

# HPTN 2023

# State of the Network

Myron S. Cohen, MD

Wafaa M. El-Sadr, MD, MPH, MPA

HPTN Principal Investigators



# Network Structure – Leaders

## Executive Committee (EC)



Myron  
S. Cohen



Wafaa  
El-Sadr

- Myron S. Cohen
- Wafaa El-Sadr
- Quarraisha Abdool Karim
- Chris Beyrer
- Sinead Delany-Moretlwe
- Deborah Donnell
- Susan Eshleman
- Sybil Hosek
- Raphael Landovitz
- Nyaradzo Mgodzi
- David Serwadda
- Sten Vermund
- Nirupama Sista
- Melissa Turner
- Darrell Wheeler
- 2 NIH Representatives

## Leadership and Operations Center (LOC) FHI 360



Nirupama  
Sista

## Statistical and Data Management Center (SDMC) SCHARP



Deborah  
Donnell

## Laboratory Center (LC) Johns Hopkins University



Susan  
Eshleman



Mark  
Marzinke

A world map in shades of green is centered on the slide. The map is semi-transparent, allowing a background of faint medical icons to be seen. These icons include a white cross on a green background, a white pill, a white syringe, and a white flask. The overall aesthetic is clean and professional, with a focus on global health and medical research.

# 78 Trials

ongoing or completed

A world map in shades of green is centered in the background. The map is overlaid on a white horizontal band. The background also features faint, light green icons of a medical cross, a pill, a person, and a molecular structure.

**172,000+**

Study participants enrolled



A world map in shades of green is centered on the page. The map is semi-transparent, allowing a white horizontal band to pass through its center. In the background, there are faint, light green icons related to science and medicine, including a DNA double helix, a medical cross, a pill, and a flask. The overall aesthetic is clean and professional, with a focus on global research.

**800+**

**Publications**

# History: HPTN Research Evolution

<b>Cates &amp; Self</b>  Vaccines Microbicides MTCT ART Prevention <b>STI Treatment</b> Substance Use <b>Behavioral</b> Structural Intervention	<b>Cates &amp; Coates</b>  Vaccines <b>Microbicides</b> <b>MTCT!!</b> ART STI Treatment Substance Use Behavioral Structural Intervention	<b>Vermund &amp; Abdool-Karim</b>  Vaccines Microbicides MTCT <b>TaSP (052) !!!!</b> STI Treatment Substance Use Behavioral Structural Intervention	<b>El-Sadr &amp; Cohen</b>  <b>Integrated Strategies:</b> Biomedical Behavioral Structural <b>Oral PrEP!!!</b> Alternate drugs, regimens, and formulations Phase I to III	<b>El-Sadr &amp; Cohen</b>  <b>LA-PrEP!!</b> <b>Multipurpose technology</b> <b>Broadly-neutralizing antibodies as PrEP</b> <b>Integrated strategies</b> - <b>Trans prevention!</b> - <b>PWID!</b> <i>Heterosexual men</i> <i>Pregnant women</i> <b>STI Vaccines ?</b>
<b>1993</b> IMC/HIVNET	<b>1999</b> HPTN I	<b>2006</b> HPTN II	<b>2013</b> HPTN III	<b>2020</b> HPTN IV

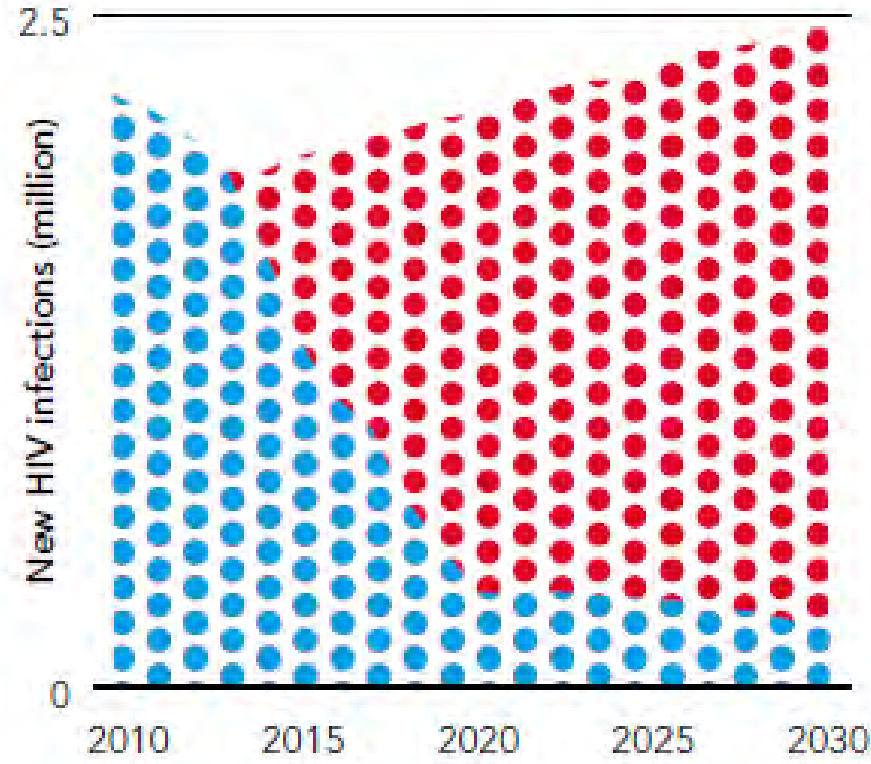
UNDETECTABLE = UNTRANSMITTABLE



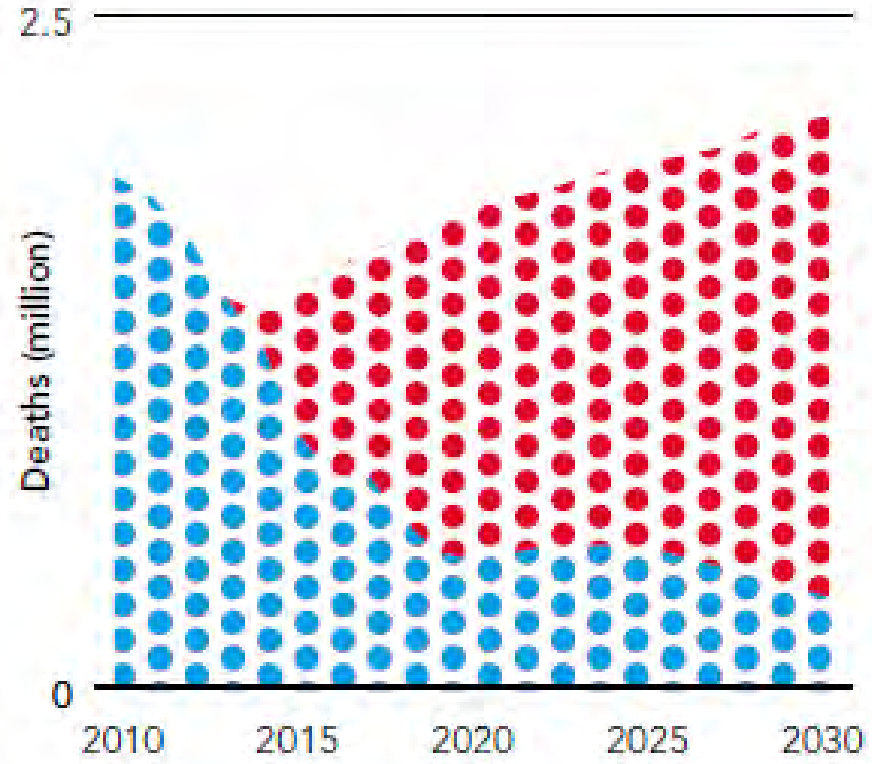
Prevention Access Campaign

# The impact of Fast-Track

## New HIV infections in low- and middle-income countries



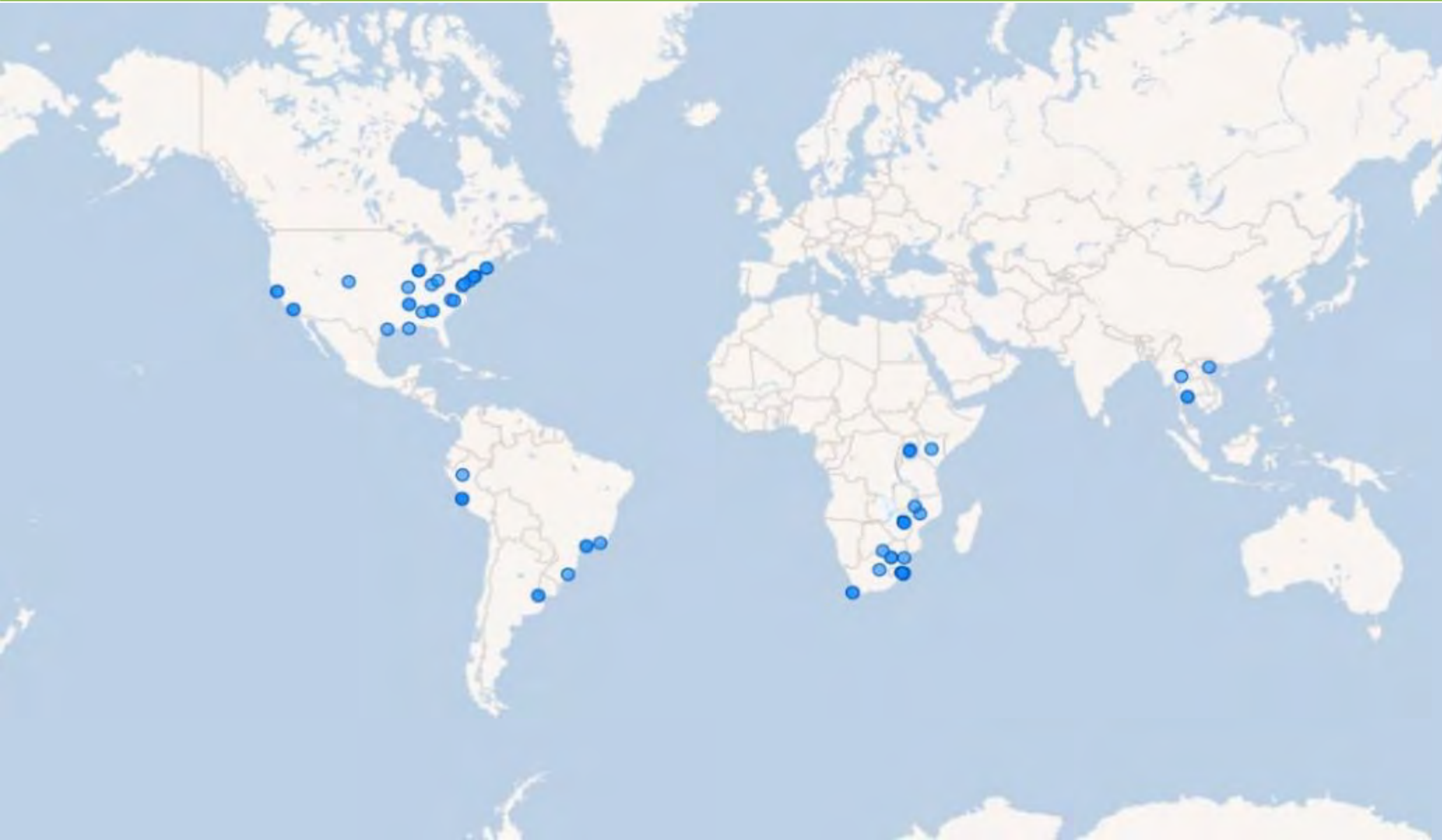
## AIDS-related deaths in low- and middle-income countries



- Business as usual (no scale-up)
- Fast-Track results (rapid scale-up)



# Forward: 2023 Clinical Research Sites



**69**

HPTN Sites

**13**

Countries

**22**

African Sites

**5**

Asian Sites

**31**

North American Sites

**11**

South American Sites

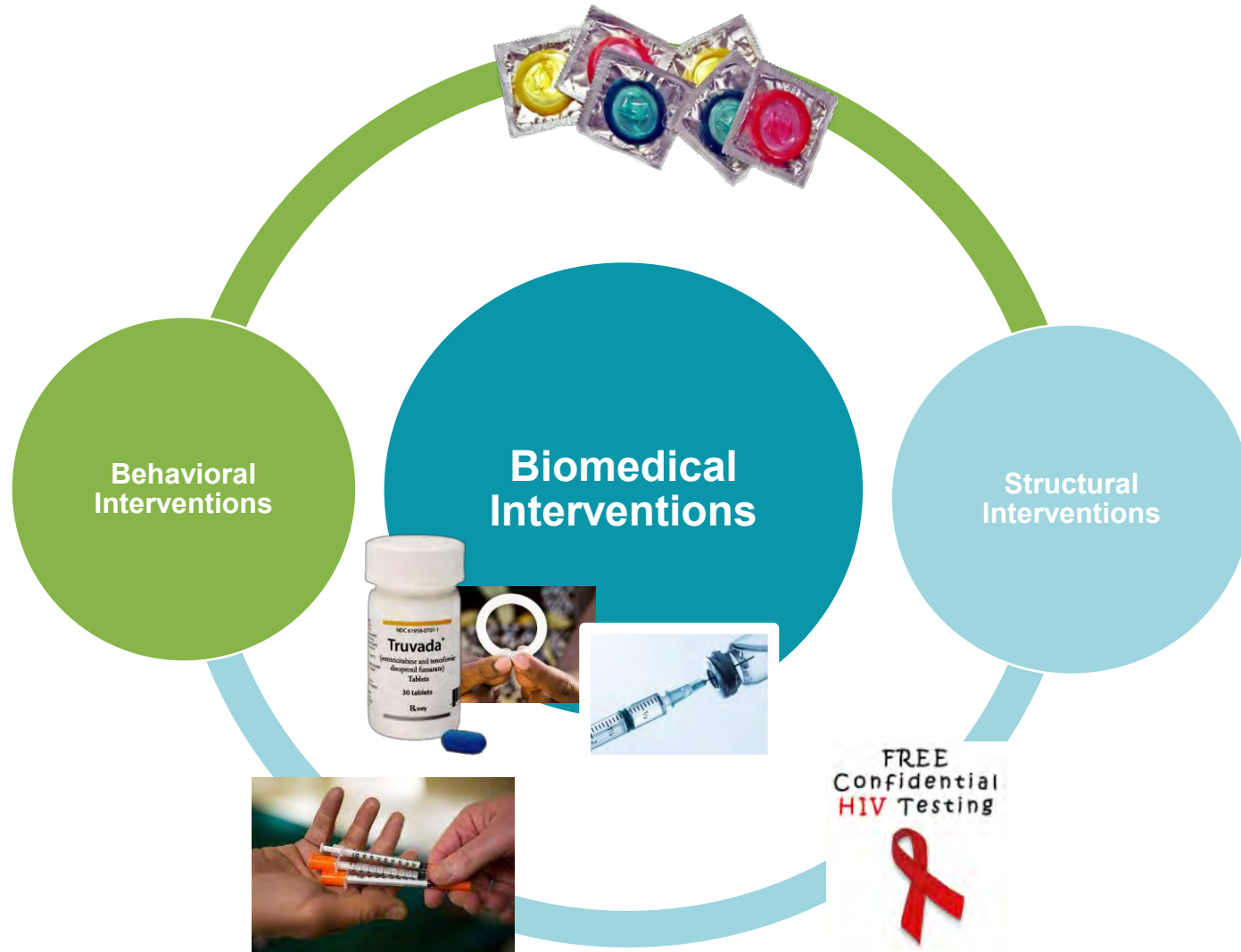
# Two Points to Consider First

- **HPTN/HVTN = The COVID Prevention Network (CovPN)**
    - Moderna, Astra Zeneca, J&J, Novavax vaccines
    - mAbs from Lilly, Regeneron and Astra Zeneca
- But.. Consider the HPTN/HVTN Opportunity Costs**

## **Recent HVTN Vaccine Trials**

- HIV vaccine development continues to prove VERY challenging
- Collaborative HVTN/HPTN bnAb research for next PrEP
- bnAb research informs vaccine development, long-term

# Achieving Population Impact





# NEXT in PrEP



**HPTN** Regional Meeting



# CAB LA PrEP IS APPROVED in the U.S.

## – What's Next?

- Open label extension (OLE) studies will estimate continued safety and protection, PK, resistance, and include pregnancy and adolescent substudies.
- CAB LA for PrEP is approved in several countries, including Botswana, Malawi, South Africa, Zambia and Zimbabwe. In addition, full EMA approval was received for use in EU countries.
- **ROUND OF APPLAUSE!!!!!!**
- New studies in development to examine the effectiveness of CAB-LA among adolescents and PWID.
- New studies to explore different routes of administration (e.g., thigh). fewer injections/year and more.
- Combine cabotegravir-LA with contraceptives in future studies?

# Pregnancy Sub-Study in HPTN 084 OLE

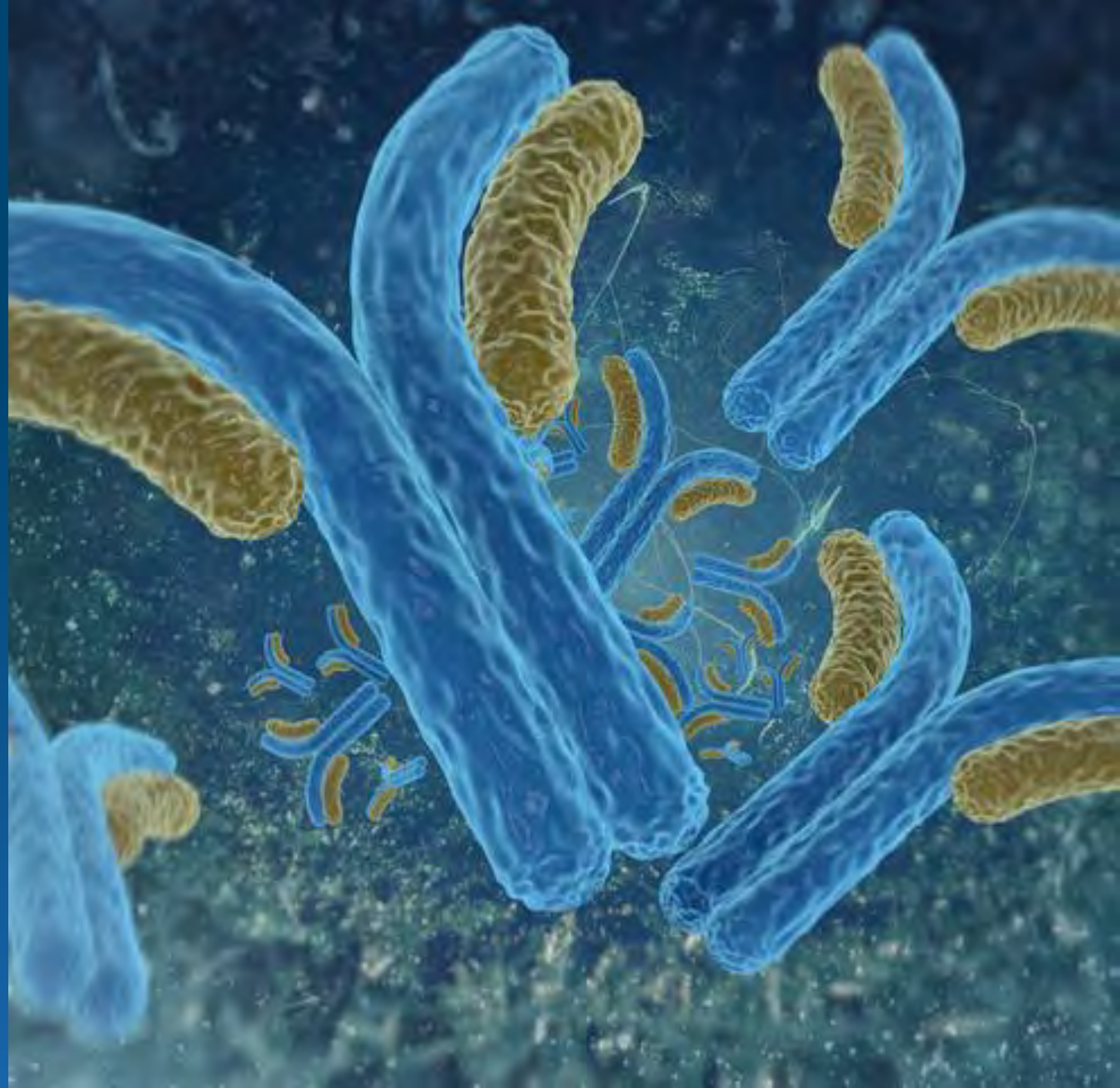
- Estimate the incidence of pregnancy among participants during the OLE period
- Evaluate safety and infant outcomes among pregnant participants
- Evaluate the PK of CAB LA among pregnant participants, combining blinded, unblinded and OLE periods
- Evaluate concentration in breastmilk and infants among women who receive CAB LA injections during pregnancy and/or the early post-partum period.

# The HPTN/Gilead Collaboration: A New paradigm



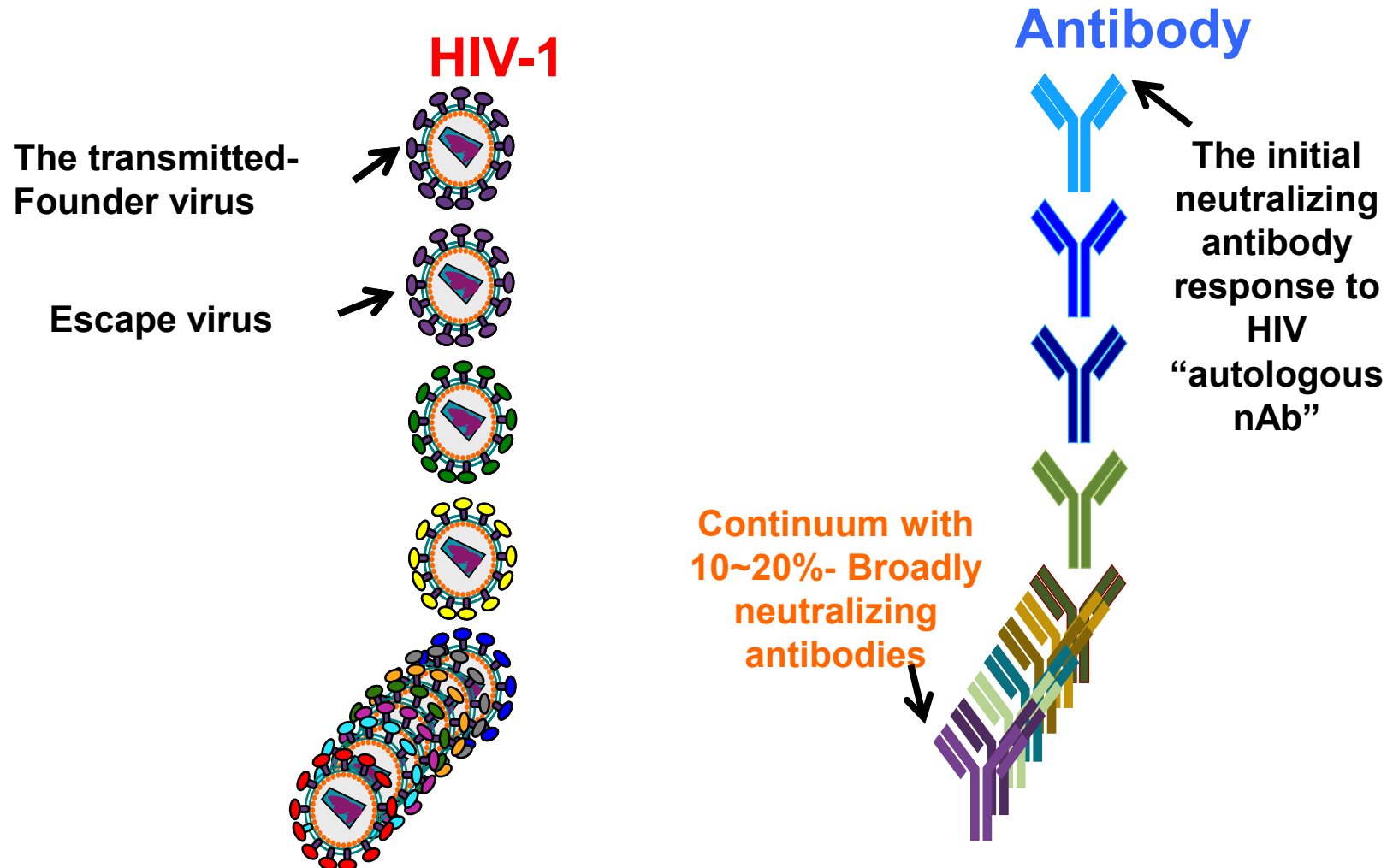
- Lenacapavir, a first-in-class selective HIV capsid inhibitor, with subcutaneous injections every 6 months
- HPTN and Gilead will develop two companion studies in collaboration:
  - **HPTN 102/Purpose 3: A lenacapavir Phase 2 PK, safety, acceptability in cis-gender women in the US**
  - **HPTN 103/Purpose 4: A phase 2 PK, safety, acceptability of lenacapavir in people who inject drugs (PWID) in the US**

# Broadly Neutralizing Antibodies for HIV Prevention





# Broadly Neutralizing Antibodies



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

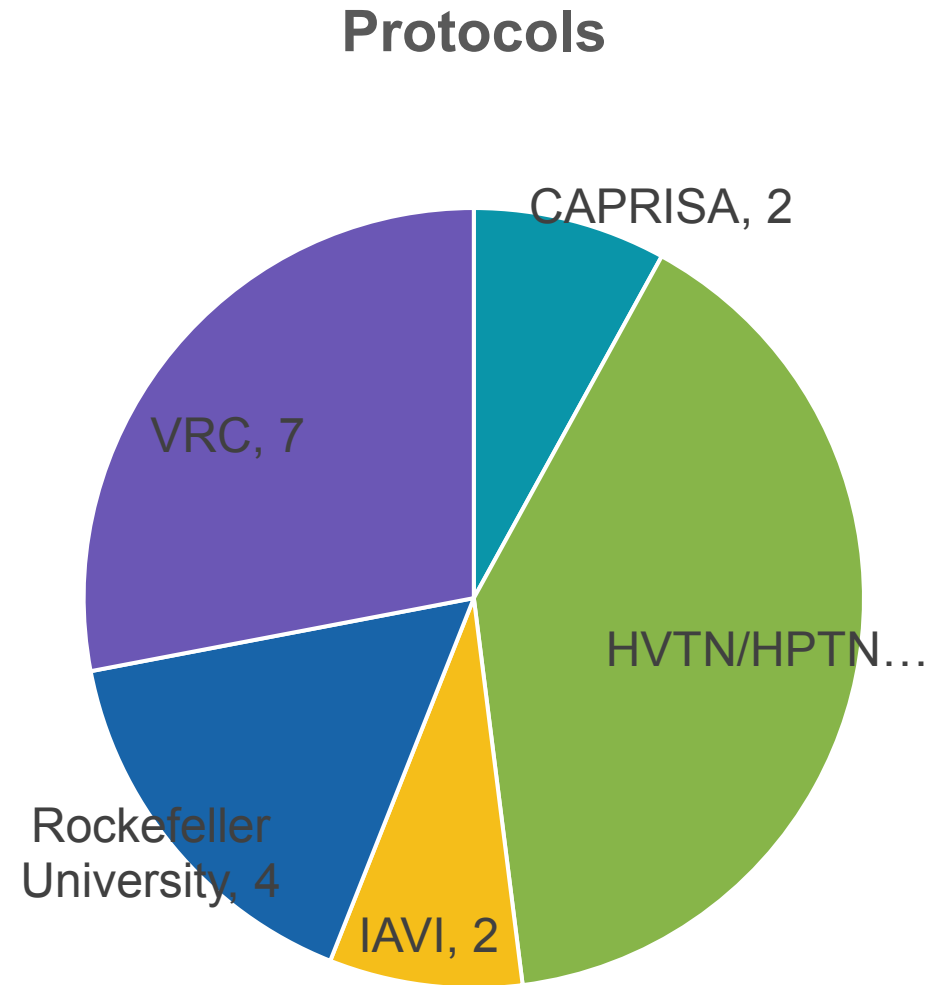
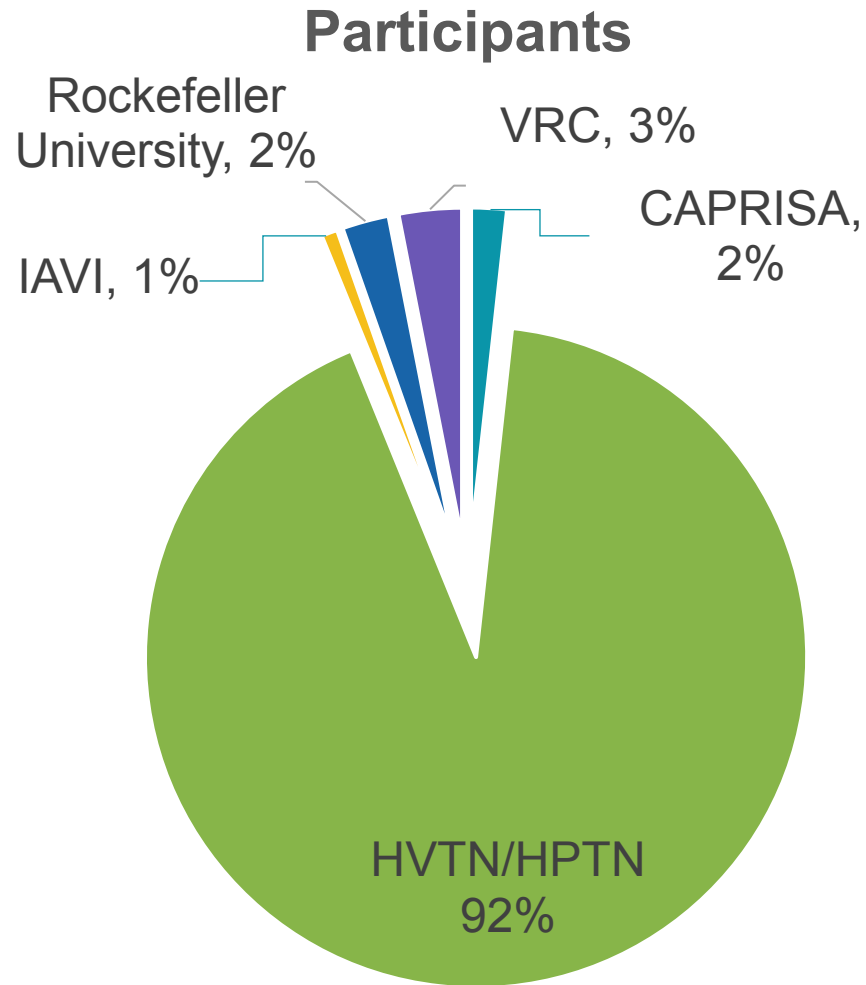
## Two Randomized Trials of Neutralizing Antibodies to Prevent HIV-1 Acquisition

L. Corey, P.B. Gilbert, M. Juraska, D.C. Montefiori, L. Morris, S.T. Karuna, S. Edupuganti, N.M. Mgodhi, A.C. deCamp, E. Rudnicki, Y. Huang, P. Gonzales, R. Cabello, C. Orrell, J.R. Lama, F. Laher, E.M. Lazarus, J. Sanchez, I. Frank, J. Hinojosa, M.E. Sobieszczyk, K.E. Marshall, P.G. Mukewerere, J. Makhema, L.R. Baden, J.I. Mullins, C. Williamson, J. Hural, M.J. McElrath, C. Bentley, S. Takuva, M.M. Gomez Lorenzo, D.N. Burns, N. Espy, A.K. Randhawa, N. Kochar, E. Piwowar-Manning, D.J. Donnell, N. Sista, P. Andrew, J.G. Kublin, G. Gray, J.E. Ledgerwood, J.R. Mascola, and M.S. Cohen, for the HVTN 704/HPTN 085 and HVTN 703/HPTN 081 Study Teams\*

- VRC01 is a broadly neutralizing antibody (bNAb) which blocks the CD4 binding site on the HIV envelope
- VRC01 was infused every 2 months x 10 to high-risk women (Africa) and MSM and transgender individuals (Americas) (n=4,600)
- Two doses of VRC01 were evaluated: 10 mg/kg and 30 mg/kg

**VRC01 neutralized highly sensitive viruses, no effect on others**

# HIV bnAb clinical trials in HIV-uninfected adults



# HVTN/HPTN HIV bnAb Clinical Trials in HIV-uninfected adults

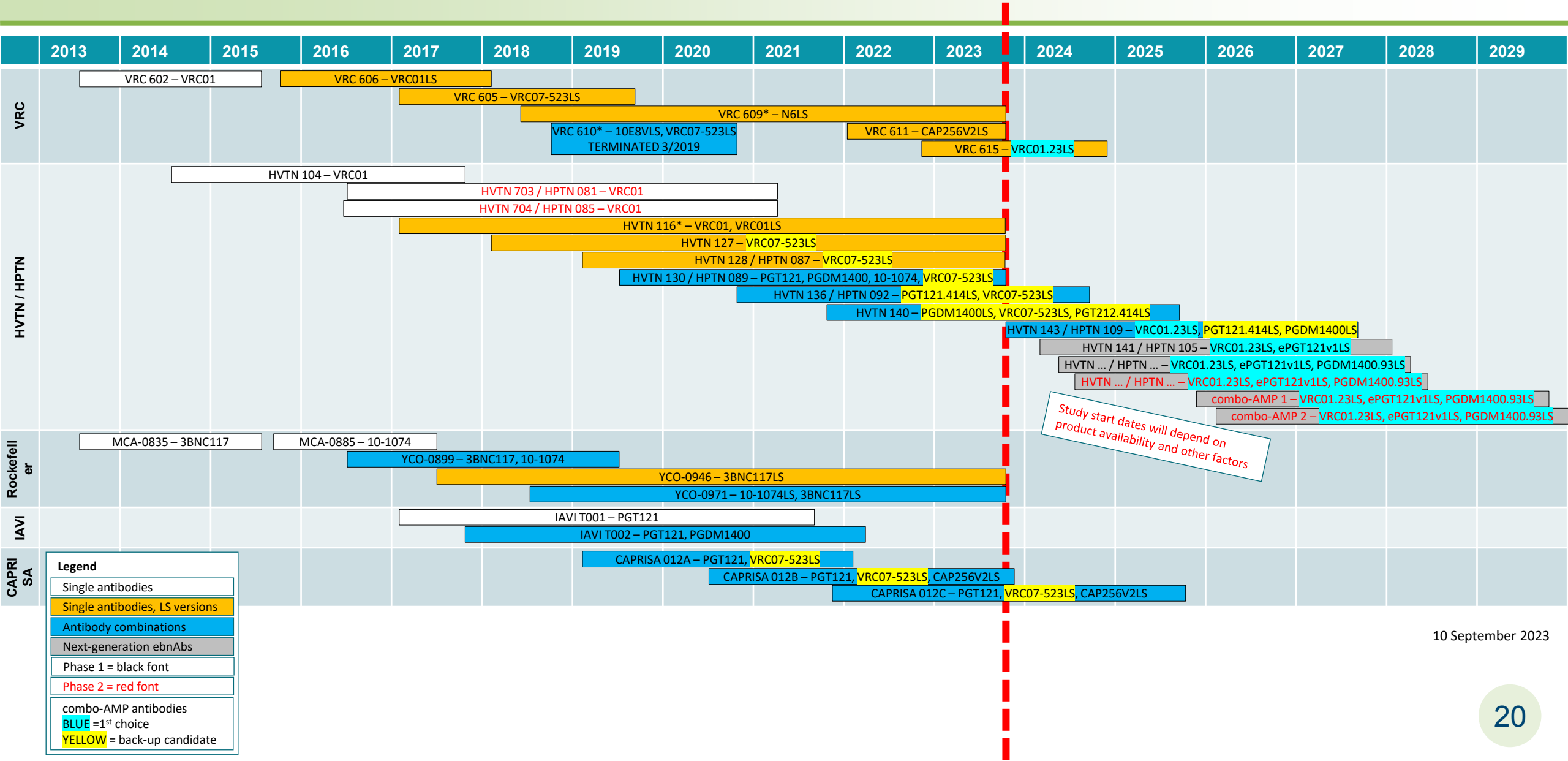
> 4900 participants  
> 50 sites  
11 countries

Clinical Trial Participants	Start	bnAb	New concepts <sup>1</sup>	Key results – the road to combo-AMP	Countries
HVTN 104 N=88	2014	• VRC01 IV, SC	<ul style="list-style-type: none"> <li>Safety, PK, PD, neutralization</li> <li>Repeat dosing up to 22 weeks</li> </ul>	<ul style="list-style-type: none"> <li>Interim PK and neutralization data informed AMP protocol development</li> </ul>	USA
HVTN 704/HPTN 085 N= 2699	2016	• VRC01 IV	<ul style="list-style-type: none"> <li>HIV prevention efficacy proof of concept</li> <li>Correlate of protection</li> </ul>	<ul style="list-style-type: none"> <li>HIV bnAb can prevent HIV acquisition</li> <li>Correlate of protection – PT<sub>80</sub> biomarker to predict protection</li> <li>HIV bnAbs are safe – safety profile equal to placebo</li> </ul>	Brazil, Peru, USA, Switzerland
HVTN 703/HPTN 081 N=1924	2016	• VRC01 IV	<ul style="list-style-type: none"> <li>HIV prevention efficacy proof of concept</li> <li>Correlate of protection</li> </ul>		Botswana, Kenya, Malawi, Mozambique, South Africa, Tanzania, Zimbabwe
HVTN 116 N=80	2017	• VRC01 IV • VRC01LS IV	<ul style="list-style-type: none"> <li>LS modification, longer half-life</li> <li>Mucosa, tissue &amp; secretions PK &amp; activity</li> </ul>	<ul style="list-style-type: none"> <li>VRC01LS ~3x longer half-life in serum, higher and prolonged levels in genital and rectal tissue</li> </ul>	South Africa, USA
HVTN 127/HPTN 087 N=124	2018	• VRC07-523LS IV, IM, SC	<ul style="list-style-type: none"> <li>IM dosing</li> </ul>	<ul style="list-style-type: none"> <li>VRC07-523LS ~2x longer half life</li> <li>Neutralization consistent after 5 doses</li> </ul>	Switzerland, USA
HVTN 128 N=28	2019	• VRC07-523LS IV	<ul style="list-style-type: none"> <li>Mucosa PK &amp; activity</li> </ul>		USA
HVTN 130/HPTN 089 N=27	2019	<ul style="list-style-type: none"> <li>VRC07-523LS IV</li> <li>10-1074 IV</li> <li>PGT121 IV</li> <li>PGDM1400 IV</li> </ul>	<ul style="list-style-type: none"> <li>2 bnAb combinations</li> </ul>	<ul style="list-style-type: none"> <li>No PK interaction</li> <li>No loss of complementary neutralization</li> <li>Greater neutralization coverage in 3 bnAb arms compared to 2 bnAb arms</li> </ul>	USA
HVTN 136/HPTN 092 N=32	2020	<ul style="list-style-type: none"> <li>VCR07-523LS IV, SC</li> <li>PGT121.414.LS IV, SC</li> </ul>	<ul style="list-style-type: none"> <li>2 LS bnAb combination</li> </ul>	<ul style="list-style-type: none"> <li>PGT121.414.LS ~3x longer half-life</li> </ul>	USA
HVTN 140/HPTN 101 N=95	2021	<ul style="list-style-type: none"> <li>VRC07-523LS IV, SC</li> <li>PGT121.414.LS IV, SC</li> <li>PGDM1400LS IV, SC</li> </ul>	<ul style="list-style-type: none"> <li>3 LS bnAb combination</li> <li>Fixed dose compared to weight-based dose</li> </ul>	<ul style="list-style-type: none"> <li>PGDM1400LS ~2.5x longer half-life</li> </ul>	Kenya, South Africa, USA, Zimbabwe
HVTN 143/HPTN 109 N=77	2023	<ul style="list-style-type: none"> <li>VRC01.23LS IV</li> <li>PGT121.414.LS IV</li> <li>PGDM1400LS IV</li> </ul>	<ul style="list-style-type: none"> <li>3 LS bnAb combination</li> <li>1<sup>st</sup> of 3 LS bnAbs to be used in 'combo AMP' in a 3 LS bnAb combination – 1 of 3</li> </ul>		South Africa
HVTN 141/HPTN 105 N= 92	2024	<ul style="list-style-type: none"> <li>VRC01.23LS IV</li> <li>ePGT121v1LS IV, SC</li> </ul>	<ul style="list-style-type: none"> <li>2<sup>nd</sup> (and 1<sup>st</sup>) of 3 LS bnAbs combination to be used in 'combo AMP' in a 2 LS bnAb combination – 2 of 3</li> </ul>		South Africa, USA
HVTN TBD/HPTN TBD N= tbd ± 92	2024	<ul style="list-style-type: none"> <li>VRC01.23LS IV</li> <li>ePGT121v1LS IV</li> <li>PGDM1400.93LS IV, SC</li> </ul>	<ul style="list-style-type: none"> <li>3<sup>rd</sup> (and 2<sup>nd</sup> and 1<sup>st</sup>) of 3 LS bnAbs combination to be used in 'combo AMP' in a 3 LS bnAb combination – 3 of 3</li> </ul>		TBD, South Africa, USA
HVTN TBD/HPTN TBD N=tbd ± 200	2024	<ul style="list-style-type: none"> <li>VRC01.23LS IV</li> <li>ePGT121v1LS IV</li> <li>PGDM1400.93LS IV</li> </ul>	<ul style="list-style-type: none"> <li>Fixed 'combo-AMP' dose compared to weight-based dose</li> <li>Safety run-in for combo-AMP</li> </ul>		TBD, South Africa, USA
Combo-AMP studies 1. Women in SSA 2. MSM & transgender N=tbd	2025/ 2026	<ul style="list-style-type: none"> <li>VRC01.23LS IV</li> <li>ePGT121v1LS IV</li> <li>PGDM1400.93LS IV</li> </ul>	<ul style="list-style-type: none"> <li>3 LS bnAbs combination                             <ul style="list-style-type: none"> <li>HIV prevention efficacy proof of concept</li> <li>Correlate of protection</li> </ul> </li> </ul>		AMP countries, TBD

<sup>1</sup>All trials evaluate safety, PK, & serum neutralization; additional protocol-specific evaluations noted here.



# HIV bnAb clinical trials in HIV-uninfected adults



Study start dates will depend on product availability and other factors

**Legend**

- Single antibodies
- Single antibodies, LS versions
- Antibody combinations
- Next-generation ebnAbs
- Phase 1 = black font
- Phase 2 = red font

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- combo-AMP antibodies
- BLUE = 1<sup>st</sup> choice
- YELLOW = back-up candidate

# NIH Criteria for a bNab PreP Trial

- **Pharmacology leads to a stable combination (i.e.no “tails”)**
- A product manufacturer
- A commercial partner
- An ethical trial design
- Feasible implementation

# Dual Prevention Pill: HPTN 104

Phase 2b, open label, randomized crossover study of DPP (co-formulated F/TDF+ ethynyl estradiol/levonorgestrel oral contraceptive pill (OCP), compared with the two tablets with daily oral F/TDF + OCP (2PR) for PrEP and pregnancy prevention in HIV-uninfected women

**Sample Size:** ~300 women 16-39 years (100 adolescents) for 48 weeks per participant

**Regulatory Sponsor:** Viatrix

**Primary Objective:**

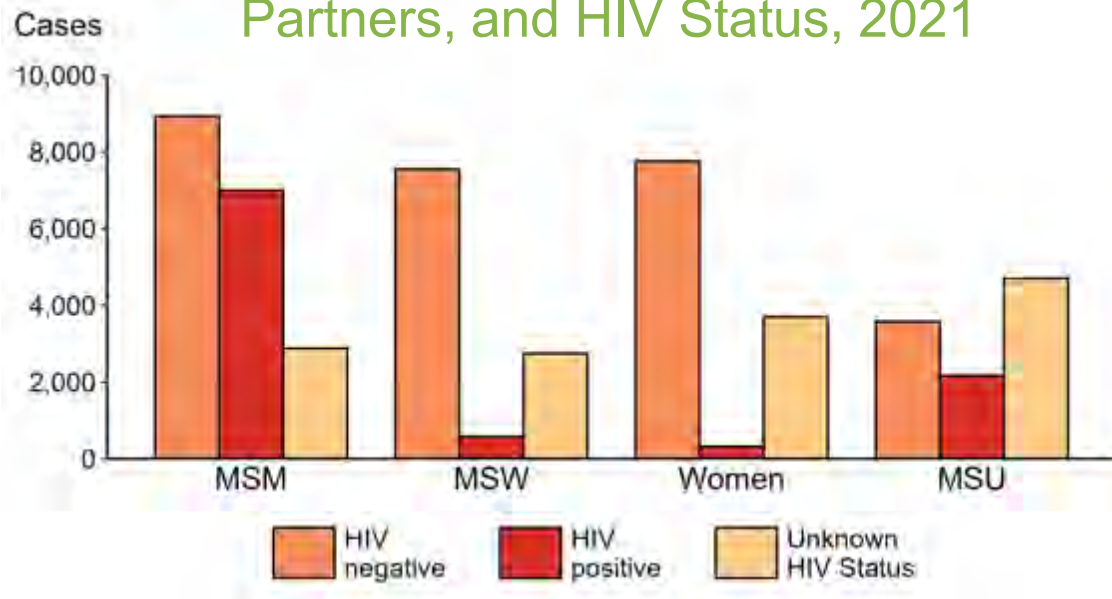
Compare PrEP adherence to the DPP versus 2PR during a randomized crossover period

Pivotal Bioequivalence results to be submitted to US FDA 2023

**Speculation: Study launched 2024. Aspiration {US FDA approval 2025!!**

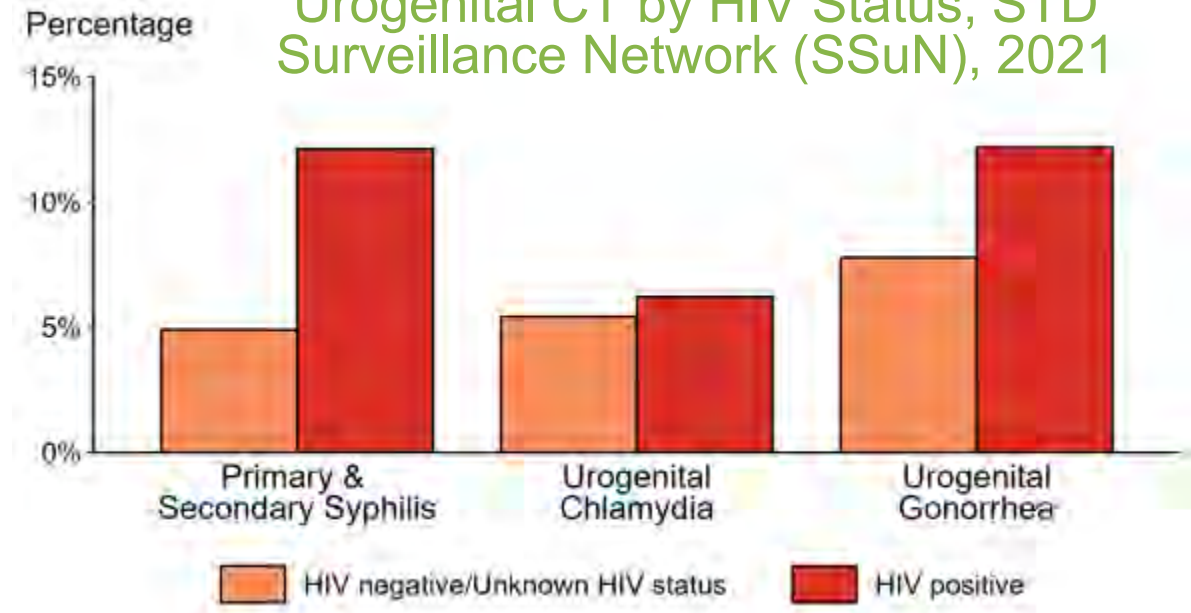
# Back to STIs and the HIV “Syndemic”

Primary & Secondary Syphilis:  
Reported Cases by Sex, Sex of Sex  
Partners, and HIV Status, 2021



Among cases with reported HIV status, 44% among MSM were HIV+, compared with 38% among men with unknown sex of sex partners, 7.1% among men who have sex with women only, and 3.9% among women

Proportion of MSM with Primary and  
Secondary Syphilis, Urogenital GC, or  
Urogenital CT by HIV Status, STD  
Surveillance Network (SSuN), 2021

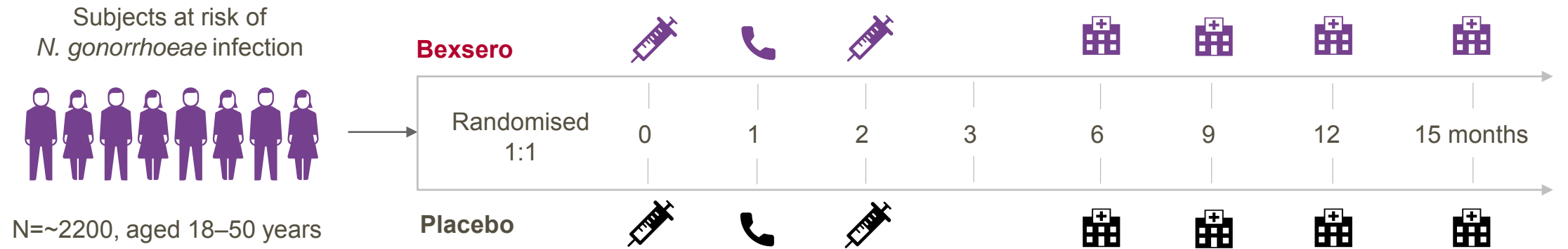


Percent with primary and secondary syphilis was higher for HIV+ compared with those not (12% vs 4.9%), similar to urogenital chlamydia (6.2% vs 5.4%) and gonorrhea (12% vs 7.8%)



# A Phase II randomized, observer-blind, placebo-controlled study to assess efficacy of meningococcal **Group B vaccine MenB+OMV NZ (Bexsero)** in preventing gonococcal infection (DMID Protocol 19-0004/HPTN 108)

- Study design** Phase II, randomised, observer-blind, placebo-controlled trial (USA and Thailand)
- Primary objective** Bexsero efficacy in preventing urogenital and/or anorectal gonococcal infection



**Recruiting** estimated completion **2024**  
**Target enrolment 2,200** to achieve **202** incident infections  
**Current enrolment 667** across 11 sites

**3 HPTN Sites in the US and (soon) Malawi**

# US Vanguard Integrated Strategies

HPTN 091: HIV Prevention, Gender-Affirmative Medical Care, and Peer Health Navigation for Transgender Women in the Americas

HPTN 094: A Study of Health Service Delivery in a Mobile Health Delivery Unit to Link Persons who Inject Drugs to Integrated Care and Prevention for Addiction, HIV, HCV and Primary Care

HPTN 096: Getting to Zero among Black MSM in the American South: Testing the Efficacy of an Integrated Strategy

# Approved Evolving Concepts

- **HPTN 111:** Uptake of HIV Self-testing and Linkage to Prevention and Care among Heterosexual Men Attending Barbershops in Uganda: A Cluster Randomized Trial
- **HPTN 112:** Improving HIV Prevention Among Heterosexual Men Seeking STI Services in Sub-Saharan Africa: Examining the Feasibility, Acceptability, and Associated Costs of a Systems-Navigator-Delivered Integrated Prevention Package
- **HPTN 113:** Double Prevention: A Vanguard Study of an Integrated Strategy of HIV PrEP and STI PEP for Young Latino Sexual Minority Men (SMM) in the Americas



# Community Engagement



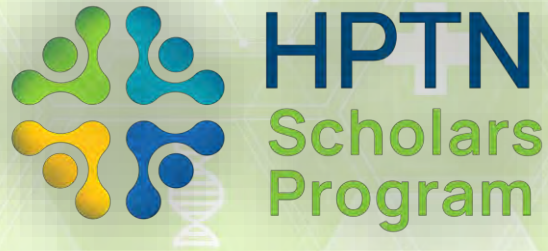
# Community Engagement

## Community Engagement is pivotal part of all HPTN studies.

A few examples:

- Advocacy for affordable post-trial access to CAB LA in countries where HPTN 083 and HPTN 084 are being conducted
- Participating in the development of all forthcoming HPTN research initiatives
- Contributed “Including pregnant and breastfeeding people in trials of novel LAED PrEP agents – perspectives from sub-Saharan Africa community stakeholders” in JIAS Special Issue





Domestic Program established in 2010

- 48 Scholars to date

International Program established in 2015

- 15 Scholars to date

60+ Scholars since 2010 (some were in multiple cohorts)

- 34% men; 66% women
- 20 datasets: HPTN 037-HPTN 082
- 50+ mentors

HPTN involvement

- Protocol Team Members (HPTN 073, 078, 094, 096)
- Protocol Team Leadership (HPTN 091, HPTN 096)
- Memberships/Observerships: Black Caucus, Scientific Committees, and Working Groups

# 2022-2023 HPTN Scholars



Dr. Tina Herrera



Dr. David Zelaya



Dr. Donte Boyd



Dr. Waru Gichane



Dr. Sophia Zamudio-Haas



Dr. Victoria Ndyabangi



Kudzai Hlahla

# Acknowledgments

**Thank you very much to all study participants, investigators and site staff, community groups, collaborators and funders**

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- National Institute of Allergy and Infectious Diseases (NIAID)
- Office of the Director (OD), National Institutes of Health (NIH)
- National Institute on Drug Abuse (NIDA)
- National Institute of Mental Health (NIMH)
- Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)
- ViiV Healthcare, Gilead Sciences, The Bill and Melinda Gates Foundation, and Viatrix
- Collaborations with HVTN, ACTG, IAVI, AVAC and Rockefeller University

Award Numbers UM1AI068619 (HPTN Leadership and Operations Center), UM1AI068617 (HPTN Statistical and Data Management Center), and UM1AI068613 (HPTN Laboratory Center)