Gilead Is Studying Lenacapavir as Twice-Yearly PrEP

Five trials are evaluation long-acting lenacapavir injections for various groups at risk for HIV.

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Five clinical trials are underway to test lenacapavir as pre-exposure prophylaxis (PrEP) in diverse populations at risk for HIV. If it is found to be effective for preventing HIV acquisition, lenacapavir could become the longest-acting PrEP option, administered by subcutaneous injection once every six months. The current longest-acting option, Apretude (cabotegravir), is administered by intramuscular injection every other month.

Lenacapavir (formerly GS-6207), from Gilead Sciences, is the first HIV capsid inhibitor. It disrupts the cone-shaped shell that surrounds the viral genetic material and essential enzymes. Laboratory studies found that the drug interferes with multiple stages of the HIV life cycle. It has a long half-life in the body, making it suitable for twice yearly administration.

In December 2022, the Food and Drug Administration approved lenacapavir, marketed as Sunlenca, for treatment-experienced people with highly resistant HIV who are unable to maintain viral suppression on their current regimen. As part of a combination regimen, lenacapavir injections every six months are effective against multidrug-resistant HIV for at least two years. Lenacapavir combination therapy also works well for first-line treatment, though it is not yet approved for this indication.

Lenacapavir's potential for twice-yearly treatment is limited by the fact that it currently has no equally long-lasting partner drugs to build a complete regimen. But it can be used alone for PrEP. Studies have shown that lenacapavir protected monkeys exposed to an HIV-like virus either via the rectum (simulating anal sex) or intravenously (simulating injection drug use).

The PURPOSE trials are evaluating twice-yearly lenacapavir injections and daily oral PrEP in different groups of people at risk for HIV. The studies will compare the rate of HIV acquisition among people who use either form of PrEP against the background (or "counterfactual") rate of infection among people who don't use PrEP.

PURPOSE 1 (NCT04994509) is evaluating the safety and efficacy of lenacapavir and tenofovir alafenamide/emtricitabine (Descovy) for cisgender adolescent girls and young women ages 16 to 25 in South Africa and Uganda. Descovy PrEP is not currently approved for people exposed to HIV

through vaginal sex. This pivotal Phase III trial is fully enrolled with more than 5,300 participants. Initial results are expected this fall.

PURPOSE 2 (NCT04925752) is evaluating the safety and efficacy lenacapavir and tenofovir disoproxil fumarate/emtricitabine (TDF/FTC, sold as Truvada or generic equivalents) for cisgender men, transgender men, transgender women and nonbinary people who have sex with men in the United States, Argentina, Brazil, Mexico, Peru, South Africa and Thailand. This Phase III trial has enrolled more than 3,000 participants; initial results are expected in early 2025.

PURPOSE 3 (NCT06101329) is studying lenacapavir and TDF/FTC as PrEP for cisgender women in the United States who are disproportionately affected by HIV, with a focus on Black women and other women of color. This Phase II trial, which aims to enroll 250 participants, will assess lenacapavir pharmacokinetics and the safety and acceptability of lenacapavir and TDF/FTC. It is expected to end in 2027.

PURPOSE 4 (NCT06101342) is studying lenacapavir and TDF/FTC as PrEP for people who inject drugs in the United States. This Phase II trial, which aims to enroll 250 participants, will assess lenacapavir pharmacokinetics and the safety of lenacapavir and TDF/FTC. It is expected to end in 2027.

PURPOSE 5 is evaluating lenacapavir and TDF/FTC in France and the United Kingdom, focusing on participants who are disproportionally affected by HIV and often underrepresented in clinical trials. This Phase II trial will look at persistence, or continuous use, of lenacapavir and TDF/FTC among people who are not currently using PrEP.

While oral PrEP is highly effective—especially for gay and bisexual men and transgender women—new options are still needed. Some people have trouble remembering to take a pill every day, some do not wish to constantly be reminded of HIV and some do not want to have pill bottles that could subject them to stigma or could be lost or stolen.

In the United States, only about a third of people who could benefit from PrEP have received a prescription, according to the Centers for Disease Control and Prevention. In Europe, it is estimated that less than 15% of people who could benefit from PrEP are using it. Access is even more limited in low- and middle-income countries.

“I am encouraged by Gilead’s long-acting prevention research program,” Jean-Michel Molina, MD, PhD, of Université Paris Cité, said in a Gilead press release. “While existing PrEP options have certainly helped transform the way HIV is prevented, offering a variety of person-centered options will be an important step towards making PrEP accessible among a greater range of people.”

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