GILEAD | Medical Information

# Yeztugo® (lenacapavir)
# Ongoing Studies for HIV-1 Pre-Exposure Prophylaxis

This document is in response to your request for information regarding Yeztugo® (lenacapavir [LEN]) and its investigational use for HIV-1 pre-exposure prophylaxis (PrEP).

Some data may be outside of the US FDA-approved prescribing information. In providing this data, Gilead Sciences, Inc. is not making any representation as to its clinical relevance or to the use of any Gilead product(s). For information about the approved conditions of use of any Gilead drug product, please consult the FDA-approved prescribing information.

**The full indication, important safety information, and boxed warnings are available at: www.gilead.com/-/media/files/pdfs/medicines/hiv/yeztugo/yeztugo_pi; www.gilead.com/-/media/files/pdfs/medicines/hiv/truvada/truvada_pi.**

## Summary


### Clinical Data on Use of Twice-Yearly SUBQ LEN for HIV-1 PrEP

LEN is indicated for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 in adults and adolescents weighing at least 35 kg who are at risk for HIV-1 acquisition.[1]

Gilead is studying LEN for the prevention of HIV-1 across multiple ongoing PURPOSE studies. Please see Table 1 for an overview of these studies.[2-4]

- PURPOSE 3 is an ongoing, phase 2, open-label, randomized study to evaluate the pharmacokinetics, safety, and acceptability of twice-yearly SUBQ LEN or once-daily FTC/TDF for HIV-1 PrEP in cisgender women in the US.[2]
- PURPOSE 4 is an ongoing, phase 2, open-label, randomized study to evaluate the pharmacokinetics and safety of twice-yearly SUBQ LEN or once-daily FTC/TDF for HIV-1 PrEP in people who inject drugs in the US.[3]
- PURPOSE 5 is an ongoing, phase 2, open-label, randomized study to evaluate the persistence, safety, acceptability and pharmacokinetics of twice-yearly SUBQ LEN or once-daily FTC/TDF for HIV-1 PrEP in people who need or want PrEP in France and the UK.[4]

### Clinical Data on Use of Once-Yearly IM LEN for HIV-1 PrEP

A phase 1, open-label study evaluated the pharmacokinetics, safety, and tolerability of two once-yearly IM formulations of LEN for HIV-1 PrEP in participants 18-55 years without HIV. Both formulations were safe and well tolerated, and demonstrated potential for once-yearly dosing.[5]

# Background: PURPOSE Studies Overview

The PURPOSE program is evaluating the efficacy and safety of LEN for PrEP given twice yearly as a SUBQ injection.[2-4] LEN for HIV-1 PrEP is currently being studied in three phase 2 studies, PURPOSE 3, 4, and 5. See Table 1 for an overview of each study design and intended population.

**Table 1. PURPOSE Studies Overview[2-5]**

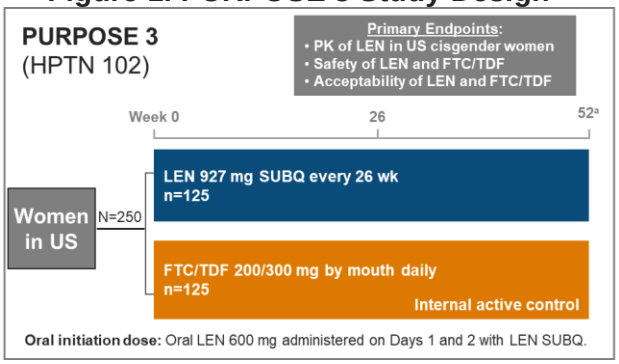
| Study | Medications | Population | Countries | Primary Endpoint |
|---|---|---|---|---|
| **PURPOSE 3** (HPTN 102) NCT06101329 | LEN, FTC/TDF | Cisgender women | US | LEN PK, safety, acceptability vs FTC/TDF |
| **PURPOSE 4** (HPTN 103) NCT06101342 | LEN, FTC/TDF | PWID | US | LEN PK, safety, acceptability vs FTC/TDF |
| **PURPOSE 5** NCT06513312 | LEN, FTC/TDF | Individuals who need or want PrEP and are not currently on PrEP | France, UK | LEN PK, safety, acceptability, tolerance, persistance vs FTC/TDF |

# Clinical Data on Use of Twice-Yearly SUBQ LEN for HIV-1 PrEP

## PURPOSE 3 Study Design

PURPOSE 3 is a phase 2, open-label, multicenter, randomized study to evaluate the PK, safety, and acceptability of LEN SUBQ injection compared with once-daily oral FTC/TDF for HIV-1 PrEP among cisgender women in the US. This study has 2 parts: a Randomized Phase and a PK Tail Phase. In the Randomized Phase, approximately 250 cisgender women will be enrolled and randomized 1:1 to either LEN 927 mg SUBQ every 26 weeks or FTC/TDF 220/300mg orally daily, and each participant will be followed for 52 weeks. Participants transitioning to the PK Tail Phase, which will be for up to an additional 78 weeks, in the LEN group will transition to FTC/TDF and participants in the FTC/TDF group will continue to receive FTC/TDF.[2]

**Figure 1. PURPOSE 3 Study Design[2,a]**

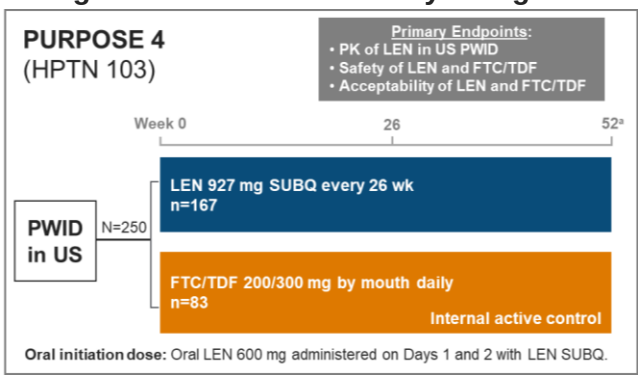



[a]After Week 52, participants in the LEN group will switch to oral FTC/TDF, and participants in the FTC/TDF group will continue to receive FTC/TDF in the PK tail phase for 78 weeks.

# PURPOSE 4 Study Design

PURPOSE 4 is a phase 2, open-label, multicenter, randomized study to evaluate the PK and safety of LEN SUBQ injection compared with once-daily oral FTC/TDF for HIV-1 PrEP among PWID. This study has 2 parts: a Randomized Phase and a PK Tail Phase. In the Randomized Phase, approximately 250 participants will be randomized in a 2:1 allocation ratio to receive 52 weeks of LEN 927 mg SUBQ every 26 weeks or FTC/TDF 220/300mg orally daily, followed by up to 78 weeks of FTC/TDF for both study drug groups in the PK Tail Phase. Following the Randomized Phase, participants in the LEN group will transition to FTC/TDF to provide coverage for the PK tail while participants in the FTC/TDF group will be provided continued access to FTC/TDF for a comparable duration.[3]

**Figure 2. PURPOSE 4 Study Design[3,a]**

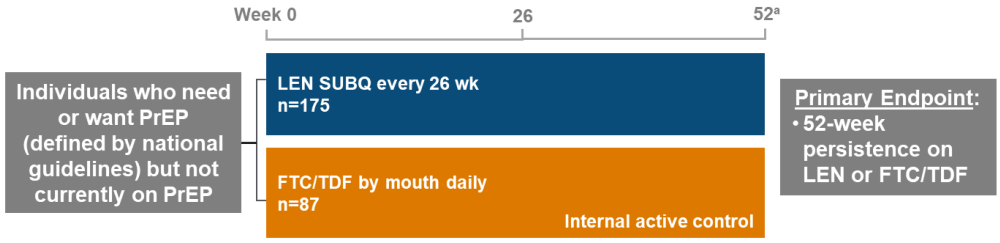



[a]After Week 52, participants in the LEN group will switch to oral FTC/TDF, and participants in the FTC/TDF group will continue to receive FTC/TDF in the PK tail phase for 78 weeks.

# PURPOSE 5 Study Design

PURPOSE 5 is a phase 2, open-label, multicenter, randomized study to evaluate the persistence, safety, acceptability, and PK of SUBQ LEN injection compared with daily oral F/TDF for HIV-1 PrEP in individuals who need or want PrEP and who are not currently taking PrEP in France and the UK. This study has 3 parts: a Randomized Phase, a LEN open-label extension (OLE) Phase, and a PK Tail Phase. In the Randomized Phase, approximately 262 participants will be randomized 2:1 in an open-label fashion to receive 52 weeks of LEN 927 mg SUBQ every 26 weeks or FTC/TDF 220/300mg orally daily. In the LEN OLE Phase, all participants will receive up to 52 weeks of SUBQ LEN, administered every 26 weeks. In the PK Tail Phase, all participants will receive up to 78 weeks of daily oral FTC/TDF.[4]

**Figure 3. PURPOSE 5: Study Design[4,a]**




[a]After Week 52, all participants will receive SUBQ LEN every 26 weeks for up to 52 weeks in the OLE Phase. After the OLE Phase, all participants will receive up to 78 weeks of daily oral FTC/TDF.

# Clinical Data on Use of Once-Yearly IM LEN for HIV-1 PrEP[5]

This phase 1, open-label study evaluated the pharmacokinetics, safety, and tolerability of two once-yearly IM formulations of LEN for HIV-1 PrEP in participants aged 18-55 years without HIV. Each dose was delivered as a single 5,000 mg ventrogluteal intramuscular injection as either formulation 1 (5% w/w ethanol) or formulation 2 (10% w/w ethanol). Plasma PK concentrations were measured over 56 weeks and participants were monitored for adverse events. Both formulations achieved rapid and sustained drug levels, with median time to maximum concentration achieved at 84.1 days (IQR 56.1–112.0) for formulation 1 and 69.9 days (IQR 55.3–105.5) for formulation 2. Adverse events were mostly grade 1 or 2, with the most common being injection-site pain in 16/20 (80%) of participants receiving formulation 1 and 15/20 (75%) of participants receiving formulation 2.[5]

# References

1. Enclosed, Gilead Sciences Inc. YEZTUGO® (lenacapavir) tablets, for oral use. YEZTUGO® (lenacapavir) injection, for subcutaneous use. U.S. Prescribing Information. Foster City, CA.
2. Gilead Sciences. Study of Lenacapavir and Emtricitabine/Tenofovir Disoproxil Fumarate (F/TDF) in Prevention of HIV in Cisgender Women in the United States (HPTN-102) (PURPOSE 3) Available at: https://clinicaltrials.gov/study/NCT06101329?term=lenacapavir%20purpose&rank=1 Accessed: 13 November 2023. 2023.
3. Gilead Sciences. Study of Lenacapavir and Emtricitabine/Tenofovir Disoproxil Fumarate (F/TDF) for Prevention of HIV in People Who Inject Drugs (HPTN-103) (PURPOSE-4) Available at: https://clinicaltrials.gov/study/NCT06101342?intr=lenacapavir&rank=5 Accessed: 07 November 2023. 2023.
4. Clinicaltrials.gov. Study of Lenacapavir Taken Twice a Year for HIV Pre-Exposure Prophylaxis(PrEP) (PURPOSE 5). Available at: https://clinicaltrials.gov/study/NCT06513312?term=lenacapavir, persistence&rank=1. Accessed: 11 November 2024. Last Updated: 21 October. 2024.
5. Jogiraju V, Pawar P, Yager J, et al. Pharmacokinetics and safety of once-yearly lenacapavir: a phase 1, open-label study. *Lancet*. 2025;405(10485):1147-1154.

# Abbreviations

AE=adverse event
FTC=emtricitabine
IM=intramuscular
IQR=interquartile range
LEN=lenacapavir
OLE=open-label extension
PK=pharmacokinetic(s)
PrEP=pre-exposure prophylaxis
PWID=people who inject drugs
SUBQ=subcutaneous
TDF=tenofovir disoproxil fumarate

# Product Label

For the full indication, important safety information, and boxed warning(s), please refer to the Yeztugo, Descovy, and Truvada US Prescribing Information available at: www.gilead.com/-/media/files/pdfs/medicines/hiv/yeztugo/yeztugo_pi; www.gilead.com/-/media/files/pdfs/medicines/hiv/truvada/truvada_pi.

# Follow-Up

For any additional questions, please contact Gilead Medical Information at:

☎1-866-MEDI-GSI (1-866-633-4474) or 🖱 www.askgileadmedical.com

# Adverse Event Reporting

Please report all adverse events to:

Gilead Global Patient Safety ☎ 1-800-445-3235, option 3 or 🖱 www.gilead.com/utility/contact/report-an-adverse-event

FDA MedWatch Program by ☎ 1-800-FDA-1088 or ✉MedWatch, FDA, 5600 Fishers Ln, Rockville, MD 20852 or 🖱 www.accessdata.fda.gov/scripts/medwatch

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