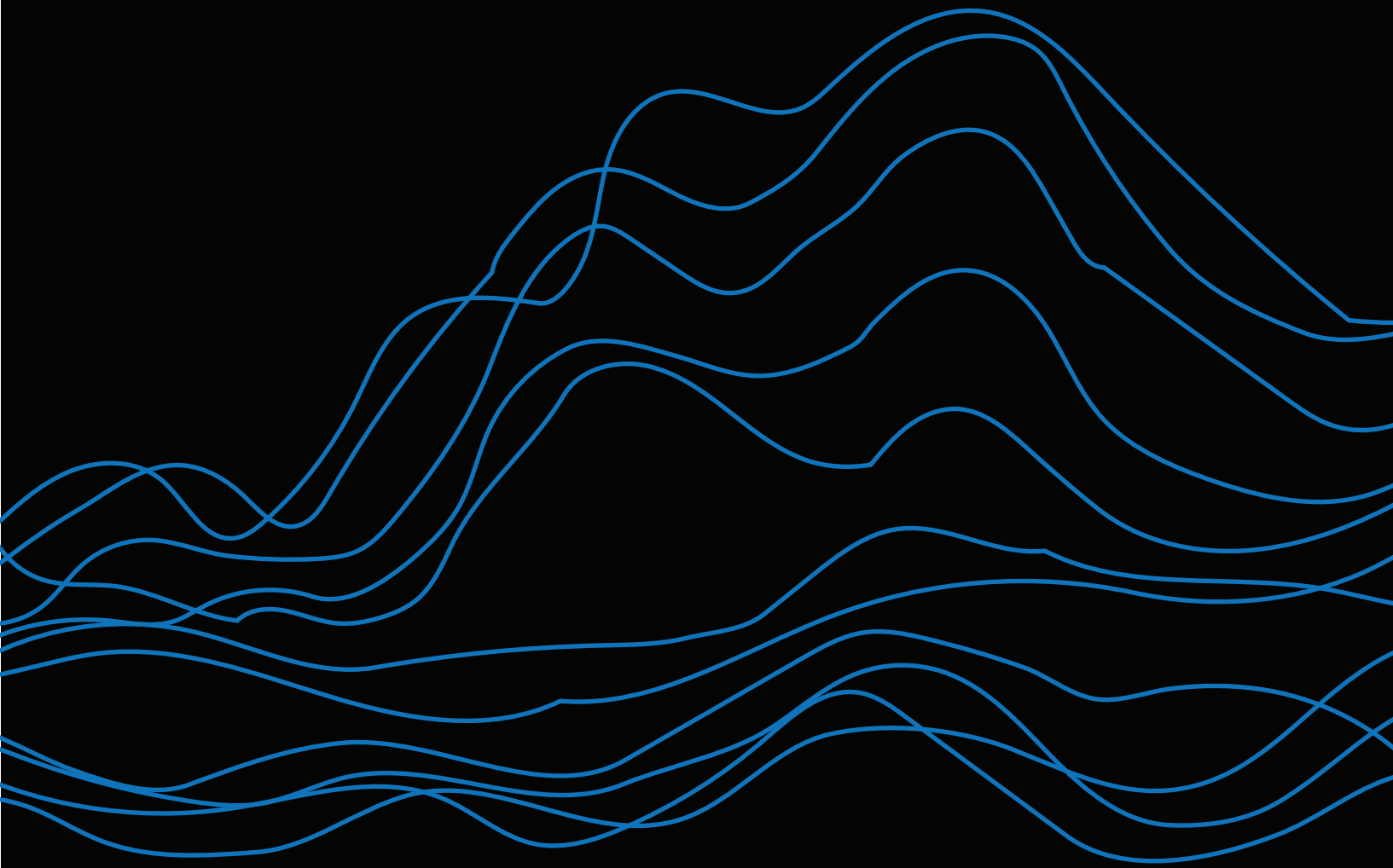
Pipeline Report » 2023

Antiretroviral Therapy



TAG
Treatment Action Group

The Antiretroviral Therapy Pipeline 2023

By Richard Jefferys

At the end of last year, the US Food and Drug Administration (FDA) approved lenacapavir (trade name Sunlenca), the first antiretroviral that works by inhibiting HIV's capsid protein, and the first to be dosed just once every six months (see table 1). The decision followed approvals by the European Union, United Kingdom, and Canada earlier in 2022.

The HIV capsid protein encapsulates the virus's genetic material and plays a role in multiple steps of the viral life cycle. Research has demonstrated that the activity of lenacapavir is unaffected by HIV resistance mutations against currently available classes of antiretrovirals. The drug is manufactured by Gilead Sciences, and the FDA indication is for "heavily treatment-experienced adults with multidrug resistant HIV-1 infection failing their current antiretroviral regimen due to resistance, intolerance, or safety considerations."

The data supporting approval derive from the CAPELLA trial, which enrolled 72 heavily treatment-experienced people with HIV whose current antiretroviral therapy (ART) was failing to suppress viral load to below 400 copies/mL. Results after 26 weeks of follow-up were published in the *New England Journal of Medicine* on May 12, 2022, with additional information on outcomes after 52 weeks presented as a poster at the 2023 Conference on Retroviruses and Opportunistic Infections (CROI).

Participants in CAPELLA had previously taken an average of nine antiretrovirals, and about half showed evidence of HIV resistance to all four main classes of ART (nucleoside reverse-transcriptase inhibitors, non-nucleoside reverse-transcriptase inhibitors, protease inhibitors, and integrase inhibitors).

An initial cohort of 36 participants whose detectable viral load had remained stable between a screening visit and study entry received a two-week period of oral lenacapavir or placebo. This study design allowed for a randomized comparison of short-term effects on HIV viral load, with 88% of lenacapavir recipients experiencing at least a 0.5 $\log_{10}$ (two-thirds) decline compared with 17% of placebo recipients. These participants were then switched to open-label lenacapavir administered by abdominal subcutaneous injection every six months, in combination with an optimized background ART regimen. An additional second cohort of 36 participants received open-label lenacapavir plus an optimized background ART regimen, with an oral lead-in for two weeks followed by subcutaneous injection every six months.

After 26 weeks of follow-up, HIV viral load was below the limit of detection in 81% of the participants in the first cohort and 89% of the participants in the second. The poster presentation at CROI 2023 reported that 78% of all participants (56 out of 72) maintained undetectable viral load after 52 weeks. The average CD4+ T-cell increase at this timepoint was 84 cells per microliter. These represent impressive results in a population with multidrug-resistant HIV.

Lenacapavir is also being investigated as a potential first-line therapy in the CALIBRATE trial. The results after 54 weeks of follow-up were published in *The Lancet HIV* in January 2023. A total of 182 participants were divided into four groups:

1. Injectable lenacapavir every 26 weeks after two weeks of oral lead-in dosing, combined with daily emtricitabine and tenofovir alafenamide for 28 weeks and then combined with daily tenofovir alafenamide.

2. Injectable lenacapavir every 26 weeks after two weeks of oral lead-in dosing, combined with daily emtricitabine and tenofovir alafenamide for 28 weeks and then combined with daily bictegravir.

3. Oral daily lenacapavir (600 mg for the first two days, followed by 50 mg daily) with daily emtricitabine and tenofovir alafenamide.

4. A control group given oral daily bictegravir, emtricitabine, and tenofovir alafenamide.

The journal article reports that most participants (93%) were male, three (2%) were transgender, a slight majority (52%) Black, and 45% of Latinx ethnicity. After 54 weeks, viral load was suppressed to undetectable levels in 90% of group one, 85% of group two, 85% of group three, and 92% of the controls. Results after 80 weeks of follow-up were presented in a poster at CROI 2023, demonstrating continued high rates of viral load suppression. The researchers conclude that "these results support ongoing evaluation and further development of LEN [lenacapavir] in combination with other long-acting partner agents."

In a commentary accompanying the paper in Lancet HIV, Chloe Orkin notes that the identity of an appropriate long-acting partner for lenacapavir is as yet unclear. Gilead is evaluating whether two long-acting broadly neutralizing antibodies (bNAbs) that the company licensed from Rockefeller University, teropavimab and zinlirvimab (formerly known as 3BNC117-LS and 10-1074-LS), might be candidates.

Preliminary results from a small ongoing phase Ib trial of the combination were described by Joe Eron in a presentation at CROI 2023. All components were dosed every six months, with the bNAbs delivered by intravenous infusion. Most participants (18 out of 20) successfully suppressed viral load to undetectable levels after 26 weeks. One participant displayed detectable viral load after 16 weeks, possibly indicating the development of resistance to one or more elements of the regimen, but achieved suppression after being switched back to their previous ART. The researchers attempted to assess whether the rebounding HIV showed evidence of resistance mutations, but because viral load levels were low, the assay failed to generate evaluable results (a known problem with HIV resistance assays). A second participant chose to leave the study at week 12 and return to oral ART, with their viral load below the limit of detection at the time of withdrawal.

The major issue associated with use of bNAbs is the presence of preexisting resistance among circulating HIV variants because the antibodies target the most variable part of the virus, the outer envelope protein. Eron's study screened potential participants for HIV resistance to teropavimab and zinlirvimab prior to enrollment, and half of those evaluated (54 of 109) showed evidence of reduced susceptibility to one or both bNAbs. While baseline resistance may present a hurdle for widespread clinical use of this type of combination, Gilead is nevertheless launching a larger phase II trial of lenacapavir, teropavimab, and zinlirvimab dosed every six months.

In addition to the long-acting injectable form of lenacapavir, Gilead has an ongoing trial evaluating the potential of oral lenacapavir combined with the integrase inhibitor bictegravir to offer a simplified switch option for people on more complicated ART regimens. The phase II portion of the study will compare daily bictegravir plus oral lenacapavir at two different doses (25 mg or 50 mg) with standard ART. After 24 weeks, the trial will shift to a phase III evaluation of a fixed dose combination of bictegravir plus oral lenacapavir compared with standard ART. The amount of oral lenacapavir included in the fixed-dose pill will be based on the results from the initial phase II dose comparison.

The most common side effects from lenacapavir in studies conducted to date were injection-site reactions, nausea, and headache. No severe adverse events have been associated with the drug. There have been at least four reported instances of lenacapavir discontinuation because of injection-site reactions, which are typically transient but rarely can persist as nodules or induration (thickening of the skin).

The development of HIV resistance to lenacapavir is possible but has been uncommon; in the CAPELLA study, the emergence of resistance mutations in eight participants was associated with a lack of other active antiretrovirals in their background combination. The FDA label warns that the drug can remain in the body at a low level for long periods, which could increase the risk of the development of resistance if doses are missed or the drug is stopped without another suppressive ART regimen being initiated.

Islatravir is an experimental nucleoside reverse transcriptase translocation inhibitor (NRTTI) developed by Merck that was until recently considered a promising long-acting oral antiretroviral, and an ideal candidate partner for lenacapavir. The two manufacturers entered into a co-development agreement for the combination in early 2021. These plans experienced a setback when it was disclosed in November 2021 that islatravir administration had been associated with unexpected declines in CD4+ T-cell and white blood counts. The news was followed rapidly by the FDA placing full or partial clinical holds on ongoing islatravir trials for both treatment and preexposure prophylaxis (PrEP).

On September 20, 2022, Merck announced a paring down of the islatravir development program. The company is now pursuing combination approaches that are considered likely to be safe based on their analyses and feedback from the FDA. This involves a phase III program combining a lower once-daily 0.25 mg dose of islatravir with the NNRTI doravirine and an amended protocol with a lower once-weekly 2 mg dose of islatravir for a phase II trial in combination with oral lenacapavir.

The islatravir once-monthly oral PrEP program has been discontinued, and the FDA partial clinical hold on studies of higher doses remains in place (current participants can continue to receive study drug, but there is no further screening and enrollment). At CROI 2023, Merck researchers presented evidence that the once-daily 0.25 mg dose and once-weekly 2 mg dose are likely to be safe because the negative effect of islatravir on white blood cell counts is dose related.

There are several new additions to the pipeline from established manufacturers (table 2). Gilead Sciences is initiating a research protocol that will assess two new candidates: GS-5894, a long-acting NNRTI, and GS-1720, a long-acting integrase inhibitor. The study is recruiting HIV-positive participants at multiple sites in the United States.

ViiV Healthcare has launched the first phase I studies of VH4524184, an integrase inhibitor, and VH4011499, a capsid inhibitor. Both are recruiting HIV-negative participants for an initial evaluation of safety, tolerability, and pharmacokinetics (the behavior of the drug in the body).

Also added from ViiV is VH3810109 (also known as GSK3810109A, and formerly called N6-LS), a long-acting bNAb licensed from the National Institutes of Health that may have the potential to partner with other long-acting antiretrovirals. Encouraging results from an ongoing phase II trial were presented at recent HIV research conferences (see entry in table 2), but the issue of resistance to bNAbs is also relevant to this candidate, with the magnitude of the viral load response among participants associated with HIV's susceptibility to the bNAb at baseline.

ViiV Healthcare's plans for moving the maturation inhibitor GSK3640254 into a phase III efficacy evaluation have been shelved. The decision isn't related to safety and efficacy but rather based on the company's focus on developing antiretrovirals that offer significant additional value compared with existing options, particularly longer-acting regimens. The abundance of daily oral regimens essentially makes for a crowded market, and it appears the potential financial payoff from progressing GSK3640254 to approval was not considered sufficient to justify the cost of further development.

HIV advocates have serious concerns about this trend toward abandonment of daily regimens because there remains a need for additional novel options for people who develop resistance to extant antiretrovirals, and more choices are always better than fewer.

TABLE 1. U.S. ADULT APPROVALS SINCE JULY 2022

Product	Class/Type	Company	FDA Approval Date	U.S. Launch Price (Annual WAC)
Lenacapavir (Sunlenca)	**Capsid inhibitor**	**Gilead**	**December 22, 2022**	**$42,250 for the first year, then $39,000**

- FDA label indication for "heavily treatment-experienced adults with multidrug resistant HIV-1 infection failing their current antiretroviral regimen due to resistance, intolerance, or safety considerations" in combination with other antiretroviral(s).
- U.S. Department of Health and Human Services Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV have added information on the use of lenacapavir in the setting of virologic failure.
- Approval based on results from a phase II/III trial (CAPELLA) evaluating lenacapavir in heavily treatment-experienced people with HIV and multidrug resistance. Results after 26 weeks of follow-up were published in the *New England Journal of Medicine* on May 12, 2022. Results after 52 weeks were reported at CROI 2023. Resistance analyses were published in the *Journal of Infectious Diseases*, September 9, 2022.
- Ongoing phase II trial (CALIBRATE) of lenacapavir in combination with approved ARVs in ART-naive people with HIV. Results at 54 weeks were published in the *Lancet HIV* in January 2023.
- Ongoing phase II and III trial investigating daily oral lenacapavir in combination with bictegravir as a switch option for people on more complex ART regimens.
- A phase II trial in combination with islatravir, in partnership with Merck (protocol amended to remove doses of islatravir higher than 2 mg).
- Two trials investigating the combination of lenacapavir with two LA broadly neutralizing antibodies, teropavimab and zinlirvimab: a phase Ib trial launched in March 2021 with preliminary results presented at CROI 2023 and a newly initiated phase II study that plans to recruit 125 participants.
- Results from a phase Ib trial in people with HIV were published in *Nature* in July 2020. Subcutaneous administration of single doses ranging from 20 to 750 mg led to decreases in HIV viral load of up to 2.2$\log_{10}$ copies/mL over 10 days, without serious adverse events. Resistance analyses published in the *Journal of Antimicrobial Chemotherapy* in January 2022 found that mutations occurred in only two out of 29 participants, who had received lower doses than those selected for efficacy trials.
- A study published in *Antimicrobial Agents and Chemotherapy* reported that the activity of lenacapavir is unimpaired by resistance mutations to the main extant classes of ARVs.

TABLE 2: ARV PRODUCTS IN DEVELOPMENT

Product	Class/Type	Company	Development Phase
Islatravir	**NRTTI**	**Merck**	**Phase III**

- A new category of ARV: NRTTI.
- All islatravir trials were placed on full or partial clinical holds in December 2021 due to declines in total lymphocyte and CD4+ T-cell counts observed among both HIV-positive and HIV-negative recipients. After further investigation and consultation with the FDA, a more limited development program investigating low once-daily or once-weekly dosing is being pursued. Treatment trials of higher doses remain on partial clinical hold (no new screening or enrollment), and the PrEP development program for HIV-negative people has been discontinued.
- Trials now include:
  - A phase III trial of a once-daily fixed-dose formulation with doravirine and 0.25 mg of islatravir for people who received the combination in earlier studies.
  - A phase III trial for treatment-naive people comparing a once-daily fixed-dose formulation with doravirine and 0.25 mg of islatravir with Biktarvy (bictegravir/emtricitabine/tenofovir alafenamide).
  - Two phase III switch studies: one for people on any standard ART regimen, and one for people receiving Biktarvy.
  - A phase II trial of once-weekly dosing of 2 mg islatravir with lenacapavir in partnership with Gilead. This protocol has been revised to reduce the weekly dose of islatravir from the originally planned 20 mg a week. Exclusion criteria have also been modified to prevent enrollment of individuals with evidence of drug resistance mutations in HIV's reverse transcriptase. The latter change was prompted by concerns that the lower islatravir dose may be insufficiently active against HIV containing these mutations.
  - Open-label follow-up study for certain participants in trials of the 0.75 mg once-daily fixed-dose formulation with doravirine.
  - Several previous trials involving higher doses are ongoing but under partial clinical holds, including phase III trials of the 0.75 mg once-daily fixed-dose formulation with doravirine in treatment-naive, virologically suppressed (two trials, switch A and switch B) and heavily treatment-experienced people with HIV and a phase IIb trial of once-weekly dosing in combination with the NNRTI MK-8507.
- Presentations at CROI 2023 described the analyses supporting the decision to evaluate 0.25 mg daily and 2 mg weekly dosing on the basis that they are unlikely to have negative effects on white blood cell counts.
- Phase IIb trial results were published in *Lancet HIV* on May 14, 2021. A brief report describing results after 96 weeks of follow-up was published in JAIDS in September 2022.
- Phase Ib safety, PK, and antiretroviral activity results were published in *The Lancet HIV* on January 3, 2020.
- Results from drug interaction studies with doravirine and dolutegravir and tenofovir disoproxil fumarate have been published, reporting no significant interactions.

Albuvirtide (Aikening)	**Fusion inhibitor**	**Frontier**	**Phase II/III**

- Approved in China in June 2018 based on 48-week data from the phase III TALENT study, which demonstrated superiority of albuvirtide plus ritonavir-boosted lopinavir over lopinavir/ritonavir plus two NRTIs as second-line therapy.
- A trial in the United States is evaluating albuvirtide in combination with the broadly neutralizing antibody 3BNC117 as LA maintenance therapy for people with suppressed viral load.
- The combination of albuvirtide and 3BNC117 was being investigated in people with multidrug-resistant HIV in a phase II trial launched in September 2020. The study was slated to end in December 2022, but the registry record hasn't been updated since September 2021, rendering the current status unclear.
- The effects of albuvirtide and 3BNC117 on the HIV reservoir and viral load rebound after an ART interruption were due to be assessed in a phase II trial, however the registry record has also been neglected and the study was never listed as open for enrollment. Inquiries to company representatives about the status of these studies have not been answered.

Product	Class/Type	Company	Development Phase
PRO 140 (leronlimab)	**CCR5 antagonist**	**CytoDyn**	**Phase II/III**

- Leronlimab is a monoclonal antibody designed to block the interaction between HIV and CCR5, the primary coreceptor the virus uses to enter and infect cells.
- In October 2022, CytoDyn voluntarily withdrew its Biologics License Application (BLA) to the FDA for the treatment of multidrug-resistant HIV because of problems with the data. The fate of the drug in the context of HIV appears very uncertain, with the company now reported to be focusing on non-alcoholic steatohepatitis.
- Former CytoDyn CEO Nader Pourhassan was indicted in December 2022 for securities fraud schemes related to leronlimab, along with an associate, Kazem Kazempour, who ran the company that managed CytoDyn's clinical trials.
- The FDA placed holds on both HIV and COVID-19 programs for leronlimab in March 2022. Participants receiving leronlimab through trial extensions were transitioned to alternative therapeutics.
- The FDA previously rejected a BLA from the manufacturer in July 2020, citing lack of information necessary for a review. The recent indictment alleges that CytoDyn was aware that the submission was inadequate but went ahead in an effort to mislead investors in the company.
- Preliminary results from the dose-escalating CD03 phase II/III evaluation of weekly subcutaneous PRO 140 as single-agent monotherapy in virologically suppressed people were presented as a poster at CROI 2019. Rates of virological failure were high in the 350 mg and 525 mg dose groups (65.9% and 33%, respectively), but suppression was better maintained in the ongoing 700 mg dose group (6 out of 43 participants experienced virological failure, defined as two consecutive viral loads ≥200 copies/mL).
- Primary efficacy results from the CD02 phase IIb/III trial of PRO 140 in treatment-experienced people were reported at ASM Microbe 2018.
- The CD01 phase IIb trial and extension study, demonstrating moderate efficacy of PRO 140 single-agent maintenance therapy, were published online in April 2018. In a paper published in *PloS Pathogens* on March 31, 2022, researchers report that five participants in the extension study were able to maintain HIV viral load suppression for over seven years while receiving the 700 mg dose.
- Dr. Jonah Sacha at Oregon Health & Science University is planning to conduct a leronlimab study in a person with HIV who requires a stem cell transplant to treat a concurrent condition. Several people with HIV, most famously Timothy Ray Brown, have been cured of the infection after receipt of stem cell transplants from donors with the CCR5Δ32 mutation (which causes immune cells to be resistant to most HIV variants), but in this case such a donor couldn't be identified. The goal of the study is to assess whether blocking CCR5 with leronlimab can protect the newly transplanted immune system cells from HIV infection and possibly achieve a cure in the absence of the CCR5Δ32 mutation.

Semzuvolimab (UB-421)	**CD4 attachment inhibitor**	**United BioPharma**	**Phase II/III**

- Results from a small phase II trial evaluating weekly or biweekly UB-421 as a single-agent maintenance therapy during an 8- or 16-week ART interruption were published in the *New England Journal of Medicine* in April 2019. No cases of virological failure (defined as >400 copies/mL) were documented.
- In August 2022, the company announced that the FDA had approved an NIAID-sponsored, 25-person phase II trial of UB-421 in combination with optimized background ART regimen in people with multidrug-resistant HIV.
- A phase III trial in combination with an optimized background ART regimen in treatment-experienced participants is planned but not yet enrolling.
- A phase II trial exploring the effects of UB-421 on the HIV reservoir and another HIV cure-related proof-of-concept phase II trial testing UB-421 in combination with the latency-reversing agent chidamide (an histone deacetylase inhibitor) have been completed, with results yet to be presented.
- A phase I trial assessing delivery via subcutaneous injection has also been completed, with results pending.

Product	Class/Type	Company	Development Phase
MK-8507	**NNRTI**	**Merck**	**Phase IIb**

- Initially evaluated in a phase I trial in 2014/2015.
- Favorable PK, antiretroviral activity, and resistance profile were reported in studies published in the *Journal of Acquired Immune Deficiency Syndromes* and *Antimicrobial Agents and Chemotherapy* in 2021.
- A study highlighting an increase in exposure to fluoride associated with MK-8507 administration was published in the *Journal of Clinical Pharmacology* on August 21, 2021. The authors state that at doses used in trials "fluoride levels are not expected to exceed a clinically relevant threshold in most individuals."
- A phase IIb trial is testing a once-weekly combination with islatravir; currently among the Merck trials placed on partial hold by the FDA (see islatravir entry above).
- A planned phase I study of MK-8507 in HIV-negative participants with mild or moderate hepatic impairment has not yet opened for enrollment.

Cabotegravir (LA), VRC07-523LS	**INSTI, bNAb**	**ViiV/Vaccine Research Center**	**Phase II**

- NIAID-sponsored phase II trial investigating the combination of LA cabotegravir with the LA bNAb VRC07-523LS developed by the Vaccine Research Center at the U.S. NIH. Participants will switch from standard ART and undergo a 46-week period of intermittent administration of LA cabotegravir + VRC07-523LS before reinstituting their oral ART regimen.
- Results from baseline screening for HIV resistance against VRC07-523LS were presented at CROI 2023. The authors report that HIV samples from approximately 70% of the potential participants met prespecified criteria for susceptibility to the bNAb, while 14% showed evidence of resistance. In the remaining cases, samples could not be evaluated because of the technical limitations of the assay.

VH3810109 (also known as GSK3810109A, N6-LS)	**bNAb**	**ViiV**	**Phase II**

- bNAb licensed from the NIH by ViiV Healthcare.
- Results from an ongoing phase II trial presented at HIV Glasgow 2022 and CROI 2023, reporting good tolerability and an average viral load reduction of 1.72 $\log_{10}$ after a single infusion. Virologic response was associated with HIV susceptibility to the bNAb (retrospectively assessed from baseline samples).
- Results are pending from a completed phase I trial investigating subcutaneous administration with recombinant human hyaluronidase PH20 (rHuPH20), which allows for large volumes of antibody to be delivered via the subcutaneous route.

GSK3739937	**Maturation inhibitor**	**ViiV/GlaxoSmithKline**	**Phase I**

- A candidate long-acting HIV maturation inhibitor. A phase I study in HIV-negative volunteers has been completed; the results were published in *Pharmacology Research and Perspectives* in June 2023, showing good tolerability and the potential for once-weekly dosing..

MK-8527	**NRTTI**	**Merck**	**Phase I**

- Merck disclosed that that MK-8527 is an NRTTI in a September 2022 press release.
- A single-dose phase I trial is recruiting in South Africa.
- A phase I trial evaluating safety, tolerability, PK, and antiretroviral activity in people with HIV in Romania has been completed.
- The results are posted to ClinicalTrials.gov and indicate viral load declines of around 1 $\log_{10}$, with no serious adverse events.

HRF-4467	**Maturation inhibitor**	**Hetero Labs Limited**	**Phase I**

- Phase I trial in HIV-negative volunteers taking place in India. Regulatory review information is available online (see page 13).
- A poster abstract about HRF-4467 was presented at the 2021 Cold Spring Harbor Retroviruses meeting, but the content is not publicly available.

Product	Class/Type	Company	Development Phase
CPT31	**Novel D-peptide HIV entry inhibitor**	**Navigen, Inc.**	**Phase I**
■ Entry inhibitor that has shown activity in the macaque model of SHIV infection. ■ A phase Ia trial in HIV-negative participants has been completed; the results are posted to ClinicalTrials.gov. ■ The manufacturer Navigen isn't planning further development but is looking to license or sell the compound to a larger pharmaceutical company (Alan Mueller, PhD, personal communication April 26, 2023, shared with permission).			
Lipovirtide	**Fusion inhibitor**	**Shanxi Kangbao Biological Product Co., Ltd.**	**Phase I**
■ A phase I trial evaluating a single injection of lipovirtide in treatment-naive people with HIV is recruiting in China. ■ A 24-person phase I trial of multiple dosing is planned but not yet recruiting.			
VH4004280	**Capsid inhibitor**	**ViiV**	**Phase I**
■ First-in-human phase I trial underway in HIV-negative volunteers evaluating the safety, tolerability, and PK of a new HIV capsid inhibitor delivered orally.			
STP0404	**Integrase inhibitor**	**ST Pharm Co., Ltd.**	**Phase I**
■ HIV-1 integrase inhibitor targeting the LEDGF/p75-integrase interaction site. ■ Results from a phase I study in HIV-negative men were presented at AIDS 2022, reporting favorable safety and PK and plans for a phase IIa clinical trial to be initiated in the United States. A company press release stated the trial would start in the fourth quarter of 2022, and it is now registered and recruiting. ■ A paper published in *PLoS Pathogens* in July 2021 described preclinical results.			
HRS5685	**Unknown**	**RetroLead (Shanghai) BioPharma Co., Ltd.**	**Phase I**
■ A phase I trial assessing safety, tolerability, and PK in HIV-negative participants is registered but not yet open for enrollment. The mechanism of action is not available in public reports, but it is likely an antiretroviral intended for the Chinese market.			
VH4524184	**INSTI**	**ViiV**	**Phase I**
■ A phase I trial evaluating safety, tolerability, PK, and effects on liver enzyme (cytochrome P450 3A) activity in HIV-negative participants is recruiting.			
VH4011499	**Capsid inhibitor**	**ViiV**	**Phase I**
■ Ongoing first-in-human phase I trial evaluating safety, tolerability, and PK in HIV-negative participants.			
GS-5894	**NNRTI**	**Gilead**	**Phase I**
■ LA NNRTI being evaluated under a phase I open-label master protocol, which is currently recruiting participants.			
GS-1720	**INSTI**		**Phase I**
■ LA INSTI being evaluated under a phase I open- label master protocol, which is currently recruiting participants.			

TABLE ABBREVIATIONS

ART: antiretroviral therapy

ARV: antiretroviral

ASM: American Society for Microbiology

bNAb: broadly neutralizing antibody

CROI: Conference on Retroviruses and Opportunistic Infections

FDA: U.S. Food and Drug Administration

INSTI: integrase strand transfer inhibitor

LA: long-acting

NIAID: U.S. National Institute of Allergy and Infectious Diseases

NIH: National Institutes of Health

NRTI: nucleoside reverse transcriptase inhibitor

NNRTI: non-nucleoside reverse transcriptase inhibitor

NRTTI: nucleoside reverse transcriptase translocation inhibitor

PK: pharmacokinetic(s)

WAC: wholesale acquisition cost