

HIV Pre-Exposure Prophylaxis (PrEP) The Future of PrEP

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Disclosures

December 2023: only FTC/TDF (Truvada), FTC/TAF (Descovy), and CAB-LA (Apretude) are approved by the U.S. Food and Drug Administration (FDA) and only for use in some, but not all, populations.

This talk will include discussion of non-FDA approved strategies for HIV prevention.

Disclaimer

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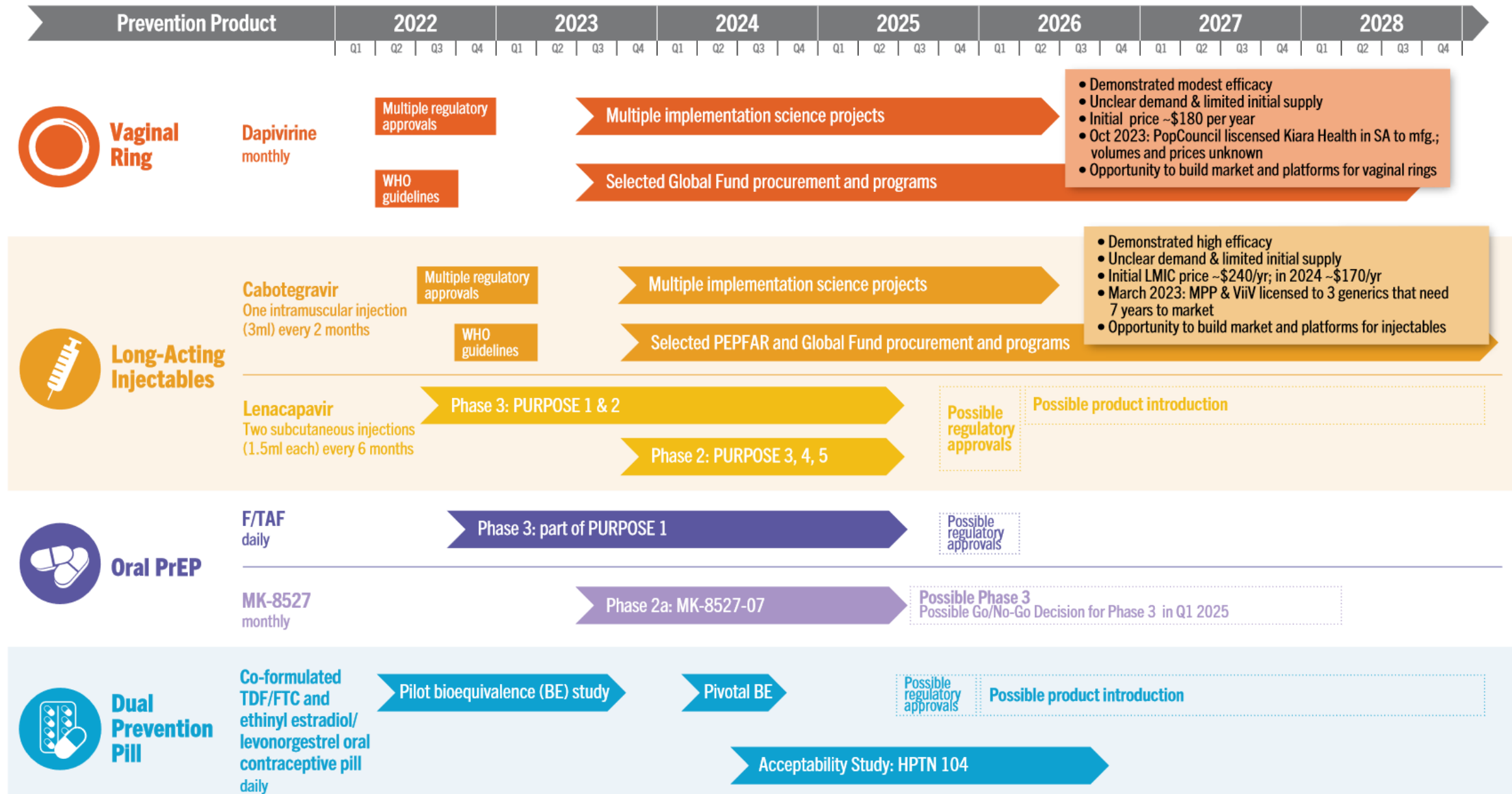
What to prescribe as PrEP (December 2023)

	IAS-USA (2022)	HHS/CDC (2021)
FTC/TDF	All persons at risk from sexual or injection exposures.	All persons at risk from sexual or injection exposures.
FTC/TAF	<ul style="list-style-type: none">- Preferred if eCrCl 30-60 mL/min or known osteoporosis- Limited to anyone whose risks do not include receptive vaginal or neovaginal sex or exclusive IDU	<ul style="list-style-type: none">- Preferred if eCrCl 30-60 mL/min or known osteoporosis- Recommended for men and TGW who have sex with men.
CAB	All persons at risk from sexual exposures and PWID with sexual risk.	All persons at risk from sexual exposures.

Why do we need more PrEP studies and PrEP options?

- Not all PrEP options are approved in all populations
- Daily pill-taking is challenging for many people
- Easier accessibility at home or other locations
- Side effects
- More options = better choices
- ? More options = more competition = lower costs ?
- ? Avoiding drug resistance in first line antiretroviral therapy ?

The Future of PrEP



- Demonstrated modest efficacy
- Unclear demand & limited initial supply
- Initial price ~\$180 per year
- Oct 2023: PopCouncil licensed Kiara Health in SA to mfg.; volumes and prices unknown
- Opportunity to build market and platforms for vaginal rings

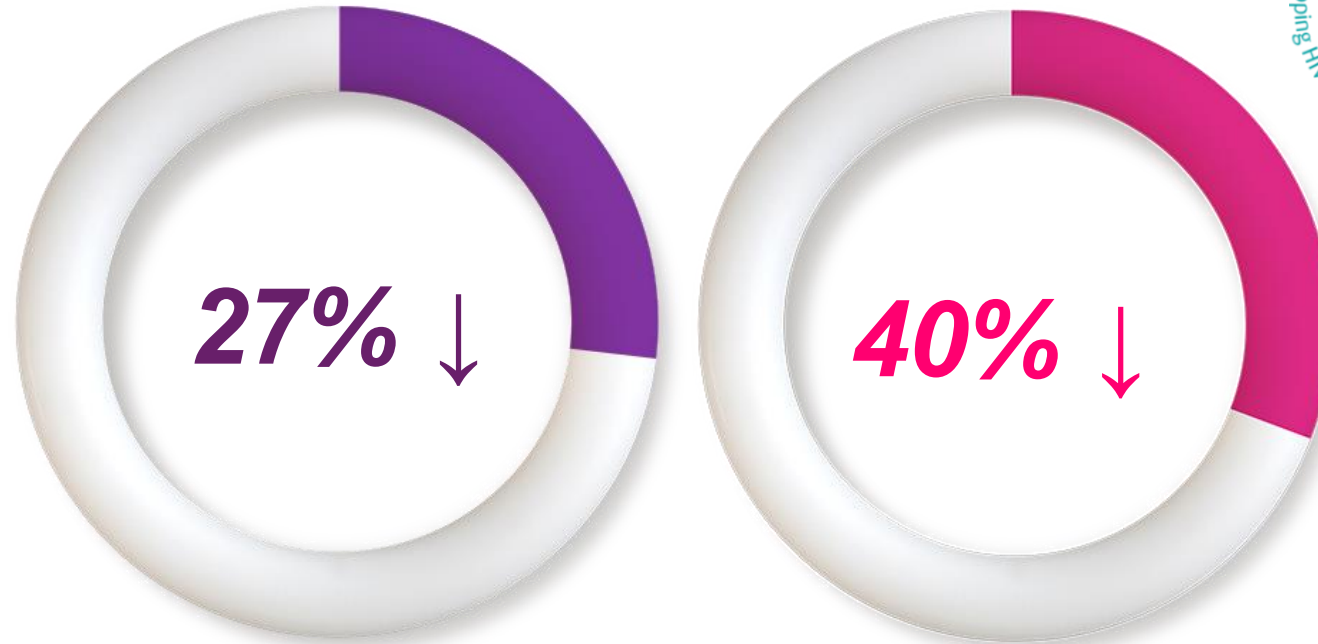
- Demonstrated high efficacy
- Unclear demand & limited initial supply
- Initial LMIC price ~\$240/yr; in 2024 ~\$170/yr
- March 2023: MPP & ViiV licensed to 3 generics that need 7 years to market
- Opportunity to build market and platforms for injectables

Vaginal ring for sustained delivery of ARV drugs

Dapivirine ring



ASPIRE



NEJM 2016; 375: 2121-32 (Baeten et al) and 2133-2143 (Nel et al.)

Adapted from Dr. Sharon Hillier's presentation at the Annual Principles of STI/HIV Research Course

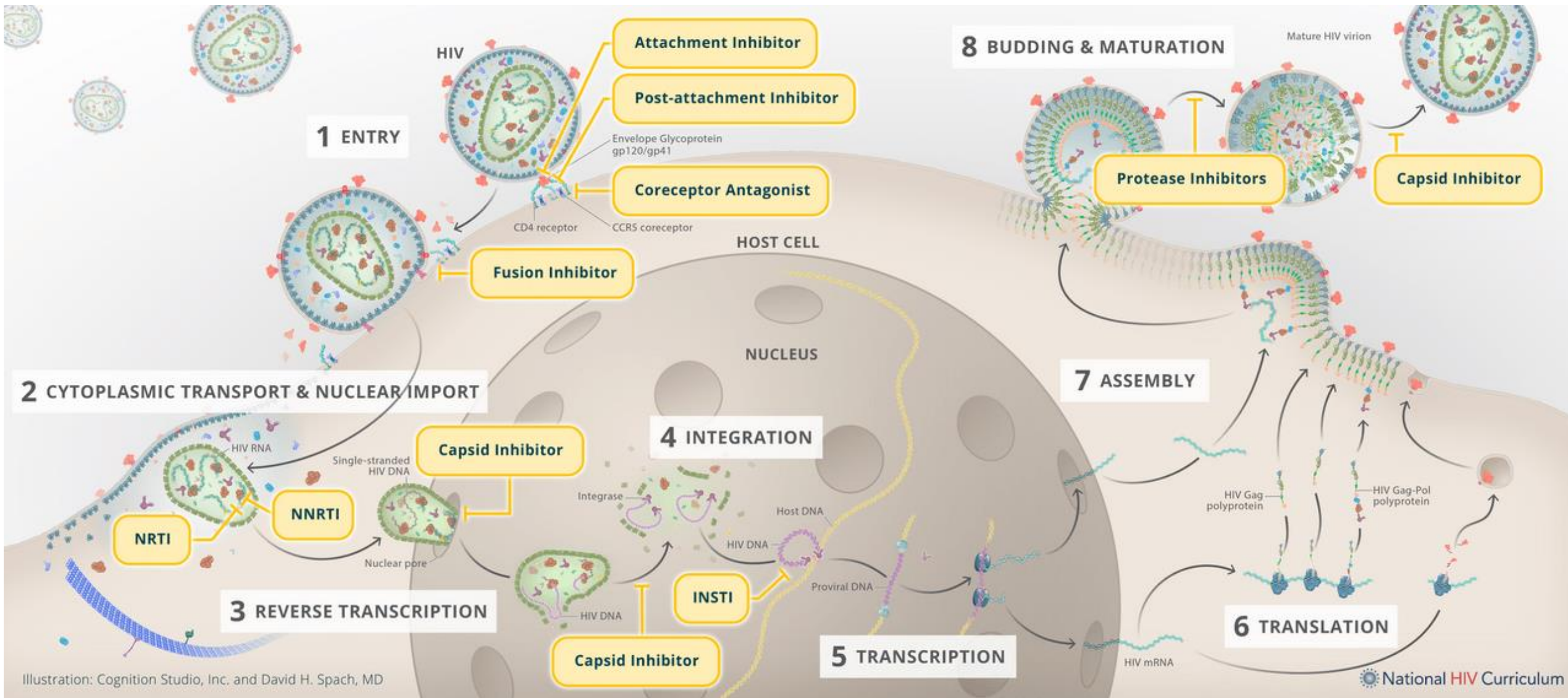


Vaginal ring for sustained delivery of ARV drugs

Future products

- Longer duration vaginal rings
 - Dapivirine ring 004 (30 days) v 008 (90 days) (Phase I, enrolling)
- Other medications
 - TDF/FTC ring (Phase I, active)
- Multipurpose rings (PrEP + contraception)
 - Dapivirine 200mg + Levonorgestrel 320mg (Phase I/II, enrolling)
 - TDF + Levonorgestrel

Capsid inhibitors



Lenacapavir as PrEP

- Lenacapavir as PrEP in an IV HIV challenge macaque model
(Swanstrom et al., EBioMedicine 2023)
- Lenacapavir as PrEP in a rectal SHIV challenge macaque model
(Bekerman et al., J Clin Invest 2023)

Prevention dosing:

Oral LEN 600mg day 1 and 2, then

Subcutaneous LEN 927mg q26 weeks (i.e. every 6 months)

PURPOSE: lenacapavir

- PURPOSE 1: lenacapavir v FTC/TAF in girls and women
phase III, n=5639, South Africa and Uganda, 1° completion 2024
- PURPOSE 2: lenacapavir v FTC/TDF in cisMSM, transgender/GNB persons
phase III, n=3000, US/ex-US sites, 1° completion 2025
- PURPOSE 3: lenacapavir v FTC/TDF in cisgender women in US (HPTN 102)
phase II, n=250, 1° completion 2027
- PURPOSE 4: lenacapavir v FTC/TDF in PWID in US (HPTN 103)
phase II, n=250, 1° completion 2027
- PURPOSE 5: lenacapavir persistence in UK and France

Long-acting oral formulations

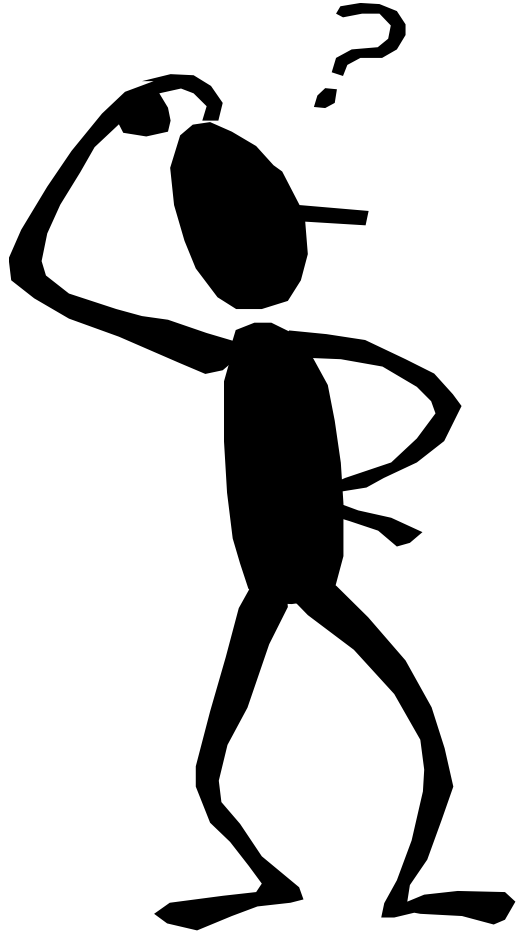
- MK-8591 = islatravir, no longer being studied for prevention
- MK-8527 taken monthly
 - NRTTI = nucleoside reverse transcriptase translocation inhibitor
 - phase IIa (safety, tolerability, PK) in low-risk participants
 - n=350, completion 2025

Dual Prevention Pill (DPP): PrEP + Contraception

- Generic maker is co-formulating
 - FTC/TDF + Levonorgestrel (0.15mg) + Ethinyl Estradiol (0.03mg) in blister pack
 - 21 combo pills + 7 peach-colored PrEP only pills
- Two crossover adherence/acceptability studies – study completion 2023
- FDA submission?



Questions?



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