

# Pipeline Report » 2022

Antiretroviral Therapy



**TAG**

Treatment Action Group

# The Antiretroviral Therapy Pipeline 2022

By Richard Jefferys

Over the quarter-century since HIV-suppressing combination regimens were first approved, antiretroviral drug development has progressed through several broad eras.

Initially, there was an impetus to develop candidates with fewer side effects and fewer pills. HIV treatment became progressively safer and simpler with the arrival of integrase inhibitors, a new class of antiretrovirals, and the advent of multi-drug regimens in single fixed-dose pills that allowed once-daily administration.

The past decade has seen an increasing focus on reducing dosing even further with long-acting (LA) drugs, both oral and injectable, in addition to the continued pursuit of antiretrovirals with novel mechanisms of action.

The U.S. Food and Drug Administration (FDA) approved the first LA injectable regimen for monthly dosing last year: Cabenuva, which contains the integrase inhibitor cabotegravir and the non-nucleoside reverse transcriptase inhibitor (NNRTI) rilpivirine.

In February of 2022, the FDA gave the green light for an option to administer Cabenuva bimonthly (every other month). The approval of bimonthly dosing is based on the phase IIIb ATLAS 2M trial. An initial publication in the *Lancet* in December 2020 described results after 48 weeks, with extended 96-week data subsequently reported in *Lancet HIV* on October 11, 2021.

Bimonthly dosing was found to meet prespecified criteria for non-inferiority compared with monthly dosing but was associated with a slightly elevated risk of virologic failure: after 96 weeks, there were nine confirmed cases in the bimonthly arm of the trial compared with two in the monthly arm (virologic failure was defined as two sequential viral load measurements greater than or equal to 200 copies/mL). All but one of these cases (in the bimonthly group) were documented during the first 48 weeks of the study. Analysis of baseline samples from six of the nine cases detected the presence of low levels of HIV containing NNRTI resistance mutations that reduce susceptibility to rilpivirine.

Results after 152 weeks of follow up were presented in a poster at CROI 2022.

An additional two cases of virologic failure occurred between weeks 96 and 152, both in the bimonthly dosing arm. As with the majority of prior cases, evidence of resistance to both NNRTIs and integrase inhibitors was observed, highlighting that viral load breakthrough on this regimen typically necessitates a switch to protease inhibitor-based ARV combinations.

In a presentation during the British HIV Association 'Best of CROI' Virtual Feedback Meeting, expert clinician Dr. Laura Waters stressed that people considering bimonthly dosing should be made aware of the potentially higher risk of virologic failure, which equates to an approximately one in forty chance after three years for bimonthly dosing compared with a one in a hundred chance after three years for monthly dosing.

Another potential concern flagged in an abstract presented at the April 2022 British HIV Association (BHIVA) conference relates to risk of NNRTI resistance after interrupting Cabenuva. The abstract describes two women with HIV and no prior NNRTI exposure who achieved virologic suppression on Cabenuva (obtained before approval through a compassionate access program) but later switched back to oral regimens to facilitate conception. Both experienced adherence difficulties, and, after HIV viral load rebounded, mutations conferring resistance to rilpivirine were documented (see P009, [BHIVA conference abstracts](#)).

The efficacy studies of Cabenuva administered oral versions of the drugs for a four-week lead-in period to assess tolerability prior to switching to the LA injectable formulation, but both [European regulators](#) and the [FDA](#) have now approved an option to start LA therapy immediately. The data supporting the approval derive from the extension phase of the FLAIR trial, which reported comparable results in cohorts of participants initiating Cabenuva either with or without the oral lead-in phase. Results were [published in \*Lancet HIV\* on October 14, 2021](#).

The labeling amendments for Cabenuva represent the only adult antiretroviral drug approvals in the United States during the past year (see table 1). Two candidates that were listed in last year's Pipeline Report are now omitted, having gained licensure in China: the NNRTI [ACC007 \(KM-023\)](#), now named AINUOVIRINE, and the NRTI [azvudine](#).

Gilead Sciences [submitted a new drug application \(NDA\)](#) to the FDA for their LA capsid inhibitor lenacapavir on June 28, 2021, based on encouraging results from the CAPELLA trial in people with multidrug-resistant HIV. The company is initially seeking an indication for people with HIV who have limited therapy options due to extensive prior treatment histories.

The HIV capsid protein forms a protective case around the virus's genetic material and plays a role in multiple steps of the virus life cycle. Lenacapavir is the first capsid inhibitor to enter late-stage clinical trials. The drug has an oral formulation for weekly dosing and a subcutaneous injection for administration every six months. Lenacapavir's targeting of the HIV capsid [enables inhibition](#) of HIV variants that are resistant to currently approved antiretrovirals.

Progress toward licensure has been delayed by [FDA concerns about the safety of the vials](#) used for the injectable formulation. The original vials were made of a material called borosilicate glass, and the concern was that incompatibility with lenacapavir solution could lead to microscopic glass particles mixing with the drug. A temporary hold was placed on trials administering injectable lenacapavir, but on May 16, 2022 [Gilead announced](#) that the issues had been resolved and all trials allowed to restart. Injectable lenacapavir is now being stored in an alternative vial made from aluminosilicate glass.

Updates on lenacapavir were presented at the 2022 Conference on Retroviruses and Opportunistic Infections (CROI). The drug continues to show promise among heavily treatment-experienced participants in [the CAPELLA trial](#), with 83% of recipients followed for 52 weeks maintaining undetectable viral loads. CD4+ T cell counts increased by an average of 83 cells per microliter. No serious adverse events have been documented; the most common side effect is injection-site reactions. The preliminary results obtained

after 26 weeks of follow up were published in the *New England Journal of Medicine* on May 12, 2022.

A separate study in treatment-naive people with HIV reported high rates of viral load suppression after 54 weeks for both oral and injectable formulations in combination with tenofovir alafenamide, bicitgravir, or emtricitabine/tenofovir alafenamide. Echoing CAPELLA, no serious adverse events occurred, and injection-site reactions were the most frequently reported side effect (three participants discontinued lenacapavir because of injection-site reactions).

Another investigational antiretroviral that has run into problems over the past year is islatravir, Merck's nucleoside reverse transcriptase translocation inhibitor (NRTTI). There was considerable excitement about islatravir's potential because of unprecedented potency (activity against HIV at low doses) and the possibility of intermittent dosing for both treatment and pre-exposure prophylaxis (PrEP).

On November 18, 2021, Merck announced an unexpected and unwelcome derailment of development plans in the form of data from an ongoing trial testing once-weekly dosing of islatravir and an experimental NNRTI, MK-8507, in people with HIV. Small but statistically significant decreases in total lymphocyte (white blood cell) and CD4 counts were observed among participants, and dosing was suspended as per the recommendation of the trial's external Data Monitoring Committee.

On December 6, Merck also disclosed a pause in enrollment of two islatravir PrEP trials in HIV-negative participants, and this was followed on December 13 by the announcement of FDA clinical holds on "oral and implant formulations of islatravir for HIV-1 pre-exposure prophylaxis (PrEP); the injectable formulation of islatravir for HIV-1 treatment and prophylaxis; and the oral doravirine/islatravir HIV-1 once-daily treatment."

All PrEP studies are on full hold, with participants no longer receiving islatravir and being offered FDA-approved once-daily regimens instead. Total lymphocyte and CD4+ T-cell counts will be monitored.

For treatment studies of doravirine/islatravir, there is currently a partial hold: participants already receiving the drug can continue, but no additional participants will be screened or enrolled. In an additional ongoing treatment trial of islatravir combined with lenacapavir as an oral once-weekly regimen, all dosing will be stopped, and participants will be instructed to restart their prior antiretroviral regimen.

The mechanism by which islatravir might affect total lymphocyte and CD4+ T-cell counts is unclear, and the subject of investigation. The outcomes of these ongoing analyses will determine whether Merck can continue the development of islatravir.

There are few new additions to the pipeline of antiretroviral agents at earlier stages of development (table 2). The only drug clearly intended for Western markets is VH4004280, a capsid inhibitor being developed by ViiV Healthcare that's undergoing first-in-human testing in HIV-negative people. An integrase inhibitor with a novel mechanism, STP0404, is being developed by a Korean company that is also collaborating with researchers at Emory University in the United States to explore the drug's potential.

**TABLE 1. U.S. APPROVALS SINCE JULY 2021**

Product	Class/Type	Company	FDA Approval Date	U.S. Launch Price (Annual WAC)
<b>Cabotegravir/ rilpivirine LA injectable formulation (Cabenuva)</b>	<b>INSTI/NNRTI</b>	<b>ViiV/Janssen</b>	<b>Bimonthly dosing option: February 1, 2022</b> <b>Approval of optional oral lead in: March 24, 2022</b>	<b>\$47,520 (initial loading doses: \$5,940)</b>
<ul style="list-style-type: none"> <li>■ Bimonthly dosing was approved based on non-inferiority with monthly dosing demonstrated in the international phase IIIb ATLAS-2M trial. 96-week data from ATLAS-2M were published in the <i>Lancet HIV</i>, October 11, 2021. Results after 152 weeks of follow up were presented at CROI 2022.</li> <li>■ On March 29, 2022, the FDA approved use in adolescents aged 12 years and older based on interim results from the MOCHA study. Acceptability data from MOCHA were presented as a poster at CROI 2022.</li> <li>■ Monthly dosing was approved January 21, 2021, based on 48-week data from two phase III randomized non-inferiority trials comparing Cabenuva to oral ARV regimens: ATLAS and FLAIR (see links for results published in the <i>New England Journal of Medicine</i>).</li> <li>■ FDA label indication: “a complete regimen for the treatment of HIV-1 infection in adults and adolescents 12 years of age and older and weighing at least 35 kg to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA &lt;50 copies/mL) on a stable antiretroviral regimen with no history of treatment failure and with no known or suspected resistance to either cabotegravir or rilpivirine.”</li> <li>■ U.S. Department of Health and Human Services Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV recommend that Cabenuva “can be used to replace an existing oral ARV regimen in people with HIV with sustained viral suppression for 3 to 6 months (optimal duration is not defined), who have good adherence and engagement in care, no baseline resistance to either medication, no prior virologic failures; who do not have active or occult HBV infection (unless the patient also is receiving an HBV active regimen); who are not pregnant or planning on becoming pregnant; and who are not receiving medications with significant drug interactions with oral (during lead-in or bridging therapy) or injectable CAB or RPV.”</li> <li>■ European regulators and the FDA have approved the option of starting LA injectable Cabenuva immediately, without a lead-in period of oral dosing. Decisions based on the results of the FLAIR trial extension phase (published in the <i>Lancet HIV</i> on October 14, 2021).</li> <li>■ ViiV Healthcare is sponsoring an implementation study investigating the use of infusion centers to administer Cabenuva in the southeastern United States (Georgia, North Carolina, and South Carolina).</li> <li>■ The ACTG is conducting the LATITUDE trial for people who face challenges adhering to daily oral ART.</li> <li>■ A completed phase I trial in HIV-negative participants investigated the PK of Cabenuva administered concomitantly as two separate IM injections in the vastus lateralis (thigh) muscles, but the results have not yet been presented. In the phase III trials, administration was via IM injections in the gluteal muscles (buttocks).</li> <li>■ A larger ongoing phase I trial in HIV-negative participants is evaluating abdominal subcutaneous injections of LA cabotegravir in addition to IM injections in gluteal or vastus lateralis muscles.</li> </ul>				

TABLE 2: ARV PRODUCTS IN DEVELOPMENT

Product	Class/Type	Company	Development Phase
Islatravir	NRTTI	Merck	Phase III
<ul style="list-style-type: none"> <li>■ A new category of ARV: NRTTI.</li> <li>■ All islatravir trials are on <u>full or partial clinical holds</u> due to declines in total lymphocyte and CD4+ T-cell counts observed among both HIV-positive and HIV-negative recipients.</li> <li>■ Trials include: <ul style="list-style-type: none"> <li>■ Phase III trials of a once-daily fixed-dose formulation with doravirine in <u>treatment-naive, virologically suppressed, and heavily treatment-experienced</u> people with HIV.</li> <li>■ Phase IIb trial of once-weekly dosing in combination with the NNRTI MK-8507.</li> <li>■ Phase II trial of once-weekly dosing of islatravir and lenacapavir in <u>partnership with Gilead</u>.</li> <li>■ Phase II trial in <u>children and adolescents</u> under 18 years old.</li> <li>■ <u>Open-label follow-up study</u> for all participants in trials of the once-daily fixed-dose formulation with doravirine.</li> <li>■ Phase IIb trial results were <u>published in Lancet HIV</u> on May 14, 2021.</li> </ul> </li> <li>■ Phase Ib safety, PK, and antiretroviral activity results were <u>published in The Lancet HIV</u> on January 3, 2020.</li> <li>■ Results from drug interaction studies with <u>doravirine and dolutegravir and tenofovir disoproxil fumarate</u> have been published, reporting no significant interactions.</li> </ul>			
Lenacapavir	Capsid inhibitor	Gilead	Phase II/III
<ul style="list-style-type: none"> <li>■ Clinical trials of injectable lenacapavir were placed on hold for several months because of FDA concerns related to the safety of the storage vial. On May 16, 2022, <u>Gilead announced</u> that the hold has been lifted and a new storage vial implemented.</li> <li>■ Trials include: <ul style="list-style-type: none"> <li>■ A <u>phase II/III trial (CAPELLA)</u> is evaluating lenacapavir in heavily treatment-experienced people with HIV and multidrug resistance. A lead-in dose of oral lenacapavir is administered over the first 14 days, followed by subcutaneous dosing every six months. Preliminary results after 26 weeks of follow up were published in the <u>New England Journal of Medicine</u> on May 12, 2022. Interim 52-week results were presented at CROI 2022.</li> <li>■ A phase II trial (CALIBRATE) of lenacapavir in combination with approved ARVs in ART-naive people with HIV was initiated in November 2019. As in CAPELLA, a lead-in dose of oral lenacapavir will be administered over the first 14 days, followed by subcutaneous dosing every 26 weeks. Interim 54-week results were <u>presented at CROI 2022</u>.</li> <li>■ A phase II trial in combination with islatravir, in <u>partnership with Merck</u>.</li> <li>■ A <u>phase I trial</u> launched in March 2021 investigating the combination of lenacapavir with two LA broadly neutralizing antibodies, teropavimab and GS-2872 (formerly known as 3BNC117-LS and 10-1074-LS).</li> </ul> </li> <li>■ Results from a phase Ib trial in people with HIV were <u>published in Nature</u> 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 copies/mL over 10 days, without serious adverse events. Resistance analyses published in the <u>Journal of Antimicrobial Chemotherapy</u> in January 2022 found that mutations occurred in only 2 out of 29 participants, who had received lower doses than those selected for efficacy trials.</li> <li>■ A study published in <u>Antimicrobial Agents and Chemotherapy</u> reported that the activity of lenacapavir is unimpaired by resistance mutations to the main extant classes of ARVs.</li> </ul>			

Product	Class/Type	Company	Development Phase
<b>Albuvirtide (Aikening)</b>	<b>Fusion inhibitor</b>	<b>Frontier</b>	<b>Phase II/III</b>
<ul style="list-style-type: none"> <li>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.</li> <li>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.</li> <li>The combination of albuvirtide and 3BNC117 is also being investigated in people with multidrug-resistant HIV in a phase II trial launched in September 2020.</li> <li>The effects of albuvirtide and 3BNC117 on the HIV reservoir and viral load rebound after an ART interruption will be assessed in a phase II trial.</li> <li>A phase I study in China is evaluating PK of albuvirtide delivered by either intravenous drip or intravenous injection in HIV-negative volunteers.</li> </ul>			
<b>PRO 140 (Ieronlimab)</b>	<b>CCR5 antagonist</b>	<b>CytoDyn</b>	<b>Phase II/III</b>
<ul style="list-style-type: none"> <li>The manufacturer, CytoDyn, is undergoing an upheaval with the previous CEO fired in January of 2022 and the FDA placing holds on both HIV and COVID-19 programs for Ieronlimab. Participants receiving Ieronlimab through trial extensions will be transitioned to alternative therapeutics. On an investor call held on March 31, 2022, the company stated that it is working to address unspecified FDA concerns and is also dealing with an ongoing Federal Exchange Commission and Department of Justice investigation.</li> <li>The FDA previously rejected a biologics license application from the manufacturer in July 2020, citing lack of information necessary for a review.</li> <li>Preliminary results from 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 <math>\geq 200</math> copies/mL).</li> <li>Primary efficacy results from CD02 phase IIb/III trial of PRO 140 in treatment-experienced people were reported at ASM Microbe 2018. A single-arm open-label trial for treatment-experienced people with HIV is now closed to enrollment.</li> <li>CD01 phase IIb trial and extension study, demonstrating moderate efficacy of PRO 140 single-agent maintenance therapy, published online in April 2018. In a paper published in <i>PLoS Pathogens</i> 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.</li> </ul>			
<b>UB-421</b>	<b>CD4 attachment inhibitor</b>	<b>United Biomedical</b>	<b>Phase II/III</b>
<ul style="list-style-type: none"> <li>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 <i>New England Journal of Medicine</i> in April 2019. No cases of virological failure (defined as <math>&gt;400</math> copies/mL) were documented.</li> <li>A larger phase III single-agent maintenance therapy trial is enrolling.</li> <li>A phase III trial in combination with optimized background regimen in treatment-experienced participants is planned but not yet enrolling.</li> <li>A phase II trial exploring effects on the HIV reservoir has been completed. Another HIV cure-related proof-of-concept phase II trial launched in late 2021 is testing UB-421 in combination with the latency-reversing agent chidamide (an HDAC inhibitor).</li> <li>A phase I trial assessing delivery via subcutaneous injection is recruiting.</li> </ul>			

Product	Class/Type	Company	Development Phase
<b>MK-8507</b>	<b>NNRTI</b>	<b>Merck</b>	<b>Phase IIb</b>
<ul style="list-style-type: none"> <li>Initially evaluated in a phase I trial in 2014/2015.</li> <li>Favorable PK, antiretroviral activity, and resistance profile were reported in studies published in the <i>Journal of Acquired Immune Deficiency Syndromes</i> and <i>Antimicrobial Agents and Chemotherapy</i> in 2021.</li> <li>A study highlighting an increase in exposure to fluoride associated with MK-8507 administration was published in the <i>Journal of Clinical Pharmacology</i> 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.”</li> <li>A phase IIb trial is testing a once-weekly combination with islatravir; currently among the Merck trials placed on hold by the FDA (see islatravir entry above).</li> <li>A planned phase I study of MK-8507 in HIV-negative participants with mild or moderate hepatic impairment has not yet opened for enrollment.</li> <li>The future of MK-8507 is unclear and may depend on the outcome of investigations into islatravir’s effects on total lymphocyte and CD4+ T cell counts. In Merck’s first press release describing the problem, it was noted that there appeared to be a dose-dependent exacerbation of the effects in participants also receiving MK-8507.</li> </ul>			
<b>GSK2838232</b>	<b>Maturation inhibitor</b>	<b>GlaxoSmithKline</b>	<b>Phase IIa</b>
<ul style="list-style-type: none"> <li>Requires combination with cobicistat boosting.</li> <li>Results from a phase IIa 10-day dose-finding trial in people with HIV were published in <i>Clinical Infectious Diseases</i> on November 26, 2019. Reported to be well tolerated, with mean viral load reduction of 1.7 log copies/mL in the highest-dose group (200 mg/day).</li> <li>Safety, tolerability, and PK results from a phase I dose-escalation trial in HIV-negative participants were published in June 2018. Additional results on PK and food effects were published in June 2020.</li> <li>A poster abstract presented at CROI 2022 noted that the drug is active against HIV-1 but lacks activity against HIV-2.</li> <li>No additional trials registered on ClinicalTrials.gov at this time.</li> </ul>			
<b>Cabotegravir (LA), VRC07-523LS</b>	<b>INSTI, bNAb</b>	<b>ViiV/Vaccine Research Center</b>	<b>Phase II</b>
<ul style="list-style-type: none"> <li>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. National Institutes of Health. Participants will switch from standard ART and undergo a 46-week period of intermittent administration of LA cabotegravir + VRC07-523LS before reinstating their oral ART regimen.</li> </ul>			
<b>GSK3640254</b>	<b>Maturation inhibitor</b>	<b>ViiV/GlaxoSmithKline</b>	<b>Phase I</b>
<ul style="list-style-type: none"> <li>A suite of phase I trials involving HIV-negative participants has been completed, including interaction studies with dolutegravir, tenofovir alafenamide/emtricitabine, and oral contraceptives (see NCT03231943, NCT03575962, NCT03836729, NCT03816696, and NCT03984825). Results indicating favorable safety and PK have been published along with data demonstrating a lack of significant interactions with dolutegravir, tenofovir alafenamide/emtricitabine, and oral contraceptives. No serious adverse events were reported.</li> <li>A phase I study exploring food effects on PK of capsule and tablet formulations was published in <i>Clinical Pharmacology in Drug Development</i> in January 2022, reporting slightly higher drug levels associated with moderate and high fat intake. The authors conclude that the data “support the use of the tablet formulation co-administered with food.”</li> <li>A Phase II proof-of-concept trial involving treatment-naïve participants living with HIV has been completed, with results published in <i>Clinical Infectious Diseases</i> in January 2022. Maximal viral load declines of approximately 2 and 1.5 logs were observed in recipients of 200 mg and 140 mg daily doses, respectively (six participants per group). Drug resistance mutations were observed in four of six participants who received the 200 mg dose for 14 days, with evidence of significantly reduced HIV susceptibility to the drug in one case, causing the monotherapy dosing period to be reduced to seven days in the other cohorts. The most commonly reported side effect was headache, and there were no discontinuations due to adverse events.</li> <li>A phase IIb trial of GSK3640254 as part of a combination ARV regimen is ongoing, with an enrollment target of 150 participants.</li> <li>A second phase IIb trial testing GSK3640254 in combination with dolutegravir and/or lamivudine was launched in 2021.</li> </ul>			



Product	Class/Type	Company	Development Phase
<b>GSK3739937 (also known as VH3739937)</b>	<b>Maturation inhibitor</b>	<b>ViiV/GlaxoSmithKline</b>	<b>Phase I</b>
<ul style="list-style-type: none"> <li>A candidate long-acting HIV maturation inhibitor. A <a href="#">phase I study</a> in HIV-negative volunteers has been completed, results are pending.</li> </ul>			
<b>MK-8527</b>	<b>Not yet publicly available</b>	<b>Merck</b>	<b>Phase I</b>
<ul style="list-style-type: none"> <li>A <a href="#">phase I trial</a> evaluating safety, tolerability, PK, and antiretroviral activity in people with HIV in Romania has been completed.</li> <li>The results are posted to <a href="#">ClinicalTrials.gov</a> and indicate viral load declines of around 1 log, with no serious adverse events.</li> </ul>			
<b>MK-8558</b>	<b>Not yet publicly available</b>	<b>Merck</b>	<b>Phase I</b>
<ul style="list-style-type: none"> <li>A <a href="#">phase I trial</a> evaluating safety, tolerability, PK, and antiretroviral activity in people with HIV in Germany and Romania has been completed.</li> <li>Results are posted to <a href="#">ClinicalTrials.gov</a> and indicate viral load declines of around 1 log at the highest doses with three reported serious adverse events and a high proportion of participants experiencing non-serious adverse events.</li> </ul>			
<b>HRF-4467</b>	<b>Maturation inhibitor</b>	<b>Hetero Labs Limited</b>	<b>Phase I</b>
<ul style="list-style-type: none"> <li><a href="#">Phase I trial</a> in HIV-negative volunteers taking place in India. Regulatory review information is <a href="#">available online</a> (see page 13).</li> <li>A poster abstract about HRF-4467 was <a href="#">presented at the 2021 Cold Spring Harbor Retroviruses meeting</a>, but the content is not publicly available.</li> </ul>			
<b>CPT31</b>	<b>Novel D-peptide HIV entry inhibitor</b>	<b>Navigen, Inc.</b>	<b>Phase I</b>
<ul style="list-style-type: none"> <li>Entry inhibitor that has <a href="#">shown activity</a> in the macaque model of SHIV infection.</li> <li>A <a href="#">phase Ia trial</a> has been completed, results are pending.</li> </ul>			
<b>Lipovirtide</b>	<b>Fusion inhibitor</b>	<b>Shanxi Kangbao Biological Product Co., Ltd.</b>	<b>Phase I</b>
<ul style="list-style-type: none"> <li>A <a href="#">phase I trial</a> evaluating a single injection of lipovirtide in treatment-naive people with HIV is recruiting in China.</li> <li>A 24-person <a href="#">phase I trial</a> of multiple dosing is planned but not yet recruiting.</li> </ul>			
<b>Teropavimab, GS-2872</b>	<b>LA bNABs</b>	<b>Gilead</b>	<b>Phase I</b>
<ul style="list-style-type: none"> <li>Two LA bNABs <a href="#">licensed from Rockefeller University</a> by Gilead. Formerly known as 10-1074-LS and 3BNC117-LS.</li> <li>A <a href="#">phase I trial</a> at Rockefeller University has been completed; results are pending.</li> <li>The bNABs are being administered in four independently sponsored HIV cure-related trials (<a href="#">NCT04319367</a>, <a href="#">NCT05300035</a>, <a href="#">NCT05079451</a>, <a href="#">NCT05245292</a>).</li> <li>The only currently registered Gilead-sponsored trial is a <a href="#">phase I evaluation</a> of the bNABs in combination with lenacapavir.</li> </ul>			
<b>VH4004280</b>	<b>Capsid inhibitor</b>	<b>ViiV</b>	<b>Phase I</b>
<ul style="list-style-type: none"> <li><a href="#">First-in-human phase I trial</a> underway in HIV-negative volunteers evaluating the safety, tolerability, and PK of a new HIV capsid inhibitor delivered orally.</li> </ul>			

Product	Class/Type	Company	Development Phase
STP0404	Integrase inhibitor	ST Pharm Co., Ltd.	Phase I
<ul style="list-style-type: none"> <li>■ HIV-1 integrase inhibitor targeting the LEDGF/p75-integrase interaction site.</li> <li>■ A paper published in <i>PLoS Pathogens</i> in July 2021 describing preclinical results states: “based on these encouraging preclinical findings, we have recently started phase I clinical studies with 200 mg STP0404 in a Single Ascending Dose (SAD) regimen.”</li> <li>■ No trials are listed in online registries, but a <a href="#">news article from 2020</a> states that approval was received to conduct a phase I study in France.</li> </ul>			
HRS5685	Unknown	RetroLead (Shanghai) BioPharma Co., Ltd.	Phase I
<ul style="list-style-type: none"> <li>■ A phase I trial assessing safety, tolerability, and PK in HIV-negative participants is <a href="#">registered</a> but not yet open for enrollment. Mechanism of action not available in public reports, but likely an antiretroviral intended for the Chinese market.</li> </ul>			

## TABLE ABBREVIATIONS

**ACTG:** AIDS Clinical Trials Group

**ART:** antiretroviral therapy

**ARV:** antiretroviral

**ASM:** American Society for Microbiology

**bNAbs:** broadly neutralizing antibody

**CAB:** cabotegravir

**CROI:** Conference on Retroviruses and Opportunistic Infections

**FDA:** U.S. Food and Drug Administration

**HBV:** hepatitis B virus

**IM:** intramuscular

**INSTI:** integrase strand transfer inhibitor

**LA:** long-acting

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

**NRTI:** nucleoside reverse transcriptase inhibitor

**NNRTI:** non-nucleoside reverse transcriptase inhibitor

**NRTTI:** nucleoside reverse transcriptase translocation inhibitor

**PK:** pharmacokinetic(s)

**RPV:** rilpivirine

**WAC:** Wholesale acquisition cost