

What science tells us and what comes next

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Disclosures

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Presentation Outline



PrEP Gap - PrEP Advantages - Existing LAI for Prevention

LEN MOA, Selecting Appropriate Patients for LEN, Dosing



PURPOSE 1 & 2 Studies

Objectives, populations, efficacy, safety, adherence, HIV incidence & resistance.



Steps for LENACAPAVIR PrEP Roll out

Dosing, Testing, Self-testing roll-out, Yearly LEN, & Summary




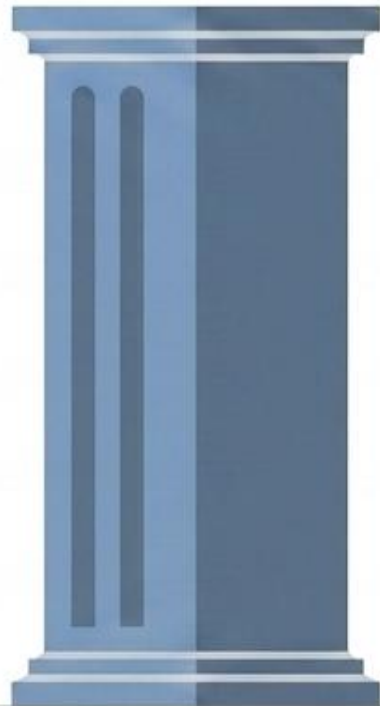
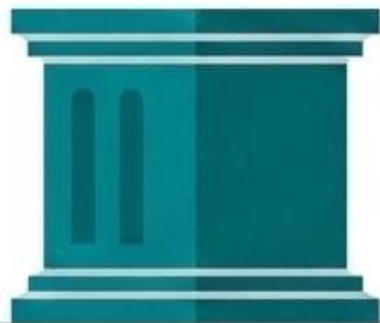
Key Recommendations

The PrEP Coverage Reality in Latin America & Caribbean (PAHO Data)



~2.3 million
people who
could benefit


~160,000
people currently
using PrEP



PAHO Data

Regional Urgency


HIV Incidence Comparison

(New infections per 1,000 uninfected population)




3x Higher
Belize remains ~3x
higher than the global
incidence.


**Concentrated
Epidemic**
Burden remains heavy
among MSM and
transgender women.









**Declining but
Elevated**
Global incidence dropped
~40% since 2010, yet
regional spikes require
targeted LAI intervention.



1. World Bank. Incidence of HIV, all (per 1,000 uninfected population) – Belize. Available at: <https://data.worldbank.org/indicator/SH.DYN.AIDS.IN.ZS?locations=BZ> Accessed May 15, 2025.
2. UNAIDS. UNAIDS Data 2024 (2024 epidemiological estimates). Geneva: UNAIDS; 2024.

Note: Estimates are modelled and may differ slightly across sources due to methodology and year.

Available Long Acting Injectables for PrEP (LAI)

Cabotegravir (CAB)	Lenacapavir (LEN)
Class: INSTI	Class: Capsid Inhibitor
Formulation: Oral tablet, IM Injection 	Formulation: Oral tablet, SC injection 
Indication: Prevention (alone) Treatment (w/RPV)	Indication: Prevention (alone) Treatment (w/OBR)
Population: PrEP: HIV neg Tx: Experienced 	Population: PrEP: HIV neg Tx: Highly Tx-Experienced 
Dosing: PrEP: Q8W Tx: Q4W or Q8W 	Dosing: Q26W or Q6M
Half-life: Oral: 41h IM: 5.6-11.5W 	Half-life: Oral: 10-12d SC: 8-12W 

PrEP (Pre-Exposure Prophylaxis) is a safe, effective, and proven way to prevent HIV before exposure.

FOR PATIENTS (Population Impact)

- UP TO ~99% EFFECTIVE**
in preventing HIV when taken as prescribed.¹
- CHOICE OF OPTIONS**
Daily oral pill or long-acting injectable (LAI) every 1–2 months.²
- IMPROVED ADHERENCE**
with less frequent dosing (monthly or every 2–6 months with LAI).^{3–5}
- GREATER PRIVACY & AUTONOMY**
in prevention decisions and care.⁶
- REDUCED STIGMA**
compared to HIV treatment-associated care.⁷
- DECREASED ANXIETY**
around HIV exposure risk.⁷
- EMPOWERS INDIVIDUALS**
to take control of their sexual health and HIV prevention.⁶

FOR PROVIDERS (Clinical & System Benefits)

- SHIFTS CARE TO PREVENTION-FIRST,**
not just treatment.⁸
- REDUCES HIV INCIDENCE**
and supports epidemic control goals, including the 95-95-95 targets.^{8,9}
- IMPROVES ENGAGEMENT**
with high-risk and underserved populations.^{6,10}
- SIMPLIFIED REGIMENS**
(especially LAI PrEP) enhance adherence and persistence.^{3–5}
- STRENGTHENS PATIENT RELATIONSHIPS**
through proactive, prevention-focused care.^{6,10}
- INTEGRATES ACROSS CARE SETTINGS**
including primary care, ID, sexual health, and community-based services.^{6,10}
- SUPPORTS PUBLIC HEALTH TARGETS**
and contributes to long-term cost savings by preventing new HIV infections.^{8,9}

Protect today.
Empower tomorrow.

KEY TAKEAWAY: PrEP transforms HIV prevention—delivering highly effective, flexible, and patient-centered protection while enabling providers to lead with prevention.

PROTECT

EMPOWER

PREVENT

SOURCES

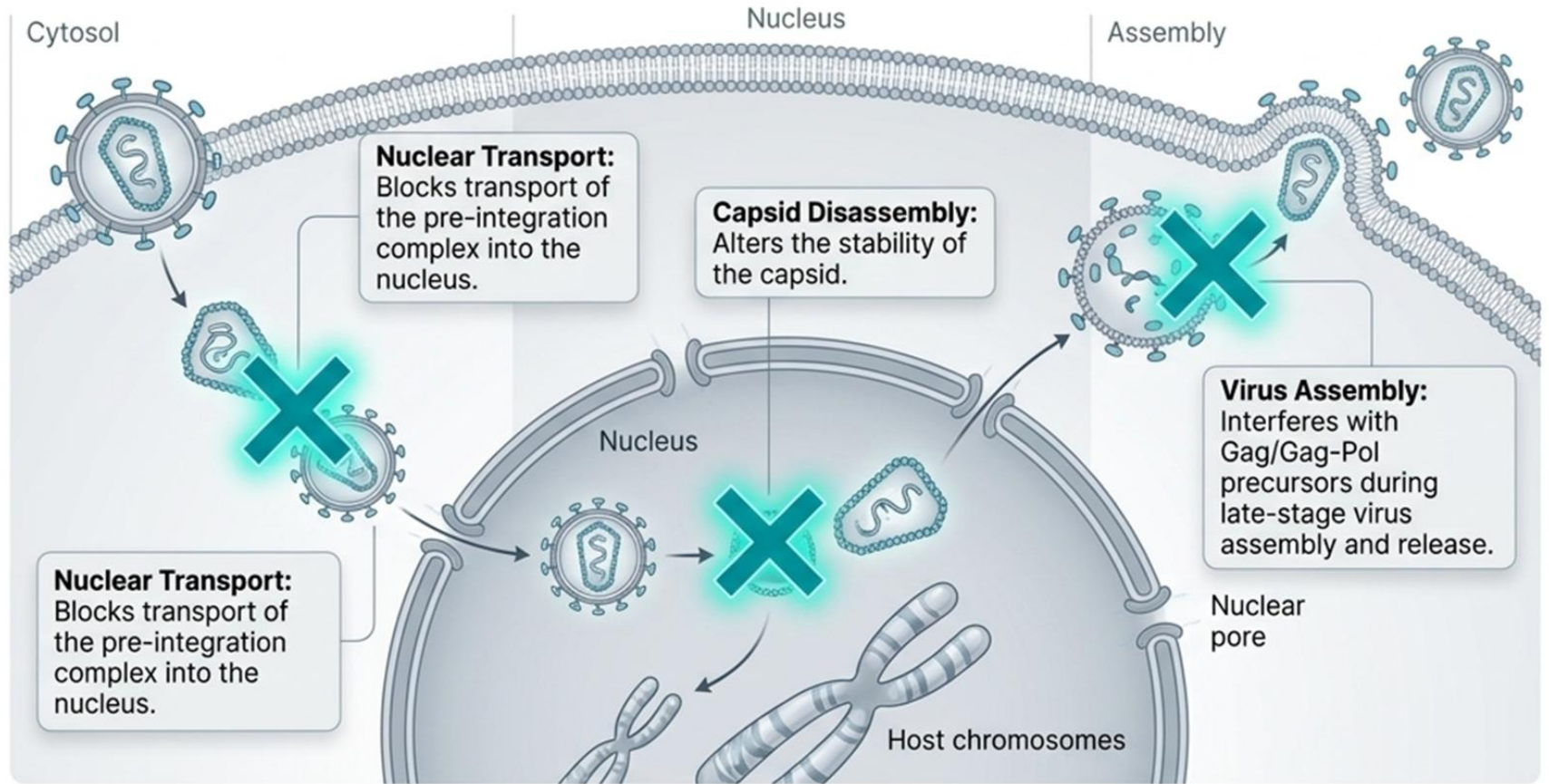
1. CDC. Preexposure Prophylaxis (PrEP). <https://www.cdc.gov/hiv/prevention/prep.html>
2. WHO. Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach. 2021.
3. Landovitz RJ, et al. Cabotegravir for HIV Prevention in Cisgender Men and Transgender Women (HPTN 083).
4. Delany-Moretlwe S, et al. Long-Acting Cabotegravir to Prevent HIV in Women (HPTN 084). *N Engl J Med.* 2022;386:1789–1799.
5. McCormack S, et al. Injectable cabotegravir vs daily tenofovir DF/emtricitabine for HIV prevention (ATLAS). *Lancet.* 2021;396:1994–2005.
6. Eisinger RW, et al. A review of oral and injectable HIV PrEP: background, current considerations, and future directions. *J Int AIDS Soc.* 2022;25:e25971.
7. Smith DK, et al. Patient and provider perspectives on PrEP stigma and experiences. *AIDS Behav.* 2020;24:2652–2662.
8. UNAIDS. Global AIDS Update 2023.
9. UNAIDS. 95-95-95 An ambitious treatment target to help end the AIDS epidemic. 2021.
10. Hosek S, et al. Implementing PrEP in clinical practice and public health settings. *Lancet HIV.* 2019;6:e474–e485.

Multi-Stage Capsid Disruption

Capsid Inhibitor

High potency:
EC₅₀ = 105 pM/L

Long half-life
(8-12 weeks SC) due to binding directly between capsid protein subunits.






N=1325; p<0.001; 95% CI [0.78, 0.92] vs. standard of care

Importance of Selecting Appropriate Individuals for LEN for PrEP







Selection and Adherence

-  Choose individuals who agree to HIV-1 testing and 6-month injection schedule.¹
-  Adherence is critical to reduce HIV-1 acquisition and resistance.¹
-  Provide counseling and reminders for dosing and testing.¹

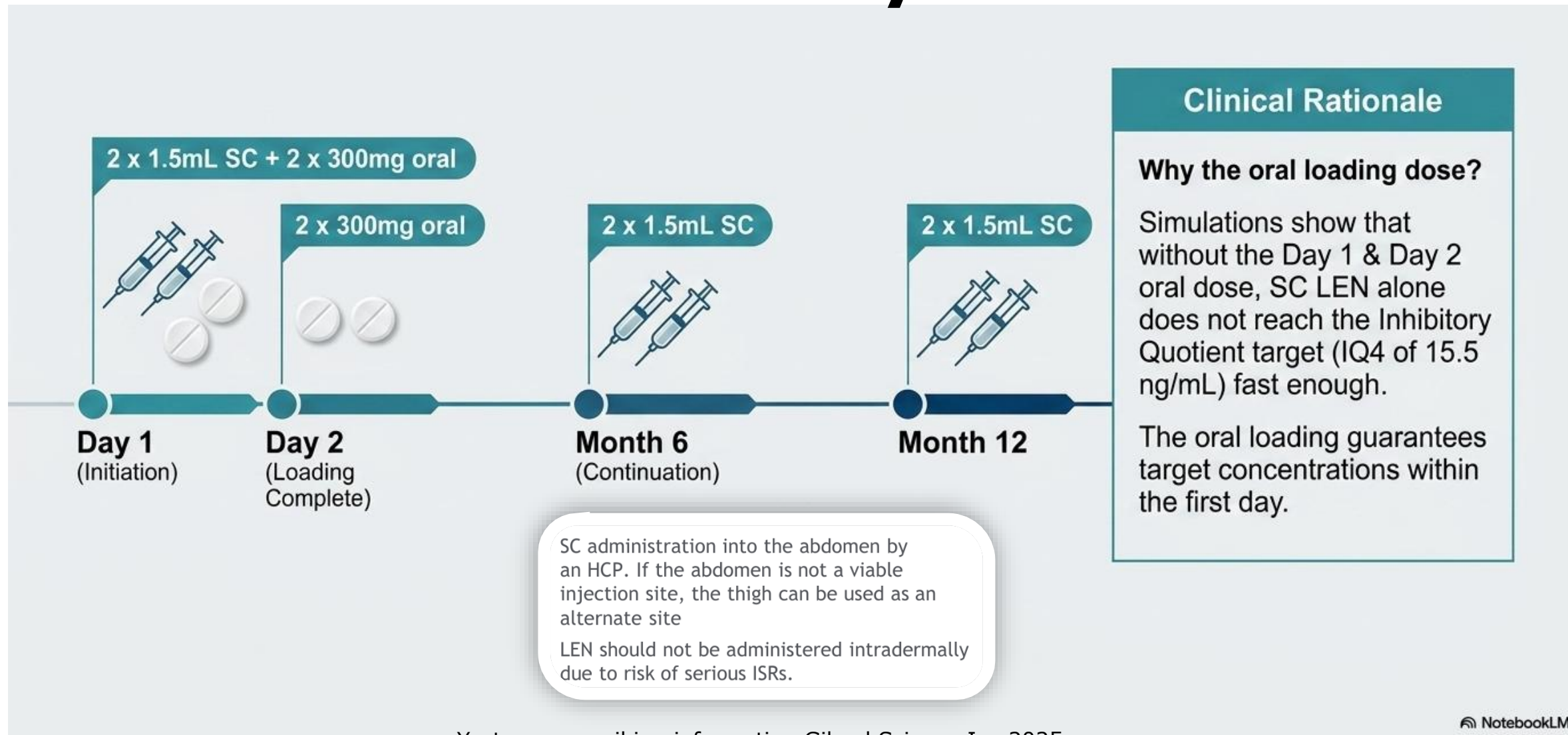


PK Tail and Resistance Risk

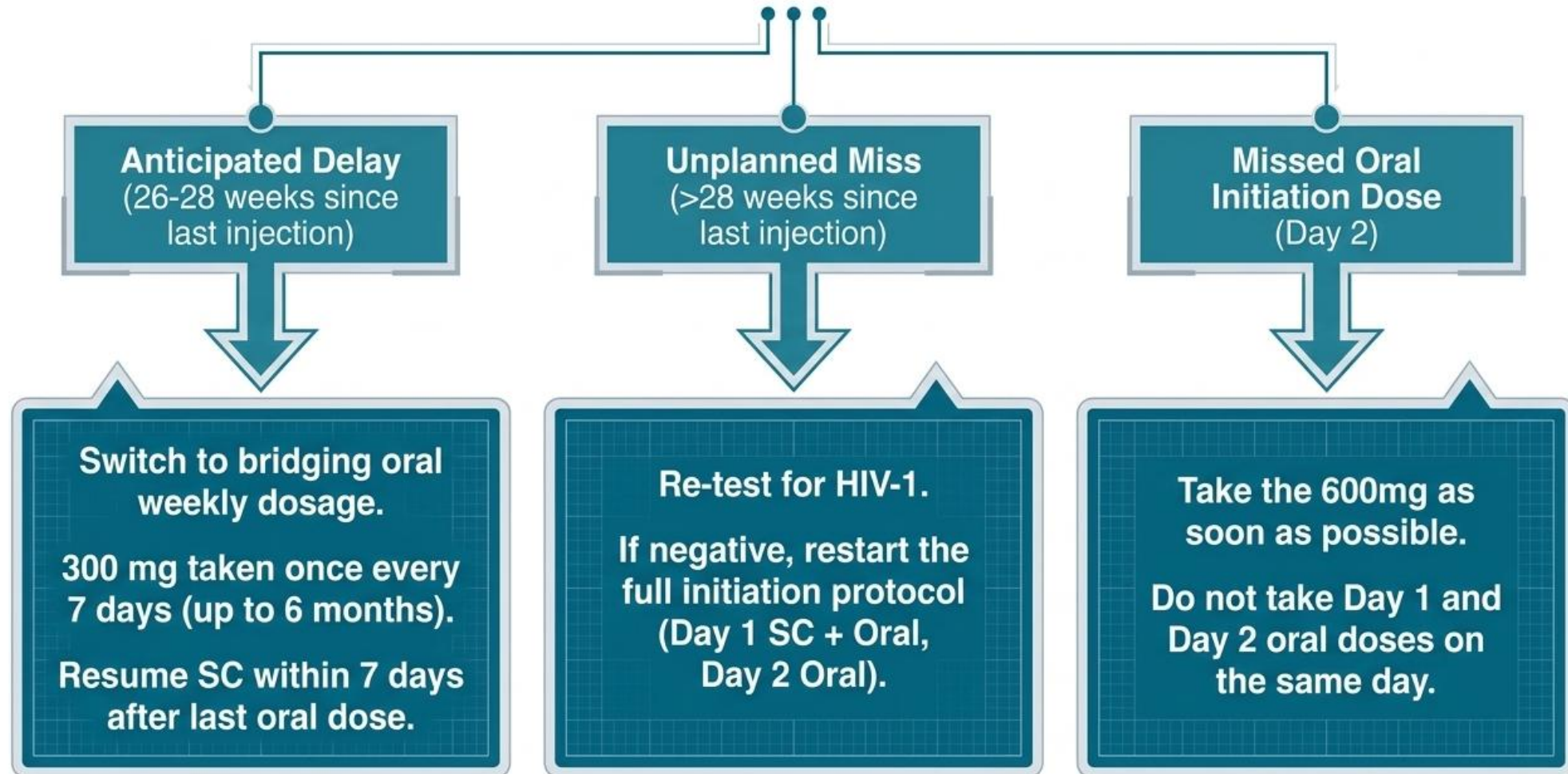
-  LEN for PrEP can remain in the body ≥ 12 months after the last injection (PK tail).¹
-  After 6 months, levels drop below target concentration.¹
-  HIV acquisition during PK tail may lead to drug resistance; assess individual's ongoing HIV risk.^{1,2}
-  Transition to other HIV prevention options, within 28 weeks of the last LEN for PrEP injection, if stopping LEN for PrEP for those with HIV-1 negative status and at continuing risk of HIV-1 acquisition.¹

Individuals should understand the need for adherence and the risk of resistance if HIV-1 is acquired during the PK tail after stopping LEN for PrEP.^{1,2}

Dosing & Administration of Twice-Yearly LEN



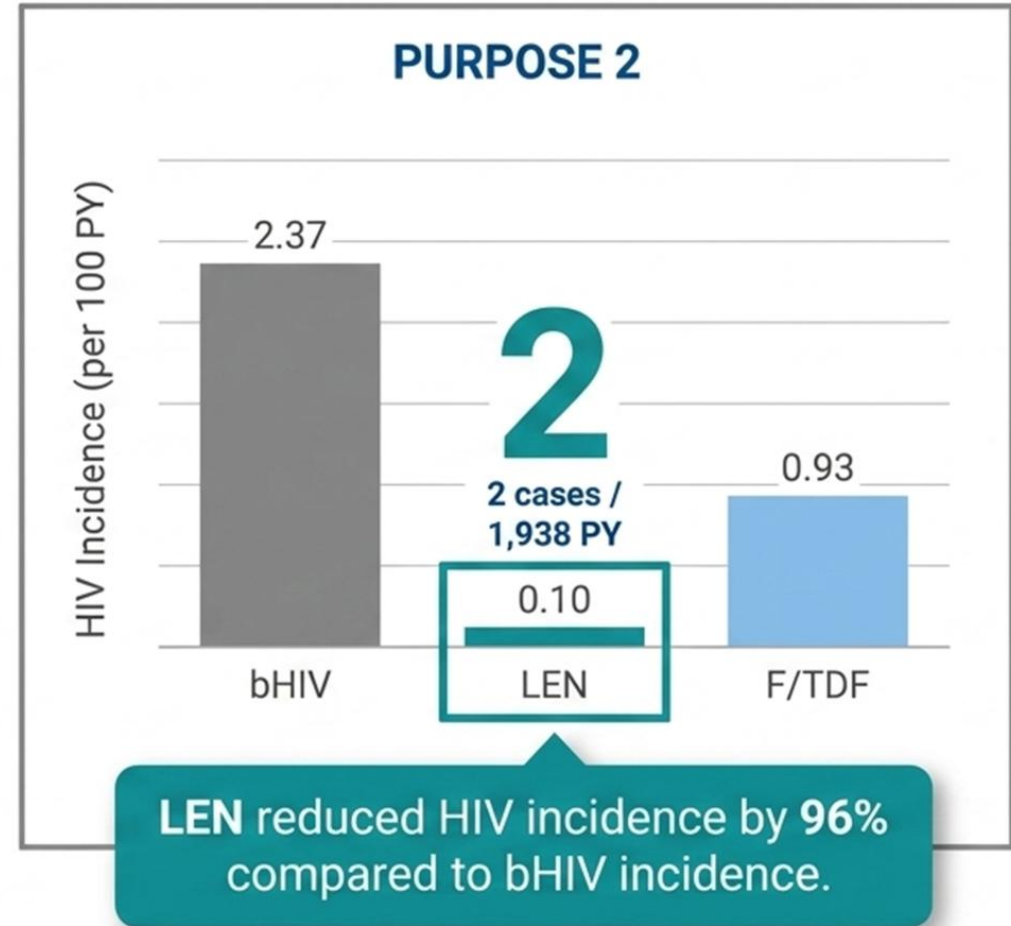
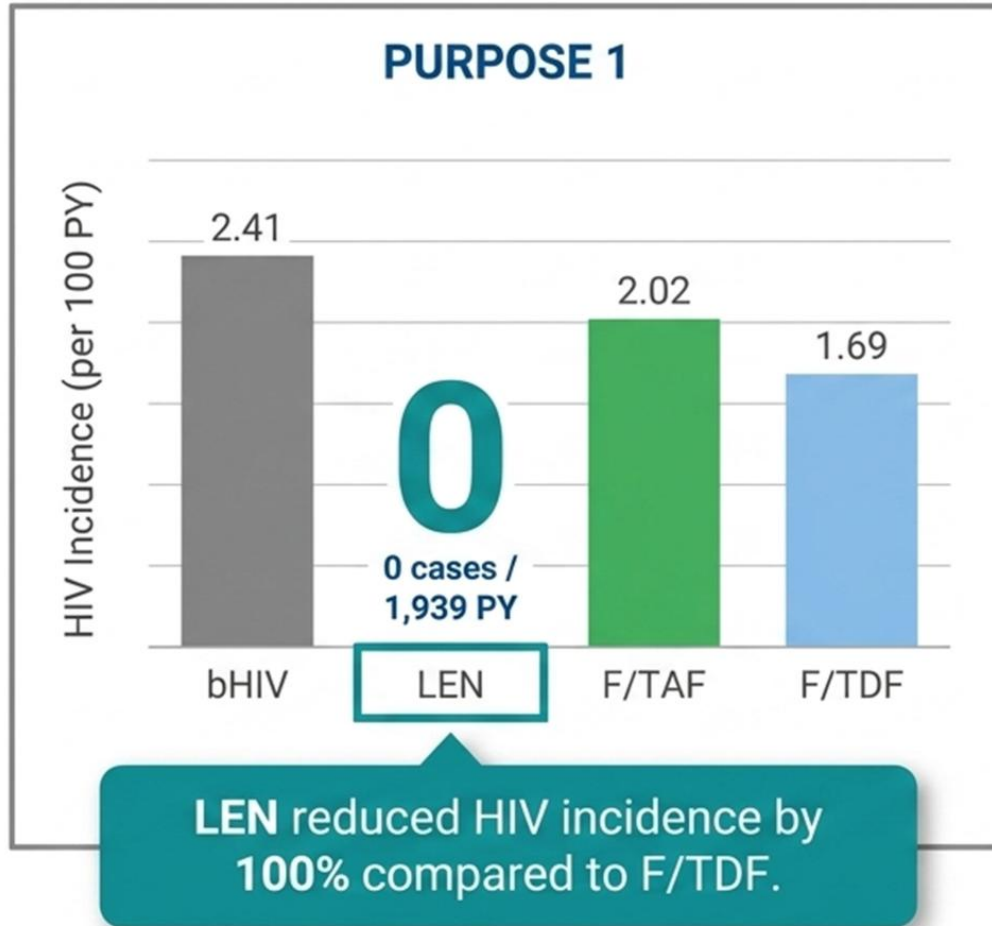
Dosing Schedule for **Missed** Twice-yearly LEN Dose



PURPOSE Trials

	PURPOSE 1	PURPOSE 2
Study Design	Phase 3, double-blind, active-controlled, multicenter randomized study	
Populations	Cisgender women (CGW), 16-25 years	CGM, TGW, TGM, and GNB individuals having sex with partners assigned male at birth, ≥16 years.
Comparators	Twice-yearly SC LEN vs. bHIV incidence and daily oral F/TDF (and F/TAF in P1).	Twice-yearly SC LEN vs. bHIV incidence and daily oral F/TDF.
Safety Context	Most common AEs were ISRs, headache, and nausea	

Twice-Yearly LEN Efficacy Primary Analysis Data

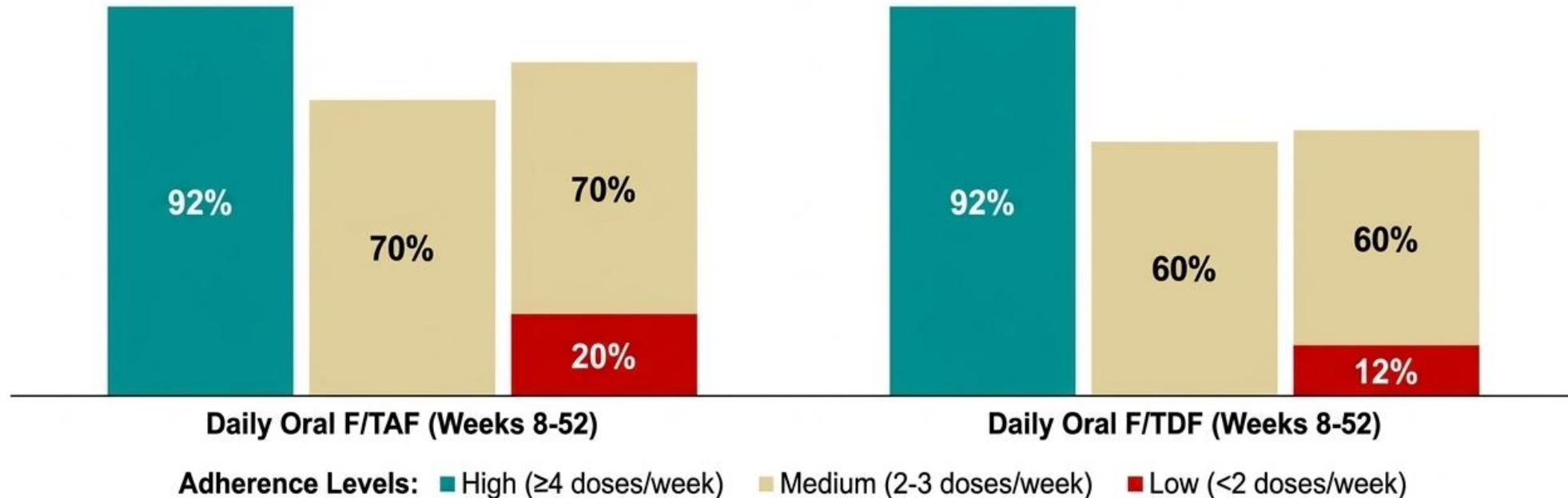


Adherence Data - PURPOSE 1&2

PURPOSE 1 Injection Adherence: 91.5% at Wk 26 → 92.8% at Wk 52

PURPOSE 2 Injection Adherence: 91% at Wk 26 → 92% at Wk 52

Most HIV acquisitions on F/TAF and F/TDF occurred in those with low adherence. LEN provides consistent, systemic protection independent of daily user behavior.



*Adherence definitions of high (≥4 doses/week), ■ Medium (2-3 doses/week), and non-protection, zkratied aeti-inference (216).

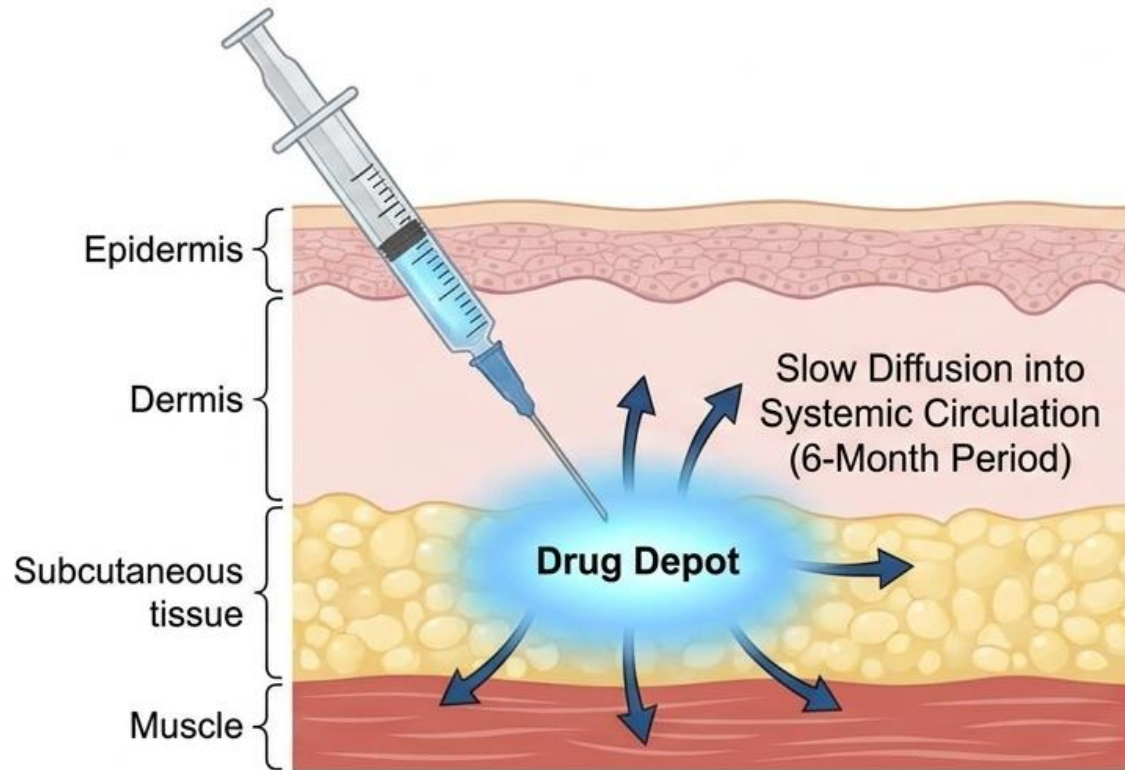
*N-values with consiamous ansist-sener protection, N=0B m=12,175, n=3,090.

NotebookLM

* In PURPOSE 1 and 2 adherence to LEN was defined as on-time injection (within 28 weeks from the last injection) and participants who presented later than 28 weeks after their previous injection were required negative HIV testing to reinitiate study product, which included reloading with oral LEN or placebo. In PURPOSE 2, preselected 10% sample of participants assessed for TFV-DP concentrations in DBS (F/TDF: low <350, medium ≥350 to <700, high ≥700 fmol/punch). † 2 participants in each group had missing data. ‡ Cases were defined as participants who had acquired HIV; up to 5 controls were selected, matched on basis of trial site and VOICE risk score for HIV acquisition. Each of 37 case participants contributed 1 sample. A trial participant could serve as a control for more than 1 case participant; 159 participants contributed 176 samples to be used as matched controls. TFV-DP levels in DBS were measured from the HIV diagnosis visit (for case participants) or time-matched visit (for controls). Randomly preselected 10% sample of participants assessed for TFV-DP concentrations (F/TAF, n=200; F/TDF, n=106).
 DBS: Dried blood spot; F/TAF: Emtricitabine/tenofovir alafenamide; F/TDF: Emtricitabine/tenofovir disoproxil fumarate; HIV: Human immunodeficiency virus; LEN: Lenacapavir; PrEP: Pre-exposure prophylaxis; TFV-DP: Tenofovir diphosphate.
 1. Bekker L-G, et al. *N Engl J Med.* 2024;391(13):1179-1192. doi: 10.1056/NEJMoa2407001. 2. Kelley C, et al. *N Engl J Med.* 2025;392(13):1261-1276. doi: 10.1056/NEJMoa2411858.



Injection Site Reactions, Drug Depot, & Nodule Formation with LEN for PrEP in PURPOSE Trials



The most common adverse drug reactions (all grades) reported in at least 5% of participants were ISRs, headache, and nausea.¹



Nodules were the most commonly reported ISR. Additional ISRs reported include pain, induration, swelling, pruritis, erythema, bruising, and warmth.¹⁻³



Upon injection, a **drug depot** forms in the SC tissue. Lenacapavir is slowly released into the systemic circulation over time. This allows for a twice-yearly continuation injection schedule.¹



The drug depot can lead to a possible reaction.¹

In PURPOSE 1 and PURPOSE 2, nodule frequency decreased with subsequent injections.^{1-3*†}

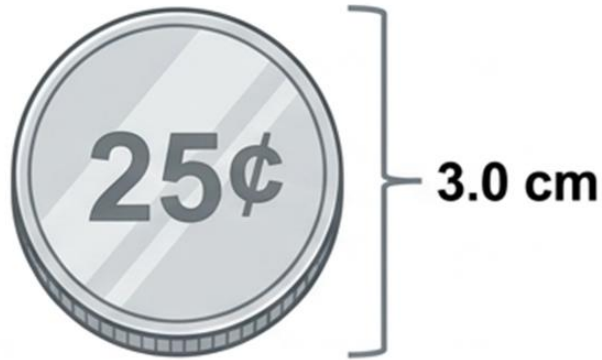
* PURPOSE 1 is a phase 3, double-blind, active-controlled, multicenter, randomized study of twice-yearly SC LEN for PrEP, daily oral emtricitabine/tenofovir alafenamide (F/TAF) or emtricitabine/tenofovir disoproxil fumarate (F/TDF) for HIV prevention in cisgender women in South Africa and Uganda. The HIV incidence in adolescent girls and young women not receiving PrEP in these countries was at least 3.5/100 person-years in recent trials. † The PURPOSE 2 study is a phase 3, double-blind, active-controlled, multicenter, randomized trial designed to evaluate safety and efficacy of twice-yearly subcutaneous LEN for PrEP for HIV prevention in cisgender gay, bisexual, and other men, transgender women, transgender men, and gender non-binary individuals who have condomless receptive anal sex with partners assigned male at birth.

ISR: Injection site reaction; LEN for PrEP: Lenacapavir for pre-exposure prophylaxis; SC: Subcutaneous.

1. YEZTUGO Prescribing Information. Gilead Sciences, Inc. 2025. 2. Bekker L-G, et al. *N Engl J Med.* 2024;391(13):1179-1192. doi: 10.1056/NEJMoa2407001. 3. Kelley C, et al. *N Engl J Med.* 2025;392(13):1261-1276. doi: 10.1056/NEJMoa2411858.

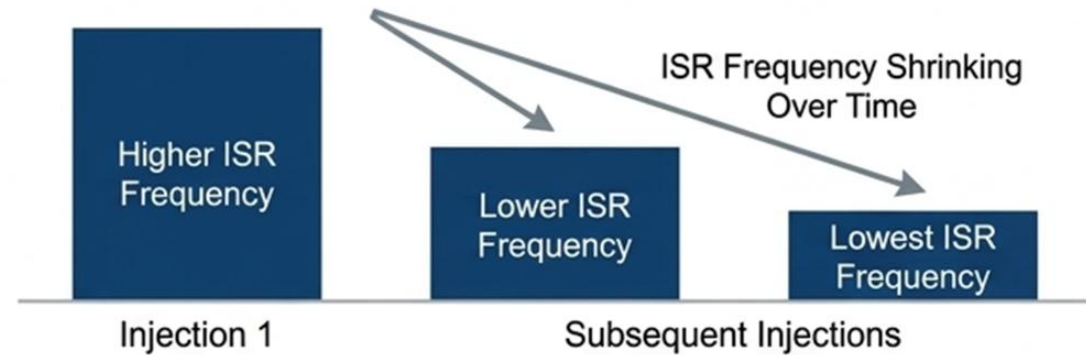
Injection Site Reactions with LEN for PrEP in PURPOSE 1 and PURPOSE 2: Nodules

The Nodule Profile



- Median maximum diameter is ~3.0 cm (roughly the size of a U.S. quarter).
- Median duration: 350 days (P1) and 297 days (P2).

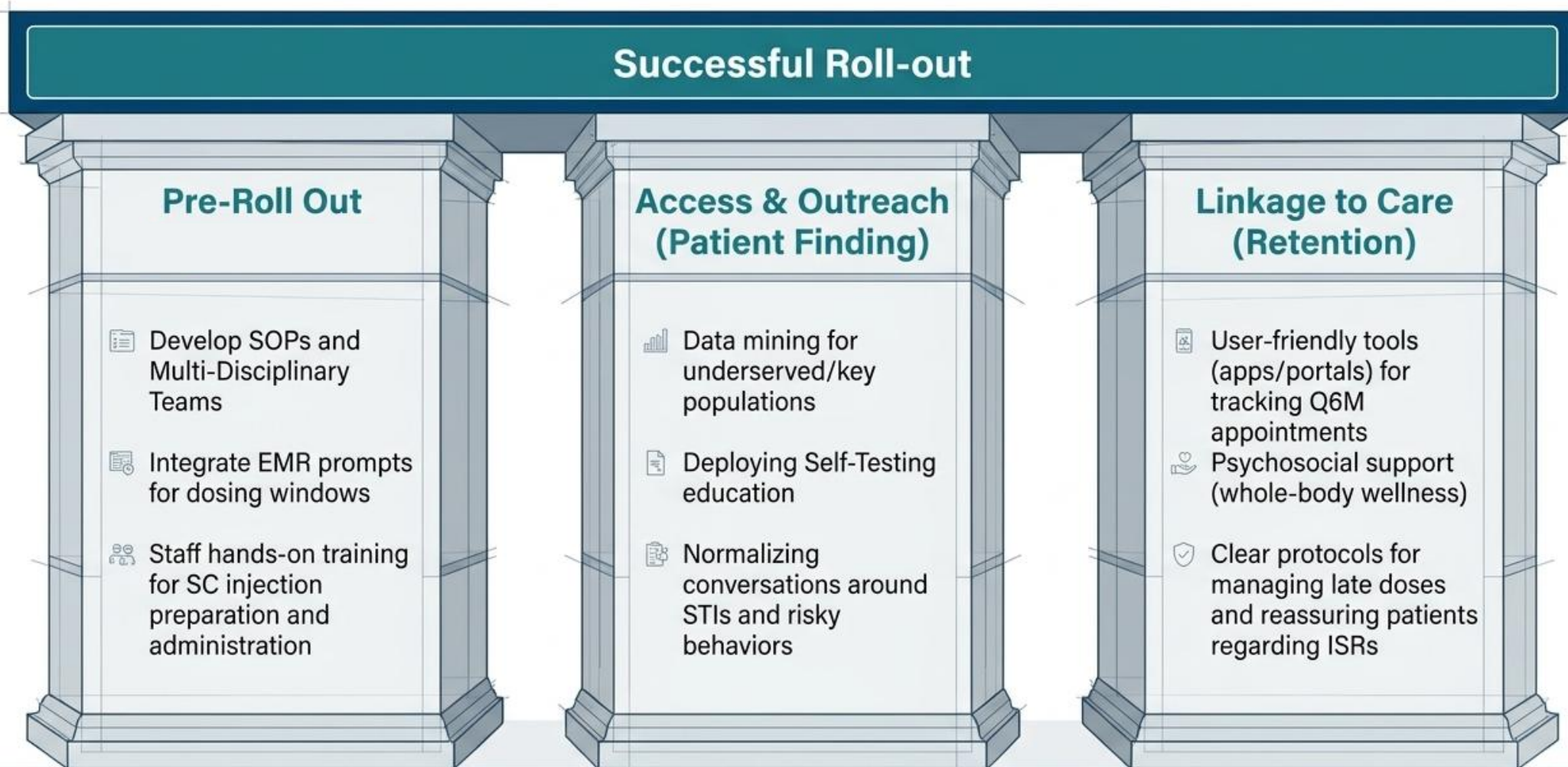
Tolerability Reality



Discontinuations due to ISRs are exceptionally low.

- Only **4 (0.2%)** participants in P1 and **26 (1.2%)** in P2 discontinued due to ISRs.
- Other common **non-ISR** AEs: Headache, Nausea, UTI/Chlamydia (similar rates observed in control groups).

Key Recommendations for Successful LENO roll out



Evolution of Science for Prevention Beyond 2026+

Population Pharmacokinetic Modeling of Once-Yearly IM LEN to Inform Phase 3 Dose Selection and Design



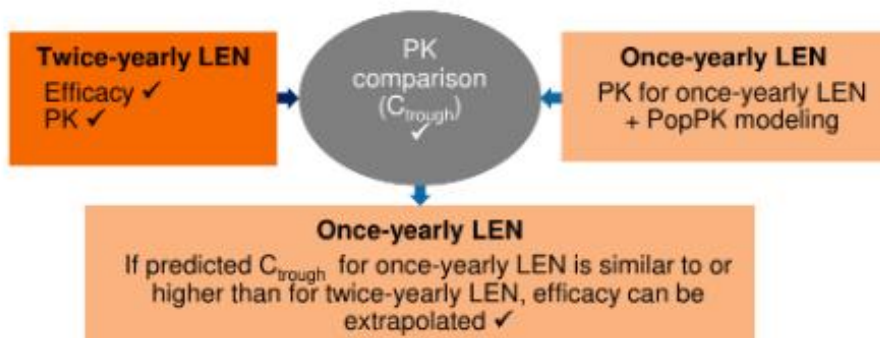
N=151

A 3-compartment PopPK model developed using data from four Phase 1 studies, providing 3378 LEN concentration measurements^a



Dose selection was based on **exposure matching**, targeting a dose where the Week 52 C_{trough} was projected to be equivalent to or greater than the observed Week 26 C_{trough} in the PURPOSE 1 and 2 trials

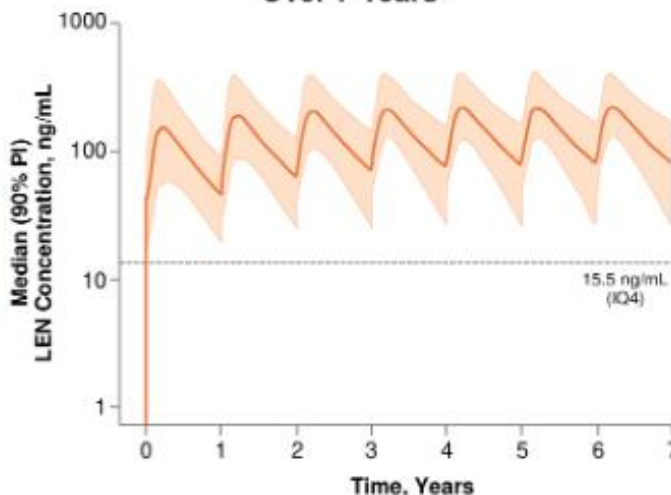
Model-Informed Drug Development Efficacy Extrapolation



Outcome

Simulation of various oral loading frequencies and potential IM LEN doses to identify a regimen projected to maintain protective drug concentrations for ≥ 52 weeks in people who need or want PrEP

Simulated Concentration of LEN for 3000 mg Once-Yearly IM Administration Over 7 Years^b



- PopPK simulations predicted a LEN IM dose of **3000 mg** would result in a Week 52 C_{trough} exceeding the observed Week 26 C_{trough} in PURPOSE 1 and 2
- **LEN 3000 mg IM** was projected to maintain **median LEN concentrations >4 times the *in vitro* IQ4 (15.5 ng/mL)** for ≥ 52 weeks
- Simulations indicated that **oral loading (600 mg on Days 1 and 2)** is required to achieve target concentrations rapidly by Day 2

A LEN dose of 3000 mg IM was predicted by PopPK modeling to be suitable for once-yearly dosing; the safety and efficacy of this dose will be investigated in the Phase 3 PURPOSE 365 study


^aOral data included doses from 300 to 1800 mg, and IM data included a single dose of 5000 mg. ^bCentral solid line is the median concentration over time and the shaded region is the 90% PI
 IQ4, inhibitory quotient 4; PI, prediction interval; PopPK, population pharmacokinetic; Q12M, every 12 months
 Hughes E, et al. CROI 2026, Poster 996







Starting LEN for PrEP in Individuals Who Completed nPEP


Guidance from the CDC

All individuals prescribed nPEP should be screened for ongoing HIV risk and transition to PrEP as appropriate.¹





Screening and Testing

-  nPEP guidelines recommend an immediate transition from nPEP to PrEP.¹
-  Complete baseline labs, including confirmation of HIV-negative status through repeat testing.¹
-  Provide adherence and risk reduction counseling.¹
-  Schedule follow-up visits for HIV, STI, and other lab tests consistent with PrEP follow-up.¹



Transitioning to PrEP

-  Maintain satisfactory ARV drug levels for PrEP (if nPEP adherence has been good).¹
-  Maximize continuous prevention measures through continuity of care.¹

Please refer to the full guidelines for complete recommendations.

ARV: Antiretroviral; CDC: Centers for Disease Control and Prevention; HIV: Human immunodeficiency virus; LEN for PrEP: Lenacapavir for pre-exposure prophylaxis; nPEP: Non-occupational post-exposure prophylaxis; STI: Sexually transmitted infection.
 1. Tanner MR, et al. Antiretroviral Postexposure Prophylaxis After Sexual, Injection Drug Use, or Other Nonoccupational Exposure to HIV – CDC Recommendations, United States, 2025. *MMWR Recomm Rep.* 2025;74(No. RR-1):1-56. doi: <http://dx.doi.org/10.15585/mmwr.rr7401a1>.

Switching to LEN for PrEP from Another PrEP Option

Testing Prior to Initiation

Clinical Considerations



Test to confirm HIV-negative status.¹



↔ Switching from other LAI PrEP

- No clinical trial data available in HIV-negative individuals switching from Q2M IM CAB to LEN for PrEP.^{2,3}
- No clinically significant DDIs expected. Injectable PrEP options have different mechanisms of action and metabolic pathways.^{2,3}
- There is no contraindication for switching to LEN for PrEP immediately in appropriate individuals.²



↔ Switching from oral PrEP

- In the OLE phase of PURPOSE 1 and PURPOSE 2, there were no reported DDIs in participants on F/TDF and F/TAF who switched directly to LEN for PrEP.⁴
- In appropriate individuals, a switch from daily oral PrEP would be immediate.⁵
- Discontinuation of agents with activity against HBV (such as F/TDF or F/TAF) can cause severe hepatitis B exacerbation in individuals living with HBV.^{6,7}
- Monitor liver function closely and consider HBV therapy if needed for these individuals.^{6,7}

CAB: Cabotegravir; DDI: Drug-drug interaction; F/TAF: Emtricitabine/tenofovir alafenamide; F/TDF: Emtricitabine/tenofovir disoproxil fumarate; HBV: Hepatitis B virus; HIV-1: Human immunodeficiency virus type 1; IM: Intramuscular; LAI: Long-acting injectable; LEN for PrEP: Lenacapavir for pre-exposure prophylaxis; OLE: Open-label extension; Q2M: Every 2 months.
 1. Clinical Guidance for PrEP, HIV Nexus: CDC Resources for Clinicians. February 10, 2025. Available at: <https://www.cdc.gov/hivnexus/hcp/prep/index.html>. Accessed February 14, 2025. 2. YEZTUGO Prescribing Information. Gilead Sciences, Inc. 2025. 3. APRETUDE Prescribing Information. ViiV healthcare; 2025. 4. Data on file. Gilead Sciences, Inc.; 2025. 5. Patel RR, Hoover KW, Lale A, Cabrales J, Byrd KM, Kourtis AP. Clinical Recommendation for the Use of Injectable Lenacapavir as HIV Preexposure Prophylaxis – United States, 2025. *MMWR Morb Mortal Wkly Rep.* 2025;74:541-549. doi: <http://dx.doi.org/10.15585/mmwr.mm7435a1>. 6. TRUVADA Prescribing Information. Gilead Sciences, Inc. 2024. 7. DESCOVY Prescribing Information. Gilead Sciences, Inc. 2025.



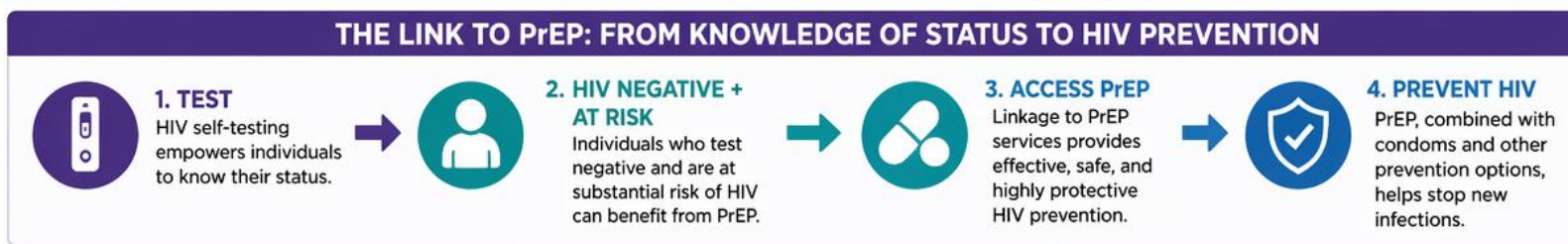


SELF-TESTING FOR HIV (HIVST): GLOBAL PITFALLS, ADVANTAGES AND LINK TO PrEP

ADVANTAGES	
	Increased access and reach Enables people to test in the privacy of their own space; reaches underserved and key populations.
	Privacy and confidentiality Reduces fear of stigma and discrimination associated with facility-based testing.
	Convenience and autonomy Allows individuals to test on their own time and terms.
	Early detection Encourages more frequent testing and earlier diagnosis.
	Supports epidemic control A critical tool to reach the 95-95-95 targets and reduce new infections.
	Cost-effective at scale Can reduce costs related to facility infrastructure and staffing.

GLOBAL PITFALLS / CHALLENGES	
	Linkage to care Risk of loss to follow-up for reactive results without effective referral systems.
	Incorrect use and result interpretation Improper testing or misunderstanding results may lead to false reassurance or anxiety.
	Psychological impact Reactive results can cause distress, anxiety, or depression without immediate support.
	Inequity and digital divide Limited access to information, digital tools, or support in low-resource settings.
	Regulation and quality assurance Variability in test quality, counterfeit products, and weak regulatory oversight.
	Data and surveillance gaps Harder to capture data for monitoring and public health response.

WHAT'S NEEDED FOR SUCCESS	
	Strong linkage systems Clear, confidential, and accessible pathways to confirmatory testing and treatment.
	User-friendly tools & instructions Simple instructions, multilingual support, and helplines.
	Psychosocial support Access to counseling, peer support, and crisis services.
	Digital and community solutions mHealth, hotlines, and community networks to support users.
	Quality assurance & regulation Ensure availability of WHO-prequalified tests and regulate supply chains.
	Data integration Innovative approaches to capture and use data for better decision-making.



HIVST + PrEP = A POWERFUL PREVENTION COMBINATION

Know your status. Protect your future.

Summary

Available LAI's

- Prevention impact in potential decrease in HIV cases if leveled up
- Capsid Inhibitor-new MOA for HIV Treatment & Prevention (PrEP)
- Purpose 1 & 2- Landmark Studies –Guideline changes for Prevention.

LEN Roll-Out Recommendations

- Prior to Rollout-Health care staff must be educated on PrEP (Science & Implementation)
- Increased Access and outreach to key population – data mining – trials
- Patient Education - linkage to care/injection adherence/available resources

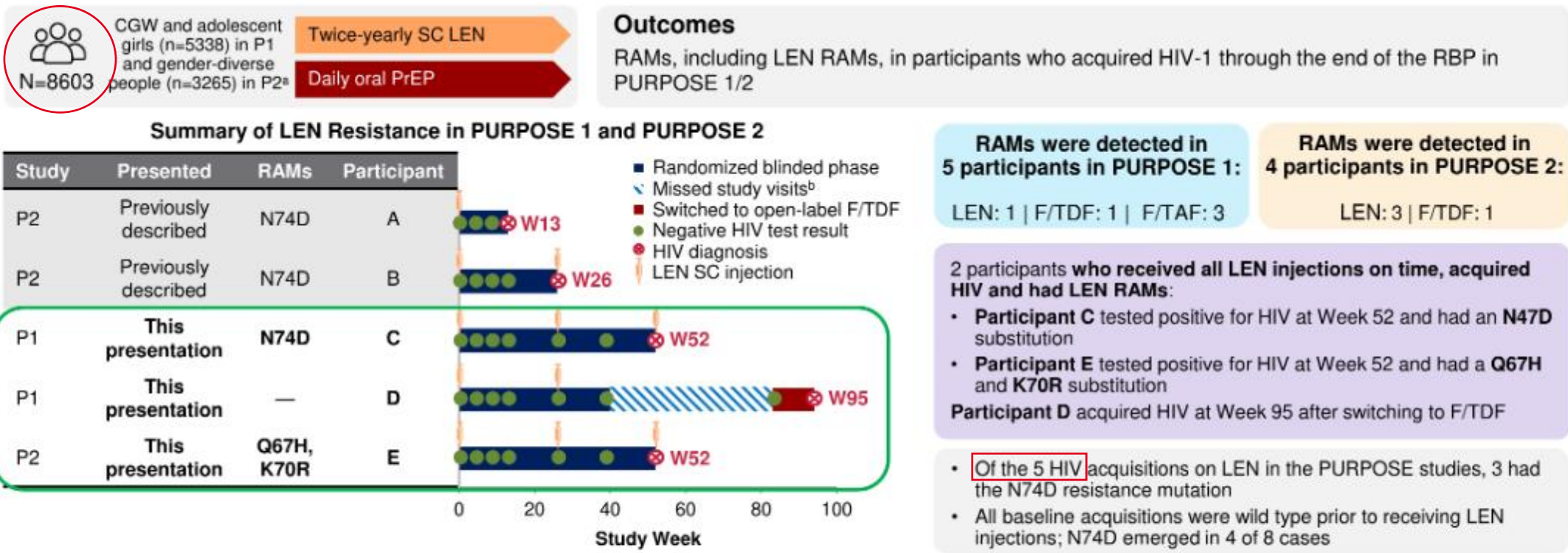
Evolution of Science for Prevention Beyond 2026+

- Lenacapavir once-yearly IM (Purpose 365)
- PrEP Switch
- Self-Testing for HIV (STHIV) – Global Pitfalls Advantages - Link to PrEP



THANK YOU

Resistance Analyses of the PURPOSE Studies Through the End of Randomized Blinded Phase



Acquisition of HIV while receiving LEN was rare, and resistance emergence was likely due to LEN monotherapy, consistent with other PrEP agents. These findings may support LEN's potential as a durable and effective long-acting PrEP option

^aIncluded in the full analysis set for primary efficacy analyses (additional participants are included in the safety analysis). ^bMissed LEN injections
 – indicates no resistance mutation was detected; CGW, cisgender women; IQ4, inhibitory quotient 4; P1, PURPOSE 1; P2, PURPOSE 2; RBP, randomized blinded phase; W, Week
 Cox S, et al. CROI 2026, Oral 130