PURPOSE
Prevention with PURPOSE

IAS 2025

# Preference for Twice-Yearly Injections vs Daily Oral Pills for HIV PrEP in Cisgender Men, Transgender Women, Transgender Men, and Gender Nonbinary People Enrolled in PURPOSE 2

Kathryn Mngadi[1], Nittaya Phanuphak[2], Juan Carlos Hinojosa[3], Karam Mounzer[4], Ricardo Vasconcelos[5], Moti Ramgopal[6], Pamela Wong[7], Lillian B Brown[7], Dylan Mezzio[7], Christoph C Carter[7], Namrata Shah[8]

[1]The Aurum Institute, Clinical Research Tembisa, Tembisa, South Africa; [2]Institute of HIV Research and Innovation—Pribta Tangerine Clinic, Bangkok, Thailand; [3]Asociación Civil Selva Amazónica, Iquitos, Peru; [4]Philadelphia FIGHT Community Health Centers—Jonathan Lax Treatment Center, Philadelphia, PA, USA; [5]Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil; [6]Midway Immunology and Research Center, Fort Pierce, FL, USA; [7]Gilead Sciences, Inc., Foster City, CA, USA; [8]Whitman-Walker Health, Washington, DC, USA

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# Acknowledgments and Presenter Disclosures


## Acknowledgments

I want to begin my talk by extending my deepest gratitude to the PURPOSE trial participants who have shared their time, experiences, and bodies for the purposes of this research, and their families and communities, the global community advisory and accountability groups, the site staff and investigators, and the members of the PURPOSE study teams. Much of the fight against HIV and AIDS relies upon people living with HIV and people who want to need PrEP continuing to put themselves forward and this research and our fight against HIV and AIDS is indebted to those past and present.


## Disclosures

- Kathryn Mngadi received funding for protocol conduct and attendance at IAS 2025 from Gilead Sciences, Inc.
- Gilead Sciences, Inc., funded the study and designed the study with input from the PIs and G-CAG. The PIs and study staff gathered data; Gilead Sciences, Inc., monitored conduct of the trial, received the data, and performed analyses. The PURPOSE 2 Study Team all vouch for the data and analysis
- Medical writing support was provided by Aimee Sherlock, MSc (Aspire Scientific Ltd, UK), and was funded by Gilead Sciences, Inc




G-CAG, Global Community Advisory Group; PI, principal investigator; PrEP, pre-exposure prophylaxis.

# Summary

## What is your main question?

What were the PrEP administration preferences of PURPOSE 2 participants (twice-yearly injections vs daily oral pills) and how did different methods of administration impact their feelings about HIV risk and PrEP adherence?

## What did you find?

Most participants preferred twice-yearly injectable PrEP and reported greater confidence in their ability to remain adherent and that they would feel more protected from HIV if PrEP were administered as twice-yearly injections versus as daily pills

## Why is it important?

Understanding PrEP administration preferences may help inform discussions with individuals about PrEP options, as well as influencing clinical practice and public health policy

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PrEP, pre-exposure prophylaxis.

# PrEP Adherence in Disproportionately Affected Populations is Suboptimal

Daily oral PrEP is efficacious for HIV prevention; however, consistent adherence is a predictor of effectiveness and remains suboptimal in many populations who are disproportionately affected by HIV incidence[1-9]

New PrEP modalities that meet the needs, routines, and preferences of more individuals are needed

LEN for PrEP is a first-in-class, multistage HIV-1 capsid inhibitor with high potency and a long half-life, supporting twice-yearly SC injection[10,11]

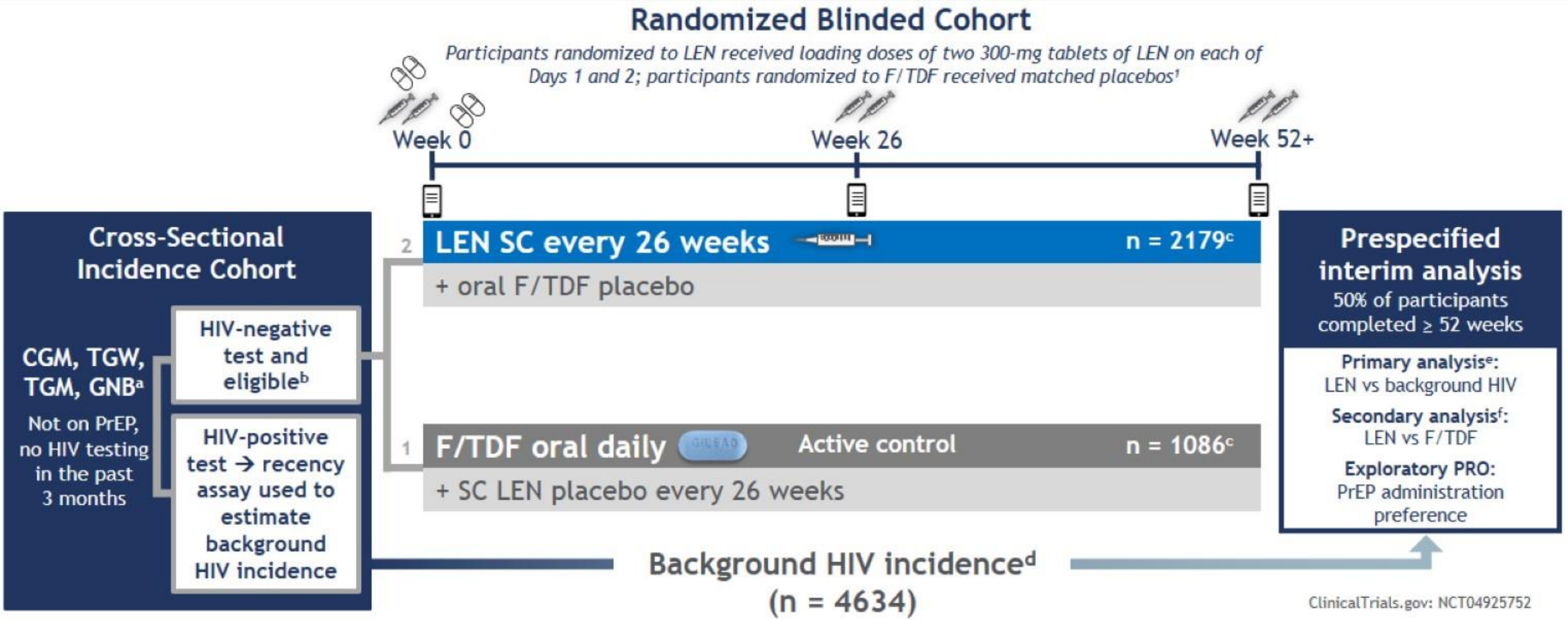
In the Phase 3 PURPOSE 2 trial (NCT04925752), twice-yearly SC LEN lowered HIV incidence by 96% compared with background incidence and by 89% compared with daily oral F/TDF in cisgender men, transgender women, transgender men, and gender nonbinary people who have sex with partners assigned male at birth[12]

**We examined the PrEP administration preferences of PURPOSE 2 participants and how different methods of administration may affect their feelings about HIV risk and PrEP adherence**

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

1. Klein H, Washington TA. *J Gay Lesbian Soc Serv*. 2020;32:99-114. 2. Baral SD, et al. *Lancet Infect Dis*. 2013;13:214-22. 3. Kanny D, et al. *MMWR Morb Mortal Wkly Rep*. 2019;68:801-6. 4. Poteat T, et al. *J Acquir Immune Defic Syndr*. 2016;72(suppl. 3):S210-9. 5. Torres TS, et al. *Lancet Reg Health Am*. 2023;28:100642. 6. CDC. https://stacks.cdc.gov/view/cdc/156513 (accessed October 24, 2024). 7. Babel RA, et al. *AIDS Behav*. 2021;25:3574-604. 8. Wang Y, et al. *AIDS Res Ther*. 2022;19:28. 9. O Murchu E, et al. *BMJ Open*. 2022;12:e048478. 10. Segal-Maurer S, et al. *N Engl J Med*. 2022;386:1793-803. 11. Link JO, et al. *Nature*. 2020;584:614-8. 12. Kelley CF, et al. *N Engl J Med*. 2025;392:1261-76.

# Participants Reported PrEP Administration Preferences at Day 1, Week 26, and Week 52 in PURPOSE 2




On Days 1 and 2, all participants received a pharmacologic loading dose of 600 mg oral LEN or matched oral placebo. [a]The first participant was screened in June 2021, the 50th-percentile participant was randomized in August 2023, and the last participant was randomized in December 2023. [b]Eligibility criteria included: age ≥ 16 years, bodyweight ≥ 35 kg, eGFR ≥ 60 mL/min, not pregnant. [c]n numbers represent the full analysis set for efficacy analyses. [d]Background HIV incidence is the incidence expected without PrEP that would have been expected in a placebo group (the counterfactual HIV incidence).[1,2] [e]IRR was assessed using a Wald test.[1,2] [f]IRR was assessed using Poisson regression. CGM, cisgender men; eGFR, estimated glomerular filtration rate; F/TAF, bictegravir/emtricitabine/tenofovir alafenamide; F/TDF, emtricitabine/tenofovir disoproxil fumarate; GNB, gender nonbinary person; IRR, incidence rate ratio; LEN, lenacapavir; PrEP, pre-exposure prophylaxis; PRO, patient-reported outcome; SC, subcutaneous; TGM, transgender man; TGW, transgender woman.

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

# Participants Reported Strength of and Reasons for Preferences

**If I could take just one kind of PrEP medication, knowing they both worked equally well, I would prefer to take PrEP medication:**

| | | |
|---|---|---|
| By injection every 6 months | I have no preference one way or the other | By a daily pill |

**I would rate my preference for the PrEP medication I prefer as[a]:**

| | | |
|---|---|---|
| Slight preference | Moderate preference | Strong preference |

**In a few words, explain the reason for your preference (or why you have no preference):**

_____(short-text-length, open-ended response)

**Thinking about the future, I would expect to be more able to take my PrEP medication without missing a dose if I received the medication:**

| | | |
|---|---|---|
| By injection every 6 months | No difference; either by injection every 6 months or by a daily pill | By a daily pill |

**Thinking about the future, I would expect to feel more protected from HIV if my PrEP medication was given to me:**

| | | |
|---|---|---|
| By injection every 6 months | No difference; either by injection every 6 months or by a daily pill | By a daily pill |

During baseline (after injection), Week 26, and Week 52 injection visits,[b] participants completed an electronic questionnaire about:

- PrEP administration preference
- How administration type impacts HIV risk perception and expected PrEP adherence

Responses were submitted privately (except for participants who required assistance to complete the questionnaires)

Results were pooled across the treatment arms and categorical responses were analyzed descriptively

The questionnaire was translated into the study languages. Participants marked one response option per multiple-choice question. [a]Participants who reported no preference for PrEP administration type did not answer this question. [b]Data may not be available for all participants at all timepoints—eg, ~50% could not reach Week 52 due to the timing of the analysis.



PrEP, pre-exposure prophylaxis; PRO, patient-reported outcome.

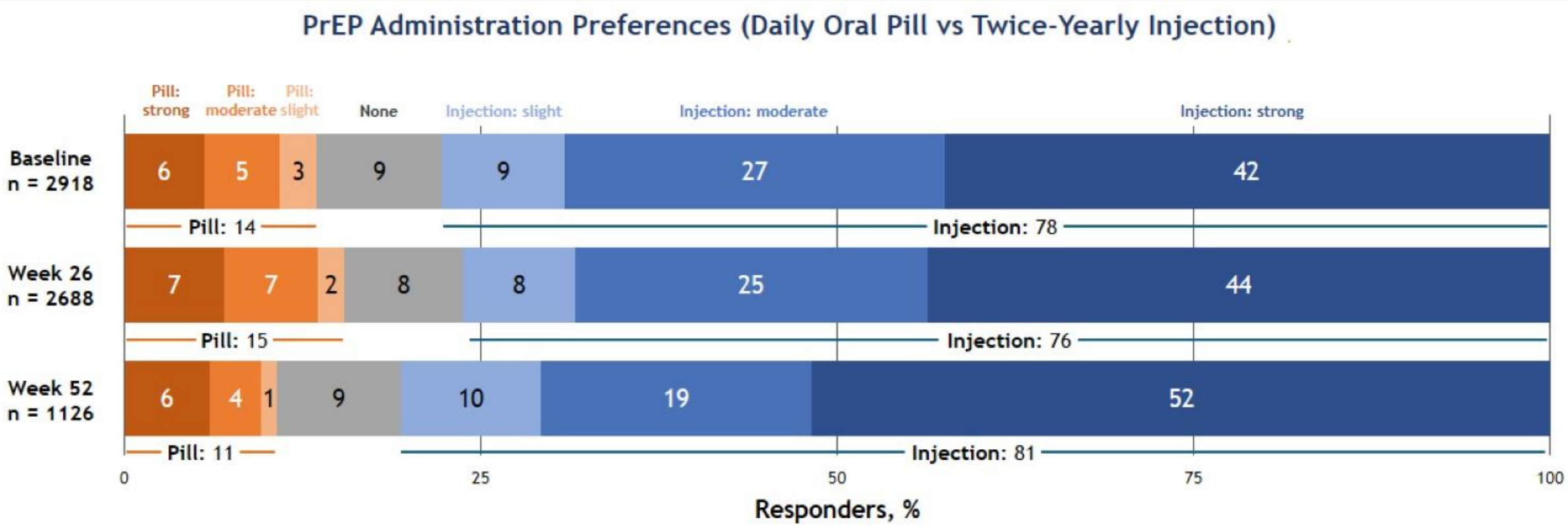
# The Majority of Participants that Attended Each Study Visit Completed a Questionnaire

- **3271 participants were randomized and dosed**
- 2918 completed the questionnaire at baseline
- 2688 completed the questionnaire at Week 26[a]
- 1126 completed the questionnaire at Week 52[a,b]



[a]At the time of primary analysis. [b]The number of participants who completed the questionnaire at Week 52 was lower due to the early stopping of the randomized blinded phase of the study.

# More than Three-Quarters of Participants Preferred Twice-Yearly Injections

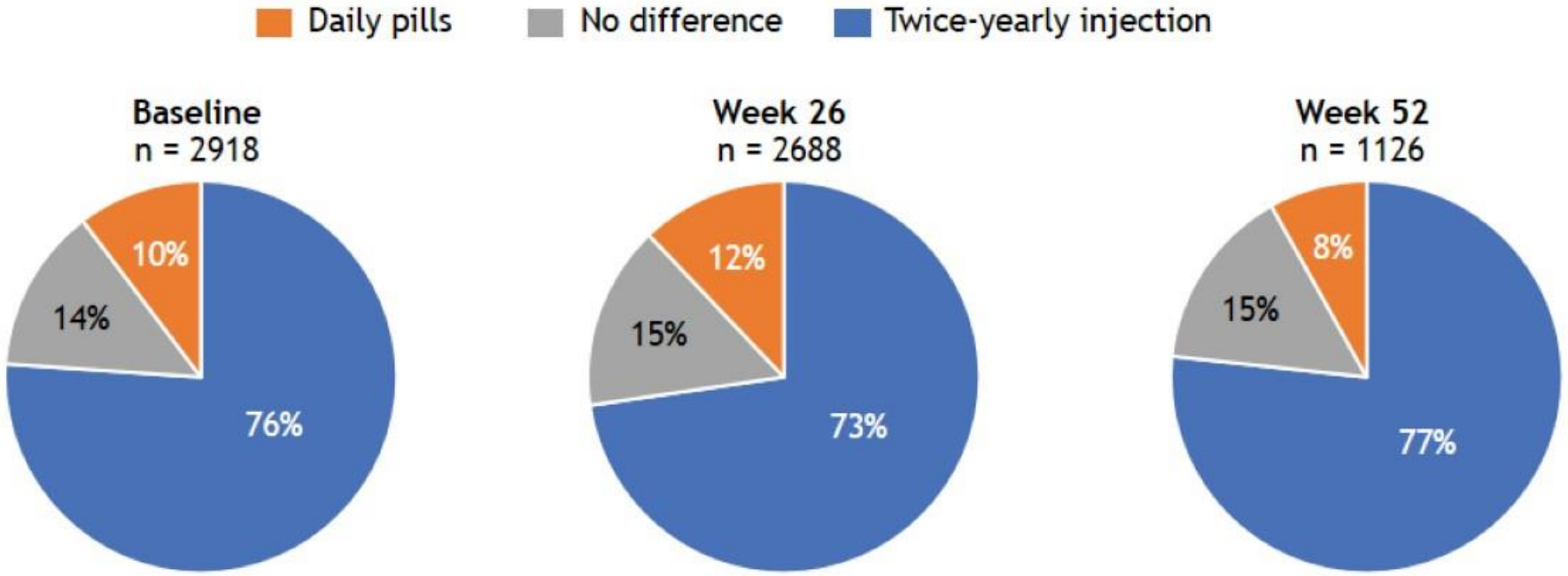



**Among those with a preference for either injection or daily pills, approximately half reported their preference as "strong"; most participants maintained their baseline preference for twice-yearly LEN through Week 52**

The population presented is based on all observed non-missing responses at each visit. Question: If I could take just one kind of PrEP medication, knowing they both worked equally well, I would prefer to take PrEP medication: 1) by injection every 6 months; 2) I have no preference one way or the other; 3) by a daily pill. Follow-up question for participants who reported a preference for pills or injections: I would rate my preference for the PrEP medication I prefer as: 1) slight preference; 2) moderate preference; 3) strong preference. Percentages may not sum to 100%, or align, due to rounding. LEN, lenacapavir; PrEP, pre-exposure prophylaxis.

# Participants Perceived High Future Adherence with Twice-Yearly Injections

"Thinking about the future, I would expect to be more able to take my PrEP medication without missing a dose if I received the medication by:"

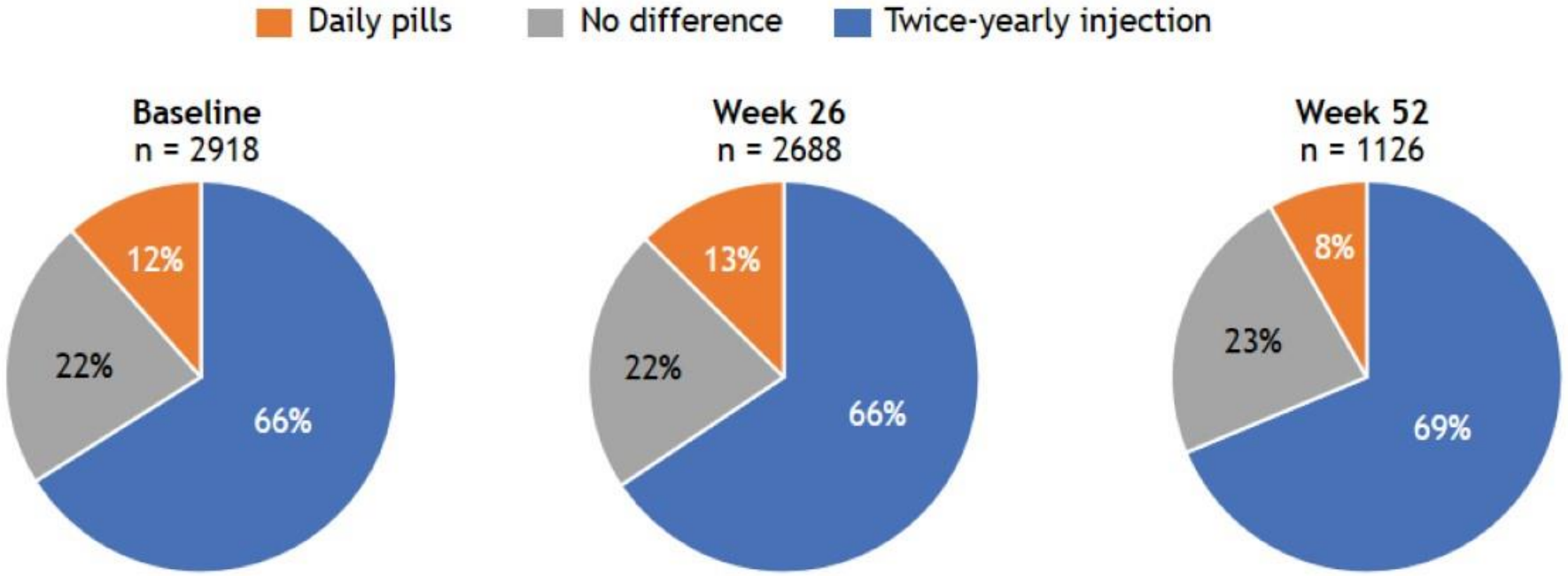



**Most participants felt that their future PrEP adherence would be better with twice-yearly injections versus daily pills**

The population presented is based on all observed non-missing responses at each visit.
PrEP, pre-exposure prophylaxis.

# Participants Perceived High Protection with Twice-Yearly Injections

"Thinking about the future, I would expect to feel more protected from HIV if my PrEP medication was given to me by:"



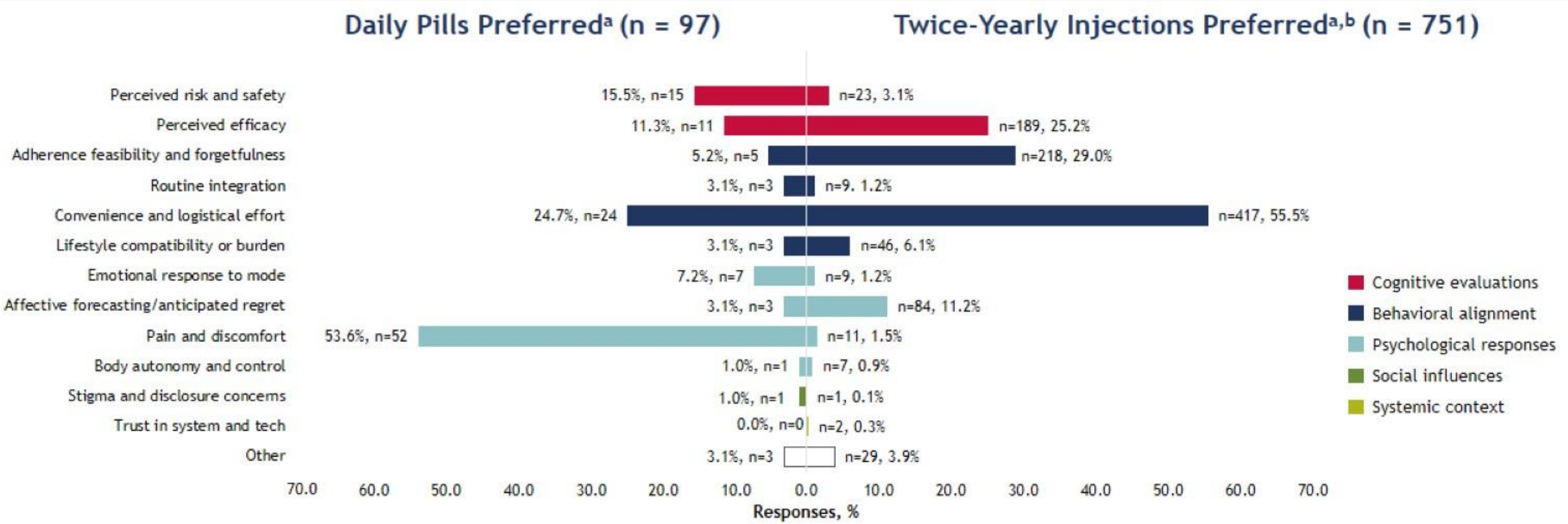

**Most participants reported that they would feel more protected from HIV with twice-yearly injections versus daily pills**

The population presented is based on all observed non-missing responses at each visit.



PrEP, pre-exposure prophylaxis.

# Perceived Efficacy, Adherence, and Convenience Motivated Preferences for Twice-Yearly Injections




**Those who favored twice-yearly injections (78%) were motivated by perceived efficacy, adherence, and convenience; participants who preferred daily pills (11%) emphasized pain and discomfort**

The nested topic structure indicated in the figure legend was predefined and reasons for preferences mapped onto this structure. Reasons shown are only those with > 0 responses. Nested topics included Cognitive Evaluations (perceived risk and safety, perceived efficacy), Behavioral Alignment (adherence feasibility and forgetfulness, routine integration, convenience and logistical effort, lifestyle compatibility or burden), Psychological Responses (emotional response to mode, affective forecasting/anticipated regret, pain and discomfort, body autonomy and control), Social Influences (social norm, partner attitude, stigma and disclosure concerns, social support), Systemic Context (trust in system and tech), Cultural Context (cultural beliefs about medication, cultural acceptance, and symbolism) and Other. [a]Responses could be included in more than one category. [b]Participants with no preference or responses that were nonsensical, vague, or unable to be translated (eg, Thai), or did not provide a reason were excluded (n=273). Free-text question: "In a few words, explain the reason for your preference (or why you have no preference)." Tech, technology.

# Conclusions

- In the most diverse Phase 3 PrEP study to date,[1] the majority of participants reported a preference for twice-yearly injectable PrEP; this preference was maintained among participants with the potential to be followed up until Week 52
- Preferences for PrEP modality were multifactorial
- Understanding preferences may help inform discussions with individuals about PrEP options
- These quantitative results are a part of a wider mixed-methods approach to understanding the participant voice in the PURPOSE program
- Twice-yearly SC LEN could increase the uptake of, adherence to, and persistence on PrEP

LEN, lenacapavir; PrEP, pre-exposure prophylaxis; SC, subcutaneous.



1. Kelley CF, et al. *N Engl J Med*. 2025;392:1261-76.

# Acknowledgments

**We extend our gratitude to the PURPOSE trial participants and their communities, our Global Community Advisory and Accountability Groups, the site staff and investigators, and all the members of the PURPOSE study teams**

## PURPOSE 2 Study Team

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# Accelerating Access for Global HIV Prevention

| Expansive licensing | Rapid technology transfer | Simultaneous submissions |
|---|---|---|
| Earliest and geographically broadest (120 countries) voluntary licensing strategy ever for an antiretroviral | Agreements with 6 generics & full technology transfer within 3 months; Global Fund 2 million people for 3 years | US Approval June 2025 EU, EUM4All, South Africa, Brazil, Canada, Australia, Switzerland & more coming |
| **Expediting Regulatory Review** | **WHO endorsement** | **Manufacturing readiness** |
| EU-M4all application enables faster reviews in low- and middle-income countries | Guidelines released July 14, 2025 & prequalification later this year will facilitate global adoption | Gilead-supplied no-profit product & partnership agreements, bridging to sustainable generic supply |

**Collaborative implementation science studies to inform sustainable access, eg South Africa (Project PrEP, UNITAID/Wits RHI; ALIGN, Gates Foundation/Desmond Tutu Health Foundation) and Brazil (ImPrEP, IUNITAID/Fiocruz)**