

What's New & Next in HIV Prevention

Update on Research & Development and Delivery

Mitchell Warren, Executive Director

4 August 2025

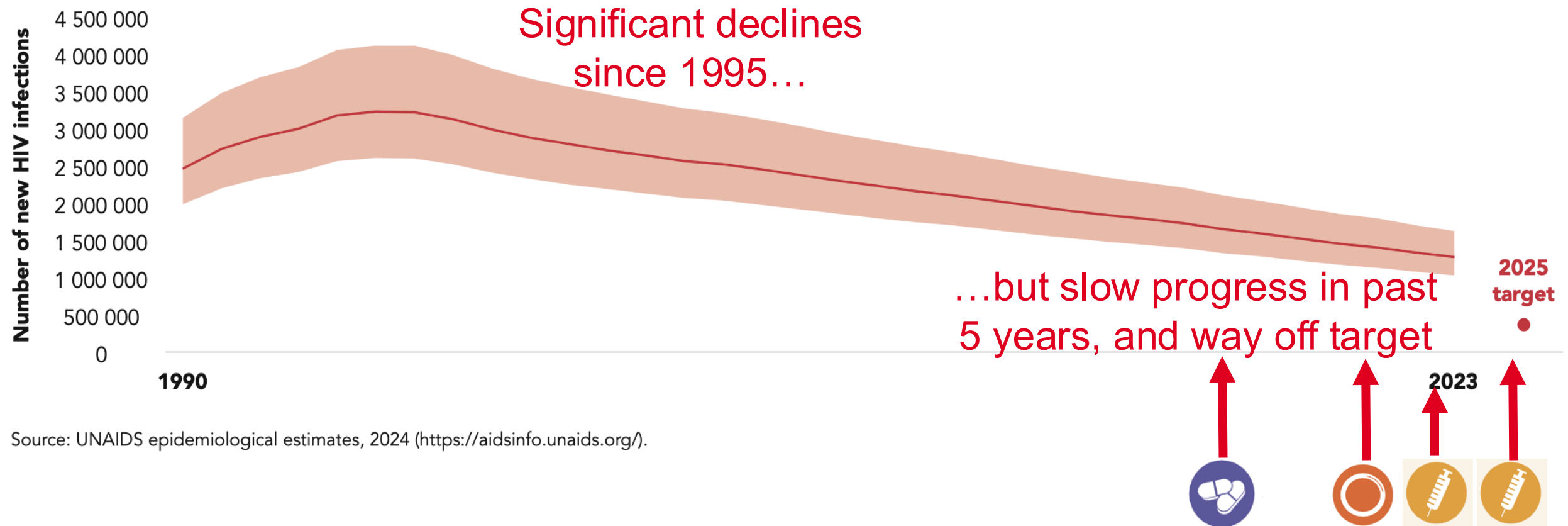
Inter-CFAR Antiretroviral for Prevention Lecture Series

Outline

- Targets made – and missed
- Language check
- Prevention journeys – for programmes and for people
- The oral PrEP experience – and the potential of a “prevention platform”
- The product pipeline
- Decisions, decision-makers and the future

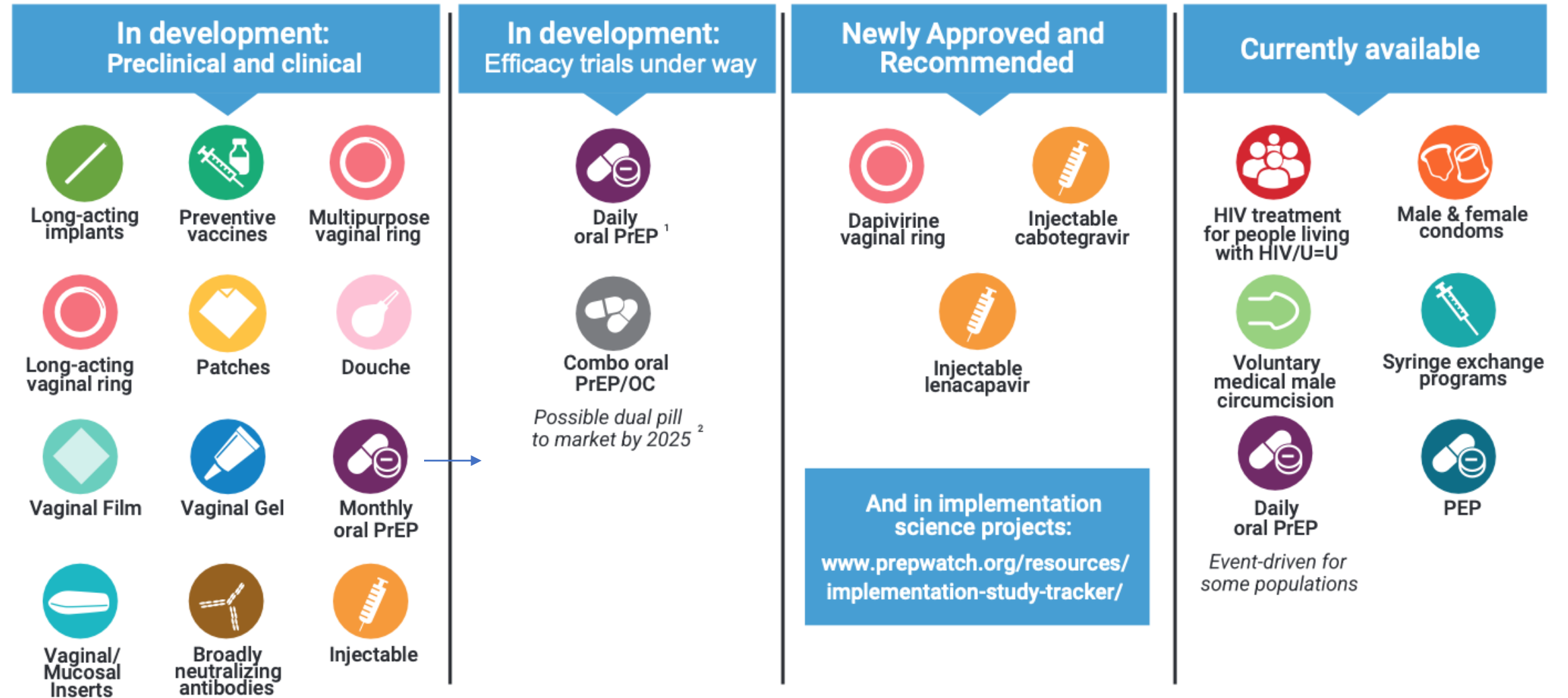
Tracking incidence against UNAIDS 2025 targets

Figure 0.1 Number of new HIV infections, global, 1990–2023, and 2025 target



Source: UNAIDS epidemiological estimates, 2024 (<https://aidsinfo.unaids.org/>).

Overview of Biomedical Px Pipeline (circa 2025)



Pipeline in Crisis: Impact of USAID & NIH Cuts

In development: Preclinical and clinical

USAID cancelled funding for pre-clinical and clinical trials, stunting critical early progress on multiple upstream HIV prevention products

NIH terminated HIV vaccine research, including research on vaccine candidates and bNabs

Long-acting implants, Preventive vaccines, Multi-purpose vaginal ring, Long-acting vaginal ring, Vaginal, Monthly oral PrEP, Vaginal Mucosal Inserts, neutralizing antibodies

In development: Efficacy & IS trials under way

NIH and USAID terminated implementation science and acceptability studies which could impact product introduction

lenacapavir, Daily oral PrEP, Combo oral PrEP/OC, Possible dual pill to market by 2025?

Newly Approved and Recommended

Introduction of promising new products in development and newly approved is at risk if USAID does not honor procurement commitments and fund prevention programs

Injectable, Vaginal ring

Currently available

Cuts to USAID's PEPFAR funding for prevention products and programs may impact access to available products, but the extent is not yet known

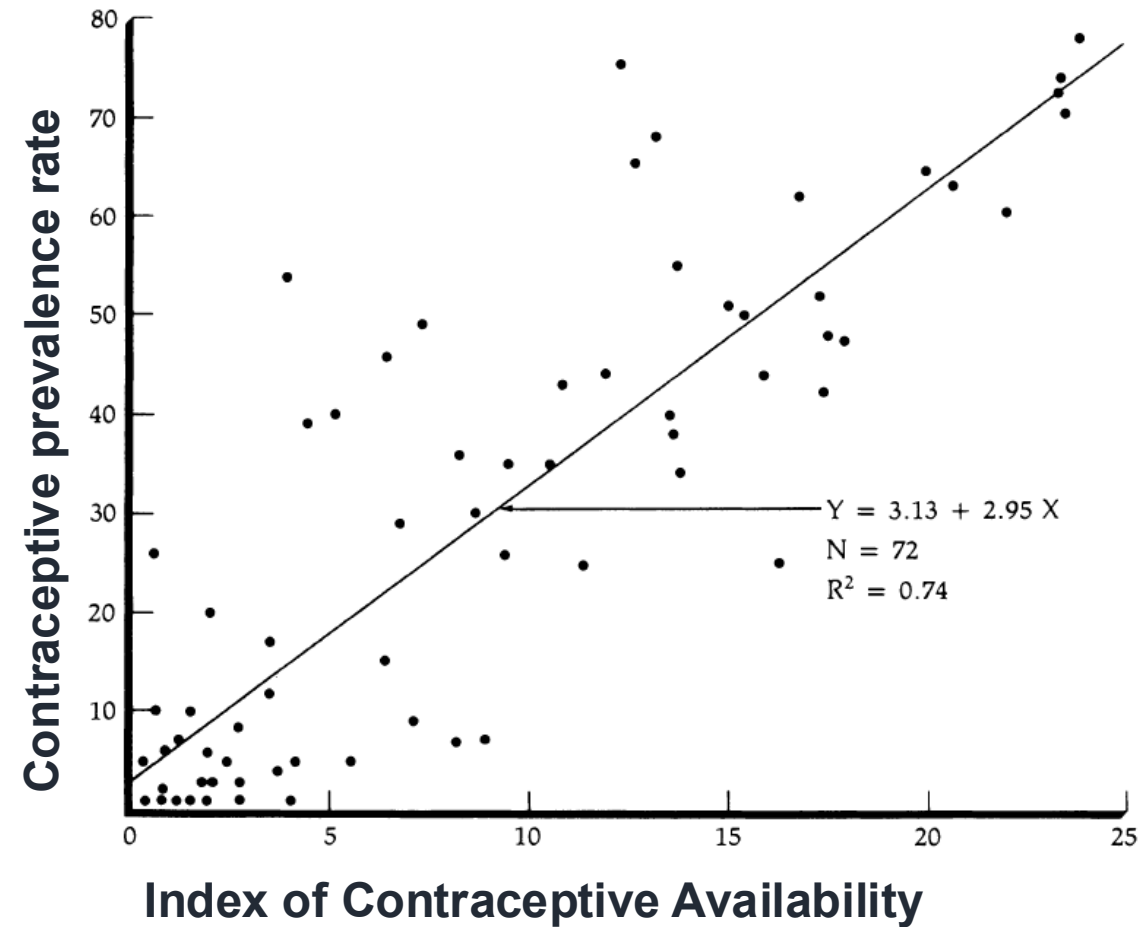
HIV treatment for people living with HIV, Male & female condoms, Voluntary medical male circumcision, PrEP, Daily oral PrEP, Event-driven for some populations.

Language Check

- Options
 - Biomedical methods that are safe and effective
 - Requires R&D of additional options to add to the “method mix”
- Choice
 - The ability for an individual to select from an array of options
 - Requires policy makers, donors, governments & implementers to make the “mix” available, accessible & affordable

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



Voices for Choice

African Women Prevention Community Accountability Board

The HIV Prevention Choice Manifesto For Women and Girls In Africa



Introduction:

The HIV Prevention Choice Manifesto is a collection of voices of African women and girls in all their diversity, feminists and HIV prevention advocates across Southern and Eastern Africa who are united in calling for continued political and financial support for HIV prevention choice.

Biomedical HIV prevention is at a historic turning

Options vs. Choice

- Effective and safe biomedical methods
- Requires R&D of additional options to add to the "method mix"



- The ability for an individual to select from an array of options
- Requires policy makers, donors, governments & implementers to make the "mix" available, accessible & affordable

▶ [HIV Prevention Choice Manifesto](#)

Global Key Population HIV Prevention Advisory Group

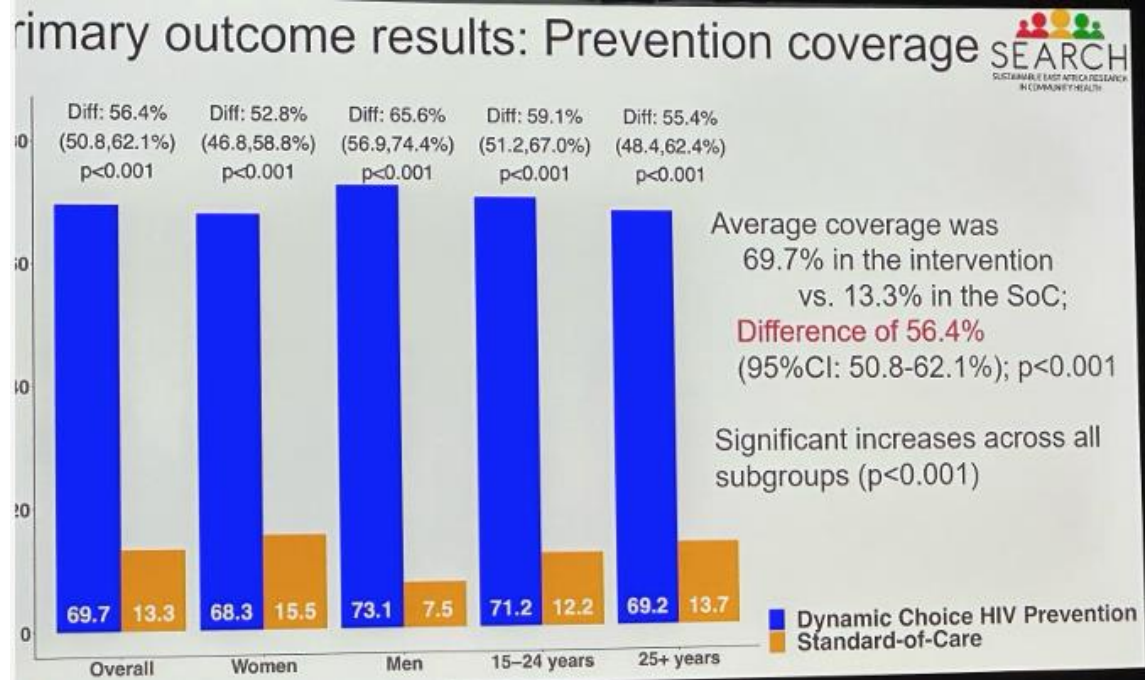
DECEMBER 2023

Global HIV Prevention Roadmap for Key Populations

This roadmap outlines a strategy for the equitable expansion and delivery of HIV prevention services to key populations (KPs) globally and regionally. It introduces a critical, coordinated approach led by KPs to accelerate the implementation of existing and new HIV prevention interventions.

▶ [Global HIV Prevention Roadmap for Key Populations](#)

Choice Matters



Secondary outcome: HIV incident infection

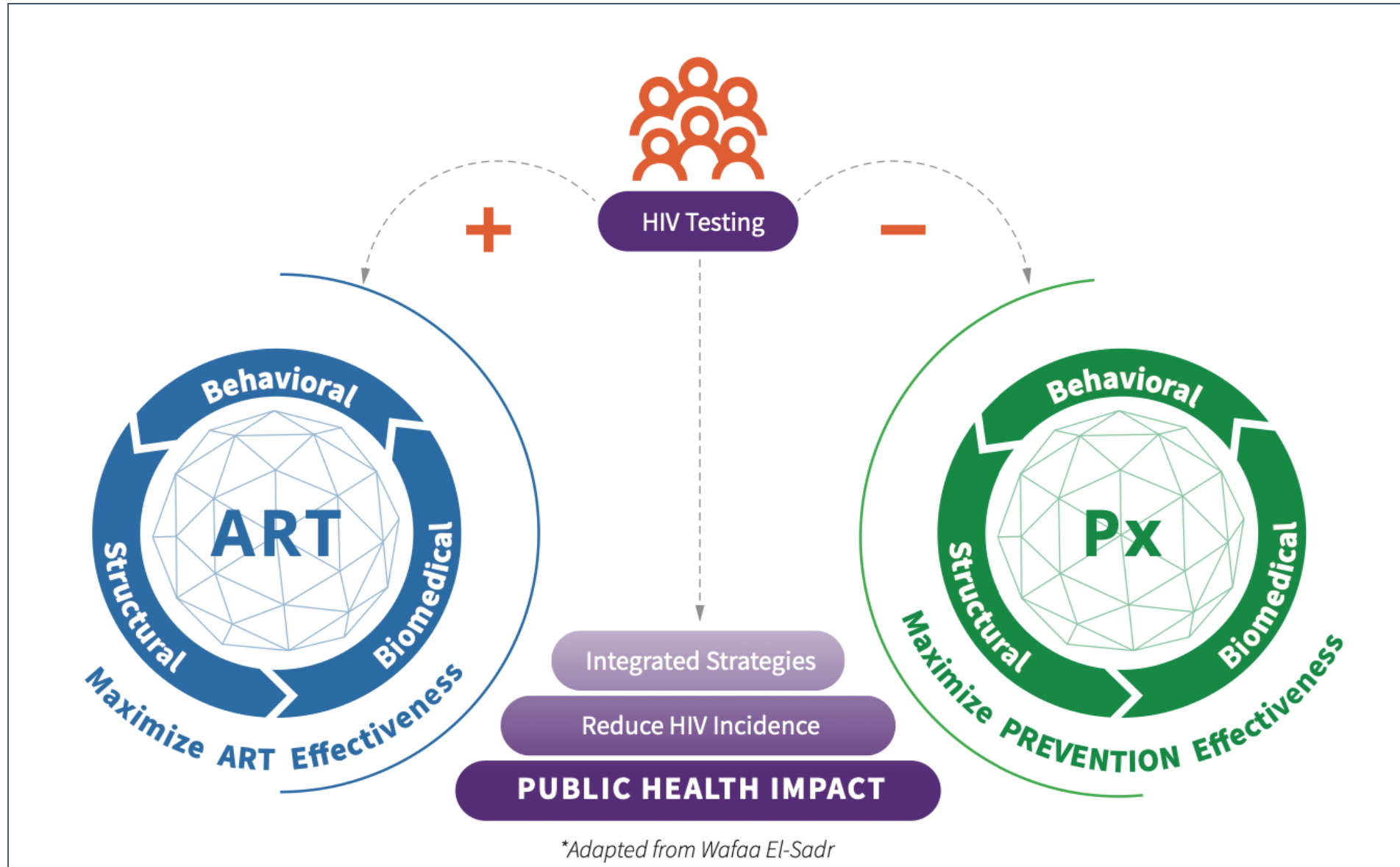
	Dynamic Choice HIV Prevention intervention	Standard of Care
Overall	0/400 PY	7/390 PY
Women	0/293 PY	5/283 PY
Men	0/107 PY	2/106 PY
15-24 years	0/113 PY	1/122 PY
25+ years	0/287 PY	6/268 PY

- 7 participants in the SoC and 0 in intervention had incident HIV infection
- Incidence rate was 0% in the intervention vs. 1.8% in the SoC
- Difference of -1.8% ($p = 0.01$)
- In addition, 1 infant born to participant in SoC was infected
 - Not included in incidence

Ever use	Dynamic Choice HIV Prevention intervention	Standard of Care
CAB-LA	56%	0%
Oral PrEP	53%	19%
PEP	2%	1%
2+ products	28%	0.4%

- Over half of participants in intervention arm used CAB-LA during the study (both men and women)
- Of those starting CAB-LA at baseline, 42% were not on any prevention product in the prior month
- 28% of intervention participants used at least 2 different products during the study

Universal Test & Connect



Parallel Universes/Journeys

Providers & Health Systems



Users



A New Journey: New Way(s) of Thinking

Key findings from a 4-year intensive user-centered design project among adolescent girls and young women

1. Think relevance – not risk reduction
2. Think habit – not adoption
3. Think relationships – not HIV
4. Think needs – not demographics
5. Think ecosystems – not interventions
6. Think options – not preferences

→ **Healthy Sexual Relationship Journey framework**

Outlines a 5 stage model that articulates the context for prevention from an AGYW perspective. Consolidates AGYW behaviour and choices relevant to HIV prevention and their influencers.

→ **AGYW Segmentation**

Differentiates by relationship motivation and associated prevention behaviour. Stage specific progression factors quantified.

→ **HIV prevention product preferences**

AGYW's preferences quantified to guide future product development.

→ **15 intervention opportunity areas**

Identified and prioritised for optimal programmatic impact.

→ **4 Design Aids**

Developed for resource allocation, optimisation of current Programmes, and designing of new interventions.

→ **22 prioritized intervention concepts**

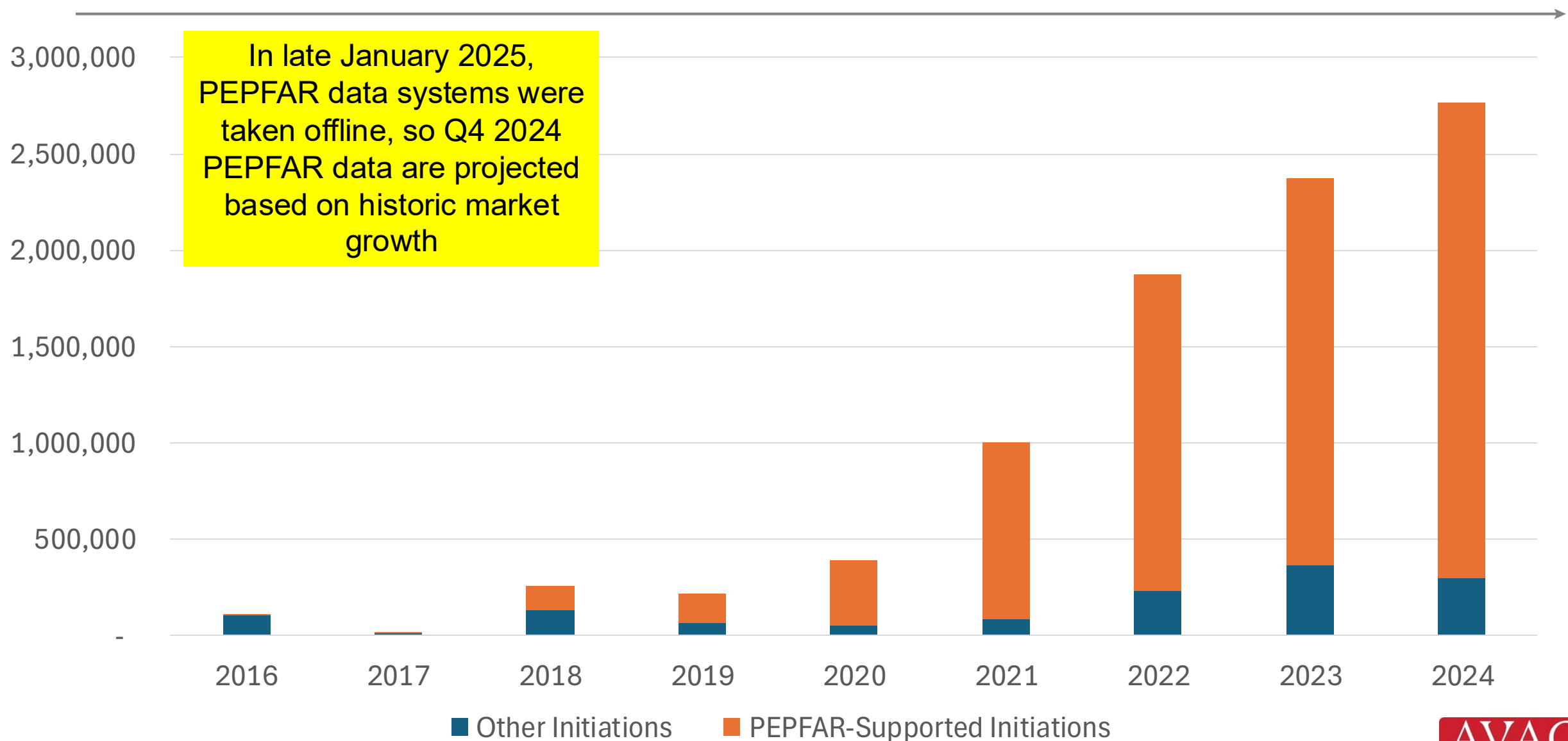
Co-created with AGYW and stakeholders.

→ **1 programme design validated through piloting**

Designed and implemented in collaboration with two IPs for high prevalence geographies in South Africa. Proven success in changing negative relationship dynamics and establishing referral support.

For more info: [Breaking the Cycle of Transmission: Increasing uptake and effective use of HIV prevention among high-risk adolescent girls and young women in South Africa](#)

PrEP Initiations to 2024



PEPFAR Stop Work Orders: Major Impacts

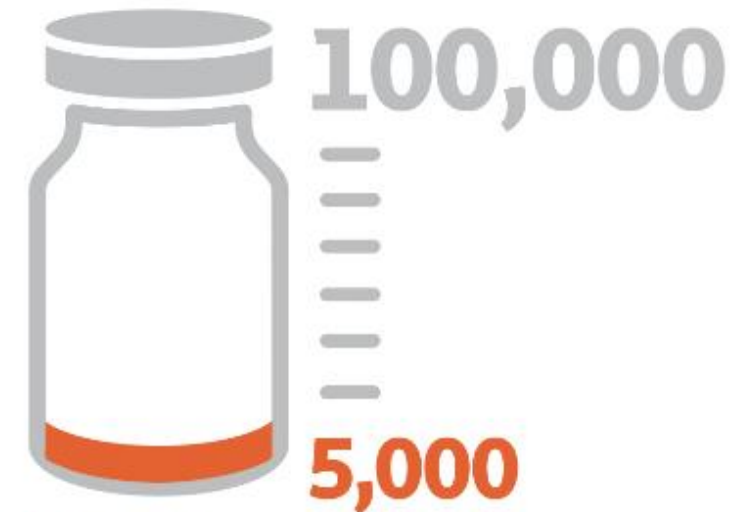
<https://www.prepwatch.org/pepfar-stop-work/>



Number of new **PrEP users** in 2024 who have **lost access to PEPFAR-supported PrEP services**

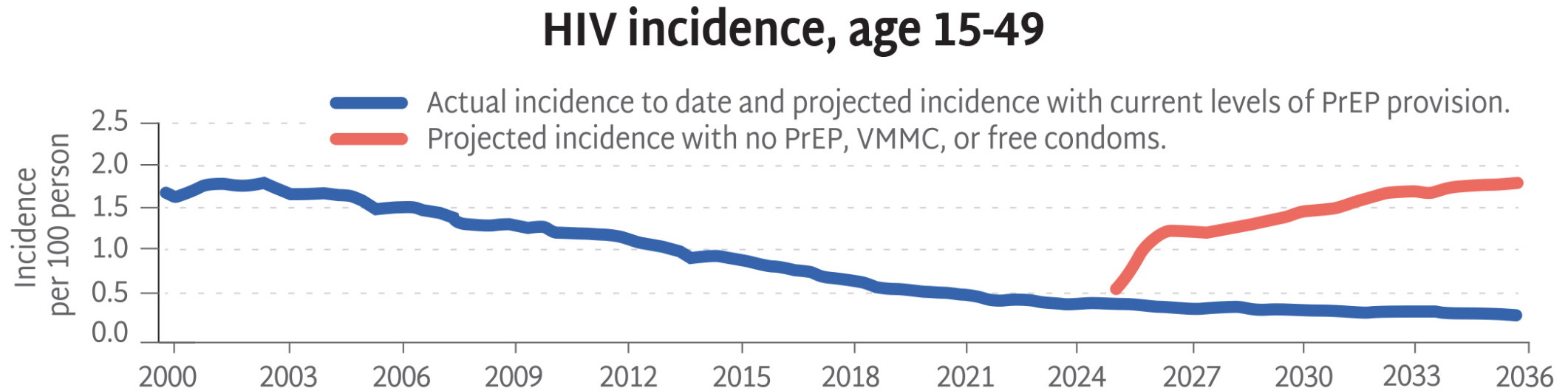


Number of people identifying as **Key Populations who have lost access to HIV prevention programming** under PEPFAR



Off Target: The PEPFAR goal of **people initiating CAB for PrEP** in 2025 is falling far short – **5k instead of 100k**

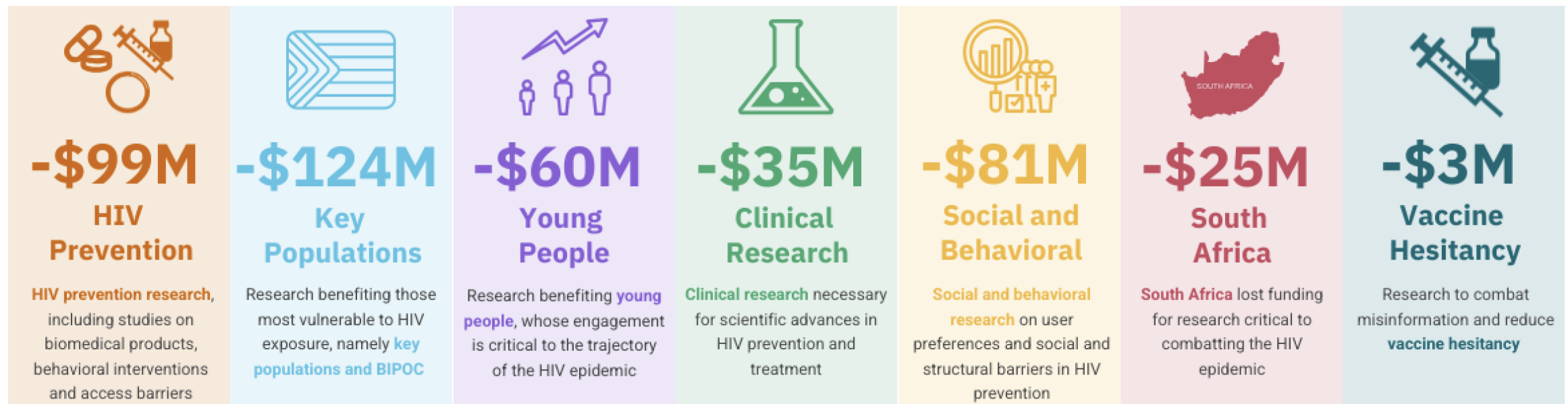
A World Without HIV Prevention



[HIV Synthesis model](#), developed by the HIV Modelling Consortium

The Cost of Cutting HIV Research

NIH terminated 191 HIV-specific grants in 2025, slashing over \$200 million from key HIV prevention research grants¹



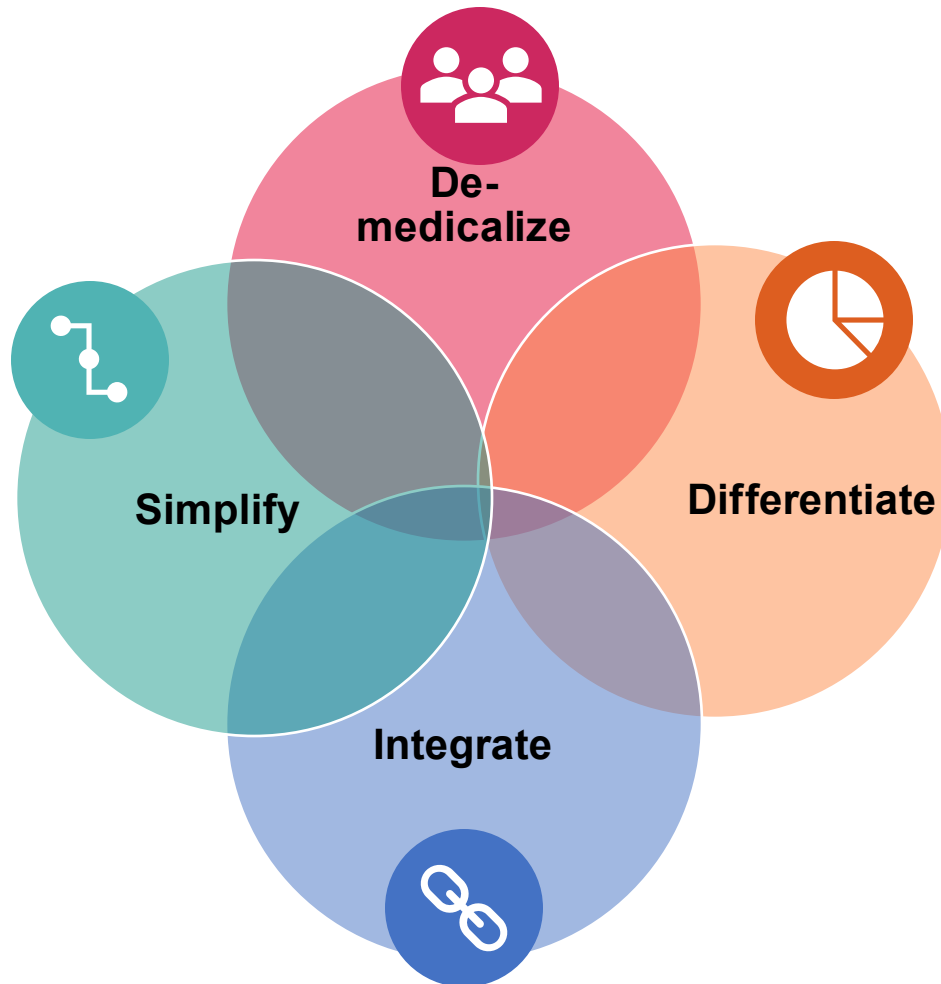
¹Grants may cover more than one research area, so total across categories shown here exceeds \$200 million in total funding lost

Potential Fallout from Cuts to HIV Prevention

Impacts on trials, including those sponsored by non-USG funders

- USG funding is the scaffold on which pharma, philanthropies and other governments invest in transformative HIV & TB science
- Trials sponsored by other research funders build on top of core and other funding provided to clinical trials units and research sites through NIH awards
- USG cuts risk infrastructure, staff/talent, training the next generation of scientists, community engagement, data sharing, biorepositories, etc.
- If South African and other international study sites and participants are excluded from enrollment, follow-up, study completion, and data collection and analysis, ongoing and planned trials are likely underpowered to produce meaningful results, wasting years of work and tens or hundreds millions of dollars
- Trials no longer able to enroll internationally will face delays and increased costs as they seek new sites and study participants elsewhere

Differentiate, Simplify and De-Medicalize



Building blocks for differentiated PrEP

Adapting the when, where, who and what



Kim Green, PATH: Bringing PrEP to the people: Democratizing access to PrEP through differentiated delivery before, during, and after COVID-19

Getting It Right This Time

Getting PrEP Rollout Right This Time:

Lessons from the Field



AVAC
Advocacy. Access. Equity.

June 2025

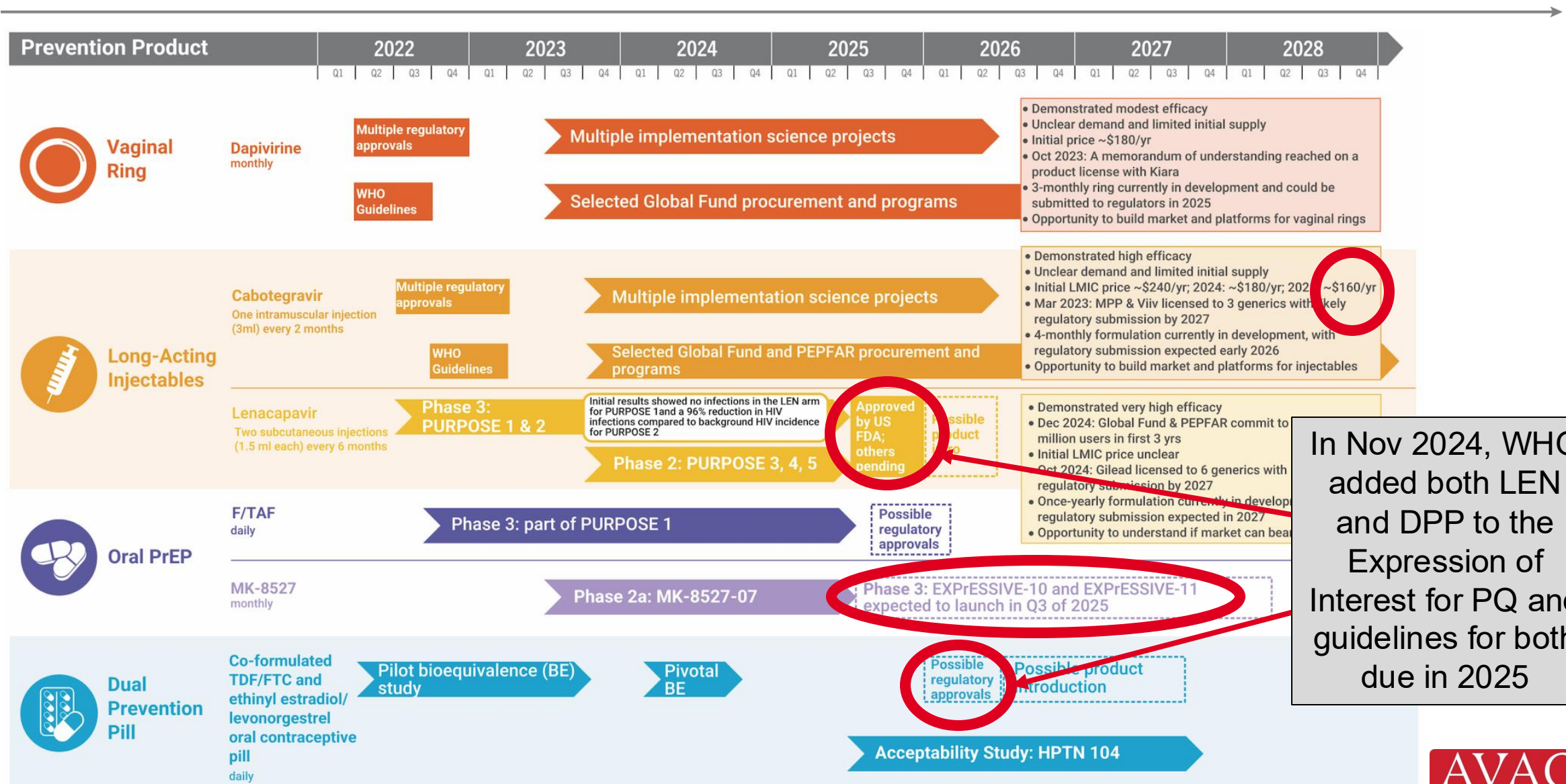
Seven countries—Brazil, Kenya, Nigeria, South Africa, Vietnam, Zambia, and Zimbabwe—exploring themes of:

- Successes and challenges with PrEP introduction and scale-up and what can be done differently now
- Public health system readiness for intron and scale-up of LEN
- Considerations for improving & accelerating regulatory approval, normative guidance, demand generation, stakeholder engagement, & health systems strengthening

www.prepwatch.org/resources/getting-prep-rollout-right

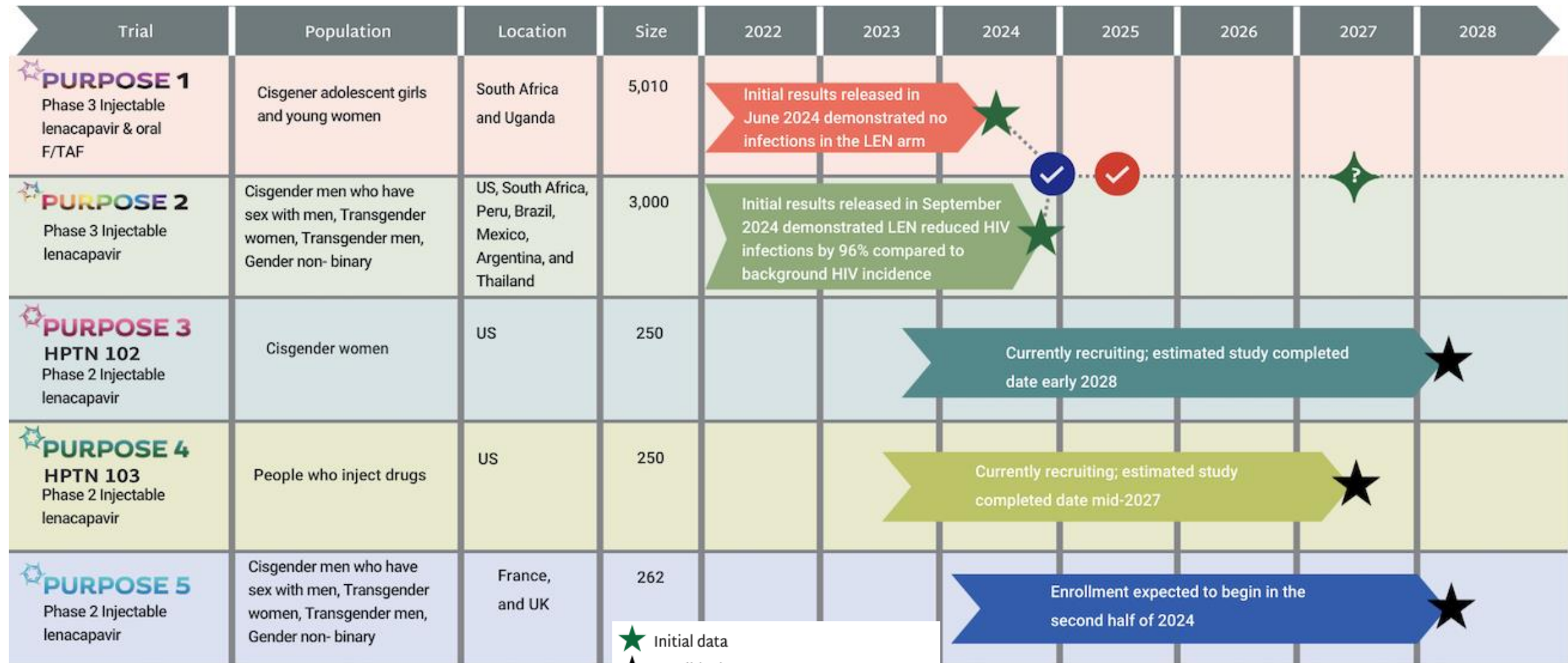
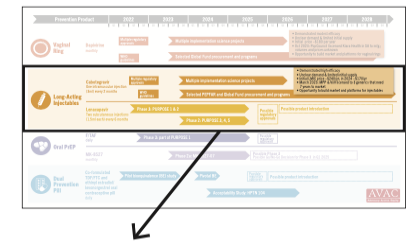
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Years Ahead in HIV Prevention Research



In Nov 2024, WHO added both LEN and DPP to the Expression of Interest for PQ and guidelines for both due in 2025

Planning for Injectable Lenacapavir



- ★ Initial data
- ★ Possible data
- ✓ Possible earliest regulatory submissions
- ✓ Possible earliest regulatory approval and market entry with product from Gilead
- ? Possible earliest generic manufacturer(s)

Getting to Zero

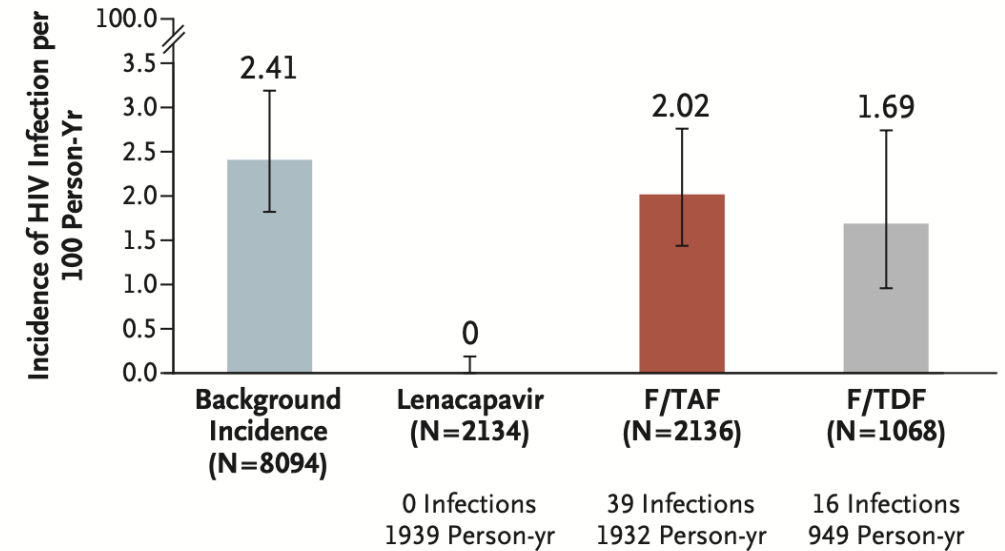
June 20, 2024

Gilead's Twice-Yearly Lenacapavir Demonstrated 100% Efficacy and Superiority to Daily Truvada® for HIV Prevention

ORIGINAL ARTICLE

Twice-Yearly Lenacapavir or Daily F/TAF for HIV Prevention in Cisgender Women

A Background HIV Incidence and HIV Incidence in Lenacapavir, F/TAF, and F/TDF Groups



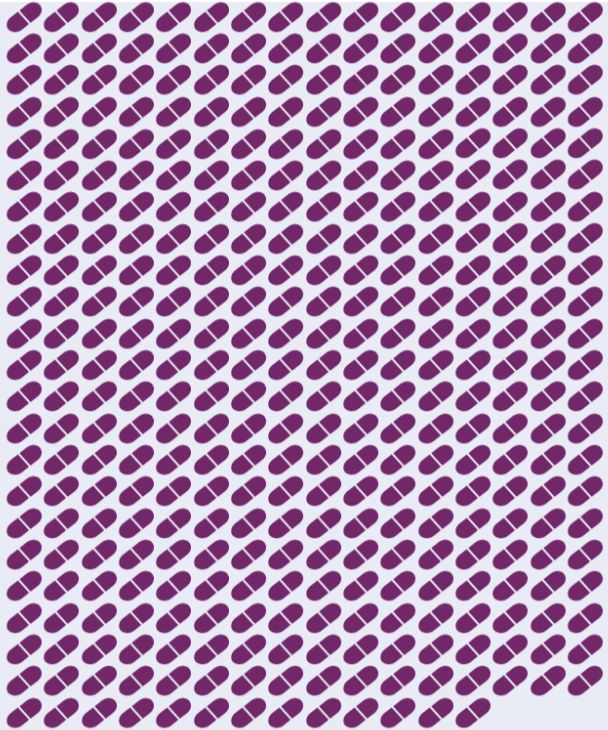














September 12, 2024

Gilead's Twice-Yearly Lenacapavir for HIV Prevention Reduced HIV Infections by 96% and Demonstrated Superiority to Daily Truvada® in Second Pivotal Phase 3 Trial

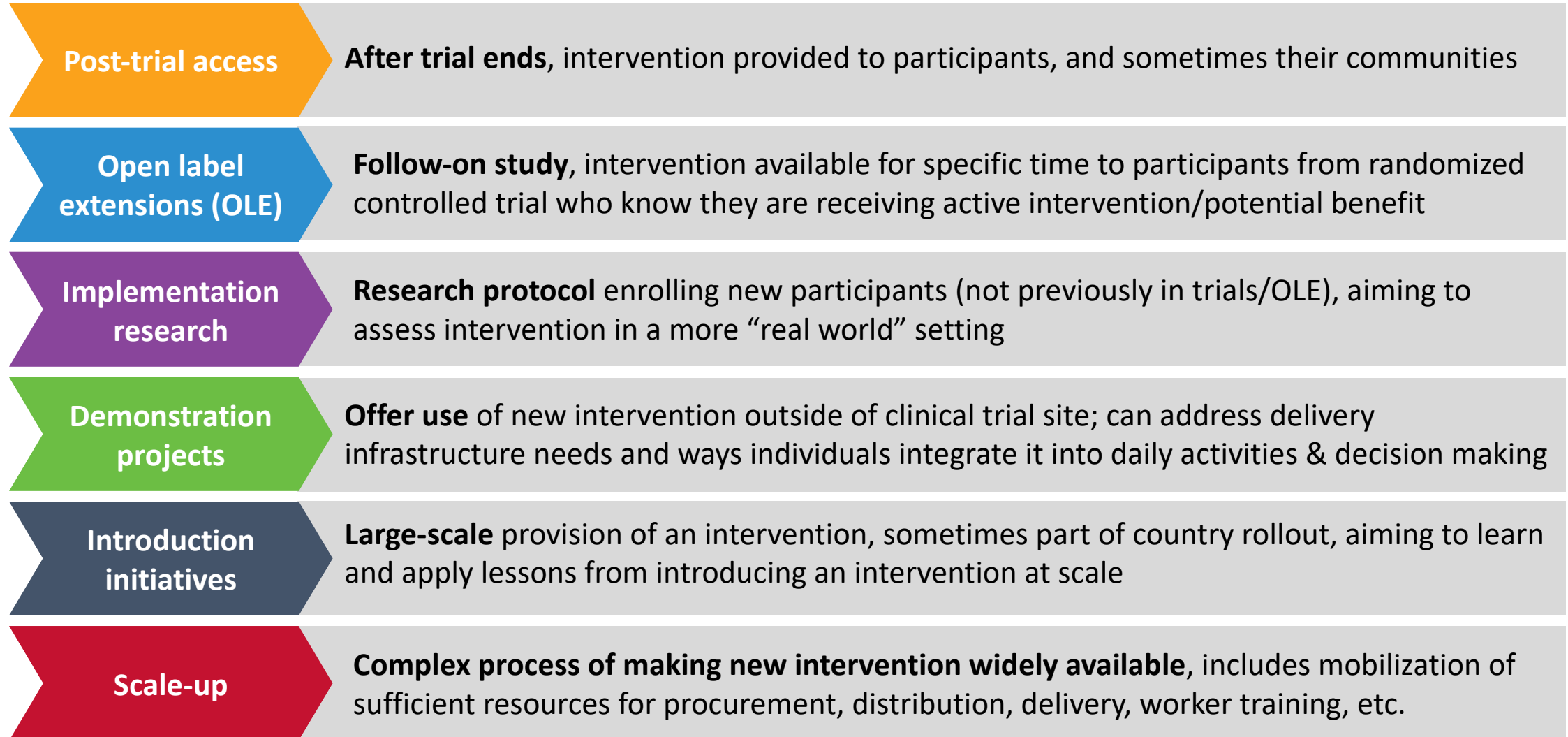
Px Options

	Tenofovir-based (FTC + TDF or TAF)	Dapivirine (DVR)	Cabotegravir (CAB)	Lenacapavir (LEN)
ARV Drug Class	Nucleoside reverse transcriptase inhibitor (NRTI)	Non-nucleoside reverse transcriptase inhibitor (NNRTI)	Integrase strand transfer inhibitor (ISTI)	Capsid inhibitor
Efficacy Established	2010, 2011	2016	2020	2024
Delivery site	Oral	Vaginal ring	Intramuscular injection in gluteal muscle (buttocks)	Subcutaneous injection in abdomen
Volume	Tablet with 300mg (TDF) or 25mg (TAF) with 200mg emtricitabine (FTC)	25 mg ring	One 3 ml injection	Two 1.5 ml injections
Frequency	Daily ; 2-1-1 dose also recommended	Monthly (<i>3-monthly ring in development</i>)	First injection followed by a second one month later, then every 2 months (<i>every 4 month dose in development</i>)	First injection along with two oral tablets, followed by two more tablets on day 2 and then injections every 6 months
Efficacy	High efficacy among all populations; highly adherent-dependent	Moderate efficacy among cisgender women; highly adherent-dependent	Very high efficacy in all populations	Very high efficacy in all populations
Regulatory	±100 approvals since 2012; recommended by WHO in 2015	9 approvals as of Oct 2024; recommended by WHO in 2021	25 approvals as of Oct 2024; recommended by WHO in 2022	Submissions to begin in 2024; guidance anticipated in 2025
Commodity Cost in LMICs, per person per yr	±\$40	\$156	≈\$160 (actual cost in UK Pounds)	TBD
Developer	Gilead Sciences	IPM/PopCouncil	ViiV Healthcare	Gilead Sciences
Generic	15+ suppliers all over the world	MOU with Kiara in SA; details to come on license and timelines	3 licenses via MPP, with expected earliest market access in 2027	6 direct licenses, with expected earliest market access in 2027

What Is a “Person Year of Protection”?

	Tenofovir-based (FTC + TDF or TAF)	Dapivirine (DVR)	Cabotegravir (CAB)	Lenacapavir (LEN)
PrEP Dosing for One Year of Protection	One pill every day for all populations (with possibility of event-driven dosing of 2-1-1 for some)	One ring every month	First injection followed by a second one month later, then every 2 months	First injection along with two oral tablets, followed by two more tablets on day 2 and then injections every 6 months
			Day 1:  1 month:  3 month:  5 month:  7 month:  9 month:  11 month: 	Day 1:    Day 2:  6 month:  

Moving a Product to the “Real World”



Posted in Support of the Coalition to Accelerate Access to Long-Acting PrEP

Potential Demand for LEN for PrEP

Totals for Top Markets

2024 Oral PrEP Initiations	2,554,082
Possible 2026 Injectable Users	1,532,449

	2024 Initiations	Possible 2026 Market
Nigeria	235,776	141,466

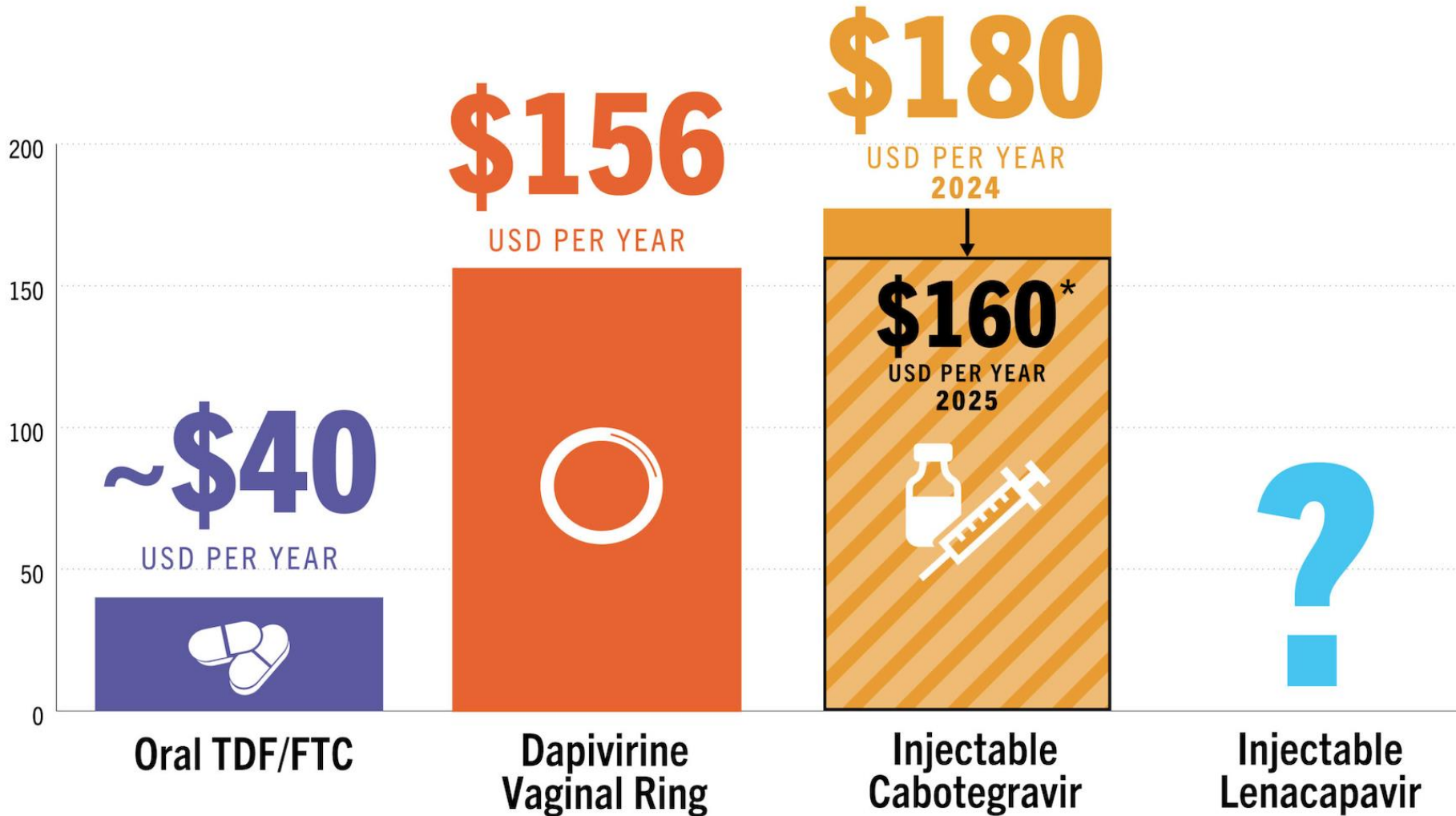
	2024 Initiations	Possible 2026 Market
Brazil	82,619	49,571

	2024 Initiations	Possible 2026 Market
Ukraine	76,454	45,872

	2024 Initiations	Possible 2026 Market
Philippines	13,191	7,915
Thailand	13,670	8,202
Vietnam	16,735	10,041

	2024 Initiations	Possible 2026 Market
Eswatini	26,369	15,821
Kenya	145,774	87,464
Lesotho	30,161	18,097
Malawi	100,485	60,291
Mozambique	205,582	123,349
South Africa	572,393	343,436
Tanzania	272,526	163,516
Uganda	265,753	159,452
Zambia	379,797	227,878
Zimbabwe	116,797	70,078

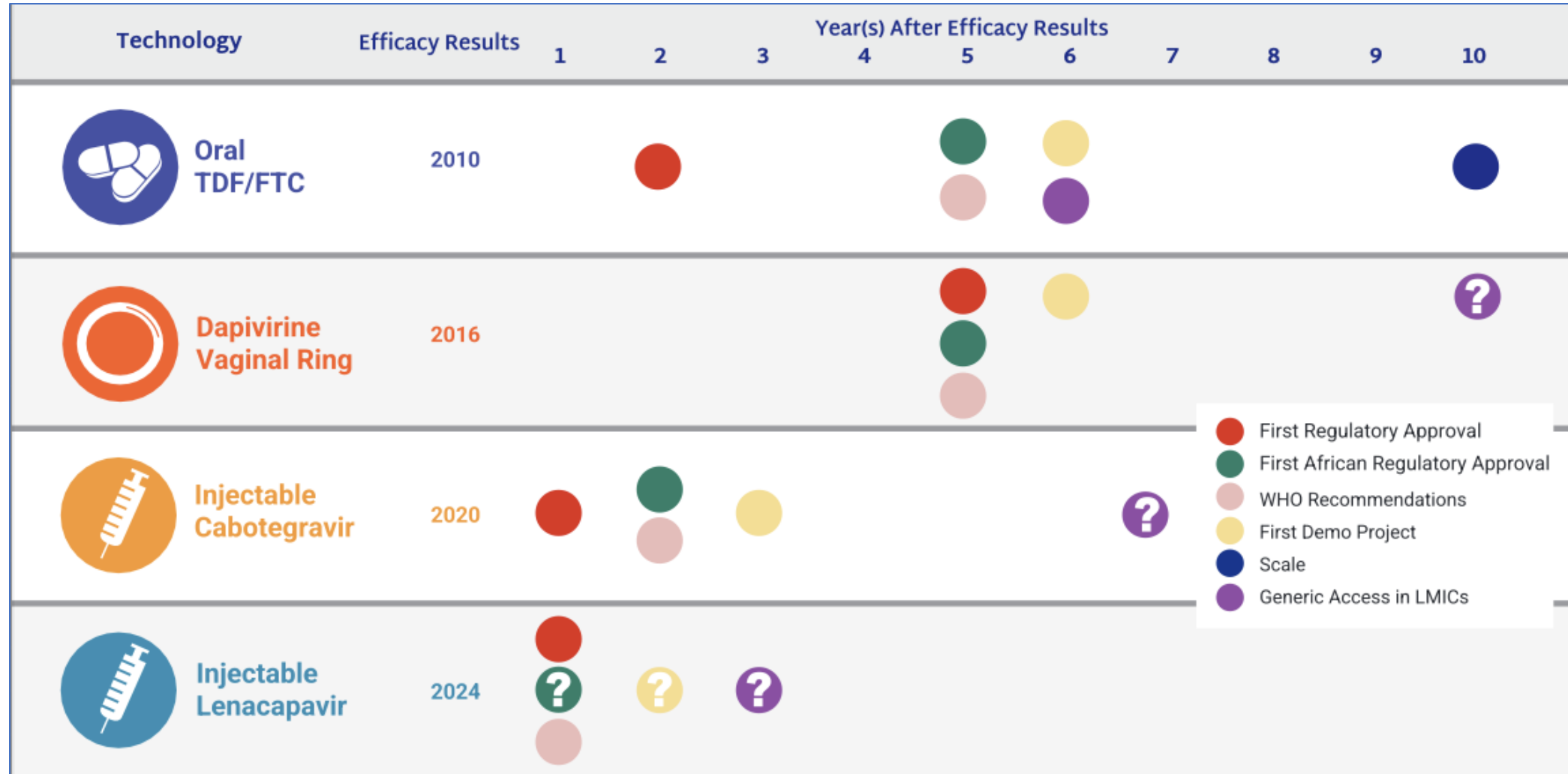
PrEP Prices in LMICs



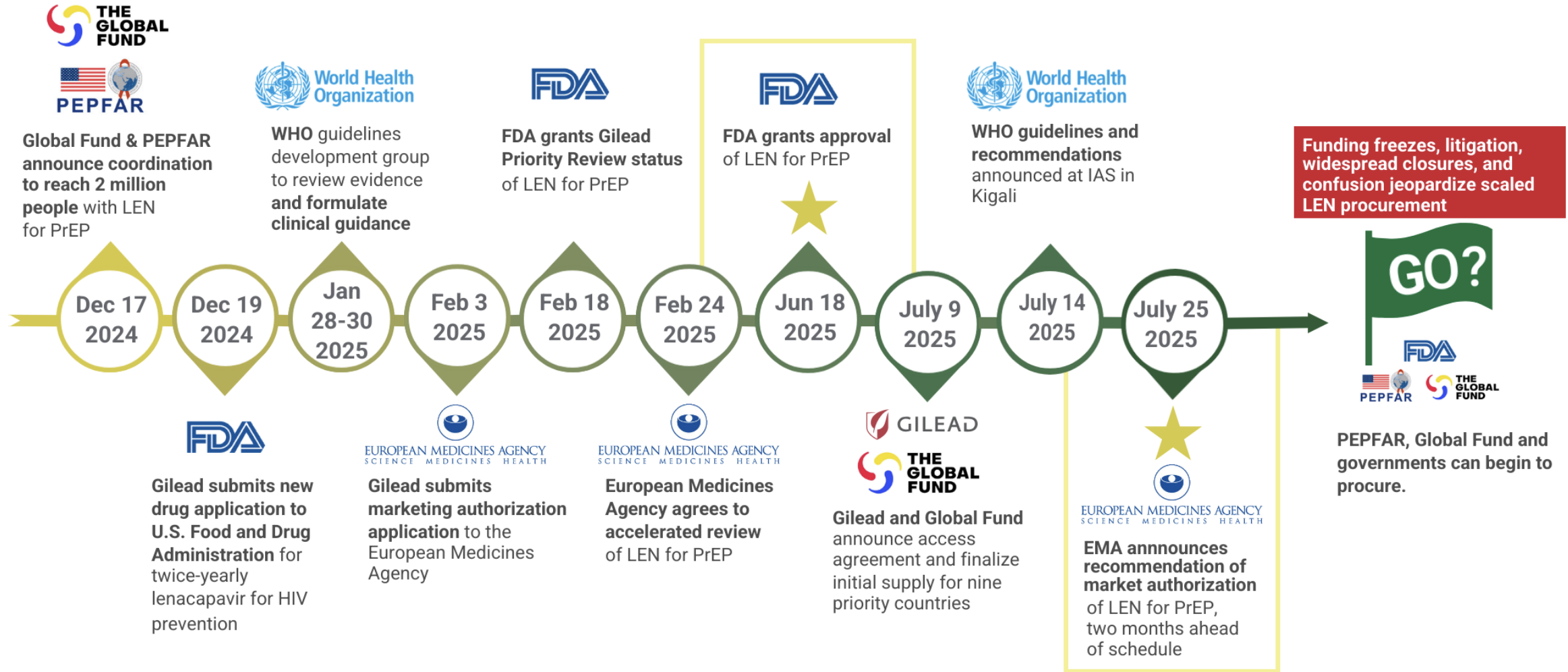
**The actual price per vial is quoted in UK Pounds but converted to US Dollars for comparison purposes.
The price is down from \$180 in 2024 to \$160 in 2025.*

Moving a Product to the “Real World”

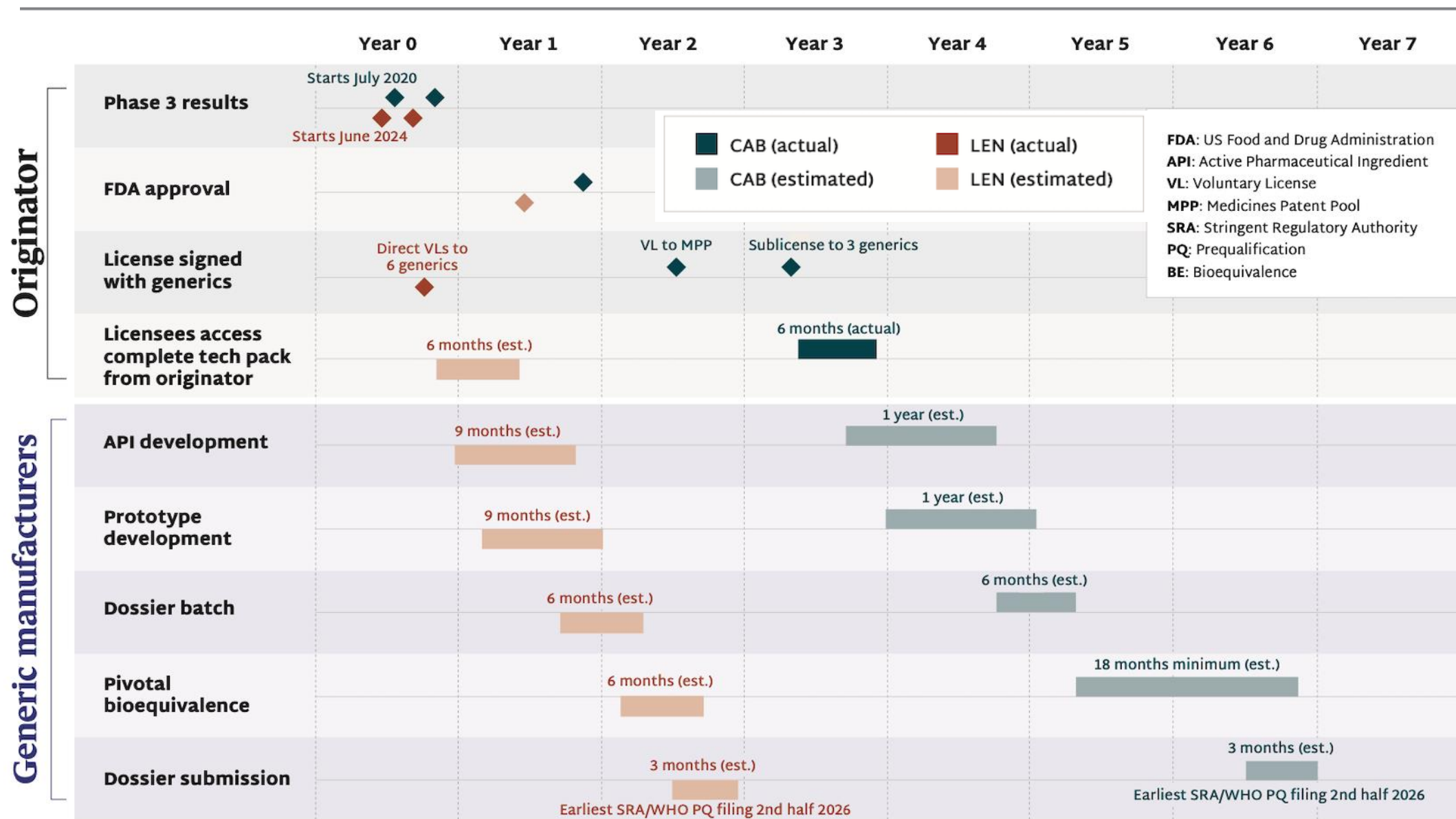
Can We Go Faster with LEN?



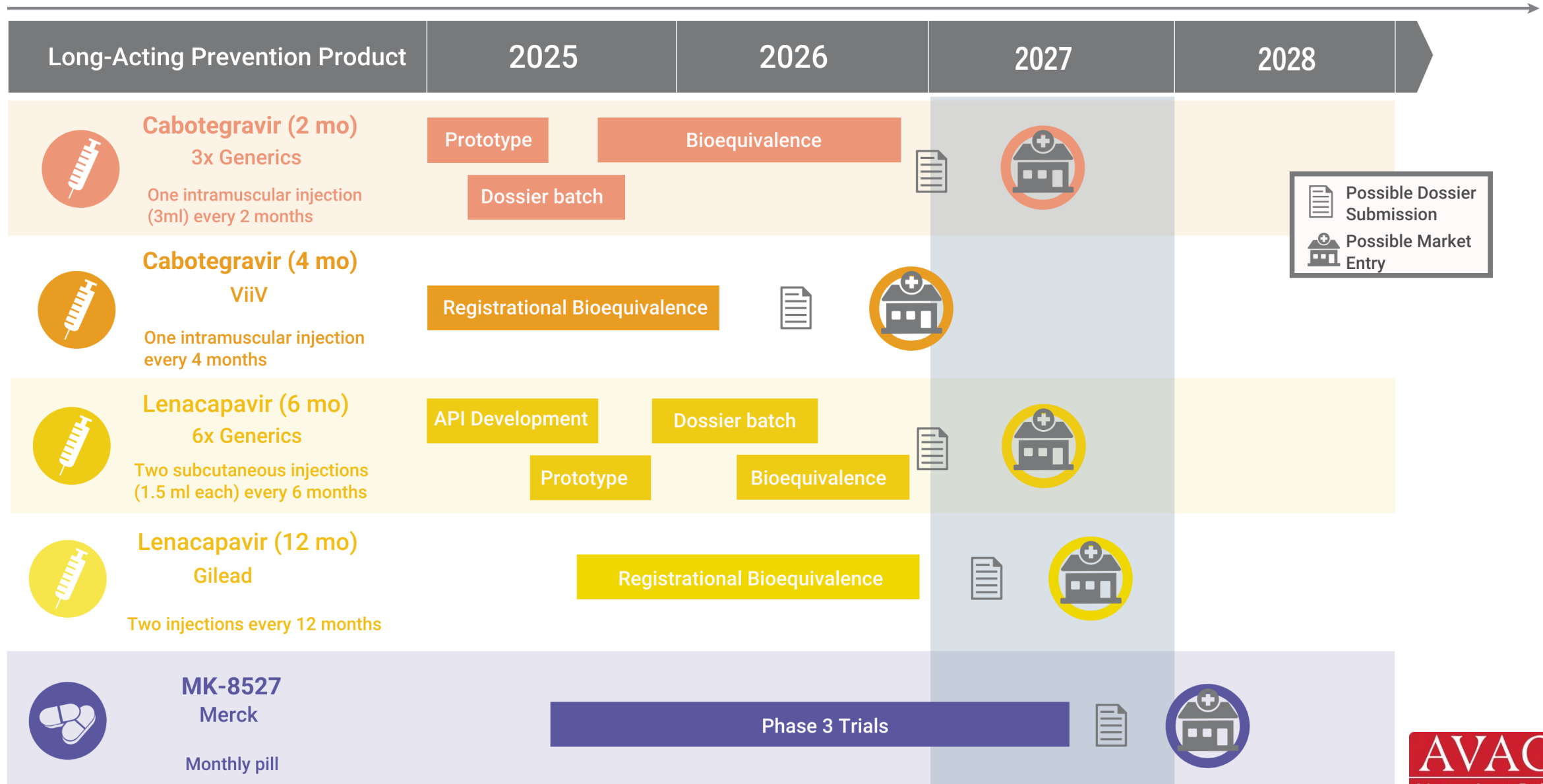
Our Best Shot at Prevention – But Now What?



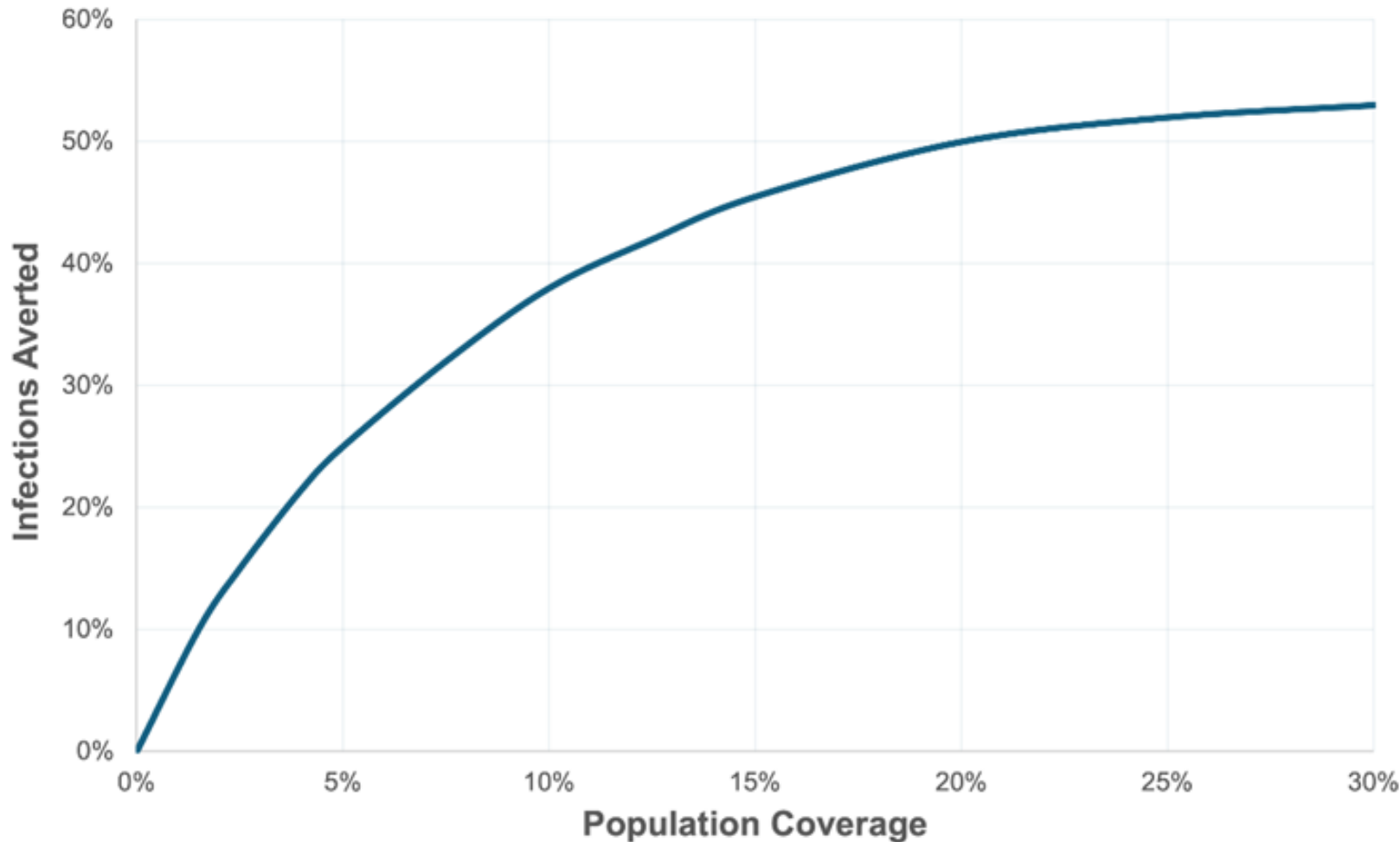
Development Timeline for Generic CAB & LEN



Innovation Pile-Up



If We Get Rollout Right: Potential Impact of LEN



Source: Gates Foundation

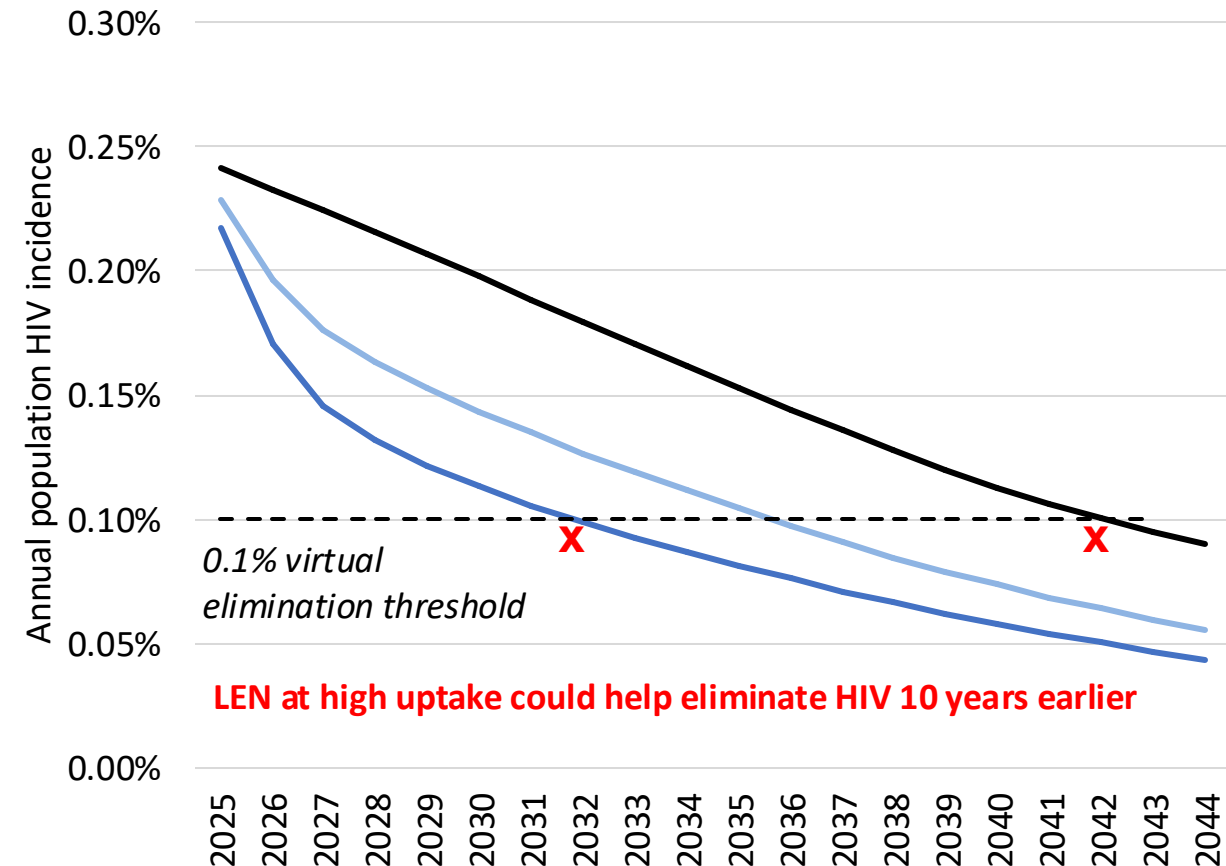
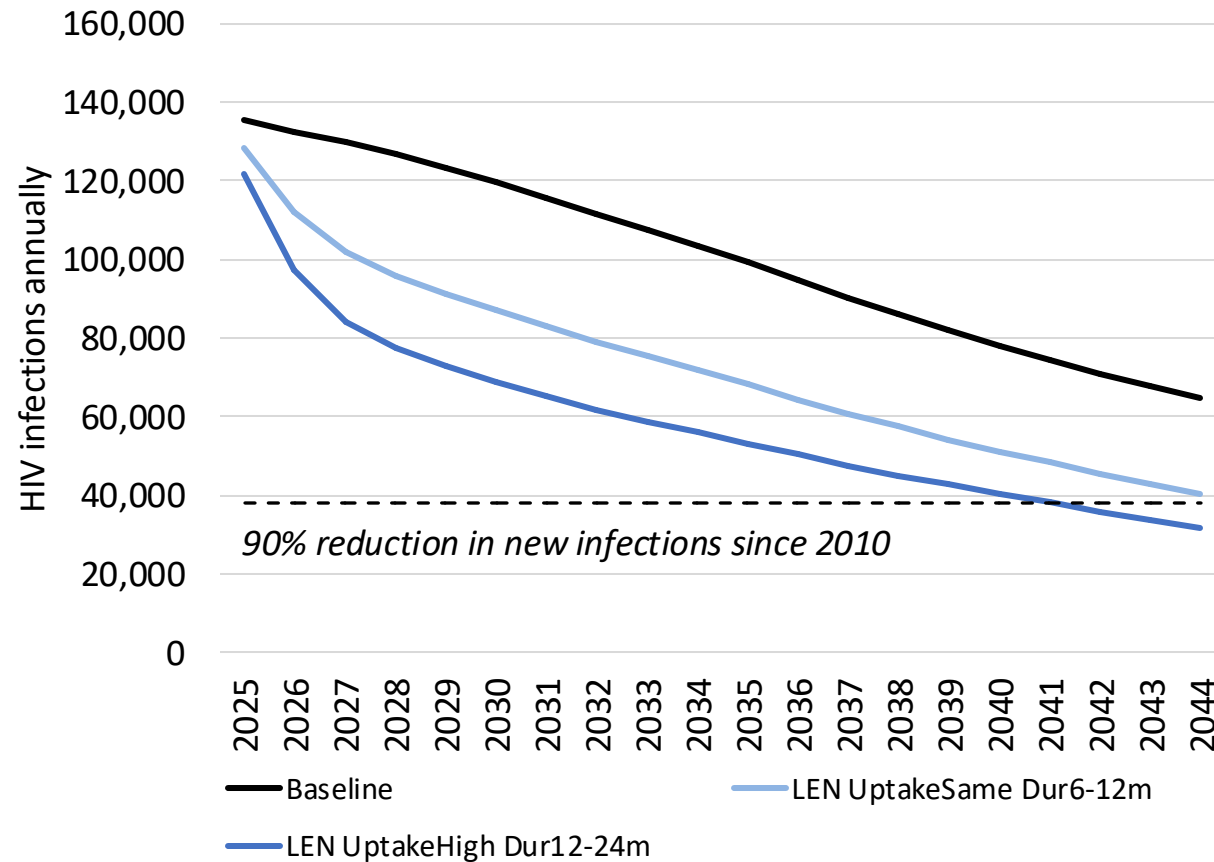
In **concentrated epidemics**, providing LEN to **3% of adult population** in the highest risk key populations **could avert ~70% of new infections**

In **generalised epidemics**, providing LEN to **~5% of the adult population and prioritising** by location and behaviour **could avert ~25-35% of new infections**

In **generalised epidemics**, providing LEN to **~20% of the adult population and prioritising** by location and behaviour **could avert 50-70% of new infections**

If We Get Rollout Right: Potential Impact of LEN

Potential Infections Averted in South Africa



Product Considerations

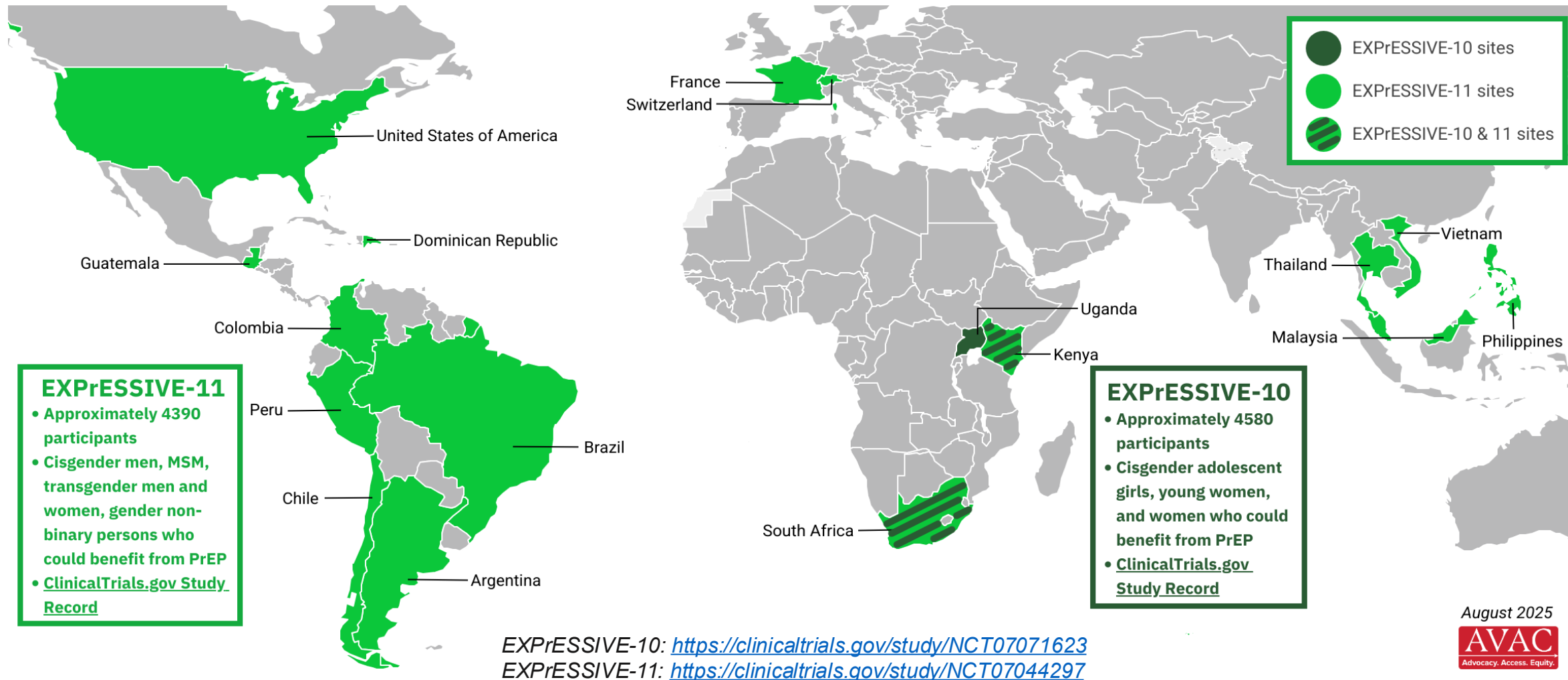
For each product, understand and balance:

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

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

EXPrESSIVE Phase 3 Trial Countries

17 countries are hosting sites of the monthly MK-8527 PrEP pill;
Q3 2025 expected launch



Accelerating Introduction of New Px

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

What we need to know – and fast

FUNDERS

- 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 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?

The Way(s) Forward

Some guiding principles

- Prioritize, Prioritize, Prioritize – like we've never prioritized before
- Don't miss out on innovation
- Think health systems – not disease- or product-specific
- Think and collaborate differently – in new ways and with different stakeholders
- Re-define sustainability – and make sure it is not just about money, and that prevention is a solid part of it
- Local ownership & leadership

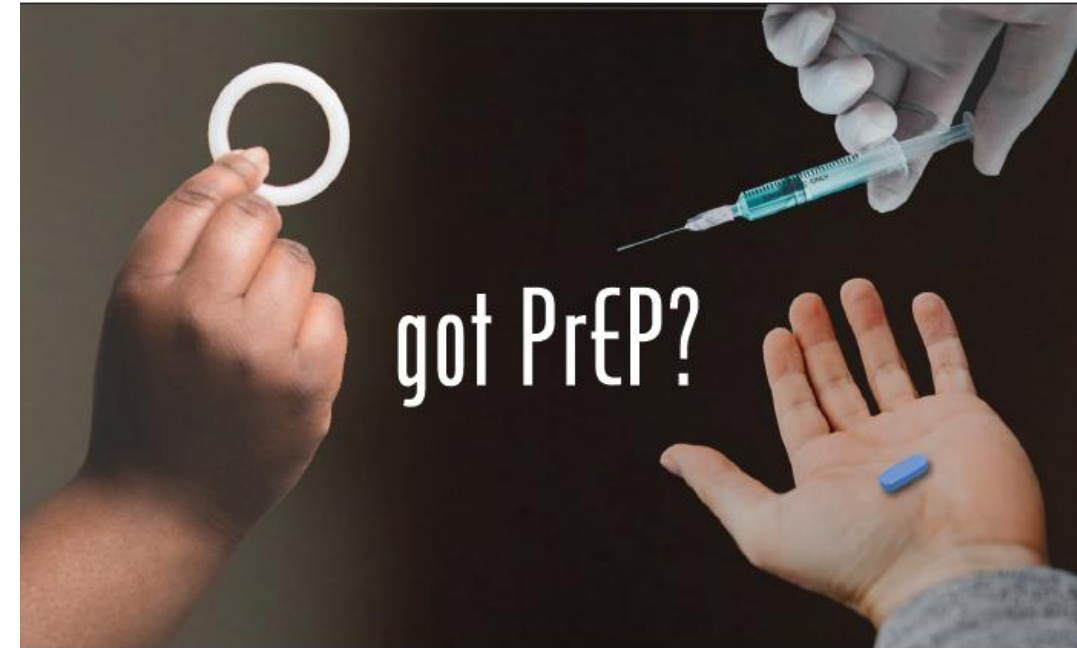
Conclusion

Much accomplished; much to do

- 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

Further Resources

- [PEPFAR Stop Work Order Tracker](#) – a live version of this slide deck
- [HIV Prevention R&D at Risk](#) – highlighting the impact of US cuts on the pipeline of HIV prevention R&D
- [PrEPWatch.org](#) – data, information, and PrEP resources
- [Global PrEP Tracker](#) – tracking PrEP initiations by country over time
- Weekly [Global Health Watch](#)
- [All things LEN](#)



For the last 8 years, AVAC has proudly worked with PEPFAR to document PrEP uptake and its impact around the world. That stopped in January with a stop work order from the US government. But protecting access to PrEP is vital. Are you leading a PrEP program? Whether supported by PEPFAR or not, we invite you to work with us to ensure global data on PrEP is not lost.

Acknowledgements

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- Helen Rees
- Mitchell Rodolph
- Kenly Sikwese
- Jacque Wambui

Gates Foundation

CIF CHILDREN'S INVESTMENT FUND FOUNDATION



BioPIC Biomedical Prevention Implementation Collaborative



COMPASS

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

