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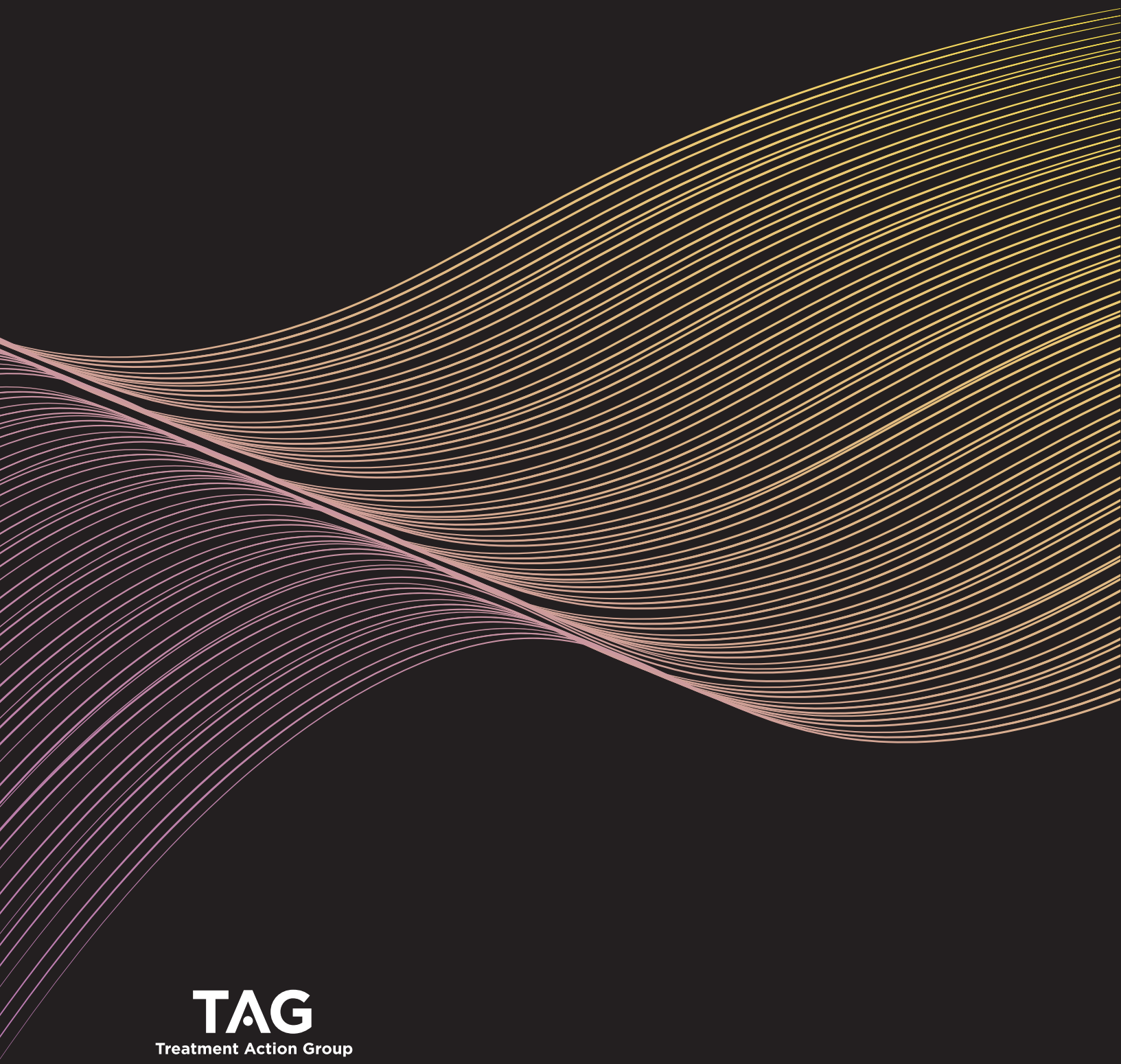
Antiretroviral Therapy



TAG
Treatment Action Group

The Antiretroviral Therapy Pipeline 2026

By Richard Jefferys

During the past year, one new antiretroviral therapy (ART) has been approved by the US Food and Drug Administration (FDA): Merck's once-daily fixed-dose doravirine (100 mg) and islatravir (0.25 mg) combination pill named IDVYNSO™ on April 21, 2026. As stated in Merck's press release, the indication is for

> *"the treatment of HIV-1 infection in adults to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA less than 50 copies per mL) on a stable antiretroviral regimen with no history of virologic treatment failure and no known substitutions associated with resistance to doravirine. IDVYNSO is contraindicated when co-administered with drugs that are strong cytochrome P450 (CYP)3A enzyme inducers and lamivudine (3TC) or emtricitabine (FTC)."*

The data supporting the FDA decision derive from two phase III switch trials showing the combination was well tolerated and noninferior to standard ART regimens after 48 weeks of follow up. Results were published in *The Lancet* earlier this year, with one trial involving participants who were receiving Biktarvy and the other enrolling participants on any standard suppressive oral ART regimen. In both studies about 98.5% of participants switched to IDVYNSO maintained viral load less than 50 copies/mL, which was slightly (but not statistically significantly) lower than those remaining on Biktarvy (99.4%) and somewhat but nonsignificantly higher than those on other standard oral ART regimens (95.1%). The incidence of side effects and discontinuations due to adverse events was similar between the arms in both trials.

Doravirine is a non-nucleoside reverse transcriptase inhibitor (NNRTI) that was approved in 2018, while islatravir becomes the first licensed nucleoside reverse transcriptase translocation inhibitor (NRTTI) (and the first novel antiretroviral to receive FDA approval since 2022). NRTTIs inhibit the HIV reverse transcriptase enzyme in a different way to other available inhibitors, demonstrating high potency as evidenced by the low dose of islatravir needed in the combination pill.

However, at least in the case of islatravir, a potential for negatively affecting CD4 T cell counts depending on the dosing regimen has stymied Merck's original plan to advance a monthly dose. The toxicity is related to the peak islatravir levels that occur after taking the higher doses that are required for the drug to be longer acting. A once-weekly form of islatravir continues to be evaluated in combination with oral lenacapavir in the ISLEND trials (see table). Merck is testing the efficacy of an alternate NRTTI candidate, MK-8527, as a monthly pre-exposure prophylaxis (PrEP) option for HIV-negative people at risk of HIV acquisition (see TAG's 2026 PrEP and Microbicides Pipeline Report).

In addition to the approval of IDVYNSO, the FDA has recently accepted and granted priority review to a new drug application from Gilead Sciences for a once-daily single pill combining the integrase inhibitor bictegravir (75 mg) and the capsid inhibitor lenacapavir (50 mg) (BIC/LEN). The application is based on the findings of the ARTISTRY-1 and -2 clinical trials, the first of which recruited individuals on stable complex ART regimens and the second involving people receiving Biktarvy – in both studies, participants were randomized to either switch to BIC/LEN or continue their current treatment.

Results from the phase III portion of ARTISTRY-1 were published in *The Lancet* in March 2026, demonstrating equivalent maintenance of HIV viral load suppression and comparable tolerability. After 48 weeks, 3 of the 371 BIC/LEN recipients (1%) and 2 of the 186 participants remaining on their current regimen (1%) had viral loads above 50 copies/mL. The average age of participants was 60, which Gilead notes is the "oldest study population in a Phase 3 HIV treatment registrational trial to date."

Similar 48-week data from ARTISTRY-2 were reported at CROI 2026, (and subsequently published in *Lancet HIV*), with BIC/LEN noninferior to Biktarvy for maintaining HIV viral load suppression. Drug-related adverse events occurred at comparable rates between the study arms (10.4% and 12.0%, respectively) and discontinuations because of side effects were infrequent (1.6% of participants in each arm). A phase II/III trial of BIC/LEN in children and adolescents with HIV is ongoing, with completion anticipated in 2030.

In January 2025 the FDA provided Gilead Sciences a Breakthrough Therapy designation for an experimental twice-yearly regimen combining the long-acting (LA) capsid inhibitor lenacapavir with two LA broadly neutralizing antibodies (bNAbs), teropavimab and zinlirvimab. A twice-yearly dosing interval for a combination HIV therapy has no precedent, prompting the FDA breakthrough designation, which facilitates more rapid review of interventions that may offer significant improvements compared to existing options. As this report was going to press, Gilead registered two new phase III efficacy trials for the combination: a comparison with switching to the approved long-acting injectable regimen Cabenuva, and a comparison with remaining on standard oral ART.

Over the past year, results have been presented from an ongoing phase II trial of the regimen indicating maintenance of viral load suppression and positive patient-reported outcomes. An HIV resistance analysis presented at CROI 2026 reported loss of susceptibility to zinlirvimab in two study participants, one of whom showed evidence of HIV developing resistance to lenacapavir. Both individuals resuppressed HIV viral load after switching to standard oral ART regiments.

As noted in TAG's 2025 Pipeline Report, baseline bNAb resistance testing is required before initiating the combination and a substantial proportion of the people with HIV who were screened for the trial were unable to enroll due to evidence of resistance to one or both bNAbs or test failure (a known issue with the technology). A pilot study subsequently assessed the regimen in people who displayed baseline HIV resistance to only one of the two bNAbs, with results published in the *Journal of Infectious Diseases* in April 2025. Of 10 participants in this analysis, 8 maintained viral load suppression, with the cases of rebound to detectable levels associated with receiving a lower bNAb dose. The authors conclude: *"Our results highlight the importance of investigating more broadly inclusive criteria for the long-acting regimen of LEN, TAB, and ZAB dosed every 6 months."*

In a potentially significant development, Gilead has registered a new phase II trial that will investigate twice-yearly injectable lenacapavir partnered with their experimental LA injectable integrase inhibitor GS-3242. The comparator groups will be people receiving oral Biktarvy. This research could represent a first step toward an unprecedented twice-yearly combination ART regimen, which would avoid the complex HIV resistance issues that accompany trying to partner bNAbs with lenacapavir. Data indicating safety, strong antiretroviral activity, and PK that may allow twice-yearly GS-3242 dosing were reported at CROI 2026.

ViiV Healthcare has reported progress toward a twice-yearly LA injectable regimen with their integrase inhibitor VH4524184 and capsid inhibitor VH4011499. Studies of each candidate presented at CROI 2026 reported that injectable administration was well tolerated in HIV-negative participants and PK supportive of dosing every six months. The company plans to initiate a phase IIb trial of injectable VH4011499 during the second half of 2026.

Less frequent oral dosing of ART is another active area of research. The most advanced candidate is the weekly oral combination of islatravir and lenacapavir currently in phase III trials made possible by a collaborative agreement between Gilead and Merck (ISLEND-1 and ISLEND-2). Results from a phase II

assessment were published in *Annals of Internal Medicine* in December 2025, showing that safety and viral load suppression at 48 weeks was comparable to Biktarvy. Similar findings after 96 weeks were described in a presentation at the European AIDS Conference (EACS 2025) in Paris.

Merck is also pursuing a once-weekly combination of islatravir with the company's experimental NNRTI ulonivirine. A phase II/III trial for people with HIV who've not yet started ART began enrolling in December 2025, while a phase II evaluation is in follow up.

Gilead is aiming to develop a proprietary weekly combination of an oral lenacapavir prodrug named lenacapavir pacfosacil (formerly GS-4182) and an experimental oral integrase inhibitor lepetegravir (formerly GS-1720). Two phase II trials have been initiated (WONDERS-1 and WONDERS-2) but were placed on hold by the FDA in June of last year due to evidence of CD4 T cell and absolute lymphocyte count declines in a subset of trial participants. The unexpected finding is reminiscent of the issue that arose with the Merck drug islatravir and is under investigation. WONDERS-1, which is investigating the combination in people switching from Biktarvy, remains on hold. The intent of WONDERS-2 was to test the approach in people with HIV who had yet to initiate ART, but the trial was terminated by Gilead in April 2026. The future of the combination remains uncertain at this juncture.

There were four new additions to the pipeline in 2026 (see table):

- Three of the entries are candidates being developed by companies in China that may be intended for the regional rather than global market:
  - CL-197, an oral nucleoside reverse transcriptase inhibitor (NRTI) being tested in a phase IIa trial in Beijing.
  - ACC017, an oral integrase inhibitor under evaluation in a phase Ib/IIa trial, also taking place in Beijing.
  - LP-98, an injectable fusion inhibitor reported to suppress simian-human immunodeficiency virus (SHIV) replication in macaques. A phase I/II trial is now ongoing in people with HIV who haven't previously received ART at a study site in Tianjin.
- VH4770359, described only as "an antiretroviral compound" in the description of a new first-in-human phase I trial registered by ViiV Healthcare. At the time of writing, the study has not yet opened for enrollment.

A major concern that continues to overshadow all HIV pipelines is the damaged state of the scientific research enterprise in the United States since the inauguration of the current political regime in January 2025. As was the case in last year's Pipeline Reports, TAG encourages everyone in the US who cares about scientific research and the development of new therapeutics — for any condition — to connect with advocacy efforts such as Stand Up for Science and Defend Public Health and make their voices heard to Congressional representatives, news outlets, and in their communities.

TABLE: ARV PRODUCTS IN DEVELOPMENT

Product	Class/Type	Company	Development Phase
Lenacapavir (Sunlenca)	**Capsid inhibitor**	**Gilead**	**Approved for people with limited options Phase II, III**

- Injectable version approved for "heavily treatment-experienced adults with multidrug-resistant HIV-1 infection failing their current ARV regimen due to resistance, intolerance, or safety considerations" in combination with other ARV(s) (see FDA label).
- 52-week results from the phase II/III CAPELLA study in people with multidrug-resistant HIV were published in *Lancet HIV* in July 2023, demonstrating high rates of viral load suppression and good safety profile. Participant-reported outcomes were described in a paper published in *AIDS & Behavior* in May 2025: health-related quality of life was maintained, with some reductions in frequency of bothersome symptoms. The 156-week results were published in *Open Forum Infectious Diseases* in December 2025: a majority of participants (43 out of 70, 61%) continued to maintain viral load less than 50 copies/mL, while 11 were above this threshold and data were missing for 16. There were 14 cases of lenacapavir resistance, and two participants discontinued the drug because of injection site nodules.
- Results from the phase III portion of the ARTISTRY-1 trial investigating a fixed-dose single daily oral lenacapavir/bictegravir tablet as a switch option for people on more complex ART regimens were published in *The Lancet* in March 2026, demonstrating equivalent maintenance of HIV viral load suppression and comparable tolerability.
- The ARTISTRY-2 phase III trial enrolled 577 people on Biktarvy for at least six months and is comparing continuing the same regimen to switching to the fixed-dose lenacapavir/bictegravir combination pill. Results reported at CROI 2026 (and subsequently published in *Lancet HIV*) indicate non-inferiority to Biktarvy for maintaining HIV viral load suppression. The results of ARTISTRY-1 and -2 have led Gilead to submit a new drug application to the FDA (see main report text).
- Phase II/III open-label study of oral lenacapavir/bictegravir for children and adolescents with HIV is currently in follow up.
- An oral weekly lenacapavir formulation is being assessed in combination with Merck's islatravir in two phase III switch trials:
  - ISLEND-1, which is recruiting people with suppressed viral load on Biktarvy and randomly assigning them to continue the current regimen or switch to weekly lenacapavir/islatravir. Preliminary results indicating non-inferiority were published in the *New England Journal of Medicine* on July 29, 2026.
  - ISLEND-2, a protocol taking the same approach but recruiting participants with suppressed viral load on any standard ART combination.
- Results of an ongoing phase II trial of the oral combination with islatravir were published in *Annals of Internal Medicine* in December 2025, reporting a high rate of viral load suppression after 24 and 48 weeks. Comparable findings from extended follow up out to 96 weeks were presented at EACS 2025 (see abstract PS15.5.LB).
- Gilead is evaluating lenacapavir combined with two LA bNAbs, teropavimab and zinlirvimab, as a potential six-monthly treatment regimen. Results from a completed phase Ib trial assessing a single administration of the combination were published in *Lancet HIV* in January 2024. A larger phase II study of the same regimen, presented at CROI 2025 and published in *Lancet Microbe* in March 2026, demonstrated high rates of viral load suppression after 26 weeks in people who switched from standard oral ART. Only 1 of 53 recipients had a viral load over 50 copies/mL at the end of follow up and there were no grade 3 or greater treatment-related adverse events or any adverse events leading to treatment discontinuation.
- A completed phase II trial (CALIBRATE) assessed lenacapavir in combination with approved ARVs in ART-naive people with HIV. Results after 54 weeks were published in *Lancet HIV* in January 2023.

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

- Islatravir is a first-in-class NRTTI with potent anti-HIV activity.
- Merck's once-daily fixed-dose islatravir (0.25 mg) and doravirine (100 mg) and combination pill named IDVYNSO™ was approved by the FDA on April 21, 2026, making islatravir the first novel ARV to receive approval since 2022 (see main report text).
- FDA approval was based on the results from two pivotal phase III switch trials: one enrolled people on any standard ART regimen, the other recipients of Biktarvy. In both cases switching to fixed-dose islatravir/doravirine met noninferiority criteria for maintaining viral load suppression after 48 weeks of follow up.
- Merck's original development plans for islatravir were derailed when clinical 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, the company shifted to a more limited program investigating low once-daily or once-weekly dosing. Treatment trials of higher doses were placed on partial clinical hold (no new screening or enrollment), and the PrEP development program for HIV-negative people has been discontinued.
- Trials now include:
  - ISLEND-1, which is recruiting people with suppressed viral load on Biktarvy and randomly assigning them to continue the current regimen or switch to weekly lenacapavir/islatravir.
  - ISLEND-2, a protocol taking the same approach but recruiting participants with suppressed viral load on any standard ART combination.
  - A phase II trial of once-weekly dosing of 2 mg islatravir with lenacapavir in partnership with Gilead. Results after 24 and 48 weeks of follow up were published in *Annals of Internal Medicine* in December 2025.
  - 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).
  - Open-label follow-up study for certain participants in trials of the 0.75 mg once-daily fixed-dose formulation with doravirine.
  - Results from the switch A and switch B islatravir studies were published in *Lancet HIV* on May 8, 2024 (see Molina et al. and Mills et al.). The results showed that switching to the islatravir regimen achieved comparable viral load suppression, but both papers note that decreases in CD4 T cell and white blood cell counts preclude further development of the 0.75 mg dose.
- Results from a trial of the 0.75 mg once-daily fixed-dose formulation with doravirine in heavily treatment-experienced people with HIV were published in the journal *AIDS* in February 2026, reporting viral load benefit but noting that further studies of the higher islatravir dose are precluded by the association with CD4 T cell decreases. The lower dose is unsuitable for this population because of inadequate suppression of drug-resistant HIV variants.
- Presentations at CROI 2023 described the analyses supporting the decision to evaluate 0.25 mg daily dosing 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, pharmacokinetics (PK), and antiretroviral activity results were published in *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.

Product	Class/Type	Company	Development Phase
Lepetegravir (formerly GS-1720)	**INSTI**	**Gilead**	**Phase II/III**

- LA integrase strand transfer inhibitor (INSTI) initially evaluated under a completed phase I open-label master protocol.
- Preliminary results presented at CROI 2024.
- Two phase II/III trials were started to test lepetegravir in combination with lenacapavir pacfosacil as an oral weekly regimen, but both were put on hold by FDA in mid-2025 due to evidence of CD4 T cell and absolute lymphocyte count declines:
  - WONDERS-1 involves participants on Biktarvy with at least six months of viral load suppression either continuing or switching to weekly lepetegravir/lenacapavir pacfosacil. At the time of writing, the trial remains on hold.
  - WONDERS-2 randomized ART-naive individuals to either weekly lepetegravir/lenacapavir pacfosacil or Biktarvy, but the trial was terminated by Gilead in April 2026.
  - In both cases the study design included a phase II portion administering separate lepetegravir and lenacapavir pacfosacil pills for the first 24 weeks, followed by a phase III assessment of a fixed-dose combination pill until week 48.

Lenacapavir pacfosacil (formerly GS-4182)	**Capsid inhibitor**	**Gilead**	**Phase II/III**

- An oral prodrug of lenacapavir.
- Being tested in combination with lepetegravir as an oral weekly regimen in two phase II/III trials (see prior lepetegravir table entry). Clinical trials currently on hold.
- Results from a completed phase I study presented at AIDS 2024, reporting drug levels twofold higher than standard oral lenacapavir, favorable tolerability, and a PK profile appropriate for weekly dosing.

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 the superiority of albuvirtide plus ritonavir-boosted lopinavir over lopinavir/ritonavir plus two NRTIs as second-line therapy.
- Three clinical trials combining albuvirtide with the bNAb 3BNC117 (NCT03719664, NCT04560569, NCT04819347) were registered many years ago with estimated completion dates in 2022. The clinicaltrials.gov records show "unknown status" but results from the trial involving people with multidrug-resistant HIV (NCT04560569) were published in *BMC Infectious Diseases* in March 2026. A substantial proportion of the 16 participants were able to suppress HIV viral load below 50 copies/mL and the authors advocate that further development is warranted.
- A poster presentation at the 2023 EACS described a possible effect in enhancing CD4 T cell recovery in people with suboptimal CD4 T cell increases on standard ART. These results were subsequently published in the journal *Frontiers in Cellular and Infection Microbiology* in June 2024.

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 to the FDA for the treatment of multi-drug-resistant HIV because of problems with the data. The fate of the drug in the context of HIV appears very uncertain, with the company reported to be focusing on nonalcoholic 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. On February 29, 2024, CytoDyn announced the hold on HIV had been lifted but, on a subsequent investor call, stated that "we're choosing to prioritize other applications at this time."
- The FDA previously rejected a Biologics License Application 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 700 mg dose group (6 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 results were published in *JAIDS* on June 1, 2025.
- The CD01 phase Ib 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 CCR5D32 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 CCR5D32 mutation. Sacha is also involved in research evaluating whether leronlimab can be delivered via an adeno-associated virus vector, with results from a macaque study published recently in *Science Translational Medicine*.

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. However, the protocol is now listed as withdrawn because of "difficulty with recruitment and drug production."
- In January 2025, researchers at NIAID published a case report of successful viral load suppression in a person with multidrug-resistant HIV for whom semzuvolimab was obtained via expanded access.
- A phase III trial in combination with an optimized background ART regimen in treatment-experienced participants was registered and projected to be completed this year, but hasn't opened for enrollment.
- 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 (a 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.

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

- Initially evaluated in a phase I trial in 2014/2015.
- A subsequent dose-ranging phase IIb switch study of ulonivirine in combination with islatravir was stopped in 2021 due to reductions in CD4 T cell and absolute lymphocyte counts related to the latter drug. Results presented at IAS 2025 showed that viral load suppression was maintained in all recipients, and dose adjustments have allowed for continued evaluation of a once-weekly ulonivirine/islatravir combination. A separate poster at IAS 2025 describes the PK analysis for selecting an appropriate weekly dose.
- A phase II/III trial of weekly ulonivirine/islatravir in people with HIV naive to ART began recruiting in December 2025.
- Favorable PK, antiretroviral activity, and resistance profile were reported in studies published in *JAIDS* 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 planned phase I study of ulonivirine in HIV-negative participants with mild or moderate hepatic impairment has not yet opened for enrollment.

N6-LS (VH3810109)	**bNAb**	**ViiV**	**Phase IIb**

- bNAb licensed from the NIH by ViiV Healthcare.
- Results were presented at CROI 2026 from an ongoing phase IIb study (the EMBRACE trial) evaluating N6-LS (delivered either via infusion or subcutaneously with rHuPH20 every four months) combined with the LA injectable integrase inhibitor cabotegravir given monthly in adults with HIV. The majority of participants who switched from a standard oral ART regimen maintained viral load suppression after 12 months of follow up (94% in the infusion group, 90% in the subcutaneous injection group). Five recipients of N6-LS experienced virologic failure but resuppressed after returning to oral ART. Injection site reactions were frequent in the subcutaneous group, and the next step of the study will only administer IV infusions of N6-LS every six months in combination with LA cabotegravir every two months.
- Results from the phase II BANNER trial were published in the *Journal of Infectious Diseases* in December 2025, following prior presentations at HIV Glasgow 2022, CROI 2023, and CROI 2024. A single infusion or subcutaneous injection was associated with a greater than 0.5 log reduction in viral load in most recipients with no serious adverse events. Virologic response was associated with HIV susceptibility to the bNAb (retrospectively assessed from baseline samples).
- A phase I trial investigating subcutaneous administration with recombinant human hyaluronidase PH20 (rHuPH20), which is intended to allow for large volumes of antibody to be delivered via the subcutaneous route, has been completed in HIV-negative participants. Results were reported at CROI 2024: injection site reactions, including grade 3 erythema (reddening of the skin), were common but typically resolved within seven days.

VH4524184	**INSTI**	**ViiV**	**Phase IIb**

- In early 2026, ViiV began a phase IIb study evaluating oral VH4524184 combined with FTC/TAF, compared to a standard HIV treatment containing dolutegravir and lamivudine (DTG/3TC).
- A small phase IIa proof-of-concept trial has been completed in 28 people with HIV who hadn't yet started ART. Results demonstrating safety and potent anti-HIV activity were presented at CROI 2025 and published in *Clinical Infectious Diseases* on June 12, 2026.
- Phase I trial of LA injectable formulations in HIV-negative people is recruiting, with preliminary favorable PK results reported at CROI 2026 that support the possibiity of twice-yearly dosing.
- Results from the first-in-human trial in HIV-negative participants published in *Clinical Infectious Diseases* in March 2025, demonstrating safety with minimal potential for significant drug interactions.
- A drug-drug interaction study looking at the effects of VH4524184 taken together with an oral contraceptive (Loestrin) in HIV-negative cisgender women has been completed.
- A phase I study to assess absorption, food effects, and the potential for drug interactions was completed in 2025.

Product	Class/Type	Company	Development Phase
VH4011499	**Capsid inhibitor**	**ViiV**	**Phase IIa**

- An international phase IIa proof-of-concept study recruited people with HIV naive to ART to assess antiretroviral activity, safety, tolerability, and PK of oral VH4011499. Results were presented at CROI 2025, indicating potent anti-HIV activity and promising safety and drug interaction profiles.
- PK results from phase I trials and modeling for future oral dose selection were presented at CROI 2026.
- A first-in-human phase I trial evaluating safety, tolerability, and PK in HIV-negative participants has been completed, with results published in *Infectious Diseases and Therapy* in April 2025.
- Preliminary results were presented at CROI 2026 from a phase I trial evaluating single and multiple ascending subcutaneous and intramuscular LA doses in HIV-negative participants. The injections were well tolerated and the PK results supportive of twice-yearly intramuscular administration. A phase IIb trial in adults naive to ART (named CINERGY) is due to be launched in the second half of 2026.
- Included in a phase I protocol assessing single and multiple ascending subcutaneous and intramuscular LA doses administered to HIV-negative participants.
- Phase I assessment of the effects of food on bioavailability completed in October 2024.

CL-197	**NRTI**	**Henan Genuine Biotech Co., Ltd.**	**Phase IIa**

- Phase IIa trial of oral CL-197 capsules taking place in Beijing, China. Development appears focused on regional market.
- Phase I trial in HIV-negative participants completed in 2024.

ACC017	**INSTI**	**Jiangsu Aidea Pharmaceutical Group Co., Ltd.**	**Phase Ib/IIa**

- Integrase inhibitor in development for regional market, a phase Ib/IIa trial in combination with FTC/TAF is ongoing in Beijing, China.
- Laboratory studies of antiretroviral activity published in the journal *Viruses* in December 2025.

GS-3242	**INSTI**	**Gilead**	**Phase II**

- LA injectable integrase inhibitor.
- A phase II trial investigating injectable GS-3242 combined with injectable lenacapavir compared to oral Biktarvy was registered in June 2026.
- A phase I trial has been completed in people with HIV naive to ART or integrase inhibitors at multiple sites in the US, Mexico, and Thailand. Results reported at CROI 2026 demonstrated strong antiretroviral activity, a low rate of mild adverse events, and PK consistent with the potential to dose "at least every four months." Higher doses amenable to twice-yearly administration are now being evaluated.

Lipovirtide	**Fusion inhibitor**	**Shanxi Kangbao Biological Product Co., Ltd.**	**Phase II**

- A phase II trial in China combining lipovirtide with lamivudine and tenofovir has been completed. To our knowledge, results have yet to be publicly presented.
- A phase I trial evaluating a single injection of lipovirtide in treatment-naive people with HIV and a 24-person phase I trial of multiple dosing have been completed in China.

LP-98	**Fusion inhibitor**	**Shanxi Kangbao Biological Product Co., Ltd.**	**Phase I/II**

- Injectable HIV fusion inhibitor candidate reported to suppress viral replication in the SHIV/macaque model (papers published in *Cell Reports* in September 2025 and *Cell* in January 2022).
- Phase I/II clinical trial in people with HIV naive to ART is underway in Tianjin, China.
- A completed phase I/II trial tested multiple subcutaneous injections in people with HIV, to our knowledge public disclosure of the results is pending.
- A completed phase I trial in China assessed safety, tolerability, and PK of LP-98 administered by either subcutaneous injection or intravenous infusion in people without HIV. The study also monitored for the induction of anti-drug antibodies against LP-98. To our knowledge, public disclosure of the results is pending.

Product	Class/Type	Company	Development Phase
MK-8527	**NRTTI**	**Merck**	**Phase I**
■ Merck disclosed that that MK-8527 is an NRTTI in a September 2022 press release. ■ Phase I trials in people with HIV completed in South Africa and Romania. ■ Results from both studies were first presented at CROI 2024, demonstrating viral load declines of around 1 log_{10}, with no serious adverse events. The data were published in *Clinical Infectious Diseases* in March 2026, with the paper's conclusion indicating that the focus is now on HIV prevention: "*The safety and PK profiles of MK-8527 support continued clinical investigation for use as once-monthly oral PrEP.*" ■ Two PrEP efficacy trials are now underway, see TAG's 2026 PrEP and Microbicides Pipeline Report. ■ Safety and PK results in HIV-negative participants published in *Clinical and Translational Science* in September 2025.			
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. ■ The phase IIa trial has been completed, with results pending. ■ A paper published in *PLoS Pathogens* in July 2021 described preclinical results.			
MK-4646	**NNRTI, TACK**	**Merck**	**Phase I**
■ Promising preclinical results with NNRTI TACK molecules reported in the journal *Science Translational Medicine* in February 2023. ■ Multiple dose phase I study in people with HIV completed at sites in Moldova and Romania. ■ Recently registered phase I trial is studying MK-4646 in combination with Biktarvy and dolutegravir in HIV-negative participants. ■ First-in-human phase I trial in HIV-negative participants completed in Belgium in 2024, results pending.			
VH4527079	**Bispecific bNAb**	**ViiV**	**Phase I**
■ Ongoing phase I trial in people with HIV and HIV-negative participants to evaluate the safety, tolerability, and PK of single and multiple doses given by subcutaneous injection or intravenous infusion.			
GS-3107	**Capsid inhibitor**	**Gilead**	**Phase I**
■ LA oral lenacapavir prodrug (converted into the active drug in the body). ■ Listed as being in a phase I trial on the Gilead website pipeline page, but the study isn't registered in clinicaltrials.gov. Information indicating the protocol is recruiting HIV-negative participants in Baltimore can be found on the Instagram account of the contract research organization Pharmaron.			
VH4770359	**N/A**	**ViiV**	**Phase I**
■ A phase I first-in-human trial to evaluate safety, tolerability, and PK of orally administered VH4770359 was registered in April 2026, no further information currently available.			

TABLE ABBREVIATIONS

ART: antiretroviral therapy

ARV: antiretroviral

ASM: American Society for Microbiology

BLA: Biologics License Application

bNAb: broadly neutralizing antibody

CROI: Conference on Retroviruses and Opportunistic Infections

EACS: European AIDS Clinical Society / European AIDS Conference

FDA: US Food and Drug Administration

INSTI: integrase strand transfer inhibitor

LA: long-acting

NIAID: US National Institute of Allergy and Infectious Diseases

NIH: National Institutes of Health

NNRTI: non-nucleoside reverse transcriptase inhibitor

NRTI: nucleoside reverse transcriptase inhibitor

NRTTI: nucleoside reverse transcriptase translocation inhibitor

PK: pharmacokinetic(s)

PrEP: Pre-exposure prophylaxis

SHIV: Simian-human immunodeficiency virus

TACK: targeted activator of cell kill