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

AVAC
Advocacy. Access. Equity.

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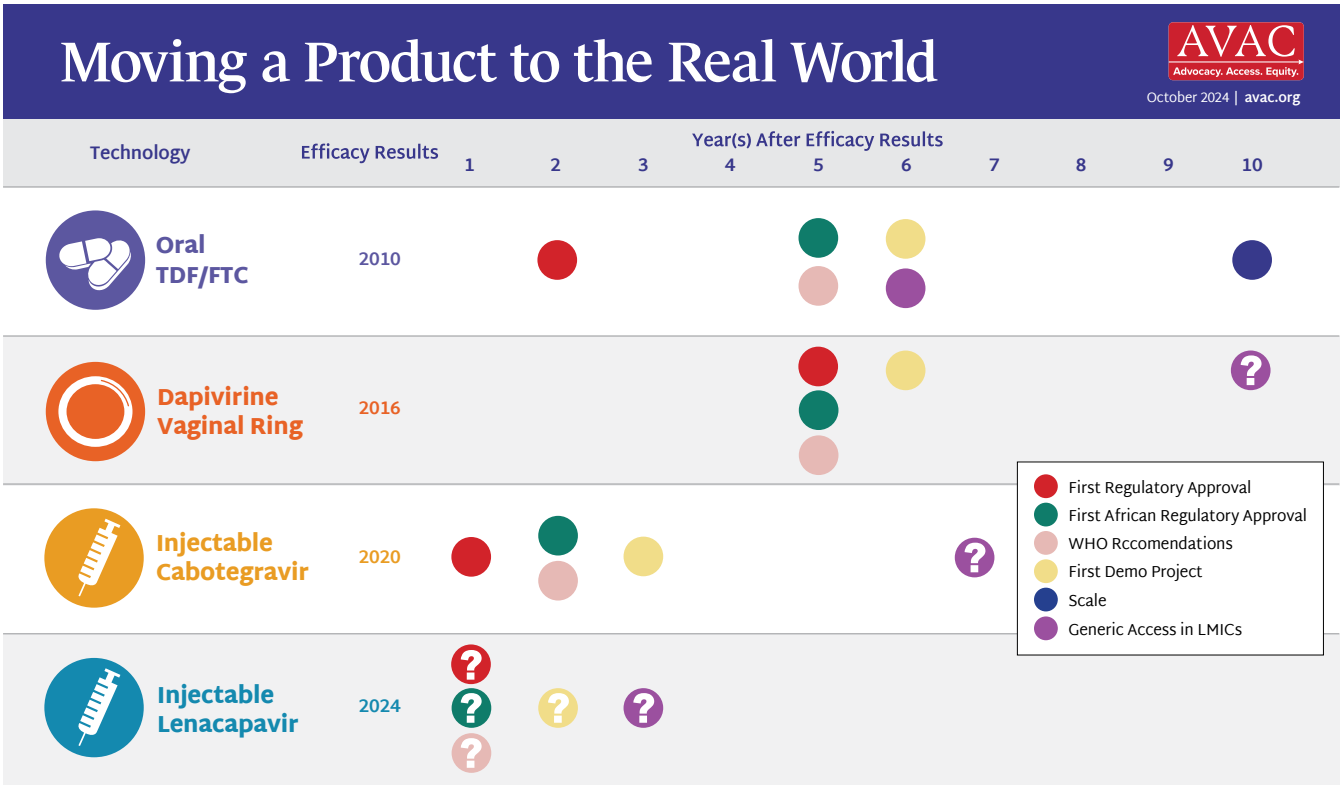
1. Background

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.



2. Guiding Principles of LEN Introduction

Since the announcement of the initial PURPOSE 1 and PURPOSE 2 trial results, there has been a great deal of excitement and trepidation regarding access to LEN, with questions regarding how long it will take for LEN to reach countries, what the price will be and when generics will become available. While the experience of the first decade of oral PrEP introduction since 2012 has shown the risks of delays in delivery and inequity in access, the more recent experience of beginning rollout for injectable cabotegravir (CAB) has proven that things can move quickly. Even greater speed, scale and equity are urgently needed, though, to translate the scientific data into public health impact – and this can only happen with coordinated and strategic actions amongst numerous and varied stakeholders; to name a few, Gilead Sciences, policy makers, normative agencies, donors, program implementers, researchers, generic manufacturers, civil society, and communities.

This document attempts to provide a comprehensive view of all the moving parts and identify priority actions and actors responsible for ensuring time is not wasted and opportunity not squandered. To consider this, the overarching goal and focus must be to **move faster, more strategically and in a more coordinated approach than** the field did with previous PrEP options, and to build upon real-time leanings from the ongoing rollout for injectable cabotegravir (CAB). To do so, the following principles must drive all parties:

- **Accelerate Speed, Scale and Equity:** Products don't end pandemics if they aren't delivered with fidelity, equity and urgency; oral PrEP and COVID vaccine delivery are the most recent reminders. 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.
- **Center the Community and User**: It is critical to center communities in design and implementation of programs and center users in actual product delivery.
- **Choice Matters**: No one product will be right for everyone, all the time. Choice leads to increased use of chosen prevention method, improved health outcomes and helps to close the gap for new infections.

- **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.
- **Work collaboratively, 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 learn from past experiences and not let 'perfect be the enemy of good'. The introduction of LEN for PrEP is a chance to reorient, reimagine and re-energize HIV prevention programs, including transparent data tracking and expanded analysis to inform decision-making..

3. Top Priorities

To ensure that the opportunities of LEN for PrEP, and PrEP choice generally, are finally seized and not squandered, a diverse array of stakeholders must act on the following top priorities over the next five years (2024-2028) with the product and with the programs that facilitate access.

	Priority	Target time
Product-specific	▪ In October, Gilead announced voluntary licenses to **six generic manufacturers** – Dr. Reddy's Laboratories Limited (India), Emcure (India), Eva Pharma (Egypt), Ferozsons Laboratories Limited (Pakistan), Hetero (India) and Mylan, a subsidiary of Viatris (India). These licenses should be made publicly available; include specific technology transfer provisions for accelerated product development;and ensure access in countries based on public health need, rather than World Bank economic classification. Generic agreements cover not only lenacapavir for HIV prevention (pending approval), but also lenacapavir for HIV treatment in heavily treatment-experienced (HTE) adults with multi-drug resistant HIV.	October 2024
	▪ To provide Gilead-supplied lenacapavir until generic versions are available, **Gilead to expedite plans for submission to regulatory agencies, including the US Food and Drug Administration (FDA)** and a robust number of additional regulatory agencies, especially in countries with high HIV burden, whether directly to national regulatory agencies or through collaborative review procedures, such as the European Medicines Agency's EU-Medicines for all (EU-M4all). Regulatory agencies should prepare to fast-track regulatory review. In October 2024, Gilead announced that it is prioritizing initial registration in 18 countries "that represent about 70% of the HIV burden in the countries named in the license": Botswana, Eswatini, Ethiopia, Kenya, Lesotho, Malawi, Mozambique, Namibia, Nigeria, Philippines, Rwanda, South Africa, Tanzania, Thailand, Uganda, Vietnam, Zambia and Zimbabwe.	Q4 2024 – Q1 2025

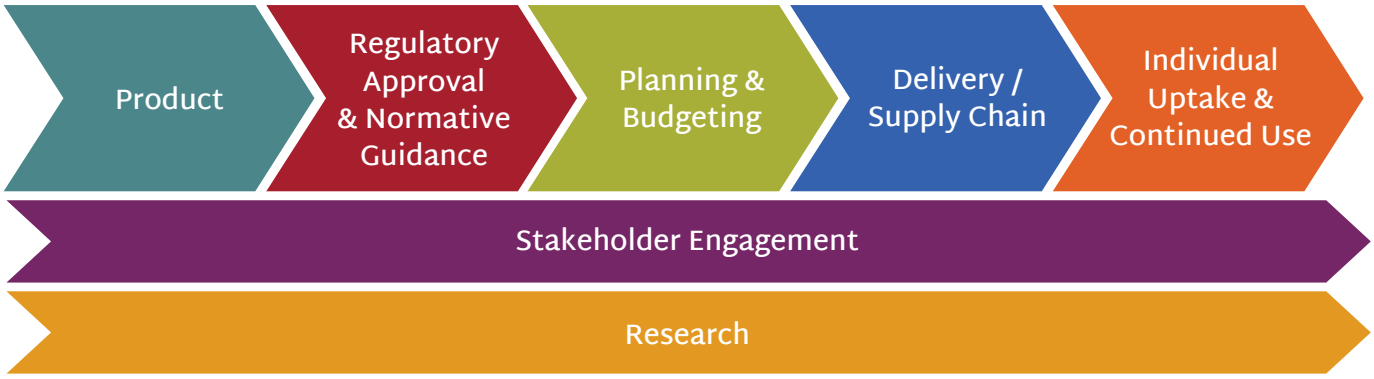
	Priority	Target time
	▪ WHO to initiate the process for **developing guidelines**, plan for a Guideline Development Group by early 2025, and ensure WHO Guidelines are in place by the time regulatory approvals might be granted, as soon as mid-2025.	By Q3 2025
	▪ **Cost-effective, affordable and transparent LEN price and volume commitment from Gilead** to support early launch and roll-out. Donors to negotiate price/volume guarantee with Gilead to ensure sustainable supply for initial introduction period until generics registered and readily available, given the 2-3 year timeline for generic preparation, manufacturing upgrades and approvals.	Q4 2024 – Q2 2025
	▪ Regulators and **WHO define bioequivalence** (BE) requirements, paving the way for approval of a generic product.	2025
	▪ Gilead to collaborate with WHO to expedite an **Expression of Interest (EOI) into the Pre-Qualification (PQ) process** to allow expedited registration in countries participating in WHO's Collaborative Procedure for Accelerated Registration process.	Q4 2024 – Q1 2025
	▪ **Donor investments** identified that could accelerate technology transfer to generic manufacturers and accelerate generic manufacturing capacity.	2025
	▪ **Sufficient Gilead capacity** to meet initial, near-term order forecast for programmatic launch.	2026
	▪ **Generic manufacturer(s) develop product** and high-volume sterile fill/finish capacity, undertake BE studies and file with regulatory authorities.	2026-2028
	▪ **Generics of LEN approved** and available for procurement.	2028
Programmatic	▪ **Collaborative implementation strategy**. 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 of product introduction, moving toward a parallel approach where research, implementation science, and scale programs are designed, funded and implemented in parallel. An initial strategy for a multi-country launch, based on current trends and PrEP experience, for scale in 2026, to include at least strategy in 8-10 countries, provinces or districts with 50,000-100,000 people per country getting access to LEN in the first two-years of introduction – including negotiation with Gilead to ensure product supply of at least 4 million doses per year to support this introduction (or one million persons per year).	Q3 2024 – Q1 2025

	Priority	Target time
	▪ **National Programs** in priority countries complete LEN registration (or secure relevant waivers); revise PrEP guidelines/ adapt WHO guidance; design provider trainings and expansive introduction efforts.	2025-2026
	▪ **Operational research/implementation science studies** identify successful, scalable delivery channels, including primary care facilities and integration with family planning services, antenatal care (ANC)/postnatal care (PNC) and key population drop-in sites, etc.; any specific testing and drug resistance issues related to a capsid inhibitor (as opposed to an integrase inhibitor like CAB); ongoing engagement with communities and civil society to ensure needs are being met; and an independent coordination mechanism.	2025-2026
	▪ **Market assessments and demand generation strategies** and forecasts, updated with data from initial projects to inform manufacturing, volume and cost and procurer budgeting, including the unique needs of potentially having two injectable PrEP options in the market.	2026 onwards

4. Pathway to Access and Impact, with proposed Next Steps

This table outlines the immediate next steps on the pathway to access and impact and includes key actors responsible for them.

The Pathway to Access and Impact



Pathway	Next steps
Product	▪ **Gilead** to publicly confirm maximum quantity and minimum price for 2025-2027. ▪ **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 2-3 years post-innovator approval). ▪ **Gilead** announced its licenses for injectable LEN to six generic manufacturers across different geographies in October 2024. ▪ **Gilead** to work with donors and generic manufacturers, including those based in Africa, to expedite technology transfer and ensure sustainable supplies of the product. ▪ **Generic manufactures** to identify capital expenditure needs and timeframe to be able to develop capacity. ▪ **WHO and regulatory agencies** to confirm bioequivalence (BE) requirements for generic LEN development and approval. ▪ **Innovative donor(s)** to fund capital investments needed for generic manufacturing to reach scale.

Regulatory Approval & Normative Guidance	▪ **Gilead** to pursue widespread registration of LEN in high-burden countries, with a target of at least 30 regulatory submissions by the end of 2025, primarily in the highest-burden countries.
	  ▪ Submissions to regulators in low- and middle-income countries especially should be simultaneous with FDA submission, and not after FDA approval.
	  ▪ Submissions either directly to national regulatory agencies or through accelerate collaborative review mechanisms like the European Medicines Agency's EU-Medicines for all (EU-M4all) program.

Pathway	Next steps
	▪ **Gilead** to provide access to relevant data and publications as soon as possible to ensure expeditious Guideline development. ▪ **WHO** to initiate Guidelines development process and plan for a Guideline Development Group by early 2025 to ensure WHO Guidelines are in place by the time regulatory approvals might be granted. ▪ **Gilead** to collaborate with WHO to expedite an Expression of Interest (EOI) into the Pre-Qualification (PQ) process to allow expedited registration in countries participating in WHO's Collaborative Procedure for Accelerated Registration process. ▪ **WHO** to work with ministries of health and national technical working groups to prepare for national adaptations of updated PrEP guidelines to be in place by the end of 2025.
Planning & Budgeting	▪ **Governments and donors** to set targets for supply and programs at scale – what is needed and possible in 2025-2026 in early introduction efforts, and what is needed from 2026 to begin programs at scale. ▪ **Donors, governments and implementing partners** design an initial programmatic launch strategy in 8-10 countries, provinces or districts with 50,000-100,000 people per country getting access to LEN in the first two-years of introduction – including negotiation with Gilead to ensure product supply of at least 4 million doses per year to support this introduction (or one million persons per year).
Delivery / Supply Chain Individual Uptake & Continued Use	▪ **Governments and donors** to ensure provider training materials and tools updated to incorporate LEN administration. ▪ **Governments and donors** to ensure that program designs 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. ▪ **Multiple stakeholders** to consider innovative demand creation strategies (for injectable PrEP and for "choice" among options) developed with process to test and iterate and share across projects – in real time and at scale.
Delivery / Supply Chain	▪ **Implementers** to report on testing requirements to ensure they do not become a barrier to LEN introduction. Testing strategies should be both robust and feasible and work with locally available tests and assays to maximize the benefits of access while minimizing the risk of undetected cases. Self-testing can be explored for initiation and continuation where relevant and should be discussed as part of WHO guideline development.

Pathway	Next steps
Research	▪ **Funders, ministries of health and implementation scientists** to define specific implementation science questions that can be embedded within programs or that require standalone implementation science studies. ▪ **CAB implementation science studies and funders** to review real-time findings to assess what might be CAB-specific and what might provide insights of injectable PrEP generally. ▪ **Implementers** to collect data and integrate learnings from PURPOSE trials on the benefit of injectable LEN as PrEP for populations that were not part of efficacy trials, to ensure no populations are left behind. ▪ **Implementers** to study and cost alternate injection sites, method switching, testing algorithms and role of oral loading dose. ▪ **Members of Global Community Accountability Groups (GCAGs) for each PURPOSE efficacy study** to remain engaged in ongoing guidance and recommendations resulting to support inclusive data-gathering.
Stakeholder Engagement	▪ **Integrate and engage civil society** in all decision-making relevant to planning and preparation for access to LEN, including designing, conducting and monitoring programs, membership on national technical working groups and in demand generation campaign development. ▪ **Leverage the GCAGs, the Civil Society Caucus of the long-acting PrEP coalition and AfroCAB**, amongst other groups, to ensure robust engagement is sustained from research to rollout.

5. Cross-stakeholder Advocacy Priorities

- **Demand equitable PrEP access and programming for choice**. This entails funding commitments, setting bold targets and embracing innovation. National governments must move with speed, scale and equity in designing, funding and implementing comprehensive and integrated PrEP programs that offer a choice of products and service delivery models.
- **Advocate for affordable pricing and building a sustainable market**. Gilead has not yet set a price for LEN for PrEP. Various cost-effectiveness analyses have shown that injectable PrEP must be priced in the range of generic daily oral TDF/FTC to be considered cost-effective. Driving the price lower and getting to parity between LEN and oral PrEP will require a low launch price from Gilead; a significant volume procurement from donors; and multiple generic companies competing for large, multi-million dose market. While this is not feasible at product launch, the field needs to collaborate to reach this price point as quickly as possible.

  It is essential to build volume in the market with supplies from Gilead at a price no higher than CAB for PrEP and to support multiple generic manufacturers to enable production at scale as quickly as possible. Advocates must demand pricing transparency and a clear, accelerated pathway to cost-effective PrEP programs over the next three years – so that when generic LEN manufactures do enter the market with approved products by 2028, they are competing and driving the price lower.

- **Hold procurers and donors for 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?
- **Work locally with research sites and PrEP progams**. Bring your advocacy know-how to sites for planned and ongoing research and PrEP programs to ensure communication, access and continued work meet your needs.

6. Recent Resources

- Lenacapavir: The case for investing in delivering HIV prevention
- The long wait for long-acting HIV prevention and treatment formulations, The Lancet
- A game-changer for PrEP if access is adequate, The Lancet
- Country-planning matrix to track introduction of next-generation PrEP
- The pipeline of products getting towards to the market
- Getting Rollout Right: Lessons from Oral PrEP
- Coalition to Accelerate Access to Long-Acting PrEP
- Coalition to Accelerate Access to Long-Acting PrEP – Status Update (updated quarterly)
- BioPIC Adaptable Product Introduction Framework
- Study Dashboard for New PrEP Options
- Statement From The Gilead's Purpose 1 Global Community Accountability Board, The African Women's Prevention Community Accountability Board, Our Partners And Community Partners

"In a perfect world, what I would love to see is that by this time next year, PEPFAR and the Global Fund, in collaboration with a number of ministries of health in countries in which they work, jointly design a program to get at least 3 million people access to lenacapavir. That they fund the program to build it, that they negotiate with Gilead to get the price as low as possible, certainly lower than cabotegravir and closer to oral prep, but a price that is in a range that's affordable at least at launch. And if we do that, and if advocates hold everybody to account to get those many millions of people access to lenacapavir from Gilead, then the license agreements would be in place with generic manufacturers. And after 2 or 3 years, by 2027 or 2028, you would see that market grow to maybe four or 5 or 6 million injectable PrEP users, and that they would be getting product at an even lower price because you'd have multiple generic companies, all competing with Gilead for the lowest possible price of a high-quality injectable product. That I think is not a fairy tale. I think that's possible if we make the collaborations possible."

- **Mitchell Warren** in AVAC's, Lenacapavir, HIV Prevention, and how to end the epidemic podcast in September 2024

7. AVAC'S Role

AVAC was founded in 1995 to advocate for the ethical development and global delivery of HIV vaccines. AVAC's current activities include a range of efforts to influence and accelerate access to the widest range of PrEP options, including LEN:

- **Advocacy**: Through the USAID-funded CASPR and Gates-funded COMPASS projects, AVAC and a range of civil society partners have pushed for implementation of the GPP Guidelines throughout the injectable PrEP efficacy trials; developed materials to understand the results and advocate for applying them; pushed PEPFAR, Global Fund and national governments to integrate injectable PrEP into guidelines, targets and programs.
- **Stakeholder Engagement**: CASPR partners engaged directly with Gilead in trial conduct and results dissemination. More recently, AVAC has worked with these and other partners to ensure civil society is actively engaged with planners and funders of implementation science projects and provided technical assistance in the creation of the African Women Prevention Community Accountability Board and the Key Population Advisory Group. As a partner in the USAID-funded MOSAIC project, AVAC is working with civil society partners to ensure ongoing stakeholder engagement in the five-country CATALYST study.
- **Production Introduction and Access**: In addition to its role within MOSAIC, AVAC continues to lead the Biomedical Prevention Implementation Collaborative (BioPIC) which serves as a clearinghouse to monitor and track HIV prevention product introduction activities; as a convener of stakeholders brought together as part of ongoing think tanks to address roadblocks to product introduction and scale-up; and as a catalyst for investments towards the HIV prevention product introduction strategy. AVAC also serves as the secretariat for the Coalition to Accelerate Access to Long-Acting PrEP.

About AVAC

AVAC is an international non-profit organization that leverages its independent voice and global partnerships to accelerate ethical development and equitable delivery of effective HIV prevention options, as part of a comprehensive and integrated pathway to global health equity. Follow AVAC on Twitter @HIVpxresearch and find more at www.avac.org.