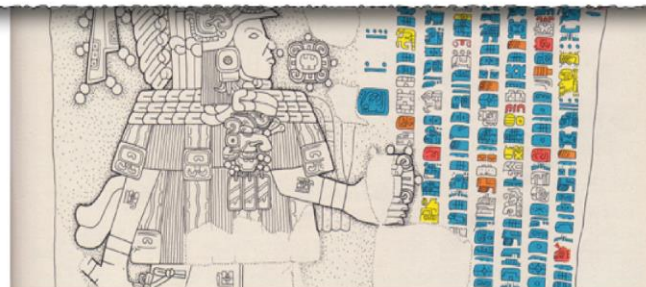
---

- 1985 – The U.S. FDA licensed the first HIV test, pioneered by Abbott
- 1993 – Quantitation of HIV-1 in plasma by competitive polymerase chain reaction (QC-PCR) useful in assessing the efficacy of antiretroviral agents, especially in early stage disease



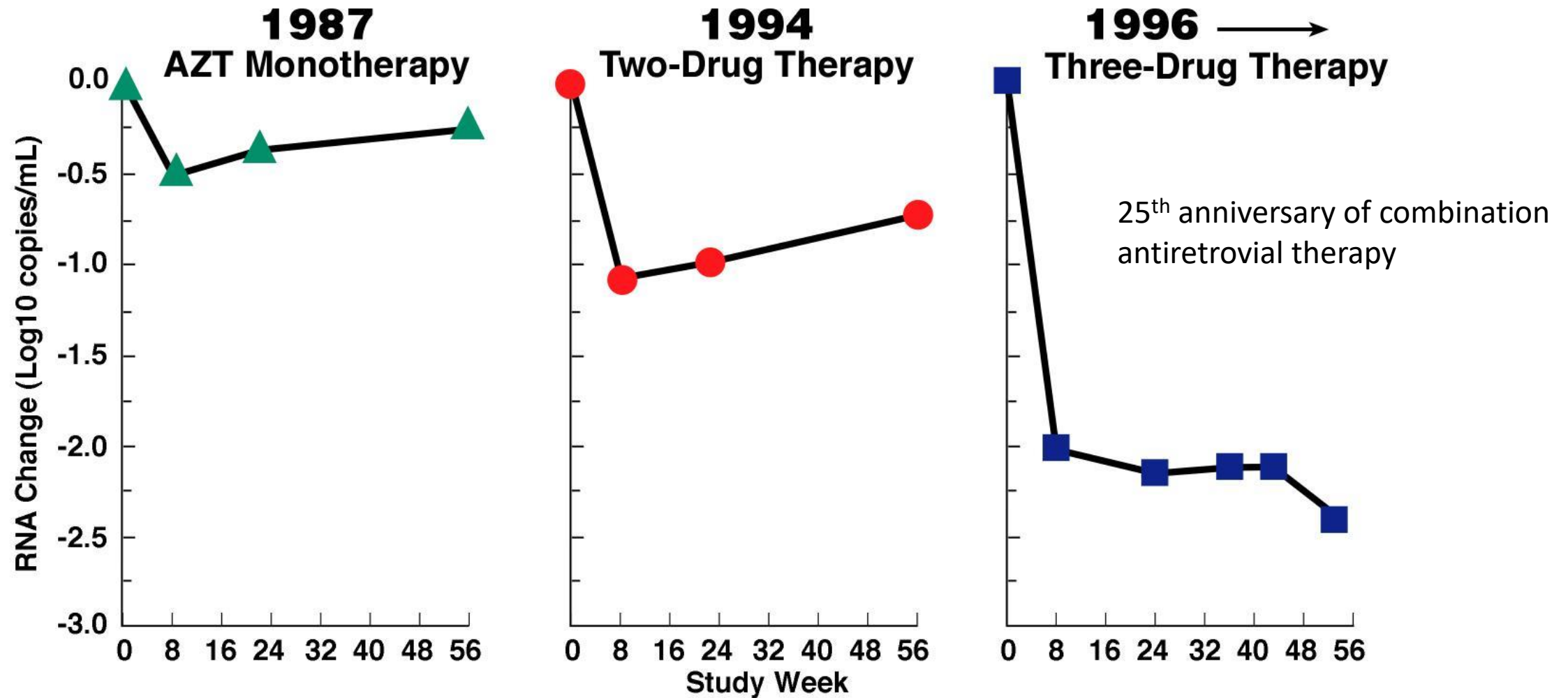
## **High Levels of HIV-1 in Plasma During all Stages of Infection Determined by Competitive PCR**

M Piatak Jr., JD Lifson, et al.



# Evolution of Treatment Strategies for HIV Disease

---



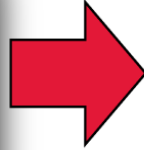
**From Treatment to “*Treatment as Prevention*” and more**

# **Treating HIV-Infected Individuals: A Triad of Pivotal ART Studies**

---

- **SMART**                      Episodic ART inferior to continuous ART
- **HPTN 052**                      Early ART reduces HIV transmission to uninfected sexual partner by 93%
- **START**                      Early ART reduces serious illness/death by 57%

**HPTN 052:  
Treatment as  
Prevention**

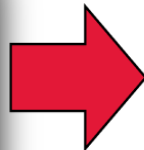


**Public  
Health  
Benefit**



**Begin treatment  
at any CD4<sup>+</sup>  
T-cell count**

**START and  
Temprano Studies:  
Early Treatment**



**Individual  
Health  
Benefit**



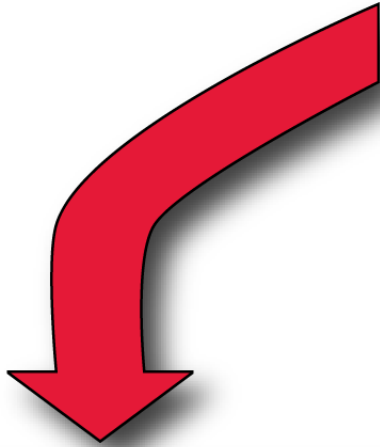
**U=U** Undetectable  
Equals Untransmittable

NAM supports the Consensus Statement on the risk of sexual transmission of HIV from a person living with HIV who has an undetectable viral load.  
[www.preventionaccess.org/consensus](http://www.preventionaccess.org/consensus)

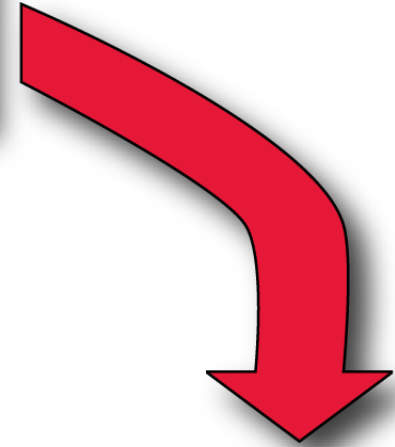
# **“Game Changing” Concept in Addressing HIV**



**Treatment = Prevention**



**Treatment  
as Prevention  
(TasP)**



**Pre-Exposure  
Prophylaxis  
(PrEP)**



# **Improvements in PrEP**

# **Optimizing HIV Prevention**

---

## **Two key priorities**

- **Pre-Exposure Prophylaxis (PrEP)**

- **Vaccine**

# **Long-Acting PrEP**



**ART-Based**

**Broadly  
Neutralizing  
Antibodies**

# **Long-Acting PrEP**



**ART-Based**

**Broadly  
Neutralizing  
Antibodies**

# Long-acting Antiretrovirals for Prevention

---



- RCT of long-acting cabotegravir vs. TDF/FTC for PrEP
- 4500 MSM and TGW in multiple countries



- RCT of long-acting cabotegravir vs. TDF/FTC for PrEP
- 3200 women in Sub-Saharan Africa



**National Institute of Allergy and Infectious Diseases**  
*Leading research to understand, treat, and prevent infectious, immunologic, and allergic diseases.*

FOR IMMEDIATE RELEASE  
Tuesday, July 7, 2020

## **Long-acting Injectable Form of HIV Prevention Outperforms Daily Pill in NIH Study**

*Both Methods Highly Effective at Preventing HIV Among Men  
Who Have Sex with Men and Transgender Women*



**National Institute of Allergy and Infectious Diseases**  
*Leading research to understand, treat, and prevent infectious, immunologic, and allergic diseases.*

FOR IMMEDIATE RELEASE  
Monday, November 9, 2020

## **Statement – NIH Study Finds Long-acting Injectable Drug Prevents HIV Acquisition in Cisgender Women**

*Long-acting Regimen More Effective Than Daily Oral Pill Among  
African Women*

# PrEP Implant Could Last More Than One Year

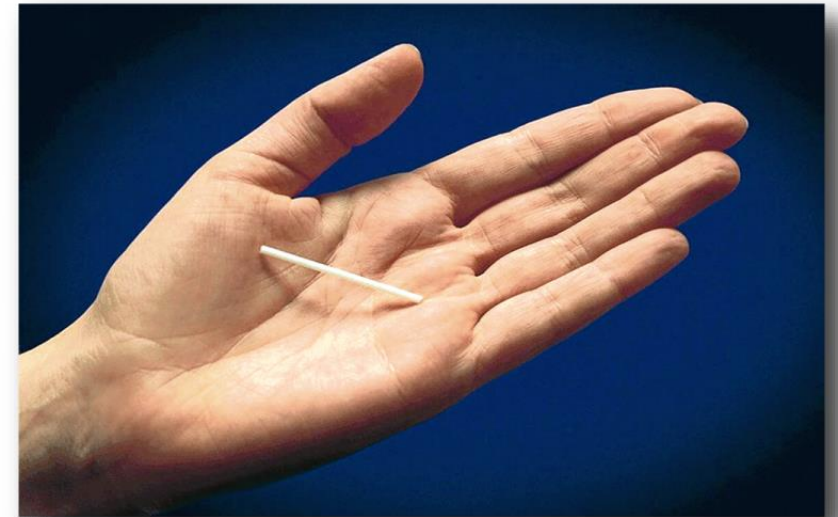
---



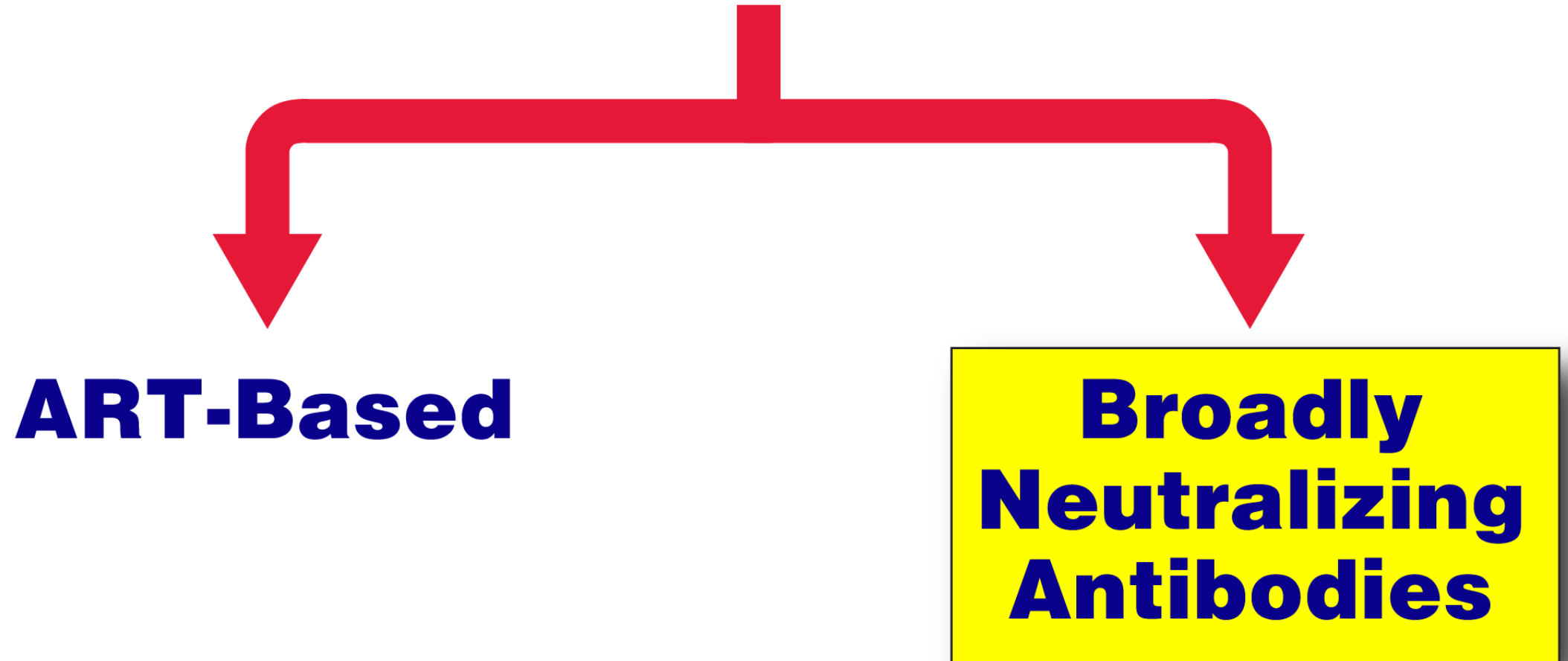
**Abstract TUAC0401LB**

## **First-in-Human Trial of MK-8591-Eluting Implants Demonstrates Concentrations Suitable for HIV Prophylaxis for at Least One Year**

RP Matthews et al.



# **Long-Acting PrEP**







The  
New England  
Journal of Medicine

Established in 1812 as THE NEW ENGLAND JOURNAL OF MEDICINE AND SURGERY

Volume 384

March 18, 2021

Number 11

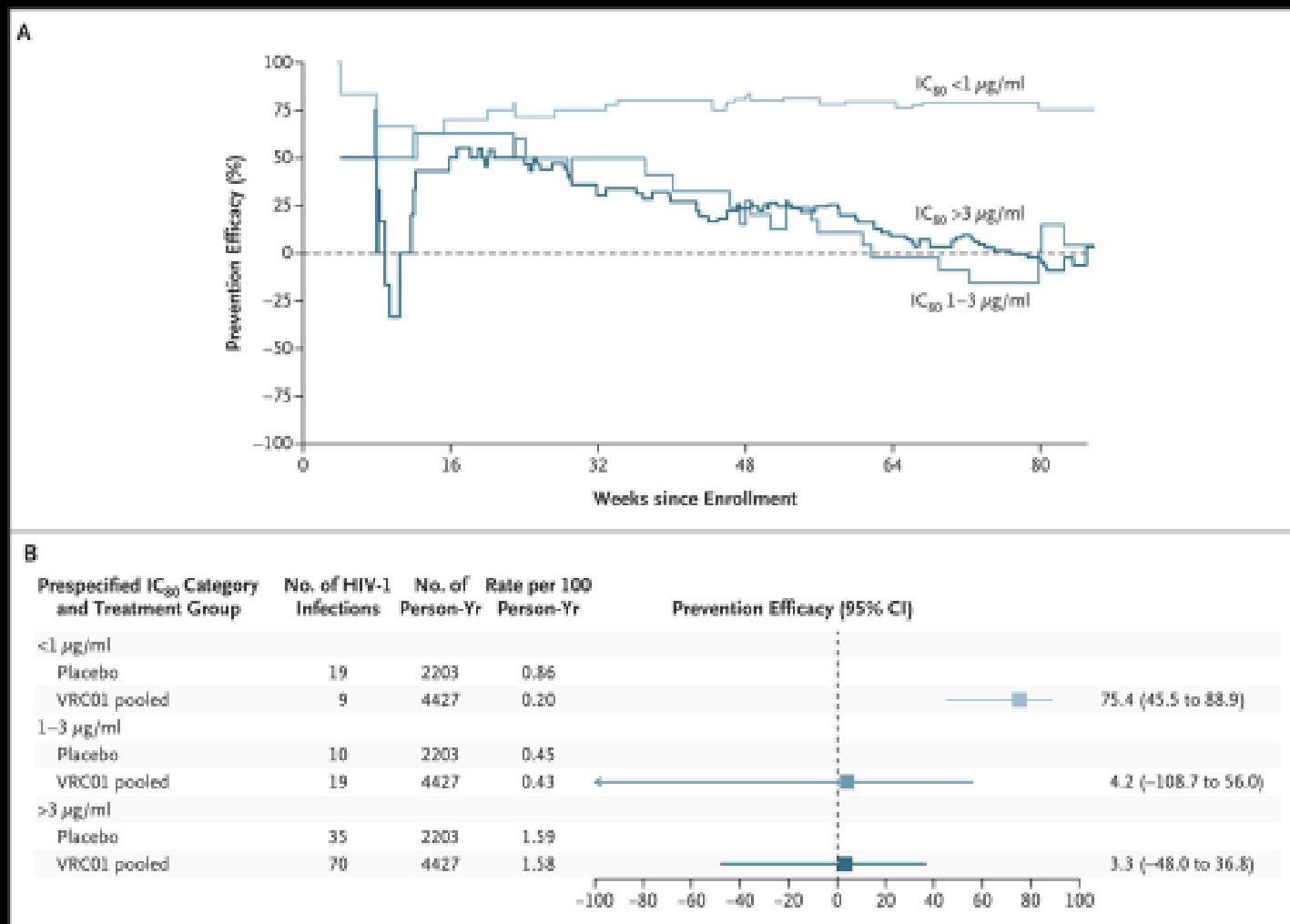
# **Two Randomized Trials of Neutralizing Antibodies to Prevent HIV-1 Acquisition**

L Corey, MS Cohen et al.

- **VRC01 did not prevent overall HIV-1 acquisition more effectively than placebo**
- **VRC01 effective at preventing acquisition of HIV strains sensitive to the bnAb**
- **AMP provided proof-of-concept that bnAb prophylaxis can be effective**

# Prevention Efficacy of VRC01 against HIV-1 of Different in Vitro Sensitivities (IC<sub>50</sub>) to VRC01.

80



# **Optimizing HIV Prevention**

---

## **Two key priorities**

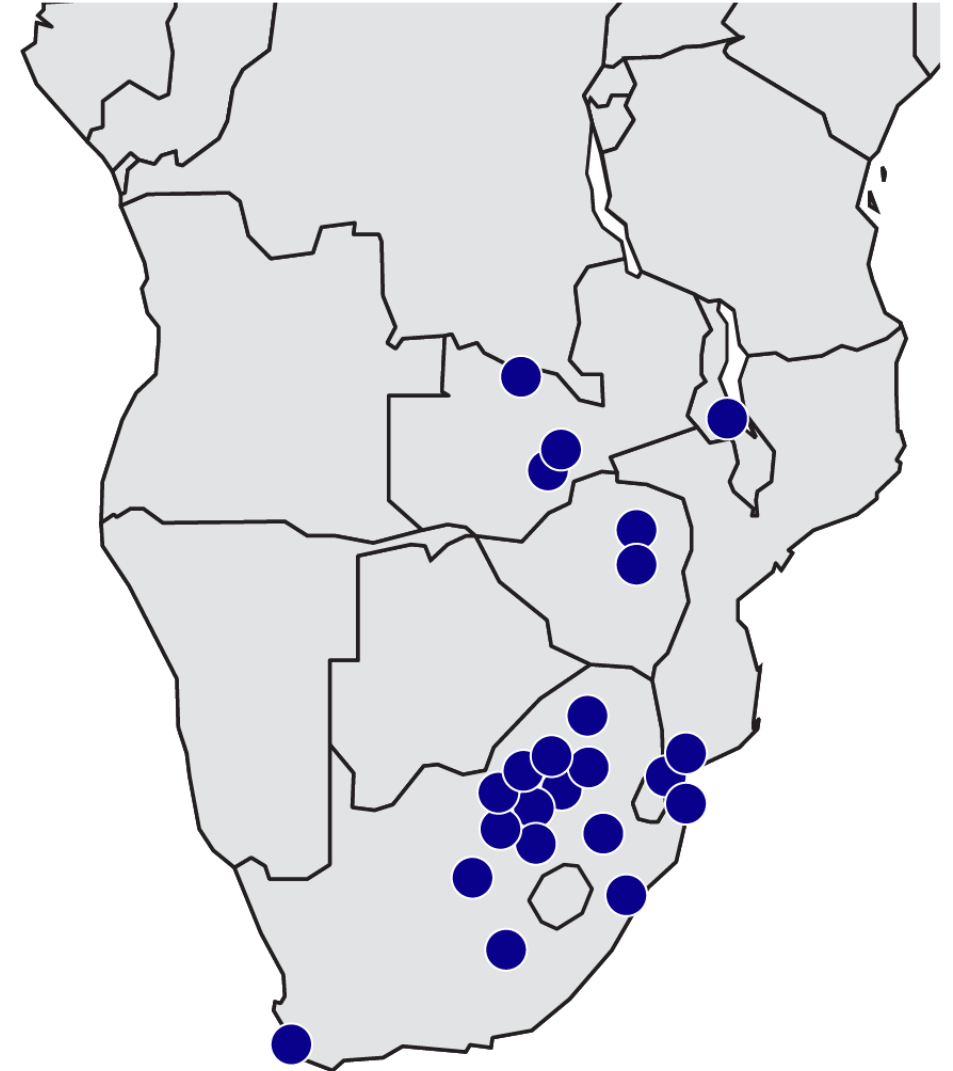
■ **Pre-Exposure Prophylaxis (PrEP)**

■ **Vaccine**

# HVTN 705/HPX2008 – Imbokodo



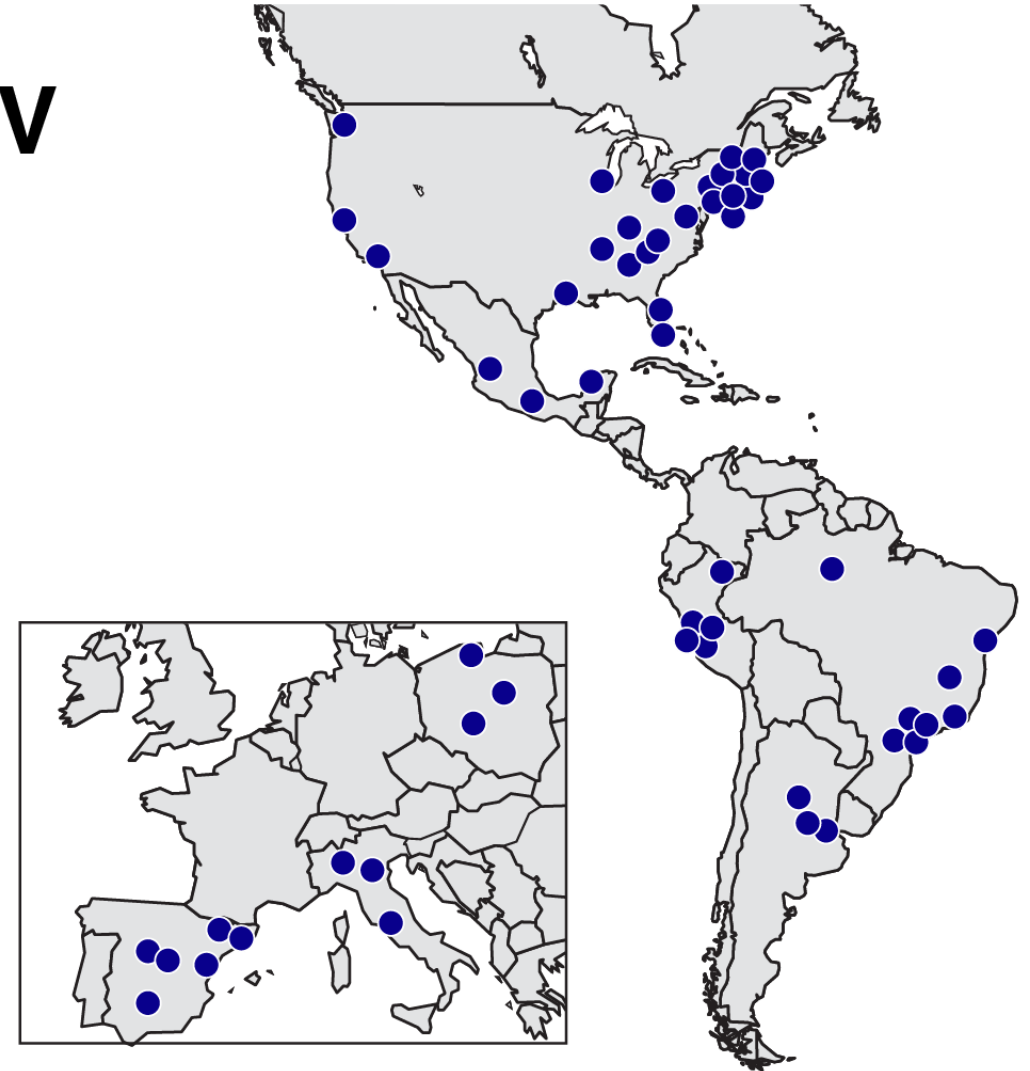
- **Quadrivalent, Ad26-vectored mosaic vaccine + HIV clade C gp140**
- **N=2,637 women in sub-Saharan Africa (fully enrolled)**
- **Launched November 2017**



# HVTN 706/HPX3002 – MOSAICO

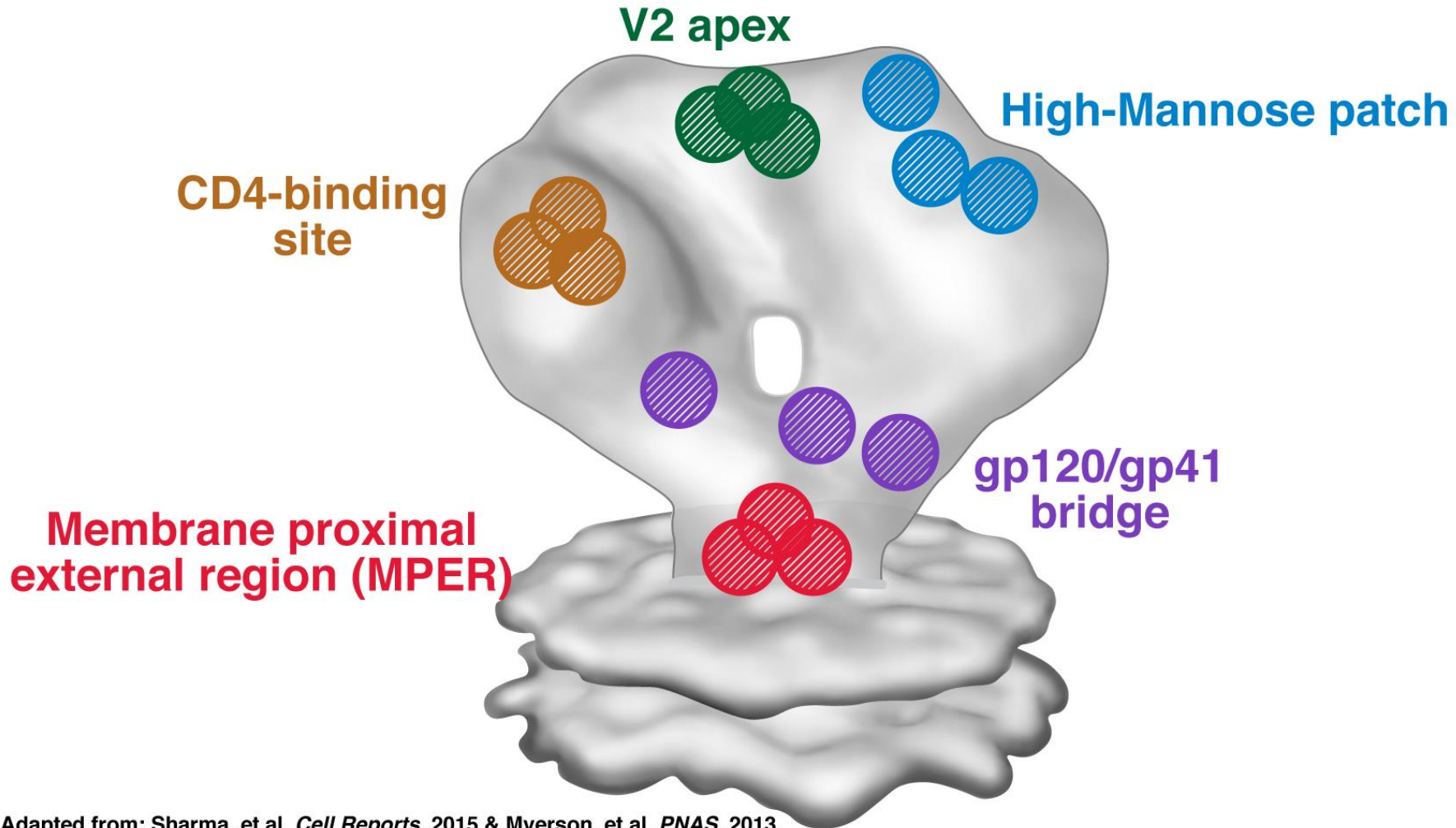


- **Quadrivalent, Ad26-vectored mosaic vaccine + bivalent HIV clade C and mosaic gp140**
- **Target N: 3,800 MSM and transgender individuals in Americas, Europe**
- **Launched Sept. 2019**



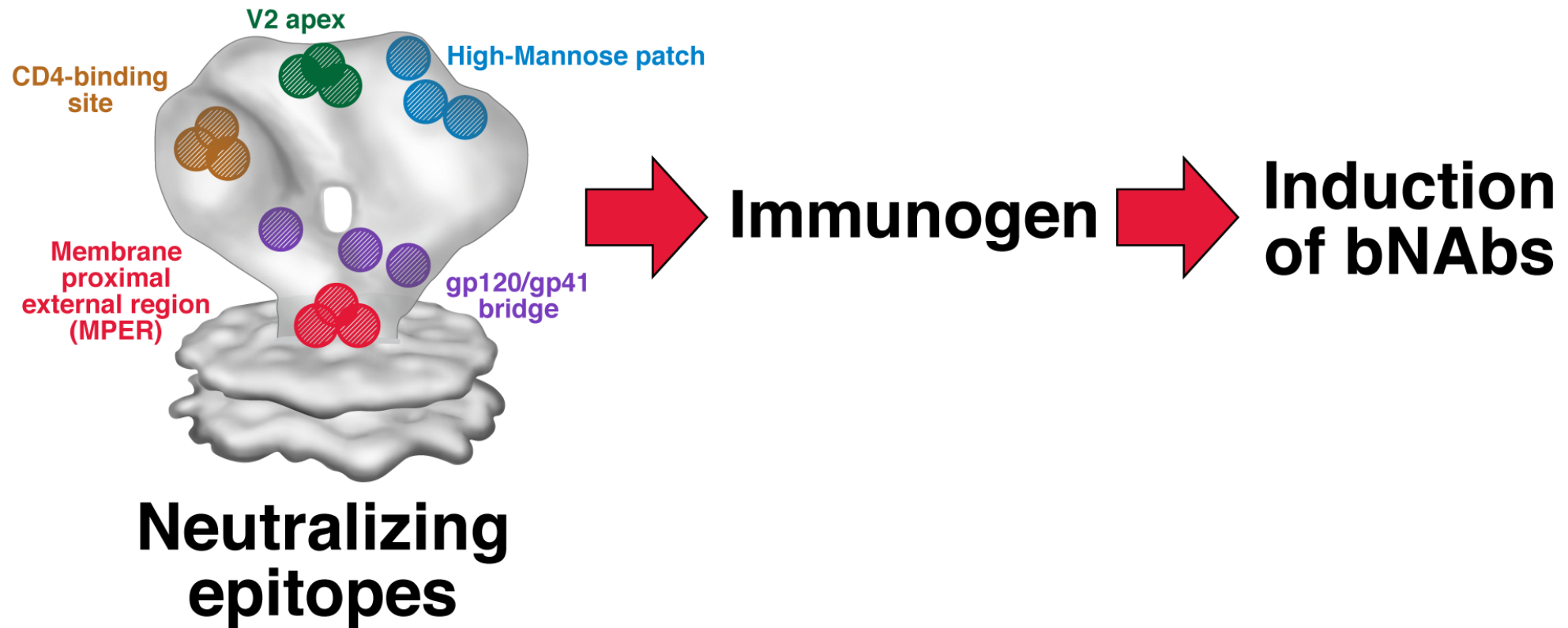
# HIV Envelope Trimer with Target Epitopes

---



# Fundamental Challenge in HIV Vaccinology: Convert Neutralizing Epitopes to Immunogens Inducing bNAbs

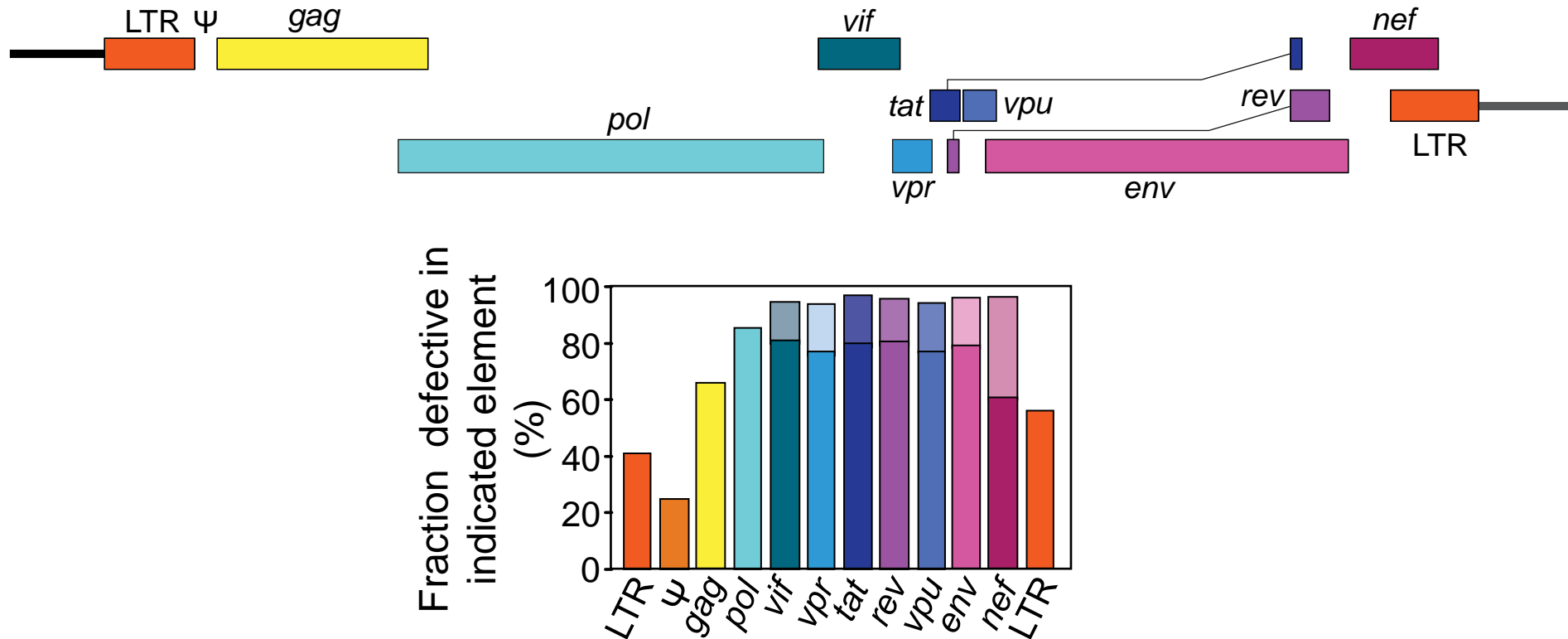
---



# **Towards a Cure – How to Measure?**

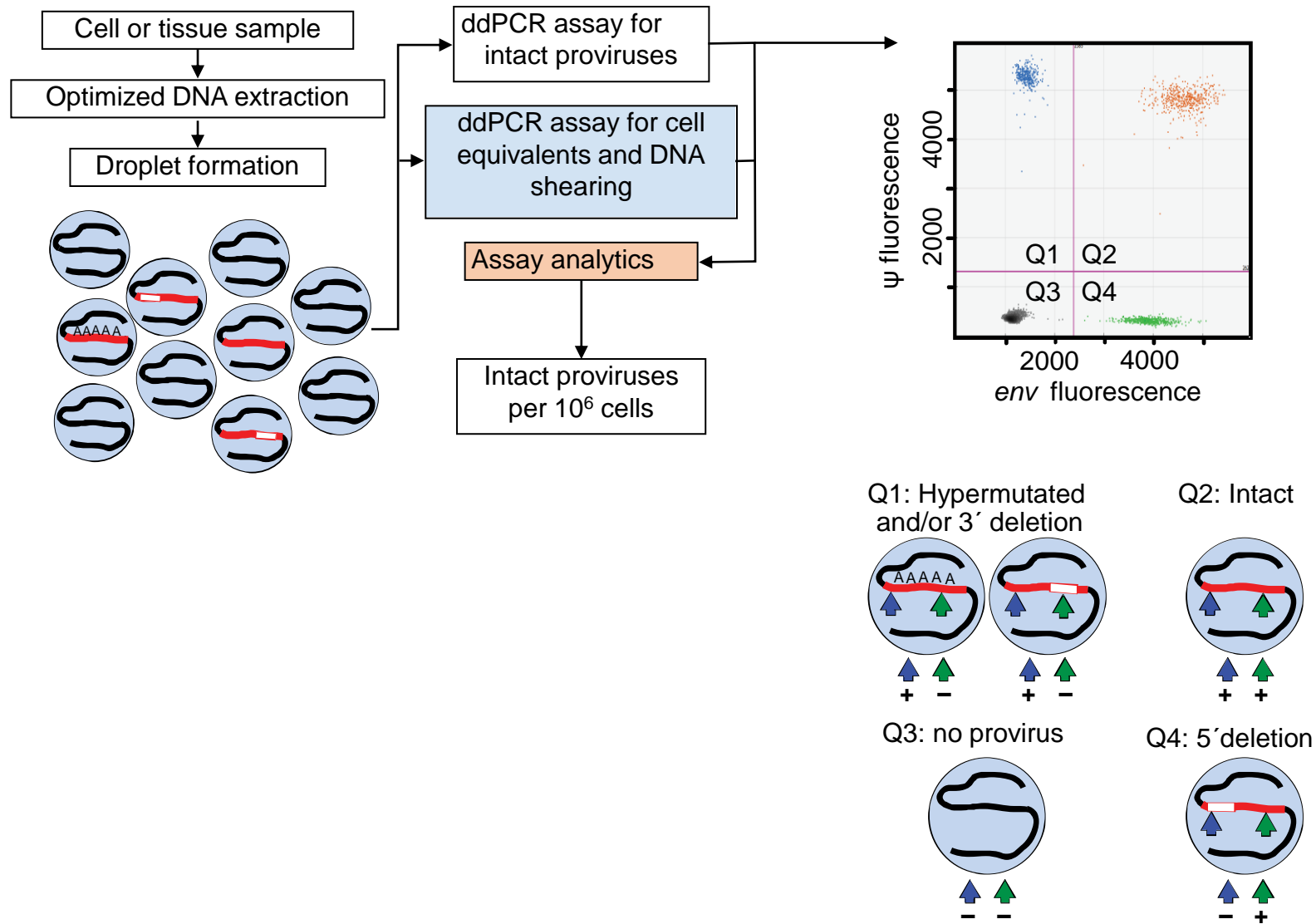


# Most Proviruses Are Defective

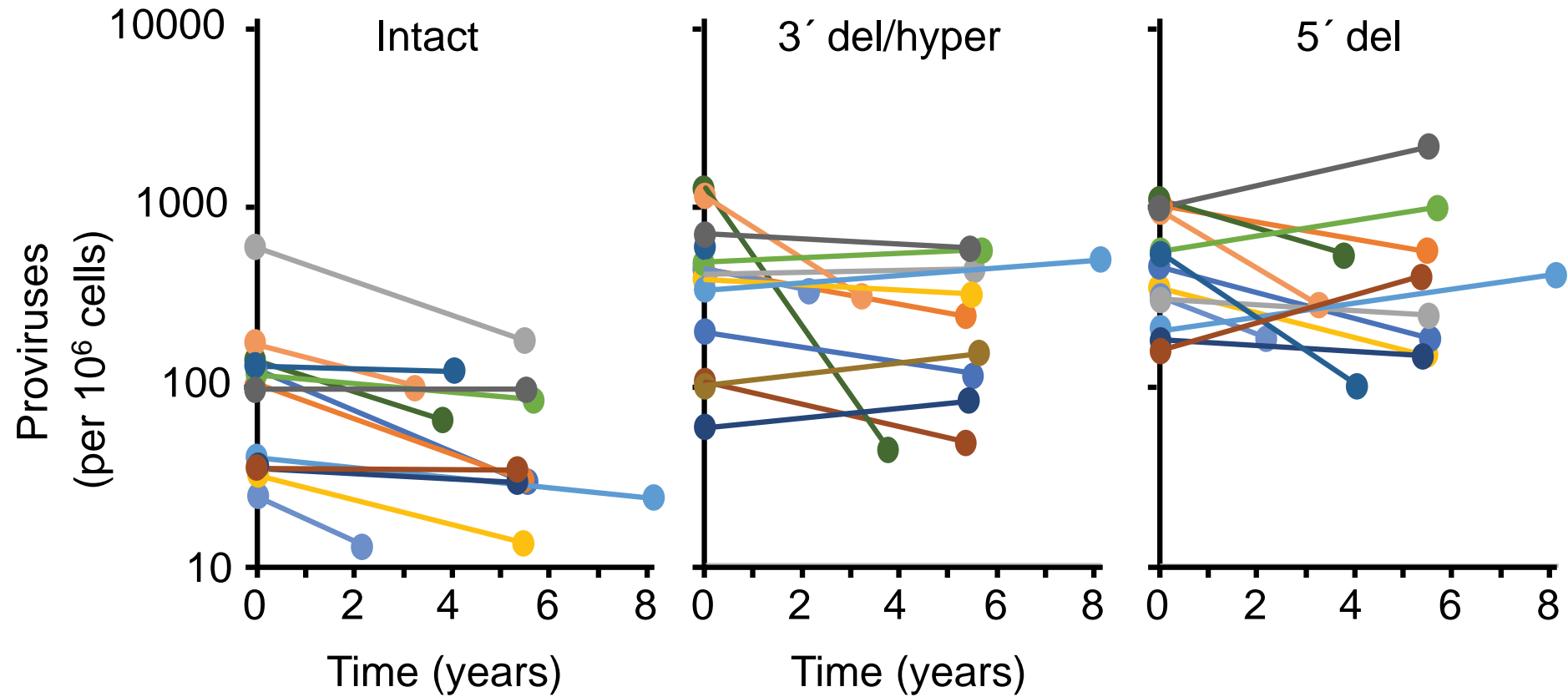


- Most proviruses are defective in most viral genes
- Cells with defective and intact proviruses may be affected differently by shock and kill interventions

# Intact Proviral DNA Assay



# Decay of Intact and Defective Proviruses



# Pathways to Sustained ART-Free HIV Remission

---

Eradicate the replication-competent HIV reservoir – classic **“cure”**

Control viral rebound without eradication of HIV in the absence of ART – **“sustained virologic remission”**



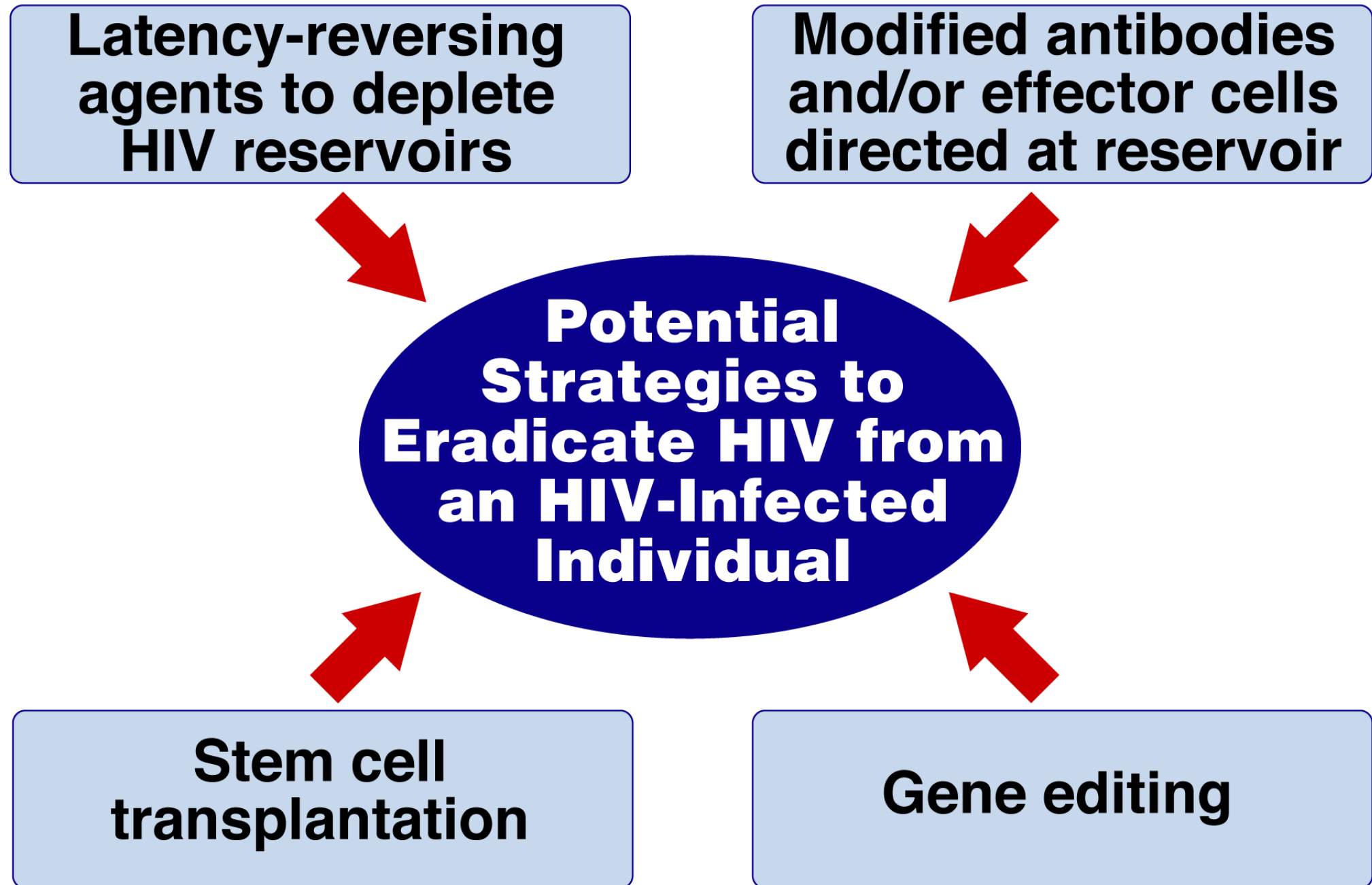
**Latency-reversing  
agents to deplete  
HIV reservoirs**

**Modified antibodies  
and/or effector cells  
directed at reservoir**

**Potential  
Strategies to  
Eradicate HIV from  
an HIV-Infected  
Individual**

**Stem cell  
transplantation**

**Gene editing**



# **ART-Free Remission of HIV Infection**

---

- **ART-free remission, but requiring intermittent or continual non-ART intervention**
- **ART-free remission resulting from induction of durable immune-mediated control of virus without further intervention**

# **Optimal Criteria for Maintaining ART-Free Remission of HIV Infections Without Direct Eradication of Virus**

---

- **Low risk to patient**
- **Scalable**
- **Potentially leads to induction of durable immune-mediated control of virus**

# Where Do We Go From Here?

---

- **Scientific challenges remain**
  - Finding a cure
    - HIV sustained remission remains elusive
  - Developing a vaccine
    - RV144 vaccine trial results did not reproduce in HPTN 702
    - Imbokodo and Mosaico are continuing
    - Scientific breakthroughs needed to reliably induce multiple bNAb lineages

*Once achieved, we need a global commitment to take to scale*



**Thank You**