

# New In the World of PrEP

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2022 Communicable Disease Summit and PrEP  
Conference



# Topics for Discussion

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- Discuss HPTN083 and HPTN084
- Drug Facts
  - Indications for Use of Injectable LA cabotegravir
  - Contraindications for Use of Injectable LA cabotegravir
    - Drug Resistance
  - Patient Education
    - Attitudes and Experiences of Patients of Different Populations
  - Patient Financial Assistance
- Limitations to Acceleration
- Opportunities and Aspirations

# HPTN 083 HPTN 083

## Active Products

Long-acting injectable cabotegravir (CAB LA), oral cabotegravir (CAB), oral TDF/FTC



## Populations

4,570 cisgender men and transgender women who have sex with men



## Locations

Argentina, Brazil, Peru, South Africa, Thailand, U.S., Vietnam



## Start Date

December 2016



## Study Design

### Non-Inferiority of CAB LA to TDF/FTC

A non-inferiority study tests whether one drug works about the same as, but not worse than, another drug.

## Study Phases

### PHASE 1

5 weeks of 2 daily oral pills – 1 active and 1 placebo



### PHASE 2

Injections every 8 weeks and daily pills for up to 3 years



### PHASE 3

Daily oral pills for up to 1 year



■ = placebo

# HPTN 084 HPTN 084

Long-acting injectable cabotegravir (CAB LA), oral cabotegravir (CAB), oral TDF/FTC



3,200 (projected) cisgender women



Botswana, Eswatini, Kenya, Malawi, South Africa, Uganda, Zimbabwe



November 2017



### Superiority of CAB LA to TDF/FTC

A superiority study tests whether one drug works better than another drug.

### PHASE 1

5 weeks of 2 daily oral pills – 1 active and 1 placebo



### PHASE 2

Injections every 8 weeks and daily pills for up to 3.5 years



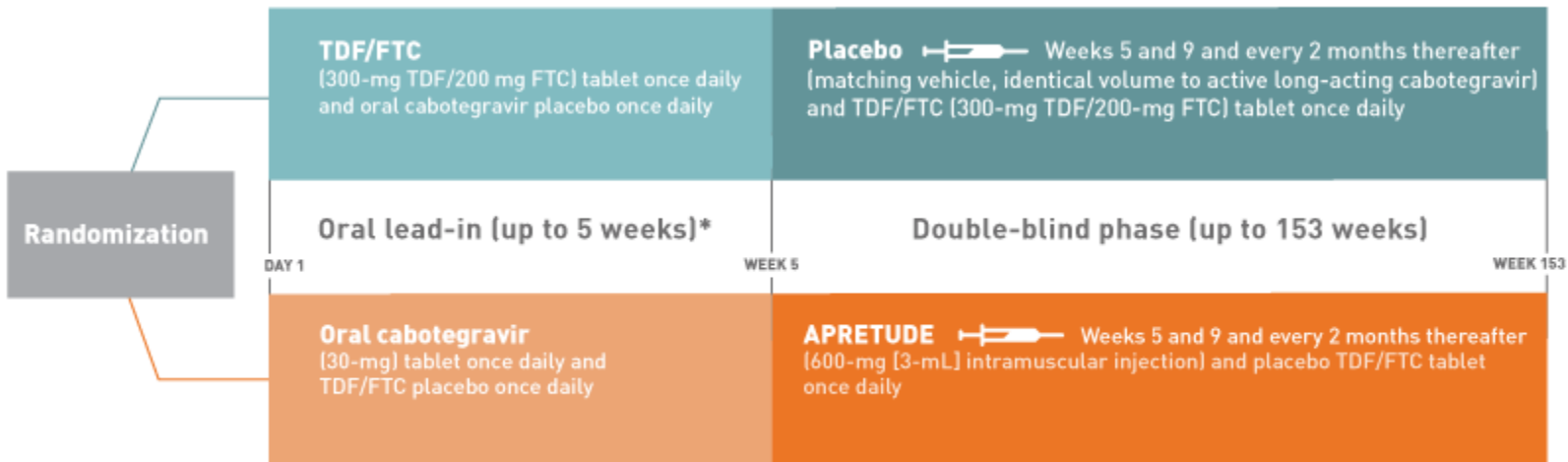
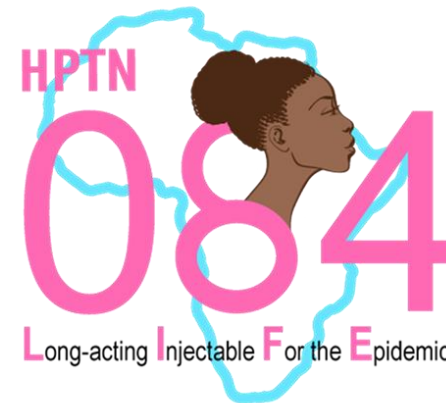
### PHASE 3

Daily oral pills for up to 1 year



# Trial Design and Primary Endpoint

Primary endpoint- Incidence of HIV-1 infection



# HTPN 083 Study

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**STUDY:** **HTPN 083** is the first study to compare the efficacy of CAB LA to daily oral TDF/FTC for HIV pre-exposure prophylaxis (PrEP). HTPN 083 enrolled 4,570 cisgender men and transgender women (TGW) who have sex with men at 43 sites in Argentina, Brazil, Peru, the United States, South Africa, Thailand, and Vietnam.

## Conclusions:

- Both agents were highly effective in HIV prevention
- The PrEP regimen containing CAB-LA was superior to a daily oral regimen of TDF/FTC, with a 66% reduction in risk of HIV infection receiving CAB compared to TDF/FTC.
- CAB-LA was well tolerated despite injection site reactions
- Peri-infection drug concentrations and detailed resistance profiles are needed to fully understand and contextualize results
- CAB is the first long-acting injectable to demonstrate robust HIV prevention and efficacy in MSM/TGW

# HTPN 084 Study

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**STUDY:** **HTPN 084** (LIFE study) is the first and only study comparing cabotegravir LA to daily oral tenofovir disoproxil fumarate/emtricitabine (TDF/FTC), for pre-exposure prophylaxis exclusively in cis-gender HIV-uninfected women. HTPN 084 enrolled 3,223 cisgender women 18 to 45 years old in sub-Saharan Africa (Botswana, Eswatini, Kenya, Malawi, South Africa, Uganda, and Zimbabwe) who were at risk for acquiring HIV.

## Conclusions:

The average age of study participants was 26 years and 57% of participants were 18-25 years old. Eighty-two percent of the women enrolled were not living with a partner, 55% reported two or more partners in the past month, with 34% had a primary partner who is reported to be living with HIV or having an unknown HIV status. A total of 39 HIV infections occurred during follow-up, with three infections in the CAB LA arm and 36 infections in the TDF/FTC arm. Approximately twelve times more incident HIV infections occurred in the TDF/FTC arm than in the CAB arm. \*\*These results meet the statistical criteria for the superiority of CAB LA compared to TDF/FTC in the HPTN 084 study population. The higher-than-expected level of adherence to TDF/FTC throughout the study and the overall low incidence rate in both arms of the study clearly demonstrate both drugs were highly effective at preventing HIV acquisition.

# Drug Facts

- Indications for Use of Injectable LA cabotegravir
- Contraindications for Use of Injectable LA cabotegravir
  - Drug Resistance
- Patient Education
  - Attitudes and experiences of Patients of different populations
- Patient Financial Assistance



# Indications

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## Indications & Usage

Apretude is an HIV-1 integrase strand transfer inhibitor (INSTI) indicated in at-risk adults and adolescents \*\* who weigh at least 35kg (77 lbs.) for PrEP to reduce the risk of sexually acquired HIV-1 infection. Individuals must have a negative HIV-1 test before initiating Apretude (with or without an oral lead-in with oral cabotegravir) for HIV-1 PrEP.

## Dose and administration

- HIV-1 Screening: Screen all individuals for HIV-1 infection immediately before initiating Apretude for HIV-1 PrEP and before each injection while taking Apretude.
- Before initiating Apretude, an oral lead-in dosing may be used for approximately 1 month with the recommended dosage to assess the tolerability of Apretude.
- For gluteal intramuscular injection only
- Recommended Dosing Schedule: Initiate Apretude with a single 600mg (3mL) injection given 1 month apart for 2 consecutive months on the last day of an oral lead-in if used or within 3 days continue with the injections every 2 months thereafter\*\*



# Contraindications

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## Contraindications

- Unknown or positive HIV-1 status
- Previous hypersensitivity reaction to cabotegravir
- Coadministration with drugs where significant decreases in cabotegravir plasma concentrations may occur (anticonvulsants & antimycobacterials)

## Warnings & Precautions

- Comprehensive management to reduce the risk of HIV-1 acquisition
- Potential risk of developing resistance to cabotegravir if an individual acquires HIV-1 either before or while taking Apretude or following discontinuation of Apretude. Reassess the risk of HIV-1 acquisition and test before each injection to confirm HIV-1 negative status
- Residual concentrations of cabotegravir may remain in the systemic circulation of the individuals for up to 12 months or longer
- Hypersensitivity reactions have been reported in association with other integrase inhibitors. Discontinue Apretude immediately if this occurs
- Hepatotoxicity has been reported in patients receiving cabotegravir. Clinical and laboratory monitoring should be considered. Discontinue if suspected.
- Depressive disorders have been reported with Apretude. Prompt evaluation is recommended for depressive symptoms.

# Adverse Reactions

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## Adverse Reactions

- The most common adverse reactions (all grades) observed in at least 1% of the subjects receiving Apretude were injection site reactions, diarrhea, headache, pyrexia, fatigue, sleep disorders, nausea, dizziness, flatulence, abdominal pain, vomiting, myalgia, rash, decreased appetite, somnolence, back pain, and upper respiratory tract infection.

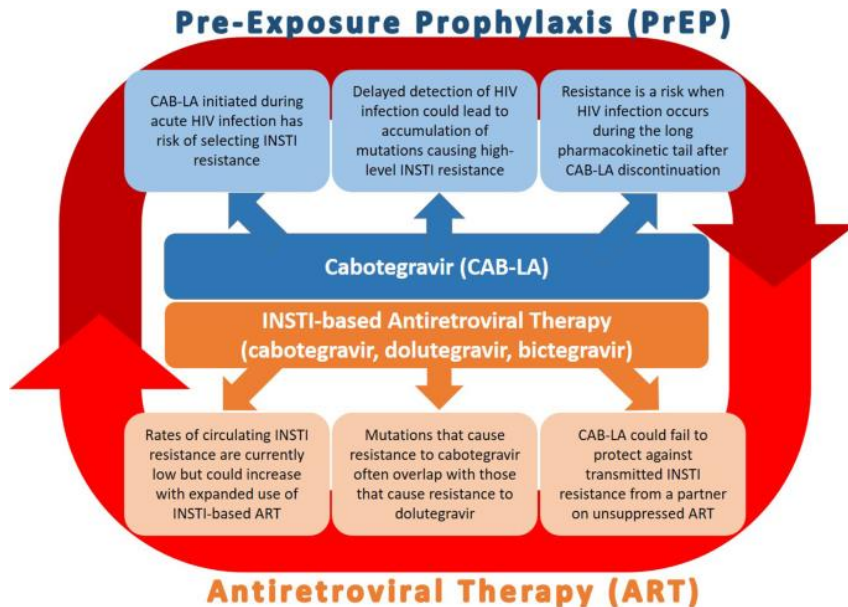
## Drug Interactions

- Drugs that induce uridine diphosphate glucuronosyltransferase (UGT1A1 or 1A9) may significantly decrease plasma concentrations of cabotegravir (anticonvulsants & antimycobacterials)
- Clinical monitoring is recommended for patients taking Methadone. No dose adjustment of methadone is required when starting coadministration with Apretude; however, maintenance therapy of methadone may need to be adjusted in some individuals.

## Use in Specific Populations

- Lactation: Assess the benefit-risk of using Apretude to the infant while breastfeeding due to the potential for adverse reactions and residual concentrations in the systemic circulation for up to 12 months or longer after discontinuation.
- Pediatrics: Not recommended in individuals weighing <35 kg.

# What about resistance?



- Incident HIV infections occurring in people on PrEP may have delayed seroconversion.
- Using the same drugs and drug classes for both prevention and treatment increases the risk of resistance and failure of both approaches.
- Implications of delayed HIV diagnosis include the development and possible transmission of resistant HIV. \*\*
- The longer half-life of CAB vs. TDF may explain the higher relative risk of emergent class drug resistance per incident HIV infection for the CAB than for TDF/FTC.
- Implications for CAB-associated resistance are greater due to the Q148R/K and R263K mutations which could be associated with virologic failure with both DTG and BIC.

# Updated Screening Recommendations for People on PrEP

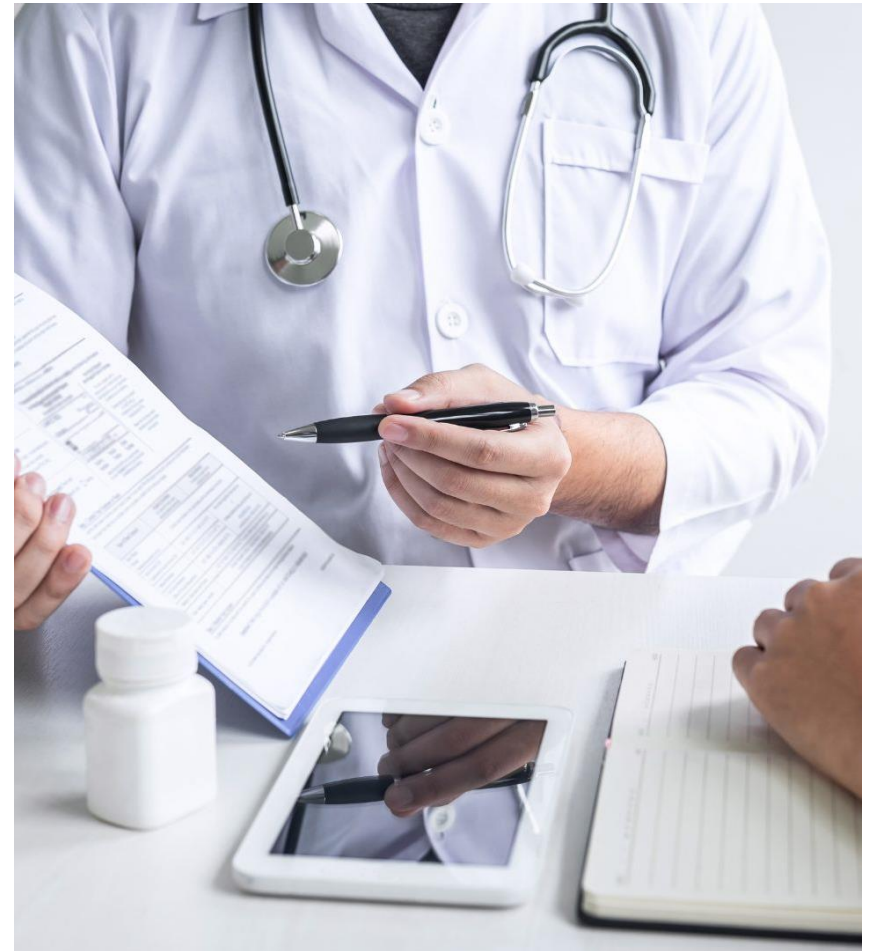
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- New CDC guidelines recommend the addition of HIV-1 viral load screening for all on PrEP. This means dual use of HIV Ag/Ab and RNA testing rather than sole Ag/Ab testing for regular screening for individuals on PrEP.
  - Rationale for change comes from analysis of incident HIV infection in HPTN 083 showing Ag/Ab assays are unpredictable for individuals on PrEP because they can remain negative or indeterminate for several additional weeks after acute infection.
  - Data from HPTN 083 shed key insights into the phenomenon of delayed seroconversion. Retrospective analysis of 51 of the HPTN 083's 52 incident HIV infections found delayed detection of infection in several cases.
    - In the CAB arm, 7 of 12 (58.3%) incident cases were not detected on routine Ag/Ab testing at a study visit, leading to a median delay of diagnosis of 98 days.
    - In TDF/FTC arm, delayed detection was found in 7 (17.9%) of the 39 incident cases, with a median delay of 31 days.
  - However viral load testing detected infection earlier in 5 of the 7 cases in the CAB arm and 6 of the 7 cases in the TDF/FTC arm.
  - Reversion of the Ag/Ab assay from reactive to nonreactive was also reported in the CAB arm.

# Patient Education

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- Attitudes and experiences of different patient populations
- Financial Assistance
- What the Provider Should Discuss with the Patient



# Attitudes and Experiences of Different Patient Populations

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- A study among MSM of color in NYC evaluated preference for a daily pill or an injection every 3 months to protect against HIV and found 79% preferred periodic injection.
- Interest in using CAB-LA to avoid “one stupid mistake” and allow for greater assurances against this possibility was more pronounced among MSM who more commonly self-reported engaging in multiple sexual partnerships than did the heterosexual participants.
- CAB-LA “affords more confidentiality and privacy than daily oral pills”. The privacy and lack of stigma were seen as an additional advantage of CAB-LA.
- In areas where PrEP is routinely used participants noted a decrease in the use of the term “Truvada whore” and instead suggested that there was actually increasing stigma linked to not being on PrEP as it was seen as being “irresponsible”
- Feelings of “invincibility” and an increase in condom-less sex were reduced because of the more frequent reminders to “stay safe” when getting their injections.
- When asked who were the “right people” the common response was “those with unstable lives, lack of routine, or an erratic schedule” such as migrant populations, homeless, substance users, or young people.
- In a nationwide sample of Black women in the US with 315 respondents, 32.1% were aware of PrEP and 40.6% were interested in using it; interest increased to 62.2% if PrEP were provided for free. Oral PrEP was preferred (62.7%) over LAI PrEP. LAI PrEP was more likely to be preferred among respondents with concerns about costs or PrEP-related stigma, and among those who reported inconsistent condom use and multiple sexual partners.

# Cost

Ready, set, PrEP (low or no cost for those who qualify)

Federal law requires that insurance plans cover certain items and services associated with PrEP.

Co-pay assistance (income not a factor)

ViivConnect- Program for PrEP shots

- Aprelude Savings Program ( Evouchers, Viiv savings cards, rebates)
- Medicare is tricky
- Medicaid variable
- PAP- no insurance

Prescription claims help- CMN sample online, PA support



# What The Provider Should Discuss with the Patient

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1. Before receiving LAI cabotegravir to reduce the risk of getting HIV-1, the patient must be HIV negative
2. Cabotegravir does not protect against pregnancy or STIs.
3. Patients should not miss doses. Missing injections will increase the risk of acquiring HIV.
4. Side effects may include allergic reactions, liver problems, depression, or mood changes.
5. Most common side effect is injection site reactions
6. Patients should tell the HCP about all the medications they take at every visit including OTC, vitamins, and herbal supplements.



# Special Considerations for Women with Childbearing Potential

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- Updated Centers for Disease Control and Prevention guidelines list multiple options for PrEP for men who have sex with men (MSM) and transgender women (TGW) including once-daily tenofovir alafenamide/emtricitabine (TAF/FTC), daily and “on-demand” tenofovir disoproxil/emtricitabine (TDF/FTC), and now CAB-LA.
- Cisgender women have 2 Food and Drug Administration (FDA)–approved options for PrEP: once-daily oral TDF/FTC or CAB-LA. TAF/FTC is currently being evaluated for PrEP in patients at risk for HIV infection due to receptive vaginal intercourse but is not currently approved for that indication. It is, however, currently approved for treatment in cisgender women with HIV when used in combination with other antiretrovirals regardless of pregnancy or childbearing status.
- Although the FDA approval for PrEP and treatment of HIV includes women of childbearing potential or women actively trying to conceive, the use of CAB-LA in these settings presents distinct challenges of which providers should be aware.

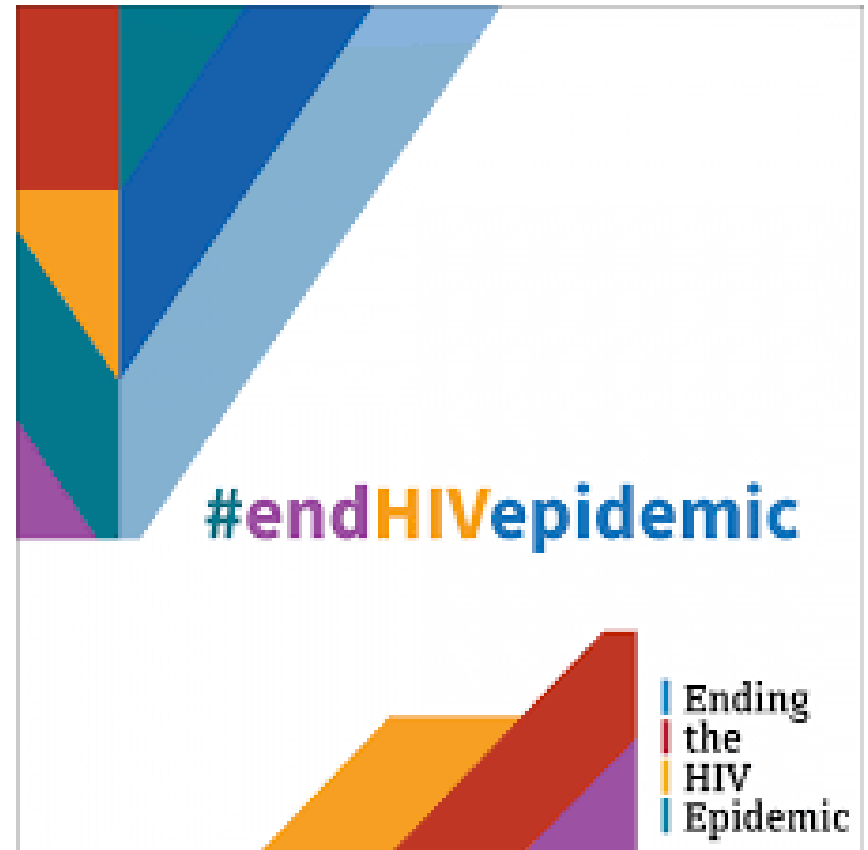
# Special Considerations for Women with Childbearing Potential <sup>2</sup>

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- A review of CAB LA pharmacokinetics highlights the potential for extended exposure to CAB at therapeutic levels even after discontinuation of the injections. Women who conceive up to 1 year or more after discontinuation of PrEP with CAB-LA may have significant CAB levels at the time of conception and during the first trimester.
- Without appropriate preconception counseling, many women may not be aware of this information, and CAB-LA is not currently recommended in women who are pregnant.
- The logistical issues of asynchronous timing of injections may create adherence difficulties for some patients. The concomitant use of reliable contraception should be advocated. Until additional data are accumulated regarding the safety of CAB-LA in pregnancy, providers may want to proceed with caution when using CAB-LA in women of reproductive potential.

# Opportunities & Aspirations for LAI Cabotegravir and Beyond

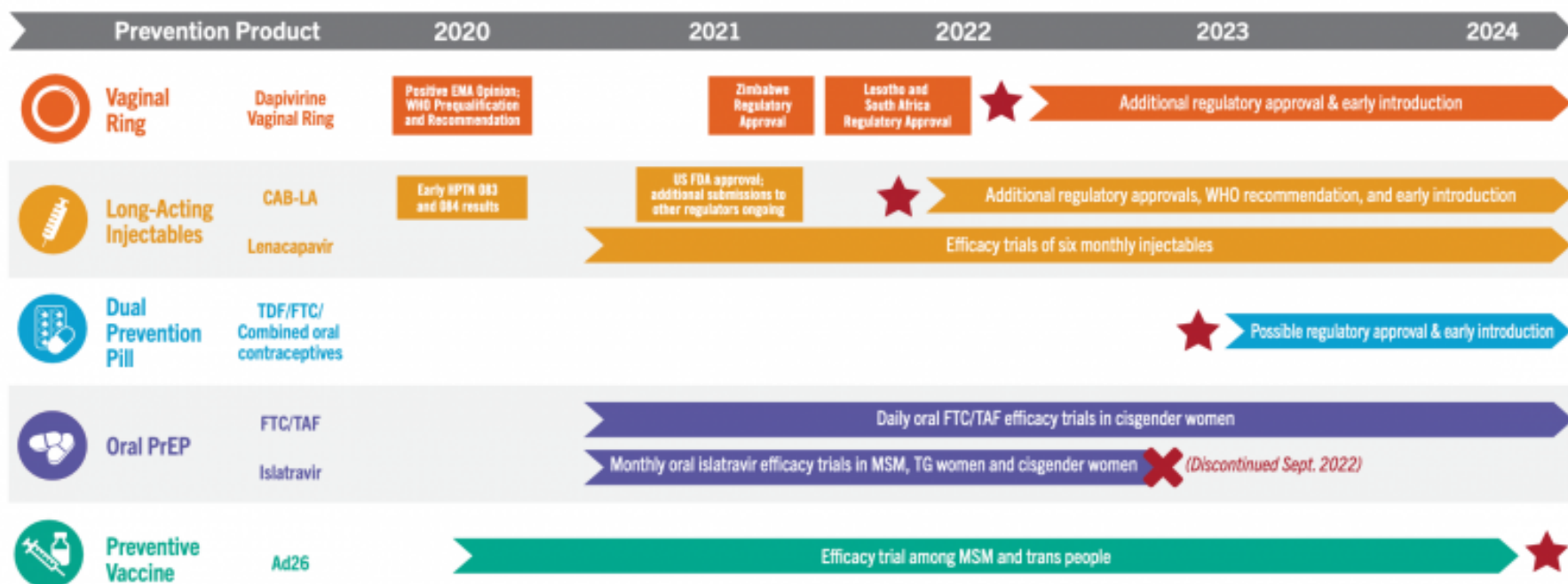
- Viiv is the developer and will be the sole supplier in the initial period. Appropriate price volume has to be identified for this initial 4-5year period.
- Voluntary licensing to generic manufacturers along with capital investments will be necessary to secure a low-cost, sustainable, enable, and diversified product supply.
- Provider training (explaining efficacy, clinic visits, side effects etc.. of all methods available)
- Testing requirements
- Data needs to be collected on the benefit of injectable CAB as PrEP population signs not part of the efficacy trials (esp. adolescents, pregnant and breast-feeding people, transmasculine and gender-nonconforming individuals)
- Research study on alternate injection sites and frequency (consider alignment with injectable contraception)



# Years Ahead in HIV Prevention Research

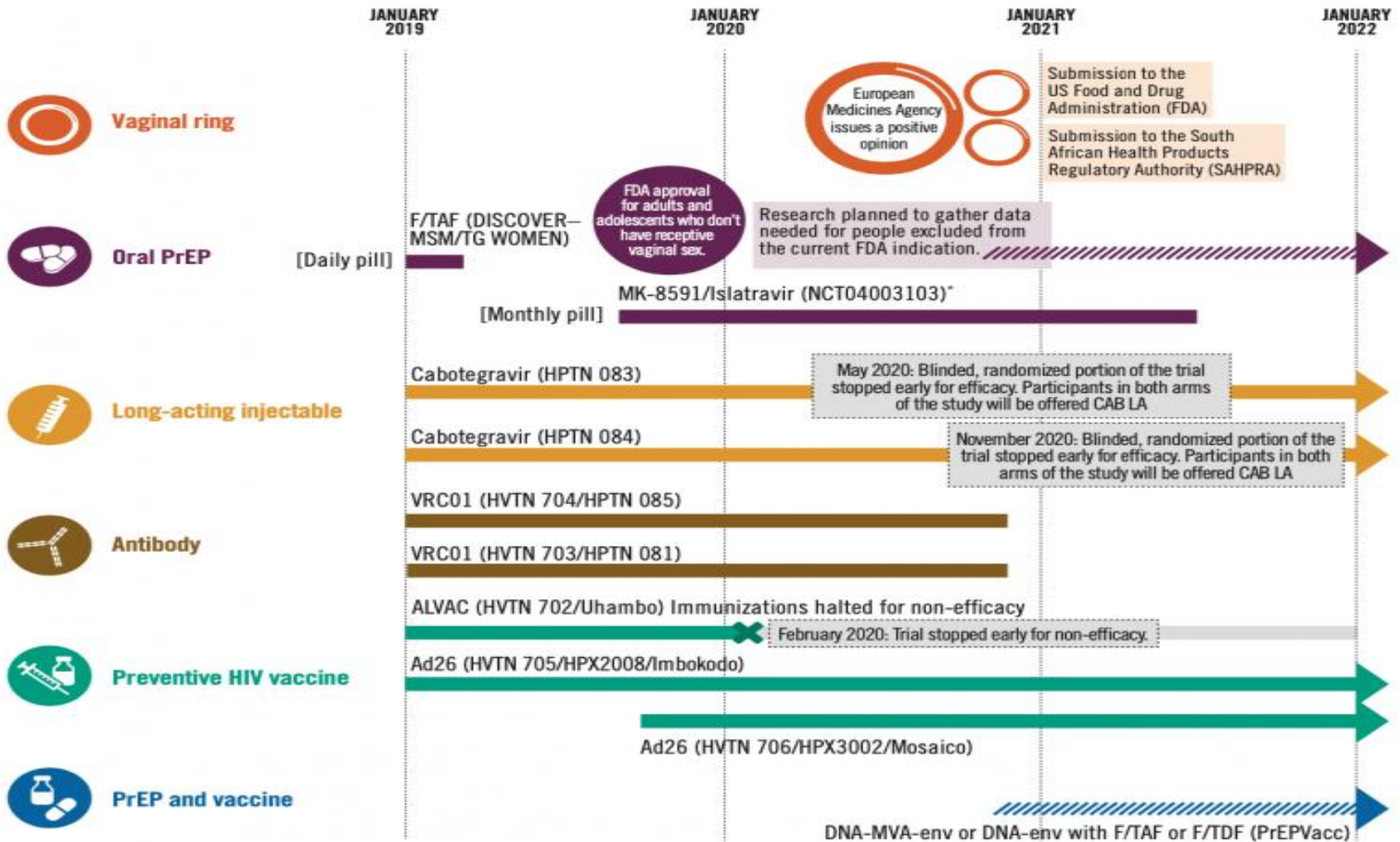
## Time to Market

★ Earliest time to market  
 ✗ Discontinued




AVAC [www.avac.org](http://www.avac.org)  
 September 2022

# Biomedical HIV Prevention Trials: Results, milestones and more





# Conclusion




 **Diagnose** all people with HIV as early as possible.



**Treat** people with HIV rapidly and effectively to reach sustained viral suppression. 

 **Prevent** new HIV transmissions by using proven interventions, including pre-exposure prophylaxis (PrEP) and syringe services programs (SSPs).



**Respond** quickly to potential HIV outbreaks to get needed prevention and treatment services to people who need them. 



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