INCLUSION
(ImplemeNtation of twiCe-yearly Lenacapavir to address Unmet needS in HIV preventION)
U.S. 2025 Request for Proposals

Through the Medical Affairs Phase 4 Investigator-Sponsored Research (ISR) and Collaborative Programs, Gilead supports the research efforts of academic institutions, clinical investigators, community-based organizations, and research networks. Gilead supports these research efforts based on the need addressed by the proposed scientific question, validity of study methodology, timing of when results will fill a data gap of interest, and lack of redundancy with previous studies/data conclusions already available. Letters of intent (LOIs) will be used to determine who will be invited to submit a full application.

The HIV epidemic remains an important public health priority, with 1.1 million Americans currently living with HIV and many more at risk of acquiring HIV.[1] While new diagnoses have declined significantly, without intervention nearly 400,000 more Americans will be newly diagnosed over 10 years despite the availability of HIV prevention options to prevent transmission. There is a real risk of an HIV resurgence due to several factors, including the lack of awareness of the public health threat that HIV poses, trends in drug use, HIV-related stigma, homophobia and transphobia, and lack of access to HIV prevention, testing, and treatment. There are proven models of effective HIV care and prevention which are based on decades of experience engaging and retaining people in effective care and pre-exposure prophylaxis (PrEP) reducing the risk of HIV acquisition from sex by up to 99% when taken as prescribed.[1]

Despite the availability of multiple PrEP options, uptake and persistence remain low in many geographical areas and among populations most in need. Per the CDC, only 36% of the 1.2 million individuals with an indication were prescribed PrEP in 2022, far short of the 50% goal by 2025.[2] PrEP use is low among populations disproportionately affected by HIV; including: Black/Latine men who have sex with men (MSM), Black cisgender women, transgender individuals, and those living in the US South.[2] Programs that deliver PrEP in convenient ways (ex. telePrEP, same-day PrEP, injectable PrEP, and pharmacy-based PrEP) and increasing the number of clinicians who offer HIV prevention services are key strategies to prevent HIV transmission.[3] Additional PrEP options could also help to address unmet needs and improve PrEP uptake, adherence, and persistence in those who need or want PrEP.

Lenacapavir is a twice-yearly injectable HIV-1 capsid inhibitor currently approved, in combination with other antiretrovirals(s), for the treatment of HIV-1 infection in heavily treatment-experienced adults with multidrug resistant HIV-1 infection failing their current antiretroviral regimen due to resistance, intolerance, or safety considerations.[4] If proven safe and effective and approved by the FDA, twice-yearly lenacapavir has the potential to help fill these unmet individual, societal, and public health needs to end the HIV epidemic. The efficacy and safety of lenacapavir for PrEP was evaluated in cisgender adolescent girls and young women in the PURPOSE 1 trial[5] and in cisgender men, transgender women, transgender men, and gender nonbinary people ≥ 16 years of age who have sex with male partners in the PURPOSE 2 trial.[6] If lenacapavir is approved by the FDA to prevent HIV, different strategies would be required to test, implement, and compare this twice-yearly injectable option. This is especially true in the context of alternative delivery settings and reaching more providers, both of which are key strategies that the CDC has identified to prevent HIV transmission and end the HIV epidemic in the US.[2]

With INCLUSION U.S., the 2025 RFP program, Gilead will evaluate and potentially support research proposals that address the following open research questions:

1. Delayed PrEP initiation is associated with increased HIV acquisition.[7] Can lenacapavir for HIV prevention be used as a potential modality for same day/rapid PrEP initiation in appropriate individuals, including use of oral PrEP for bridging prior to first injection?
2. What is the RW effectiveness of lenacapavir for HIV prevention including persistence, adherence, satisfaction, QOL, and safety (including ISRs)?
3. What is the comparative effectiveness of lenacapavir for HIV prevention vs currently available PrEP options on adherence, persistence, reported satisfaction, HCRU/clinic burden, and costs?
4. Evaluate implementation outcomes (e.g., feasibility, acceptability, adherence, persistence) of new clinical tools, resources, and strategies using lenacapavir for HIV prevention in appropriate individuals,

within the following settings:
    - Clinics currently offering PrEP
    - Routine healthcare (ex. primary care, family planning, etc…)
    - In non-clinical settings (ex. Drop in centers)
5. How does the real world use of lenacapavir for HIV prevention impact experiences, perceptions, preferences, and satisfaction with PrEP modalities, including willingness to initiate PrEP and stay on PrEP, for those who need or want PrEP?
6. There are many people in the US with an unmet need for PrEP. How can individuals who need or want PrEP be identified?

Please note:

- ***The use of lenacapavir for PrEP to reduce the risk of HIV-1 infection is investigational and has not been approved by the U.S. Food and Drug Administration (FDA) or any other regulatory authority; the efficacy and safety for this use has not been established.***
- ***Only proposals where study sites, participants, and investigators are located in the United States will be considered.***
- ***Initiation of studies through this RFP will be contingent upon FDA approval of lenacapavir for PrEP in the population being studied.***
- ***Requests for drug supply will not be considered if the provision of drug impacts the question being addressed. For example, those assessing real world implementation of lenacapavir for HIV prevention.***

Proposals should include descriptions of:

- Incorporation of community and/or user/participant involvement in study planning and study design/protocols;
- Clear scientific objectives and endpoints, based on sound scientific hypotheses;
- Appropriate, defined, and specific data collection/evaluation methods;
- Scalability and sustainability of the program after funding completion (when applicable);
- Generalizability to other settings; and
- Feasibility of completion of the project within 18 months, followed by rapid data dissemination and presentation of results.
- Plans to present and publish results in scientific forums and peer-reviewed journals.

As the study sponsor, the principal investigator will be responsible for compliance with all laws and regulations applicable to research sponsors, including satisfying local requirements and obtaining all necessary regulatory approvals prior to beginning the study.

Key Dates & Program Specifics:

Stage 1: Letter of Intent (LOI: a concise overview of proposed project and total estimated budget)

- **November 22, 2024**: LOI submission window opens
- **January 24 at 11:59pm PST, 2025**: LOI submission window closes

LOIs must be submitted via the online GOPTICS portal (https://gileadmedaffairs.appiancloud.com/suite/portal/login.jsp)

LOIs are not binding documents on either party. The purpose of the LOI is to provide a brief summary of the proposed study to enable Gilead to determine on a preliminary basis whether the proposed study and related budget are aligned with the criteria, timeline and scope of this RFP.

Any questions about the INCLUSION RFP 2025 program or application process can be submitted to your local Gilead Medical Scientist or INCLUSION@gilead.com.

Stage 2: Full Application Submission (complete proposal with detailed budget)

All those who have submitted an LOI will be informed of the outcome of the LOI review by March 3, 2025. Certain applicants will be invited to submit a full application, including a detailed budget. The timelines for submission and review of full applications are as follows:

- **April 4 at 11:59pm PST, 2025:** Deadline for receipt of full application
- **June, 2025:** Notice of full application outcome

Full applications must be completed in GOPTICS following approval to submit (https://gileadmedaffairs.appiancloud.com/suite/portal/login.jsp)

Investigators who meet criteria for a standard Gilead ISR (https://www.gilead.com/science-and-medicine/research/investigator-sponsored-research) and have a proven track record of conducting research in HIV prevention are encouraged to apply.

The program provides awards for research completed in up to 18 months. Awards shall be for research purposes only; ***routine medical care or other costs associated with routine medical care will not be considered for funding.***

Budget Considerations

Gilead plans to award a total of approximately $5,000,000 in funds for research proposals under the INCLUSION RFP 2024 Program, dependent upon availability of funds and receipt of meritorious applications. Any proposal greater than $500,000 should be discussed with your Gilead Medical Scientist prior to submission.

Gilead's approval of awards will depend on the availability of funds and receipt of meritorious and complete proposals. Awards shall be granted solely on the merit of the research and alignment with the criteria of this program.

Review Process

Letters of Intent (LOI) will be rigorously reviewed by a Gilead internal committee. Each complete LOI that meets program requirements will be assigned to multiple reviewers. Each reviewer will review the LOI and evaluate how well the proposal addresses the RFP, the potential impact of the study, the strength of the objectives/study design, sustainability/scalability of the proposal/intervention, and the site's and study team's ability to recruit the proposed study population and execute on study objectives. Investigators with the top submissions will be offered the opportunity to submit a full application including a detailed budget, adequate and proportional to the study's scope, which will be similarly reviewed.

No Guarantee of Funding

Gilead reserves the right to approve or decline any application at its sole discretion. Submission of an LOI or a full application does not guarantee funding. Applications are reviewed by an internal review committee.

No Inducement or Reward

Gilead approval of awards does not take into account the past, present, or future volume or value of any business or referrals between the parties. Awards are not being given, directly or indirectly, as an inducement or reward with respect to the past or potential future purchase, utilization, recommendation or formulary placement of any Gilead product. Further, except for the use of the Gilead product in an approved award/research, the awardee is not required to purchase, order, recommend or prescribe to any patients any products manufactured by or available through Gilead.

About Gilead Sciences

Gilead Sciences, Inc. is a biopharmaceutical company that discovers, develops and commercializes innovative therapeutics in areas of unmet medical need. The company's mission is to advance the care of

patients suffering from life-threatening diseases worldwide. Gilead has operations in more than 30 countries worldwide, with headquarters in Foster City, California.

Footnote: Lenacapavir, a human immunodeficiency virus type 1 (HIV-1) capsid inhibitor, in combination with other antiretroviral(s), is indicated for the treatment of HIV-1 infection in heavily treatment-experienced adults with multidrug-resistant HIV-1 infection failing their current antiretroviral regimen due to resistance, intolerance or safety consideration. ***The use of lenacapavir for PrEP to reduce the risk of HIV-1 infection is investigational; it is not approved for this use, and the efficacy and safety for this use has not been established.***

References:

1. HIV.gov, Ending the HIV Epidemic in the US: https://www.hiv.gov/federal-response/ending-the-hiv-epidemic/overview. Accessed October 30, 2024.
2. CDC, Ending the HIV Epidemic in the US Goals: https://www.cdc.gov/ehe/php/about/goals.html. Accessed October 30, 2024.
3. AIDSVu Public Data Resource: https://aidsvu.org/prep/. Accessed October 30, 2024.
4. Sunlenca USPI, Gilead Sciences, July 2024. Available at: https://www.gilead.com/-/media/files/pdfs/medicines/hiv/sunlenca/sunlenca_pi.pdf
5. Bekker L-G, et al. *N Engl J Med*. July 2024 [ePub]. doi: 10.1056/NEJMoa2407001
6. https://clinicaltrials.gov/study/NCT04925752
7. Tao L, et al. IDWeek 2023, Poster 1557