Twice-Yearly HIV Treatment on the Horizon

Three experimental antiretrovirals could become components of future long-acting HIV treatment regimens.

May 18, 2026 By Liz Highleyman

Three experimental antiretrovirals could become components of future long-acting HIV treatment regimens, according to research presented at the Conference on Retroviruses and Opportunistic Infections.

ViiV Healthcare's VH-499 could be the second approved HIV capsid inhibitor after lenacapavir. ViiV's VH-184 is a novel integrase inhibitor with a high barrier to resistance, while GS-3242 is a next-generation integrase inhibitor from Gilead Sciences. Oral versions of all three drugs demonstrated potent antiviral activity and good safety profiles in early small studies, setting the stage for the first trials of long-acting injectable formulations.

In a Phase I study of injectable VH-499, 65 HIV-negative adults were randomly assigned to receive a single subcutaneous injection in the abdomen or intramuscular injection in the buttocks using various doses or a placebo. Nearly 90% had at least one injection site reaction (ISR), but these were mostly mild and temporary. People who received subcutaneous injections reported more ISRs, including nodules, than those who got intramuscular shots. The pharmacokinetic profile supports twice-yearly dosing.

The VH-184 Phase I study enrolled 76 HIV-negative adults. They received a single sub-cutaneous or intramuscular injection of various doses of two formulations of VH-184 or a placebo. Again, most participants had at least one ISR, usually mild and brief. Formulation B was both better tolerated and lasted longer than Formulation A, and it is expected to maintain an effective drug concentration if given every four to six months.

A Phase I study of injectable GS-3242 enrolled 34 HIV-negative adults. They received various doses or a placebo administered as a single intramuscular injection in the thigh. Nearly 90% of those who received the highest dose experienced ISRs. The half-life ranged from 50 to 76 days,

supporting a dosing interval of at least four months; additional cohorts are evaluating a six-month interval.

Phase II clinical trials of these pipeline drugs are expected to start this year. Ultimately, VH-499 and VH-184 could be combined with experimental ultra-long-acting formulations of cabotegravir or ViiV's broadly neutralizing antibody lotivibart in a twice-yearly regimen. GS-3242 could be partnered with lenacapavir or Gilead's investigational antibodies teropavimab and zinlirvimab.
