

# What's New & Next in HIV Prevention

*A Review of the HIV Prevention Pipeline from Research to Rollout*

**The Choice Manifesto Launch**

8<sup>th</sup> September 2023

Kampala Uganda

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# Outline







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- Where we are today, and what's coming up for HIV prevention R&D
- Where are the products furthest ahead in the pipeline
- Update on DVR & CAB 4 PrEP implementation
- What can be done now to accelerate introduction of new prevention products







# UNAIDS 2020 targets: Where we landed

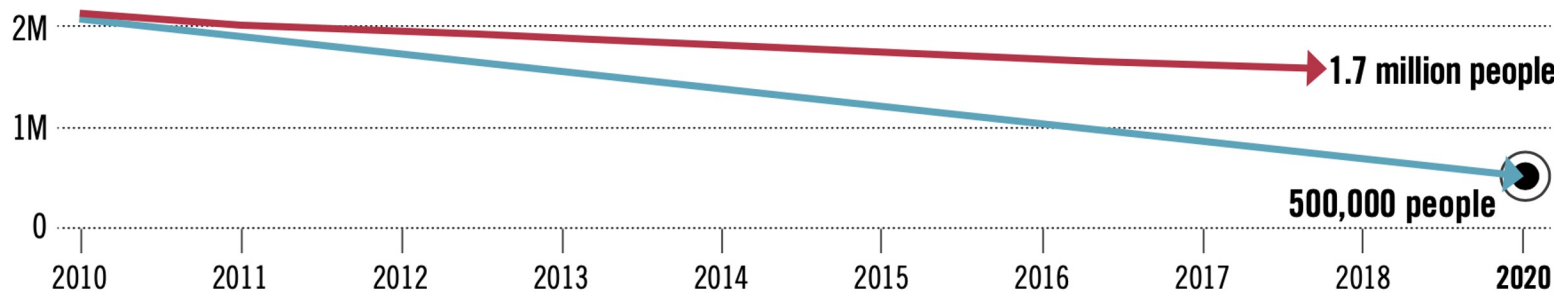


### What Model Assumed

-  90% key population covered
-  90% of AGYW (key locations)
-  >6bn condoms (SSA) per year
-  3m PrEP
-  5m VMMC per year
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  - Funding (additional \$6.5bn per year)
  - Testing, treatment, virologic suppression in PLHIV worldwide: 90-90-90

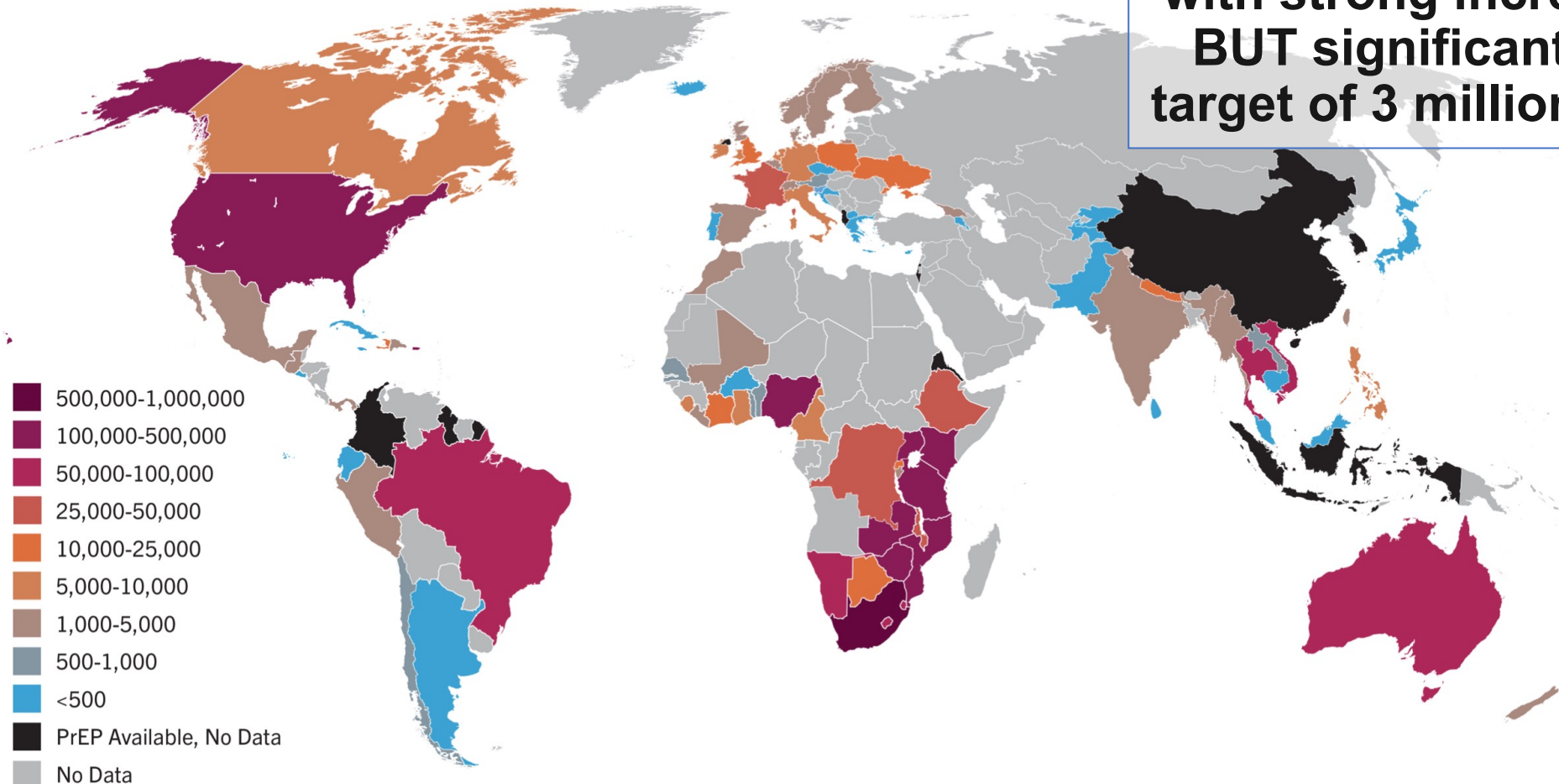
### What Was Implemented

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  - 47% for sex workers
  - 33% for gay men & other MSM
  - 32% for PWID\*
-  34% of AGYW in key locations covered\*\*
-  <3bn condoms (SSA)\*\*\* per year
-  Approx 385,000 PrEP\*\*\*\*
-  4.1m VMMC per year in 2018
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  - Flat funding
  - Testing, treatment, virologic suppression in PLHIV worldwide: 79-78-86 with large disparities



# Global PrEP Uptake – 10+ years in

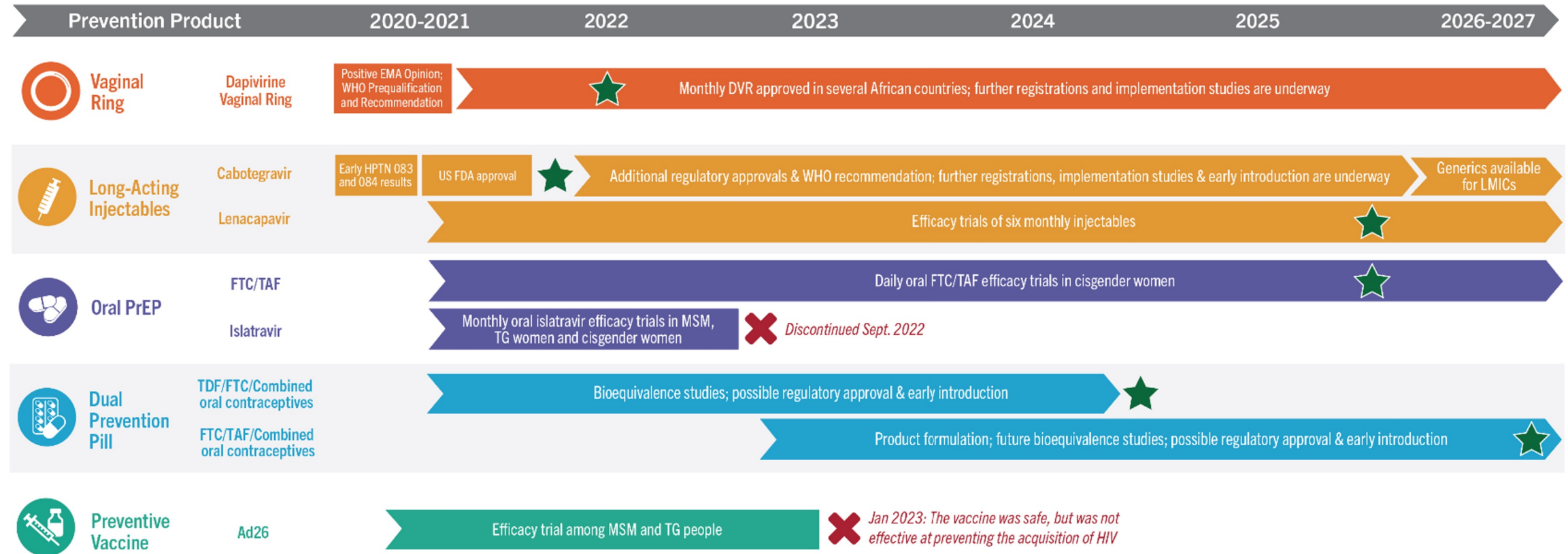
Approx. total PrEP **initiations**:  
3.8 million  
with strong increases in 2022 –  
**BUT** significantly missed UN  
target of 3 million **users** by 2020



# Years Ahead in HIV Prevention Research

## Time to Market

★ Earliest time to market  
 ✗ Discontinued



# The Current State of HIV Prevention R&D Efficacy

Px Option	Populations	Next Steps	Time to Market
<b>Male &amp; female condoms</b>	All at risk	Market at scale	Approved for decades
<b>VMMC</b>	Heterosexual men	Re-energize post-COVID restrictions	2007 Recommended in 14 priority counties in E/SA since
<b>Daily Oral TDF/FTC</b>	All at risk	Scale-up demand creation and support for continuation	2012 US approval ; 2015 first African approvals
<b>Event-driven Oral TDF/FTC</b>	MSM	Integrate as per guidelines	2019 WHO recommendation
<b>Daily Oral TAF/FTC</b>	All except “those at risk via receptive vaginal sex”	Efficacy trial in cisgender women in Africa started 2021	2019 FDA partial approval; ±2025 for cisgender women
<b>Dapivirine Vaginal Ring</b>	Women	WHO guidelines; National regulatory approvals in 2021/2; & product intro in 2022	2020 positive EMA opinion and WHO pre-qualification; multiple African approvals
<b>Injectable Cabotegravir</b>	Studied in multiple populations	Regulatory submissions mid-2021	As of 5/23 approved in US, Australia, Zim, SA, Malawi; additional approvals pending
Six-monthly injectable Lenacapavir	Being studied in multiple populations	Two efficacy trials started in 2021	Likely earliest approvals ±2025
Dual Px Pill (TDF/FTC/COC)	Women	Bioequivalence studies ongoing	Likely earliest approvals ±2024
Ad 26 Vaccine	Studied in multiple populations	Efficacy trial in Africa ended with lack of efficacy; MSM/TG trial continuing	Regulatory pathway and timelines unclear
VRC 01 bNAb infusion	Studied in multiple populations	No overall efficacy, but proof of concept Multiple combo bNABs in development	NA – not intended for licensure; alternate combos in development
Monthly Oral Islatravir	Being studied in multiple populations	Two efficacy trials started in 2021, but discontinued in September 2022	NA – not going forward, but Merck is looking at alternate monthly pill options

# ARV/Drug-Based Product Pipeline Overview

PRE-CLINICAL			PHASE I		PHASE II	PHASE III/IIIb/IV	DELIVERY SYSTEM	ACTIVE DRUG
TAF <b>CONRAD</b>	MAVR TNFV Nigerian Institute for Medical Research	CAB ViiV	ELVG TAF <b>CONRAD</b>	DSO3 <b>Pop Council</b>		F/TAF Gilead Daily	Diaphragm	5P12 5P12-RANTES
CAB <b>CONRAD</b>	CAB PATH/Queens University Belfast	MAVR ViiV/Pfizer	TNFV Johns Hopkins	DPVR <b>Pop Council</b> <sup>1</sup> 3-monthly		LEN Gilead 6-monthly	Enema	ACZX Acyclovir-Zovirax
CAB <b>CONRAD</b>	DSO3 Queen's University Belfast		ISL Merck <sup>3</sup>	MK20 University of Pittsburgh		CAB ViiV-GSK <sup>2</sup> 2-monthly	Intramuscular injection	AMPR Amphora
TNFV Gilead	BNAB Rockefeller University		TAF Oak Crest /CAPRISA	GRFS University of Pittsburgh		Merck <sup>3</sup> 1-monthly	Implant	BNAB Broadly neutralizing antibody
F/TAF Houston Methodist	TAF RTI		OB2H Orion			DPVR <b>Pop Council</b> 1-monthly	Micro-array patch	CAB Cabotegravir/ GSK 744
5P12 Mintaka	DPVR University of Pittsburgh						Non-specific mucosal insert	CRGN Carrageenan
<b>Multipurpose Prevention Technologies (MPTs)</b>								
ETED ACZX TNFV Auritec	PC05 PATH /Pop Council /Kessel	F/TDF MAB UMass and Planet Biotechnology /Oak Crest /MassBiologics	TAF ELVG <b>CONRAD</b>		TNFV <b>CONRAD</b>	F/TAF ETED LVGR <b>Pop Council /Medicines360</b> <sup>4</sup>	Oral pills	DPVR LVGR <b>Pop Council</b>
ACZX TNFV <b>CONRAD</b>	CAB PRGT PATH/Queens University Belfast	DPVR PRTV LVGR University of North Carolina	DPVR LVGR <b>Pop Council</b>		TNFV LVGR <b>CONRAD</b>	F/TDF ETED LVGR <b>Viatrix</b> <sup>4</sup>	Subcutaneous injection	Vaginal film
CAB LVGR <b>CONRAD</b>	ETGS GRFS ETED <b>Pop Council</b>	ETGS ISL ETED University of North Carolina					Vaginal gel	Vaginal insert
TNFV EFAV i3S/University of Porto	CRGN GRFS <b>Pop Council /Evofem Biosciences</b>	DPVR LVGR PRTV University of North Carolina					Vaginal ring	
PRGT ISL Magee-Women's Research Institute /University of Pittsburgh	RTI <sup>5</sup>	ISL University of North Carolina						
F/TDF MAB Oak Crest /University of North Carolina		PPCM Yaso Therapeutics						

<sup>1</sup> This is a Bioequivalency trial with the monthly DVR.

<sup>2</sup> Dec. 2021 Approved by the FDA; Aug. 2022 Approved by the Australian regulatory agency

<sup>3</sup> Discontinued in Sept. 2022

<sup>4</sup> These two dual pill products are undergoing bioequivalency trials. The drug components are approved, but not in their combination. Therefore, it does not follow the traditional R&D pathway.

<sup>5</sup> Non-specific to any drug; for development of a long-acting biodegradable implant suitable for an MPT use to protect against pregnancy and HIV. See SCHIELD Implant for more information.

*The Future of ARV-Based Prevention and MPTs, AVAC, 2022*

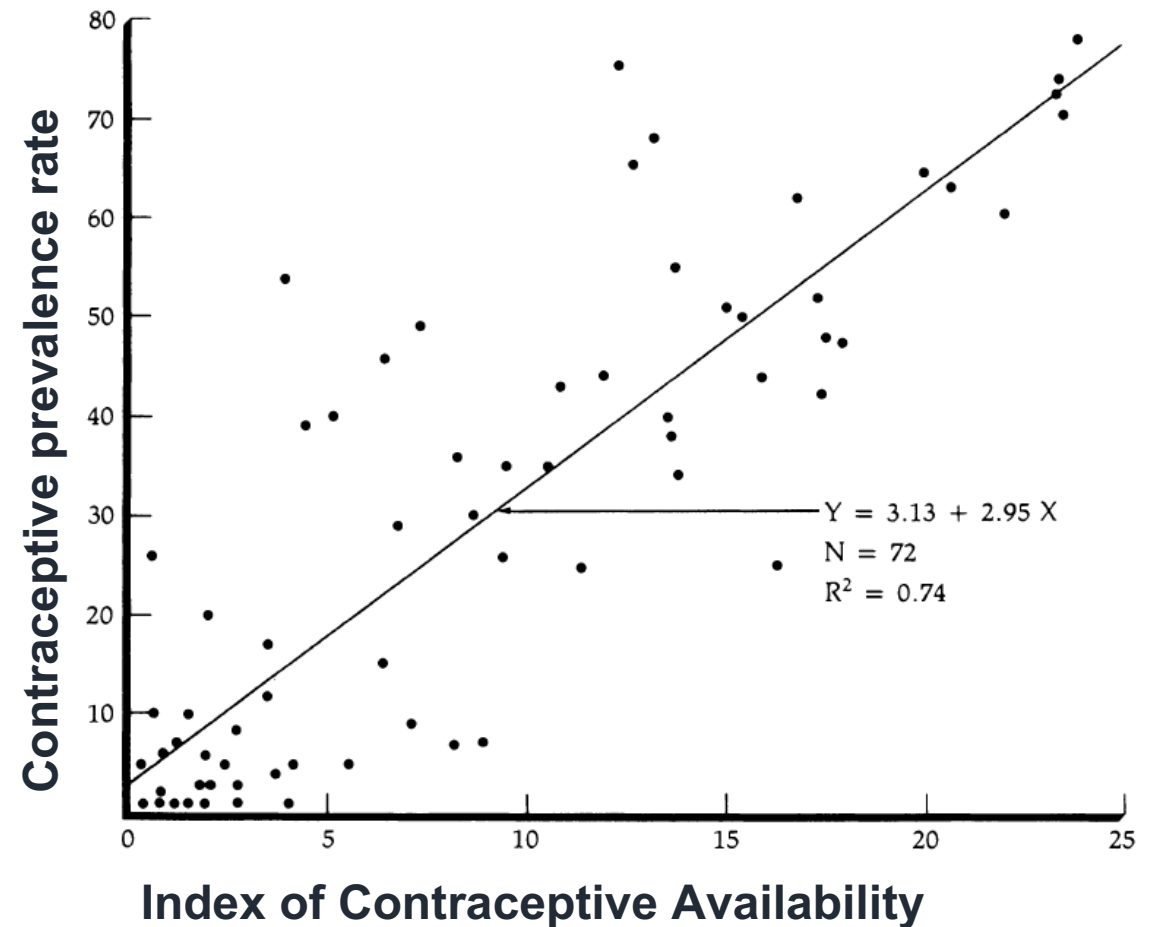
# Prevention Paradigm 2021 and beyond

Different Strokes for Different Folks		
Method	Contraception	HIV Prevention
Behavior	✓	✓
Barrier Methods	✓	✓
Gels	✓	✓ – not registered
Rings	✓	✓ – EMA positive opinion; WHO PQ
Oral pill	✓	✓✓ (for some) ? – monthly, dual px in development
Injectables	✓	✓ – ARV ? – 1 bNAb, 1 vax in Phase 3, 1 new ARV entering Ph 3; others in development
Implants	✓	? – multiple in preclinical
Surgical procedures	✓	✓
Treatment		✓



# Choice Matters

- WHO systematic review (231 articles) showed increased choice associated with:
  - **Increased persistence** on chosen method
  - **Better health outcomes**
  - **12% increase in contraceptive prevalence for each additional method**
- Similar to contraceptive needs: different people have different HIV prevention needs at different times



# Monthly Dapivirine Vaginal Ring (DVR)



## Features

- A flexible silicone vaginal ring developed by IPM
- Slowly releases the ARV dapivirine over one month
- Shelf-life: Up to 60 months when stored at or below 30°C
- No cold chain needed for storage



## Benefits

- Women-initiated
- Self-inserted monthly
- Discreet
- Does not interfere with sex and menses

## Evidence



- Reduced HIV risk in Phase III trials: 35% in The Ring Study, 27% in ASPIRE (*n=4500*)
- Open-label extension studies saw increased adherence, suggested greater risk reduction (*increasing to 63% and 39% from Phase III*)

## Additional Research



- Additional studies – in AGYW (REACH), pregnant (DELIVER) and breastfeeding (B-PROTECTED) women show promising interim results on adherence and safety

# Dapivirine Vaginal Ring

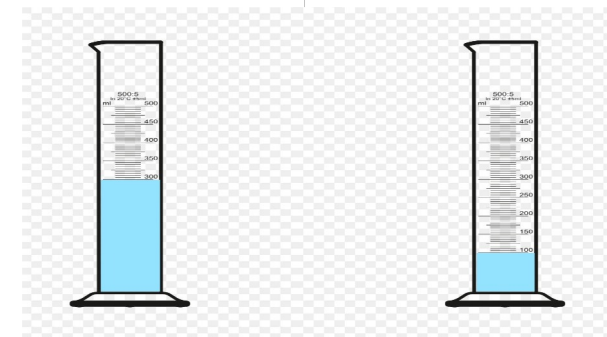
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- In July 2020, European Medicines Agency (EMA) announced a positive scientific opinion on DVR as an additional HIV prevention option for cisgender women age 18 and older in developing countries to reduce their HIV risk
- Considered under EMA's Article 58, in cooperation with WHO, to “facilitate access to essential medicines in developing countries using the same rigorous standards as for products intended for use in the European Union”
- In November 2020, WHO prequalified DVR (to facilitate access to medicines that meet unified standards of quality, safety and efficacy)
- In January 2021 WHO included the ring in the consolidated HIV guidelines; recommended DVR as an additional option
- EMA/WHO combination expedited submissions to African National Medicines Regulatory Authorities (NMRAs) with multiple national approvals in 2022 & 2023

# Long-acting Injectable Cabotegravir

- A new HIV drug by ViiV/GSK that stops the virus from integrating into DNA, similar to dolutegravir.
- A nano-formulated drug, minuscule in size, now soluble in water, designed to address challenges with low solubility.
- J&J has also developed Cabenuva, a combo of CAB and injectable rilpivirine as an HIV treatment
- In two trials, HPTN 083 and HPTN 084, injections of CAB-LA every two months were safe and substantially lowered HIV risk.

	CAB-LA	DMPA-IM
<i>Location</i>	Gluteal muscle (buttocks)	Upper arm or gluteal muscle (buttocks)
<i>Frequency</i>	Every 2 months	Every 3 months
<i>Volume</i>	3 mL	1ml



# CAB for PrEP updates

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- FDA approved in Dec 2021; ViiV filed with other regulatory authorities, approvals happening on rolling basis (current approvals: US, Australia, Zimbabwe, South Africa, Malawi, Botswana, Brazil)
- WHO guidelines released in July 2022
- Currently offering all participants choice between the two safe and effective options in formal Open Label Extension phase of trials
- Additional sub-studies & sub-analyses underway for various sub-populations
- Multiple implementation studies launching and underway

# CAB for PrEP Updates (continued)

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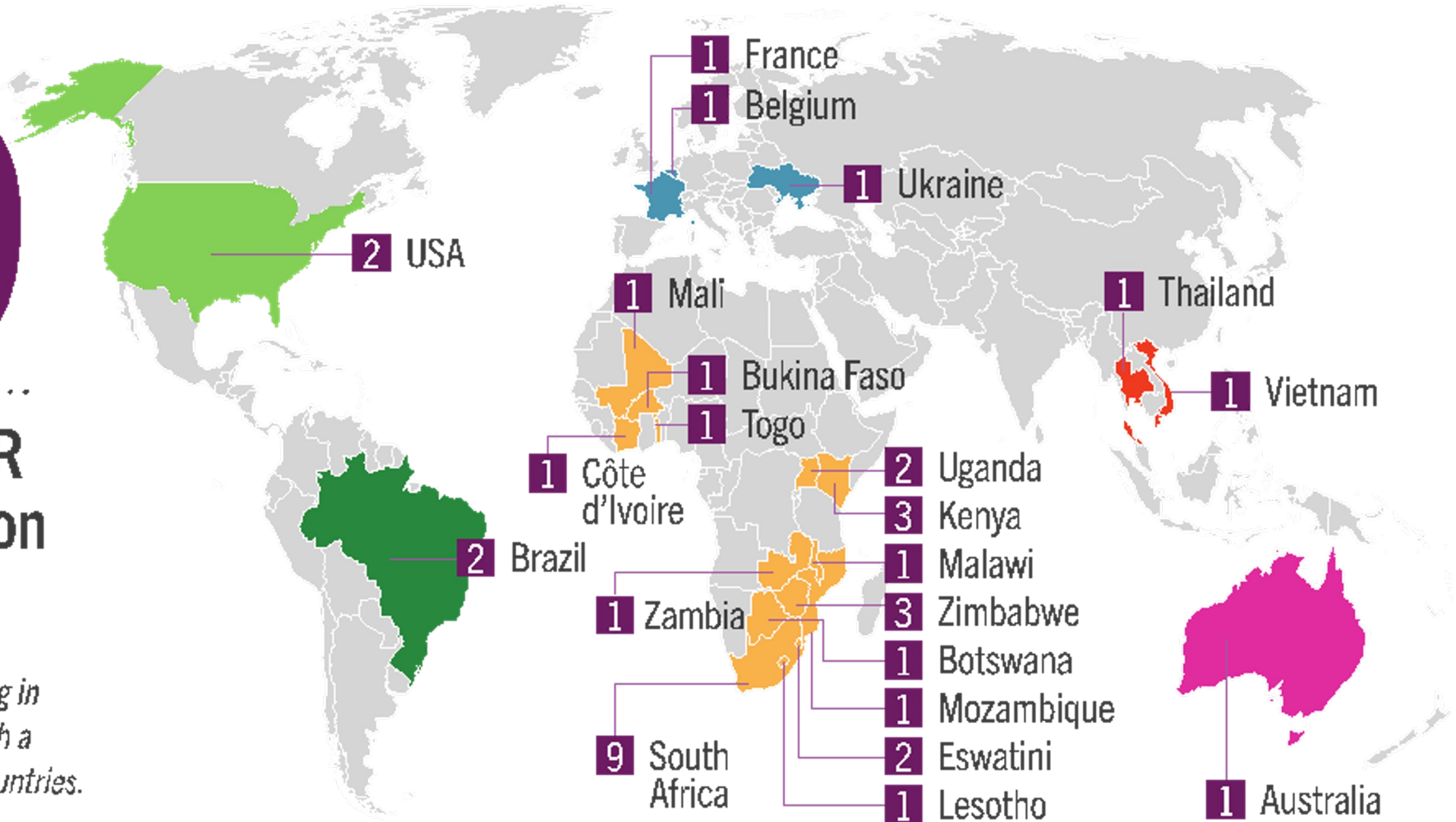
- Zimbabwe, South Africa & Malawi approvals include quite permissive labels in terms of age, oral lead-in, use in pregnancy and testing
- Eight implementation science projects approved
- PEPFAR procurement plans and COP agreements in 6 countries
- Global Fund and CIFF partnership in 6 countries
- Limited supplies available from ViiV thru 2023, pending additional mill approval from FDA to expand
- Three generic sub-licenses from MPP announced in March 2023
- Coalition to Accelerate Access to Long-Acting PrEP working with wide range of stakeholders

# PrEParing for New Products – Geographically

# 29

## CAB and DVR Implementation Studies

*Some studies are happening in more than one country, with a total of 29 studies in 22 countries.*



# PrEParing for New Products – Geographically

BUT, significant questions remain about timing:

- National regulatory approvals of product
- Product supply – manufacturing capacity, timing, shipping
- Actual product delivery to participants
- Answers to critical questions to inform models, policies, program design, procurement, investment

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East and Southern Africa, with  
others in East Asia and Pacific,  
Europe, Latin America and  
Caribbean, North America,  
Southeast Asia and West Africa.

*Some studies are happening in more than one country, with a total of 25 studies in 32 countries.*



# Product Considerations

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For each product, understand and balance:

Clinical	Policy & Programs	Personal
<ul style="list-style-type: none"><li>■ Biologic efficacy</li><li>■ Dosing/duration</li><li>■ Reversibility</li><li>■ Side effect profile</li><li>■ Systemic/Topical</li></ul>	<ul style="list-style-type: none"><li>■ Delivery channel(s)</li><li>■ Health system burden</li><li>■ Product cost</li><li>■ Program cost</li><li>■ Provider training</li><li>■ Demand creation</li></ul>	<ul style="list-style-type: none"><li>■ User effectiveness</li><li>■ User preference</li><li>■ User burden</li><li>■ Discretion of use</li><li>■ Contribution to stigma</li></ul>

It's never just "the product" – it's the program;  
new options can't solve for everything

# Parallel Universes/Journeys

## Providers & Health Systems

Who is at risk?

Where do I find them?

When I can test them?

What do I tell them?

Where can I provide px info and products to them?

What px options can I provide them?

Oral, ring, injectable, condoms, DPP?

## Users

What do I want?

Who do I want to talk with about sex and relationships?

Do I want an HIV test?

Where do I want to get an HIV test?

Do I need and want HIV prevention?

What kind of HIV px do I want?

Oral, ring, injectable, condoms, DPP?

Where and from whom do I want it?

Choice

Choice

# Accelerating Introduction of New Prevention

Those who Use; Those who Choose; Those who Pay the Dues

FUNDERS

## *What we need to know – and fast*

- What is the cost for procurement AND for programming?
- What is the cost-effectiveness?
- What is the market size, generally and relative to other PrEP products?
- How will introduction affect the current market share and size of other PrEP?

PROGRAMS

- What policies need to change to plan for & introduce new option?
- How to overcome siloes in procurement & service delivery?
- What type of training & support do providers need?
- What are optimal service delivery platforms and communication channels?

USERS

- Who prefers which option, and what are their motivators and barriers?
- Where/from whom do potential users desire to hear about and access product?
- How will product use/preference change over time?
- How can we increase & support adherence?
- What is the end user's path to initiation and continued, effective use?
- How can peer groups/influencers be leveraged to support uptake & adherence?
- How can providers be supported to have more knowledge and empathy?
- How can the product be packaged to better support uptake/ adherence?

# Now What?

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- **Translate biomedical options into viable choices** for users, providers and health systems
  - Introduce new options as part of marketing and programming for choice
  - Identify (and differentiate) service delivery models that work for users
  - Ask and answer critical implementation science questions for each product, while building prevention platforms for the future
- Understand **testing and initiation needs** for PrEP
- Ensure **robust civil society engagement** in intro/implementation research and planning
- **Procurement/commodity funding** – for launch and ongoing
- **Provider training** – both clinical guidelines AND appropriate counseling, support, empathy
- **Realistic targets** for interventions, especially intro – and not just coverage targets
- Identify what **products can “solve for”** – and what they can’t
- Ensure we do better, **more equitable** intro with ring and injectable than with oral PrEP and COVID-19 vaccines

# Much accomplished; much to do

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- Fill the **product introduction gaps**
  - Accelerate time from regulatory approval to intro to impact
  - Demand-creation and program platforms for prevention generally
  - Differentiated (and integrated) service delivery for px
- Fill the **product development gaps**
  - Longer-acting & event-driven
  - User-friendly & developed WITH users
  - Dual-purpose & multi-purpose methods

# Resources

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- [Biomedical HIV Prevention Research in 2022 and Beyond](#)
- [Lessons Lessons From Oral PrEP Programs And Their Implications for Next Generation Prevention](#)
- [Understanding the EMA Opinion and Next Steps for the Dapivirine Vaginal Ring](#)
- [An Advocates' Primer on Long-Acting Injectable Cabotegravir for PrEP](#)
- [A Plan for Accelerating Access and Introduction of Injectable CAB for PrEP](#)
- [Dapivirine Ring Early Introduction Considerations: 7 Country Analysis](#)
- [BioPIC CAB-LA initial introduction strategy](#)
- [Biomedical Prevention Implementation Collaborative \(BioPIC\) Adaptable Framework for Product Introduction](#)
- [Developing and Introducing a Dual Prevention Pill](#)
- [Dual Prevention Pill Market Preparation and Introduction Strategy](#)
- [Evolving Designs for HIV Prevention Trials and Next-Gen Trial Summary](#)

[www.avac.org](http://www.avac.org)

[www.PrEPWatch.org](http://www.PrEPWatch.org)

# Resources

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- Podcast: [\*New Products are Needed & a New Paradigm is Essential: A new era in prevention?\*](#)
- Summary slide decks:
  - [Advocates Guide to CAB for PrEP](#)
  - [Advocates' Guide to Product Introduction](#)
  - [Advocates' Guide to HIV Testing and PrEP](#)
- [AVAC's Plan for Accelerating Access and Introduction of Injectable CAB for PrEP & summary document](#)
- [Advocates' Primer on Injectable Cabotegravir for PrEP: Trials, Approvals, Rollout and More](#)
- [Implementation Science Questions for CAB for PrEP](#)
- [Implementation Study Tracker](#)
- [Cost of Goods Sold \(COGS\) Analyses: FAQ Brief – AVAC & CHAI](#)
- [\*A New Shot Guards Against HIV, but Access for Africans Is Uncertain\*](#) – New York Times
- [Global PrEP Tracker](#) (that includes DVR and CAB in addition to long-standing oral PrEP info)
- [Lessons Lessons From Oral PrEP Programs & Implications for Next Generation Prevention](#)
- [BioPIC CAB-LA Initial Introduction Strategy](#)
- [BioPIC Adaptable Framework for Product Introduction](#)
- [Dual Prevention Pill Market Preparation and Introduction Strategy](#)

# Thank You!

## Coalition to Accelerate and Support Prevention Research (CASPR)



**Cooperative Agreement No. AID-OAA-A-16-00031**  
**HIV Vaccine and Biomedical Prevention Research Project—Objective 3**

