

# Pipeline Report » 2024

PrEP and Microbicides



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Treatment Action Group

# PrEP and Microbicides Pipeline 2024

By Richard Jefferys

Major news for the pre-exposure prophylaxis (PrEP) pipeline was announced on June 20, 2024, when Gilead Sciences [issued a press release](#) disclosing that their twice-yearly injectable HIV capsid inhibitor lenacapavir demonstrated 100% efficacy in the PURPOSE 1 HIV prevention trial. Participants in the research protocol were 5,368 young cisgender women aged 16–25 in South Africa and Uganda, representing populations currently facing an extremely high lifetime risk of HIV acquisition. According to the press release, there were no cases of HIV acquisition among the 2,134 women in the lenacapavir group – the first time an HIV incidence rate of zero has been reported in an efficacy trial of any candidate prevention intervention.

The PURPOSE 1 results haven't yet been presented or published, but will be featured at the [AIDS 2024 conference](#) in Munich in late July. The study included two additional arms in which 2,136 cisgender women received Descovy and 1,068 received Truvada: there were 39 and 16 cases of HIV acquisition in these arms, respectively. All study participants are now being offered open label lenacapavir.

A novel aspect of the PURPOSE 1 design is that there was no placebo arm: the HIV incidence in different arms was compared to the background incidence in the population. Lenacapavir demonstrated efficacy by this metric (which was the primary endpoint), with the HIV incidence rate of zero contrasting with a background incidence rate of 2.41 per 100 person-years (2.4%). A secondary endpoint formally demonstrated that lenacapavir was statistically superior to Truvada.

There was no significant difference between HIV incidence in the Descovy group and the background incidence. Gilead [has been justifiably criticized](#) for not studying Descovy in cisgender women sooner, and while this trial was intended to address that concern the results don't provide evidence that could support licensure as PrEP for this population.

The lenacapavir results are understandably viewed as extremely encouraging, but many questions remain. Key among them is how rapidly the drug can be made affordable and accessible to those most in need. The majority of cases of HIV acquisition that are currently occurring in the world could be conceivably be prevented, but the most recent new PrEP option with the high efficacy – CAB LA – is still only available to relatively few. It's vital that lenacapavir is licensed and made available more rapidly.

Prior to the announcement of the PURPOSE 1 outcome, the [People's Medicines Alliance](#) and a coalition of over 300 prominent people [wrote to Gilead](#) demanding that the company enter into an agreement with the Medicines Patent Pool (MPP) to allow manufacturing of cheap generic versions of lenacapavir. In a statement issued on the [same day as the results](#), Gilead claims to be committed to working to ensure access, but the details are vague and appear to suggest voluntary licenses will be issued to individual generic manufacturers rather than entering into an agreement with the established MPP. Gilead also indicated that before filing with regulatory authorities for a PrEP indication they're waiting for the results of [PURPOSE 2](#), a partner trial assessing lenacapavir efficacy among 3,295 cisgender men, transgender women, transgender men, and gender-nonbinary individuals who have sex with partners assigned male sex at birth.

Additionally, the details of the PURPOSE 1 findings are likely to be important. Lenacapavir administration can be associated with the formation of nodules under the skin at the site of injection and, as with any intervention, understanding acceptability among different populations will be crucial. In studies of CAB LA, a very low number of cases of HIV acquisition occurred that were difficult to diagnose because the drug inhibited the replication of the virus in the body to low levels. A similar situation could theoretically occur with lenacapavir, but the information available is too limited to know if tests for low amounts of HIV genetic material have been performed in PURPOSE 1.

Beyond PURPOSE 1 & 2, Gilead is also sponsoring several additional ancillary studies:

- PURPOSE 3 is a collaboration with the HIV Prevention Trials Network (HPTN) that will evaluate the pharmacokinetics (PK), safety, and acceptability of twice-yearly injectable lenacapavir versus daily Truvada for PrEP in 250 cisgender women in the United States.
- PURPOSE 4 is another collaboration with the HPTN that will evaluate the same parameters in people who inject drugs, also with an enrollment target of 250 participants. All participants in both studies will be switched to Truvada PrEP after 52 weeks.
- PURPOSE 5 is taking place in France and the United Kingdom and, according to a Gilead press release, “has an intentional focus on recruiting participants from groups across France and the United Kingdom that are disproportionately affected by HIV and often underrepresented in clinical trials.” The protocol doesn’t appear to be entered into European or international clinical trial registries.

Events of the course of the next year will be critical for determining the full potential of lenacapavir PrEP, and whether the impressive and unprecedented benefits for cisgender women in PURPOSE 1 can be realized for all the people in greatest need.

CAB LA PrEP dosed every two months is now approved in many countries, but the manufacturer ViiV is continuing to investigate the possibility of extending the dosing interval. An ongoing study is assessing new formulations and also looked at whether recombinant human hyaluronidase PH20 (rHuPH20) could allow delivery of higher CAB LA doses by easing passage through the subcutaneous space. As reported at the 2024 Conference on Retroviruses and Opportunistic Infections (CROI), the latter approach was stymied by injection site reactions and unfavorable PK, but a new formulation of 800 mg in 2 ml showed promise for dosing every four months (injected either subcutaneously or intramuscularly) and remains in clinical development. The company hopes to eventually extend to twice-yearly dosing either with CAB or other antiretrovirals that are earlier in their developmental pipeline.

Since the publication of last year’s Pipeline Report, Merck has disclosed its decision to discontinue efforts to develop an implant formulation of islatravir for PrEP (a planned research protocol has been withdrawn). Islatravir is a novel antiretroviral nucleoside reverse transcriptase translocation inhibitor (NRTTI) that was originally slated to be investigated as an oral monthly PrEP option; however, an adverse effect on lymphocyte counts at higher doses has precluded further development for this indication. Treatment studies testing lower doses are continuing.

Merck is now focusing on an alternate experimental NRTTI, MK-8527, as a potential once-monthly oral PrEP candidate. Results from initial safety and PK studies in participants without HIV were presented at CROI 2024: there were no serious adverse events and drug absorption parameters supported further development. A phase IIa trial is now ongoing, testing low, medium, and high monthly doses in adults at low risk of HIV acquisition.

The only other newly registered study of a possible PrEP candidate involves an injectable fusion inhibitor named LP-98 being developed by a manufacturer in China, Shanxi Kangbao Biological Product Co., Ltd. The first-in-human trial is currently recruiting at the Henan Provincial Hospital for Infectious Diseases (Zhengzhou Sixth People's Hospital). A study published in the journal Cell in 2022 reported that LP-98 was highly efficacious as PrEP in rhesus macaques challenged with the simian HIV counterpart SIVmac239 or the HIV/SIV hybrid SHIV SF162P3.

Last year's PrEP pipeline table included the CAPRISA 018 trial investigating a tenofovir alafenamide subdermal implant in South African women, but this study was stopped due to a high rate of adverse reactions prompting early removal of implants (see CROI 2024 poster presentation). These results prevented a planned expansion into a phase II safety evaluation.

An extremely significant development for oral PrEP approaches that occurred over the past year is the emergence of evidence that differences in efficacy among cisgender women compared to men weren't necessarily driven by biological factors, as was originally inferred. New analyses suggest efficacy is similar when adherence levels are comparable and speculation that cisgender women required higher adherence levels to achieve efficacy may have been misplaced. These findings open up the possibility that on-demand oral PrEP could be an option for cisgender women at risk for HIV acquisition.

Over the past year, two new trials have been initiated of a microbicide candidate containing tenofovir alafenamide and the integrase inhibitor elvitegravir in a vaginal or rectal insert. The vaginal insert research is being conducted by MATRIX, a USAID project to advance the research and development of innovative HIV prevention products for women.

The MATRIX 001 phase I study will evaluate the safety and PK of the vaginal insert in an estimated 60 cisgender women at sites in Kenya, South Africa, and the U.S. Another related study, MATRIX 002, plans to assess candidate placebo prototype vaginal films at sites in Kenya, South Africa, Zimbabwe, and the U.S.

The rectal insert study is sponsored by CONRAD and aims to enroll 24 participants at Emory University in Atlanta, Georgia. The goal is to build on promising findings from a previous phase I assessment that were reported at CROI 2023.

The high efficacy of available PrEP options makes the development of alternative approaches challenging, but community advocates, researchers, and other stakeholders continue to emphasize the importance of providing people with choices to suit their individual needs and preferences. While the pipeline of novel PrEP and microbicide interventions remains narrow, it's encouraging to note that it has not closed entirely and a range of novel possibilities are still being pursued.

**Table 1: Pre-exposure Prophylaxis (PrEP)**

| Agent  | Class/Type | Manufacturer/Sponsor | Delivery | Status   |
|--|------------|----------------------|----------|--|
| <p>Cabotegravir</p> <p><a href="#">NCT06134362</a><br/>(long-term follow up of participants in HPTN 083, HPTN 084, and associated substudies)</p> <p><a href="#">NCT03164564</a> (cisgender women)</p> <p><a href="#">NCT02720094</a> (MSM and transgender women)</p> <p><a href="#">NCT06033547</a> (new formulations F or G in adults without HIV)</p> <p><a href="#">NCT05418868</a> (subcutaneous delivery with recombinant human hyaluronidase PH20)</p>  | INSTI      | ViiV Healthcare      | IM, SC   | <p>Phase III</p> <p>Phase IIb/III</p> <p>Phase I</p> |
| <ul style="list-style-type: none"> <li>Approved by the FDA for adults and adolescents at risk of HIV acquisition on December 20, 2021, World Health Organization guidelines recommending CAB LA as an HIV prevention option issued July 28, 2022.</li> <li>Also on July 28, 2022, ViiV Healthcare and the Medicines Patent Pool <a href="#">announced</a> a voluntary licensing agreement designed to allow for generic manufacture and “help enable access in 90 countries.”</li> <li>Results from HPTN 083 and 084 were published in the <i>New England Journal of Medicine</i> and <i>The Lancet</i>, respectively. Open-label extension phases of both trials are ongoing.</li> <li>A report on the first year of the open-label phase of HPTN 083 was <a href="#">published in the Lancet HIV</a> 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). The authors note that diagnosis of HIV infection was challenging and delayed in cases that occurred closer to CAB LA administration because suppression of viral replication delayed and diminished the levels of HIV antigen and anti-HIV antibodies detected by standard tests. 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.</li> <li>A presentation on the open-label extension phase of HPTN 084 <a href="#">at the IAS 2023 conference</a> reported that a high proportion of participants (78%) chose CAB LA as their favored PrEP option.</li> <li>The most recently initiated <a href="#">phase I trial</a> is testing two new potentially longer-acting formulations codenamed F or G in participants without HIV.</li> <li>A trial launched in June 2022 (<a href="#">NCT05418868</a>) is investigating new formulations with the potential for dosing every four months. Preliminary results were <a href="#">reported at CROI 2024</a>. The study also assessed whether <a href="#">recombinant human hyaluronidase PH20 (rHuPH20)</a> can improve delivery of CAB LA, but this approach has been discontinued due to high rates of injection site reactions and unfavorable PK.</li> <li>A <a href="#">substudy of HPTN 83</a> investigated the safety, tolerability, and acceptability of CAB LA among HIV-uninfected adolescents assigned male at birth, including men who have sex with men, 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 nine participants enrolled. Results are pending.</li> <li>A <a href="#">phase I trial</a> assessing PK, safety, tolerability, and acceptability of CAB LA in adult Chinese men at low risk for HIV acquisition has been completed with results <a href="#">published in Antimicrobial Agents and Chemotherapy</a> on March 15, 2022.</li> </ul> |            |                      |          |  |

| Agent  | Class/Type       | Manufacturer/Sponsor                  | Delivery  | Status    |
|--|------------------|---------------------------------------|-----------|-----------|
| <p>Lenacapavir</p> <p><a href="#">NCT04994509</a> (PURPOSE 1)</p> <p><a href="#">NCT04925752</a> (PURPOSE 2)</p> <p><a href="#">NCT06101329</a> (PURPOSE 3, HPTN 102)</p> <p><a href="#">NCT06101342</a> (PURPOSE 4, HPTN 103)</p> <p>PURPOSE 5 (unregistered)</p>   | Capsid inhibitor | Gilead                                | SC, oral  | Phase III |
| <ul style="list-style-type: none"> <li>■ 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.</li> <li>■ Gilead is sponsoring two phase III efficacy trials: <ul style="list-style-type: none"> <li>■ <a href="#">PURPOSE 1</a> evaluated lenacapavir, Descovy, or Truvada PrEP in 5,368 young women aged 16–25 in South Africa and Uganda. Results were announced on June 20, 2024 (see main text). All participants are now being offered open label lenacapavir.</li> <li>■ <a href="#">PURPOSE 2</a> is evaluating lenacapavir or Truvada PrEP in 3,295 cisgender men, transgender women, transgender men, and gender nonbinary people who have condomless receptive anal sex with partners assigned male at birth. The study has sites in Argentina, Brazil, Mexico, Peru, Puerto Rico, South Africa, and the United States. Results are expected in the second half of 2024 or early 2025.</li> </ul> </li> <li>■ Additional smaller studies focused on PK, safety, and acceptability are ongoing in cisgender women and people who inject drugs in the United States (<a href="#">PURPOSE 3/HPTN 102</a> and <a href="#">PURPOSE 4/HPTN 103</a>, respectively) as well as in vulnerable populations in France and the United Kingdom (<a href="#">PURPOSE 5</a>). The opening of <a href="#">PURPOSE 3 &amp; 4</a> was announced by the National Institutes of Health on June 4, 2024.</li> </ul> |                  |                                       |           |           |
| <p>Tenofovir alafenamide + emtricitabine (Descovy), tenofovir disoproxil fumarate + emtricitabine (Truvada)</p> <p><a href="#">NCT04937881</a></p>   | NtRTI/NRTI       | University of California, Los Angeles | Oral PrEP | Phase III |
| <ul style="list-style-type: none"> <li>■ A study in pregnant and postpartum women in South Africa to establish benchmarks of TFV diphosphate concentrations as measures of adherence in this population. Either Descovy or Truvada will be administered once daily under direct observation for eight weeks during pregnancy and for eight weeks in the postpartum period. The trial is now completed with a total of 50 participants, <a href="#">results have been submitted</a> to the <a href="#">clinicaltrials.gov</a> registry but not yet published.</li> </ul>  |                  |                                       |           |           |
| <p>MK-8527</p> <p><a href="#">NCT06045507</a></p>  | NRTTI            | Merck                                 | Oral PrEP | Phase IIa |
| <ul style="list-style-type: none"> <li>■ 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 <a href="#">suitable for oral monthly dosing</a>.</li> <li>■ A phase IIa trial is ongoing in people at low risk for HIV acquisition, and the company hopes to eventually pursue efficacy trials.</li> </ul>   |                  |                                       |           |           |

| Agent  | Class/Type                     | Manufacturer/Sponsor                        | Delivery  | Status         |
|--|--------------------------------|---|-----------|----------------|
| LP-98<br><a href="#">NCT05933824</a>   | Fusion inhibitor               | Shanxi Kangbao Biological Product Co., Ltd. | SC, IV    | Phase I        |
| <ul style="list-style-type: none"> <li>Injectable HIV fusion inhibitor candidate reported to have prevention efficacy in the SIV/macaque model.</li> <li>A phase I trial in China is assessing safety, tolerability, and PK of LP-98 administered by either subcutaneous injection or intravenous infusion in people without HIV. The study will also monitor for the induction of antibodies against the inhibitor (anti-drug antibodies [ADA]).</li> </ul>   |                                |   |           |                |
| Aspirin<br><a href="#">NCT03629327</a>   | Nonsteroidal anti-inflammatory | University of Manitoba                      | Oral PrEP | Not applicable |
| <ul style="list-style-type: none"> <li>An ongoing trial is recruiting 300 women in Nairobi to assess the potential for aspirin to induce immune quiescence in the female genital tract. The goal 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.</li> <li>Results from a pilot study (<a href="#">NCT02079077</a>), published in <i>Frontiers in Immunology</i> 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.</li> </ul> |                                |   |           |                |

Table 2: Topical/Local PrEP and Multipurpose Technologies

| Agent  | Class/Type | Manufacturer/Sponsor                                      | Delivery             | Status                  |
|--|------------|---|----------------------|-------------------------|
| <b>Microbicide Rings, Gels, Enemas, Films, and Other Insertables</b>   |            |   |                      |                         |
| Dapivirine ring<br>NCT05416021 (relative bioavailability trial of DPV ring-004 and DPV ring-008)<br>NCT03965923 (pregnant women)   | NNRTI      | Population Council (vaginal ring); DAIDS/MTN (rectal gel) | Monthly vaginal ring | Phase IIIb<br>Phase IIa |
| <ul style="list-style-type: none"> <li>■ Licensed by regulatory authorities in Kenya, South Africa, Uganda, Zambia, and Zimbabwe.</li> <li>■ The Population Council <u>acquired the rights</u> to develop the DPV ring from IPM in October 2022.</li> <li>■ Preliminary results from a demonstration project in Zimbabwe, as reported by AIDSMap, suggest the HIV incidence among users over the first six months was similar to that observed with oral PrEP in other studies.</li> <li>■ An analysis of the reduction in HIV acquisition risk per sex act in the phase III efficacy trial published in the <i>Journal of Infectious Diseases</i> 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 potentially encouraging, the wide confidence interval (CI) is an indicator of considerable uncertainty regarding the precise level of efficacy.</li> <li>■ Results from a completed study in pregnant women were published in the <i>Journal of AIDS</i> 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.”</li> <li>■ A phase IIIb safety evaluation of a monthly DPV ring in pregnant women and breastfeeding mother-infant pairs <u>has been completed</u>. Results were presented at CROI 2023, reporting a favorable safety profile.</li> <li>■ Results from the REACH study reporting high acceptability among adolescent girls and young women were <u>published in the Lancet HIV</u> in October 2023.</li> <li>■ Acceptability data from the ASPIRE efficacy trial were <u>published in the journal AIDS and Behavior</u> in March 2021.</li> <li>■ Phase I MTN-036/IPM 047 assessed the potential of a three-month vaginal ring. Results, <u>presented at CROI 2021</u>, 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 <i>PLoS One</i> on February 22, 2022. A larger trial comparing the standard ring with a three-month version containing a DPV dose of 100 mg has recently been completed in South Africa. Results are pending.</li> <li>■ The phase I trials MTN-026 and MTN-033 investigated a rectal DPV gel in men and women. Results from MTN-026 were presented at R4P 2021 and published in the journal <i>AIDS Research and Human Retroviruses</i> in April 2022. Rectal tissue concentrations were found to be inadequate, and the study authors concluded that “a long-acting reformulation or higher dose is likely needed to provide protection from anal sex.” Similar findings from MTN-033 were <u>published in the journal Antimicrobial Agents and Chemotherapy</u> in October 2022.</li> </ul> |            |   |                      |                         |
| TAF/EVG<br>NCT06274398   | NRTI/INSTI | CONRAD  | Rectal insert        | Phase I                 |
| <ul style="list-style-type: none"> <li>■ A new phase I study investigating multiple doses is recruiting in the U.S. at Emory University in Atlanta, Georgia, sponsored by <u>CONRAD</u>, as predicted last year by Dr. Sharon Riddler in an <u>interview with Juan Michael Porter II</u> for TheBodyPro.com.</li> <li>■ 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 <u>press release</u>), indicating safety and the potential to suppress HIV infection of rectal tissue for up to three days.</li> </ul>   |            |   |                      |                         |



| Agent   | Class/Type      | Manufacturer/Sponsor          | Delivery               | Status    |
|---|-----------------|-------------------------------|------------------------|-----------|
| TAF/EVG<br><a href="#">NCT06087913</a>  | NRTI/INSTI      | CONRAD                        | Vaginal insert         | Phase I   |
| <ul style="list-style-type: none"> <li>Results from a previous phase I study of the vaginal insert were published in April 2023, reporting that the intervention was found safe and acceptable and achieved drug concentrations that supported further development.</li> </ul>  |                 |                               |                        |           |
| Tenofovir<br>HPTN 106 (in development)  | NtRTI           | Johns Hopkins University/HPTN | Enema                  | Phase I   |
| <ul style="list-style-type: none"> <li>A phase II study is being planned by the HIV Prevention Trials Network (HPTN 106), with the latest projected date for starting enrollment being July 2024.</li> <li>Results of DREAM-01 were published in the <i>Journal of Infectious Diseases</i> 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.</li> <li>Results from another phase I trial, DREAM-03, were presented as a poster at CROI 2022. The investigators reported that a TFV douche prior to receptive anal sex produced good drug coverage of the colorectal tract. Based on their results, the authors recommend administration prior to receptive anal sex in future studies.</li> <li>DREAM-02, a third phase I study assessing the TFV enema used in sequence with tap water enemas, has been completed with results pending.</li> <li>A phase I study of the safety, PK, PD, and acceptability of a one-dose TFV douche in adolescents aged 15–24 (ATN DREAM) has been completed. Limited preliminary results are posted in the <a href="#">clinicaltrials.gov registry entry</a> and suggest that the product was safe, but to our knowledge the findings have not yet been presented or published.</li> </ul> |                 |                               |                        |           |
| OB-002H   | CCR5 antagonist | Orion Biotechnology           | Vaginal and rectal gel | Phase I   |
| <ul style="list-style-type: none"> <li>A study published in 2009 reported prevention of vaginal transmission of SHIV SF162P3 in a macaque model.</li> <li>At the 2021 R4P conference, results were presented from a phase I trial assessing the safety, acceptability, and PK profile of single and multiple doses administered either vaginally or rectally. Local adverse events were reported to be mild and transient, and there was no systemic absorption. A majority of the 30 participants found the gel acceptable and would consider use for HIV prevention if licensed. Study results were published in <i>AIDS Research and Human Retroviruses</i> on April 30, 2021.</li> <li>In December 2021, Orion Biotechnology announced a partnership with Evofem Biosciences that will assess the combination of OB-002H with Phexxi vaginal gel, with the aim of developing an MPT. The current status of the program is unclear.</li> </ul>   |                 |                               |                        |           |
| <b>Multipurpose Technologies</b>  |                 |                               |                        |           |
| Tenofovir + levonorgestrel<br><a href="#">NCT03762382</a>   | NtRTI/HC        | CONRAD                        | Vaginal ring           | Phase IIa |
| <ul style="list-style-type: none"> <li>The CDC and CONRAD collaborated on a phase IIa, 90-day safety, adherence, and acceptability study of IVRs releasing TFV with and without LNG among women in western Kenya (NCT03762382). A presentation of interim results at R4P 2021 indicated 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 <i>Scientific Reports</i> in July 2022 reported that the IVRs were safe and didn't adversely affect genital microbiota. According to a substudy published in September 2022, acceptability was good, although women expressed concerns about potentially negative community perceptions.</li> <li>Full results from the trial were published in <i>Frontiers in Reproductive Health</i> in June 2023, finding that the products were safe and achieved desired local drug levels.</li> <li>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 <i>PLoS One</i> 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 <i>Frontiers in Cellular and Infection Microbiology</i> in March 2022.</li> </ul>  |                 |                               |                        |           |

| Agent  | Class/Type                       | Manufacturer/Sponsor | Delivery                 | Status   |
|--|----------------------------------|----------------------|--------------------------|----------|
| DPP capsule (dual prevention pill containing Truvada PrEP and combined oral contraceptive)<br><a href="#">NCT04778527</a><br><a href="#">NCT04778514</a>   | NtRTI/HC                         | Population Council   | Oral                     | Phase II |
| <ul style="list-style-type: none"> <li>Being developed by a coalition of partners for prevention of pregnancy and HIV infection in high-need countries.</li> <li>Two phase II crossover trials comparing acceptability of DPP capsule versus individual PrEP and contraceptive pills among adolescent girls and young women are being conducted, as described in a paper in <i>BMJ Open</i> published in March 2024. One study in Zimbabwe enrolled 30 participants and has been completed while the second is ongoing and closed to recruitment with 96 participants in South Africa. Results are pending.</li> </ul>   |                                  |                      |                          |          |
| Dapivirine + levonorgestrel<br><a href="#">NCT05041699</a>   | NNRTI/HC                         | Population Council   | Three-month vaginal ring | Phase Ia |
| <ul style="list-style-type: none"> <li>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.</li> <li>A phase I study of 90-day administration either continuously or on a cyclic schedule (28 days in/two 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).</li> <li>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 <i>PLoS One</i> on June 5, 2024.</li> <li>A 90-day phase Ib study of the safety and PK of two different vaginal ring formulations (<a href="#">NCT05041699</a>) is ongoing at sites in Oregon and Pennsylvania.</li> </ul> |                                  |                      |                          |          |
| PC-6500 (0.1% griffithsin in a carrageenan gel)  | Cell-viral fusion-blocking agent | Population Council   | Vaginal gel              | Phase I  |
| <ul style="list-style-type: none"> <li>The Population Council has completed a phase I study evaluating the safety of griffithsin for vaginal use. Results were published in <i>PLoS One</i> in January 2022, with the product reported to be safe. Cervicovaginal lavage samples from study participants were capable of inhibiting both HIV and HPV. The authors conclude that the intervention is “a safe and promising on-demand multipurpose prevention technology product that warrants further investigation.”</li> </ul>  |                                  |                      |                          |          |

## ABBREVIATIONS

**CAB LA:** long-acting cabotegravir  
**CDC:** Centers for Disease Control and Prevention  
**CONRAD:** Contraception Research and Development  
**CROI:** Conference on Retroviruses and Opportunistic Infections  
**DAIDS:** Division of AIDS  
**DPP:** dual prevention pill  
**DPV:** dapivirine  
**DVR:** dapivirine vaginal ring  
**EVG:** elvitegravir  
**FDA:** U.S. Food and Drug Administration  
**FTC:** emtricitabine  
**HC:** hormonal contraception  
**HPTN:** HIV Prevention Trials Network  
**HPV:** human papillomavirus  
**IM:** intramuscular injection  
**INSTI:** integrase strand transfer inhibitor  
**IPM:** International Partnership for Microbicides  
**IV:** intravenous administration  
**IVR:** intravaginal ring  
**LNG:** levonorgestrel  
**MPT:** multipurpose prevention technology  
**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