Pipeline Report » 2022

PrEP and Microbicides

TAG
Treatment Action Group

The PrEP and Microbicides Pipeline 2022

By Richard Jefferys

The past year has seen several significant developments in the pre-exposure prophylaxis (PrEP) and microbicides pipeline.

Results from two pivotal efficacy trials evaluating bimonthly injections of the long-acting integrase inhibitor cabotegravir (CAB LA) were published, with both studies demonstrating superiority to oral PrEP with Truvada. The U.S. Food and Drug Administration (FDA) approved CAB LA for PrEP on December 20, 2021.

In a very welcome departure from the debacle that surrounded licensure of the drug Descovy for PrEP in 2019, an efficacy study of CAB LA in cisgender women (HPTN 084) was conducted almost in parallel with a similar trial in cisgender men and transgender women who have sex with men (HPTN 083). The availability of results in women allowed the FDA to approve CAB LA (trade name Apretude) for all adults and adolescents at risk of HIV acquisition. The language on the label states: "Indicated in at-risk adults and adolescents weighing at least 35 kg for PrEP to reduce the risk of sexually acquired HIV-1 infection." Descovy, meanwhile, remains unapproved for "individuals at risk from receptive vaginal sex," and, despite many promises from the manufacturer Gilead Sciences, a trial intended to generate data in women has yet to do so.

Results from HPTN 083 were published in the *New England Journal of Medicine* on August 12, 2021. The trial recruited 4,566 participants and randomly assigned them to receive either CAB LA or Truvada PrEP. In the initial analysis, there were 13 cases of HIV acquisition in the CAB LA arm compared with 39 in the Truvada arm, which represents a 66% reduction in HIV incidence. Statistically, the difference is of sufficient magnitude to demonstrate superiority of CAB LA PrEP.

The trial enrolled a diverse cohort from seven countries (Argentina, Brazil, Peru, Thailand, the United States, Vietnam, and South Africa). Two-thirds of participants were under 30 years of age, and 12% identified as transgender women. In the United States, approximately half of the participants identified as Black or African American.

Raphael Landovitz, the trial's principal investigator, presented an update on the results at the Conference on Retroviruses and Opportunistic Infections (CROI) 2022. Over the entire blinded period (when participants were unaware of which arm they were in), there were 14 cases of HIV acquisition among CAB LA recipients compared with 41 in those receiving Truvada, which also equates to a 66% reduction in HIV incidence.

Landovitz also reported data from the first year after the study was unblinded, allowing participants to continue their originally assigned PrEP interventions (the protocol has since been amended to offer CAB LA to all participants). During this period, 11 CAB LA and 33 Truvada recipients acquired HIV, maintaining the difference in efficacy (statistically, a 67% reduction in HIV incidence). Overall HIV incidence in the trial population was about 1.5-fold higher during this open-label period, which was partly associated with declines in adherence to both CAB LA injections and oral Truvada. This finding stresses the importance of adherence support for people who opt to use CAB LA for PrEP now that it is approved.

A total of seven unexplained breakthrough cases of HIV infection have so far been documented in participants who received all their CAB LA injections on time. The researchers are working to better understand this rare phenomenon. In a separate presentation at CROI 2022, Susan Eshleman reported that sensitive HIV RNA tests can identify breakthrough cases of HIV acquisition, facilitating the prompt initiation of combination antiretroviral therapy (ART). Both the FDA label and most recent CDC guidance recommend this approach to reduce the risk of recipients who have acquired HIV continuing on CAB LA monotherapy and potentially developing resistance to integrase inhibitors.

Detailed descriptions of the circumstances associated with cases of HIV acquisition among HPTN 083 participants were published in a paper in the *Journal of Infectious Diseases* in November 2021.

Results from the HPTN 084 trial in cisgender women were published in *The Lancet* on April 1, 2022. The final efficacy analysis included 3,178 participants (1,592 in the CAB LA arm and 1,586 in the Truvada arm) enrolled in seven African countries: Botswana, Eswatini, Kenya, Malawi, South Africa, Uganda, and Zimbabwe. Four cases of HIV acquisition were documented in the CAB LA arm and 36 in the Truvada arm. Statistically, this indicated clear superiority of CAB LA, with recipients experiencing an 88% reduction in risk compared with participants randomized to receive Truvada.

In contrast to HPTN 083, all the HIV acquisition events in the CAB LA arm could be explained: in two instances no CAB LA injections had been received, and in one case low drug levels were present due to delayed injection visits. A retrospective analysis revealed that the fourth person had already acquired HIV prior to CAB LA administration.

A poster presentation at CROI 2022 reported on outcomes among women in the CAB LA arm who became pregnant, noting that none of the pregnancies were associated with neural tube defects or other congenital anomalies. The data derive from participants who stopped CAB LA injections at the time pregnancy was confirmed, and additional studies are investigating outcomes among women who choose to continue CAB LA through pregnancy during the open-label phase of HPTN 084.

In both efficacy trials, CAB LA had a good safety profile, with injection-site reactions being the most prominent side effect. Discontinuations due to side effects were infrequent. In HPTN 084 there was evidence of greater early weight gain among CAB LA recipients, but subsequently weight gain became comparable in both arms of the trial.

In his CROI 2022 presentation, Raphael Landovitz reported that applications for regulatory approval of CAB LA PrEP have been submitted in Australia, Brazil, Botswana, Kenya, Malawi, South Africa, Uganda and Zimbabwe, with additional submissions planned.

A critical consideration now that CAB LA PrEP has emerged from the pipeline is cost. ViiV Healthcare, the manufacturer of CAB LA, is charging the exorbitant price of $3,700 per dose in the United States, or $22,200 per year. On May 27, 2022, after several months of inconclusive statements and in response to sustained pressure from a global coalition of activists led by AfroCAB, ViiV Healthcare announced a commitment to issuing a voluntary license to the Medicines Patent Pool (MPP) "to help enable at scale access to cabotegravir LA for PrEP in low- and middle-income countries [LMICs]." If successfully negotiated, licensing will allow generic manufacturing of CAB LA for LMICs. In the interim, ViiV has committed to supplying CAB LA PrEP at an undisclosed "non-profit price" for public programs "in low-income, least developed and all sub-Saharan African countries."

The World Health Organization is expected to issue recommendations for the use of CAB LA PrEP during the International AIDS Conference in Montreal this summer. Activists are asking PEPFAR and other donors as well as country governments to rapidly develop concrete plans for comprehensive access to CAB LA to help prevent 15 million new HIV infections over the coming years. Oral Truvada PrEP has been approved for a decade, and both access and uptake remain profoundly inadequate, particularly in communities that bear the highest burdens of HIV infection. Lessons must be learned from these failures if PrEP is to fulfill its promise.

The dapivirine vaginal ring has become the first female-controlled microbicide PrEP product to achieve regulatory approval, first from the Medicines Control Authority of Zimbabwe on July 6, 2021, followed by the South African Health Products Regulatory Authority on March 11, 2022 (rollout in South Africa is now pending review by the National Department of Health). Additional applications are in process in other eastern and southern African countries. Disappointingly, an application to the FDA had to be voluntarily withdrawn because the agency deemed the results likely insufficient to support approval in the U.S. context.

The FDA's reluctance to consider the ring has global implications, because approval by the agency is required for products to be distributed by PEPFAR. Activists are vigorously expressing concerns that both PEPFAR and USAID are "backing away" from supporting the dapivirine vaginal ring as an HIV prevention option (USAID has recently ceased their support for the development of a potential 90-day version of the ring). Ongoing advocacy is aiming to ensure that the dapivirine vaginal ring is made available to all women who might stand to benefit.

Encouraging dapivirine ring acceptability data were presented at CROI 2022. The REACH (Reversing the Epidemic in Africa with Choices in HIV prevention) study was conducted by the Microbicide Trials Network and recruited 247 HIV-negative adolescent girls and young women aged 16–21 years at sites in Uganda, South Africa, and Zimbabwe. Participants sequentially received the dapivirine ring (which is replaced monthly) and daily oral Truvada PrEP, each for six months, and then for the final six months of the trial participants could decide to use one of these options, or neither.

Nearly all (98%) of the 227 participants who took part in the choice period opted to use one of the two HIV prevention products being offered; of these, 67% chose to use the ring and 31% chose to use Truvada PrEP. Only 2% preferred not to use either option. Most participants used their product of choice some or most of the time. The results suggest there is potential for the dapivirine ring to contribute significantly to HIV prevention in the young women who are most at risk in these high-incidence locations.

Two antiretrovirals considered as very promising for PrEP have experienced setbacks since the 2021 edition of TAG's Pipeline Report. Merck's islatravir belongs to a new class of drugs called nucleoside reverse transcriptase translocation inhibitors (NRTTIs), which strongly inhibit HIV's reverse transcriptase enzyme by multiple mechanisms. Two phase III efficacy trials evaluating monthly oral dosing for PrEP were initiated in late 2020.

Unfortunately, news emerged from Merck in November 2021 indicating a problem: decreases in total lymphocyte (white blood cell) and CD4 counts were observed among islatravir recipients in a combination treatment study with an experimental NNRTI (MK-8507). Based on the recommendation of the trial's external Data Monitoring Committee, dosing was suspended.

The news subsequently got worse: Merck revealed on December 6, 2021, that enrollment in islatravir PrEP trials was being paused, and a few days later there was an announcement that the FDA has placed a clinical hold on oral, implant, and injectable formulations of islatravir for PrEP (as well as all treatment studies, although in some cases there is a partial hold that allows continued dosing for participants who have already started islatravir). Islatravir dosing has been stopped in all PrEP trials, with participants being offered FDA-approved once-daily regimens instead. Total lymphocyte and CD4+ T-cell counts are being monitored to assess how they recover.

According to a presentation by Merck researcher Jay Grobler at a scientific workshop in February 2022, the average decrease in lymphocyte counts among HIV-negative people in the phase 2 PrEP trial was -21% in the 60 mg dose group and -36% in the 120 mg dose group. However, counts remained within the normal range, and no increases in adverse clinical events were documented.

Investigations into potential causes of the lymphocyte count declines are underway. Until additional results become available, it is impossible to predict whether continued development of islatravir will be possible.

Gilead's long-acting inhibitor of the HIV capsid protein, lenacapavir, was also struck by misfortune. On December 21, 2021, the company announced that the FDA has placed a hold on studies of the injectable formulation because of safety concerns related to the vials being used to store the drug. Specifically, the agency identified a potential incompatibility between the vials and the drug formulation that risked microscopic glass particles becoming mixed into the solution.

All trials of injectable lenacapavir temporarily ceased dosing, with no new participants being screened or enrolled. On May 16, 2022, Gilead announced that a new vial made from aluminosilicate glass has been cleared for use by the FDA, allowing the hold on trials of injectable lenacapavir to be lifted. Notably, the issue has caused a further delay to the already benighted Gilead study that is intended to provide data on Descovy PrEP in women.

A range of other potential systemic and topical PrEP candidates remain in the pipeline, although their potential for progressing to licensure is often unclear. The efficacy of injectable CAB LA PrEP has set a high bar, but choices remain essential for people at risk of HIV acquisition who may not find bimonthly injections (or other currently approved oral PrEP options) acceptable.

Table 1: Pre-Exposure Prophylaxis (PrEP)

Agent	Class/Type	Manufacturer/Sponsor	Delivery	Status
Cabotegravir **NCT03164564 (cisgender women)** **NCT02720094 (MSM and transgender women)** **NCT04692077 (adolescents assigned male at birth)**	**INSTI**	**ViiV Healthcare**	**IM**	**Phase III (HPTN 084)** **Phase IIb/III (HPTN 083)** **Phase II**
■ Approved by the FDA for adults and adolescents at risk of HIV acquisition on December 20, 2021. ■ Results from HPTN 083 and 084 were published in the *New England Journal of Medicine* and *The Lancet*, respectively. Open-label extension phases of both trials are ongoing. ■ A substudy of HPTN 83 is investigating 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. Enrollment target is 50 participants, and the estimated completion date is May 2023. ■ 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. Results were published in *Antimicrobial Agents and Chemotherapy* on March 15, 2022.				
Islatravir (MK-8591) **NCT04644029 (Impower-022)** **NCT04652700 (Impower-024)** **NCT04003103** **NCT05115838 (Implant)** **NCT05130086**	**NRTTI**	**Merck**	**Monthly oral PrEP, implant**	**Phase III** **Phase IIa** **Phase II**
■ Islatravir is an investigational antiretroviral drug classed as an NRTTI. The drug is reported to be highly potent with a long half-life, allowing for intermittent dosing. ■ All PrEP trials are currently subject to a full clinical hold due to evidence of declines in lymphocyte counts associated with islatravir administration. Dosing has been stopped and participants are being offered approved PrEP options as an alternative. ■ A presentation by Jay Grobler at the 2022 Long-Acting/Extended Release Antiretroviral Research Resource Program (LEAP) Investigator Meeting and Annual Workshop reported average declines in lymphocyte counts of -21% in 60 mg dose group and -36% in the 120 mg dose group in a phase IIa PrEP trial. ■ Prior to the clinical hold, interim results were reported at R4P 2021 from the IIa trial assessing safety, tolerability, and PK of once-monthly oral doses of either 60 mg or 120 mg compared with placebo in adults at low risk for HIV infection. ■ Two phase III efficacy trials were recruiting cisgender women (Impower-022) and cisgender men and transgender women who have sex with men (Impower-024); both are now on hold. ■ A phase II open-label study in trans and gender diverse individuals (NCT05130086) is planned but on hold. ■ Results from a phase I study evaluating interactions between islatravir and the oral contraceptive levonorgestrel/ethinyl estradiol were published in the *Journal of the International AIDS Society* in December 2021, indicating no requirement for dose adjustments. ■ Implant formulations are also in development. Phase I testing of a prototype implant showed potential for once-yearly administration, with results published in *Nature Medicine* in October 2021. A phase IIa study of a radiopaque matrix implant (NCT05115838) is planned but on hold.				

Agent	Class/Type	Manufacturer/Sponsor	Delivery	Status
Lenacapavir	**Capsid inhibitor**	**Gilead**	**SC, oral**	**Phase III**
■ An inhibitor of the HIV capsid protein. The LA formulation for subcutaneous injection is administered once every six months. ■ Gilead is sponsoring two phase III efficacy trials: ■ PURPOSE 1 is evaluating lenacapavir and Descovy compared with Truvada PrEP in young women aged 16-25 in South Africa. The trial plans to enroll 5,010 participants. ■ PURPOSE 2 is evaluating lencapavir compared with Truvada PrEP in 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 the United States, Puerto Rico and South Africa and plans to enroll 3,000 participants. ■ Trials were temporarily placed on hold by the FDA in December 2021 because of concerns related to the safety of the storage vials for injectable lenacapavir. On May 16, 2022, Gilead announced that the issue had been resolved and the hold lifted.				
Tenofovir alafenamide + emtricitabine (Descovy), tenofovir disoproxil fumarate + emtricitabine (Truvada)	**NtRTI/ NRTI**	**University of California, Los Angeles**	**Oral PrEP**	**Phase III**
■ A study in pregnant and postpartum women in South Africa to establish benchmarks of tenofovir 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.				
Tenofovir alafenamide subdermal implant **PACTR201809520959443**	**NtRTI**	**Centre for the AIDS Programme of Research in South Africa**	**Implant**	**Phase I/II**
■ A phase I/II trial to evaluate the safety, acceptability, tolerability, and PK in women (CAPRISA 018) is underway in South Africa. As described in a paper published in *BMJ Open*, an initial phase I portion of the study aims to determine the optimal dosing, implant location, and implant replacement interval before proceeding to a larger phase II trial.				
Aspirin **NCT03629327**	**Nonsteroidal anti-inflamma-tory**	**University of Manitoba**	**Oral PrEP**	**N/A**
■ Trial 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. ■ Results from a pilot study (NCT02079077) were published in *Frontiers in Immunology* in November 2021, indicating that aspirin levels were detectable in the genital tract and associated with significant declines in the proportion 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				
Dapivirine **NCT03965923** **(pregnant women)**	**NNRTI**	**IPM (vaginal ring/gel/film); DAIDS/MTN (rectal gel)**	**Monthly vaginal ring**	**Phase IIIb** **Phase IIa**
■ Licensed by regulatory authorities in Zimbabwe and South Africa. ■ Phase IIIb safety evaluations of monthly DPV ring in pregnant women and breastfeeding mother-infant pairs have been completed; results are pending. ■ Results from the REACH study investigating acceptability among adolescent girls and young women were presented at CROI 2022 (see main report text). ■ 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 were presented at CROI 2021, demonstrating 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. ■ 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. 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 were reported from MTN-033 at the same conference.				
TAF/EVG **NCT04047420**	**NRTI/INSTI**	**CONRAD and MTN**	**Rectal insert**	**Phase I**
■ A phase I trial (MTN-039) evaluating safety, acceptability, and concentrations of drug in the rectal tissue completed follow-up on April 7, 2021. Results are pending.				
Tenofovir **NCT04195776** **(DREAM-02)** **NCT04686279** **(ATN DREAM)**	**NtRTI**	**Johns Hopkins University**	**Enema**	**Phase I**
■ Results of DREAM-01 were presented at the 2018 R4P conference. The study 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. ■ 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. ■ DREAM-02, a third phase I study assessing the TFV enema used in sequence with tap water enemas, is now enrolling. ■ A phase I study of the safety, PK, PD, and acceptability of a one-dose TFV douche in adolescents aged 15–24 (ATN DREAM) is recruiting participants.				
IQP-0528	**NNRTI**	**ImQuest U19**	**Rectal gel**	**Phase I**
■ A phase I study looking at safety and PK for rectal use of IQP-0528 completed in June 2019. Results were published in *AIDS Research and Human Retroviruses* in January 2021, demonstrating safety and tissue concentrations above the target for HIV inhibition lasting ~3–24 hours after dosing. In three female participants, rectal administration did not lead to detectable levels in cervicovaginal tissue. The study authors suggest that the short half-life of the drug may make it better suited to episodic use.				

Agent	Class/Type	Manufacturer/Sponsor	Delivery	Status
DS003	**EI**	**IPM**	**Vaginal tablet**	**Phase I**
■ Phase I IPM 042 was a double-blind, randomized, placebo-controlled, dose-escalation trial to evaluate the safety and PK of DS003 vaginal tablets administered to healthy HIV-negative women. Results were presented at the 2018 R4P conference, showing safety and achievement of potentially protective drug levels in tissues (see Chantél et al., abstract P05.08 and Nuttall et al., abstract P21.02, *AIDS Research and Human Retroviruses* 2018 34:S1). ■ A laboratory study published in the journal *AIDS* in October 2021 reported activity in mucosal tissue explants and concluded that DS003 should be considered for further development. ■ Considered as a candidate for combining with dapivirine in a vaginal ring, but research is currently paused because of funding limitations.				
MK-2048 **NCT04319718**	**INSTI**	**NIAID**	**Vaginal film**	**Phase I**
■ Ongoing phase I trial at the University of Pittsburgh assessing the safety and PK of two different doses of an extended-release vaginal film designed to deliver drug for seven days.				
OB-002H	**CCR5 antagonist**	**Orion Biotechnology**	**Vaginal and rectal gel**	**Phase I**
■ Study published in 2009 reported prevention of vaginal transmission of SHIV SF162P3 in a macaque model. ■ 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 *AIDS Research and Human Retroviruses* on April 30, 2021. ■ 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.				
Multipurpose Technologies				
Tenofovir + levonorgestrel **NCT03762382**	**NtRTI/HC**	**CONRAD**	**Vaginal ring**	**Phase IIa**
■ 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. Full results from the 90-day assessment were published in *Frontiers in Cellular and Infection Microbiology* in March 2022. ■ CDC and CONRAD are collaborating on an ongoing 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.				
DPP capsule (dual prevention pill containing Truvada PrEP and combined oral contra-ceptive) **NCT04778514** **NCT04778527**	**NtRTI/HC**	**Population Council**	**Oral**	**Phase II**
■ Being developed by a coalition of partners for prevention of pregnancy and HIV infection in high-need countries. ■ Two phase II crossover trials comparing acceptability of DPP capsule versus individual PrEP and contraceptive pills among adolescent girls and young women are registered with clinicaltrials.gov, one located in Zimbabwe and the other in South Africa. Both are listed as not yet open for recruitment as of May 2022.				

Agent	Class/Type	Manufacturer/Sponsor	Delivery	Status
Dapivirine + levonorgestrel NCT05041699	**NNRTI/HC**	**IPM**	**Three-month vaginal ring**	**Phase Ia**
■ Phase I study evaluating PK and safety of a vaginal ring containing DPV and LNG (MTN-030/IPM 041) completed in 2017, with results presented at the 2018 R4P conference (abstract OA12.02LB). A 14-day period of evaluation showed the ring to be well tolerated and that it achieved the desired drug levels. ■ 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). ■ A 90-day phase Ia study of the safety and PK of two different vaginal ring formulations is registered in clinicaltrials.gov (NCT05041699) but not yet recruiting.				
MB66	**Anti-HIV + anti-HSV antibodies**	**LeafBio, Inc.**	**Vaginal film**	**Phase I**
■ MB66 combines monoclonal antibodies specific for HIV (VRC01-N) and herpes simplex virus (HSV8-N) in a film for vaginal application as microbicide. ■ Phase I study assessing safety, PK, and PD completed in July 2018, with results published in the journal *PLoS Medicine* in February 2021. MB66 was found to be well tolerated with antibody levels considered likely to be protective maintained for 24 hours after administration.				
PC-6500 (0.1% griffithsin in a carrageenan gel)	**Cell-viral fusion-blocking agent**	**Population Council**	**Vaginal gel**	**Phase I**
■ The Population Council has completed a phase I study evaluating the safety of griffithsin (GRFT) for vaginal use. Results were published in *PLoS One* 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."				

ABBREVIATIONS

CAB LA: long-acting cabotegravir

CDC: Centers for Disease Control and Prevention

CGN: carrageenan

CONRAD: Contraception Research and Development

CROI: Conference on Retroviruses and Opportunistic Infections

DAIDS: Division of AIDS

DPV: dapivirine

EI: entry inhibitor

EVG: elvitegravir

FDA: U.S. Food and Drug Administration

FTC: emtricitabine

HC: hormonal contraception

HSV: herpes simplex virus

IM: intramuscular injection

INSTI: integrase strand transfer inhibitor

IPM: International Partnership for Microbicides

IVR: intravaginal ring

LA: long-acting

LNG: levonorgestrel

MSM: men who have sex with men

MTN: Microbicide Trials Network

NIAID: National Institute of Allergy and Infectious Diseases

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

PEPFAR: The U.S. President's Emergency Plan for AIDS Relief

PK: pharmacokinetics

PrEP: pre-exposure prophylaxis

R4P: HIV Research for Prevention Conference

SC: subcutaneous injection

TAF: tenofovir alafenamide

TFV: tenofovir