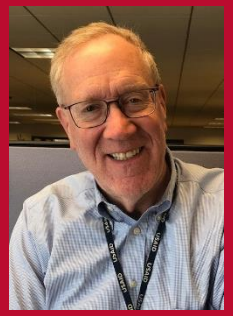
USAID's Support to Global Health Research and Development
Webinar Series:
HIV/AIDS

Alison Cheng
Implementation Science Branch Chief, Research Division, Office of HIV/AIDS



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USAID
FROM THE AMERICAN PEOPLE

USAID's Support to Global Health Research & Development: HIV/AIDS

Where Are We Now?

An estimated 2 million people are newly infected with HIV every year

In sub-Saharan Africa, 1 in 20 adults is living with HIV

Women still make up almost 60% of new HIV infections in sub-Saharan Africa. In many developing countries, women still lack the power to negotiate currently available approaches to protect themselves against HIV.

Research Vision and Mission

Vision

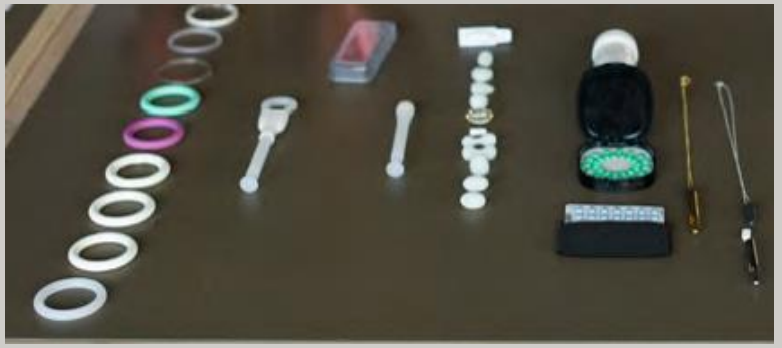
To end the AIDS epidemic through the discovery and implementation of high-impact public health tools, technologies and interventions.

Mission

Promote research, development, evaluation and the use of high-impact public health tools, technologies, and interventions for HIV and AIDS prevention, care, and treatment

Research Goals

Accelerate development and clinical testing of novel HIV vaccine candidates and build global capacity for vaccine research



Strengthen the programmatic evidence base for HIV and AIDS prevention, care, and treatment to achieve epidemic control

© International AIDS Vaccine Initiative: Jean-Marc Giboux/Getty Images

Develop, test, and introduce microbicides for women to reduce the risk of HIV infection

HIV Vaccine Research

Development of enhanced bnAbs as a prevention tool for young women and adolescent girls

Devin Sok, PhD | Director, Antibody Discovery and Development

USAID Webinar | 21 March 2018

ADVANCE Microbicides

Program goal

Develop an enhanced bnAb prevention product that has a higher likelihood for efficacy, acceptability, and affordability of use among adolescent girls and young women

INVESTIGATORS

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Program Lead & Director of Antibody Discovery and Development, IAVI

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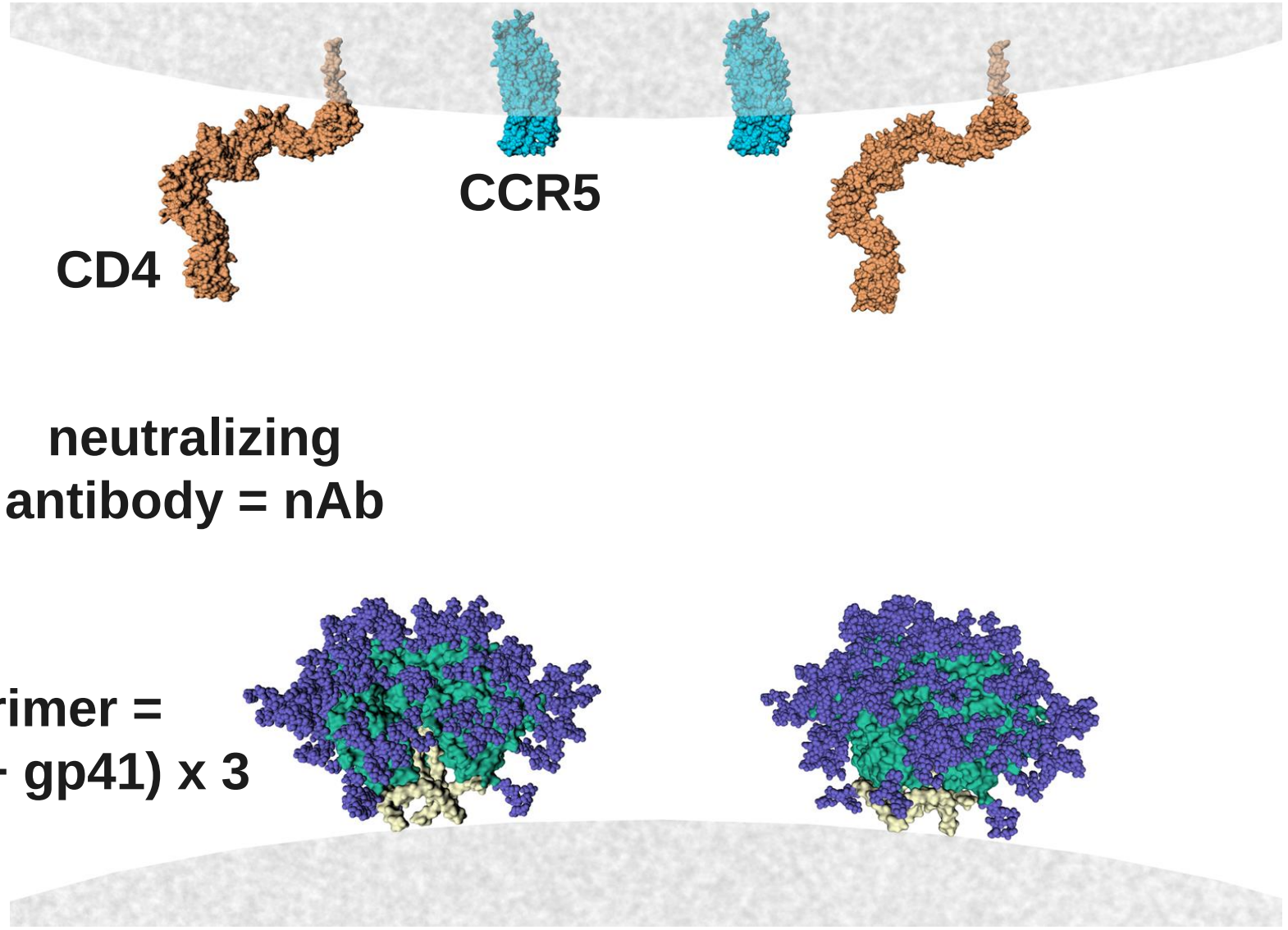
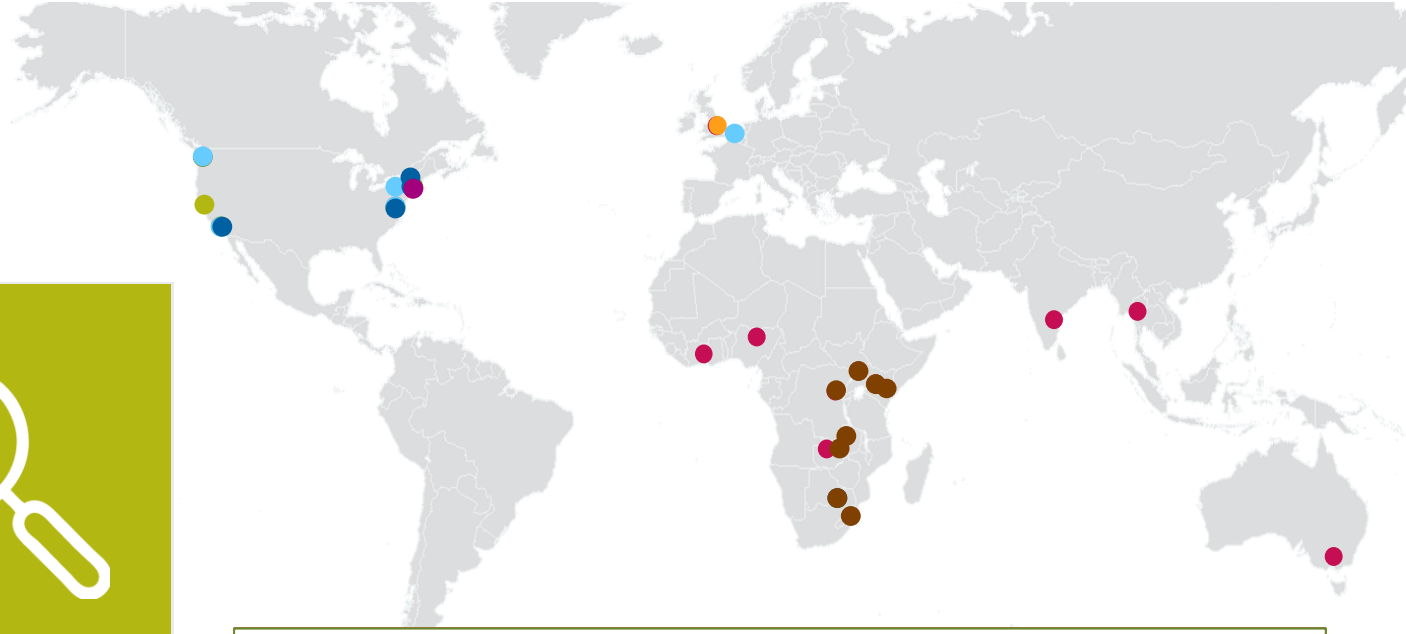
Regional Director, Africa

Neutralizing antibodies bind to the HIV Env trimer to prevent HIV from infecting target cells



Protocol G catalyzing the vaccine field

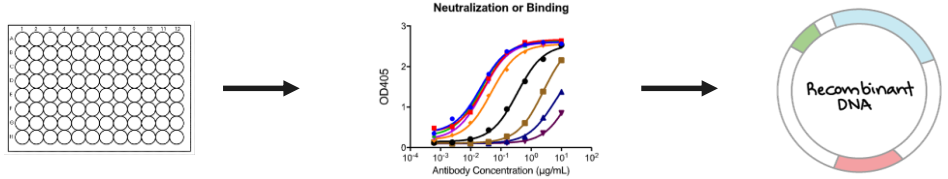


1 2 3

8 End-to-End bnAb Discovery to Development 4

7 6 5

Ab isolation

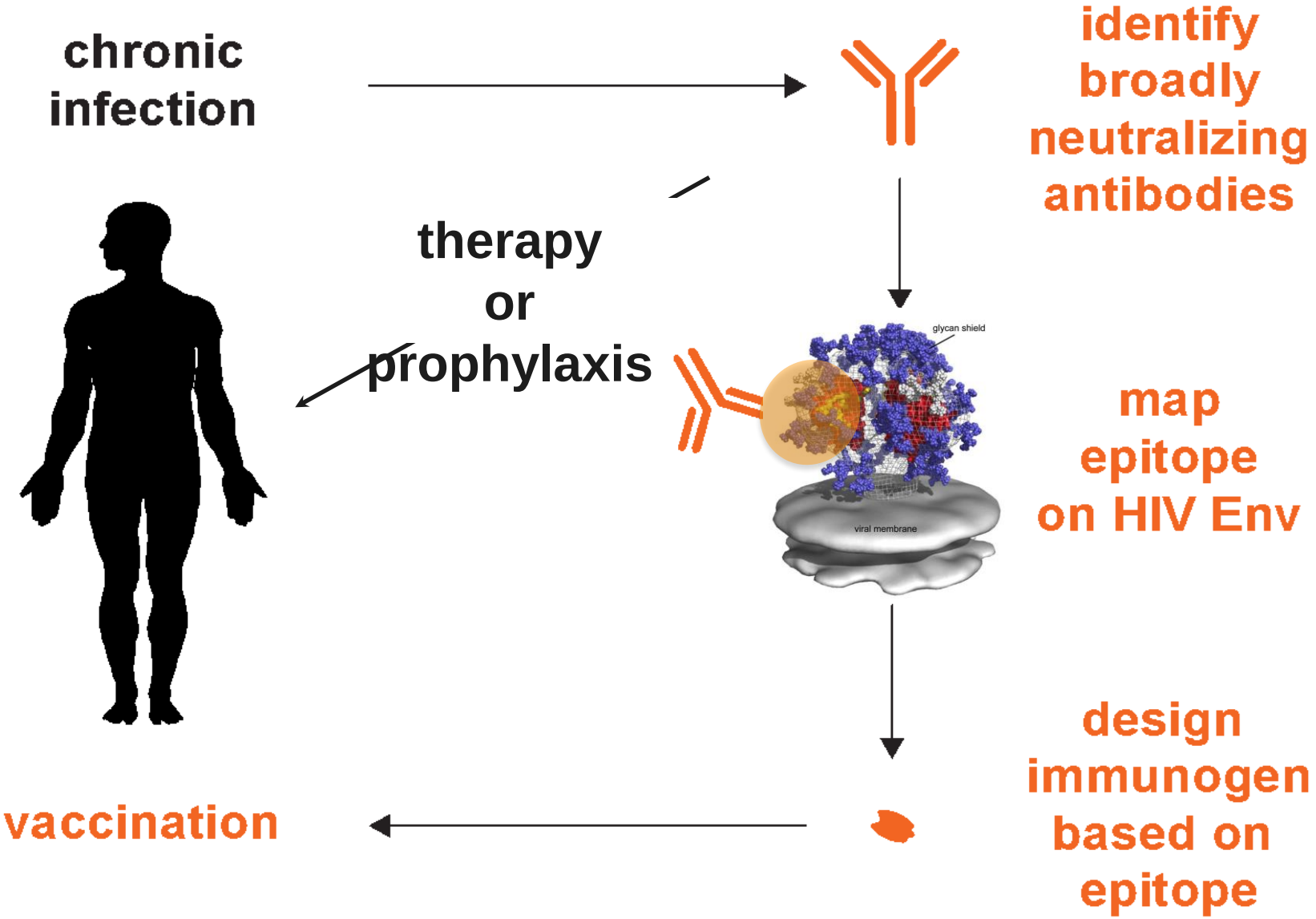


Activate Memory B cells → **Agnostic screen for function** → **Clone & express**

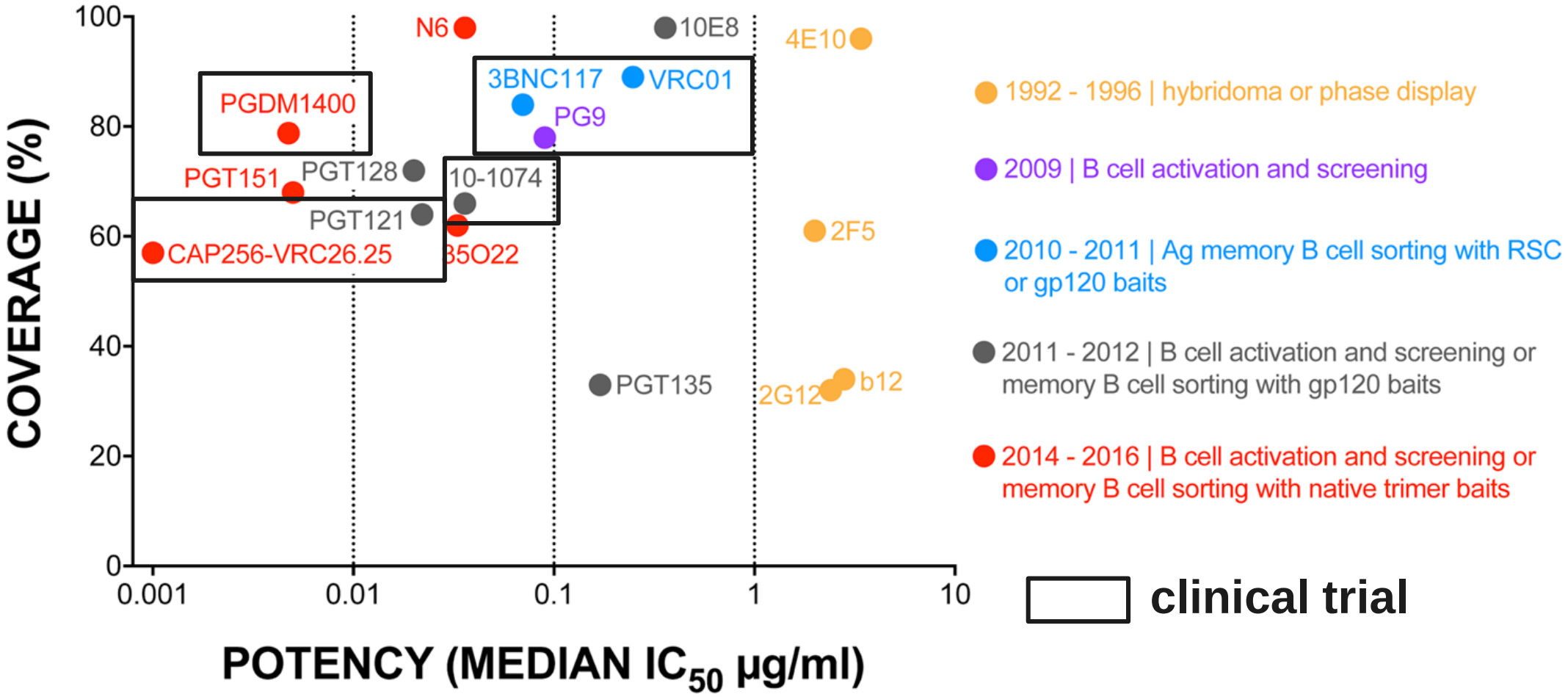
> 200 broadly neutralizing antibodies were isolated using innovative techniques. Over 80 bnAbs were isolated from Protocol G.

2009 - Present

Still active in HIV vaccine research, but can antibodies be used in the meantime for HIV prevention?

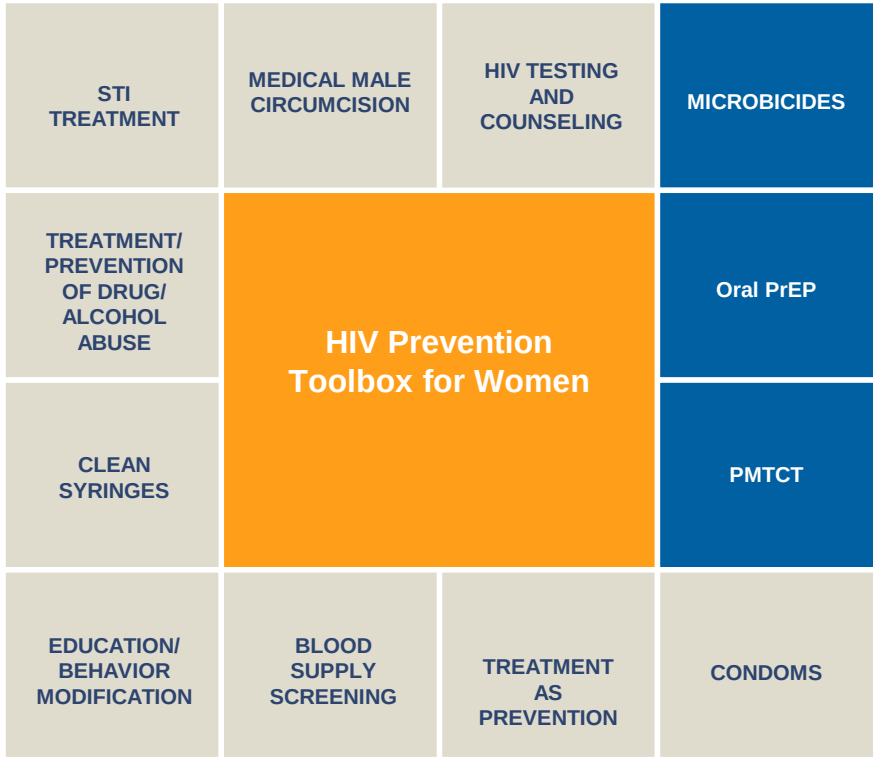


Innovation in antibody discovery has led to the discovery of increasingly potent antibodies, which has made the use of antibodies for prevention a possibility



HIV Prevention Toolbox

A single product or approach will not stop the pandemic



We need a diversity of prevention options and programs in order to address the diverse needs of adolescent girls and young women in sub-Saharan Africa

EXISTING PREVENTION PRODUCTS

ARV-BASED MICROBICIDES
- Tenovofir gel
- Dapivirine ring

PrEP
- Tenofovir
- Cabotegravir
- Rilpivirine

PMTCT
- Antiretrovirals

CASE FOR ADDING ENHANCED BNABS TO PREVENTION TOOLBOX

LONG-ACTING
- Reduced frequency of administration

MECHANISM OF PROTECTION
- Protection at the site of infection
- Elimination of infected cells distally from the site of infection

LOW TOXICITY
- Growing market of biologics
- Very few cases of adverse side effects, generally well-tolerated

DISCREET
- Subcutaneous delivery every 3 to 4 months

What are the roadblocks for using broadly neutralizing antibodies for prevention?

AFFORDABILITY

- Lower dose required to afford protection
- Long acting to reduce frequency of administration
- Lower manufacturing costs

OPTIMAL TARGET PRODUCT PROFILE

- Subcutaneous delivery to ease delivery
- Safety and limited adverse side-effects
- Stability to ensure delivery to target regions and supply chain
- Efficacy to ensure broad protection against diversity of HIV

ADOLESCENT GIRLS AND YOUNG WOMEN

- Product development to ensure efficacy in women
- End user research to ensure acceptability by women most at risk

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HIV bnAbs for prevention

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MAIN RESEARCH ACTIVITIES

- IMPROVED POTENCY
- EXTENDED HALF LIFE
- BINDING AT LOW PH
- POLYREACTIVITY
- END USER RESEARCH

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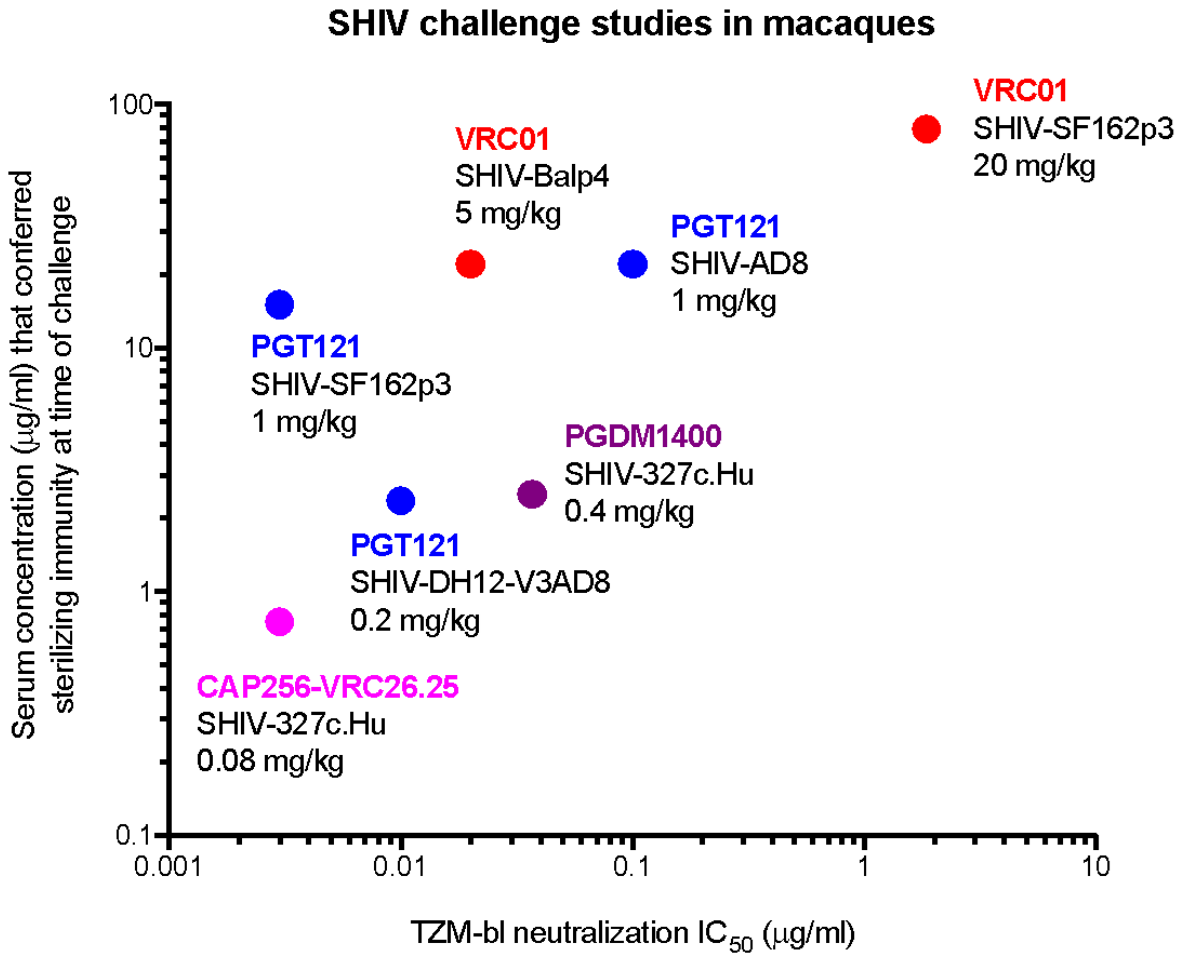
The more potent the antibody, the less that will be needed to confer protection

HIGHER POTENCY = LOWER DOSE

LOWER DOSE = LOWER MANUFACTURING COST

POTENCY THROUGH DIRECTED EVOLUTION



Passive transfer shiv challenge studies

In vitro neutralization (IC80) correlates with the dose required to afford protection against the challenge virus

The more potent the antibody the less it will cost per dose

HIGHER POTENCY = LOWER DOSE

LOWER DOSE = LOWER MANUFACTURING COST

POTENCY THROUGH DIRECTED EVOLUTION

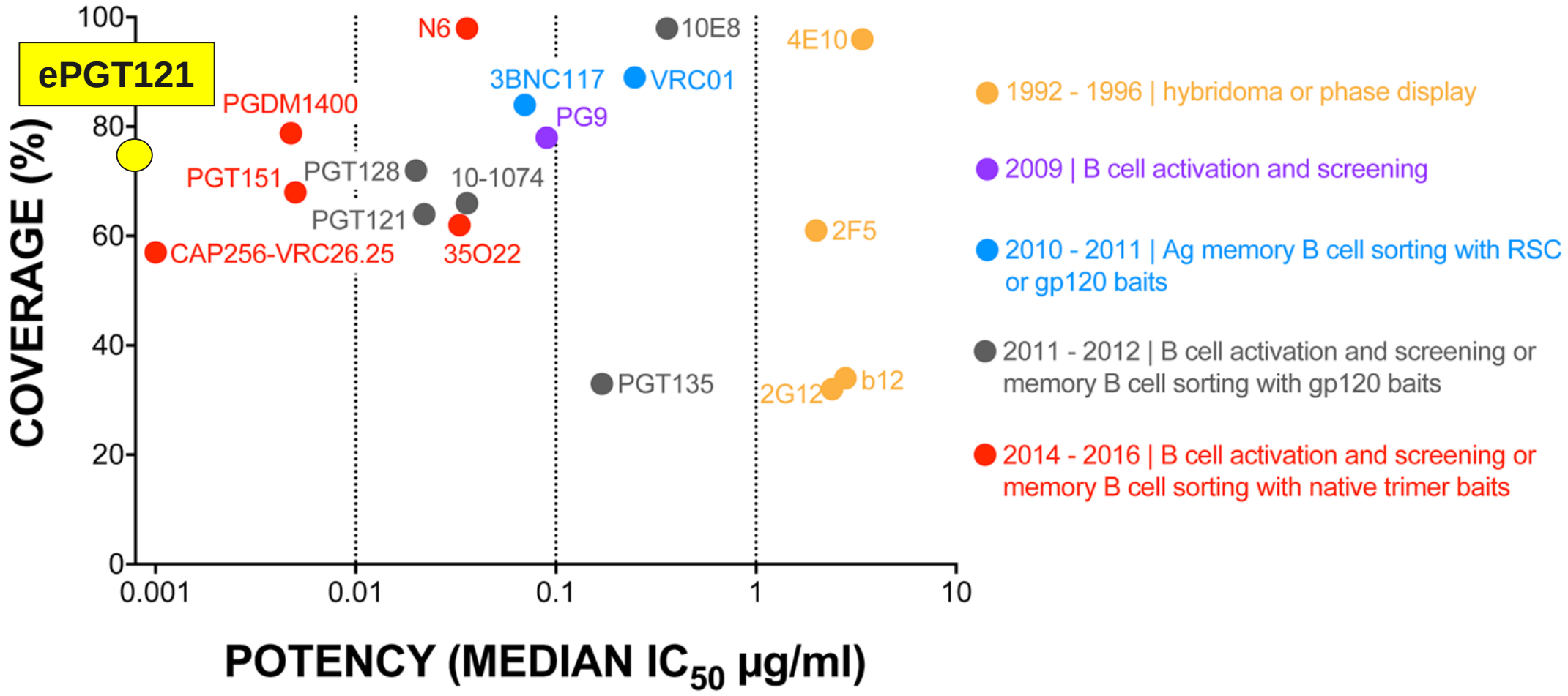
Cost comparison between ARVs and monoclonal antibodies

ARV costs ($60-122/year for first-line) are estimated based on WHO ARV regiment guidelines for adults. Calculations were done assuming an average weight of 62 kg* per individual and a manufacturing cost of $30/g** of antibody.

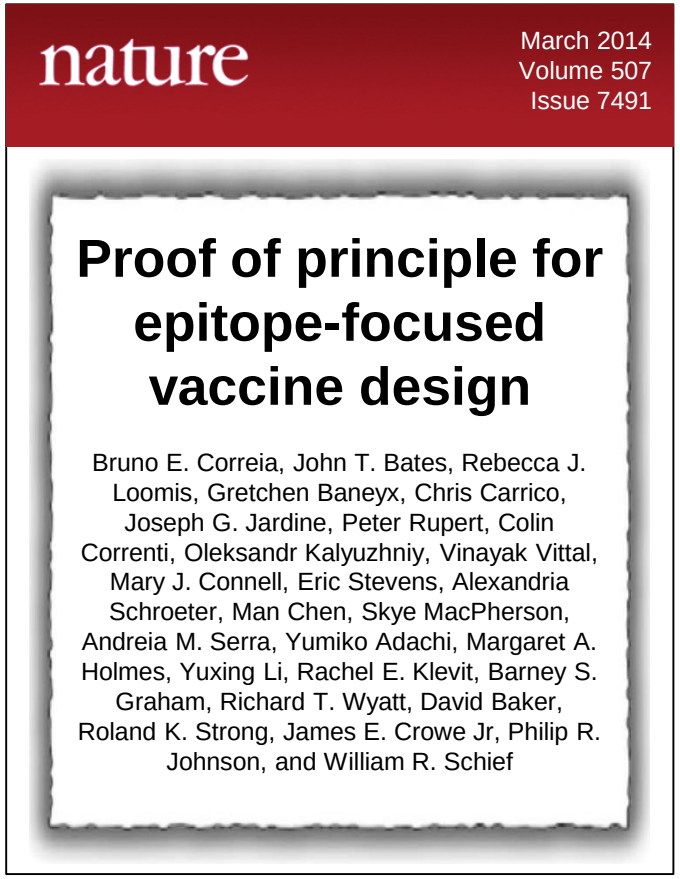
*London School of Hygiene & Tropical Medicine
**IAVI Report - Making it to Manufacturing

		Every Year	Every 4 Mo	Every 3 Mo	Every 2 Mo	Every 1 Mo
WHO ARV regime for adults	1st line ARV	$60-122				
30 mg/kg	1 mAb	$ 55.80				
	2 mAb cocktail					
	3 mAb cocktail					
10 mg/kg	1 mAb	$ 18.60	$ 55.80	$ 74.40	$ 111.60	
	2 mAb cocktail	$ 37.20	$ 111.60			
	3 mAb cocktail	$ 55.80				
1 mg/kg	1 mAb	$ 1.86	$ 5.58	$ 7.44	$ 11.16	$ 22.32
	2 mAb cocktail	$ 3.72	$ 11.16	$ 14.88	$ 22.32	$ 44.64
	3 mAb cocktail	$ 5.58	$ 16.74	$ 22.32	$ 33.48	$ 66.96

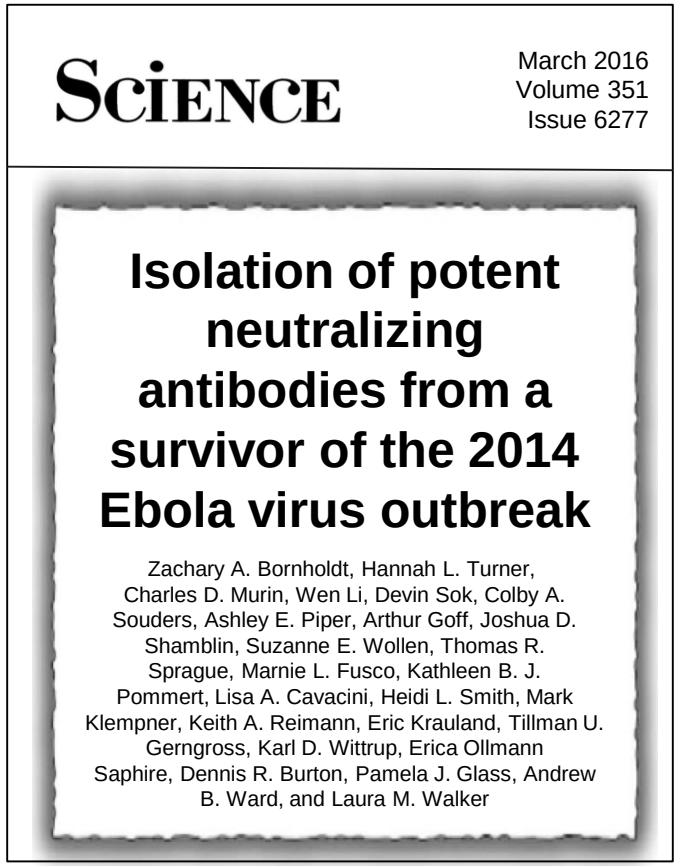
Comparing the breadth and potency of the engineered bnAb compared to others



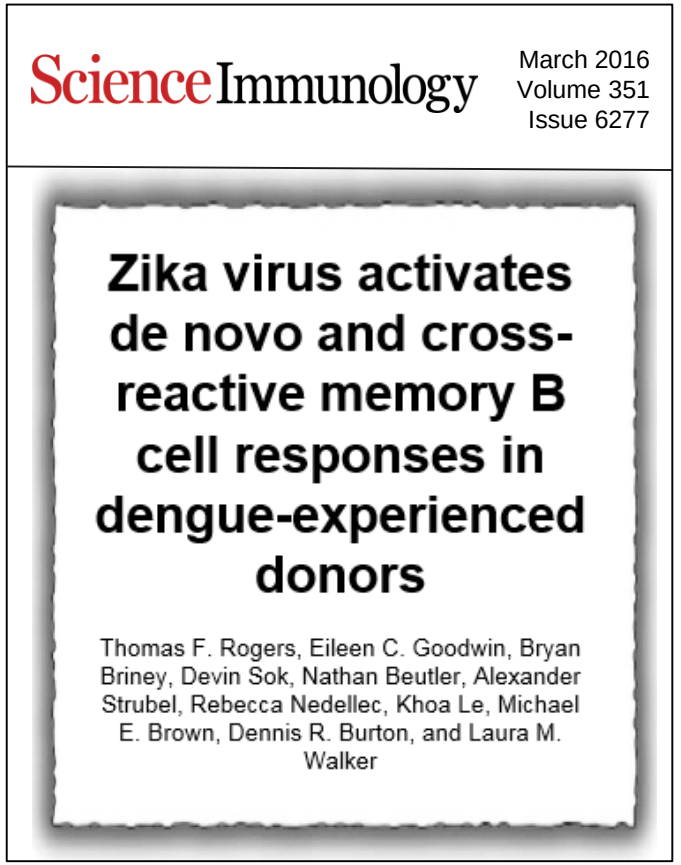
Investments in HIV research fuels prevention research for other infectious diseases



Rational vaccine design for RSV



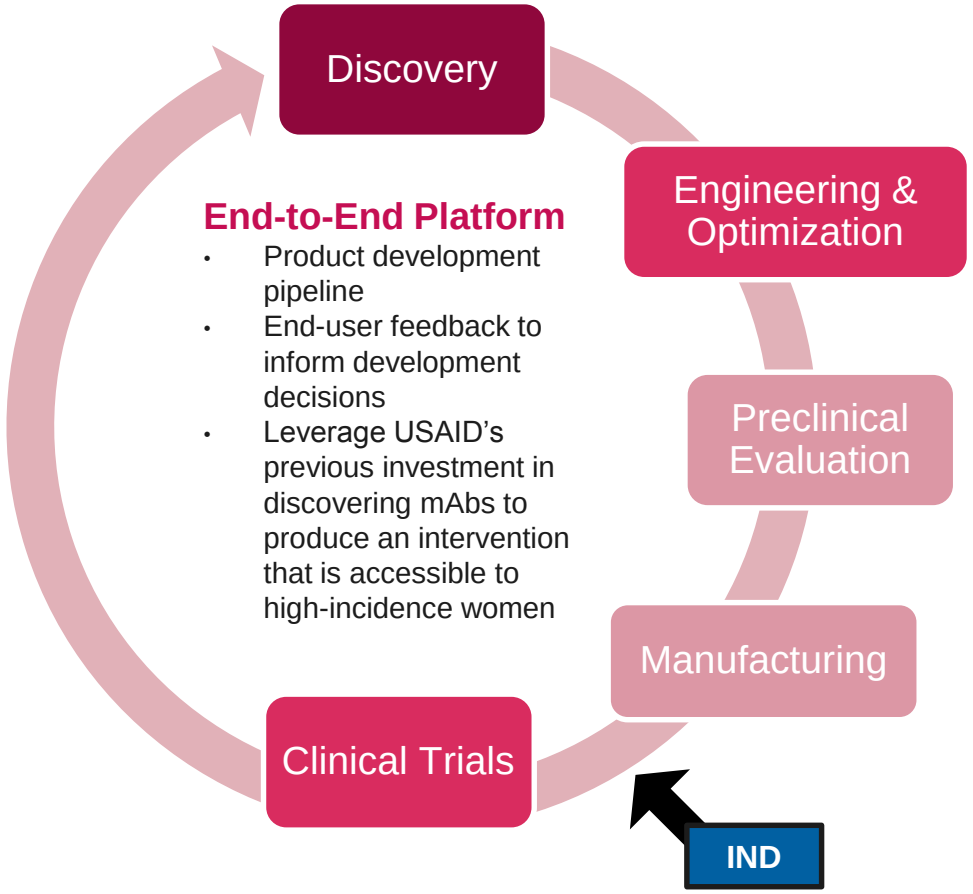
Ab discovery for Ebola



Ab discovery for Zika

Program Goal

Develop enhanced broadly neutralizing antibodies (ebnAbs) for use as prophylaxis for **adolescent girls and young women**



End-to-End Platform

- Product development pipeline
- End-user feedback to inform development decisions
- Leverage USAID's previous investment in discovering mAbs to produce an intervention that is accessible to high-incidence women

DISCOVERY

Status: **Complete**

Leverage:
Protocol G Samples

ENGINEERING & OPTIMIZATION

Years: **2 / 3**

Leverage:
South-south collaboration, Indian partners for antibody evaluation, African partners for end user research, Antibody discovery and engineering experience

Activities:
- **bnAb engineering** *(IAVI, TSRI, IPI, UiO)*
- **Passive protection study** *(IAVI, TSRI, WPRC, UPenn)*
- **End user research** *(IAVI, Regional African Centers)*
- **Antibody evaluation** *(IAVI, THSTI, NCBS)*

PRECLINICAL EVALUATION

Years: **2 / 3 / 4**

Leverage:
US and Indian partners for preclinical evaluation

Activities:
- **Passive protection study** *(IAVI, TSRI, WPRC, UPenn)*
- **pK analysis of antibodies in macaques** *(IAVI, TSRI, WPRC)*
- **Evaluation of macaque experiments** *(IAVI, THSTI, NCBS)*

MANUFACTURING

Years: **4 / 5**

Leverage:
Collaboration with government of India and partnerships with Indian manufactuers (e.g., Serum Institute), **Expertise of IAVI's Vaccine Development Center**

Activities:
- **Low cost manufacturing** *(IAVI, Indian partners)*

CLINICAL TRIALS

Years: **5+**

Leverage:
Clinical CRCs in Africa for evaluation of clinical trials, expertise of IAVI's Vaccine Development Center, IAVI's IND applications for existing bnAbs

Activities:
- **Evaluation of clinical trials** *(IAVI, THST, IAVI African CRCs)*

Institutions: International AIDS Vaccine Initiative (IAVI), The Scripps Research Institute (TSRI), Institute for Protein Innovation (IPI), Wisconsin Primate Research Center (WPRC), University of Pennsylvania (UPenn), Translational Health Science and Technology Institute (THSTI), National Center for Biological Sciences (NCBS)

iavi International AIDS Vaccine Initiative

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Ministry of Foreign Affairs of the Netherlands

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And many other generous individuals from around the world

As of June 2017

Implementation Science Research

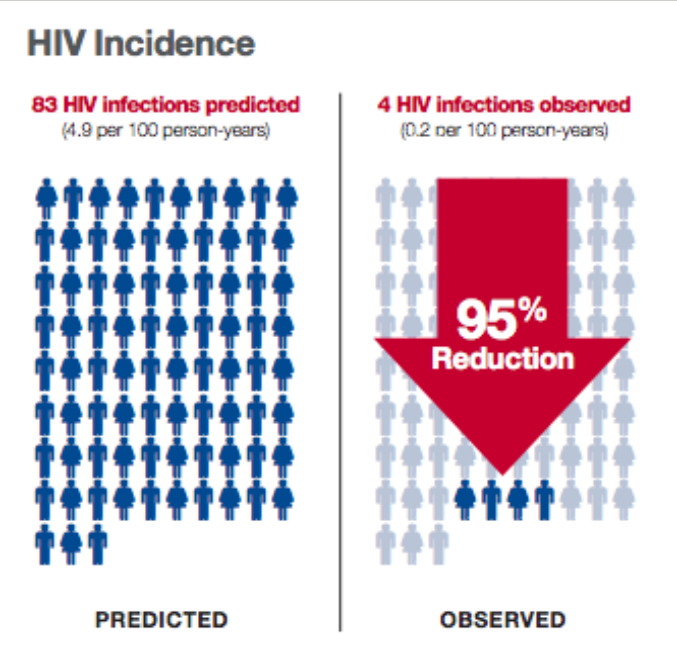
USAID HIV Implementation Science

Leading IS research activities	• Implementing research aligned with PEPFAR and OHA's priority objectives of achieving epidemic control, support for OVC, sustainable financing and data quality
Promoting capacity strengthening for IS	• Creating partnerships with local researchers and institutions, and providing opportunities to further their research agendas and build long term sustainability
Catalyzing partnerships and IS data utilization	• Engaging key stakeholders before and during all IS studies and working together to interpret findings and decide upon programmatic recommendations
Disseminating IS findings	• Sharing the results of USAID funded research across multiple platforms, leveraging different approaches for different audiences, and aligning research data to epidemic control objectives

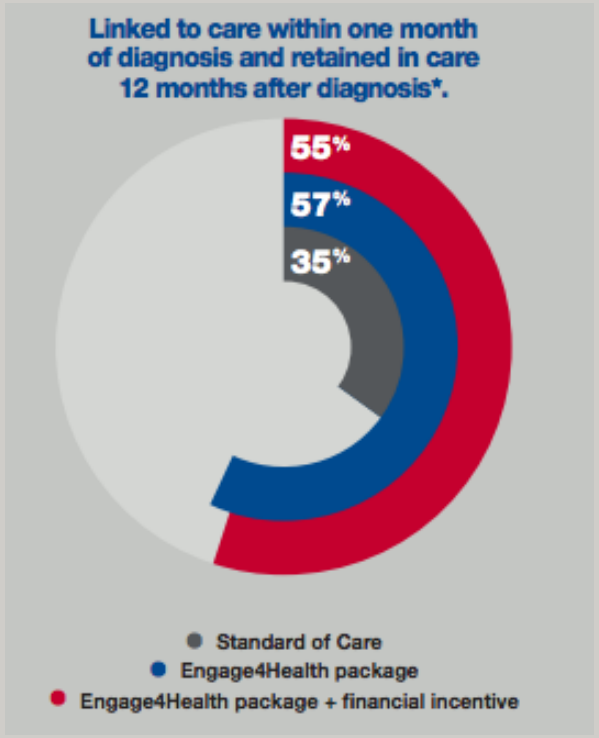
Results Highlights- IS Annual Program Statement

Partners Demonstration Project (U of Washington):

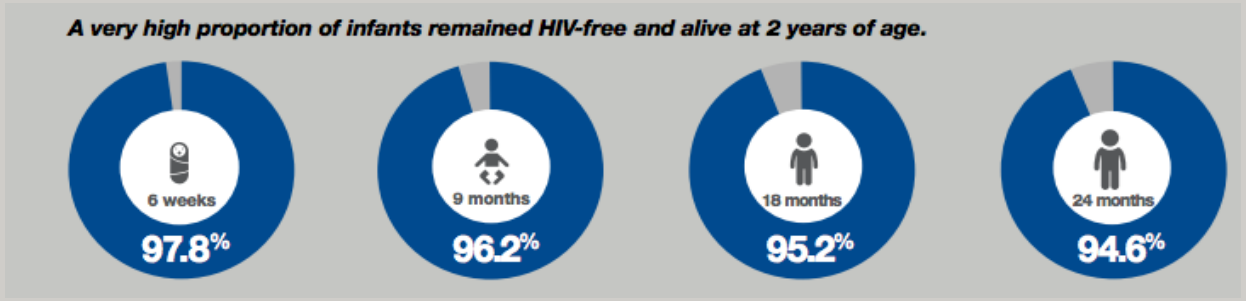
- High uptake of PrEP for serodiscordant couples
- High viral suppression for partners on ART
- 95% reduction in HIV incidence



Engage4Health (ICAP):
Interventions to improve linkage and retention



Kabeho Study (EGPAF):
Real world evaluation of PMTCT Option B+ implementation



* Graphics by Project SOAR

IS: HIV Prevention 2.0 Study

Objective: Develop and Evaluate Integrated Stigma Mitigation Interventions (ISMI)

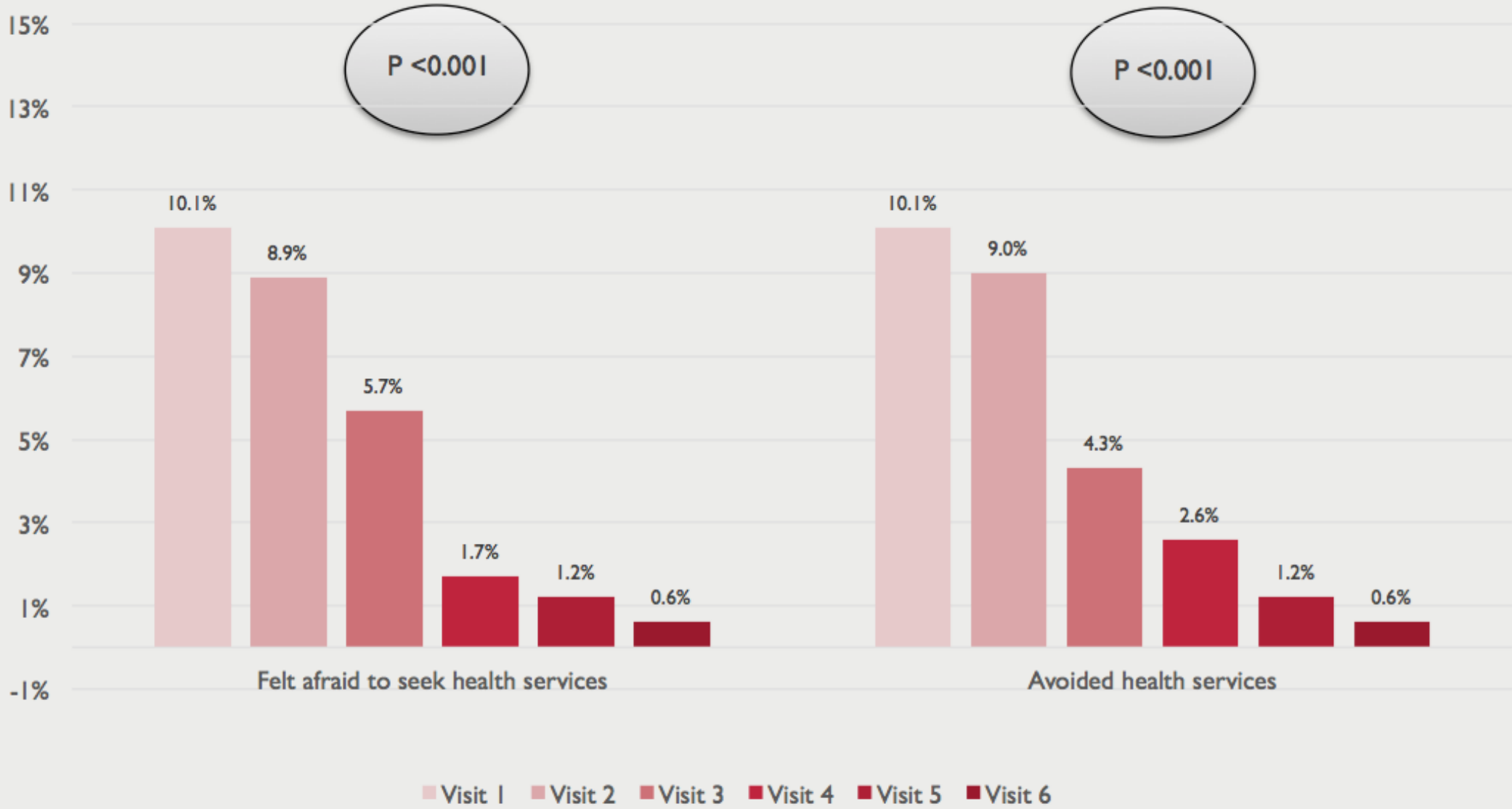
- Specific Aim 1: Systematically review the literature for existing stigma metrics that have been used for MSM and FSW.
- Specific Aim 2: Use mixed methods approaches to characterize unbiased estimates of the current coverage of HIV prevention and treatment services as well as barriers and facilitators to the uptake of these services among MSM and FSW in Senegal.
- Specific Aim 3: Use a prospective cohort (followed 24 mo) of MSM and FSW in Senegal to evaluate ISMI

enda santé

JOHNS HOPKINS
BLOOMBERG SCHOOL
of PUBLIC HEALTH

IRESSEF
Institut de Recherche en Santé de Surveillance Epidémiologique et de Formation

Anticipated Health Care Stigma Among Men Who Have Sex With Men



HIV outcomes among men who have sex with men

HIV status of cohort participants:

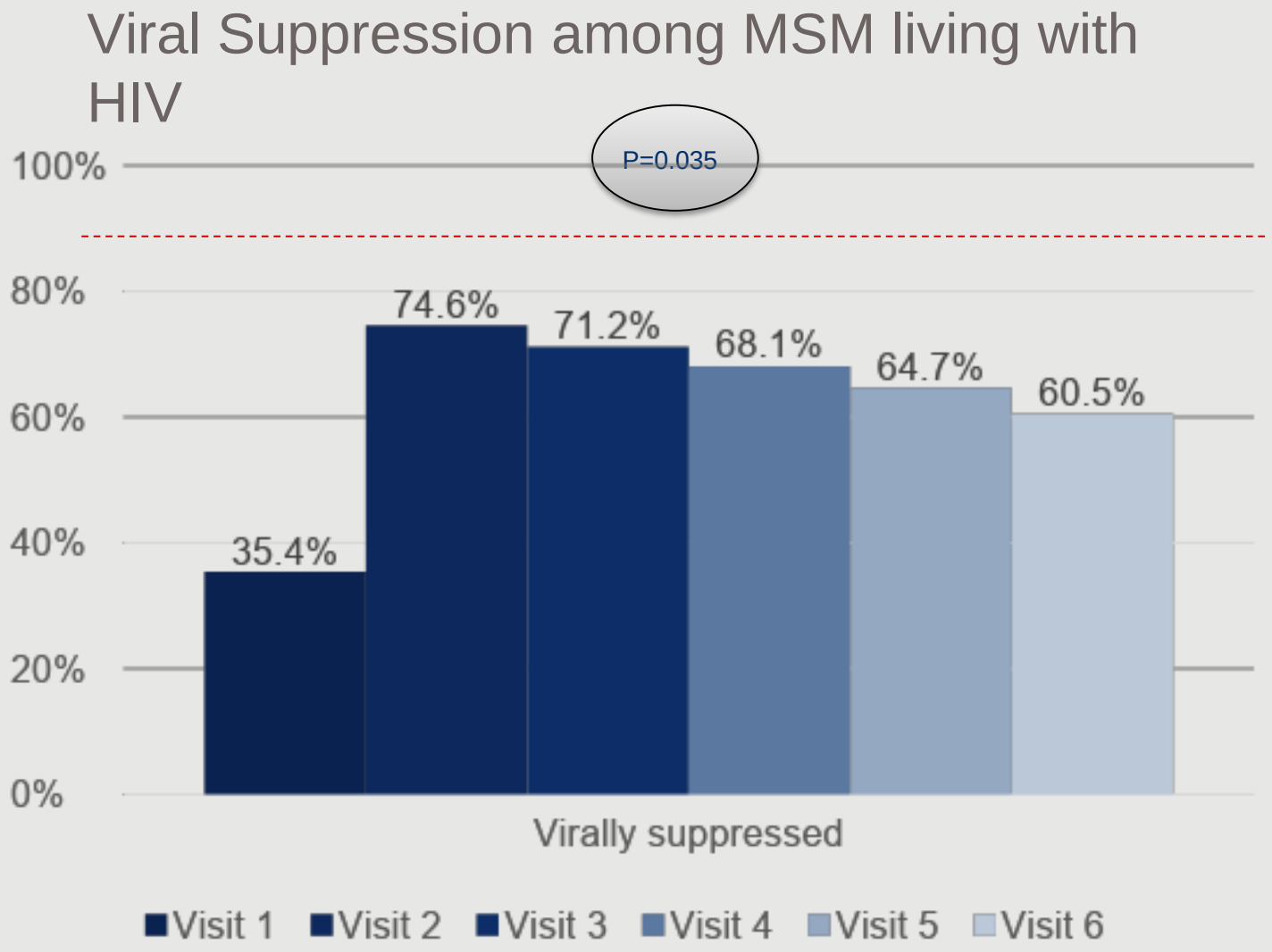
- 40.3% (73/181) living with HIV

HIV incidence over 24 months:

- 5.4/100 person-years

Self reported currently being on ART

- 95.4% at visit 1 of cohort
- Did not significantly change over time

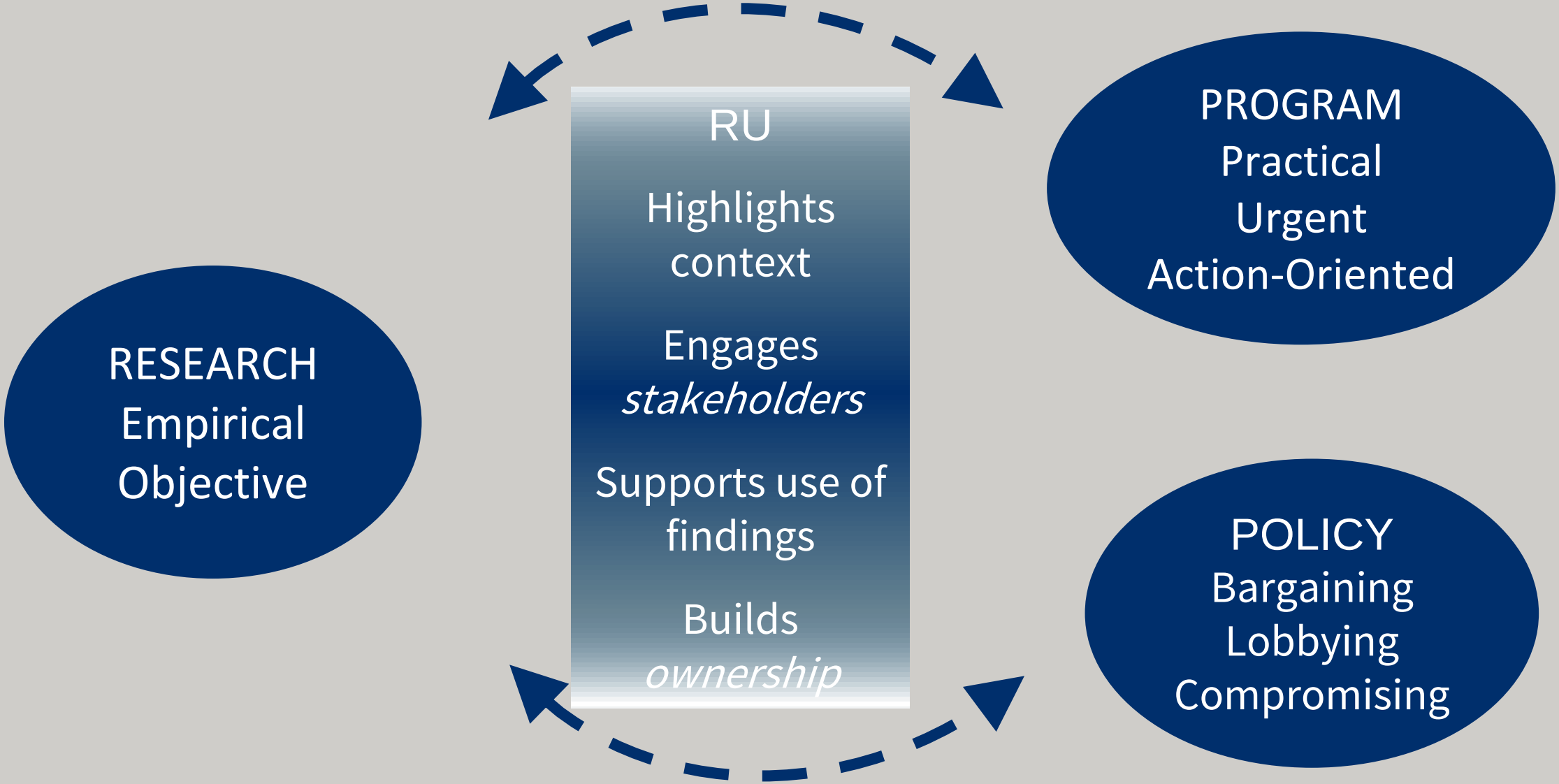


Project SOAR Overview

Project SOAR (Supporting Operational AIDS Research)

- 2014-2019
- 58 activities/studies in 23 countries
- Consortium of research partners- led by Pop Council:
  - Key partners: EGPAF, Johns Hopkins University, University of North Carolina, Avenir Health, Palladium
  - Over 30 local research partners
- http://www.projsoar.org/

Project SOAR: Strong Emphasis on Research Utilization



How IS Contributes to Achieving 90-90-90

- Assessing new innovations
- Measuring feasibility, impact and cost
- Addressing country-level key program gaps and questions

Identify PLHIV

- Self testing
- Reaching men
- Novel size estimation for KPs
- Early infant diagnosis

Initiate ART

- Test and Start
- Enhanced linkage to care
- Differentiated service delivery

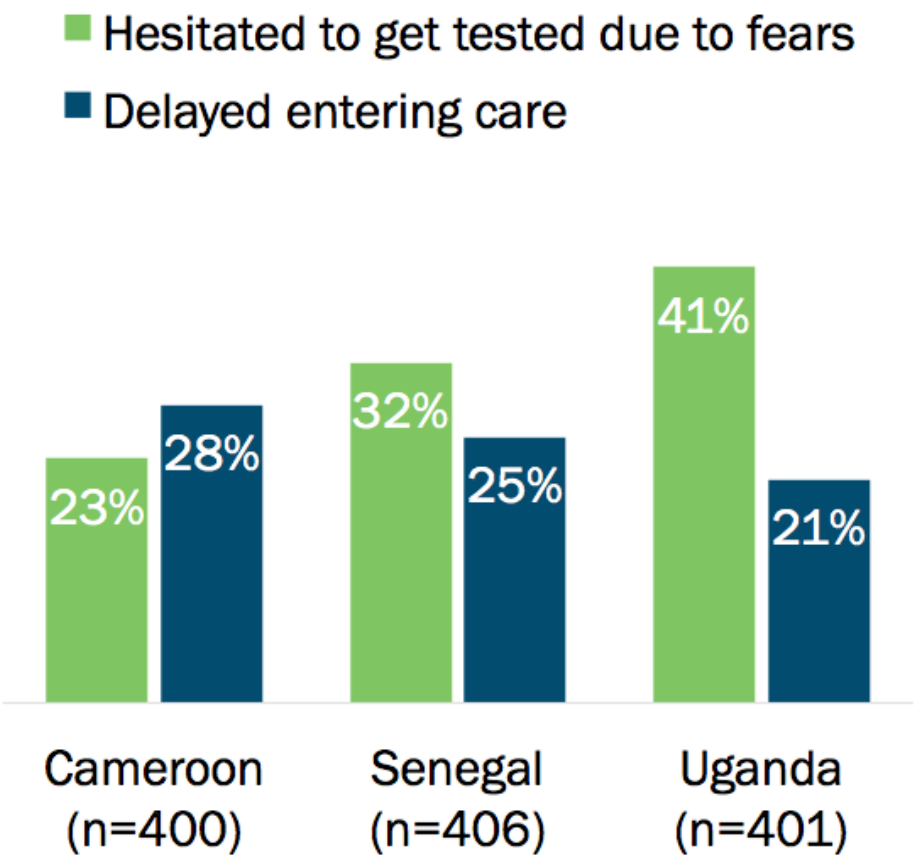
Retain & Viral Suppression

- Stigma mitigation
- Adolescent transition
- Family ART
- Community adherence groups

Updating the PLHIV Stigma Index

- Stigma Index was developed by IPPF, UNAIDS, GNP+, ICW; launched in 2008
- Questionnaire-based methodology to quantify stigma and discrimination – implemented by PLHIV among PLHIV
- Complements experiences of individuals with the collective diverse experiences of a community of PLHIV
- Provides for evidence-informed advocacy, policy reform, and service delivery
- Builds capacity of PLHIV networks
- USAID/PEPFAR supported an update in 2017, coordinated by Project SOAR, eg questions on key populations and HIV treatment

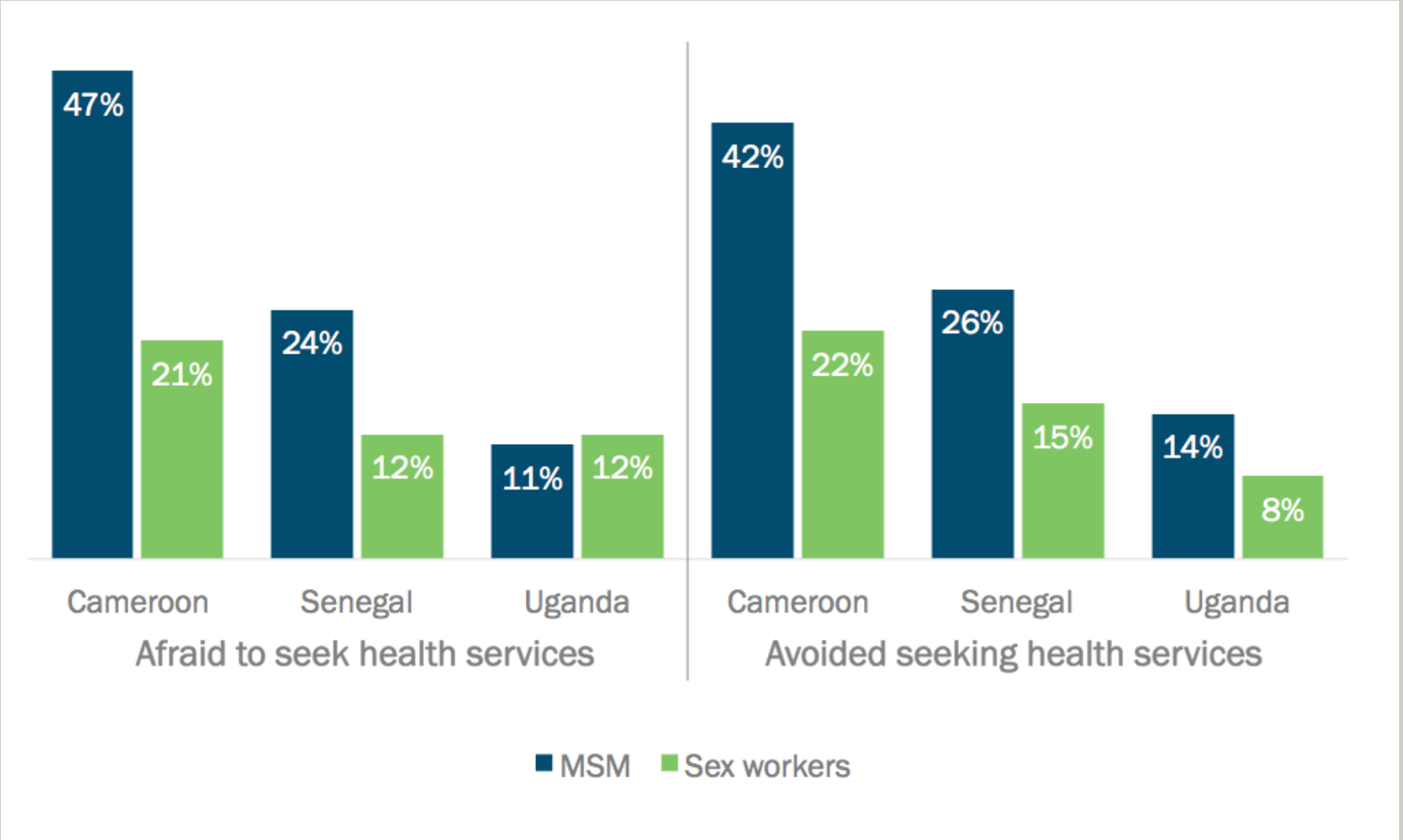
Stigma Index Pilot Results 2017: Stigma Affects HIV Care Cascade



Delayed entering care because:

- *Not ready to deal with HIV infection (16–33%)*
- *Worried others would find out status (11–13%)*
- *Afraid health workers would treat me badly or disclose status without consent/had a bad experience with a health worker previously (4–11%)*

Stigma Toward Key Populations Impedes Health Seeking Behavior



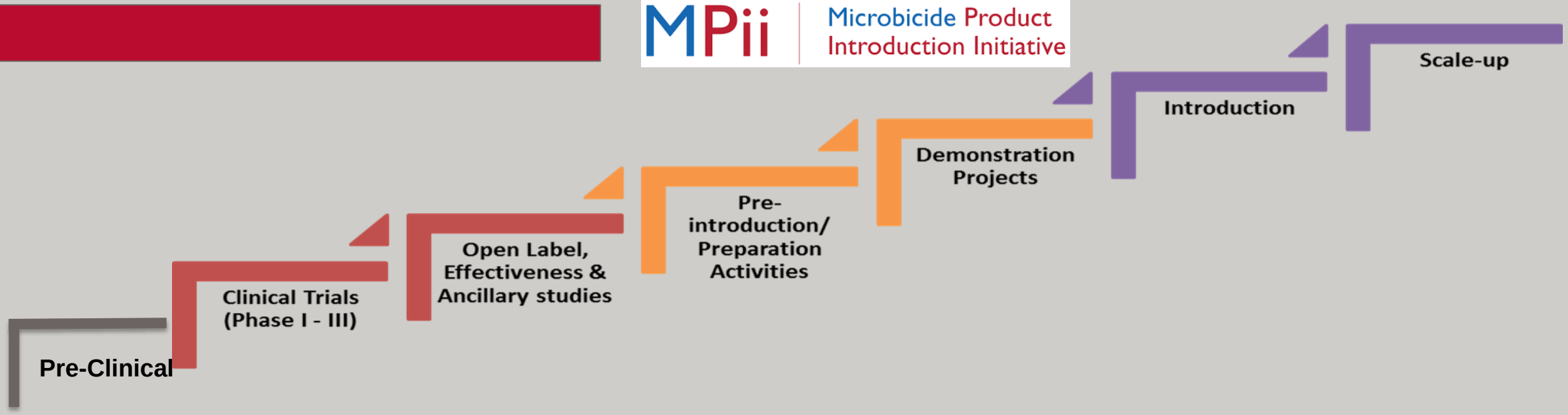
Microbicide Research

What is a Microbicide?

Biomedical products that women can use to protect themselves from HIV infection

Microbicide Development

MPii Microbicide Product Introduction Initiative



T1 - Translation to Human
(Move a molecule into product)

T2 - Translation to Patients/Practice
(Generate the "real world" evidence)

T3 - Translation to Program
(Introduce in existing health systems and scale-up)

- **Minimize delays** in introducing HIV/AIDS prevention
- Better **prepare national health systems to deliver** new HIV prevention products to Women

Considerations for Microbicide Priorities

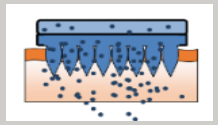


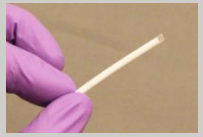


PLANNING AND BUDGETING	SUPPLY CHAIN MANAGEMENT	DELIVERY PLATFORMS	Uptake and Adherence	EFFECTIVE USE & MONITORING
• Cost of goods	• Stability • Packaging	• HCW training required • Frequency of visits • Prescription vs OTC • Self administered	• Acceptability • Discretion* • Reversibility* • Ease of use • Access channels* • Additional benefits • Product Choice	• Dosing frequency* • Side effects

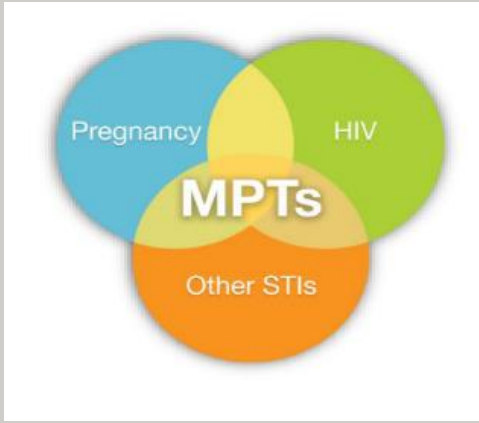
***Greater diversity in these attributes = greater potential health impact**

Potential Products

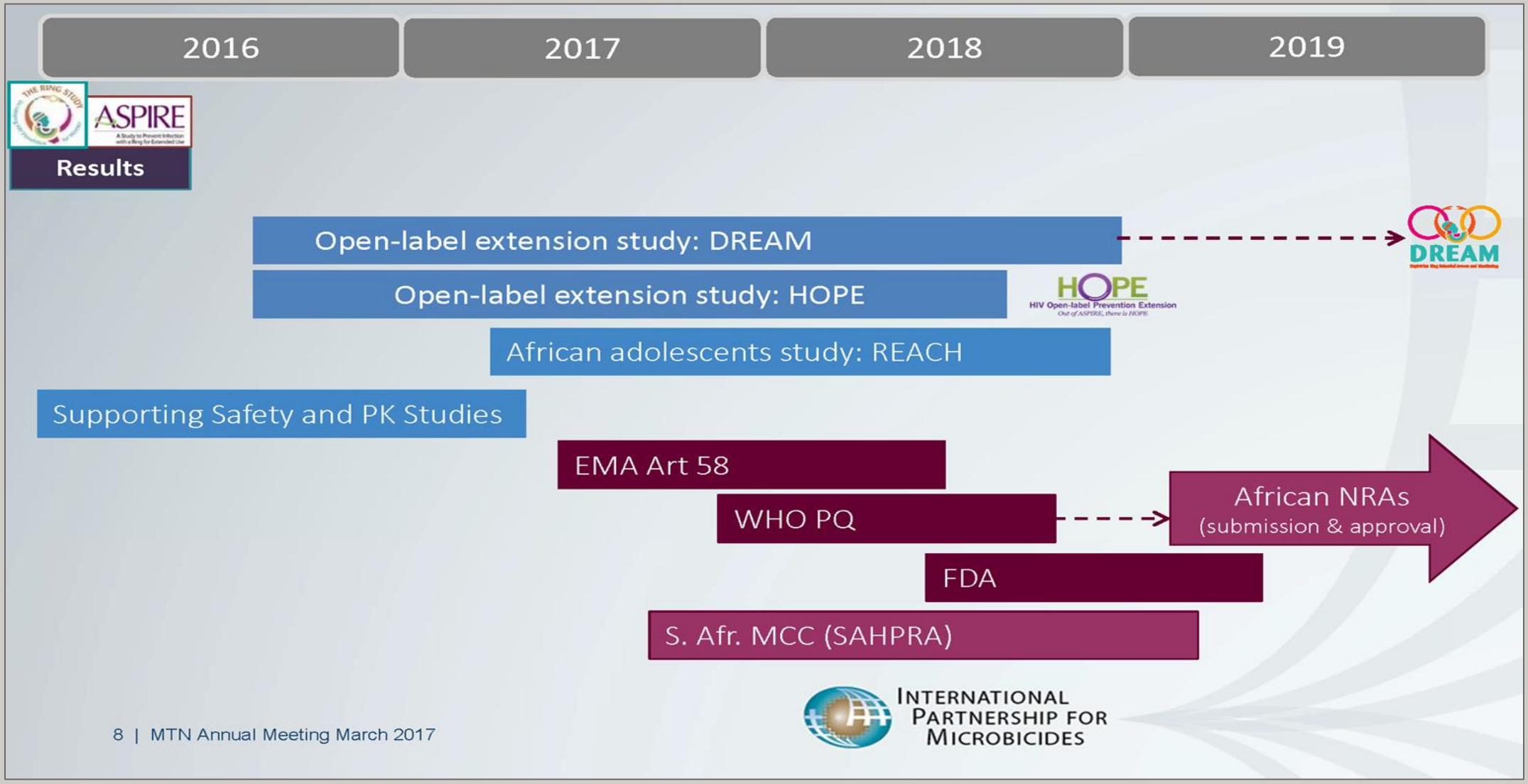




Product	Target dosing	Active Ingredients
Vaginal Ring	1 month	Dapivirine
Oral Tablets	On-demand	F/TAF TAF
Microarray Patch	≤ 3 months	TBD
Biodegradable Implant	1 year	TAF/LNG
Vaginal Inserts	On-Demand	TAF EVG GRFT



Spotlight: Dapivirine Ring Timeline



Preparing for Introduction

To **accelerate introduction and access with advances** in biomedical technologies and new approaches for HIV prevention.

CHARISMA
Agency in Relationships & Safer Microbicide Adherence

EMOTION
ENHANCING MICROBICIDE UPTAKE

GEMS
GLOBAL EVALUATION OF MICROBICIDE SENSITIVITY

POWER
Prevention Options for Women Evaluation Research

OPTIONS
OPTIMIZING PREVENTION TECHNOLOGY INTRODUCTION ON SCHEDULE

PrEP & Intimate Partner Violence

Human Centered Design

PrEP Resistance Monitoring

Cost Effective, Scalable Delivery

Systems Thinking, Technical Assistance

End User Level

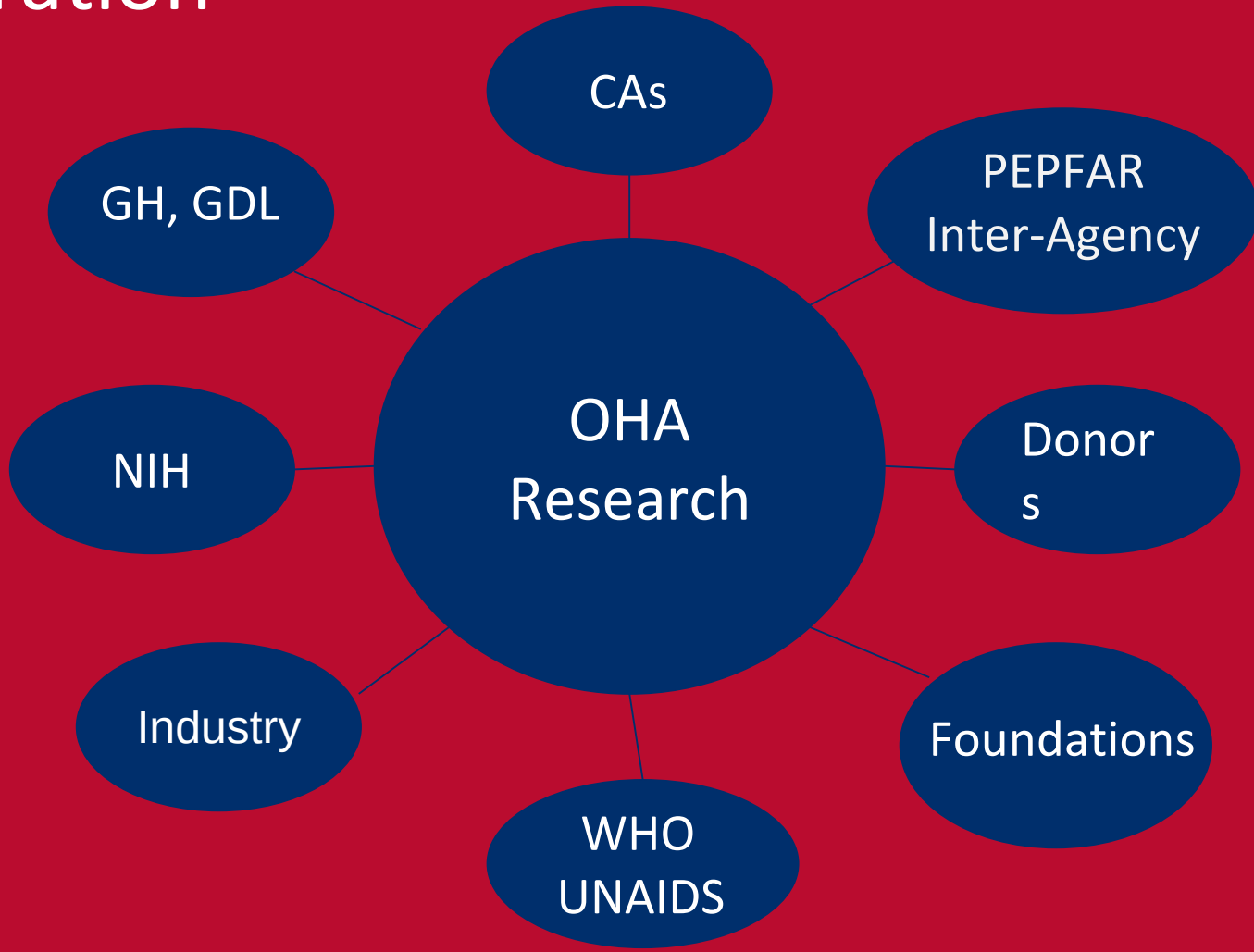
Facility Level

National/Sub-national

Incorporating End-User Preferences

Research to increase product uptake and use

Collaboration



Thank you!

Questions?

Q&A

Please submit your questions in the chat box on the screen to the right.

Any questions not addressed during the session can be submitted to **info@ghpod.com** and will be answered by email.

Thank you for joining us today!

Please join us for our third seminar

Global Health Grand Challenges

Wednesday, March 28, 12-1PM

https://ghpod.adobeconnect.com/usaid_gh_rd/

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