Lenacapavir Efficacy, Safety, and Pharmacokinetics in Adolescents and Adults in PURPOSE 1

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Disclosures

- Gilead Sciences funded and designed the study with input from the PIs and G-CAG. The PIs and study staff gathered data; Gilead Sciences monitored the conduct of the trial, received the data, and performed analyses
- Medical writing support was provided by Simon Wigfield, PhD, of Aspire Scientific Ltd (Bollington, UK), and was funded by Gilead Sciences, Inc.

G-CAG, Global Community Advisory Group; **PI**, principal investigator.

Adolescents Are Often Excluded From Registrational HIV Prevention Trials, Delaying Access to New Options

The PURPOSE program is the first to intentionally include adolescents in Phase 3 HIV prevention trials

Adolescents account for a significant number of **new infections** globally.[1] Clinical data in adolescents for new prevention options are not available until **several years after approval in adults**

Daily adherence to medications, including PrEP, is often lower among adolescents than in adults[2,3]

LEN is a **first-in-class**, multistage HIV-1 capsid inhibitor with **high potency** and a **long half-life**, supporting **twice-yearly SC injection**[4,5]

We describe our approach to adolescent inclusion and compare the efficacy, safety, and PK of LEN in adolescents aged 16 and 17 years versus adults aged 18-25 years in the PURPOSE 1 trial

HIV, human immunodeficiency virus; **LEN**, lenacapavir; **PK**, pharmacokinetics; **PrEP**, pre-exposure prophylaxis; **SC**, subcutaneous.

1. UNICEF. https://data.unicef.org/topic/hivaids/adolescents-young-people/ (accessed Jan. 15, 2025). 2. Kim S-H, et al. *AIDS*. 2014;28:1945-56. 3. Tanner MR, et al. *MMWR Recomm Rep*. 2020;69:1-12. 4. Link JO, et al. *Nature*. 2020;584:614-18. 5. Segal-Maurer S, et al. *N Engl J Med*. 2022;386:1793-803.

Engagement on Ethical and Responsible Adolescent Inclusion Before and During PURPOSE 1

COMMUNITY

- Consulted key stakeholders, such as adolescent medicine experts and community advocates, to ethically and responsibly include adolescents

REGULATORS

- Engaged regulatory authorities on the safe inclusion of adolescents
  - Required an independent review of safety data from the first 300 adult participants before adolescent enrollment

ETHICAL REVIEW ACTIVITIES

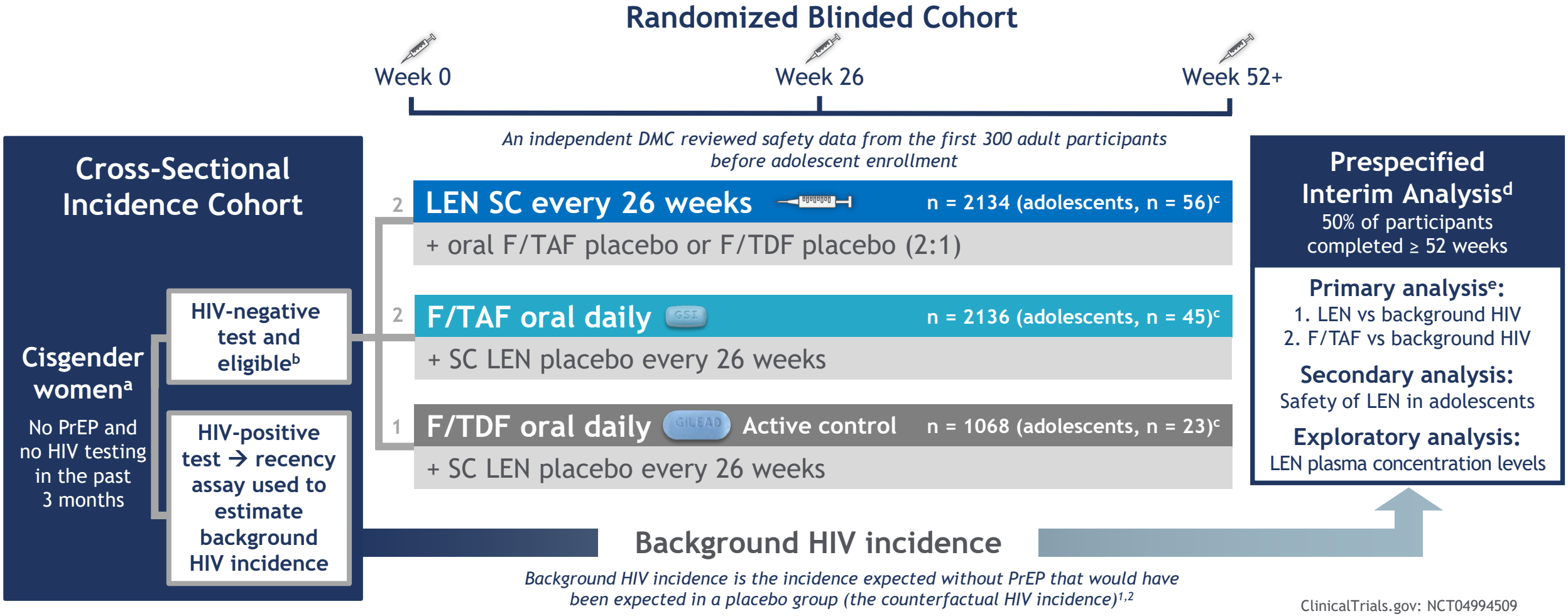
- Organized area-specific informed consent initiatives
  - Community consultation process led to parental consent waivers from some IRBs
  - Emancipated adolescents could consent for themselves in other locales

TRIAL CONDUCT

- Shared best practices from experienced sites, eg, early clinic and weekend visits to accommodate adolescents' schedules

IRB, institutional review board.

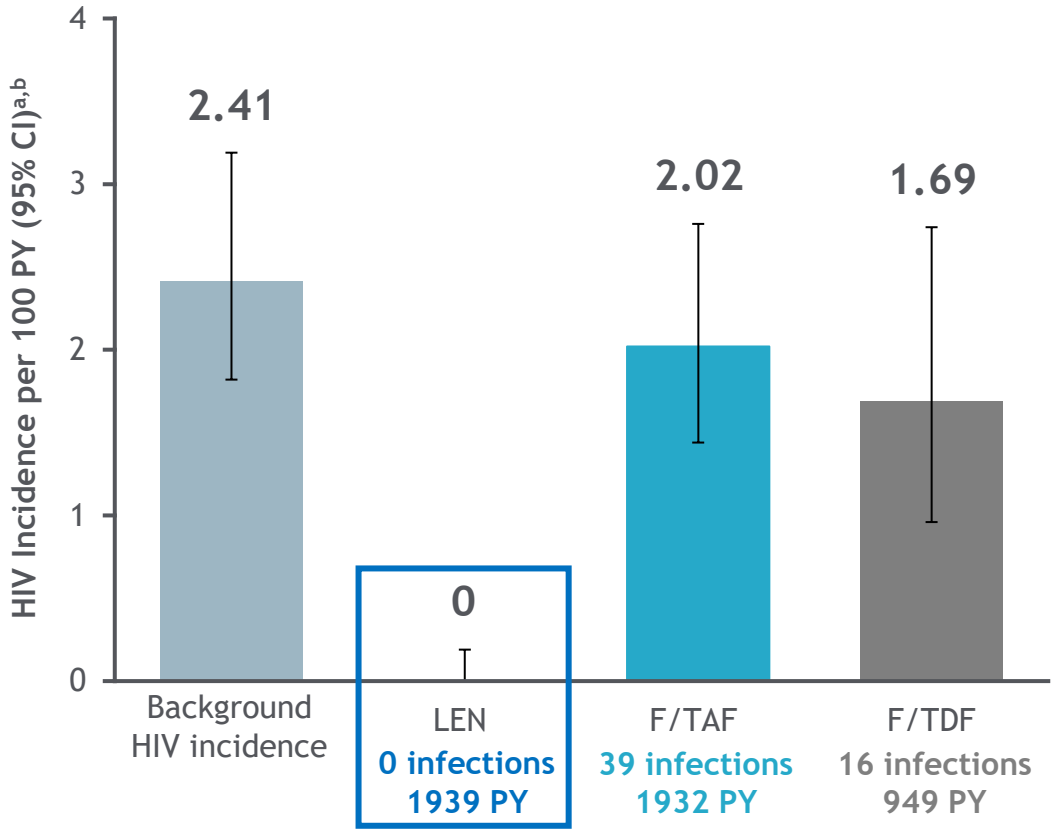
PURPOSE 1 Study Design



[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]Since the randomized blinded phase was stopped early due to an efficacy outcome, the interim analysis served as the primary analysis. [e]IRR was assessed using a Wald test or likelihood ratio test if there were zero infections.[1,2] **DMC**, data monitoring committee; **eGFR**, estimated glomerular filtration rate; **F/TAF**, emtricitabine/tenofovir alafenamide; **F/TDF**, emtricitabine/tenofovir disoproxil fumarate; **IRR**, Incidence rate ratio; **LEN**, lenacapavir; **PrEP**, pre-exposure prophylaxis; **SC**, subcutaneous.

1. Gao F, et al. *Stat Commun Infect Dis.* 2021;13:20200009. 2. Shao Y, Gao F. *Stat Commun Infect Dis.* 2024;16:20230004.

Zero HIV Infections in Adolescents Receiving LEN



Adolescents

LEN n = 56	F/TAF n = 45	F/TDF n = 23
0 infections per 42 PY	0 infections per 33 PY	0 infections per 18 PY

In the **PURPOSE 1 trial**, **zero HIV infections** occurred in **adolescents** in the **LEN**, **F/TAF**, and **F/TDF** arms

LEN demonstrated 100% efficacy for HIV prevention in adolescent and adult cisgender women[1,2]

Adolescents were defined as being aged 16 and 17 years.
[a]Overall n: background HIV incidence, 8094; LEN, 2134; F/TAF, 2136; and F/TDF, 1068. [b]95% CIs: background HIV incidence, 1.82-3.19; LEN, 0-0.19; F/TAF, 1.44-2.76; and F/TDF, 0.96-2.74.
CI, confidence interval; **F/TAF**, emtricitabine/tenofovir alafenamide; **F/TDF**, emtricitabine/tenofovir disoproxil fumarate; **HIV**, human immunodeficiency virus; **LEN**, lenacapavir; **PY**, person-years.

1. Bekker L-G, et al. *N Engl J Med*. 2024;391:1179-92. 2. Bekker L-G, et al. Oral presented at: 25th International AIDS Conference; July 22–26, 2024; Munich, Germany.

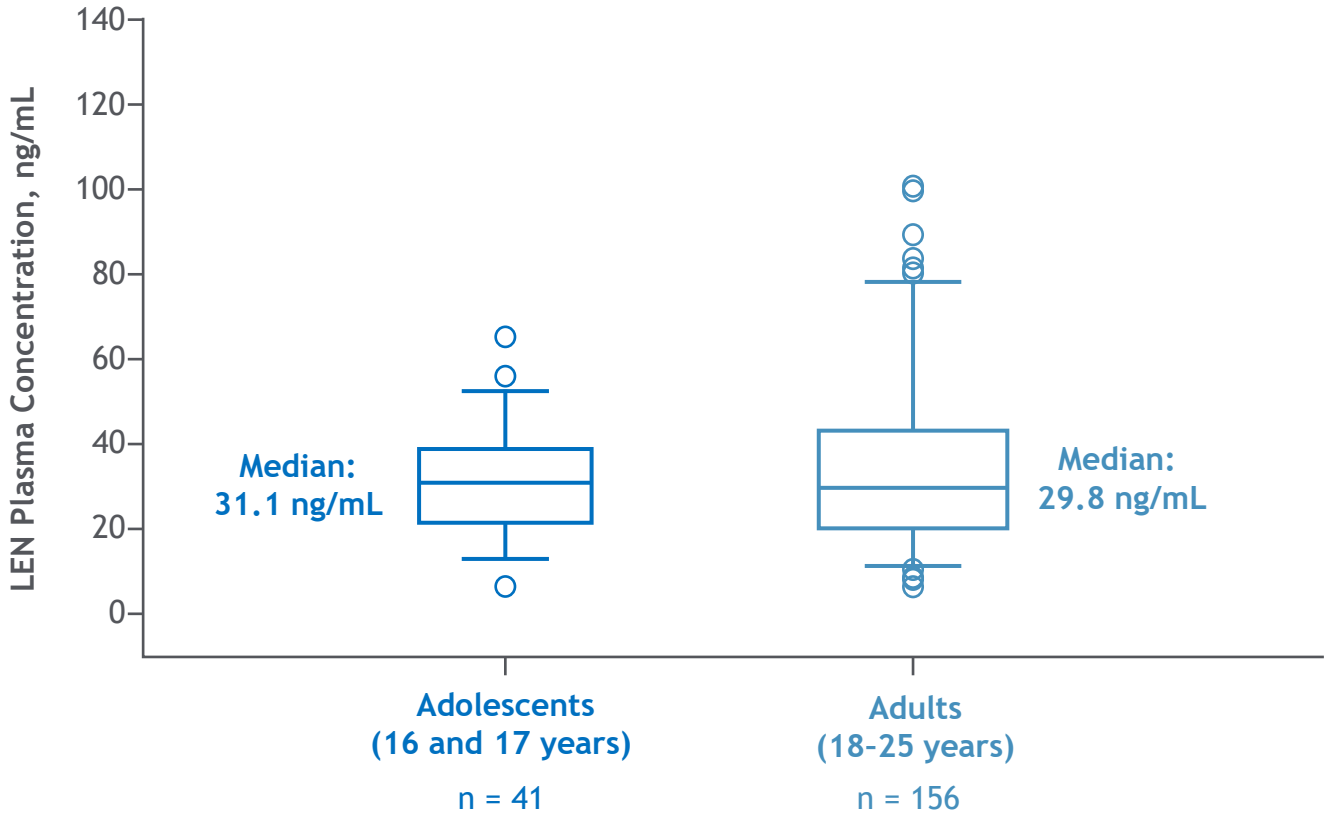
LEN Was Safe and Well Tolerated in Adolescents

AE, n (%)	Adolescents (16 and 17 years) n = 56	Adults (18-25 years) n = 2084
Any AE[a]	53 (94.6)	1840 (88.3)
AE related to study drug[a]	40 (71.4)	1337 (64.2)
Serious AEs[a]	1 (1.8)[b]	58 (2.8)
AEs leading to discontinuation of study drug[a]	0	5 (0.2)[c]
AEs occurring in ≥ 10% of participants in the adolescent group[a]		
Injection-site nodule	42 (75.0)	1323 (63.5)
Injection-site pain	18 (32.1)	651 (31.2)
Headache	9 (16.1)	276 (13.2)
Genitourinary chlamydia infection	7 (12.5)	293 (14.1)
Laboratory abnormalities, n with ≥ 1 post-baseline result[d]	55	2073
Any grade ≥ 1	49 (89.1)	1881 (90.7)
Grade ≥ 3	6 (10.9)[e]	110 (5.3)

Adverse events were generally similar between adolescents and adults receiving LEN

[a]AEs are treatment emergent in participants who received at least one dose of study drug; AEs exclude injection-site reactions; AEs coded according to the Medical Dictionary for Regulatory Activities, Version 27.0. [b]n = 1 for pyelonephritis. [c]n = 1 for each of the following: nausea, decreased creatinine renal clearance, increased hepatic enzymes, spontaneous miscarriage, and suicide attempt/major depression. [d]Severity grades were defined by Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric AEs, Version 2.1. [e]Two participants had decreased creatinine clearance, two participants had decreased hemoglobin, one participant had increased creatinine kinase, and one participant had both decreased creatinine clearance and proteinuria. **AE**, adverse event; **LEN**, lenacapavir.

LEN Plasma Concentrations at Week 26 (C_{trough}) in Adolescents Versus Adults[a]



Observed LEN plasma concentrations were generally comparable between adolescents and adults

[a]Excludes participants who became pregnant and those who received oral LEN bridging.
Plasma LEN concentration data in adolescents were collected at weeks 4, 8, 13, 26 and every 13 weeks thereafter. Values below the limit of quantitation were treated as zero.
Box = Q1 and Q3; horizonal line inside box = median; whiskers = 5th and 95th percentiles.
C_{trough}, trough concentration; **LEN**, lenacapavir; **Q1**, first quartile; **Q3**, third quartile.

Conclusions

- In the PURPOSE 1 trial, the intentional efforts to include adolescents resulted in early and robust enrollment approximately 2.5- to 5-fold higher than in typical adolescent-dedicated studies
- No HIV seroconversions were observed among adolescents receiving LEN
- LEN was safe and well tolerated in adolescents aged 16 and 17 years
- LEN PK levels in adolescents were generally comparable to those in adults
  - This supports extrapolation of efficacy in adolescents

Inclusion of adolescents in the PURPOSE 1 trial yielded data at the primary analysis that could contribute to early inclusion in the label and guidelines, and lead to accelerated access for adolescents who need or want PrEP

HIV, human immunodeficiency virus; **LEN**, lenacapavir; **PK**, pharmacokinetic; **PrEP**, pre-exposure prophylaxis.

PURPOSE 1 Acknowledgments

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- This study was funded by Gilead Sciences, Inc.
- All authors contributed to and approved the presentation; medical writing support was provided by Simon Wigfield, PhD, of Aspire Scientific Ltd (Bollington, UK), and was funded by Gilead Sciences, Inc.

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Lenacapavir for PrEP at CROI 2025

AM

Oral: Lenacapavir Efficacy, Safety, and Pharmacokinetics, in Adolescents and Adults in PURPOSE 1
(Katherine Gill)
Time: 10:29 AM PT
Session: (S0-3) Maternal-Child Health and Treatment of Malignancies;
San Francisco Ballroom A

Oral: Pharmacokinetics and Safety of Once-Yearly Formulations of Lenacapavir
(Renu Singh)
Time: 10:29 AM PT
Session: (S0-7) Antivirals For HIV, MPXV, and SARS-CoV-2: New Drug Strategies and Resistance;
San Francisco Ballroom B

Oral: Adherence to F/TAF in Cisgender Women Prevents HIV with Low Risk of Resistance or Diagnostic Delay
(Flavia Matovu Kiweewa)
Time: 10:29 AM PT
Session: (S0-12) Expanding the Prevention Toolbox;
San Francisco Ballroom D

PM

Poster (1230): PURPOSE 1: Preference for Twice-Yearly Injection vs Daily Oral Pills for HIV PrEP in Cisgender Women
(Leila E Mansoor)
Time: 2:30–4.00 PM PT
Session: (S-05) PrEP Implementation: Hopes, Dreams, and Aspirations

Late Breaker Poster (1234): Qualitative Assessment of Acceptability and Preferences for Injectable and Oral PrEP in PURPOSE 1
(Elizabeth T Montgomery)
Time: 2:30–4.00 PM PT
Session: (S-06) Innovations in PrEP Products

PURPOSE: Update on Global Lenacapavir Regulatory Filings

- The **FDA** has accepted New Drug Applications for lenacapavir for PrEP under priority review, with a PDUFA date of June 19, 2025[a]
- The **European Medicines Agency (EMA)** has validated Gilead's submission for a Marketing Authorization Application (MAA) and EU-Medicines for All (EU-M4all) application for lenacapavir for PrEP, both to be assessed in parallel under Accelerated Assessment[b]
  - The EU-M4all application seeks an opinion that can be leveraged by national regulatory agencies outside the EU, including in low and lower-middle income countries, to facilitate more expedited review processes in their respective countries and potentially accelerate access to lenacapavir for PrEP
- Gilead is executing an access strategy that prioritizes speed and enables the most efficient paths for the regulatory review, approval of and access to lenacapavir for PrEP in regions around the world
- Gilead is continuing to innovate to develop longer-acting injectable and oral formulations for lenacapavir for PrEP

PURPOSE 1 NCT identifier: NCT04994509; PURPOSE 2: NCT04925752; PURPOSE 3: NCT06101329; PURPOSE 4: NCT06101342. PURPOSE studies available at: https://www.purposestudies.com (accessed October 4, 2024). [a]https://www.gilead.com/news/news-details/2025/us-fda-accepts-gileads-new-drug-applications-for-twice-yearly-lenacapavir-for-hiv-prevention-under-priority-review (accessed Mar 3, 2025). [b]https://www.gilead.com/company/company-statements/2025/gilead-submits-marketing-authorization-applications-to-european-medicines-agency-for-twice-yearly-lenacapavir-for-hiv-prevention (accessed Mar 3, 2025).
EU, European Union; PDUFA, Prescription Drug User Fee Act; **PrEP**, pre-exposure prophylaxis.