Advocates' Guide to Lenacapavir

Trial results, and steps toward ensuring access

June 2025

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Outline

- Overview of the Pipeline
- What is Lenacapavir?
- Overview of the PURPOSE Program
- PURPOSE 1 and PURPOSE 2 Studies
- Regulatory Updates
- PURPOSE 1 and PURPOSE Stakeholder Engagement Efforts
- From Research to Rollout
- Next Steps
- Advocacy Issues
- Resources

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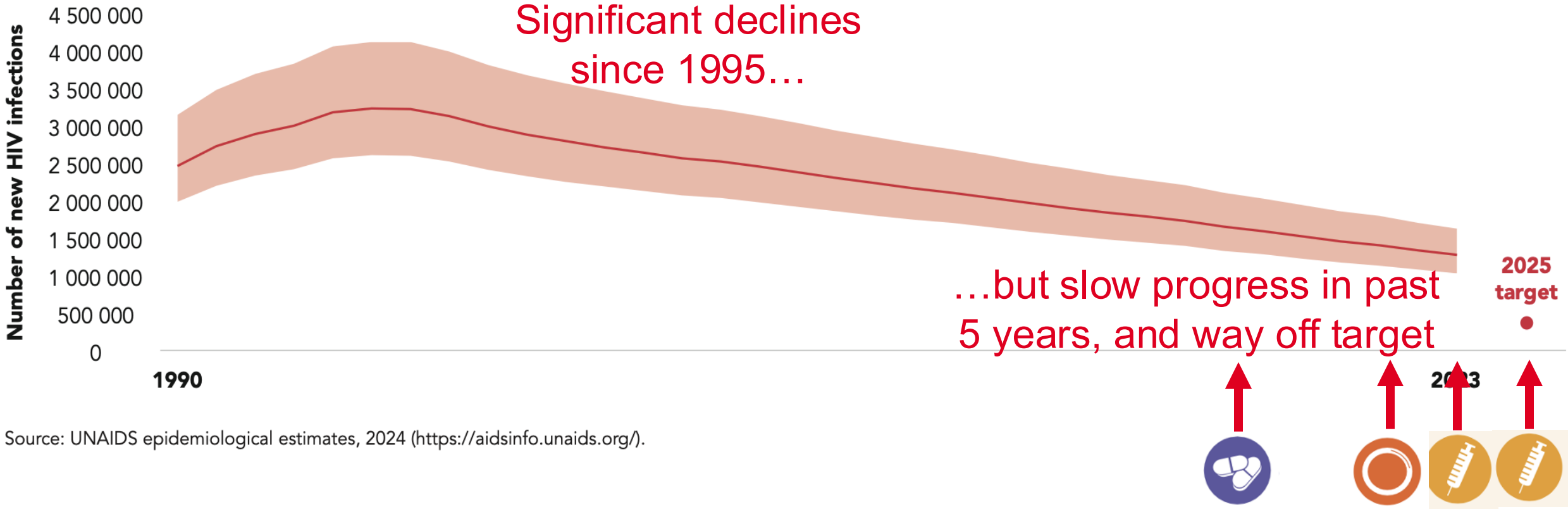
Overview of the Pipeline

Tracking 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/).

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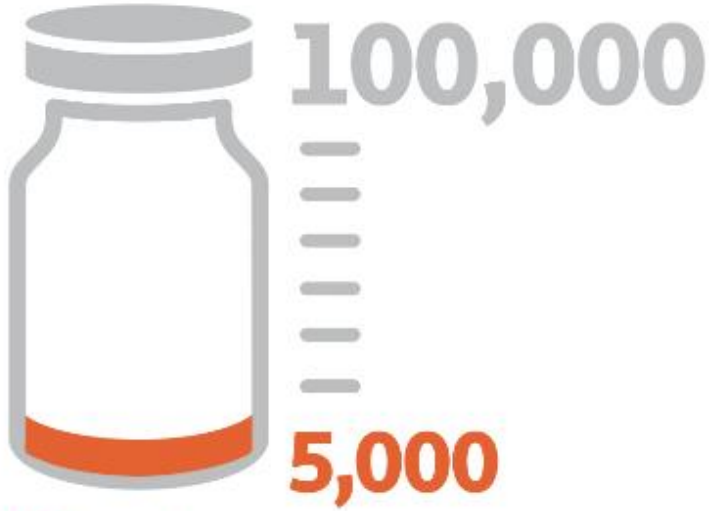
PrEP Initiations to 2024

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**

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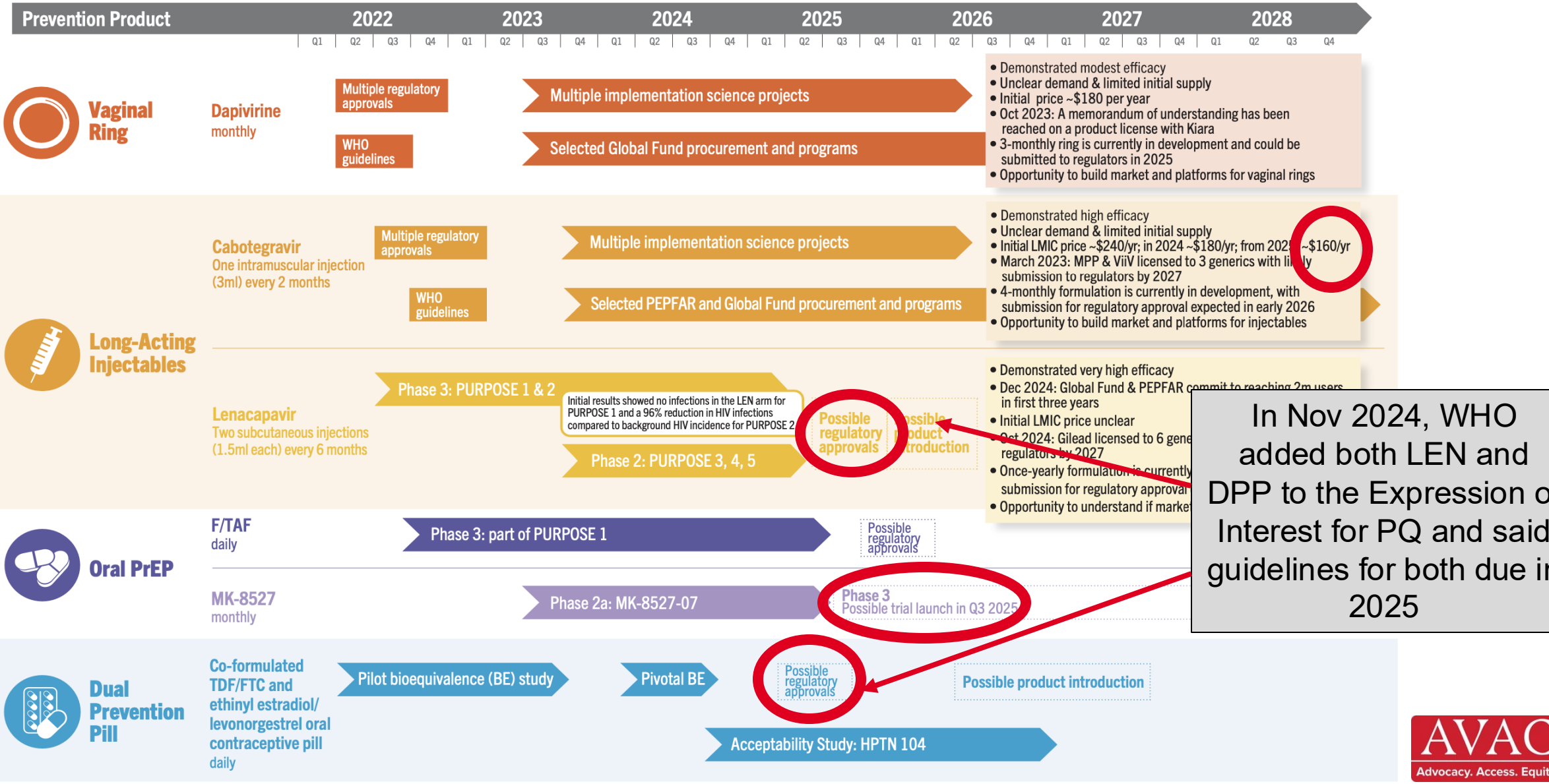
Updated Pipeline



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

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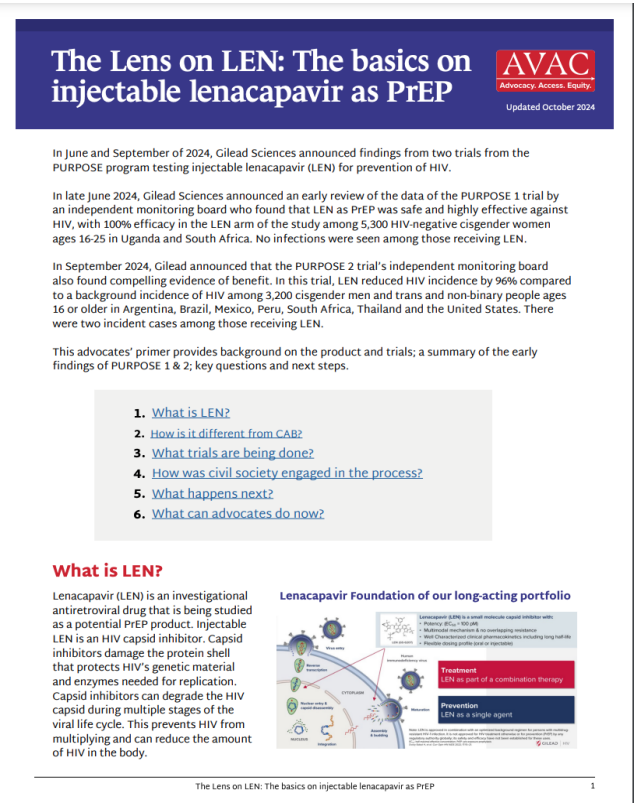
What is Lenacapavir (LEN)?

What is LEN?

Basics are outlined in the *Lens on LEN*

- Injectable lenacapavir (LEN) is an HIV capsid inhibitor
- LEN for PrEP is delivered in two subcutaneous injections in the abdomen once every six months
- There is also an oral loading dose—two at the time of the first injection and two more a day later
- Developed by Gilead Sciences, which is currently the sole manufacturer; six generics have licenses
- Approved since 2022 for treatment against multi-drug resistant HIV in combination with other ARVs
- Once-yearly LEN for PrEP is in development, with Phase I data showing promising results and possibly to market by 2028



The Lens on LEN: The basics on injectable lenacapavir as PrEP

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Updated October 2024

In June and September of 2024, Gilead Sciences announced findings from two trials from the PURPOSE program testing injectable lenacapavir (LEN) for prevention of HIV.

In late June 2024, Gilead Sciences announced an early review of the data of the PURPOSE 1 trial by an independent monitoring board who found that LEN as PrEP was safe and highly effective against HIV, with 100% efficacy in the LEN arm of the study among 5,300 HIV-negative cisgender women ages 16-25 in Uganda and South Africa. No infections were seen among those receiving LEN.

In September 2024, Gilead announced that the PURPOSE 2 trial's independent monitoring board also found compelling evidence of benefit. In this trial, LEN reduced HIV incidence by 96% compared to a background incidence of HIV among 3,200 cisgender men and trans and non-binary people ages 16 or older in Argentina, Brazil, Mexico, Peru, South Africa, Thailand and the United States. There were two incident cases among those receiving LEN.

This advocates' primer provides background on the product and trials; a summary of the early findings of PURPOSE 1 & 2; key questions and next steps.

1. What is LEN?
2. How is it different from CAB?
3. What trials are being done?
4. How was civil society engaged in the process?
5. What happens next?
6. What can advocates do now?

What is LEN?

Lenacapavir (LEN) is an investigational antiretroviral drug that is being studied as a potential PrEP product. Injectable LEN is an HIV capsid inhibitor. Capsid inhibitors damage the protein shell that protects HIV's genetic material and enzymes needed for replication. Capsid inhibitors can degrade the HIV capsid during multiple stages of the viral life cycle. This prevents HIV from multiplying and can reduce the amount of HIV in the body.

Lenacapavir Foundation of our long-acting portfolio

Treatment
LEN as part of a combination therapy

Prevention
LEN as a single agent

The Lens on LEN: The basics on injectable lenacapavir as PrEP 1

Check out *Lens on LEN* here: https://avac.org/resource/report/the-lens-on-len/

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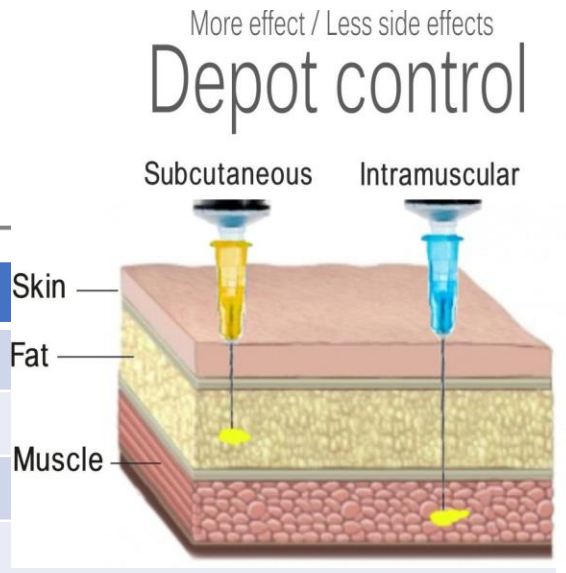
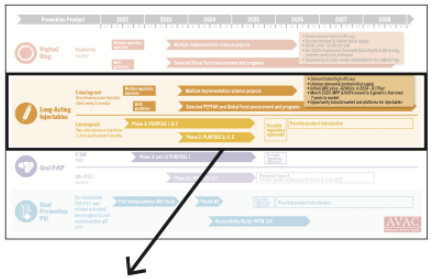
Side by Side: CAB and LEN



	Injectable Cabotegravir (CAB)	Injectable Lenacapavir (LEN)
ARV Drug Class	Integrase Strand Transfer Inhibitor	Capsid Inhibitor
Injection Type	Intramascular	Subcutaneous
Injection Site	Gluteal Muscle (buttocks)	Abdomen
Injection Volume	One 3ml injection	Two 1.5ml injections, with oral loading dose
Frequency/Interval	First injection, followed by a second one a 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.
Efficacy	Very high efficacy in all populations	Very high efficacy in all populations
Regulatory Approvals and Guidelines	25 regulatory approvals (in 56 countries) as of 31 March 2025 and 6 pending WHO recommendation as additional prevention option in July 2022	**US FDA:** decision expected by 19 June 2025 **WHO:** Guidelines expected by July 2025. **EMA:** Under accelerated review for Europe and via Medicines for All pathway for LMICs **LMICs:** Gilead submitted applications in several priority markets, including South Africa and Brazil
Price in LMICs	Approx $160 per year	TBD
Developer/Manufacturer	ViiV Healthcare	Gilead Sciences
Generic Manufacturers	Three licenses through MPP to Aurobindo, Cipla & Viatris – all Indian-based manufacturers, with expected earliest market access in 2027	Six licenses to Dr. Reddy's Laboratories Limited (India), Emcure (India), Eva Pharma (Egypt), Ferozsons Laboratories Limited (Pakistan), Hetero (India) and Mylan (a subsidiary of Viatris, with a subsidiary in India)

Overview of the Purpose Program

Planning for Injectable Lenacapavir



Trial	Population	Location	Size	2022	2023	2024	2025	2026	2027	2028
PURPOSE 1 Phase 3 Injectable lenacapavir & oral F/TAF	Cisgender adolescent girls and young women	South Africa and Uganda	**5,010**	Initial results released in June 2024 demonstrated no infections in the LEN arm						
PURPOSE 2 Phase 3 Injectable lenacapavir	Cisgender men who have sex with men, Transgender women, Transgender men, Gender non-binary	US, South Africa, Peru, Brazil, Mexico, Argentina, and Thailand	**3,000**		Initial results released in September 2024 demonstrated LEN reduced HIV infections by 96% compared to background HIV incidence					
PURPOSE 3 **HPTN 102** Phase 2 Injectable lenacapavir	Cisgender women	US	**250**			Currently recruiting; estimated study completed date early 2028				
PURPOSE 4 **HPTN 103** Phase 2 Injectable lenacapavir	People who inject drugs	US	**250**			Currently recruiting; estimated study completed date mid-2027				
PURPOSE 5 Phase 2 Injectable lenacapavir	Cisgender men who have sex with men, Transgender women, Transgender men, Gender non-binary	France and UK	**262**			Enrollment expected to begin in the second half of 2024				

- Possible efficacy data
- Possible earliest regulatory submissions
- Possible earliest regulatory approval and market entry with product from Gilead
- Possible earliest generic manufacturer(s)

PURPOSE 1 and PURPOSE 2 Studies

The Time Is Now

The NEW ENGLAND JOURNAL of MEDICINE

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

Twice-Yearly Lenacapavir for HIV Prevention in Men and Gender-Diverse Persons

The Real PURPOSE of PrEP — Effectiveness, Not Efficacy

Rochelle P. Walensky, M.D., M.P.H., and Lindsey R. Baden, M.D.

Long-Acting HIV Medicines and the Pandemic Inequality Cycle — Rethinking Access

Winnie Byanyima, M.Sc., Linda-Gail Bekker, M.B., Ch.B., Ph.D., and Matthew M. Kavanagh, Ph.D.

NEJM Journal Watch

DECEMBER 8TH, 2024

Who's Going to Get Lenacapavir for HIV Prevention?

Paul E. Sax, MD

Gilead under fire over HIV drug licensing

New licensing agreements for production of a generic version of HIV drug lenacapavir have been heavily criticised by activists who say they are too restrictive. Ed Holt reports.

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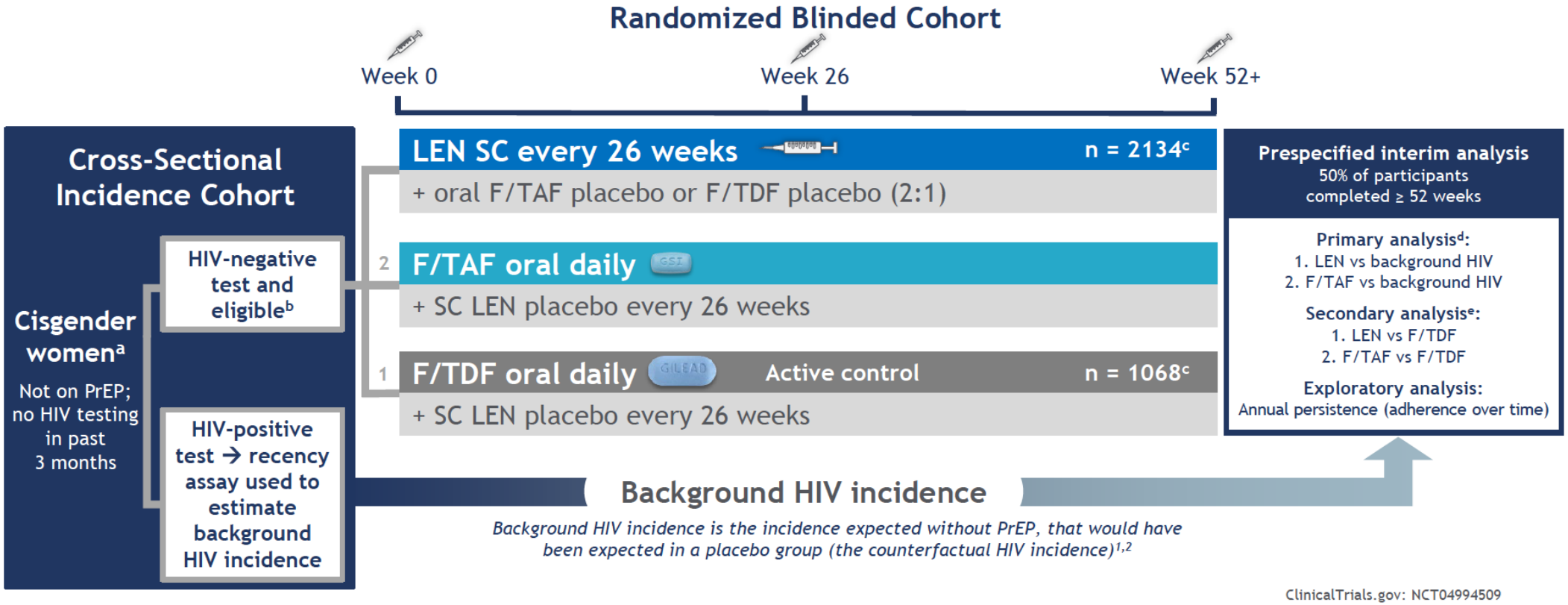
PURPOSE I Study Design

PURPOSE 1 Study Design

LEN and F/TAF for PrEP among Cisgender Women



ClinicalTrials.gov: NCT04994509

[a]The first participant was screened in August 2021, the 50th percentile participant was randomized in May 2023, and the last participant was randomized in September 2023. [b]Eligibility criteria included: weight ≥ 35 kg, eGFR ≥ 60 mL/min, not pregnant. [c]n numbers represent the full analysis set for efficacy analyses. [d]IRR was assessed using a Wald test or likelihood ratio test if there were zero infections.[1,2] [e]IRR was assessed using Poisson regression or an exact conditional Poisson regression model in case of zero infections. **eGFR**, estimated glomerular filtration rate; **F/TAF**, emtricitabine/tenofovir alafenamide; **F/TDF**, emtricitabine/tenofovir disoproxil fumarate; **HIV**, human immunodeficiency virus; **IRR**, Incidence rate ratio; **LEN**, lenacapavir; **PrEP**, pre-exposure prophylaxis; **SC**, subcutaneous. 1. Gao F, et al. *Stat Commun Infect Dis.* 2021;13(1):20200009. 2. Shao Y, Gao F. *Stat Commun Infect Dis.* 2024;16(1):20230004.

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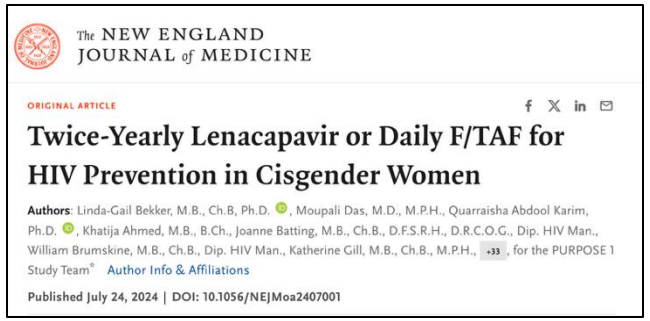
PURPOSE I Results

Highlights:

- Enrolled 5368 participants in South Africa and Uganda
- LEN showed superior results vs. daily oral PrEP
- Zero HIV infections among participants receiving twice-yearly LEN
- Lower HIV incidence with LEN compared to:
  - Background HIV rates
  - Daily oral F/TDF



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

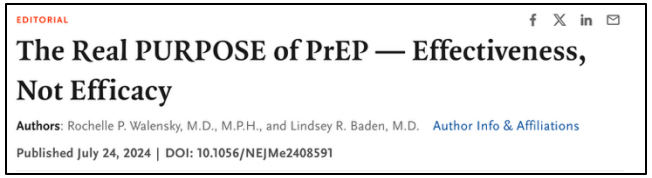
Twice-Yearly Lenacapavir or Daily F/TAF for HIV Prevention in Cisgender Women

Authors: Linda-Gail Bekker, M.B., Ch.B, Ph.D., Moupali Das, M.D., M.P.H., Quarraisha Abdool Karim, Ph.D., Khatija Ahmed, M.B., B.Ch., Joanne Batting, M.B., Ch.B., D.F.S.R.H., D.R.C.O.G., Dip. HIV Man., William Brumskine, M.B., Ch.B., Dip. HIV Man., Katherine Gill, M.B., Ch.B., M.P.H., +33, for the PURPOSE 1 Study Team* Author Info & Affiliations

Published July 24, 2024 | DOI: 10.1056/NEJMoa2407001

AIDS Activists Delight in HIV Prevention Trial Results – And Press Gilead to Lower Price of 'Miracle Drug'

HIV and AIDS 24/07/2024 · Kerry Cullinan



EDITORIAL

The Real PURPOSE of PrEP — Effectiveness, Not Efficacy

Authors: Rochelle P. Walensky, M.D., M.P.H., and Lindsey R. Baden, M.D. Author Info & Affiliations

Published July 24, 2024 | DOI: 10.1056/NEJMe2408591

Doctor behind trial of HIV prevention drug recounts breakthrough moment

Prof Linda-Gail Bekker receives ovation at Aids summit after presenting trial results of 'miracle' drug lenacapavir

The New York Times

New Drug Provides Total Protection From H.I.V. in Trial of Young African Women

An injection given just twice a year could herald a breakthrough in protecting the population that has the highest infection rates.

The long wait for long-acting HIV prevention and treatment formulations

CrossMark

Willem Daniel Francois Venter, Monica Gandhi, Simiso Sokhela, Kenly Sikwese, Helen Bygrave, Louis Da Gama, Ndiviwe Mphothulo, Lise Jamieson, Mark J Siedner, Anton Pozniak, Pablo Rojo, Solange L Baptiste, Jacque Wambui, Gesine Meyer-Rath, Brian Honerman, Mitchell Warren, Linda Gayle-Bekker, Phumla Sinxadi, Simon Collins, Jessica Burry, Karlien Möller, Polly Clayden, Andrew Owen, Andrew Hill

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PURPOSE I Results

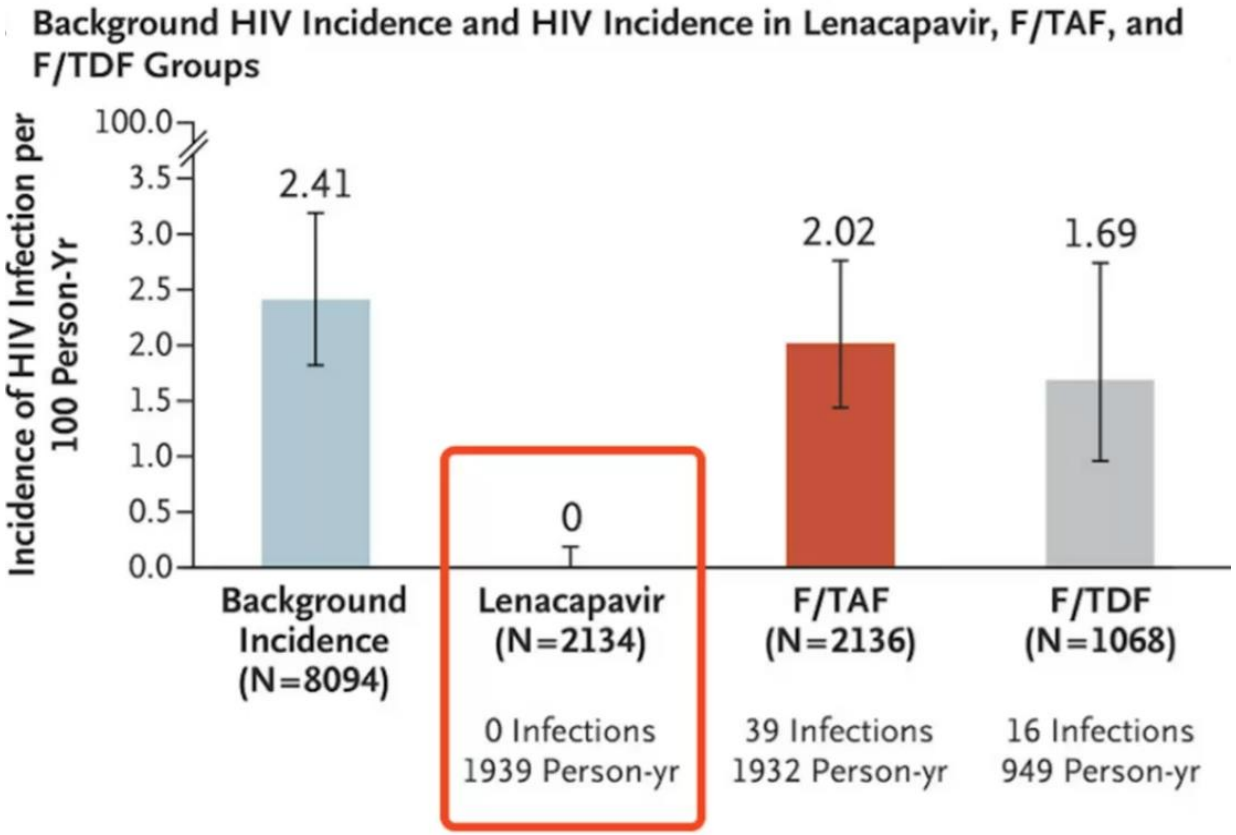
55 total HIV infections:

- **38** in **F/TAF** group
- **16** in **TDF/FTC** group
- **0** in **LEN** group
- Background HIV incidence: 2.41%

Side Effects:

- Similar rates of headaches & UTIs across all study arms
- Less nausea & vomiting with LEN compared to daily pill groups
- Injection site reactions = most common issue with LEN
  - Only 4 participants (0.2%) stopped due to this

Area to Watch: Infant exposure & long-term effects in pregnant participants



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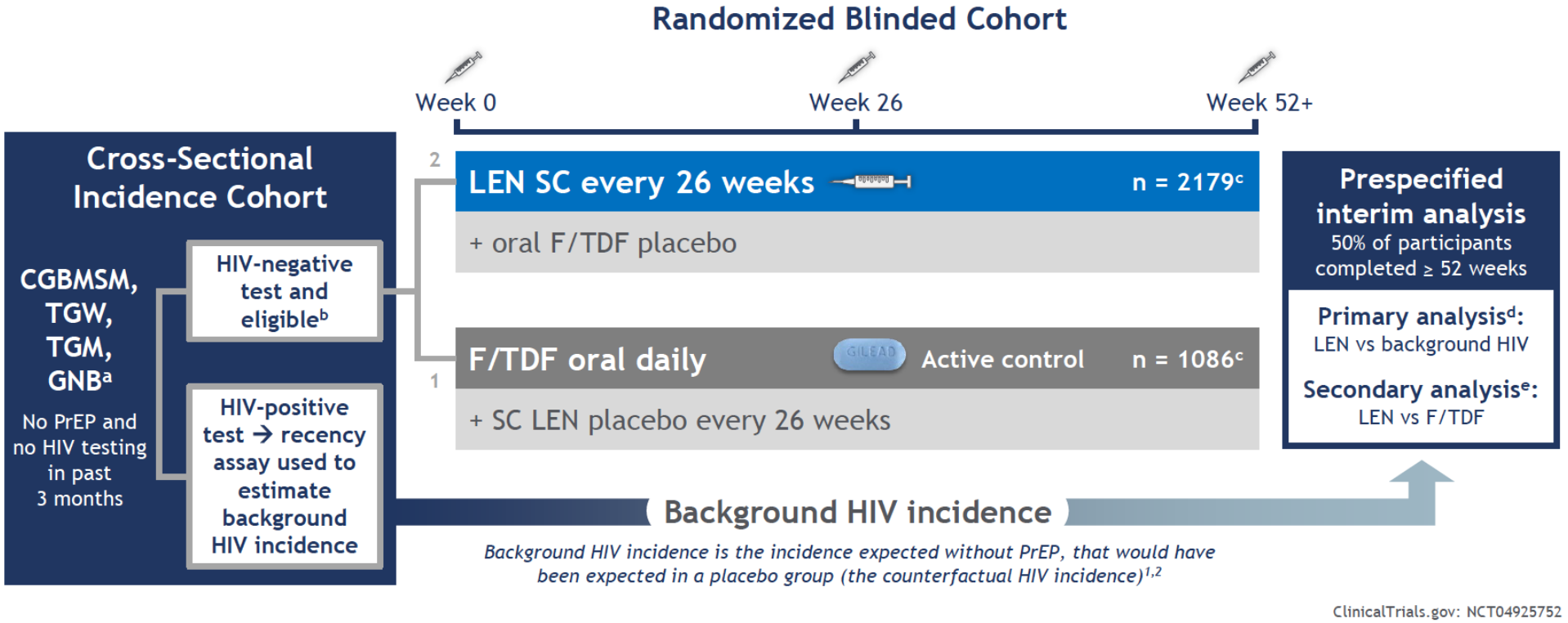
PURPOSE II Study Design

PURPOSE 2 Study Design



ClinicalTrials.gov: NCT04925752

All participants had real-time HIV testing with an FDA-approved, rapid, point-of-care, fourth-generation antigen-antibody test and a central laboratory fourth-generation antigen-antibody test, which, if positive, was confirmed by an HIV-1/2 antibody differentiation assay, and, if the results were discrepant, a qualitative HIV RNA test was conducted. All participants also had a quantitative HIV-1 RNA test (Roche Cobas 6800 HIV-1 test) during screening (lower limit of quantification, 20 copies/mL). HIV-1 cases were defined as participants with ≥ 1 of the following laboratory results: positive HIV-1/2 differentiation assay, positive HIV-1 RNA qualitative test, or HIV-1 RNA quantitative test ≥ 200 copies/mL. On Days 1 and 2, all participants received a loading dose of 600 mg oral LEN or matched oral placebo. [a]The first participant was screened in June 2021, the 50th percentile participant was randomized in August 2023, and the last participant was randomized in December 2023. [b]Eligibility criteria included: age ≥ 16 years, weight ≥ 35 kg, eGFR ≥ 60 mL/min, not pregnant. [c]n numbers represent the full analysis set for efficacy analyses. [d]IRR was assessed using a Wald test.[1,2] [e]IRR was assessed using Poisson regression. CGBMSM, cisgender gay and bisexual men who have sex with men; eGFR, estimated glomerular filtration rate; FDA, US Food & Drug Administration; F/TDF, emtricitabine/tenofovir disoproxil fumarate; GNB, gender nonbinary individuals; IRR, incidence rate ratio; TGM, transgender men; TGW, transgender women. 1. Gao F, et al. *Stat Commun Infect Dis*. 2021;13:20200009. 2. Shao Y, Gao F. *Stat Commun Infect Dis*. 2024;16:20230004.

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PURPOSE II Results

Highlights:

- Enrolled 3,295 participants from Argentina, Brazil, Mexico, Peru, South Africa, Thailand & US
- LEN showed superior results vs daily oral TDF/FTC
- LEN reduced HIV infections by 96% compared to background HIV rates and by 89% compared to daily oral TDF/FTC rates
- Two HIV infections among 2180 participants receiving twice-yearly LEN

Press Releases

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

Updated Statement on Access Planning in High-Incidence, Resource-Limited Countries for Lenacapavir for HIV Prevention

Foster City, Calif., September 12, 2024 – Today, Gilead announced that the company's twice-yearly injectable HIV-1 capsid inhibitor, lenacapavir, demonstrated superiority to background HIV incidence (bHIV) and once-daily oral Truvada® for the investigational use of HIV prevention at an interim analysis of a second pivotal Phase 3 clinical trial.

This preventive drug could be a 'game changer' in ending the HIV epidemic

SEPTEMBER 17, 2024 · 8:09 AM ET

By David Cox, Maria Isabel Barros Guinle

Lenacapavir Looks to Revolutionize HIV Prevention

New PURPOSE 2 study results show the superiority of twice-yearly injectable PrEP to once-a-day oral Truvada

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PURPOSE II Results

11 total HIV infections:

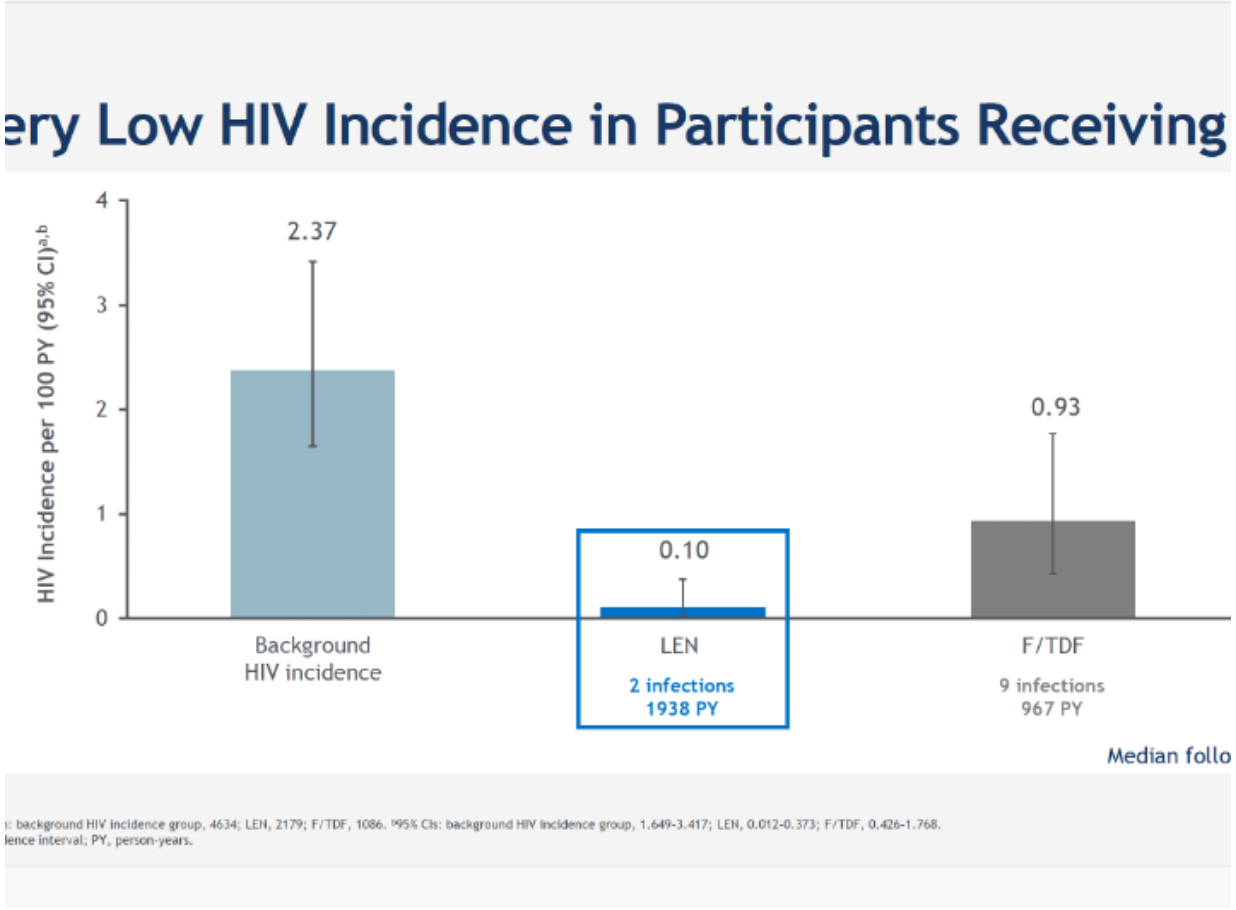
- **9** in **TDF/FTC** group (in 1086 participants)
- **2** in **LEN** group (among 2180 participants)
- Background HIV incidence: 2.37%

Side Effects:

- Nodules – common in the LEN group, compared to the TDF/FTC group.
- Injection-site pain
- Erythema – mostly observed in PURPOSE 2
- Injection site reactions = most common issue with LEN
  - 26 participants stopped due to this
- All injection-site reactions (ISRs) were mostly grade 1 & 2 and resolved on their own over time and diminished with subsequent injections

Area to Watch

- Real-world implications of injection site nodules (e.g., duration, induration) and contraindications of LEN with other medications, including treatments for migraines or with use of Cialis & Viagra



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More about the 2 Infections in the LEN Group

Participant 1	Participant 2
▪ Transgender woman with latent syphilis diagnosed and treated at baseline ▪ Engaged in transaction sex ▪ Diagnosed with HIV-1 at week 13 with standard HIV testing ▪ Participant received on-time LEN injections	▪ Cisgender gay man with rectal chlamydia diagnosed and treated at screening ▪ Diagnosed with HIV-1 at week 26 with standard HIV testing ▪ Participant received on-time LEN injections

Key Observations:

- Both participants
  - Showed no evidence of delayed HIV diagnoses by RNA or LEVI syndrome
  - Had LEN concentrations consistent with 10% random subset of participants and comparable to prior studies
  - Presented with an N74E capsid mutation at HIV diagnosis
- The N74D capsid mutation:
  - Is not a naturally occurring or transmuted mutation
  - Was determined not to be caused by LEN

Possible explanation:

- Both individuals were likely exposed to partners in the acute phase of HIV infection, potentially associated with very high viral loads

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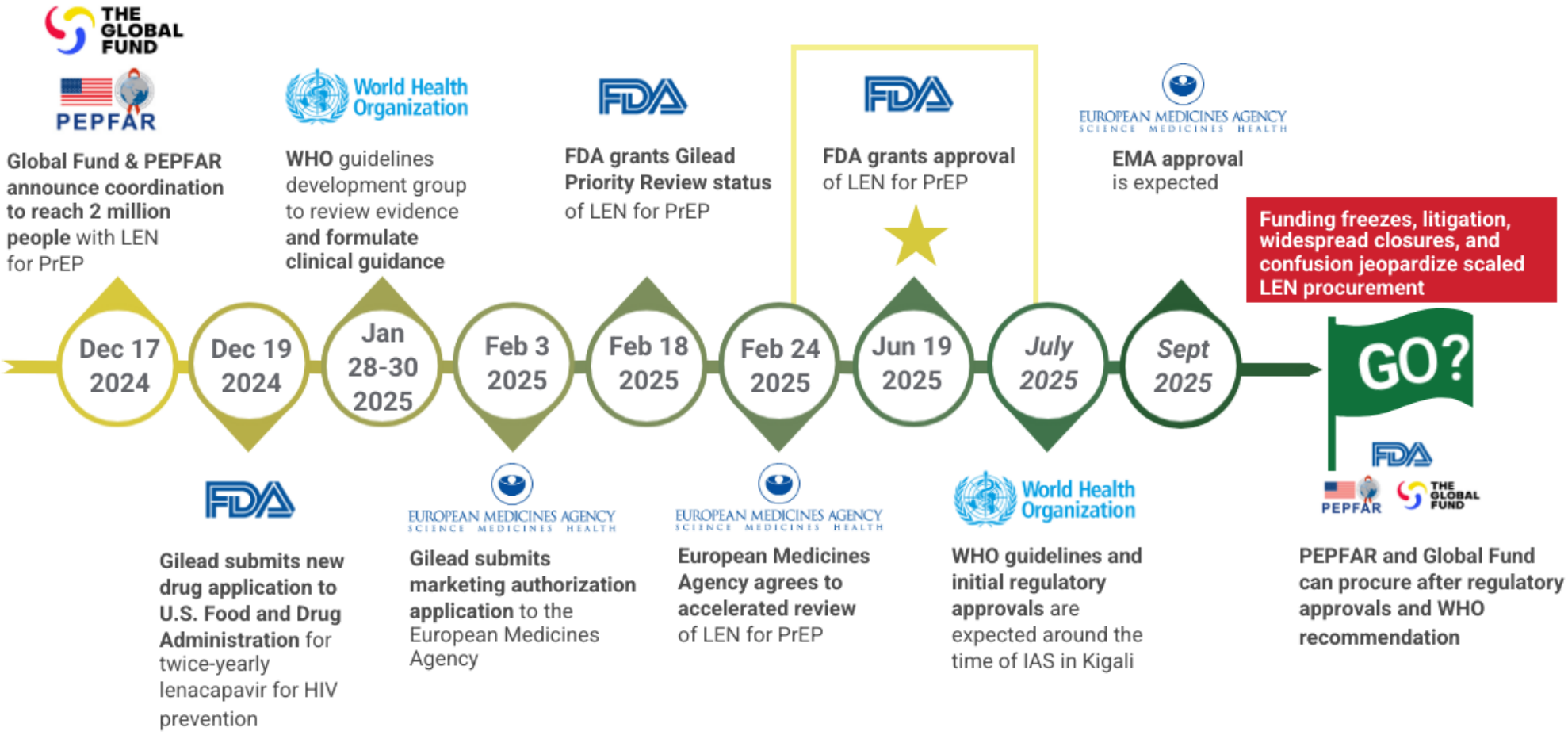
Regulatory Updates

Our Best Shot at Prevention – But Now What?



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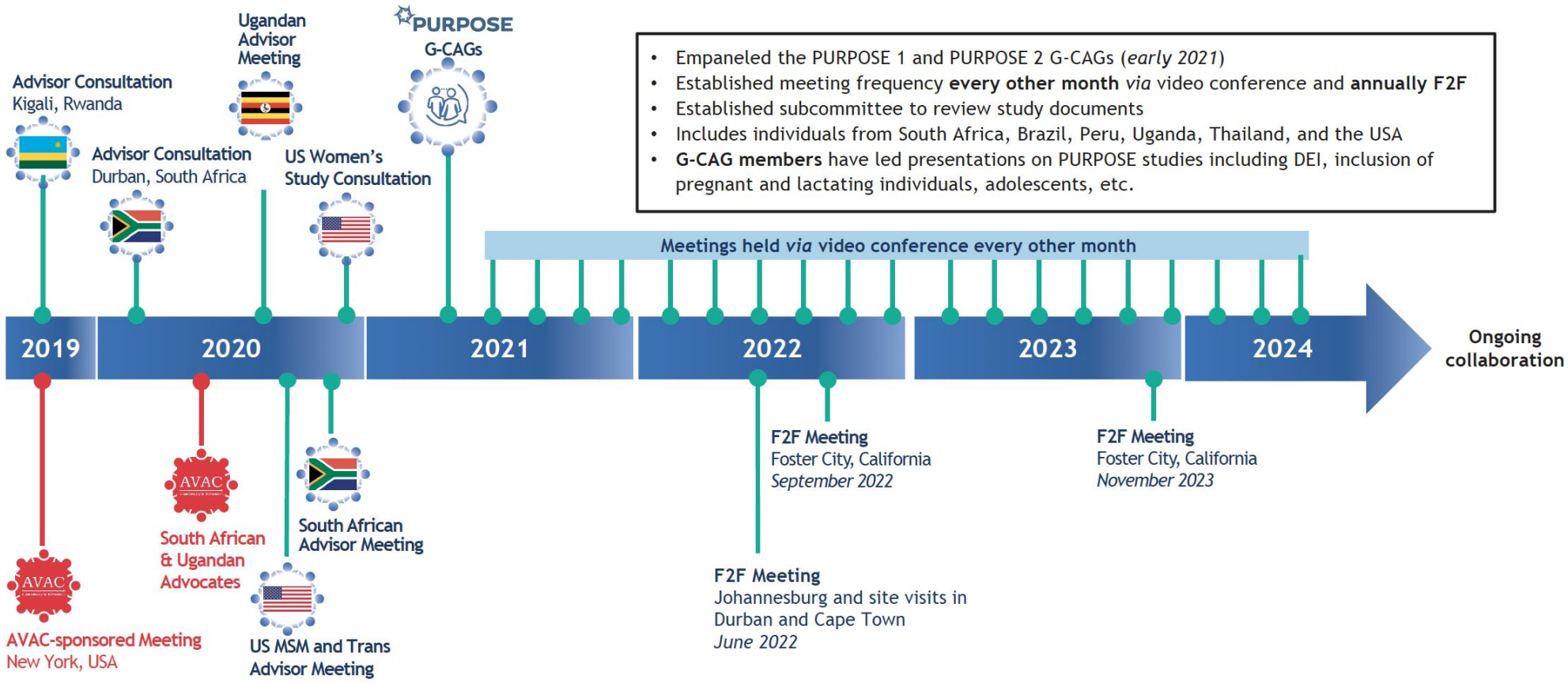
P1 & P2 Stakeholder Engagement Efforts

Stakeholder Engagement in PURPOSE Program

Figure 5. Timeline of Advisor Engagement During the PURPOSE Program



DEI, diversity, equity, and inclusion; F2F, face-to-face; G-CAG, Global Community Advisory Group; MSM, men who have sex with men.

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Gilead's Stakeholder Engagement in PURPOSE

- **Early and Consistent Engagement:** Gilead established Global Community Accountability Groups (G-CAGs) early in the PURPOSE program to ensure community input from study design to implementation
- **Community-Centered Trial Design:** Involve community voices in protocol design, consent materials, and messaging
- **Broad Representation:** G-CAG members represent communities and potential end-users from South Africa, Uganda, Brazil, Peru, Thailand & US, ensuring diverse and inclusive perspectives
  - P1 GCAG included AGYW, pregnant & lactating people (PLPs), and advocates who represent them
- **Structured Participation:** Guided by clear Terms of Reference and workplans, G-CAG members regularly met virtually and annually during face-to-face meetings
- **GPP in Action:** Helped build trust, ensure relevance, and promote ethical inclusion of historically excluded populations
- **Influence on Protocols:** G-CAG feedback shaped critical aspects of the trial
  - Tailored consent processes for adolescents
  - Respect for reproductive choice without mandatory contraception
  - Continued participation of PLPs with reconsent
  - Screening and support for intimate partner violence

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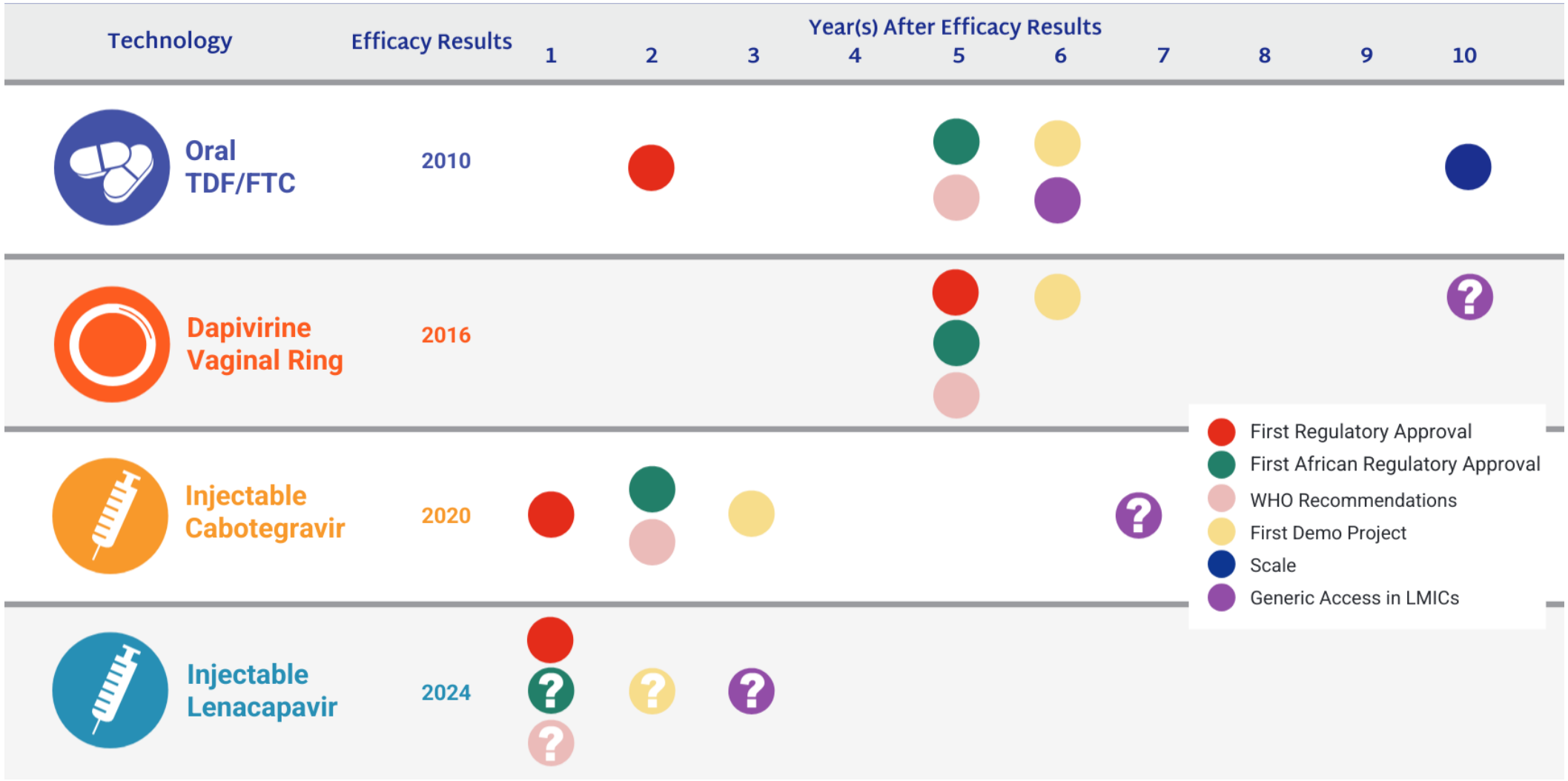
From Research to Rollout

Moving a Product to the "Real World"



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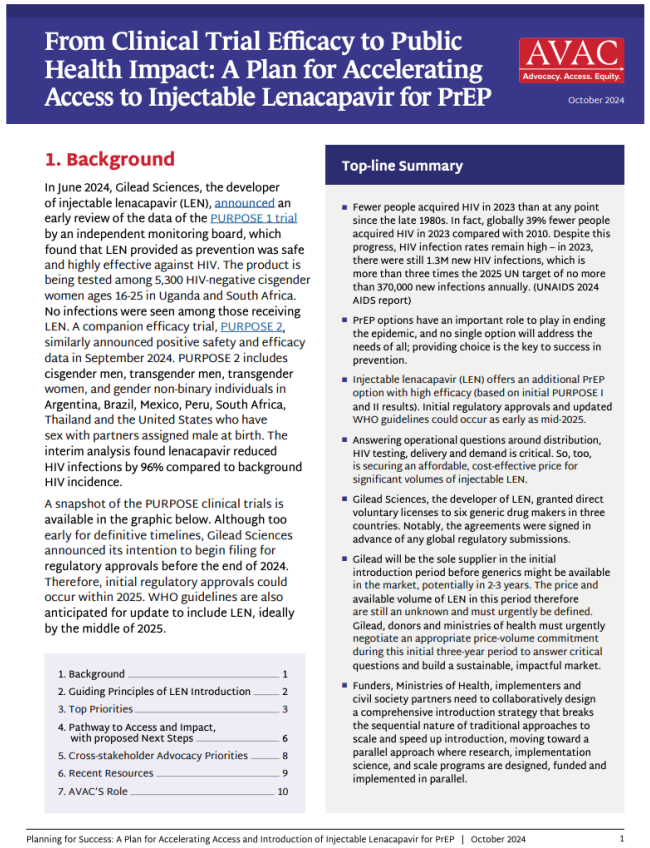
Understanding LEN Rollout

	A Plan for Accelerating Access to Injectable Lenacapavir for PrEP	*Gears of LEN for PrEP Rollout*
Purpose	Outlines a high-level strategy to ensure equitable, ethical, and accelerated access by coordinating regulatory approvals, financing, manufacturing, and demand generation	Provides a clear roadmap for accelerating the rollout, highlighting what must do. Aligning technical, policy, and procurement workstreams across governments, donors, civil society, and industry to deliver LEN at scale by 2028
Key Themes	▪ "Speed, Scale & Equity" ▪ Fast-track regulatory approvals ▪ Transparent pricing & supply commitments ▪ Global & regional licensing equity ▪ Community-centered demand generation ▪ Data transparency & integrated service delivery	▪ Three-phase rollout framework ▪ Clear pricing benchmarks from $100 (Phase 0) to <$40 (Phase 2) ▪ Defined roles for donors, governments, Gilead, WHO, and communities ▪ Regulatory milestones and volume planning ▪ Pathway to generics and sustainable access
Focus	**Advocacy Focus:** ▪ Push for Gilead transparency and equitable licensing (including Latin America & Africa) ▪ Strengthen community engagement and implementation science ▪ Call for integration into national programs and funding mechanisms	**Implementation Focus:** ▪ Who does what and when ▪ Timeline for supply chain readiness ▪ Forecasting needs and national preparedness ▪ Key country and regional milestones

Plan for Accelerating Access to LEN

- **Fast-Track Regulatory Approvals**
  - Expedite WHO guideline development (expected mid-2025) – to align with regulatory approvals
  - Urge **regulatory agencies to fast-track reviews and approvals, particularly** in high-burden countries
  - **Ensure Gilead submits in-country applications promptly for broader global access**
- **Ethical Concerns: Exclusion of Latin America in Voluntary Licensing**
  - **Voluntary licenses** granted to six generic manufacturers (India, Egypt, Pakistan) **before regulatory submissions**—a positive move
  - **None of the generic manufacturers selected by Gilead** are located in **Latin America**, where PURPOSE 2 trial was conducted
  - Gilead **did not prioritize Latin America for voluntary licensing**, despite significant trial participation
  - Urge **Gilead to expand voluntary licensing agreements** to include manufacturers in **Africa and Latin America** to ensure **regional equity in access**



From Clinical Trial Efficacy to Public Health Impact: A Plan for Accelerating Access to Injectable Lenacapavir for PrEP

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October 2024

1. Background

In June 2024, Gilead Sciences, the developer of injectable lenacapavir (LEN), announced an early review of the data of the PURPOSE 1 trial by an independent monitoring board, which found that LEN provided as prevention was safe and highly effective against HIV. The product is being tested among 5,300 HIV-negative cisgender women ages 16-25 in Uganda and South Africa. No infections were seen among those receiving LEN. A companion efficacy trial, PURPOSE 2, similarly announced positive safety and efficacy data in September 2024. PURPOSE 2 includes cisgender men, transgender men, transgender women, and gender non-binary individuals in Argentina, Brazil, Mexico, Peru, South Africa, Thailand and the United States who have sex with partners assigned male at birth. The interim analysis found lenacapavir reduced HIV infections by 96% compared to background HIV incidence.

A snapshot of the PURPOSE clinical trials is available in the graphic below. Although too early for definitive timelines, Gilead Sciences announced its intention to begin filing for regulatory approvals before the end of 2024. Therefore, initial regulatory approvals could occur within 2025. WHO guidelines are also anticipated for update to include LEN, ideally by the middle of 2025.

Top-line Summary

- Fewer people acquired HIV in 2023 than at any point since the late 1980s. In fact, globally 39% fewer people acquired HIV in 2023 compared with 2010. Despite this progress, HIV infection rates remain high – in 2023, there were still 1.3M new HIV infections, which is more than three times the 2025 UN target of no more than 370,000 new infections annually. (UNAIDS 2024 AIDS report)
- PrEP options have an important role to play in ending the epidemic, and no single option will address the needs of all; providing choice is the key to success in prevention.
- Injectable lenacapavir (LEN) offers an additional PrEP option with high efficacy (based on initial PURPOSE I and II results). Initial regulatory approvals and updated WHO guidelines could occur as early as mid-2025.
- Answering operational questions around distribution, HIV testing, delivery and demand is critical. So, too, is securing an affordable, cost-effective price for significant volumes of injectable LEN.
- Gilead Sciences, the developer of LEN, granted direct voluntary licenses to six generic drug makers in three countries. Notably, the agreements were signed in advance of any global regulatory submissions.
- Gilead will be the sole supplier in the initial introduction period before generics might be available in the market, potentially in 2-3 years. The price and available volume of LEN in this period therefore are still an unknown and must urgently be defined. Gilead, donors and ministries of health must urgently negotiate an appropriate price-volume commitment during this initial three-year period to answer critical questions and build a sustainable, impactful market.
- Funders, Ministries of Health, implementers and civil society partners need to collaboratively design a comprehensive introduction strategy that breaks the sequential nature of traditional approaches to scale and speed up introduction, moving toward a parallel approach where research, implementation science, and scale programs are designed, funded and implemented in parallel.

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Gears of Lenacapavir for PrEP Rollout

The rollout of lenacapavir represents not just a scientific breakthrough, but a pivotal moment in global health equity. Stakeholders must act decisively to seize this opportunity, ensuring that all populations—regardless of geography, income, or identity—benefit from this innovative prevention tool.

The Gear Framework for Lenacapavir for PrEP Rollout

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Phases of LEN Rollout

- Donors and procurers: Provide clear volume forecasts/ commitments to Gilead.
- National governments: Prepare early implementation plans, comprehensive programs and guidelines to and maximize access.
- WHO: PQ Expression of interest. Develop robust guidelines with diverse stakeholders.
- Foundations, development banks, and partners: Lead discussions on innovative financing and public-private partnerships.
- Gilead: Manufacture products (18-month lead time), announce VLs, submit FDA/EM4All, and support advocacy for demand generation activities.
- UNAIDS: High-level diplomacy to prioritize HIV prevention with health and finance ministers.
- UNITAID/international actors: Advocate for rapid regulatory approvals from national governments, structure financing arrangements

- Gilead to manufacture up to 10 million vials (TBD) for shipment.
- National governments/procurement agencies: Secure necessary import documentation, waivers, and supply routes.
- LEN registrations: Expected approval in several countries, with costed targets and ambitious rollout plans.
- Community engagement, demand generation, and implementation science: Prioritized with support from PEPFAR, Global Fund, CIFF, and UNITAID.
- Stakeholder advocacy: Partnerships with UNAIDS and others are key to maintaining political momentum and financial support.
- Generic lenacapavir: Efforts to secure raw materials and begin production, targeting availability by 2028.

- LEN expected to be approved in over 50 countries, with generic options lowering costs and increasing access.
- Vigilance is required to help generic manufacturers secure regulatory approvals, PQ, maintain stable supply chains, and prevent stockouts.
- Community engagement and involvement of affected populations are key to reducing stigma and educating on new prevention options.
- Real-time implementation science should focus on practical application.
- Sustainable funding from international aid, domestic investment, and innovative financing is essential for scaling efforts.
- Integrating long-acting PrEP into broader health services
- More choice to come online potentially (new products, modalities)

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Recent LEN Announcement – December 2024

★ ★ ★

Global Fund, PEPFAR Announce Coordinated Effort to Reach 2 Million People with Lenacapavir for PrEP to Significantly Reduce Global HIV Infections

PEPFAR RELEASE

DECEMBER 17, 2024

"The Global Fund and PEPFAR are aiming to secure sustainable arrangements for countries to access this new, potentially game-changing HIV prevention innovation – backed by a significant commitment from CIFF, and with support from BMGF – that would enable access to lenacapavir for at least 2 million people over three years in countries supported by PEPFAR and the Global Fund."

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Recent LEN Announcement – December 2024

★ ★ ★

Global Fund, PEPFAR Announce Coordinated Effort

The Global Fund will roll out the twice-yearly anti-HIV jab — with or without Pepfar

Ida Jooste – March 4, 2025

BHEKISISA
CENTRE FOR HEALTH JOURNALISM

PEPFAR and the Global Fund.

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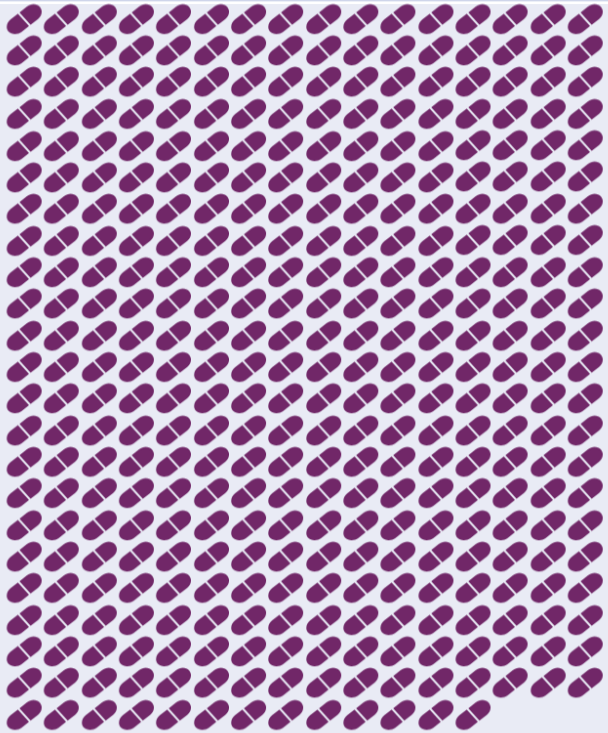
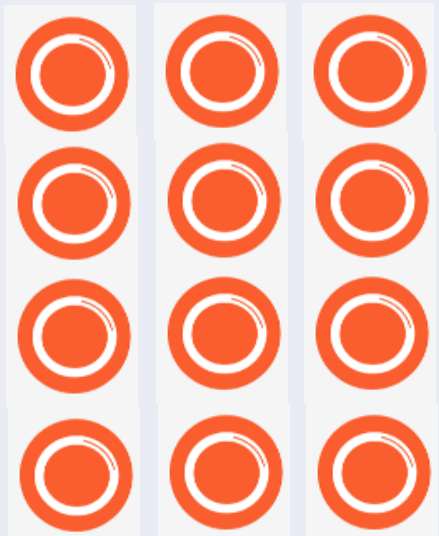
What Is a "Person Year of Protection"?

	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:

What Is a "Person Year of Protection"?

PEPFAR & Global Fund committed to "2 million person years of protection over 3 years"

- 1 year of protection is 4 vials of LEN and 4 pills
- So, 8 million vials for 2 million people
- Its 10M doses because we know not everyone will come back year on year, so a rough guess
- Gilead said can manufacture 10 M vials per year if they get orders
- This would ideally start in October 2025 and scale up from there.
- Media is talking about doses, but what is really meant is person years of protection

- Key message: Our biggest barrier to speed, scale and equity is

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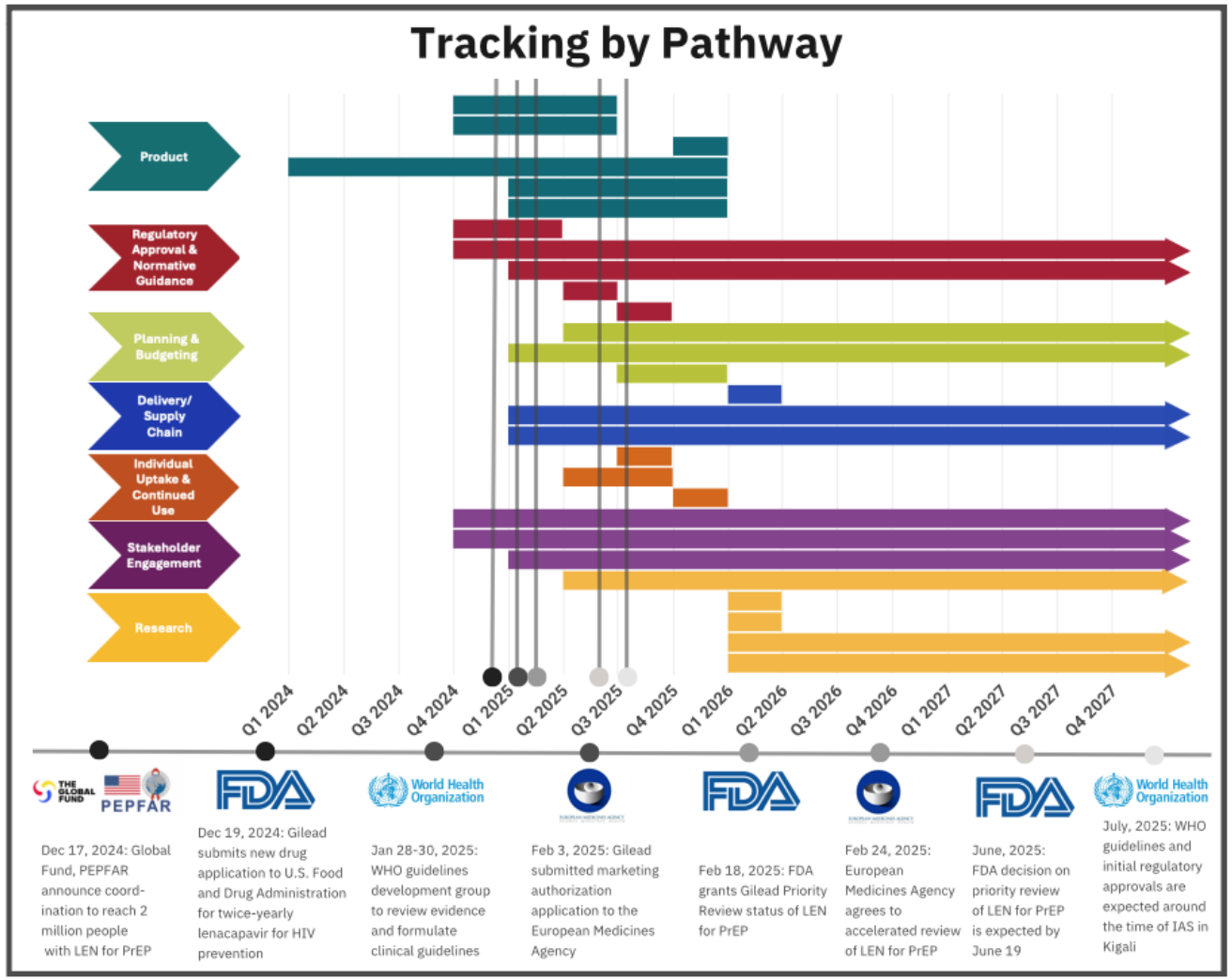
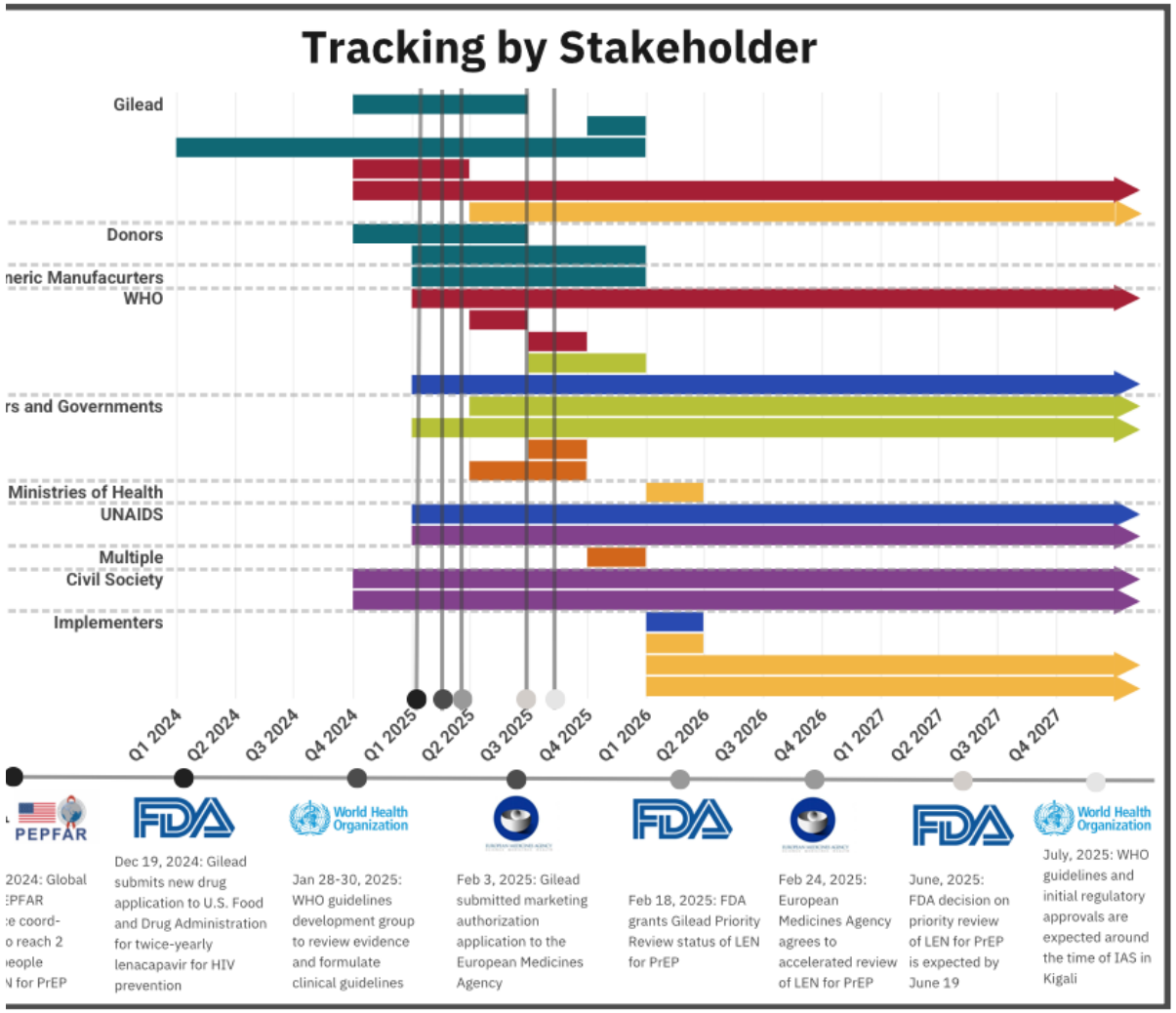
Tracking Lenacapavir Rollout





https://www.prepwatch.org/tracking-lenacapavir-rollout/

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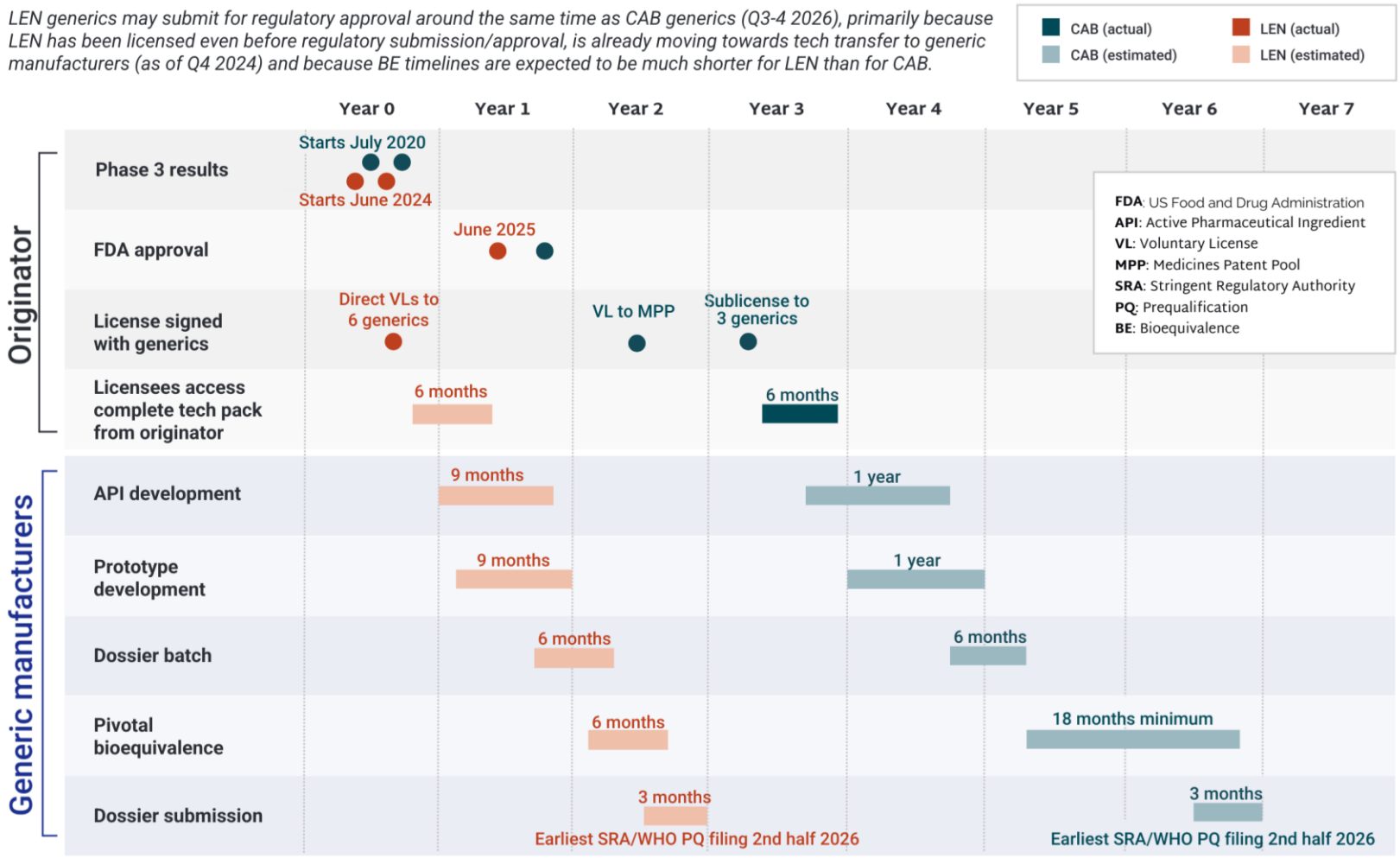
Development Timeline for Generic CAB & LEN

LEN generics may submit for regulatory approval around the same time as CAB generics (Q3-4 2026), primarily because LEN has been licensed even before regulatory submission/approval, is already moving towards tech transfer to generic manufacturers (as of Q4 2024) and because BE timelines are expected to be much shorter for LEN than for CAB.



This graphic aims to exhibit average timelines, but it is important to acknowledge that each generic manufacturer will move at different timelines and that unanticipated delays can happen at any step of the processes shown above. This graphic therefore aims to estimate timelines but should be used as a guideline rather than taken as 100% definitive.

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Lenacapavir: Once-Yearly PrEP Injection

- **Next-generation LEN**: New once-yearly formulation entering a registrational bio-equivalence (BE) trial in late 2025
- **Sustained protection**: Phase 1 results show drug levels exceeding those in PURPOSE studies, maintained for at least 12 months (≥ 56 weeks)
- **Innovative delivery**: Administered via two intramuscular injections (5mL each), avoiding nodules seen with subcutaneous injections
- **Efficient dosing**: Lower doses shown to sustain protective levels, enabling annual administration
- **Well-tolerated**: Only mild-to-moderate side effects, primarily brief injection site pain
- **Fast-tracked potential**: Does not require large efficacy trial; possible regulatory approval by 2027

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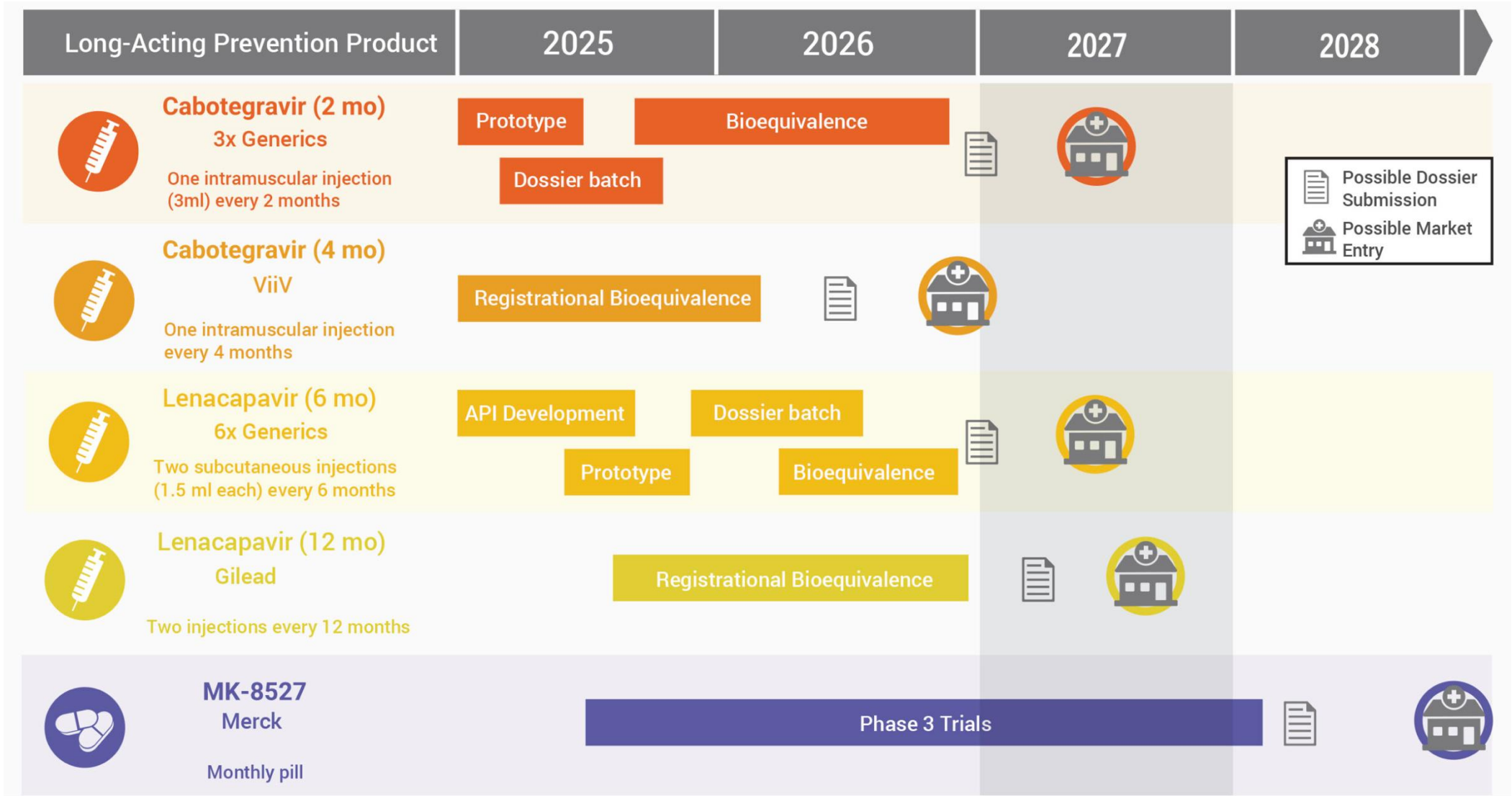
Long-Acting PrEP of the Future



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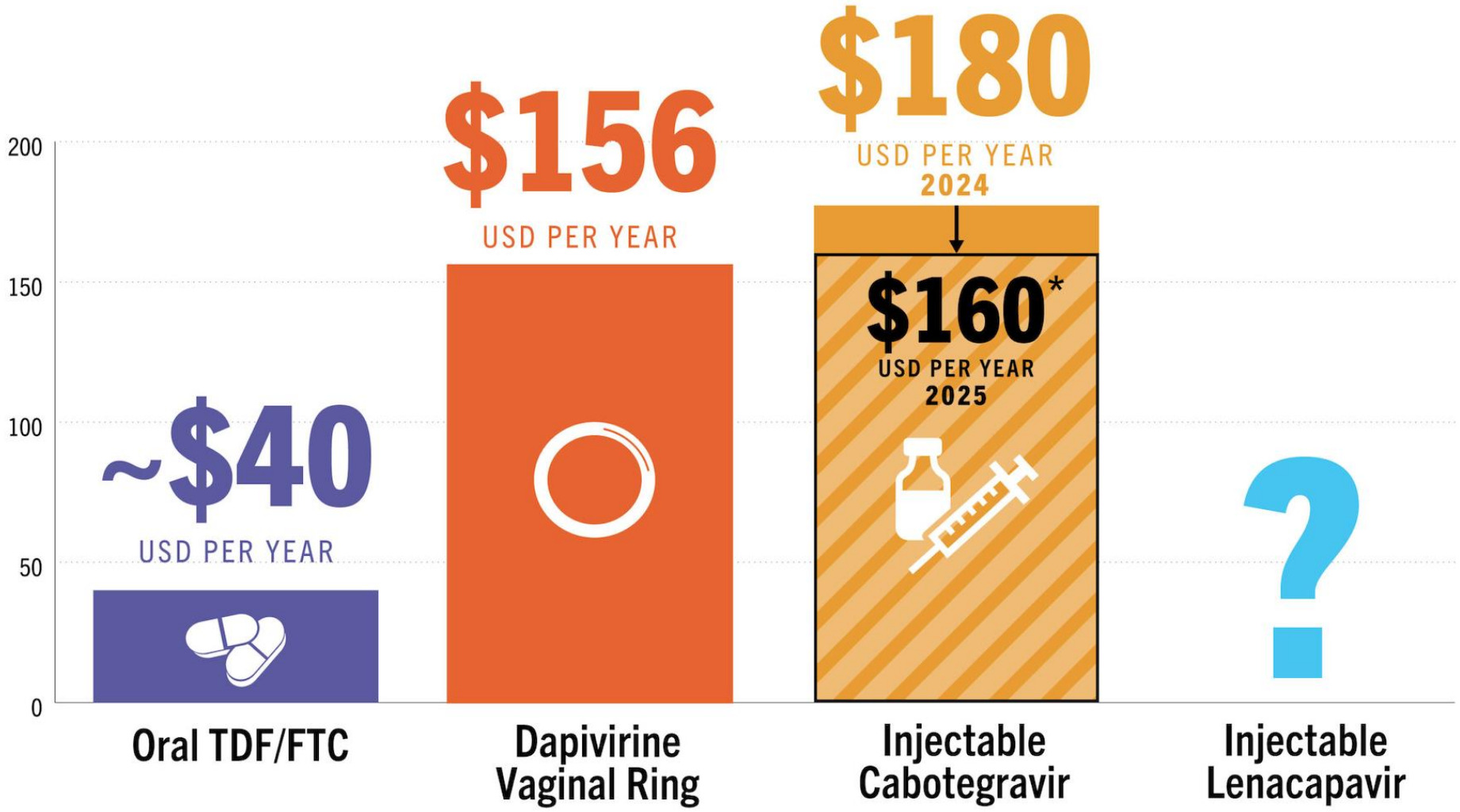
Advocacy Issues

Summary of Critical Issues to Shape Advocacy

Priority	Key Actions
Equitable Pricing & Supply Commitments	• Re-frame rollout in context of limited USG funding availability and PEPFAR support • Secure affordable pricing agreements, negotiate price and volume guarantees, and ensure transparent cost-effectiveness analysis to maintain support
Accountability from Gilead	• Ensure transparent engagement, push for volume availability, advocate for price transparency and not-for-profit pricing based on public health need
Demand Generation and PrEP Integration	• Strengthen in-country demand building on lessons learned from oral PrEP, anchor demand gen in PrEP choice, integrate PrEP guidelines and push for integrated service delivery, and promote task shifting and community-led advocacy
Regulatory Approvals & Guidelines	• Expedite WHO guideline development, urge regulatory agencies to accelerate approvals, and ensure broad global access
Exclusion of Latin America in Voluntary Licensing	• Advocate for inclusion of Latin America in voluntary licensing
Generic Manufacturing & Technology Transfer	• Monitor voluntary licenses, ensure technology transfer provisions, and push for expedited regulatory pathways for generics.
Multi-Country Launch Strategy & Implementation Science	• Support parallel research, implementation, and scale-up, advocate for 2 million LEN users annually, and enable broader healthcare worker involvement
Data Transparency & Continuous Learning	• Establish real-time tracking systems, use lessons from past PrEP rollouts, and ensure regular advocacy engagement

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.

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Cost of Goods Sold (COGS) Analysis for LEN

J Antimicrob Chemother. 2024 Nov 4;79(11):2906-2915. doi: 10.1093/jac/dkae305.

Lenacapavir to prevent HIV infection: current prices versus estimated costs of production

Andrew Hill [1], Jacob Levi [2], Cassandra Fairhead [2], Victoria Pilkington [3], Junzheng Wang [4], Madison Johnson [5], Jevon Layne [5], David Roberts [5], Joseph Fortunak [5]

- COGS is defined as the direct cost to manufacture a product
- COGS do not include research and development expenses, or fixed costs to set up manufacturing processes because these are not part of the ongoing manufacturing costs – more on COGS here
- In 2024, Hill & colleagues calculated a generic price dropping to $40 annually if the market grew to 10 million users per year
- Updated analysis following growing generic interest in 2025 suggests that L:EN could be mass produced for $35 to $46 a year, if there was annual demand for 2M people, falling to $25 at scaled up production of 5M to 10M people per year
  https://papers.ssrn.com/sol3/papers.cfm?abstract_id=5293409

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Advocacy for Affordable Pricing

- Gilead has not yet set a price for LEN for PrEP
- Various cost-effectiveness analyses show injectable PrEP must be priced in the range of generic daily oral to be cost-effective
- While it may not be possible at product launch, the field needs to collaborate to reach this price point as quickly as possible
  - Build volume in the market with initial supplies from Gilead at a price lower than CAB for PrEP
  - Support multiple generic manufacturers to enable (and accelerate) production at scale and lower prices
  - Demand pricing transparency and a clear, accelerated pathway to cost-effective PrEP programs

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Next Steps

- **Hold all decision-makers on LEN accountable**
  - Is there clarity about next steps?
  - Are there targets and milestones in place?
  - Is there adequate funding and available product to support rollout?
  - How might decisions be made about who would get the product first, if it's licensed and introduced through phased rollout?
- **Hold Gilead accountable**
  - Continued engagement
  - Volume availability
  - Price transparency
  - Not-for-profit pricing based on country needed and not World Bank economic status
- **Advocate for inclusion of Latin America** in voluntary licensing and push for regional equity
- **Build in-country demand** for prevention & PrEP – and apply lessons from oral PrEP and differentiated service delivery
- **Ensure guidelines integrated for PrEP delivery across products**
- **Monitor voluntary licenses**, ensure technology transfer provisions, and push for expedited regulatory pathways for generics

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Useful Resources

Gears of Lenacapavir for PrEP Rollout

From Clinical Trial Efficacy to Public Health Impact: A Plan for Accelerating Access to Injectable Lenacapavir for PrEP

The Lens on LEN: The Basics on Injectable Lenacapavir as PrEP

These and more at
https://avac.org/lenacapavir/

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Thank You!


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