PURPOSE 2

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Annual Persistence to Twice-Yearly Lenacapavir Versus Daily Oral F/TDF for PrEP in the PURPOSE 2 Trial

Onyema Ogbuagu[1], Karam Mounzer[2], Ricardo S Diaz[3], Carlos Brites[4], Marcelo H Losso[5], Javier R Lama[6], Anchalee Avihingsanon[7], Ramin Ebrahimi[8], Christoph C Carter[8], Jenna Yager[8], Lillian B Brown[8], Morakane Makwela[9], Kenneth H Mayer[10,11]

[1]School of Medicine, Yale University, New Haven, CT, USA; [2]Philadelphia FIGHT Community Health Centers – Jonathan Lax Treatment Center, Philadelphia, PA, USA; [3]Universidade Federal de São Paulo, São Paulo, Brazil; [4]Complexo Hospitalar Universitário Professor Edgard Santos, Salvador, Brazil; [5]Hospital General de Agudos José María Ramos Mejía, Buenos Aires, Argentina; [6]Asociacion Civil Impacta Salud y Educacion, Lima, Peru; [7]The HIV Netherlands Australia Thailand Research Collaboration, Thai Red Cross AIDS Research Centre and Center of Excellence in Tuberculosis, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand; [8]Gilead Sciences, Inc., Foster City, CA, USA; [9]Setshaba Research Centre, Soshanguve, South Africa; [10]Harvard Medical School, Cambridge, MA, USA; [11]The Fenway Institute, Boston, MA, USA

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Presenter Disclosures

- Onyema Ogbuagu received active grants from NIAID and NIH Fogarty International Center; served on an advisory board for Gilead Sciences, Inc. and ViiV Healthcare; and is a member of the Department of Health and Human Services panel for HIV treatment guidelines for adults and adolescents
- Gilead Sciences, Inc. funded the study and designed the study with input from the PIs and G-CAGs. The PIs and study staff gathered data; Gilead Sciences, Inc. monitored conduct of the trial, received the data, and performed analyses
- Medical writing support was provided by Simon Wigfield, PhD (Aspire Scientific Ltd, UK), and was funded by Gilead Sciences, Inc.

G-CAG, Global Community Advisory Group; **NIAID**, National Institute of Allergy and Infectious Diseases; **NIH**, National Institutes of Health; **PI**, principal investigator.

PrEP Uptake, Adherence, and Persistence are Suboptimal Globally

In PURPOSE 2, twice-yearly SC LEN was safe and reduced HIV incidence by 96% compared with background incidence in cisgender men and gender-diverse individuals[1], communities that have historically struggled with adherence and persistence

Daily oral PrEP with consistent adherence is highly efficacious; however, **adherence can be challenging,** which directly **reduces effectiveness**[2,3]

An efficacious, **long-acting agent** could eliminate the need for daily oral adherence and increase persistence, thereby increasing PrEP effectiveness

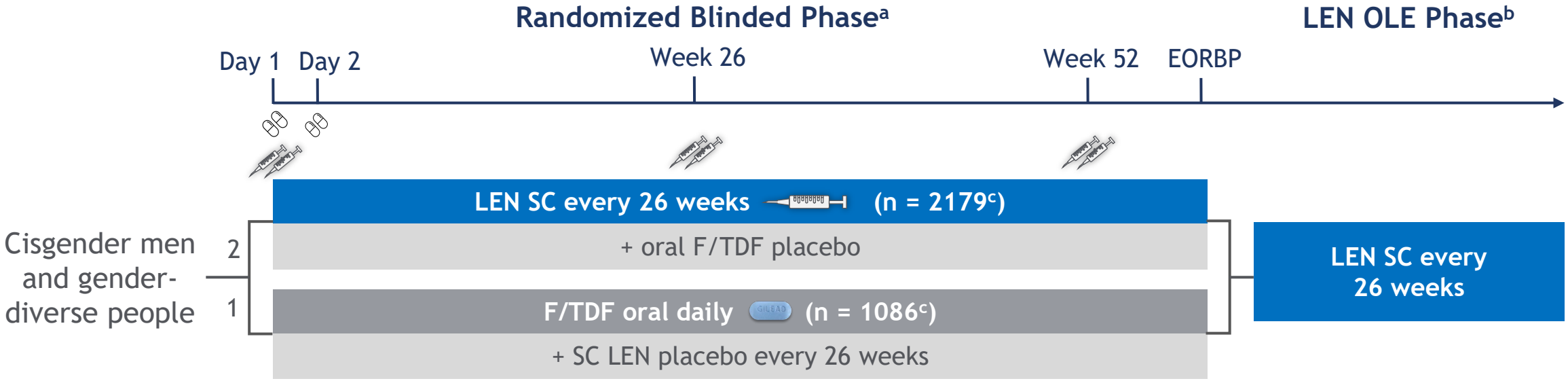
LEN is a **first-in-class**, multistage HIV-1 capsid inhibitor with **high potency** and a **long half-life**, supporting **twice-yearly SC injection**[4,5]

We performed a PURPOSE 2 subanalysis to characterize annual persistence, defined as consistent adherence over 1 year, to twice-yearly SC LEN and daily oral F/TDF

F/TDF, emtricitabine/tenofovir disoproxil fumarate; **LEN**, lenacapavir; **PrEP**, pre-exposure prophylaxis; **SC**, subcutaneous.

1. Kelley CF, et al. *N Engl J Med*. 2025;392:1261-76. **2.** Landovitz RJ, et al. *Clin Infect Dis*. 2024;79:1197-207. **3.** Marrazzo J, et al. *JAMA*. 2024;331:930-7.
4. Segal-Maurer S, et al. *N Engl J Med*. 2022;386:1793-803. **5.** Link JO, et al. *Nature*. 2020;584:614-8.

Participants in PURPOSE 2 were Randomized to Receive LEN or F/TDF



Study population: Cisgender men and gender-diverse people ≥ 16 years old who are at risk of HIV acquisition[d]

Present analysis objective

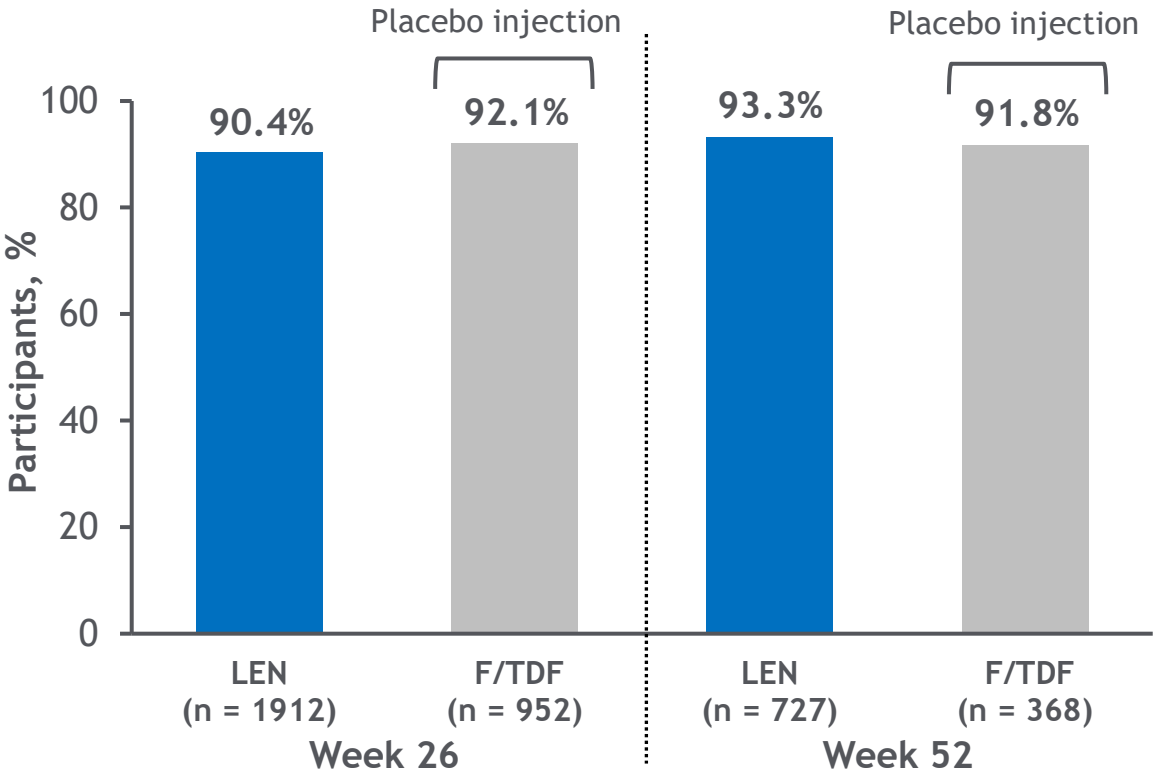
- To evaluate persistence, defined as sustained adherence over one year

ClinicalTrials.gov: NCT04925752

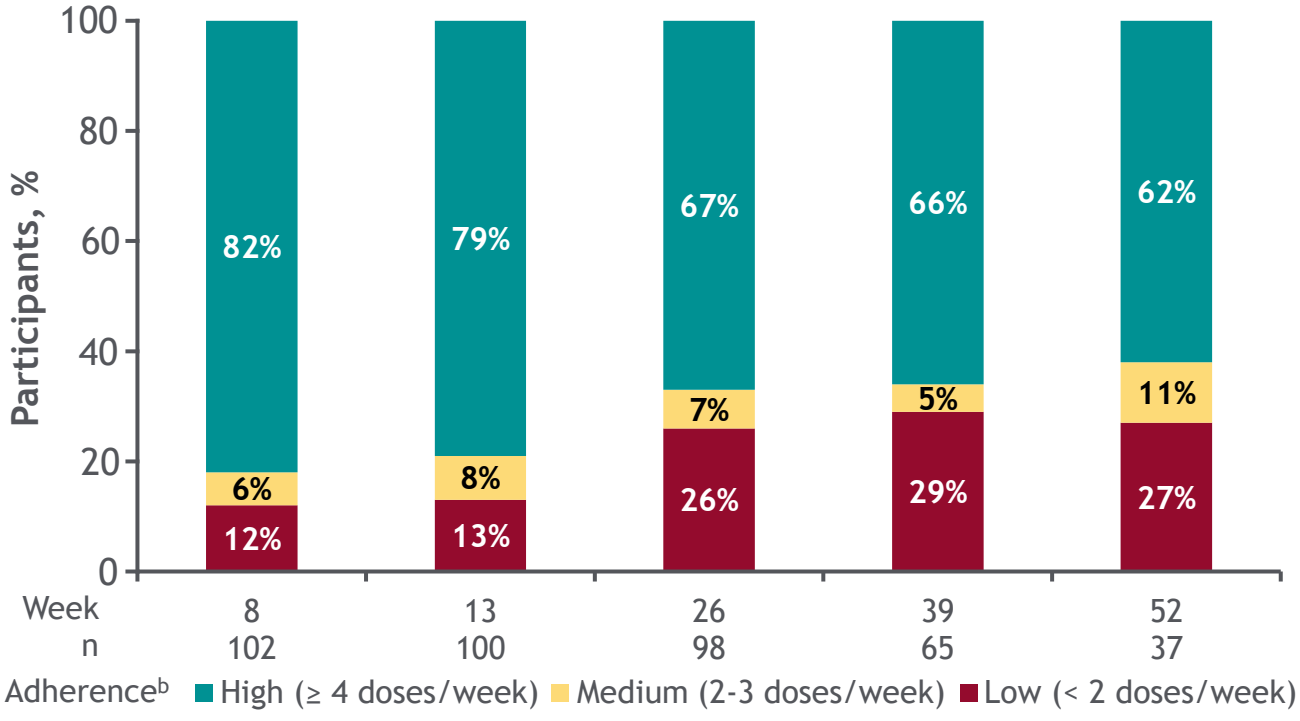
[a]Participants randomized to LEN received loading doses of two 300-mg tablets of LEN on each of Days 1 and 2 and SC LEN 927 mg on Day 1 and then every 26 weeks (± 7 days); participants randomized to F/TDF received matched placebos at these times. [b]Participants randomized to LEN in the RBP who chose to participate in the LEN OLE phase received SC LEN every 26 weeks (± 7 days) and had study visits every 13 weeks (± 7 days). Participants randomized to F/TDF in the RBP who chose to participate in the LEN OLE phase received SC LEN on LEN OLE Day 1 and every 26 weeks thereafter; these participants also received an oral LEN loading dose on LEN OLE Days 1 and 2 and had study visits at LEN OLE Day 1, Weeks 4 and 8 (± 2 days), Week 13 (± 7 days), and then every 13 weeks (± 7 days) thereafter. [c]Included in the full analysis set for primary efficacy analyses (additional participants are included in the safety analysis). [d]Cisgender men, transgender women and men, and non-binary people aged ≥ 16 years who have condomless receptive anal sex with partners assigned male at birth.
EORBP, end of randomized blinded phase; **F/TDF**, emtricitabine/tenofovir disoproxil fumarate; **LEN**, lenacapavir; **OLE**, open-label extension; **RBP**, randomized blinded phase; **SC**, subcutaneous.

Adherence to Injections was High

Injection Adherence (Study Population)[a]



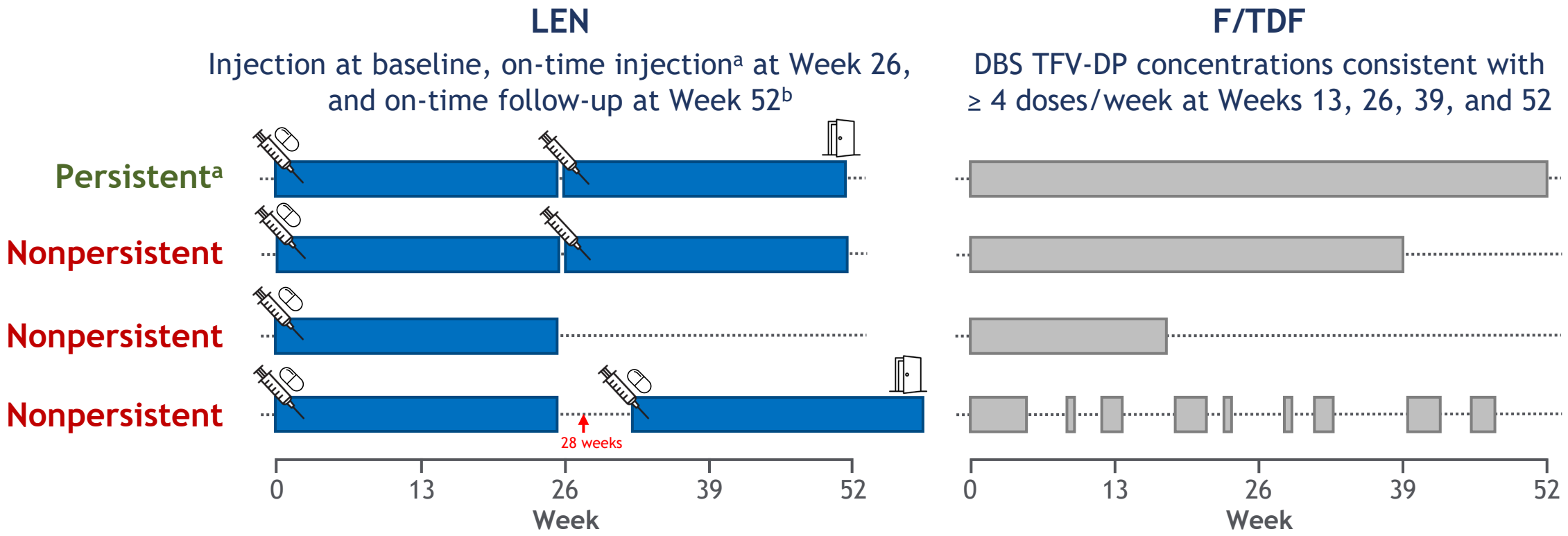
Adherence by TFV-DP Concentrations in 10% Cohort (F/TDF)



On-time adherence to injections was high
Most participants initially had a high adherence to daily oral F/TDF; however, adherence declined over time[1]

Adherence to LEN was defined as on-time injection (≤ 28 weeks after the last injection) at Weeks 26 or 52. Adherence to F/TDF was assessed using intracellular TFV-DP levels in DBS at Weeks 8, 13, 26, 39, or 52. [a]Participants on LEN who presented later than 28 weeks required negative HIV testing to reinitiate study product, which included reloading with oral LEN or placebo. [b]A randomly preselected 10% sample of participants were assessed for TFV-DP concentrations in DBS (adherence cutoffs for F/TDF: low < 350, medium ≥ 350 to < 700, high ≥ 700 fmol/punch). **DBS**, dried blood spot; **F/TDF**, emtricitabine/tenofovir disoproxil fumarate; **LEN**, lenacapavir; **TFV-DP**, tenofovir diphosphate. **1.** Kelley CF, et al. *N Engl J Med*. 2025;392:1261-76.

Defining Annual Persistence to PrEP:
Combined Assessment of Adherence and Continuation Over 1 Year



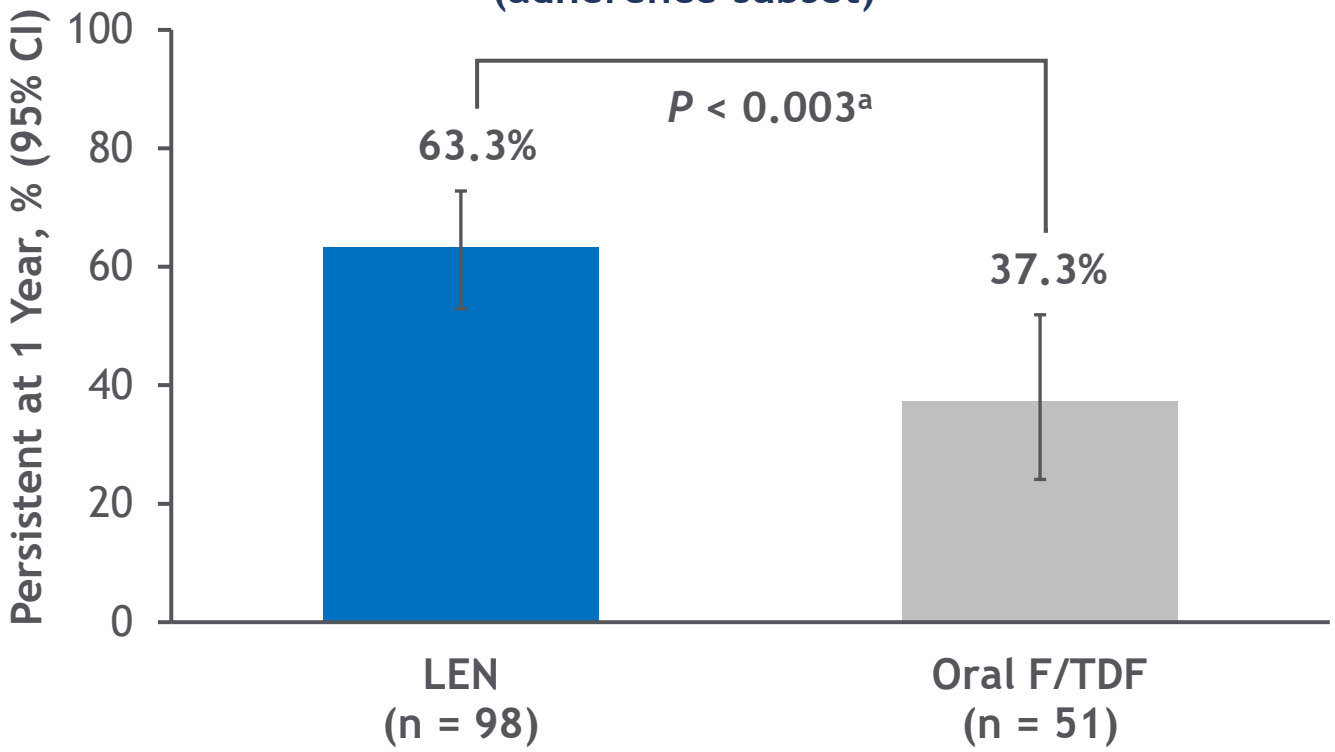
Annual persistence was characterized in a random, preselected 10% sample of participants (limited to those who had ≥ 1 year of study follow-up at the time of the primary analysis)

Nonpersistence to PrEP included participants who discontinued study drug for any reason. [a]On-time injection at Week 26 and on-time follow-up visit at Week 52 was defined as within 28 weeks after the last injection. The proportion of participants with persistence through Week 52 was reported for each study group with 2-sided 95% exact CIs based on the Clopper-Pearson method. [b]A ± 2-week window was permitted for the Week 26 LEN injection and follow-up at Week 52.

CI, confidence interval; **DBS**, dried blood spot; **F/TDF**, emtricitabine/tenofovir disoproxil fumarate; **LEN**, lenacapavir; **PrEP**, pre-exposure prophylaxis; **TFV-DP**, tenofovir disphosphate.

Higher Annual Persistence on Twice-Yearly LEN Versus Daily Oral F/TDF

Annual persistence in the randomly preselected 10% sample of participants (adherence subset)



Non-persistence

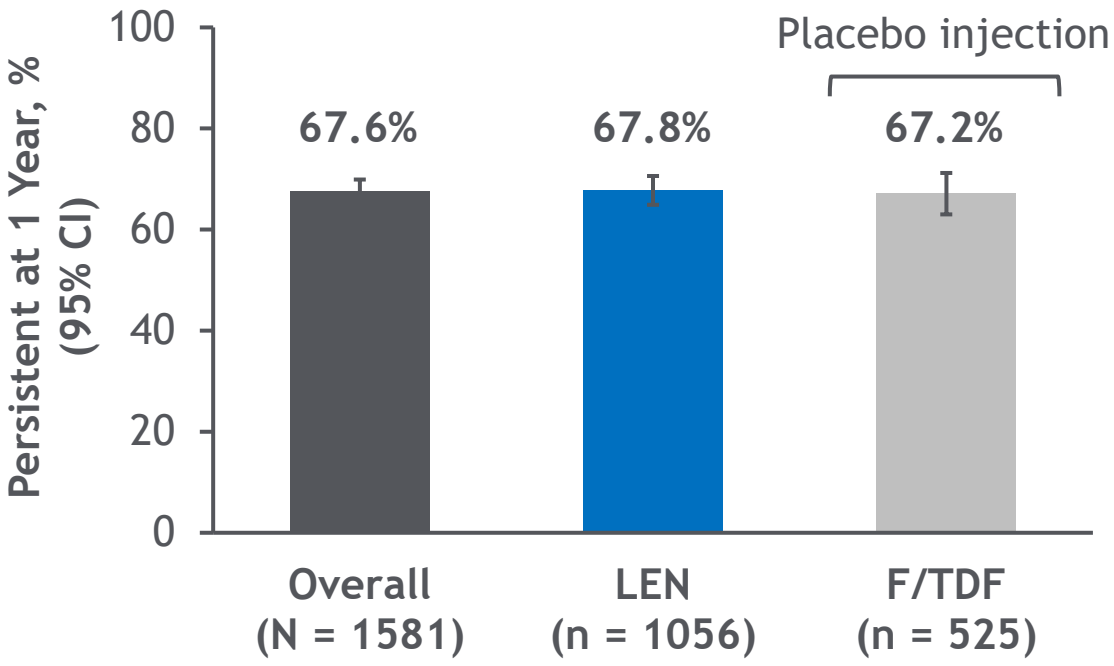
- Of the 36 **LEN participants** who were nonpersistent:
  - 21 were due to missed Week 26 injection
  - 14 were due to not having an on-time Week 52 visit
    - 5 were due to data entry delay[b]
  - 1 was due to late Week 26 injection
- Of the 32 **F/TDF participants** who were nonpersistent:
  - 18 had ≥ 1 missing DBS samples
  - 14 ≥ 1 DBS concentrations consistent with < 2 doses/week on average over the preceding 8-12 weeks

Annual persistence was significantly higher on twice-yearly LEN than on daily oral F/TDF, which helps elucidate the LEN efficacy findings in PURPOSE 2

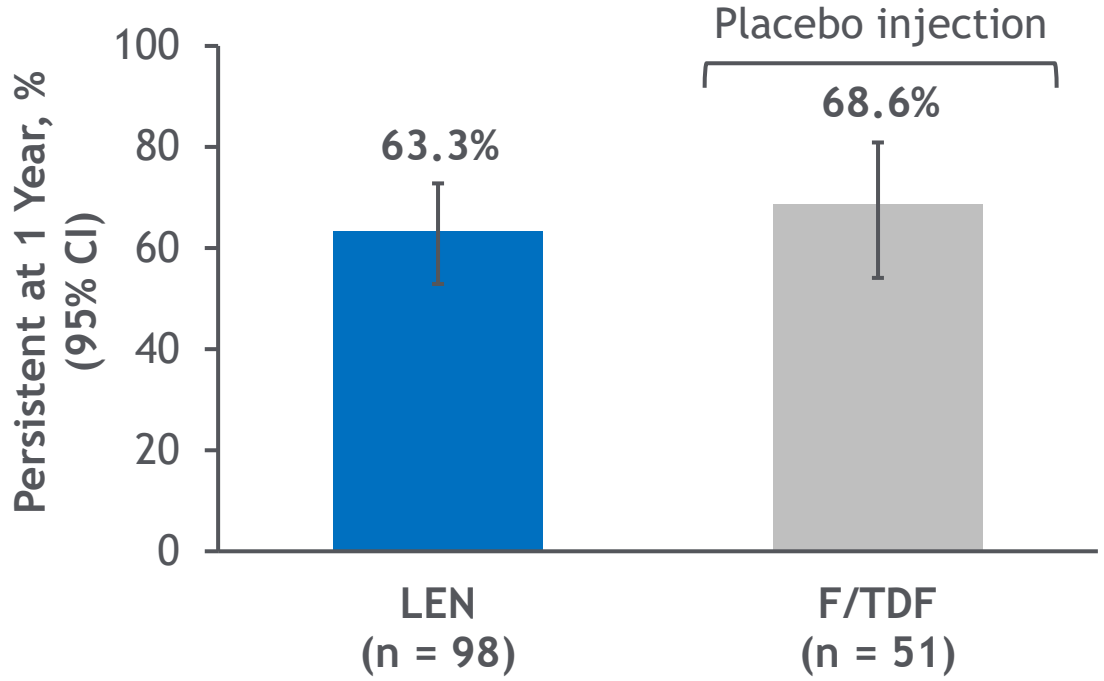
[a]*P* value was calculated based on Fisher's exact test.[b]5 participants were deemed nonpersistent due to data entry delay at the time of primary analysis but had on-time Week 52 visits.
CI, confidence interval; **DBS**, dried blood spot; **F/TDF**, emtricitabine/tenofovir disoproxil fumarate; **LEN**, lenacapavir.

Annual Persistence was Similar Between LEN Injections and Placebo Injections

Annual persistence to SC injection (whole study population)



Annual persistence to SC injection (adherence subset: randomly preselected 10% sample of participants)



Annual persistence on LEN injections was similar to persistence on placebo injections in the F/TDF group

CI, confidence interval; **F/TDF**, emtricitabine/tenofovir disoproxil fumarate; **LEN**, lenacapavir; **SC**, subcutaneous.

Conclusions

- We observed significantly higher annual persistence with twice-yearly SC LEN vs daily oral F/TDF, utilizing a conservative definition of persistence that accounts for adherence and continuation. This supports the superior efficacy of LEN vs F/TDF in PURPOSE 2
  - Similar findings were observed in the PURPOSE 1 study among cisgender adolescent girls and young women[1]
- Future studies should assess longer-term persistence to PrEP

The greater persistence on twice-yearly SC LEN vs daily oral F/TDF supports the potential for LEN to have a greater public health impact than that of daily oral PrEP

F/TDF, emtricitabine/tenofovir disoproxil fumarate; **LEN**, lenacapavir; **PrEP**, pre-exposure prophylaxis; **SC**, subcutaneous.

1. Bekker L-G, et al. Oral presented at: HIV Glasgow; November 10–13, 2024; Glasgow, UK.

Acknowledgments

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PURPOSE 2 Study Team

Maribel Acevedo-Quiñones, Allison L Agwu, Suvaporn Anugulruengkitt, Anchalee Avihingsanon, Joanne Batting, Jose A Bazan, Paul Benson, Vladimir Berthaud, Jill Blumenthal, Indira Brar, Cynthia Brinson, Carlos Roberto Brites Alves, Pedro Cahn, Thomas B Campbell IV, Valeria D Cantos, Michelle Cespedes, Ploenchan Chetchotisakd, Jesse Clark, Meredith Clement, Katya Corado, Gonzalo Corral, Catherine Creticos, Gordon Crofoot, Edwin DeJesus, Ricardo S Diaz, Craig Dietz, Susanne Doblecki-Lewis, David F Dougherty, Ian Frank, James W Galbraith, Jorge Antonio, Gallardo Cartagena, Aditya Gaur, Beatriz Gilda Jegerhorn Grinsztejn, Marcus Guimaraes De Lacerda, Michael Guyton-Nunley, Shawn Hassler, Christine Heumann, Juan Carlos Hinojosa Boyer, Theo Hodge, Moises A Huaman, Richard Kaplan, Colleen F Kelley, Sasisopin Kiertiburanakul, Javier R Lama Valdivia, Anthony LaMarca, Marcelo Losso, Christopher Lucasti, Morakane Alicia Caroline Makwela, Weerawat Manosuthi, Kenneth H Mayer, Eric G Meissner, Ivan Melendez-Rivera, Anthony Mills, Kathryn Mngadi, Caryn G Morse, Karam Mounzer, Nkosiphile Ndlovu, Richard M Novak, Onyema Ogbuagu, Alma Minerva Perez Rios, Nittaya Phanuphak, Jose Henrique Pilotto, Jorge Pinto, Jose Valdez Ramalho Madruga, Moti Ramgopal, Jeffrey Reeves, Lina Rosengren-Hovee, Peter J Ruane, Kamla Sanasi-Bhola, Breno Santos, Tanya Schreibman, Hyman Scott, Namrata Shah, Peter Shalit, Jihad Slim, LaShonda Spencer, Khuanchai Supparatpinyo, Javier Valencia, Cornelius N Van Dam, Olivia T Van Gerwen, Ricardo Vasconcelos, Jose Gabriel Vasquez Cerro, Jennifer Veltman, Robert Woolard, Kimberly Workowski, Ashraf Zadshir, Zwelethu Zwane

QR Code

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The same approach to evaluate annual persistence of LEN for PrEP vs daily oral F/TDF is being used in PURPOSE 5 in France and the UK

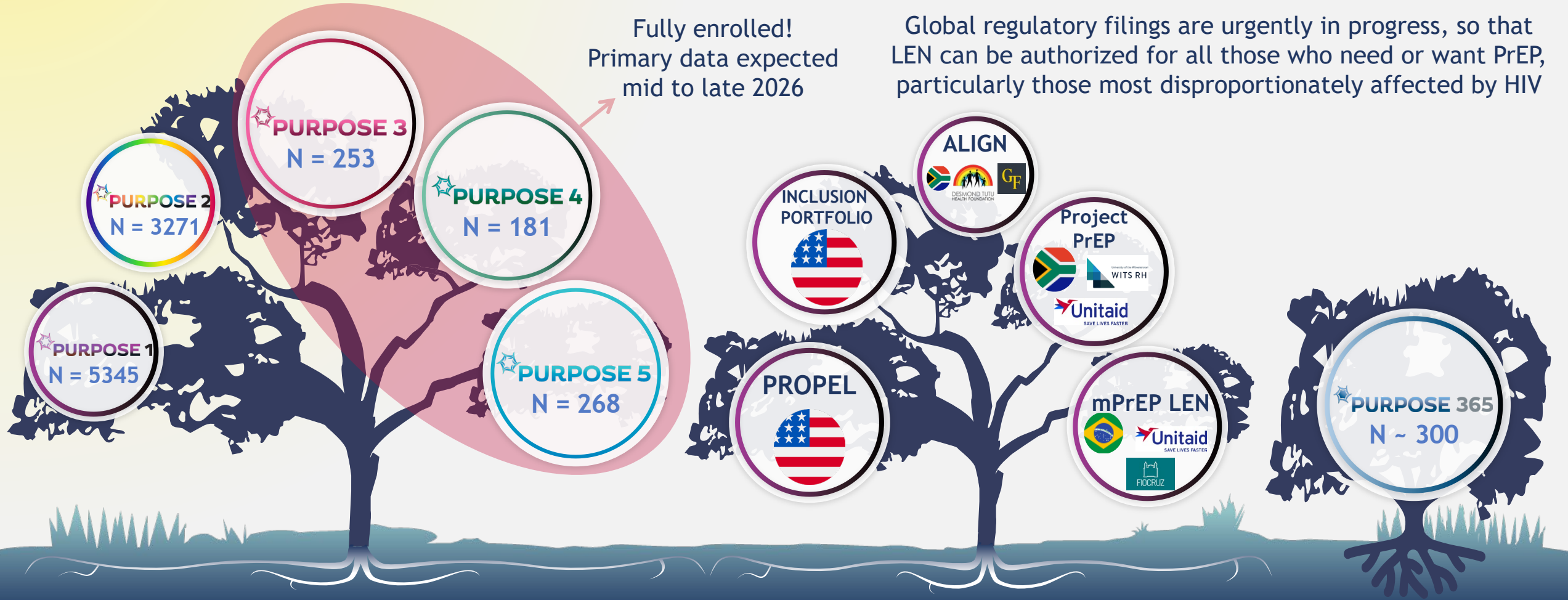
EACS Oral PS08.5: Recruitment of Disproportionately Affected Populations in the PURPOSE 5 Study Evaluating Lenacapavir for PrEP in France and the UK (Jean-Michel Molina)

SCAN ME

A Growing PURPOSE Portfolio

Fully enrolled!
Primary data expected
mid to late 2026

Global regulatory filings are urgently in progress, so that LEN can be authorized for all those who need or want PrEP, particularly those most disproportionately affected by HIV



#preventionwithpurpose

#accesswithpurpose

PURPOSE 1: NCT04994509; PURPOSE 2: NCT04925752; PURPOSE 3: NCT06101329; PURPOSE 4: NCT06101342; PURPOSE 5: NCT06513312; PURPOSE 365: NCT07047716.
LEN, lenacapavir; **PrEP**, pre-exposure prophylaxis.

PURPOSE studies. https://www.purposestudies.com (accessed August 15, 2025).