Long-Acting PrEP Status as of April 2024

Tracking Progress towards Access for New Long-Acting HIV PrEP Products

DETAILED REPORT

A quarterly update from the Secretariat of the Coalition to Accelerate Access to Long-Acting PrEP

SECRETARIAT:

AVAC
Advocacy. Access. Equity.

Important Note

This report is developed by AVAC, Secretariat to the Coalition to Accelerate Access to Long-Acting PrEP, to synthesize the current status of long-acting PrEP. This is done in service to the wider ecosystem - the report is not a deliverable of the Coalition or representative of the views of the individual institutions that make up the Coalition.

Document Structure

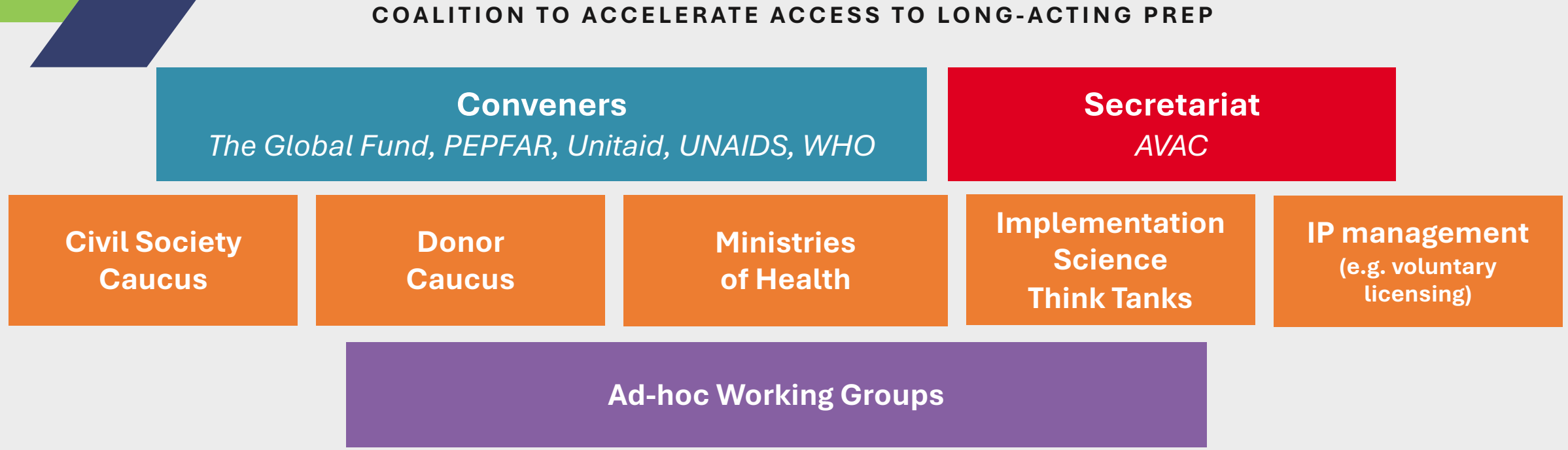
- Executive Summary
- Long-Acting HIV PrEP Coalition Purpose, Rationale, and Structure
- Long-Acting HIV PrEP Coalition Proposed Priorities 2024
- Long-Acting HIV PrEP Pipeline update
- Tracking progress to market of new Long-Acting (LA) PrEP products

Cabotegravir (CAB)

Dapivirine Vaginal Ring (DVR)

Executive Summary

Coalition Structure



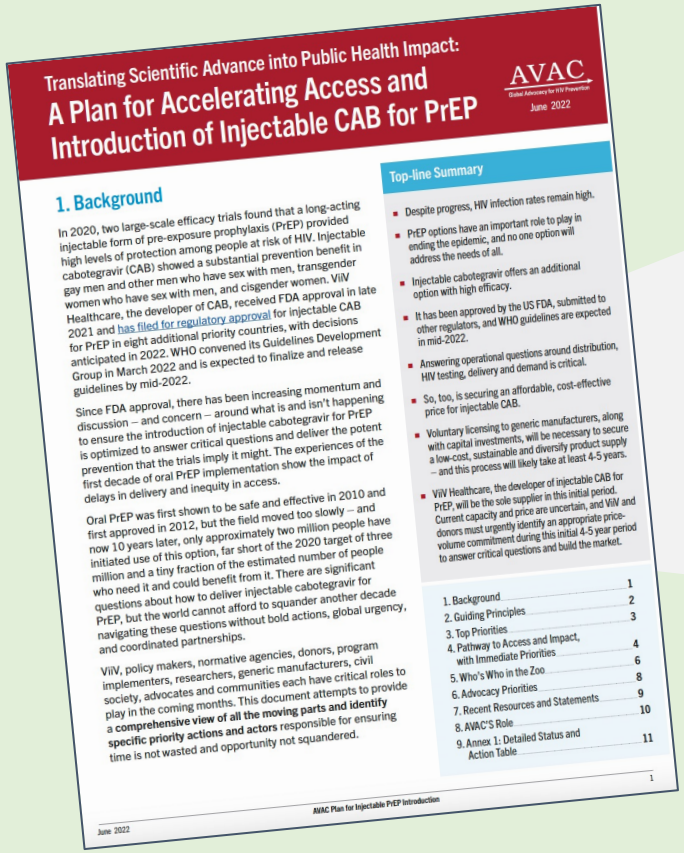
The Coalition aims to:

- The Coalition is convened by the Global Fund, PEPFAR, Unitaid, UNAIDS and WHO, with AVAC as the Secretariat.
- Build on lessons learned from oral PrEP and coordinate stakeholders activities
- Jointly develop strategies to identify and overcome access challenges for new PrEP options in near-term (injectable CAB and DVR, including generics) and medium- to long-term (injectable LEN and future products)
- Ensure new, longer-acting PrEP options reaching the market will be available and equitably accessible to all who need them more quickly than ever before

In June 2022, the ‘Plan for CAB’ document was published

It is a comprehensive view of the pathway to market for CAB and identified specific priority actions along the product pathway to ensure that opportunity was not squandered in introducing injectable CAB for PrEP.

A Plan for Accelerating Access and Introduction of Injectable CAB for PrEP — June 2022



Translating Scientific Advance into Public Health Impact:
A Plan for Accelerating Access and Introduction of Injectable CAB for PrEP

AVAC
Global Advocacy for HIV Prevention
June 2022

1. Background

In 2020, two large-scale efficacy trials found that a long-acting injectable form of pre-exposure prophylaxis (PrEP) provided high levels of protection among people at risk of HIV. Injectable cabotegravir (CAB) showed a substantial prevention benefit in gay men and other men who have sex with men, transgender women who have sex with men, and cisgender women. ViiV Healthcare, the developer of CAB, received FDA approval in late 2021 and has filed for regulatory approval for injectable CAB for PrEP in eight additional priority countries, with decisions anticipated in 2022. WHO convened its Guidelines Development Group in March 2022 and is expected to finalize and release guidelines by mid-2022.

Since FDA approval, there has been increasing momentum and discussion – and concern – around what is and isn't happening to ensure the introduction of injectable cabotegravir for PrEP is optimized to answer critical questions and deliver the potent prevention that the trials imply it might. The experiences of the first decade of oral PrEP implementation show the impact of delays in delivery and inequity in access.

Oral PrEP was first shown to be safe and effective in 2010 and first approved in 2012, but the field moved too slowly – and now 10 years later, only approximately two million people have initiated use of this option, far short of the 2020 target of three million and a tiny fraction of the estimated number of people who need it and could benefit from it. There are significant questions about how to deliver injectable cabotegravir for PrEP, but the world cannot afford to squander another decade navigating these questions without bold actions, global urgency, and coordinated partnerships.

ViiV, policy makers, normative agencies, donors, program implementers, researchers, generic manufacturers, civil society, advocates and communities each have critical roles to play in the coming months. This document attempts to provide a **comprehensive view of all the moving parts and identify specific priority actions and actors** responsible for ensuring time is not wasted and opportunity not squandered.

Top-line Summary

- Despite progress, HIV infection rates remain high.
- PrEP options have an important role to play in ending the epidemic, and no one option will address the needs of all.
- Injectable cabotegravir offers an additional option with high efficacy.
- It has been approved by the US FDA, submitted to other regulators, and WHO guidelines are expected in mid-2022.
- Answering operational questions around distribution, HIV testing, delivery and demand is critical.
- So, too, is securing an affordable, cost-effective price for injectable CAB.
- Voluntary licensing to generic manufacturers, along with capital investments, will be necessary to secure a low-cost, sustainable and diversify product supply – and this process will likely take at least 4-5 years.
- ViiV Healthcare, the developer of injectable CAB for PrEP, will be the sole supplier in this initial period. Current capacity and price are uncertain, and ViiV and donors must urgently identify an appropriate price-volume commitment during this initial 4-5 year period to answer critical questions and build the market.

4. Pathway to Access and Impact, with Immediate Priorities

This table outlines the immediate priorities across the pathway to access and impact and includes key actors responsible for them, while ***Annex 1: Detailed Status and Action Table*** provides a more detailed description of Status and Key Questions/Priorities/Next Steps for each issue area.

The Pathway to Access and Impact

Priority actions identified along each part of the pathway to access and impact (outlined on next slide).

Document link: https://avac.org/resource/report/translating-scientific-advance-into-public-health-impact-a-plan-for-accelerating-access-and-introduction-of-injectable-cab-for-prep/

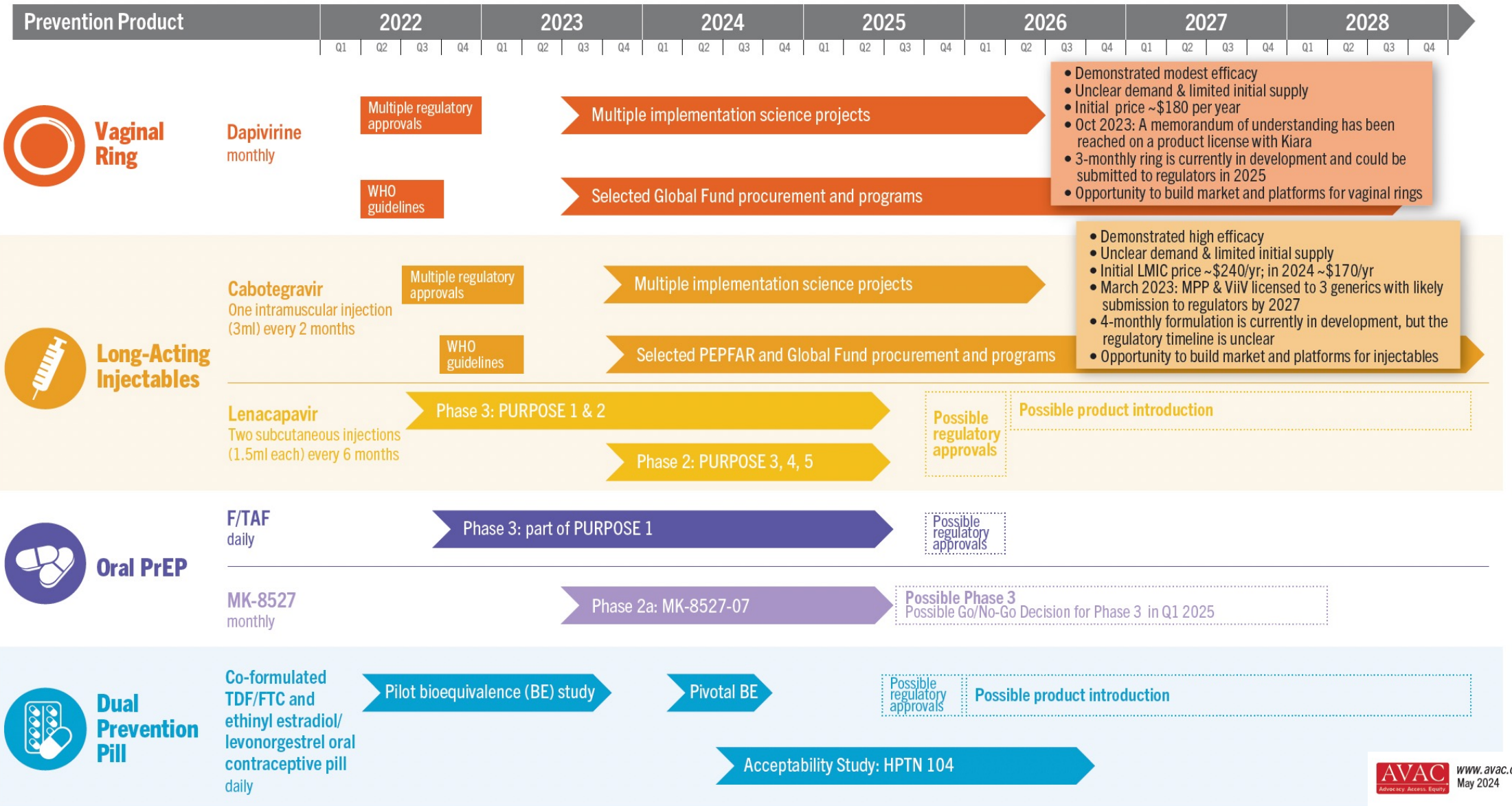
Progress on Pathway to Access & Impact for LA PrEP

The next slides will review each product along the pathway to access

Cabotegravir (CAB)

Dapivirine Vaginal Ring (DVR)

Updated Product Pipeline



Product Overview

	Product		Brand Name	Developer	First Regulatory Approval	Number of other approvals	LMIC price	
							Originator	Generic / local manufacturing
Vaginal Ring	Dapivirine		DapiRing	PopCouncil	2021 (Medicines Control Agency of Zimbabwe)	11 countries	$156 / year ($13/ring x 12 rings)	Possible local manufacturing in South Africa (Kiara Health), pending license and funding
Long-Acting Injectables	Cabotegravir		Apretude* (injection for HIV PrEP)	ViiV	2021 (US FDA)	48 countries (including EMA)	Approx. $180/year (£23.50/vial x 6 inj. = £141/year)	3 generic manufacturers signed voluntary license in March 2023; tech transfer ongoing
	Lenacapavir		*Product in phase 3 clinical trial; results anticipated be end of 2024*					
Oral PrEP	F/TAF	Cis men/trans women	Descovy	Gilead	2019	96 countries	Price unknown	2 generic manufacturers with tentative FDA approval; price unknown
		Cis women			*Product in phase 3 clinical trial; results anticipated be end of 2024*			
	MK-8527		TBD	Merck	*Products in Phase 2 clinical trial; Phase 3 could begin in 2025*			
Dual Prevention Pill	Co-formulated TDF/FTC and ethinyl estradiol/ levonorgestrel oral contraceptive pill		*Products in pivotal bioequivalence study; could reach market in 2025*					

*Brand name Vocabria for HIV treatment

Moving A Product to the "Real World"

Technology	Efficacy Results	Year(s) After Efficacy Results 1	2	3	4	5	6	7	8	9	10
Oral TDF/FTC	2010		First Regulatory Approval			First African Regulatory Approval; WHO Rccomendations	First Demo Project; Generic Access in LMICs				Scale
Dapivirine Vaginal Ring	2016					First Regulatory Approval; First African Regulatory Approval; WHO Rccomendations	First Demo Project				?
Injectable Cabotegravir	2020	First Regulatory Approval	First African Regulatory Approval; WHO Rccomendations	First Demo Project				?			

- First Regulatory Approval
- First African Regulatory Approval
- WHO Rccomendations
- First Demo Project
- Scale
- Generic Access in LMICs

Long-Acting PrEP—Current Status as of March 2024

	CAB	DVR	LEN
Product (pricing, manufacturing, generics)	Current price from ViiV made public: £23.50/vial (approx. $180/year). Voluntary license granted from MPP to 3 generics	MOU signed with Kiara Health to manufacture DVR in South Africa	Both PURPOSE 1 & 2 clinical efficacy trials fully enrolled; results anticipated by end of 2024.
Regulatory Approval & Normative Guidance	Approved in 48 countries; WHO pre-qualification in 2023	Approved in 11 countries, 2 pending review/appeal, 3 submissions in preparation. WHO PQ in 2021	
Planning & Budgeting	Total 2023-2025 volume: 1.2M doses for non-commercial supply (955k for programs; remainder for studies)	400k rings available currently, 500k additional projected for 2024-25; initial procurement in several countries for supplies via Global Fund GC7	
Delivery & Supply Chain	PEPFAR have delivered programmatic supply in 4 countries (Ukraine, Zambia, Zimbabwe & Malawi) since Q1 2024	Currently, 1,052 product initiations on DVR since Q4 2023	
Stakeholder Engagement	Establishment of the Coalition's Civil Society (CS) Caucus; facilitating reoccurring meetings with stakeholders.		
Research	Implementation studies ongoing or planned in 22 countries	Implementation studies ongoing in 7 countries	
Monitoring & Evaluation	Continued monitoring and assessment of initiations via trackers and think tanks. Understand country-specific product introduction issues to inform programmatic rollout		

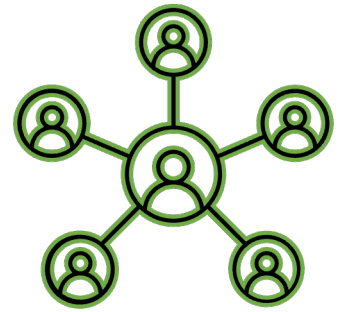
Long-Acting PrEP— Proposed Priorities for 2024

As of March 2024	CAB	DVR	LEN
Product (pricing, manufacturing, generics)	Collaborate with ViiV to understand procurement plans, build demand and accelerate generics progress	Collaborate with PopCouncil on price/volume for 2024/25 & plans for local mfg with Kiara; track development of 3-monthly & dual-purpose rings	Engage with Gilead now to influence access and pricing and encourage transparency
Regulatory Approval & Normative Guidance	Monitor progress on the need to remove oral CAB development and registration from sublicence agreements	Advocate for additional submission in high-burden countries and understand what data PEPFAR may need to consider programmatic procurement	Follow-up with Gilead on their stated plans to work with national and regional African regulatory mechanisms
Planning & Budgeting	Build demand in country and develop long-term demand forecast	Build demand in country and develop long-term demand forecast	Request Gilead to articulate plan for oral F/TAF once the PURPOSE 1 trial results are available
Delivery & Supply Chain	Track current implementation studies and share early insights; continue to identify and address evidence gaps	Track current implementation studies and share early insights; continue to identify and address evidence gaps	TBD later in 2024
Stakeholder Engagement	Create collective advocacy strategies and continue to integrate civil society thinking	Create collective advocacy strategies and support implementation of HIV Prevention Choice Manifesto	TBD later in 2024
Research	Ensure further studies are planned to research long-term effects, and continue to identify gaps in product introduction by country	Advocate for further research on long-term effects and use in conjunction with other prevention methods	Start discussing plan for IS studies with Gilead
Monitoring & Evaluation	Continue to coordinate modeling exercises; assess gaps in in product introduction by country. Push to advance a learning agenda for programmatic rollout	Continue to assess gaps in in product introduction by country. Push to advance a learning agenda for programmatic rollout	TBD later in 2024

Coalition Purpose, Rationale, and Structure

What is the purpose of the Coalition

The Coalition to Accelerate Access to Long-Acting PrEP **brings together donors, civil society, ministries of health, implementation science think tanks and partner organizations** to ensure an accelerated, equitable, sustainable, and collaborative approach to optimizing access to new long-acting PrEP options



Coordinated action

Jointly developed strategies

Coalition's objective is practical:
To coordinate key stakeholder activities on long-acting PrEP access, including jointly developing strategies to identify and overcome access challenges for new PrEP options available now and those in the pipeline.

What is the need for the Coalition to exist?

There is a **deep need to apply lessons learned from oral PrEP and create plans to overcome the unique challenges for new prevention options**, with the aim that new, longer-acting PrEP options will be quickly and equitably accessible to all who need them - especially on low- and middle-income countries (LMICs).

Learning Lessons from the rollout of oral PrEP

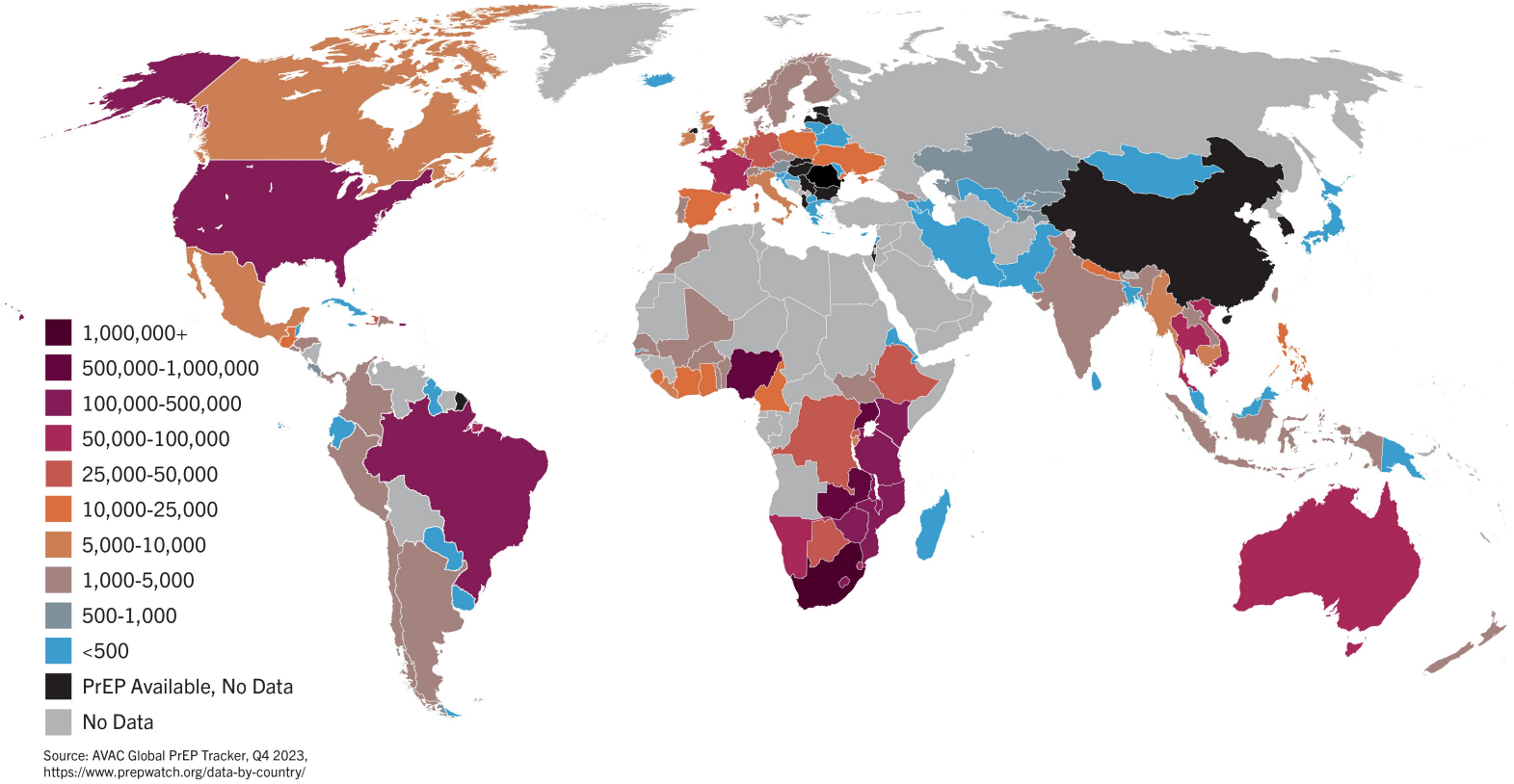
- **More than 10 years ago, research showed oral PrEP was safe and effective in preventing HIV.** In 2012, it was approved for use by the US Food and Drug Administration and subsequently recommended for all people at substantial risk of HIV by the WHO.
- **But the global health delayed action and now in 2024, only 5.67 million people have initiated oral PrEP use***, only a fraction of the estimated number of people who could benefit from it. With new, longer-acting PrEP options reaching the market, the global health field needs to bring bold actions, global urgency, and coordinated partnerships to meet the challenges of product access, roll-out, and use.
- **Coordinated, strategic action is needed to ensure that science is translated into public health impact without unnecessary delay**.

* Cumulative number of initiations from 2012 to September 2023, https://data.prepwatch.org/

Global PrEP Uptake – 12+ years in

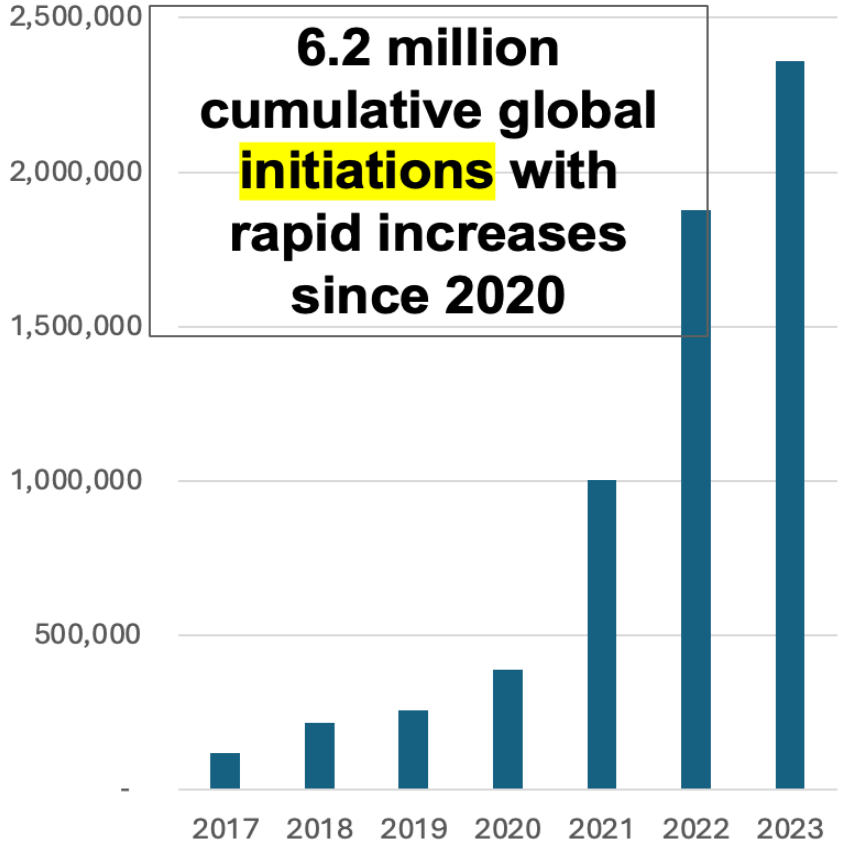
Over 6.2 million cumulative global PrEP initiations globally as of Q4 2023.

PREP INITIATIONS BY COUNTRY, DECEMBER 2023



Source: AVAC Global PrEP Tracker, Q4 2023, https://www.prepwatch.org/data-by-country/

PREP INITIATIONS OVERTIME



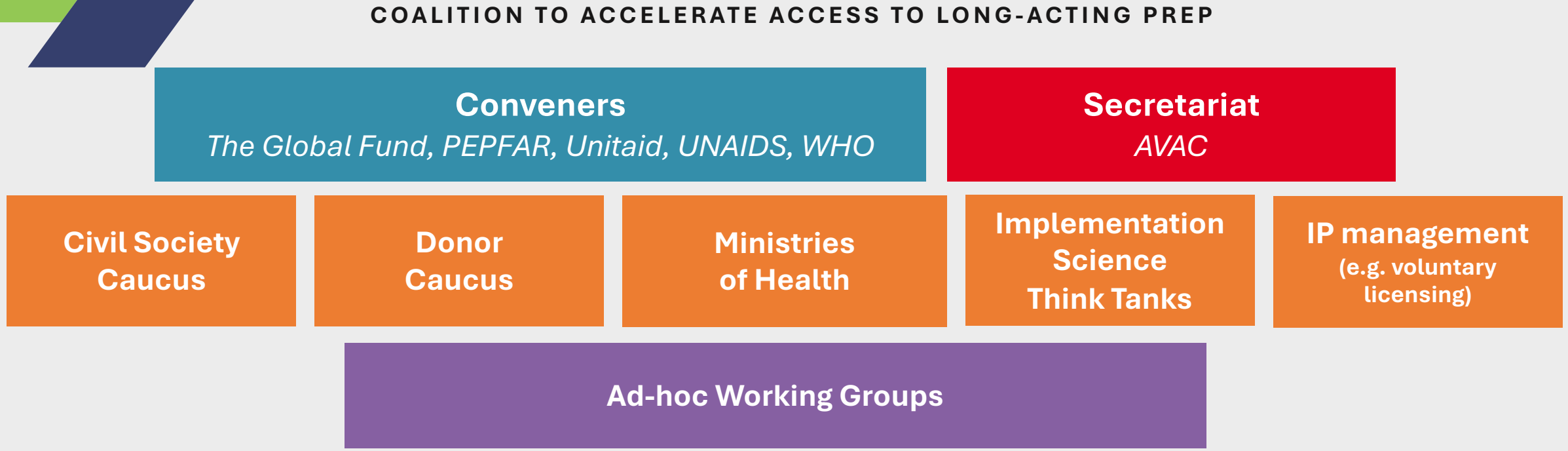
https://data.prepwatch.org/

Coalition Principles

The Coalition is committed to the following guiding principles in driving engagement with all stakeholders:

1. **Lead with Equity:** Products don't end pandemics if they aren't delivered with equity and urgency; oral PrEP and COVID vaccine delivery are the most recent reminders.
2. **Center the Community and User:** It is critical to center communities in design and implementation of programs and center users in actual product delivery.
3. **Accelerate Scale and Speed:** We need to break the sequential nature of traditional approaches to scale and speed up introduction. Part of accelerating speed is moving toward a parallel approach where research, implementation science, and scale programs are designed, funded and implemented in parallel.
4. **Deliver Impact:** Priorities and targets for the next 12 months must focus on building a pathway to public health impact. Assess and set a deadline for analyzing current operational studies and another deadline for when a coverage target towards impact could be in place.
5. **Work with what we know, while continually adding to the evidence-base:** There is still much we don't know about the newest products reaching the market, but there is also a lot we do know. We must not let the perfect be the enemy of the good and learn from past experiences. The introduction of new prevention products is a chance to reorient, reimagine and re-energize HIV prevention programs.
6. **Strategically link with long-acting treatment efforts:** While the Coalition is focused on long-acting prevention options, many of the products also have possible treatment indications. The Coalition will coordinate with long-acting treatment groups and ensure that bidirectional communications and information-sharing between the Coalition and these groups are collaborative and consistent and maximize efficient and effective coordination to ensure access for both prevention and treatment, when feasible, and open communication between prevention and treatment stakeholders

Coalition Structure



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- Ensure new, longer-acting PrEP options reaching the market will be available and equitably accessible to all who need them more quickly than ever before

The Coalition Civil Society Caucus

COALITION TO ACCELERATE ACCESS TO LONG-ACTING PREP

Conveners
The Global Fund, PEPFAR, Unitaid, UNAIDS, WHO

Secretariat
AVAC

Civil Society Caucus

Donor Caucus

Ministries of Health

Implementation Science Think Tanks

IP management (e.g. voluntary licensing)

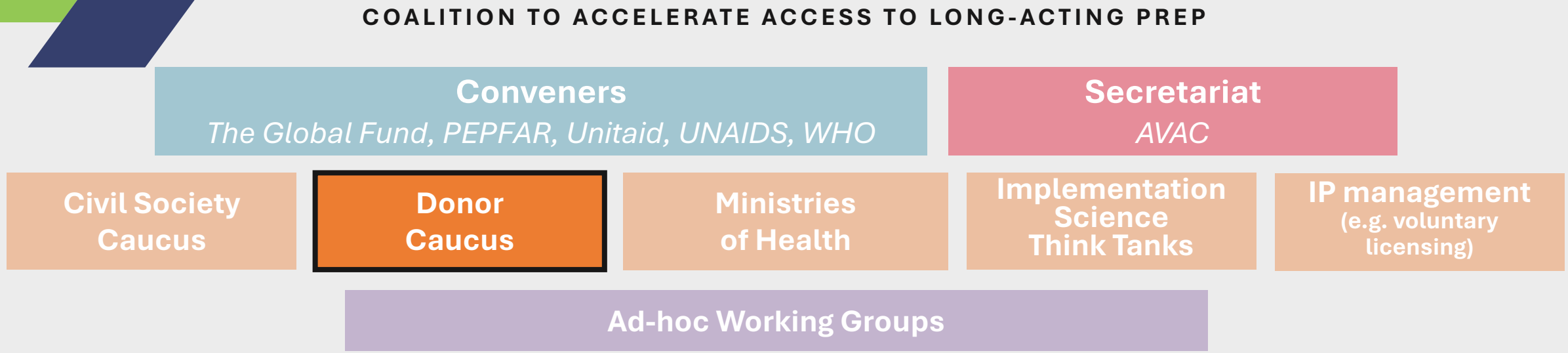
Ad-hoc Working Groups

- Established in 2022 to ensure civil society expertise influences the rollout of long-acting HIV PrEP options.
- The group meets bi-monthly for updates on long-acting PrEP activities, direct engagement with key stakeholders, and shared strategy development.

This Caucus includes representation from:

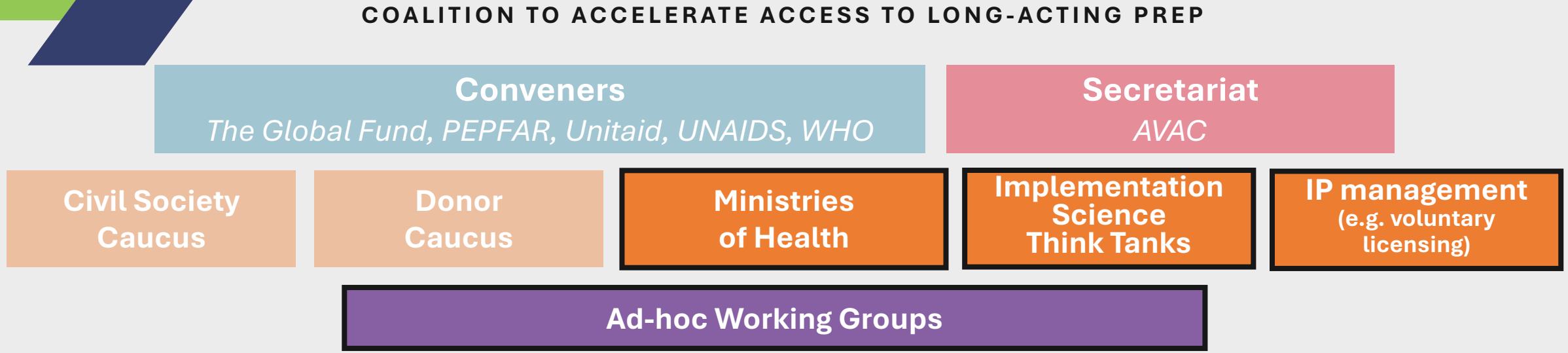
- African Women Community Prevention Accountability Board
- AfroCAB
- APCOM
- Global Black Gay Men Connect (GBGMC)
- Coalition to Accelerate and Support Prevention Research (CASPR)
- Global Key Population Advisory Group
- other civil society groups working on long-acting PrEP introduction.

The Coalition Civil Society Caucus



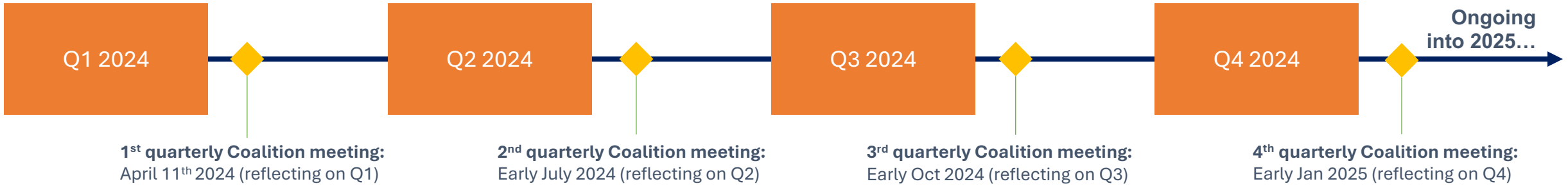
- Established in 2019, the Donor Caucus includes Bill and Melinda Gates Foundation, CDC, CIFF, The Global Fund, PEPFAR, Unitaid, USAID, and WHO
- This donor-only forum is a platform for confidential conversations among donors to ensure alignment on longer-acting PrEP investments.

The Coalition Civil Society Caucus



- The Coalition includes representatives from Ministries of Health in early introduction countries, including South Africa, Zambia, Vietnam, and Brazil.
- The Coalition collaborates with ongoing and planned implementation science projects through participation in the Biomedical Prevention Implementation Collaborative (BioPIC) and the bi-monthly think tanks that link projects on key issues that are coordinated by WHO and AVAC.
- The Coalition collaborates with the MPP on generic licensing efforts.
- Ad-hoc Working Groups can be convened as and when needed and membership will include representation of relevant technical experts, Ministries of Health, and civil society organizations.

Quarterly Coalition Meetings



The purpose of Coalition meetings is two-fold:

1. For each stakeholder group to provide updates on priority issues, identify cross-cutting issues and cross-pollinate between stakeholder groups.
2. To serve as a reminder to all Coalition stakeholders of their responsibility to influence key opinion leaders on a global scale to recognize, participate and implement the outputs of the Coalition.

IMPORTANT

Prior to each quarterly meeting, the Secretariat will publish a quarterly report reviewing the current status of Long-Acting PrEP products along the product pathway.

Proposed Coalition Priorities 2024

Coalition Coordination Updates

Proposed Priorities for 2024

- Identify and work on **priority actions (per product and product-agnostic).**
- Establish and **maintain a fully operational and agile Coalition that connects essential stakeholders for collaborative decision-making**.
- Enhance and **optimize coordination efficiency and effectiveness among donors, normative agencies, national governments, implementers, civil society, and product developers** to achieve more streamlined and impactful collaboration.
- Establish a **structured and strategic approach to effectively convey information, messages, and ideas about the Coalition** to the various stakeholders and audiences.
- **Implement a system to track, report and disseminate quarterly progress on LA PrEP** to ensure accountability, transparency, and foster trust among stakeholders.

Proposed Coalition Priority #1 (Page 1)

Identify and work on **priority actions (per product and product-agnostic).**

- **Define priority actions per product**
  - Cabotegravir (CAB)
  - Dapivirine Vaginal Ring (DVR)
  - Lenacapavir (LEN)
  - Dual Prevention Product (DPP)
- **Define product-agnostic priority actions**

Proposed Coalition Priority #1 (Page 2)

Focus on priority actions (per product and product-agnostic).

Product-specific			
CAB			
1	Requests to outline what can be done on the process side to reduce prices and pass those along to countries	6	Monitor progress on the need to remove oral CAB development and registration from sublicence agreements.
2	Expand lowest pricing eligibility criteria to ensure MICs can access CAB at non-profit price	7	Address country-level product-sharing issues
3	Build demand-side support and in-country demand	8	Explore opportunities to expand access to generics under the license
4	Advance a learning agenda for programmatic roll-out, aiming to share this via a regular platform	9	Work with ViiV to solve for packaging issues causing vial breakage in “last mile” delivery (incl. communication with IS sites if this proves to be practical issue)
5	Understand procurement to date and plans for 2024 and 2025, based on ViiV’s current forecast	10	Advocate for an appropriate price for generics

Proposed Coalition Priority #1 (Page 3)

Focus on priority actions (per product and product-agnostic).

Product-specific			
	LEN	DVR	DPP
1	Engage with Gilead now to influence pricing & access and to encourage transparency & generic production.	Schedule call with PopCouncil to discuss local manufacturing plan with Kiara Health; current pricing with plans for reductions; and current and planned volumes in 2024/25	Include DPP as an option within Coalition discussions
2	Request Gilead to articulate plan for oral F/TAF once the PURPOSE 1 trial results are available.	Document and disseminate what has been procured to date and current DVR available volumes for 2024-2025	Include other new, longer-acting PEP/PrEP products as an option within Coalition discussions
3	Start discussing plan for IS studies with Gilead	Develop plans to increase demand for DVR	
4	Follow-up with Gilead on their stated plans to work with national and regional regulatory mechanisms.	Understand specifically what data PEPFAR needs to learn in the current implementation science projects to consider larger programmatic procurement	
5	Proactively dissuade message that the market should “wait for LEN”	Draft clear messaging about DVR from Coalition, including ways in which GF and PEPFAR can partner as per PEPFAR SAB recommendation	

Proposed Coalition Priority #1 (Page 4)

Focus on priority actions (per product and product-agnostic).

	Product-agnostic
1	Build a picture of "investment case" for product innovation in HIV PrEP
2	Build out key questions for each product particularly CAB, LEN, DPP, and DVR
3	Develop framework for understanding demand, uptake and user interest in CAB and DVR (and eventually LEN and DPP) to develop a demand forecast as data begin to accrue from studies and programs
4	Link with Global Health Strategies-led coalition for LA treatment

Tracking Progress to Market of New Long-Acting (LA) PrEP Products

CAB Priorities as outlined in June 2022 'The Plan for CAB' document

Pathway	Immediate Priorities
Product	▸ **ViiV** to license injectable CAB to the Medicines Patent Pool (MPP). ▸ **The MPP and ViiV** to work with generic manufacturers and donors, including Africa-based manufacturers, to expedite technology transfer and ensure sustainable supplies of the product. ▸ **Generic manufactures, with MPP**, to identify capital expenditure needs and timeframe to be able to develop capacity. ▸ **Innovative donor(s)** to fund capital investments needed for generic manufacturing to reach scale. ▸ **ViiV** to confirm publicly, maximum quantity and minimum price for 2022-2025. ▸ **Donors** to negotiate this price/volume guarantee to ensure sustainable supply for initial introduction period, given the timeline for generic licensing agreements and manufacturing upgrades (likely 4-5 years).
Regulatory Approval & Normative Guidance	▸ **Eight regulators** currently reviewing injectable CAB for PrEP to ensure priority review. ▸ **ViiV** to pursue widespread registration of CAB in high-burden countries. ▸ **ViiV** to register with WHO Pre-Qualification (PQ) to allow expedited registration in countries participating in WHO's Collaborative Procedure for Accelerated Registration process.
Planning & Budgeting	▸ **Governments and donors** to set targets for supply and programs at scale – what is needed and possible in 2022-2023 in implementation science projects, and what is needed from 2024 to begin programs at scale.
Delivery / Supply Chain	▸ **Large, resourced and coordinated implementation studies** to begin immediately to answer critical questions about how CAB performs outside the clinic setting and across populations. ▸ **Provider training** materials and tools updated to incorporate CAB administration and implementation studies that assess the feasibility of task-shifting to expand the cadres of providers that are authorized and trained to administer injections and that offer choice (explaining efficacy, clinic visits, side effects, etc. of all methods available) and assist in shared decision-making. ▸ **Innovative demand creation** strategies (for injectable PrEP and for "choice" among options) developed with process to test and iterate, and share across projects.
Individual Uptake & Continued Use	
Delivery / Supply Chain	▸ **Testing requirements** should not become a barrier to CAB introduction. Testing strategies should be both robust and feasible and work with locally available tests and assays to, maximize the benefits of access to CAB while minimizing the risk of undetected cases.
Research	▸ **Data to be collected on the benefit of injectable CAB as PrEP for populations that were not part of efficacy trials**, especially adolescents, pregnant and breast-feeding people, and transmasculine and gender non-conforming individuals. ▸ **Study alternate injection sites and frequency of injections**, recognizing that the impact of injectable CAB holds the potential to expand, if the injection schedule could align with injectable contraception.
Stakeholder Engagement	▸ **Integrate and engage civil society** in all decision-making relevant to planning and preparation for access to CAB, including designing, conducting and monitoring implementation studies and delivery programs.

Progress on Pathway to Access & Impact for LA PrEP

The next slides will review each product along the pathway to access

Cabotegravir (CAB)

Dapivirine Vaginal Ring (DVR)

Tracking progress to market of new Long-Acting (LA) PrEP products

Injectable Cabotegravir
(CAB)

CAB for PrEP – Product Summary

Complete | Some progress | No progress

	Proposed priorities outlined in 'Plan for CAB' (July 2022)	Status as of March 2024	Progress
1	ViiV to license injectable CAB to the Medicines Patent Pool.	In July 2022, ViiV and MPP signed the license; and in March 2023 sublicences to three generic manufacturers were signed	
2	MPP and ViiV to work with generic manufacturers and donors, including Africa-based manufacturers, to expedite technology transfer and ensure sustainable supplies of the product.	Technology transfer package transferred to generic licensee in October 2023, and technology transfer support is ongoing until the end of generic product development.	
3	Generic manufactures, with MPP, to identify capital expenditure needs and timeframe to be able to develop capacity.	Discussions between MPP, ViiV and generic manufacturers are ongoing.	
4	Innovative donor(s) to fund capital investments needed for generic manufacturing to reach scale.	No additional CapEx identified	
5	ViiV to confirm publicly maximum volume/quantity and minimum price for 2022-2025.	**Non-profit price**: ViiV confirmed £24.70/vial in 2023 (confidentially) and £23.50/vial in 2024 (publicly). Prices in 2025 and beyond are unclear. ViiV cites eligibility criteria to access non-profit price; all low-income countries (LICs), least developed countries (LDCs), and Sub-Saharan African countries. **Volumes**: ViiV making 955,000 vials available for programmatic use in addition to 116,000 for HPTN trials and 129,000 for implementation studies from 2023 - 2025.	
6	Donors to negotiate this price/volume guarantee to ensure sustainable supply for initial introduction period, given the timeline for generic licensing agreements and manufacturing upgrades (likely 4-5 years).	Manufacturing has some constraint due to process, e.g. currently one mill in operation, second mill coming online in Q3 2024.	

CAB for PrEP – Product Price

Confidentiality on non-profit price lifted in October 2023

~$40
USD per year
Oral Pill

VS

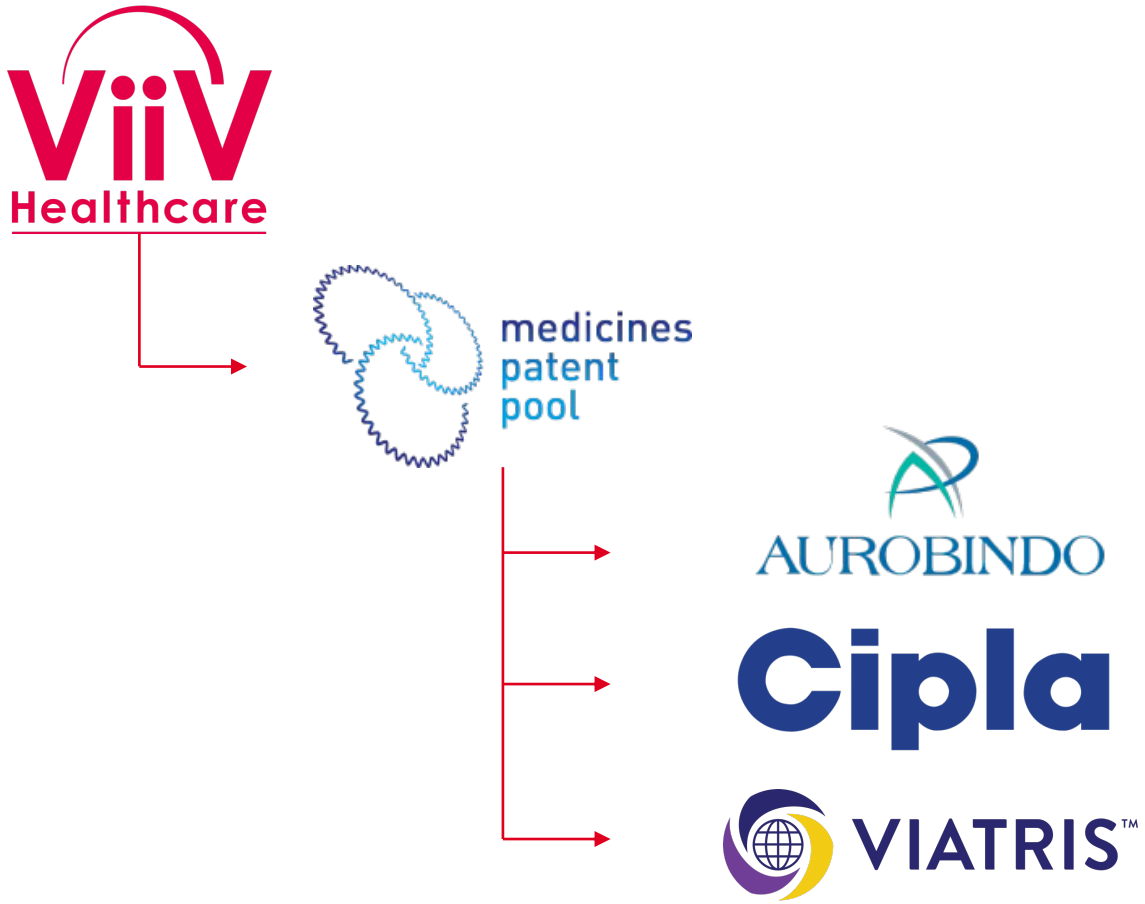
~ $180 *
USD per year
Injectable

- Need for ViiV to confirm non-profit pricing for <u>all</u> Low- and Middle-Income Countries
- ViiV may confirm further price reductions beyond 2024

* £23.50 / vial as confirmed by ViiV in October 2023.

CAB for PrEP – Generics for CAB

Sublicences granted to three generic manufacturers.



- Coalition members, advocates, and other stakeholders successfully advocated for license from ViiV to Medicines Patent Pool (MPP).
- Cipla has plans to manufacture in India as well as in South Africa.

CAB for PrEP – Generics for CAB

However, it will likely take 3-4 years before product reaches market.

AUROBINDO

Cipla

VIATRIS™

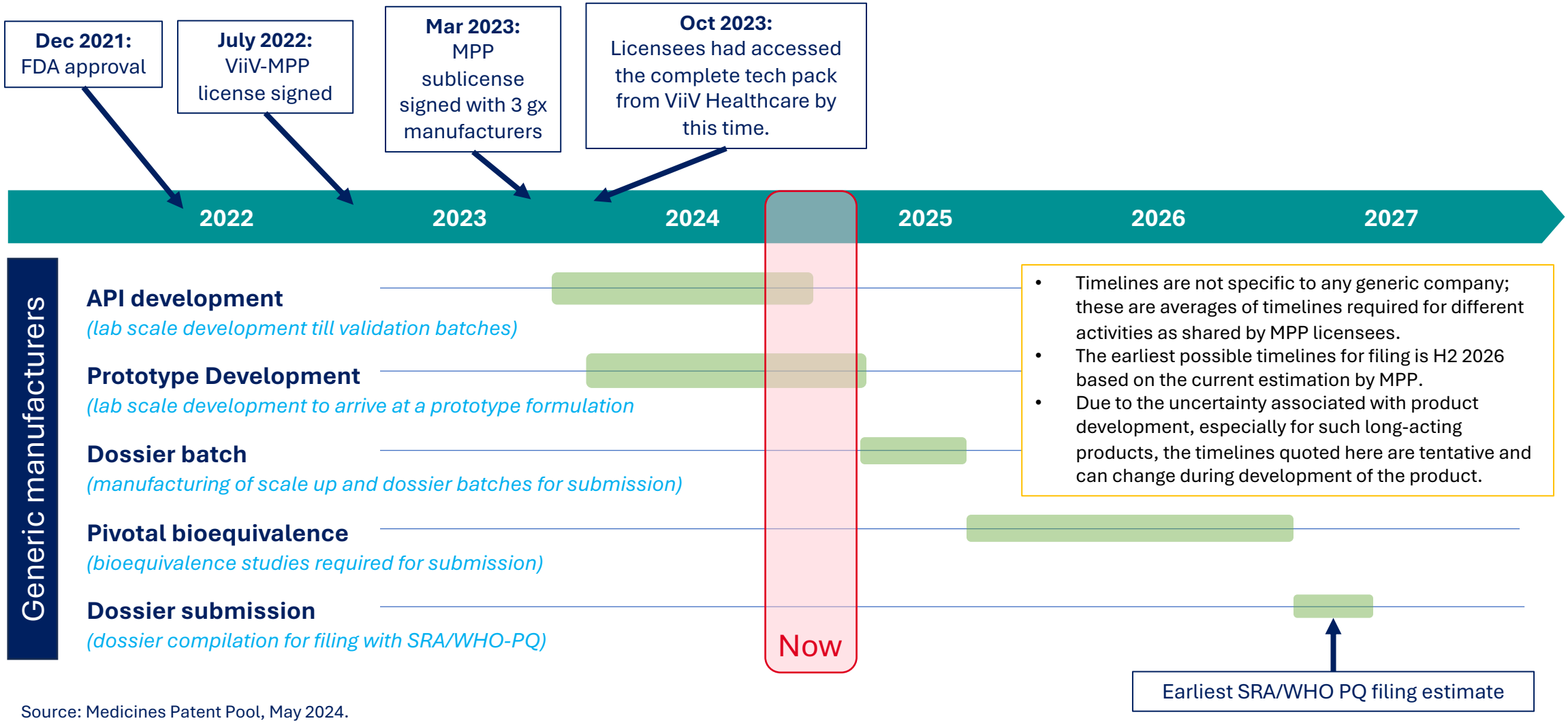
Each generic manufacturer needs to complete a bioequivalence study (BE) for its generic CAB product

Assuming best case for BE studies and regulatory approvals, **the earliest anticipated entry of a generic is 2027**

- Generic manufacturers were chosen based on their existing capability and infrastructure required to make CAB
  - However, generic CAB products will still need to complete bioequivalence studies (BE), with this BE study itself expected to take at least a year (not including recruitment)
- Each generic manufacturer generics will go through a staged process for filings and supplies across regions, likely prioritizing where needs are perceived to be highest.
- Note that, currently the CAB-LA license requires generic manufacturers to develop both injectable and oral formulations of cabotegravir – this adds complexity
  - Stakeholders are monitoring progress on the need to remove oral CAB development and registration from sublicence agreements

CAB for PrEP – Generics for CAB

Development timelines for CAB show that the earliest anticipated timeline for filing is H2 2026.



Source: Medicines Patent Pool, May 2024.

CAB for PrEP – Next Steps for Product

PRICE

- Advocate for price reduction from 2024 onwards.
- Advocate for expanded lowest pricing eligibility criteria to ensure MICs can access CAB at non-profit price.

PROCUREMENT

- Understand procurement to date and plans for 2024 and 2025, based on ViiV's current forecast.
- Address country-level product-sharing issues.

DEMAND

- Build demand side support and in-country demand.

GENERICS

- Monitor progress on the need to remove oral CAB development and with regulators to understand requirements and data gathering for request to modification in some labels – *(also mentioned in regulatory / clinical guidance section)*.
- Technology transfer will continue throughout (and until the end of) generic product development.
- Advocate to define a target price for generics and potentially negotiating some form of price guarantee with generics based on market shaping approach.

FINAL VERSION

CAB for PrEP - Regulatory Approval & Normative Guidance Summary

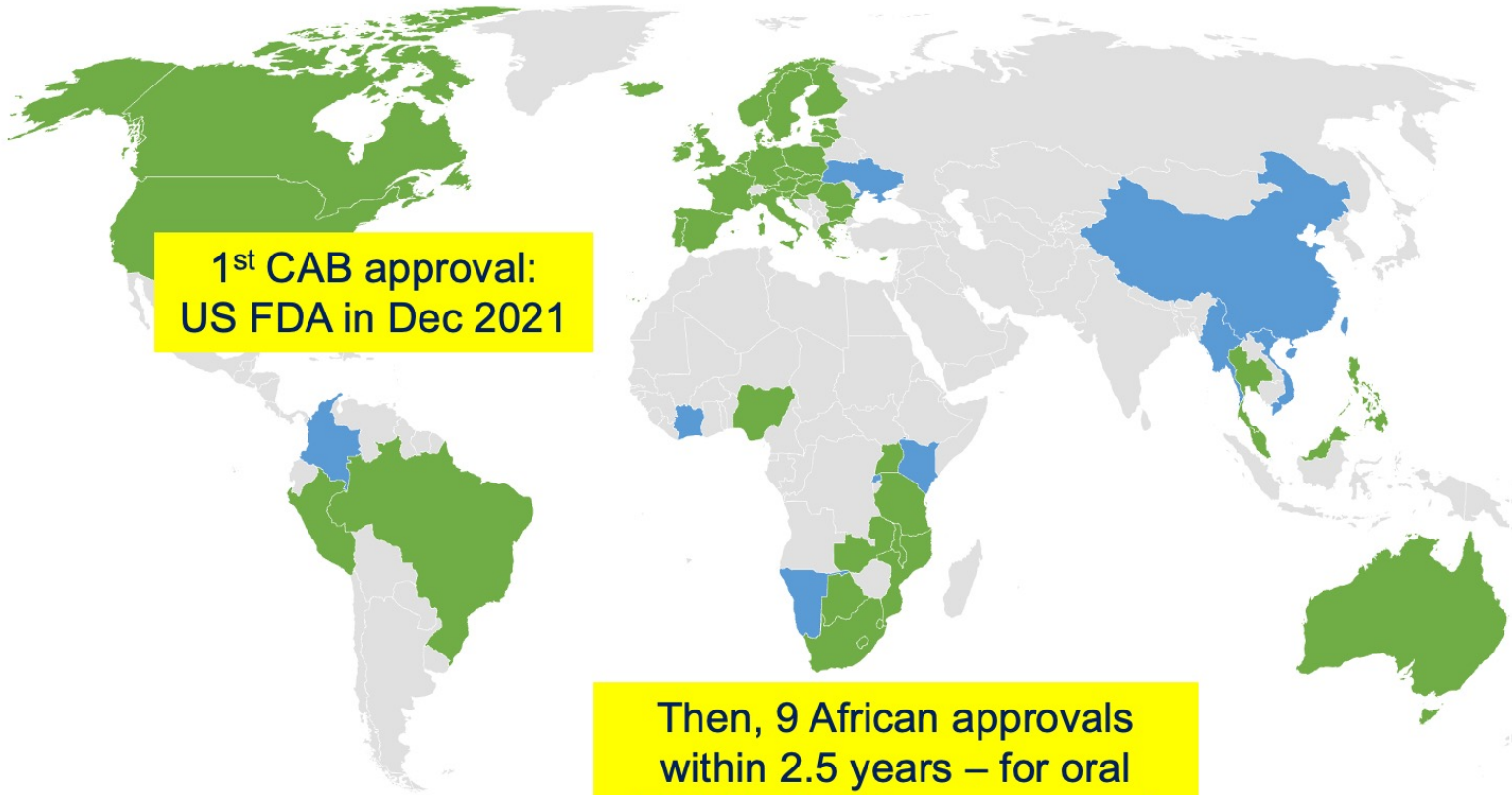
Complete | Some progress | No progress

	Proposed priorities outlined in 'Plan for CAB' (July 2022)	Status as of March 2024	Progress
1	Eight regulators currently reviewing injectable CAB for PrEP to ensure priority review.	CAB has been approved in 18 countries and the European Medicines Agency (totaling 48) and there are submissions for approval in 12 others. Countries shown in next slide.	
2	ViiV to pursue widespread registration of CAB in high-burden countries*.	Out of the 34 high-burden countries, 17 have acquired or are pending approval.	
3	ViiV to register with WHO Pre-Qualification (PQ) to allow expedited registration in countries participating in WHO's Collaborative Procedure for Accelerated Registration process.	CAB added to WHO's expression of interest list in April 2022 with prequalification normally expected about two years later. CAB for PrEP added to WHO guidelines in July 2022 with adaptation for in-country guidelines pending. PQ granted in December 2023.	

* High-burden countries are classified as the following 25 PEPFAR priority countries and the additional 9 listed in the Global Prevention Coalition Prevention Roadmap

CAB for PrEP - Regulatory Approval & Normative Guidance Summary

19 regulatory approvals; 10 pending



1st CAB approval: US FDA in Dec 2021

Then, 9 African approvals within 2.5 years – for oral TDF/FTC, 3.5 years passed after FDA approval before **any** African approvals

Approved	Pending
1. Australia	1. China
2. Botswana	2. Columbia
3. Brazil	3. Côte d'Ivoire
4. Canada	4. Kenya
5. EMA	5. Myanmar
6. Malawi	6. Namibia
7. Malaysia	7. Rwanda
8. Mozambique	8. Taiwan
9. Nigeria	9. Ukraine
10. Peru	10. Vietnam
11. Philippines	
12. South Africa	
13. Tanzania	
14. Thailand	
15. Uganda	
16. UK	
17. US	
18. Zambia	
19. Zimbabwe	

As of May 2024

AVAC
Advocacy. Access. Equity.

CAB for PrEP – Next Steps for Regulatory Approval & Normative Guidance

EXPAND AND ACCELERATE APPROVALS

- Advocate with ViiV for additional regulatory submissions in high-burden countries.
- Accelerate currently pending approvals and push for submissions in high burden countries as identified by the HIV Prevention Coalition, and those prioritized by PEPFAR.
- Identify partners who can support national medical regulatory authorities to rapidly review CAB and define bioequivalence pathway for generics.

ADVOCATE

- Advocate for in-country adaptation and adoption of CAB for PrEP guidelines.

GENERICS

- Monitor progress on the need to remove oral CAB development and registration from sublicence agreements *(also mentioned in product section)*.

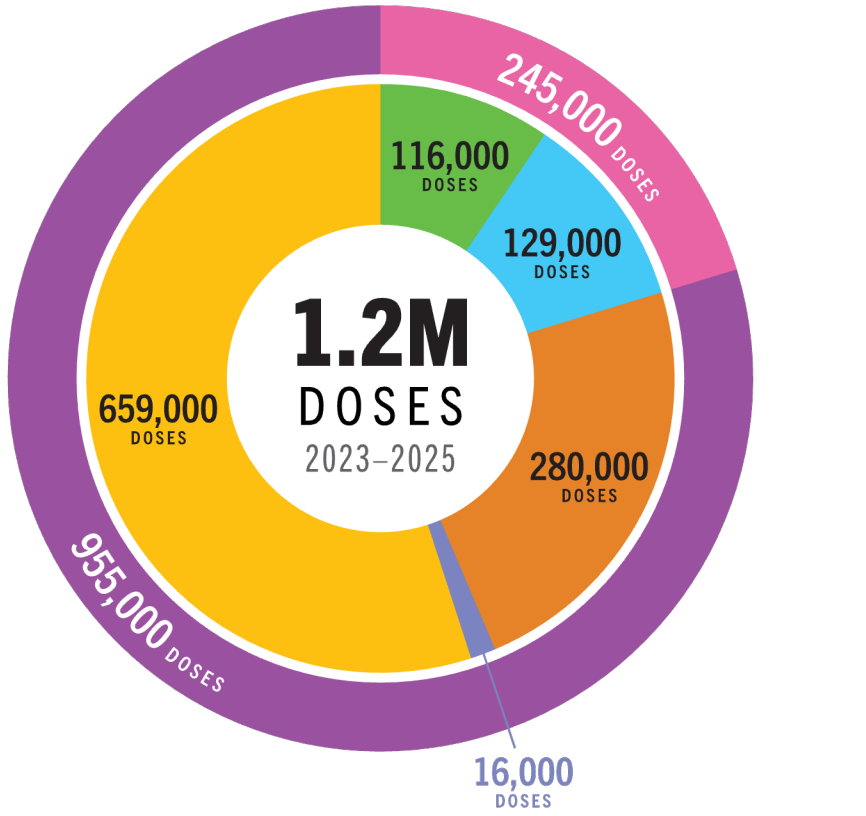
CAB for PrEP – Planning & Budgeting

Complete | Some progress | No progress

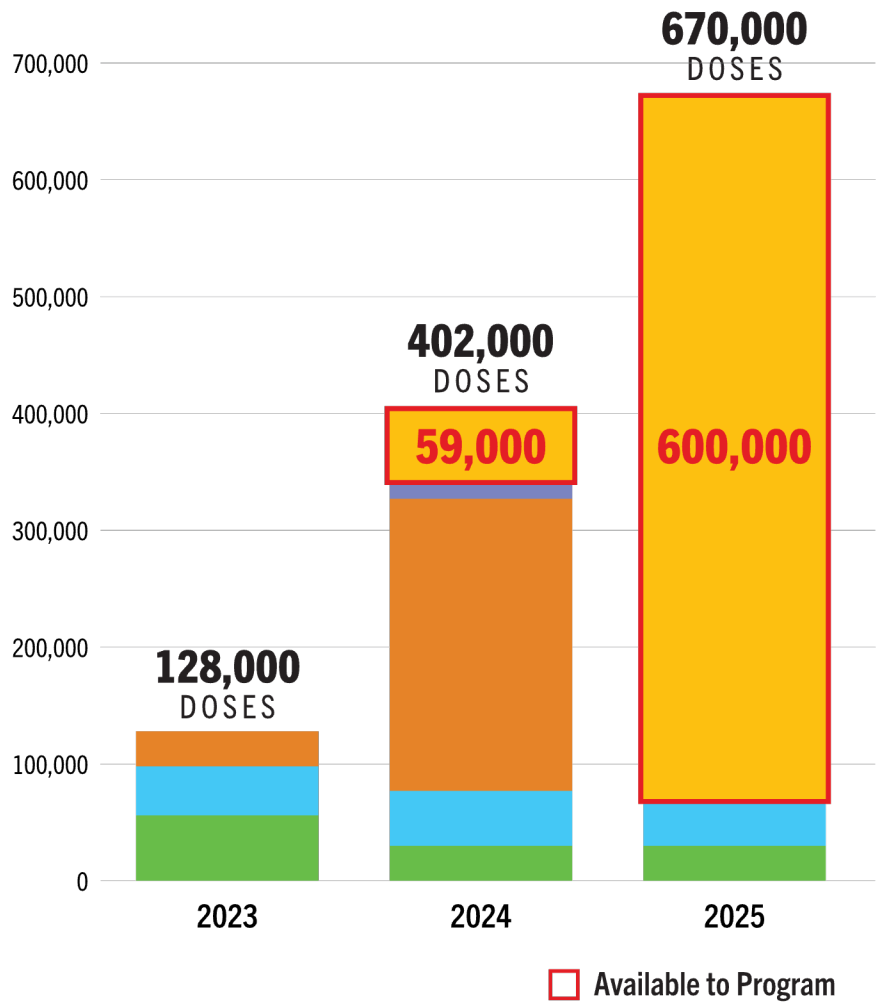
	Proposed priorities outlined in 'Plan for CAB' (July 2022)	Status as of March 2024	Progress
1	Governments and donors to set targets for supply and programs at scale – what is needed and possible in 2022-2023 in implementation science projects, and what is needed from 2024 to begin programs at scale.	Ambitious PEPFAR and Global Fund (GF) supply targets set for 2023-2025. PEPFAR has procured 250k to date.	

CAB for PrEP – Planning & Budgeting

Current (April 2024) allocation of Non-Commercial CAB for PrEP Supply in Low- and Middle-Income Countries, 2023-2025* — **BY CATEGORY**

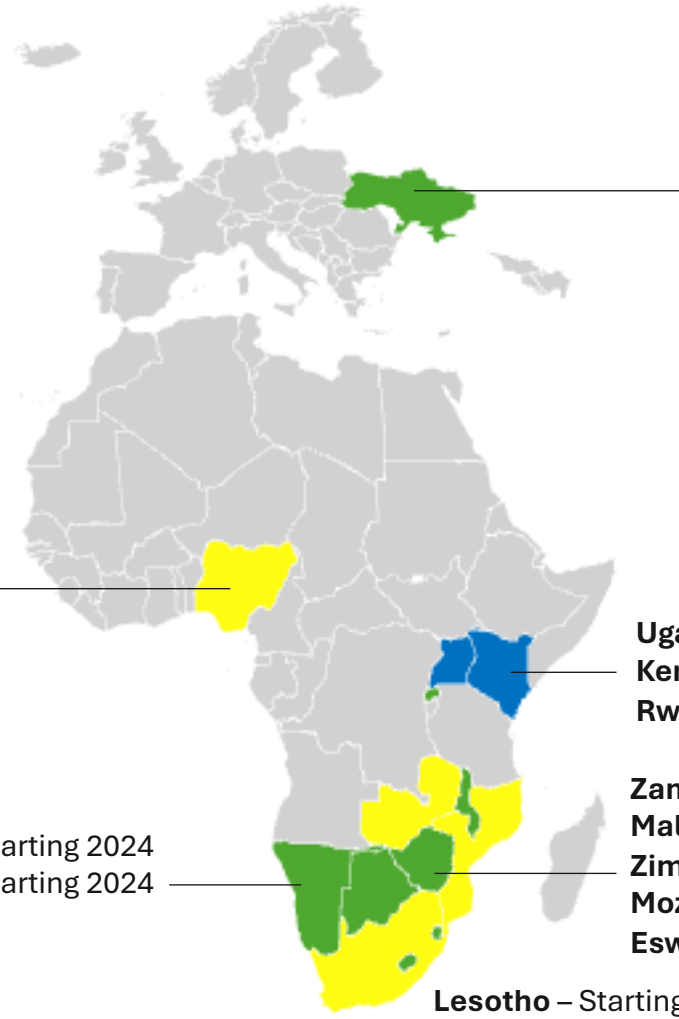


Current (April 2024) allocation of Non-Commercial CAB for PrEP Supply in Low- and Middle-Income Countries, 2023-2025* — **BY YEAR**



CAB for PrEP – Planning & Budgeting

Accomplishments and Work as of March 2024



Ukraine – 100 People

Nigeria – Starting 2024 and $6.5M

Uganda – $3M
Kenya – $3M
Rwanda – Starting 2024

Zambia – 6,000-12,000 people and $3M
Malawi – 10,000 people
Zimbabwe – 2,000 people
Mozambique – Starting 2024 and $3.75M
Eswatini – Starting 2024

Namibia – Starting 2024
Botswana – Starting 2024

Lesotho – Starting 2024
South Africa – Starting 2024 and $5.75M

- PEPFAR Procurement
- Global Fund(GF) Matching Funds
- PEPFAR + GF Matching Funds

Last Updated: March 2024

CAB for PrEP – Next Steps for Planning & Budgeting

PRODUCT MARKET

- Build demand-side support and in-country demand.
- Need to build sustainable markets; and continue to support on country prioritization for procurement and funding.
- Link modellers and Implementation Science (IS) leads so modellers can use latest IS data to refine models for demand and impact forecasting.

SUPPLY

- Push for additional volumes to be available for PEPFAR, GF and national procurement.
- Support other donors and governments to set supply targets.

PROGRAMMATIC

- Advance a learning agenda for programmatic roll-out, aiming to share this via a regular platform *(also mentioned in monitoring and evaluation section)*.

FINAL VERSION

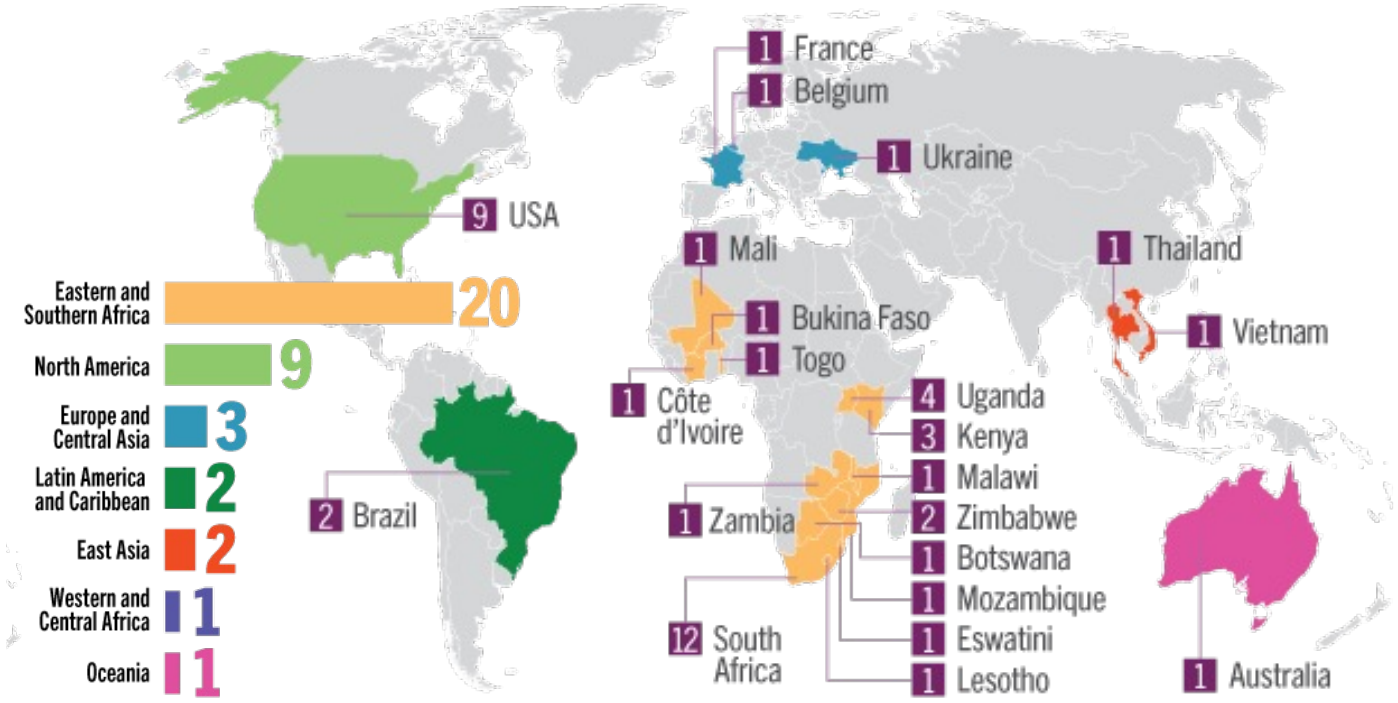
CAB for PrEP – Delivery & Supply Chain

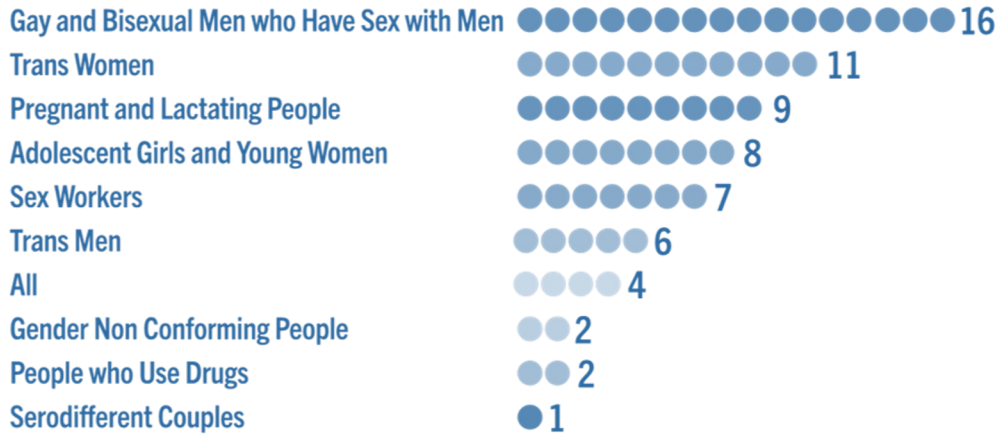
Complete | Some progress | No progress

	Proposed priorities outlined in 'Plan for CAB' (July 2022)	Status as of March 2024	Progress
1	Large, resourced and coordinated implementation studies (IS) to begin immediately to answer critical questions about how CAB performs outside the clinic setting and across populations.	Of the 34 planned and ongoing IS for CAB for PrEP, 9 have committed supply from ViiV. PEPFAR has procured larger volumes for programmatic activities in five additional countries with additional launches to come.	
2	Provider training materials and tools updated to incorporate CAB administration and implementation studies that assess the feasibility of task-shifting to expand the cadres of providers that are authorized and trained to administer injections and that offer choice and assist in shared decision-making.	Extensive work done has been done by WHO, Jhpiego, MOSAIC, and others to develop materials to better equip providers with the knowledge they need to distribute CAB to their patients. Many of these materials can be found on PrEPWatch.org.	
3	Innovative demand creation strategies developed with process to test then iterate and share across projects.	The USAID funded project, MOSAIC, has been leading demand generation for PrEP including positioning in adolescents and young women. However, there is need for more investments to implement at scale (geography and populations).	
4	Testing requirements should not become a barrier to CAB introduction. Testing strategies should be both robust and feasible and work with locally available tests and assays to, maximize the benefits of access to CAB while minimizing the risk of undetected cases.	WHO guidelines and regulatory approvals / labels are permissive so that testing does not become a barrier to CAB introduction.	

CAB for PrEP – Delivery & Supply Chain

As of March 2024, of the **38 ongoing** and planned implementation studies for CAB for PrEP, **11** have committed supply from ViiV and **5** are receiving supply from PEPFAR.*





Note: Currently, only four countries are in active programmatic rollout – the USA, Zambia, Zimbabwe and Malawi.

*Note that since some studies are multi-country, the # of countries does not match to the # of studies.

Last Updated: March 2024

CAB for PrEP – Next Steps for Delivery & Supply Chain

DELIVERY

- Follow programmatic rollout in case of any potential "last mile" delivery issues.

STUDY TRACKING

- Tracking all the studies for new PrEP options and sharing updates in real time via PrEPWatch (prepwatch.org/studies).
- Adding published results to the study tracker as they are made available.

INFORMING FUTURE STUDIES

- Evidence gaps continue to be identified and addressed through the Implementation Science Think Tanks.
- Mapping studies' primary research questions against critical implementation science questions to identify and address remaining gaps.
- Convening implementers, researchers, MoH representatives, donors, and CSOs to share emerging evidence from implementation studies and turning these into actionable insights.
- Convening implementers and modelers to share research insights and establish a formal framework for data sharing, ensuring that models are built from the latest evidence.
- Advocate for parallel approach where ongoing research, implementation science, and scale-up programs can be designed, funded, and implemented in parallel.

CAB for PrEP – Stakeholder Engagement

Complete Some progress No progress

	Proposed priorities outlined in 'Plan for CAB' (July 2022)	Status as of March 2024	Progress
1	Integrate and engage civil society in all decision-making relevant to planning and preparation for access to CAB, including designing, conducting and monitoring implementation studies and delivery programs.	Establishment of the Coalition's Civil Society (CS) Caucus, with members from 17 international organizations, to strengthen transparency, share updates and perspectives, and create dialogue between CS and conveners. CS Caucus members nominated three representatives to act on behalf of the caucus at Coalition meetings and are responsible for sharing and disseminating information between the caucus and other stakeholders. Facilitate bi-monthly meetings with the CS Caucus Hosted Civil Society Symposium including sessions with PEPFAR, PopCouncil, ViiV and Gilead. Invite the caucus and other civil society organizations to attend the Quarterly Coalition Meeting	

CAB for PrEP – Stakeholder Engagement

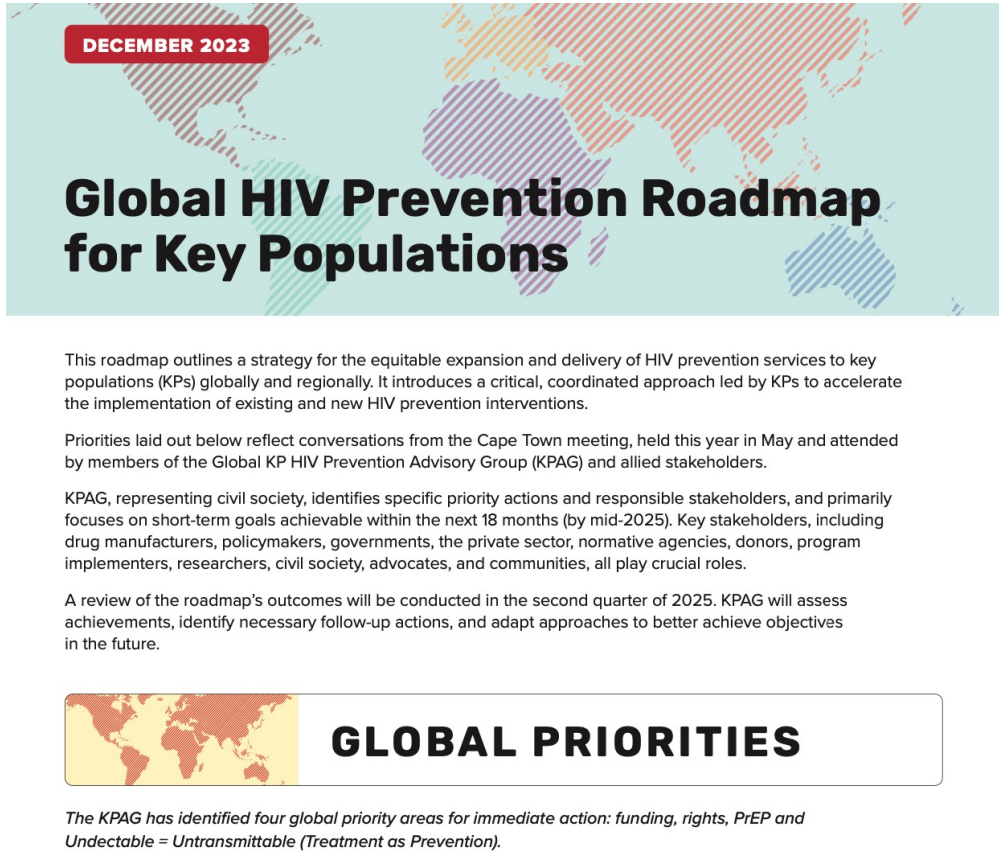
CSO Caucus Participating Organizations	
Organization	**Area Servicing**
ACTS 101	Uganda
Advocacy for Prevention of HIV & AIDS (APHA)	South Africa
African Women's HIV Prevention Community Accountability Board	Africa
AfroCAB	Africa
AGE Africa	Africa
Alliance for Public Health	Ukraine
APCOM	Asia and the Pacific
AVAC	Global
Coalition to Accelerate & Support Prevention Research (CASPR)	Global; East & Southern Africa
Frontline AIDS	Global
Global Black Gay Men Connect (GBGMC)	Global
Global Network of People Living with HIV (GNP+)	Global

CSO Caucus Participating Organizations	
Organization	**Area Servicing**
Coalition for Health Promotion and Social Development (HEPS – Uganda)	Uganda
International Community of Women living with HIV/AIDS Eastern Africa (ICWEA)	Eastern Africa
ITPC	South Africa
Key Population Advisory Group	Global
Outright International	Global
Prevention Access Campaign (PAC)	Global
Pangaea Zimbabwe AIDS Trust (PZAT)	Zimbabwe
Treatment Advocacy and Literacy Campaign (TALC)	Zambia
WACI Health	Africa

CAB for PrEP – Stakeholder Engagement

Voices for Choice: African Women Prevention Community Accountability Board Choice Manifesto, and Key Population Advisory Group Prevention Roadmap

[HIV Prevention Choice Manifesto]



[KP Prevention Roadmap]

CAB for PrEP – Next Steps for Stakeholder Engagement

ADVOCATE

- Create collective advocacy strategies to address most pressing barriers to access.

COLLABORATION

- Continue to integrate and engage civil society in decision-making relevant to planning and preparation for access, including designing, conducting and monitoring implementation studies and delivery programs.
- Coordinate, support, and provide a platform for Coalition engagement with next-generation PrEP product developers to keep product developers transparent and accountable to their commitments.

CAB for PrEP – Research

Complete | Some progress | No progress

	Proposed priorities outlined in 'Plan for CAB' (July 2022)	Status as of March 2024	Progress
1	Data to be collected on the benefit of injectable CAB as PrEP for populations that were not part of efficacy trials, especially adolescents, pregnant and breast-feeding people, and transmasculine and gender non-conforming individuals.	There are 38 planned and ongoing implementation studies for CAB for PrEP. More information can be found on the Integrated Study Dashboard Under BioPIC, Implementation Science Think Tanks have explored and identified strategies for inclusion of pregnant and lactating populations and trans populations in implementation science studies.	
2	Study alternate injection sites and frequency of injections, recognizing that the impact of injectable CAB holds the potential to expand, if the injection schedule could align with injectable contraception.	Data from HPTN 084 showed potential for three-monthly injection, but not sufficient for a regulatory process. ViiV is developing an every four-month formulation (Phase 1 data presented at CROI in March 2024) Alternate injection site not being prioritized.	

CAB for PrEP – Research

As of March 2024

Country	CAB for PrEP Regulatory Status	DVR Regulatory Status	HPTN 083/084 Studies	Ring/ASPIRE Studies	PURPOSE 1/2 Studies	PEPFAR CAB Procurement 2023-2025 (# people)	Global Fund PrEP Matching Funds	Approved Implementation Studies	Planned Implementation Studies
Botswana	Approved	Approved	✓					1	
Eswatini	Via South Africa	Approved	✓			Starting 2024/25		1	1
Ethiopia		To file in 2023							
Kenya	Pending	Approved	✓			Priority waitlist	$3,000,000	3	
Lesotho	Via South Africa	Approved				Starting 2024/25		1	
Malawi	Approved	Pending	✓	✓		10,000		1	
Mozambique	To file in 2023	To file in 2023					$3,750,000		1
Namibia	Pending	Pending							
Rwanda	Pending	Approved							
South Africa	Approved	Approved	✓	✓	✓	Starting 2024/25	$5,750,000	11	1
Tanzania	Pending	Under Appeal							
Uganda	Pending	Approved	✓	✓	✓		$3,000,000	4	
Zambia	Approved	Approved				8,000- 10,000	$3,000,000	1	
Zimbabwe	Approved	Approved	✓	✓		10,000- 12,000		2	1
Nigeria	Pending	To file in 2023				Priority waitlist	$6,500,000		
Togo									1

- A Product Introduction Country Planning Matrix has been created and is being maintained, consolidating information on approvals, studies, and procurement by country
- The matrix will continue to be updated in real time to identify gaps in product introduction plans by country

Country Planning for Product Introduction Matrix

CAB for PrEP – Next Steps for Research

FUTURE STUDIES

- Guide additional gaps to be answered by future studies.
- Further research on long-term effects and use in conjunction with other prevention methods.

TRACKING

- Continually update and monitor product introduction via Country Planning Matrix database in real time to identify gaps in product introduction plans by country.
- Disseminate updates based on new research and epidemiological data.
- Tracking, synthesizing, and sharing early learnings from on-going studies for advocacy and scale-up.

CAB for PrEP – Monitoring & Evaluation

Complete Some progress No progress

	Proposed priorities outlined in 'Plan for CAB' (July 2022)	Status as of March 2024	Progress
1	Data to be collected on the benefit of injectable CAB as PrEP for populations that were not part of efficacy trials, especially adolescents, pregnant and breast-feeding people, and transmasculine and gender non-conforming individuals.	There are currently 32 ongoing studies with 14 including adolescents, 12 including pregnant and breast-feeding people, and 9 transmasculine and gender non-conforming individuals. Data will be collected on an ongoing basis and shared via the Product Introduction Matrix, Integrated Study Dashboard, and Global PrEP Tracker.	N/A – rollout just started

CAB for PrEP – Next Steps for Monitoring & Evaluation

EVALUATION PROCESS

- Continue to coordinate modeling exercises.
- Advocate for "PrEP dispensed by method" as new indicator.

TRACKING

- Data will be collected on an ongoing basis and shared via the Product Introduction Matrix, Integrated Study Dashboard, and Global PrEP Tracker.
- Map early IS insights to initial WHO/BioPIC Implementation Science Questions for CAB for PrEP, and update as needed.

PROGRAMMATIC

- Advance a learning agenda for programmatic roll-out, aiming to share this via a regular platform *(also mentioned in planning and budgeting section)*.

Tracking progress to market of new Long-Acting (LA) PrEP products

Dapivirine Vaginal Ring (DVR)

DVR – Product Summary

Complete | Some progress | No progress

	Priorities	Status as of March 2024	Progress
1	PopCouncil to work with generic manufacturers and donors, including Africa-based manufacturers, to expedite technology transfer and ensure sustainable supplies of the product.	MOU signed with Kiara Health in South Africa. No clear timeline for resource mobilization, technology transfer, manufacturing scale up, potential volumes or price.	
2	Kiara Health to identify capital expenditure needs and timeframe to be able to develop capacity.	No clear timeline or plan in place.	
3	Innovative donor(s) to fund capital investments needed for generic manufacturing to reach scale.	No additional CapEx identified.	
4	PopCouncil to confirm publicly maximum volume/quantity and price for 2024/25.	**Non-profit price**: PopCouncil confirmed commodity price between $12-15 per ring for current volumes. **Volumes**: 115K rings have been shipped to countries (both sold or donated); 500k rings produced by end of 2023 – packaged and ready for sale; additional 500k to be produced by end of 2024	

DVR – Product Summary

Complete Some progress No progress

	Priorities	Status as of March 2024	Progress
5	Donors to negotiate this price/volume guarantee to ensure sustainable supply for initial introduction period, given the timeline for generic licensing agreements and manufacturing upgrades	Supply constrained by the number / capacity above; any reduction dependent on increased volume	
6	Track, synthesize, and share learnings ongoing studies on the three-month ring	One study, MTN-036/IPM 047 has been conducted. The three-month rings were well-tolerated and achieved higher dapivirine concentrations compared with the monthly ring. These findings support further evaluation of three-month rings for HIV prevention.	

DVR – Product Manufacturer

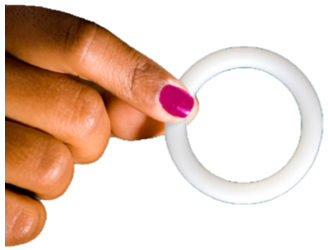
PopCouncil purchased the DVR from IPM and working on local manufacturing partnership

- PopCouncil acquired the DVR from IPM in 2022.
- PopCouncil announced in November 2023 their memorandum of understanding (MOU) with Kiara Health (South Africa). The goal is that this exclusive license for local manufacturing for the DVR in the currently approved 11 territories will allow Kiara health to substantially lower the cost of the product over the next few years.
- Awaiting plans from Kiara Health for local manufacturing. Unclear on timeline for development of first ring.

*PopCouncil 2023, https://popcouncil.org/media/innovative-hiv-prevention-product-for-women-that-promotes-choice-dapivirine-vaginal-ring-dvr-gains-momentum-across-africa/.

DVR – Product Price and Initiations

VS



- Kiara Health's acceleration of local manufacturing may eventually bring the price down further, although this may take several years.
- Current initiations: Since Q4 2023, there have been 1,502 initiations of the ring *
- Current product Distribution is via PopCouncil partnership with Imres BV

* Cumulative number of initiations, https://data.prepwatch.org/. This means that the number potentially accounts for the same user re-initiating use of a ring after stopping, rather than 1,502 separate users. Number shown does not include use of rings in implementation studies.

DVR – Next Steps for Product

LOCAL MANUFACTURING

- PopCouncil to support Kiara Health accelerate local manufacturing.
- PopCouncil to share details volumes available for 2024/25.
- Kiara Health to share plans for local manufacturing.

PRICE

- Donors / Coalition to negotiate for lower pricing.

COMMUNICATION STRATEGY

- Draft clear messaging about DVR from Coalition, including ways in which GF and PEPFAR can partner as per PEPFAR SAB recommendation.

NEW PRODUCT

- Track development of new product – PoP Council is developing a longer duration DVR for three months versus one month to significantly lower annual costs and offer a woman a more convenient option to protect themselves. Development of this longer duration ring will be completed and submitted for regulatory approval by late 2024 to mid 2025, after which Kiara Health will assume a leading role in ensuring its access.

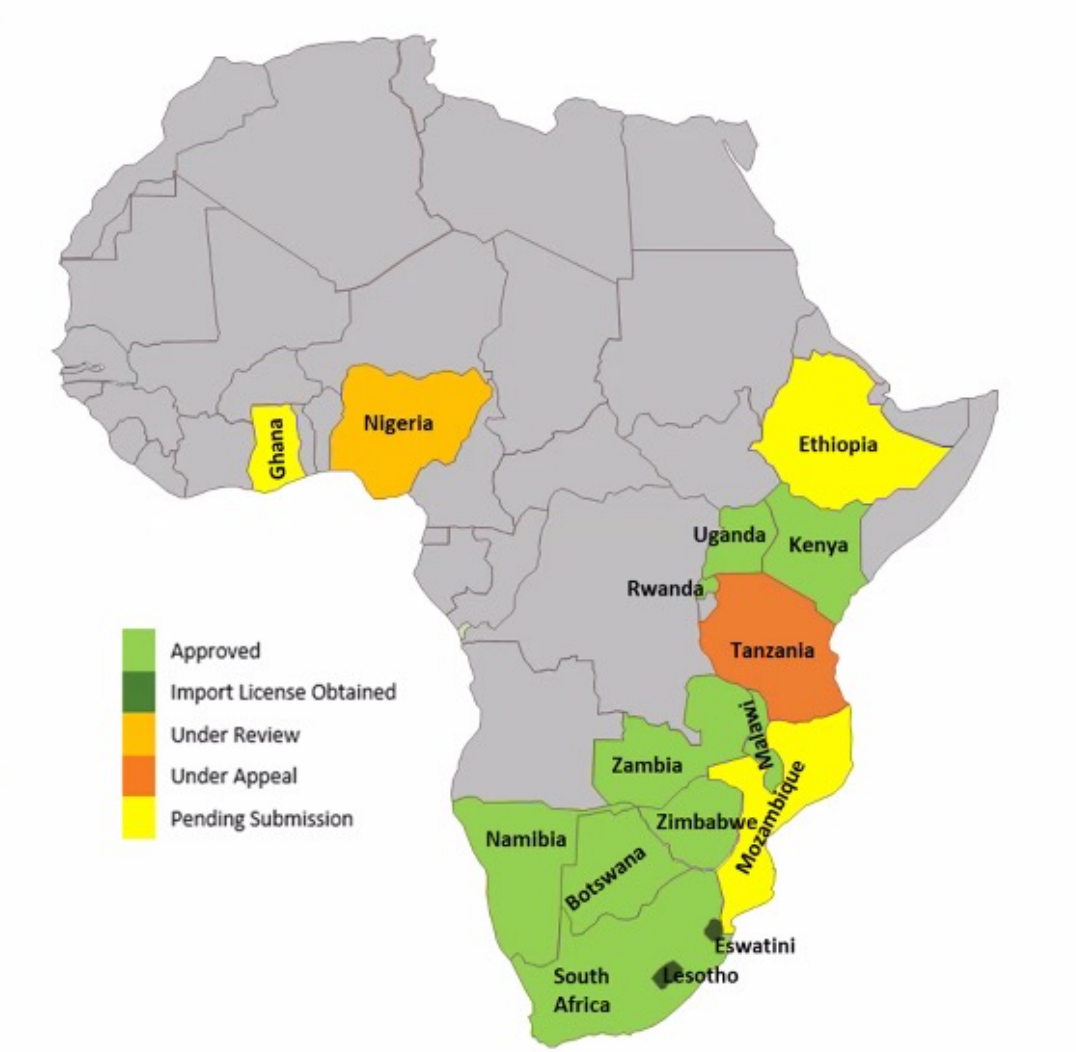
DVR – Regulatory Approval & Normative Guidance Summary

Complete | Some progress | No progress

	Priorities	Status as of March 2024	Progress
1	EMA positive scientific opinion and WHO recommendation and PQ hopefully to accelerate African regulatory approvals	DVR has been approved in 11 African countries; more approvals pending.	
2	Expand registration and guidance for DVR use among pregnant and lactating populations.	**DELIVER**: Enrolled 150 pregnant participants, ages 18 to 40, participants (DVR: 101 and Oral PrEP: 49). In this first study of a long-acting HIV prevention agent in pregnancy, adverse pregnancy outcomes and complications were uncommon when DVR and TDF/FTC were used in the third trimester of pregnancy and were similar to rates observed in the communities where the study is being conducted. **B-PROTECTED**: Enrolled 197 mother-infant pairs (DVR: 148, Oral PrEP: 49). Results indicate high uptake of study product in both arms with extremely low concentrations of dapivirine (DVR arm) detected in infant plasma samples. In the oral PrEP arm, tenofovir diphosphate concentrations from infant DBS were all below the lower limit of quantitation.	

DVR – Regulatory Approval & Normative Guidance Summary

11 regulatory approvals; **2** pending review/appeal; **3** submissions in preparation as of March 2024



APPROVED

1. Botswana
2. Eswatini
3. Kenya
4. Lesotho
5. Malawi
6. Namibia
7. Rwanda
8. South Africa
9. Uganda
10. Zambia
11. Zimbabwe

UNDER REVIEW

1. Nigeria

PENDING

1. Ethiopia
2. Ghana
3. Mozambique

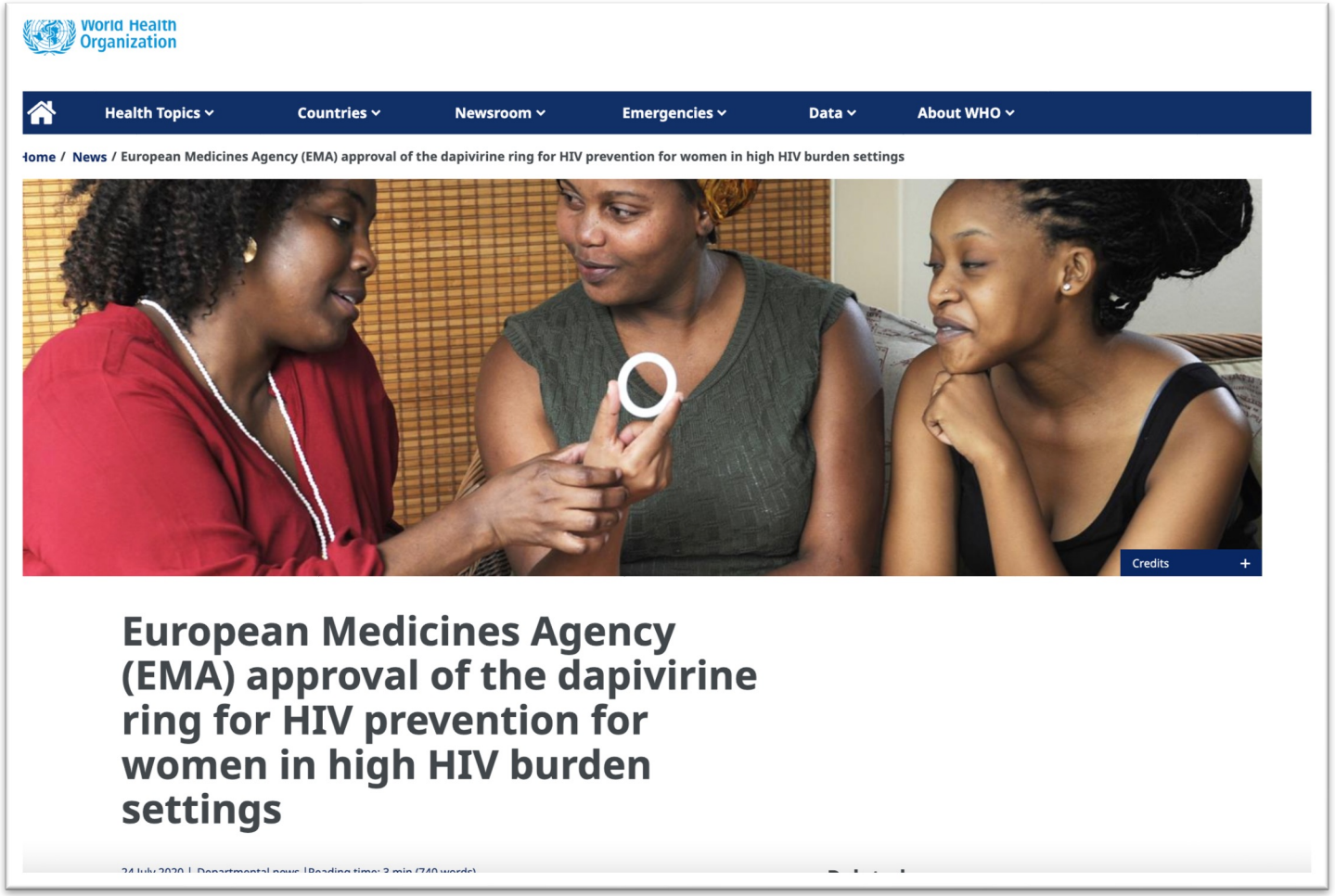
UNDER APPEAL

1. Tanzania

Last Updated: March 2024

DVR – Regulatory Approval

No approval by the FDA, and currently not being pursued



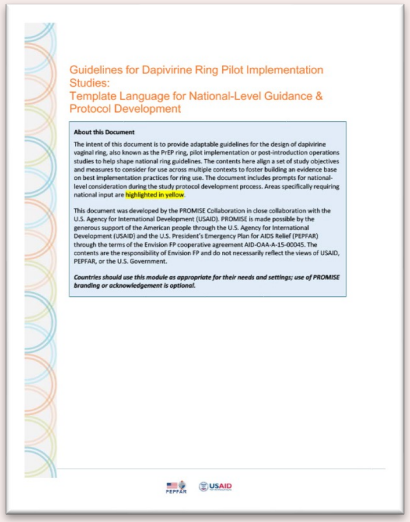
- In 2020, DVR received a positive scientific opinion from the EMA for use in women over 18 years old in high HIV burden settings.
- In the United States, a New Drug Application (NDA) for DVR was submitted to the FDA by IP
- However, in December 2021, the application was withdrawn by IPM due to the unlikelihood of approval.

https://www.who.int/news/item/24-07-2020-european-medicines-agency-(ema)-approval-of-the-dapivirine-ring-for-hiv-prevention-for-women-in-high-hiv-burden-settings

DVR – Normative Guidance Summary

In 2021, DVR received WHO recommendation and guidelines

- In 2021, the WHO recommended*^ DVR as an additional prevention choice for women at substantial risk of HIV.
  - Current evidence suggests that oral daily PrEP, when taken as prescribed, has greater efficacy for HIV prevention than the dapivirine vaginal ring.
  - Oral PrEP should be offered at sites where the ring is provided to enable women to make a choice.



Guidelines for PrEP Ring Pilot Implementation Studies – Template language for national-level guidance and protocol development

- PEPFAR and USAID created a template^^ based on a document originally developed by the dapivirine ring task force within the PrEP Technical Working Group, led by the Ministry of Health of the Government of Zambia.
- It is designed for policymakers and government technical specialists to use to apply uniform objectives, study design features, and measures across pilot implementation and other operations research studies for ring introduction, in collaboration with investigator teams.

*https://www.who.int/news/item/26-01-2021-who-recommends-the-dapivirine-vaginal-ring-as-a-new-choice-for-hiv-prevention-for-women-at-substantial-risk-of-hiv-infection
^ https://www.who.int/publications/i/item/9789240031593
^^https://www.prepwatch.org/resources/guidelines-for-prep-ring-pilot-implementation-studies/

DVR – Regulatory Approval & Normative Guidance Summary

EXPAND AND ACCELERATE APPROVALS

- Advocate for additional submissions in high burden countries.
- Understand specifically what data PEPFAR needs to learn in the current implementation science projects to consider larger programmatic procurement; and to acquire FDA approval.
- Encourage data to build case for PEPFAR procurement.

ADVOCATE

- Advocate for in-country adaptation and adoption of CAB for PrEP guidelines.

TRACKING

- Ongoing updates based on new research and epidemiological data.

DVR – Planning & Budgeting

Complete | Some progress | No progress

	Priorities	Status as of March 2024	Progress
1	Governments and donors to set targets for supply and programs at scale – what is needed and possible in 2024-2025 in implementation science projects, and what is needed to begin programs at scale.	Global Fund has received funding from CIFF for a Prevention Matching Fund which can support procurement; initial DVR procurement in several countries for programmatic supplies via GC7. PEPFAR has committed to an initial purchase of DVR for implementation science projects, including CATALYST Study in five countries and SEARCH in Kenya and Uganda. 400k rings available currently, 1M projected for 2024-25. Initial DVR programmatic procurement in several countries for supplies via GC7.	

DVR – Next Steps for Planning & Budgeting

PRODUCT MARKET

- Develop plan to build demand-side support and in-country demand.
- Identify potential opportunities for further analyses and funding strategies for scale-up.

SUPPLY

- Identify in-country targets with ministries of health
- Document and disseminate what has been procured to date and current DVR available volumes for 2024 and 2025

PROGRAMMATIC

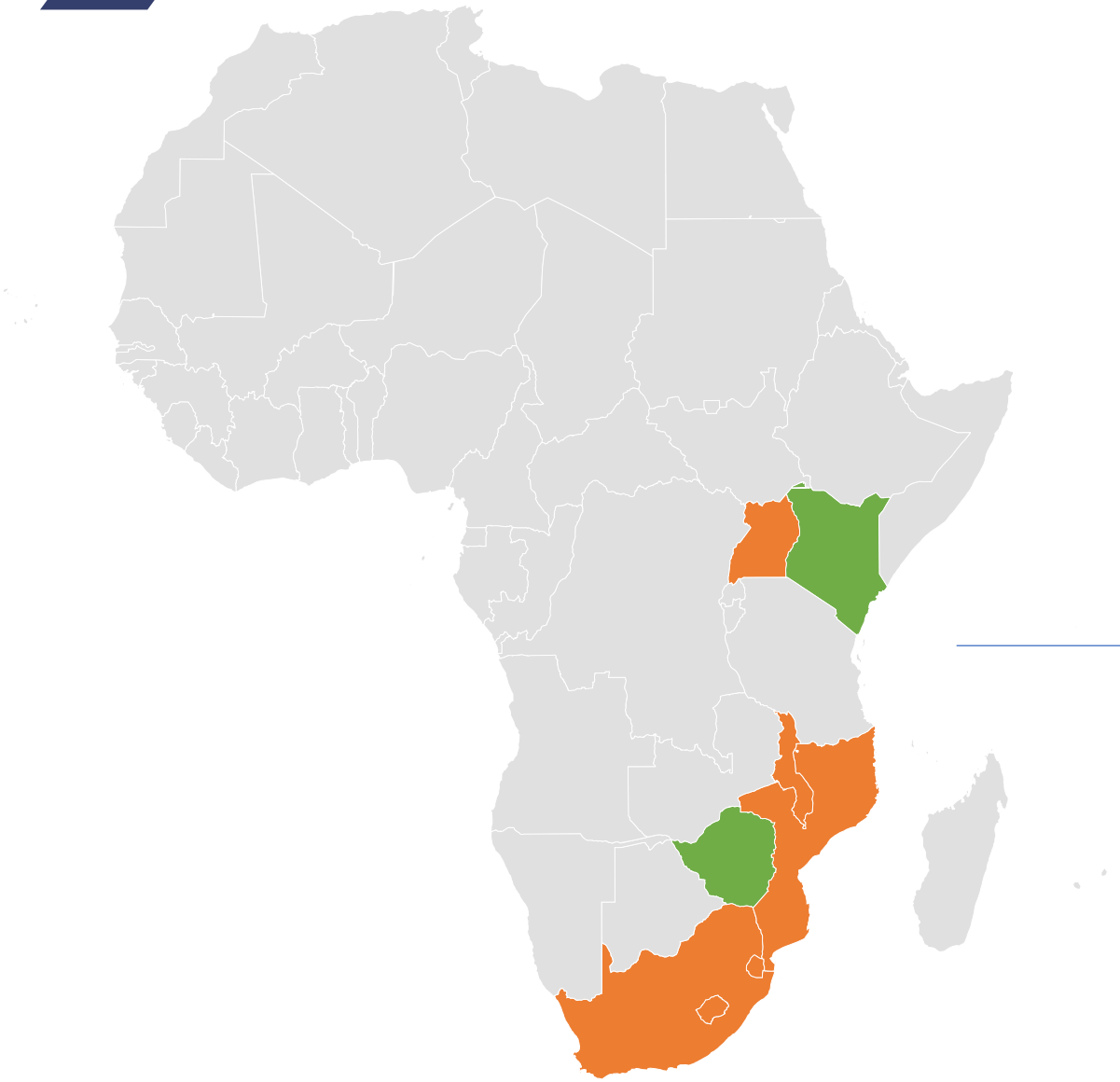
- Advance a learning agenda for programmatic roll-out, aiming to share this via a regular platform (*also mentioned in delivery & supply chain section)*

DVR – Delivery & Supply Chain

Complete Some progress No progress

	Priorities	Status as of March 2024	Progress
1	Large, resourced and coordinated implementation studies (IS) to begin immediately to answer critical questions about how DVR performs outside the clinic setting and across populations.	13 ongoing & planned implementation studies (7 countries) offering DVR as part of choice.	

DVR – Delivery & Supply Chain



13 ongoing & planned implementation studies in **7** countries as of March 2024

ONGOING

1. **Eswatini**
2. **Mozambique**
3. **Lesotho**
4. **South Africa**
5. **Uganda**

BOTH

1. **Kenya**
2. **Zimbabwe**

Note: Currently, 1,052 product initiations on DVR since Q4 2023 (in Uganda, Zimbabwe, and South Africa).

Last Updated: March 2024

DVR – Next Steps for Delivery & Supply Chain

STUDY TRACKING

- Track all the studies for new PrEP options and share updates on DVR in real time.
- Add published results to the study tracker as they are made available.

INFORMING FUTURE STUDIES

- Guide additional gaps to be answered by future studies.

PROGRAMMATIC

- Advance a learning agenda for programmatic roll-out, aiming to share this via a regular platform *also mentioned in planning and budgeting section)*.

DVR – Stakeholder Engagement

Complete | Some progress | No progress

	Priorities	Status as of March 2024	Progress
1	Integrate and engage civil society in all decision-making relevant to planning and preparation for access to CAB, including designing, conducting and monitoring implementation studies and delivery programs.	Establishment of the Coalition's Civil Society (CS) Caucus, with members from 17 international organizations, to strengthen transparency, share updates and perspectives, and create dialogue between CS and conveners. CS Caucus members nominated three representatives to act on behalf of the caucus at Coalition meetings and are responsible for sharing and disseminating information between the caucus and other stakeholders. Facilitate bi-monthly meetings with the CS Caucus Hosted Civil Society Symposium including sessions with PEPFAR, PopCouncil, ViiV and Gilead. Invite the caucus and other civil society organizations to attend the Quarterly Coalition Meeting Development of Choice Manifesto	

DVR – Stakeholder Engagement

CSO Caucus Participating Organizations	
Organization	**Area Servicing**
ACTS 101	Uganda
Advocacy for Prevention of HIV & AIDS (APHA)	South Africa
African Women's HIV Prevention Community Accountability Board	Africa
AfroCAB	Africa
AGE Africa	Africa
Alliance for Public Health	Ukraine
APCOM	Asia and the Pacific
AVAC	Global
Coalition to Accelerate & Support Prevention Research (CASPR)	Global; East & Southern Africa
Frontline AIDS	Global
Global Black Gay Men Connect (GBGMC)	Global
Global Network of People Living with HIV (GNP+)	Global

CSO Caucus Participating Organizations	
Organization	**Area Servicing**
Coalition for Health Promotion and Social Development (HEPS – Uganda)	Uganda
International Community of Women living with HIV/AIDS Eastern Africa (ICWEA)	Eastern Africa
ITPC	South Africa
Key Population Advisory Group	Global
Outright International	Global
Prevention Access Campaign (PAC)	Global
Pangaea Zimbabwe AIDS Trust (PZAT)	Zimbabwe
Treatment Advocacy and Literacy Campaign (TALC)	Zambia
WACI Health	Africa

DVR – Next Steps for Stakeholder Engagement

ADVOCATE

- Create collective advocacy strategies to address most pressing barriers to access.
- Ongoing engagement and education efforts to increase awareness and acceptance.
- Support the implementation of the HIV Prevention Choice Manifesto.

COLLABORATION

- Work alongside healthcare providers, policymakers, and community organizations.
- Continue to integrate and engage civil society in decision-making relevant to planning and preparation for access, including designing, conducting and monitoring implementation studies and delivery programs.
- Partner with Busara to work on human centered design and segmentation work in countries in the Global South.
- Coordinate, support, and provide a platform for Coalition engagement with product developers to keep product developers transparent and accountable to their commitments.

DVR – Research

Complete | Some progress | No progress

	Proposed Priorities	Status as of March 2024	Progress
1	Data to be collected on use of DVR among adolescents and among pregnant and lactating populations.	**REACH study**: exploring how adolescent girls and young women in sub-Saharan Africa use the DVR and daily oral PrEP, and their preferences for these approaches. Of these, 67 percent chose to use the ring and 31% chose to use PrEP – only 2 percent didn't want to use either. **DELIVER study**: assessing the safety of the DVR and Truvada as daily oral pill in pregnant women. Of the 750 women who will be enrolled, 500 will use the vaginal ring. **B-PROTECTED study**: evaluating the safety of Dapivirine Vaginal Ring and oral PrEP use by women who are breastfeeding.	

DVR – Research

Completed and ongoing studies

REVERSING THE EPIDEMIC IN AFRICA WITH CHOICES IN HIV PREVENTION

REACH

STUDY COMPLETE

REACH explored how adolescent girls and young women in sub-Saharan Africa use the DVR and daily oral PrEP, and their preferences for these approaches.

Nearly all (**98 percent**) of the 227 participants who took part in the choice period opted to use one of the two HIV prevention products being offered.

Of these, **67% chose to use the ring and 31% chose to use PrEP** – only 2% didn't want to use either.

deliver

A Study of PrEP and the Dapivirine Ring in Pregnant Women

STUDY ONGOING

Launched in January 2020, DELIVER is assessing the safety of the monthly DVR and Truvada as daily oral PrEP in pregnant women. Of the 750 women who will be enrolled, 500 will use the vaginal ring. The study is the **first to be conducted of the Dapivirine Vaginal Ring during pregnancy**.

Breastfeeding PrEP & Ring Open-label Trial

B PROTECTED

ONGOING STUDY

Launched in August 2020, B-PROTECTED is evaluating the safety of Dapivirine Vaginal Ring and oral PrEP use by women who are breastfeeding. B-PROTECTED will **enroll up to 200 mothers and their breastfed babies**.

DVR – Next Steps for Research

FUTURE STUDIES

- Guide additional gaps to be answered by future studies.
- Further research on long-term effects and use in conjunction with other prevention methods.

TRACING

- Ongoing updates based on new research and epidemiological data.
- Tracking, synthesizing and sharing early learnings from on-going studies for advocacy and scale-up.

DVR – Monitoring & Evaluation

Complete Some progress No progress

	Proposed Priorities	Status as of March 2024	Progress
1	Data to be collected on the benefit of DVR for populations that were not part of efficacy trials, especially adolescents, pregnant and breast-feeding people, and transmasculine and gender non-conforming individuals.	Data will be collected on an ongoing basis and shared via the Product Introduction Matrix, Integrated Study Dashboard, and Global PrEP Tracker.	

DVR – Next Steps for Monitoring & Evaluation

TRACKING

- Data will be collected on an ongoing basis and shared via the Product Introduction Matrix, Integrated Study Dashboard, and Global PrEP Tracker.

PROGRAMMATIC

- Advance a learning agenda for programmatic roll-out, aiming to share this via a regular platform *(also mentioned in planning and budgeting section)*.

Tracking progress to market of new Long-Acting (LA) PrEP products

Injectable
LEN

Proposed Injectable LEN Priorities

- PURPOSE 1 and 2 are fully enrolled, with results expected by end 2024
- The following priorities in parallel:
  - Engage with Gilead now to influence access and pricing and encourage transparency
  - Request Gilead to articulate plan for oral F/TAF once the PURPOSE 1 trial results are available.
  - Start discussing plan for IS studies with Gilead
  - Follow-up with Gilead on their stated plans to work with national and regional African regulatory mechanisms
  - Proactively dissuade message that the market should “wait for LEN”

Appendix

Oral PrEP Pricing

Oral PrEP Pricing Comparative History

Drug	Price/Year	Timing
US List Price for Truvada (TDF/FTC)	$21,108	Approved 7/2012
US List Price for Descovy (TAF/FTC)	$22,140	Approved 10/2019
US List Price for generic TDF/FTC	$17,460	From 5-11/2021 (1 generic)
US List Price for generic TDF/FTC	$396	From 11/2021 (multiple generics)
LMIC Price for generic TDF/FTC	$40	Since 12/2015 when approved

Comparative PrEP Pricing

New Injectables/ Ring PrEP Pricing

Drug	Price/Year	Timing
US List Price for originator CAB-LA (Apredtude) (injectable)	$22,200	Approved 12/2021
LMIC Price for originator CAB-LA (injectable)	±$240	“Not-for-profit” 3/2022 (CDA)
LMIC Price for originator CAB-LA (injectable)	±$180	“Not-for-profit” 1/2023 (CDA)
LMIC Price for originator CAB-LA (injectable)	±$170	“Not-for-profit” 10/2023 **(public)**
LMIC Price for generic injectable	???	Below $100/yr, based on COGS?
List Price for dapivirine vaginal ring	$156	From IPM/PC; SA mfg to come…