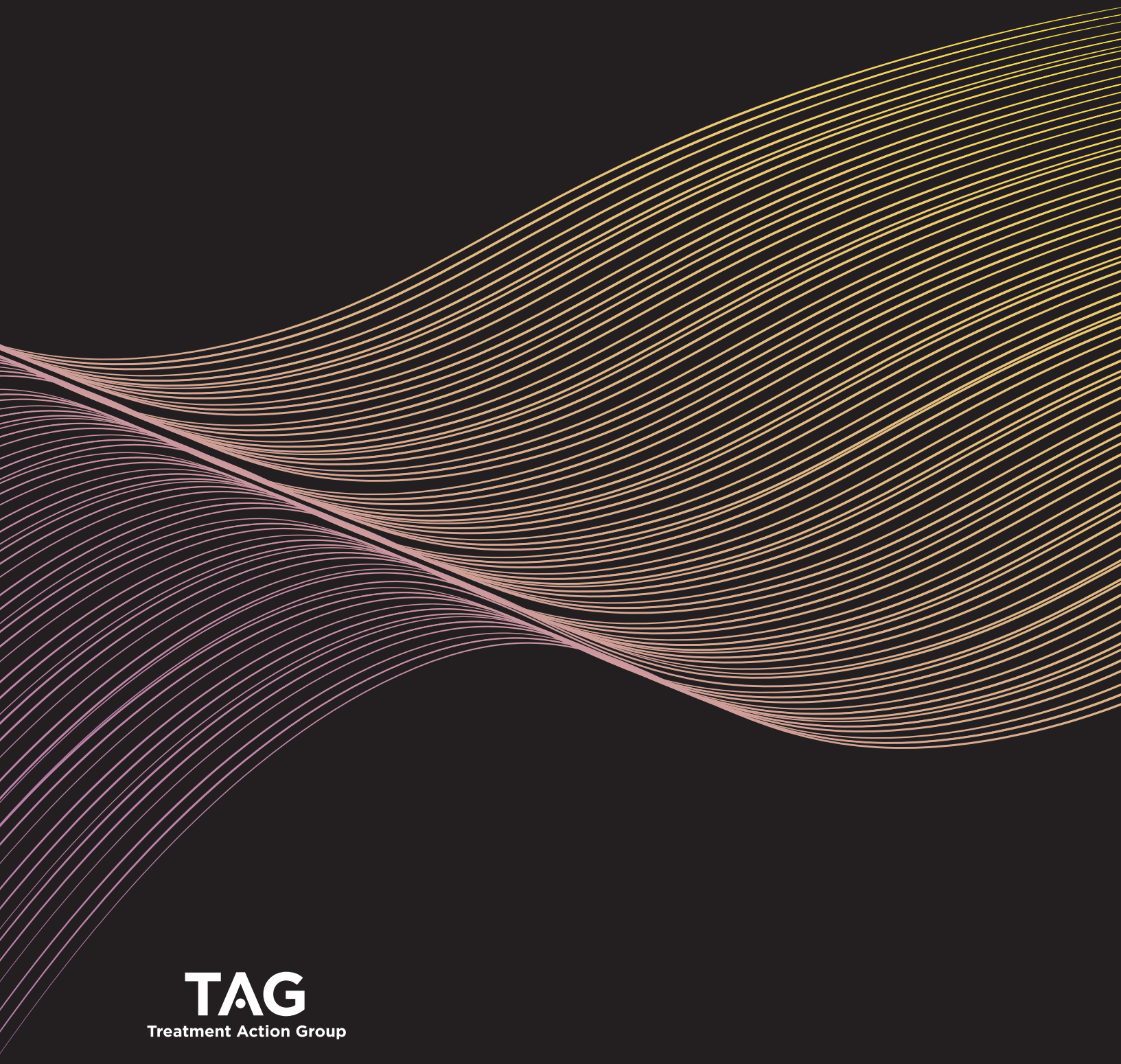
Pipeline Report » 2026

PrEP and Microbicides



TAG
Treatment Action Group

PrEP and Microbicides Pipeline 2026

By Richard Jefferys

Significant developments for the pre-exposure prophylaxis (PrEP) pipeline over the past year include Merck's launching of two efficacy trials testing monthly oral alimatravir (formerly known as MK-8527) and Gilead filing an application with the Food and Drug Administration (FDA) to approve a weekly oral lenacapavir pill for HIV prevention.

The two Merck PrEP efficacy trials are currently enrolling, with estimated completion dates in 2027:

- EXPrESSIVE-11 is recruiting cisgender men, transgender women, transgender men, and gender nonbinary persons aged 16 years or over at risk of exposure to HIV via receptive anal sex. The protocol will enroll an estimated 4,390 participants at sites in Argentina, Brazil, Chile, Colombia, Dominican Republic, France, Guatemala, Kenya, Malaysia, Peru, Philippines, South Africa, Switzerland, Thailand, and the United States.

- EXPrESSIVE-10 is recruiting an estimated 4,580 cisgender women (aged 16–30 years) at risk of exposure to HIV via heterosexual sex at sites in Kenya, South Africa, and Uganda.

Alimatravir is a nucleoside reverse transcriptase translocation inhibitor (NRTTI) with potent anti-HIV activity. The drug has demonstrated protection against infection in the SIV/macaque model, and studies in people with and without HIV have shown safety and generated the data used to select the dosing regimen for the efficacy trials.

Ahead of the trial results, Merck has announced an access plan that involves voluntary licensing deals with seven generic drug manufacturers to supply alimatravir for 129 low- and middle-income countries. The plan has received some praise as a proactive step toward enhancing access, but activists have pointed out that it doesn't go far enough because it omits multiple middle-income countries with significant HIV prevalence.

The advancement of alimatravir has supplanted Merck's original plan for developing a long-acting oral PrEP option with another NRTTI, islatravir. That plan was derailed by an unanticipated adverse effect on lymphocyte counts precluding the advancement of islatravir for monthly administration. Research into more frequent dosing for HIV treatment has continued, leading to the recent approval of a daily islatravir/doravirine combination pill.

Gilead's effort to gain FDA PrEP licensure for once-weekly oral lenacapavir is based on the robust prevention efficacy obtained with the twice-yearly injectable form of the drug in the PURPOSE 1 and PURPOSE 2 trials. The application was unexpected and may indicate that Gilead is seeking to advance their product to market ahead of Merck's potential monthly oral PrEP option.

Injectable lenacapavir's infrequent dosing has made it a focus for global PrEP rollout, and the company is hoping to further improve convenience with the launch of the first clinical trial of once-yearly administration based on supportive pharmacokinetics (PK) data. Several other studies of twice-yearly lenacapavir are in follow up but no longer recruiting participants:

- PURPOSE 3, a collaboration with the HIV Prevention Trials Network (HPTN) assessing the PK, safety, and acceptability of twice-yearly injectable lenacapavir versus daily Truvada for PrEP in 253 cisgender women in the United States.

- PURPOSE 4, another collaboration with the HPTN evaluating the same parameters in 181 people who inject drugs.

- PURPOSE 5, taking place in France and the United Kingdom with, according to Gilead, *"an intentional focus on recruiting participants from groups across France and the United Kingdom that are disproportionally affected by HIV and often underrepresented in clinical trials."* The study has enrolled 268 participants.

The innovative design of the PURPOSE 1 efficacy trial in cisgender women allowed for participants who became pregnant to continue with the study, generating encouraging data on the safety and PK of lenacapavir PrEP in this population. Results were published in Lancet HIV on July 16, 2026, and the authors conclude, *"these data support accelerated access for lenacapavir in pregnant and lactating women."*

ViiV Healthcare was the first manufacturer to receive approval for long-acting injectable PrEP with the integrase inhibitor cabotegravir (trade name Apretude) given every other month. The company is now assessing expanding the dosing interval with "ultra long-acting" (ULA) formulations, including a 191-person phase 2b study and a phase I assessment of switching from the approved long-acting cabotegravir to an ULA version administered every four months.

New PrEP & microbicide clinical trials registered since the 2025 edition of the Pipeline Report include:

- A phase 2b assessment of a single dual prevention pill (DPP) compared to a two-pill regimen (2PR) in cisgender women sponsored by HPTN. The DPP contains emtricitabine/tenofovir disoproxil fumarate (FTC/TDF) plus a combined ethinyl estradiol/levonorgestrel oral contraceptive (COC), the 2PR consists of a daily oral FTC/TDF pill and a separate COC pill. Study sites are located in Eswatini, Uganda, and Zimbabwe, with recruitment anticipated to begin later this year.

- Yaso Therapeutics Corporation's phase I study evaluating the safety and PK of the contraceptive YASO GEL (PPCM-01). The protocol will use samples to conduct laboratory investigations of antimicrobial activity against both *Neisseria gonorrhoeae* and HIV based on previously reported findings with the polyphenylene carboxymethylene component of the gel.

The funding and policy environment since the change of US administration in January 2025 continues to pose a vast challenge to advancing new interventions, not just for HIV prevention and treatment but for all conditions. The latest threat is a heinous proposal from the Office of Management and Budget to assert political control over all federal grantmaking, which has received nearly half a million public comments – the vast majority in opposition. The HIV clinical trial networks that are vital for developing improved therapeutics and prevention options are also in peril, with progress toward awarding the next seven year cycle of funding currently stalled.

As noted in all TAG's HIV Pipeline Reports since the election, it's vital that people in the US who care about science and medical research connect with advocacy efforts such as Stand Up for Science and Defend Public Health to do whatever they can to alert Congressional representatives, media, and their communities about the crisis.

Table 1: Pre-exposure Prophylaxis (PrEP)

Agent	Class/Type	Manufacturer/Sponsor	Delivery	Status
Cabotegravir NCT06134362 (long-term follow up of participants in HPTN 083, HPTN 084, and associated substudies) NCT03164564 (cisgender women) NCT06741397 (four-month dosing interval) NCT06786520 (switch from two-month to four-month dosing formulations) NCT05418868 (subcutaneous delivery with recombinant human hyaluronidase PH20) NCT06970223 (Phase I tolerability and acceptability study with lenacapavir)	INSTI	ViiV Healthcare	IM, SC	Phase III Phase IIb/III Phase II Phase I

- Approved by the FDA for adults and adolescents at risk of HIV acquisition on December 20, 2021, World Health Organization guidelines recommending long-acting cabotegravir (CAB LA) as an HIV prevention option issued July 28, 2022.
- Also on July 28, 2022, ViiV Healthcare and the Medicines Patent Pool announced a voluntary licensing agreement designed to allow for generic manufacture and to "help enable access in 90 countries."
- Massachusetts General Hospital is sponsoring ASCEND, an implementation study in people who inject drugs.
- Johns Hopkins University is sponsoring a phase I trial testing the safety, PK, and pharmacodynamics (PD) of CAB LA with a particular focus on interactions with therapeutic hormones.
- Phase I and phase II studies of CAB LA formulations designed for administration every four months are fully enrolled and in follow up.
- Results from HPTN 083 and 084 were published in the *New England Journal of Medicine* and *The Lancet*, respectively. The open-label extension phase of HPTN 084 remains ongoing, HPTN 083 is now completed.
- An April 2025 paper in the *Lancet HIV* reported findings from the HPTN 084-1 study, indicating that CAB LA is a *"safe, tolerable, and acceptable option for the prevention of HIV in adolescent girls."*
- Secondary analysis from HPTN 083 demonstrating maintenance of efficacy in the setting of bacterial sexually transmitted infections was published in *Clinical Infectious Diseases* in November 2024.
- Preliminary results from a secondary analysis from HPTN 084 describing safety and PK in pregnant women was reported in the Journal of the *International AIDS Society* in January 2025.
- A tertiary evaluation of PK interactions between cabotegravir and hormonal contraceptives in HPTN was published in the *Journal of the International AIDS Society* in October 2025, reporting that *"clinically significant interactions between CAB-LA and HC [hormonal contraception] are not expected."* A plan to also assess hormonal contraceptive interactions with F/TDF in the control arm was stymied by low adherence.
- The unique challenges of diagnosing HIV infection in recipients of CAB LA PrEP were described in a July 2024 paper in the *New England Journal of Medicine*. The authors note that the presence of the drug can suppress viral replication leading to delayed and diminished levels of HIV antigen and anti-HIV antibodies detected by standard tests.
- A report on the first year of the open-label phase of HPTN 083 was published in the *Lancet HIV* in November 2023. CAB LA continued to show high efficacy compared to Truvada, but adherence to both interventions declined and 18 additional cases of HIV acquisition were documented among recipients (most occurred more than six months after the last injection). In terms of adverse events, higher rates of hypertension, total and LDL cholesterol, malaise, and proctitis were observed in CAB LA recipients and continue to be carefully monitored.
- A presentation on the open-label extension phase of HPTN 084 at the IAS 2023 conference reported that a high proportion of participants (78%) chose CAB LA as their favored PrEP option; the results were subsequently published in *PLoS One* in October 2024.
- A phase I trial testing two new potentially longer-acting formulations codenamed F or G in participants without HIV has been completed, with results submitted to clinicaltrials.gov on July 20, 2026, and pending publication.
- A trial launched in June 2022 (NCT05418868) is investigating new formulations with the potential for dosing every four months. Preliminary results were reported at CROI 2024. The study also assessed whether recombinant human hyaluronidase PH20 (rHuPH20) can improve delivery of CAB LA, but this approach has been discontinued due to high rates of injection site reactions and unfavorable PK.

Agent	Class/Type	Manufacturer/Sponsor	Delivery	Status
▪ A substudy of HPTN 083 investigated the safety, tolerability, and acceptability of CAB LA among HIV-uninfected adolescents assigned male at birth, including men who have sex with men (MSM), transgender women, and gender-nonconforming people. The enrollment target was 50 participants, but the study is now listed as completed as of July 2023 with a total of 9 participants enrolled. Favorable results were reported at the 2024 R4P conference. ▪ ViiV Healthcare is sponsoring a phase I tolerability and acceptability study with HIV-negative participants that involves switching from CAB LA to lenacapavir or vice versa. Preliminary results published in *Advances in Therapy* indicate greater acceptability of intramuscular cabotegravir injections, but follow up is short (22 days) and the design doesn't take into account other considerations such as the different dosing intervals in real world use. ▪ A phase I trial assessing PK, safety, tolerability, and acceptability of CAB LA in adult Chinese men at low risk for HIV acquisition has been completed, with results published in *Antimicrobial Agents and Chemotherapy* on March 15, 2022.				
Lenacapavir NCT07047716 (PURPOSE 365) NCT04994509 (PURPOSE 1) NCT04925752 (PURPOSE 2) NCT06101329 (PURPOSE 3, HPTN 102) NCT06101342 (PURPOSE 4, HPTN 103) NCT06513312 (PURPOSE 5) NCT06970223 (Phase I tolerability and acceptability study with CAB LA)	Capsid inhibitor	Gilead	SC, oral	Phase III Phase I

▪ An inhibitor of the HIV capsid protein approved by the FDA for use as a treatment in December 2022. The long-acting formulation for subcutaneous injection is administered every six months.
▪ Injections every six months approved for PrEP by the FDA on June 18, 2025.
▪ Gilead sponsored two phase III efficacy trials:
  ▪ PURPOSE 1 evaluated lenacapavir, Descovy, or Truvada PrEP in 5,368 young women aged 16–25 in South Africa and Uganda. Results were published in the *New England Journal of Medicine* on July 24, 2024. An update presented at CROI 2026 reported that a further 78 incident cases of HIV acquisition occurred after the primary analysis and before the end of randomization, 2 in the lenacapavir arm and 52 in the Truvada arm. No new safety concerns have emerged.
  ▪ PURPOSE 2 compared lenacapavir to Truvada PrEP in 3,295 cisgender men, transgender women, transgender men, and gender nonbinary persons who have condomless receptive anal sex with partners assigned male at birth. Study sites located in Argentina, Brazil, Mexico, Peru, Puerto Rico, South Africa, and the United States. Results were published in the *New England Journal of Medicine* on November 27, 2024. Extended follow up described at CROI 2026 documented a further 15 cases of HIV acquisition before the conclusion of the randomized blinded phase, 3 among lenacapavir recipients and 12 in the Truvada group. As with PURPOSE 1, the safety profile of lenacapavir was unchanged.
  ▪ All participants in both trials have been offered open-label lenacapavir and follow up continues.
▪ A phase III trial of a once-yearly formulation has enrolled 339 people and is in follow up. PK modeling data supporting the feasibility of the yearly schedule was presented at CROI 2026.
▪ A substudy involving 124 adolescent participants in PURPOSE 1 was presented at CROI 2025, reporting that lenacapavir was safe and well tolerated with similar PK to adults.
▪ Additional smaller studies focused on PK, safety, and acceptability are ongoing in cisgender women and people who inject drugs in the United States (PURPOSE 3/HPTN 102 and PURPOSE 4/HPTN 103, respectively) as well as in vulnerable populations in France and the United Kingdom (PURPOSE 5).
▪ Promising results reported for once-yearly administration at CROI 2025 and in the *Lancet*.
▪ ViiV Healthcare is sponsoring a phase I tolerability and acceptability study with HIV-negative participants that involves switching from CAB LA to lenacapavir or vice versa. As noted in the previous table entry, preliminary results have been published in *Advances in Therapy*.				

Agent	Class/Type	Manufacturer/Sponsor	Delivery	Status
Alimatravir (formerly MK-8527) NCT07044297 (EXPrESSIVE-11) NCT07071623 (EXPrESSIVE-10) NCT07600775 (interaction study with rifampin)	NRTTI	Merck	Oral PrEP	Phase III Phase I

- An alternate NRTTI PrEP candidate being developed by Merck after the discontinuation of islatravir. Reported to be a highly potent inhibitor of HIV replication and suitable for oral monthly dosing.
- Two phase III efficacy trials now underway:
  - EXPrESSIVE-11, recruiting cisgender men, transgender women, transgender men, and gender nonbinary persons aged 16 years or over at risk of exposure to HIV via receptive anal sex. The protocol will enroll an estimated 4,390 participants at sites in Argentina, Brazil, Chile, Colombia, Dominican Republic, France, Guatemala, Kenya, Malaysia, Peru, Philippines, South Africa, Switzerland, Thailand, and the United States.
  - EXPrESSIVE-10 is recruiting an estimated 4,580 cisgender women (aged 16–30 years) at risk of exposure to HIV via heterosexual sex at sites in Kenya, South Africa, and Uganda.
- A phase IIa trial has been completed with people at low risk for HIV acquisition. A presentation at CROI 2026 described how the PK data from this and prior phase I studies contributed to dose selection for the phase III efficacy trials.
- Phase I PK study is completed, with favorable results from phase I PK studies conducted in Belgium published in *Clinical and Translational Science* in September 2025.
- A phase I trial has assessed PK in breast milk, plasma, and blood in lactating female participants, with results posted to clinicaltrials.gov.
- Several phase I evaluations of potential drug interactions are pending or completed, including:
  - A trial investigating interactions with rifampin, a drug used to treat latent tuberculosis.
  - In combination with carbamazepine, assessing whether drugs that induce the liver enzyme CYP3A4 alter the PK of alimatravir.
  - With the approved PrEP intervention Truvada (TDF/FTC).
  - With the oral contraceptive levonorgestrel and Ethinyl estradiol; results were presented at AIDS 2024 indicating alimatravir can be safely co-administered.

LP-98 NCT05933824	Fusion inhibitor	Shanxi Kangbao Biological Product Co., Ltd.	SC, IV	Phase I

- Injectable HIV fusion inhibitor candidate reported to have prevention efficacy in the SIV/macaque model.
- An exploratory phase I/II trial in people with HIV is ongoing in China.
- A phase I trial in China assessing safety, tolerability, and PK of LP-98 administered by either subcutaneous injection or intravenous infusion in people without HIV has been completed. The study also monitored for the induction of antibodies against the inhibitor (anti-drug antibodies). Results are pending.

Aspirin NCT03629327	Nonsteroidal anti-inflam-matory	University of Manitoba	Oral PrEP	Not applicable

- A trial that recruited women in Nairobi to assess the potential for aspirin to induce immune quiescence in the female genital tract has been completed. Analysis is now ongoing, with results pending. The aim is to develop a method of HIV prevention that works by reducing the availability of target cells for the virus at the site of exposure.
- Results from a pilot study (NCT02079077), published in *Frontiers in Immunology* in November 2021, indicate that aspirin levels were detectable in the genital tract and were associated with significant declines in the proportion of activated, potentially HIV-susceptible CD4+ T cells.

Table 2: Topical/Local PrEP and Multipurpose Technologies

Agent	Class/Type	Manufacturer/Sponsor	Delivery	Status
Microbicide Rings, Gels, Enemas, Films, and Other Insertables				
Tenofovir NCT06560684 (HPTN 106)	NtRTI	Johns Hopkins University/ HPTN	Enema	Phase II

- The HPTN 106 phase II study was completed in June 2026, with results pending. Participants were randomized to one of two eight-week on-demand product sequences: tenofovir (TFV) douche followed by oral F/TDF or oral F/TDF followed by TFV douche. For additional background, see the educational webinar sponsored by AVAC's Choice Agenda in August 2024.
- Information from the DREAM-04 study was published in *JAIDS* in May 2025, with lyophilized sachets appearing preferable to spray-dried.
- Results from a phase I trial, DREAM-03, were presented as a poster at CROI 2024. The approach was well tolerated, but the researchers note that use of nonmedicated douches after a TFV douche may reduce TFV levels.
- DREAM-02, a phase I study assessing the TFV enema used in sequence with tap water enemas has been completed, with results initially presented as a poster at CROI 2022 and subsequently published in the *Journal of Infectious Diseases* in May 2025. The investigators reported that a TFV douche prior to receptive anal sex produced good drug coverage of the colorectal tract. Based on the results, the authors recommended administration prior to receptive anal sex in future studies.
- A phase I study of the safety, PK, PD, and acceptability of a single-dose TFV douche in adolescents aged 15–24 (ATN DREAM) has been completed. Partial results were published in the journal *AIDS and Behavior* in May 2025, reporting that the approach was highly acceptable among young MSM, followed by additional information on safety, PK, and acceptability in the *Journal of Infectious Diseases* in June 2025.
- Results of DREAM-01 were published in the *Journal of Infectious Diseases* in November 2023. The trial was a phase I, open-label, dose-escalation, and variable osmolarity study to compare the safety, PK, PD, and acceptability of three formulations of a TFV enema. All three produced tissue concentrations above target levels and were well tolerated with no grade 2 or greater adverse events reported. Favorable acceptability results were reported in the journal *Sexually Transmitted Infections* in September 2024.

Dapivirine vaginal ring	NNRTI	Population Council (vaginal ring)	Monthly vaginal ring	Phase I (three-month ring)

- Licensed by regulatory authorities in Botswana, Eswatini, Kenya, Lesotho, Rwanda, South Africa, Uganda, and Zimbabwe.
- The Population Council acquired the rights to develop the dapivirine (DPV) vaginal ring from the International Partnership for Microbicides in October 2022, in partnership with manufacturer IMRES B.V.
- A trial in South Africa testing a three-month version of the ring containing a DPV dose of 100 mg reported results at the R4P 2024 conference, demonstrating superior PK to the monthly ring. The data were submitted to the European Medicines Agency for regulatory review in November 2025. The Population Council plans to follow with applications for approvals in sub-Saharan Africa and other regions, working in collaboration with Avantor's NuSil® brand silicone products on the three-month ring.
- Results from a completed phase IIIb trial in breastfeeding mother-infant pairs (MTN-043) were published in the *Lancet HIV* in February 2025, demonstrating safety and very limited drug exposure among infants, which, the authors state, *"support the recommendation for DVRs [dapivirine vaginal rings] as an additional HIV prevention choice during breastfeeding."*
- Additional data from the MTN-042 phase IIIb trial, addressing safety after initiation during the second trimester of pregnancy and in infants potentially exposed in utero, were published in *Lancet HIV* in November 2025 and March 2026, respectively. The authors note: *"Together with available maternal safety data, this supports use of the DVR and oral PrEP by pregnant women to prevent HIV."*
- Results from a demonstration project in Zimbabwe were published in *PLoS Global Public Health* in March 2025, indicating that the HIV incidence among ring users was similar to that observed with oral PrEP. Rates of continuation after six months of follow up were higher among ring users (64% versus 16% for oral PrEP). Participants cited the need for longer term application than monthly, supporting the advancement of the three-month formulation.
- An analysis of the reduction in HIV acquisition risk per sex act in the phase III efficacy trial published in the *Journal of Infectious Diseases* in December 2023 found that *"consistent ring use was associated with a 63% (95% CI, 33%–80%) per-sex-act HIV-1 risk reduction."* While encouraging, the wide confidence interval (CI) is an indicator of considerable uncertainty regarding the precise level of efficacy.

Agent	Class/Type	Manufacturer/Sponsor	Delivery	Status
▪ Results from a completed study in pregnant women were published in the *Journal of AIDS* in January 2024. The study abstract concludes: *"Adverse pregnancy outcomes and complications were uncommon when DVR and TDF/FTC were used in the third trimester of pregnancy, suggesting a favorable safety profile for both prevention products."* ▪ Results from the REACH study reporting high acceptability among adolescent girls and young women were published in the *Lancet HIV* in October 2023. ▪ Acceptability data from the ASPIRE efficacy trial were published in the journal *AIDS and Behavior* in March 2021. ▪ Phase I MTN-036/IPM 047 assessed the potential of a three-month vaginal ring. Results, presented at CROI 2021, demonstrate that the extended-duration rings were well tolerated and achieved higher DPV levels compared with monthly rings, supporting further evaluation. Acceptability data were published in *PLoS One* on February 22, 2022.				
TAF/EVG NCT06274398	NRTI/INSTI	CONRAD	Rectal insert	Phase I
▪ A phase I study sponsored by CONRAD investigating multiple doses has been completed at Emory University in Atlanta, Georgia. To our knowledge, results are pending. ▪ Researchers affiliated with CONRAD have published papers describing the tenofovir alafenamide/elvitegravir (TAF/EVG) formulation and a potential combination with doxycycline in the *Journal of Controlled Release* and *AAPS PharmSciTech*, respectively. ▪ Results from a phase I trial of the rectal insert (MTN-039) evaluating safety, acceptability, and concentrations of drug in the rectal tissue were presented at CROI 2023 (see abstract and related press release), indicating safety and the potential to suppress HIV infection of rectal tissue for up to three days.				
TAF/EVG NCT06087913	NRTI/INSTI	CONRAD	Vaginal insert	Phase I
▪ This trial at sites in the US, Kenya, and South Africa was completed but terminated prior to analysis due to the destruction of USAID by the current US administration. ▪ Results from a previous phase I study of the vaginal insert were published in *Frontiers in Cellular and Infection Microbiology* in April 2023, reporting that the intervention was found safe and acceptable and achieved drug concentrations that supported further development.				
Multipurpose Technologies				
Tenofovir + levonorgestrel NCT03762382	NtRTI/HC	CONRAD	Vaginal ring	Phase IIa
▪ The Centers for Disease Control and Prevention (CDC) and CONRAD collaborated on a phase IIa, 90-day safety, adherence, and acceptability study of intravaginal rings (IVRs) releasing TFV with and without levonorgestrel (LNG) among women in western Kenya (NCT03762382). Results were published in *Frontiers in Reproductive Health* in June 2023, indicating that the IVRs were safe and delivered drug levels likely to be associated with prevention of HIV and pregnancy. A subsequent publication in the journal *Scientific Reports* in July 2022 reported that the IVRs were safe and didn't adversely affect genital microbiota. According to a substudy published in *Contemporary Clinical Trials* in September 2022, acceptability was good, although women expressed concerns about potentially negative community perceptions. ▪ CONRAD has completed two phase I, safety, PK, and PD studies of the TFV/LNG IVR. Favorable results from a one-month evaluation were published in *PLoS One* in June 2018, and similarly positive findings from a 90-day study were presented at R4P 2021. Results from the 90-day assessment were published in *Frontiers in Cellular and Infection Microbiology* in March 2022.				

Agent	Class/Type	Manufacturer/Sponsor	Delivery	Status
DPP capsule (dual prevention pill containing Truvada PrEP and combined oral contraceptive) NCT07288190	NtRTI/HC	Population Council	Oral	Phase II

- Being developed by a coalition of partners for prevention of pregnancy and HIV acquisition in high-need countries.
- A phase 2b trial sponsored by the HPTN is expected to begin recruiting later this year. The study will compare a single DPP tablet to a 2PR in cisgender women. The DPP contains FTC/TDF plus a COC, the 2PR consists of a daily oral FTC/TDF pill and a separate combined COC pill. Study sites are located in Eswatini, Uganda, and Zimbabwe.
- Two phase II crossover trials comparing acceptability of an older, larger DPP capsule versus individual PrEP and contraceptive pills among adolescent girls and young women (as described in a paper in *BMJ Open*) have been conducted.
  - A study in Zimbabwe enrolled 30 participants, with results published in *AIDS & Behavior* in November 2025. The regimens were found safe, but adherence measured by dried blood spots was low and no differences in preference, acceptability, and adherence were identified.
  - The second trial enrolled 96 participants in South Africa, with results published in *JAIDS* in February 2026. Again adherence measured by dried blood spots was low, with a significant preference for the 2PR. The researchers note that the newer and smaller coformulated DPP tablet now under evaluation may achieve better acceptability.

Dapivirine + levonorgestrel NCT05041699	NNRTI/HC	Population Council	Three-month vaginal ring	Phase Ib

- A 90-day phase Ib study of the safety and PK of two different vaginal ring formulations (NCT05041699) at sites in Oregon and Pennsylvania has been completed; results are pending.
- A phase I study evaluating PK and safety of a vaginal ring containing DPV and LNG (MTN-030/IPM 041) was completed in 2017, with results presented at the 2018 R4P conference (abstract OA12.02LB). A 14-day period of evaluation showed the ring was well tolerated and achieved the desired drug levels.
- A phase I study of 90-day administration either continuously or on a cyclic schedule (28 days in/2 days out) was completed in October 2019 (MTN-044/IPM 053/CCN019, NCT03467347). Results demonstrating achievement of drug levels predicted to be efficacious in preventing HIV and pregnancy were presented at R4P 2021. The products were safe, with only one grade 4 adverse event reported (anemia related to cyclic use).
- A paper describing the results of both the MTN-030/IPM 041 and MTN-044/IPM 053/CCN019 studies was published in the open access journal *PLoS One* on June 5, 2024.
- Acceptability data from the MTN-030/IPM 041 and MTN-044/IPM 053/CCN019 studies was published in *PLoS One* in January 2025, showing higher acceptability of the monthly compared to the 90-day ring, with unanticipated vaginal bleeding emerging as a concern.

YASO GEL (PPCM-01) NCT07281404	Antimicrobial/ HC	Yaso Therapeutics Corporation	Gel	Phase I

- Pending phase I clinical trial will evaluate the safety and PK of YASO GEL in healthy adult participants. Samples will be used to conduct laboratory investigations of antimicrobial activity against both *Neisseria gonorrhoeae* and HIV, based on previously reported findings with the polyphenylene carboxymethylene (PPCM) component of the gel.

ABBREVIATIONS

CAB LA: long-acting cabotegravir

CDC: Centers for Disease Control and Prevention

COC: combined ethinyl estradiol/levonorgestrel oral contraceptive

CONRAD: Contraception Research and Development

CROI: Conference on Retroviruses and Opportunistic Infections

DPP: dual prevention pill

DPV: dapivirine

DVR: dapivirine vaginal ring

EVG: elvitegravir

FDA: U.S. Food and Drug Administration

FTC: emtricitabine

F/TDF: tenofovir disoproxil fumarate/emtricitabine

HC: hormonal contraception

HPTN: HIV Prevention Trials Network

IAS: International AIDS Society

IM: intramuscular injection

INSTI: integrase strand transfer inhibitor

IPM: International Partnership for Microbicides

IV: intravenous administration

IVR: intravaginal ring

LNG: levonorgestrel

MSM: men who have sex with men

MTN: Microbicide Trials Network

NNRTI: non-nucleoside analogue reverse transcriptase inhibitor

NRTI: nucleoside analogue reverse transcriptase inhibitor

NRTTI: nucleoside reverse transcriptase translocation inhibitor

NtRTI: nucleotide analogue reverse transcriptase inhibitor

PD: pharmacodynamics

PK: pharmacokinetics

PrEP: pre-exposure prophylaxis

R4P: HIV Research for Prevention Conference

SC: subcutaneous injection

TAF: tenofovir alafenamide

TDF: tenofovir disoproxil fumarate

TFV: tenofovir