

AVAC

Global Advocacy for HIV Prevention

The Science of Oral PrEP and the Next Generation Pipeline

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10 October, *Second European PrEP, U=U and Biomedical Prevention Summit*

Oral PrEP Basics

- Truvada (TDF/FTC) as only PrEP agent until this year
- PrEP reduces HIV risk across all types of exposures, sexes and genders and dosing regimens
- No significant side effects, generally
- Drug resistance can occur if an undiagnosed person with HIV starts PrEP or acquires HIV while taking PrEP inconsistently
- People with high risk can also be highly adherent to PrEP

Oral PrEP works if you take it

- 96% protective with high adherence (4 or more doses/week)
 - iPrEx OLE in cis men and trans women
 - P3 and HPTN 082 demonstration studies in cis women
- WHO: Oral PrEP fully protective after 7 days of continuous use for all sites (anal, vaginal, injection)
- Daily, oral TDF/FTC for all
- 2-1-1, event driven dosing for men who have sex with men



PrEP 2.0: the research pipeline

“Although TDF-based oral PrEP has been shown to be highly effective, it’s reliance on adherence for effectiveness has prevented the realization of its full potential for reducing incidence. The future of PrEP is characterized by a robust development pipeline.”

—Lara Esteves Coelho, PrEP 2.0 new drugs and technologies in the pipeline

HIV Px R&D Spectrum





Currently available

-  HIV treatment for people living with HIV
-  Oral PrEP with TDF/FTC
-  PrEP
-  Voluntary medical male circumcision
-  Male & Female Condoms
-  Syringe exchange programs









In regulatory review

-  Dapivirine vaginal ring

In development: Efficacy trials Under way

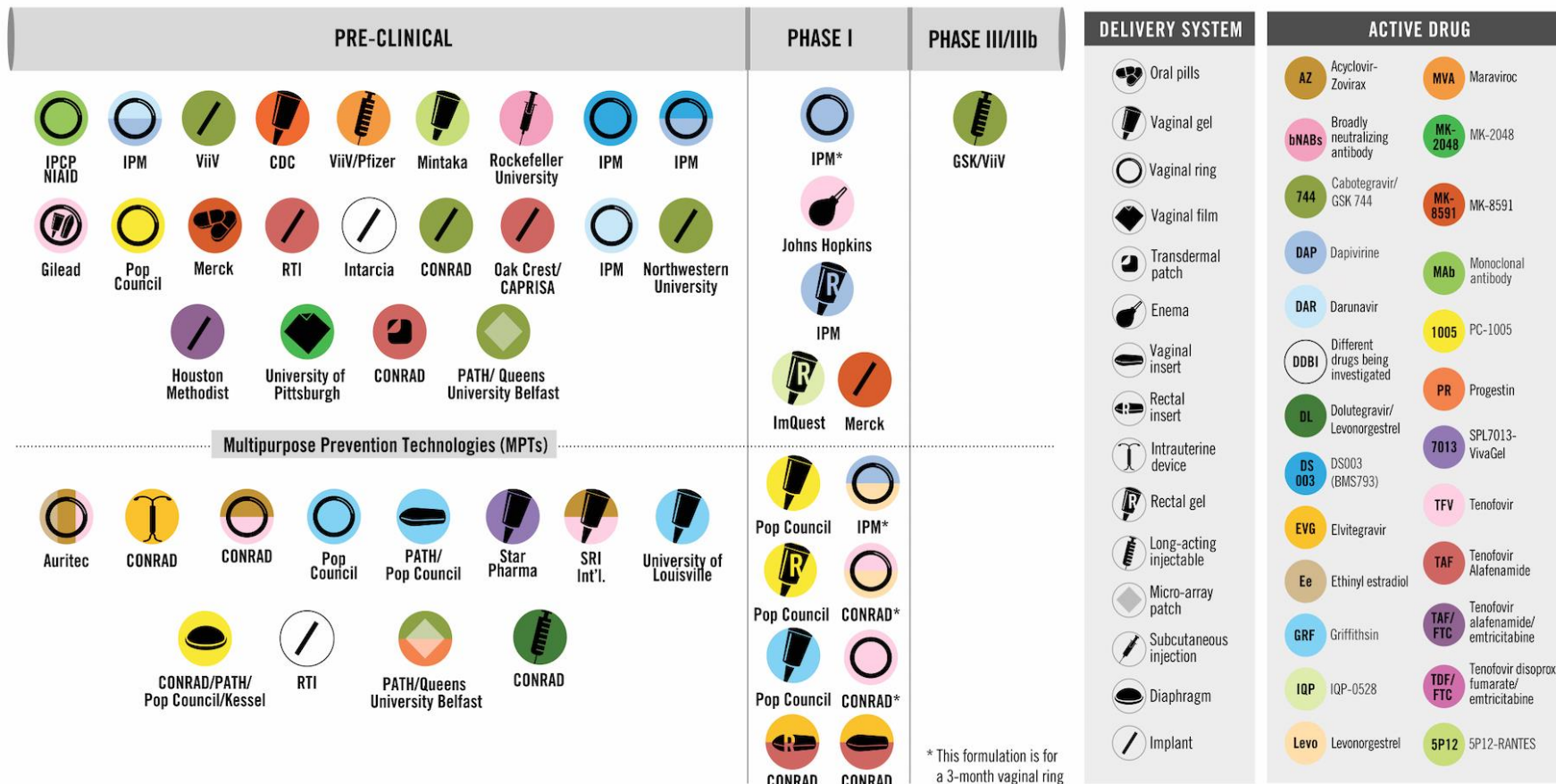
-  Oral PrEP with F/TAF
-  Preventive vaccines
-  Long-acting injectable
-  Broadly neutralizing antibodies

In development: Various pre-clinical and clinical

-  Long-acting Oral PrEP
-  Preventive vaccines
-  Long-acting implants
-  Broadly neutralizing antibodies
-  Inserts
-  Patches
-  Multipurpose vaginal ring
-  Combo Oral PrEP/OC

The Future of ARV-Based Prevention and More (September 2019)

The pipeline of non-vaccine HIV prevention products includes oral pills, vaginal rings, vaginal and rectal gels, vaginal films, long-acting injectable antiretrovirals and more. Also pictured are the range of multipurpose prevention technologies in development that aim to reduce the risk of HIV and STIs and/or provide effective contraception for women. (Visit www.avac.org/hvad for vaccine and broadly neutralizing antibody pipelines.)



What's what?



- DISCOVER study: Compared F/TAF to TDF/FTC or Descovy to Truvada ONLY in MSM and trans women in Europe and North America
- Results: F/TAF is non-inferior to TDF/FTC, aka **”NOT BETTER THAN Truvada”**
- FTAF shows minor improvements in bone density and renal health, but higher obesity and cardiovascular profile
- Absence of safety and efficacy data
 - in cis-gender women, trans men and IDU’s
 - 2-1-1 or event-driven
- Patented, expensive

- This month, the US FDA approved F/TAF for PrEP “excluding individuals at-risk from receptive vaginal sex.”
- Studies of vaginal tissue concentrations following oral F/TAF have been mixed compared to TDF/FTC. Descovy may work differently in vaginal exposures, so studying efficacy in these populations is important
- FDA requires Gilead to conduct a trial in cis-women and AGYW.
- What about trans men? IDUs?
- Gilead filing with EMA?

Other agents, injectables, vaccines

- Once-monthly pill, MK-8591, Phase 2b
- Long-acting injectable (every 8 weeks), cabotegravir, 2 efficacy trials ongoing in MSM and trans women and in cis women
 - What factors influence adherence to injection sites?
 - What to do with drug tail? Oral PrEP?
 - Interactions with cross-sex hormone therapy unknown
 - Excludes trans-women with butt implants
 - Results in 2021
- Mosaico vaccine, Phase 3 in European and North American MSM and trans*, results 2023+
- Imbokodo sister study in women in Africa, results 2022
- HVTN 702 women and men in Africa, results 2021

Immuno-prophylaxis

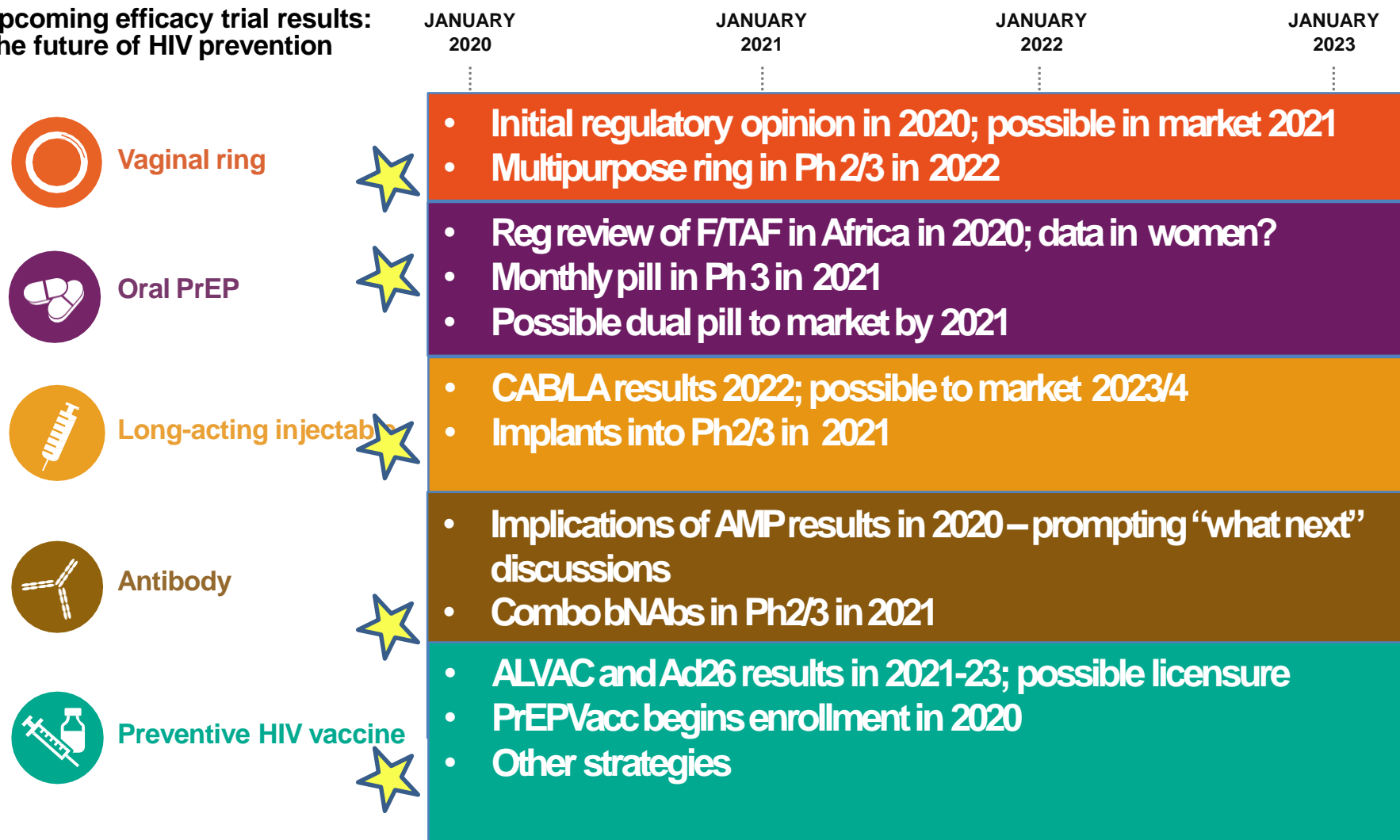
- Broadly neutralizing antibodies/bNAbs
 - Infused engineered bNAbs can clear free virus or virus-infected cells, interfering with viral reservoir
 - Safe allowing for long intervals between infusions
 - But is intravenous administration a feasible public health intervention?
 - Phase 2b proof of concept, VRCO1 (AMP) injection every 8 weeks (a site in Switzerland, the Americas and Africa), results in 2020
 - Need for combined bNAbs to avoid resistance

Rings, gels, implants, patches

- Monthly dapivirine vaginal ring
 - Reduced risk by up to 56%
 - EMA decision pending for African countries
- 3 month dapivirine and tenofovir rings in Phase I
- Multipurpose prevention technologies
 - Prevention of STIs, HIV and pregnancy
 - Vaginal rings, dual pills (PrEP/OC), microbicide gels in or approaching early phase studies
- Implants: subdermal PrEP
 - Removable (unlike long-acting injectables); biodegradable
- Transdermal PrEP, e.g. microneedle delivery
 - Ease of discontinuation
 - Potential study of delivery of cabotegravir

R&D Pipeline – Future Milestones

Upcoming efficacy trial results: The future of HIV prevention



Is Europe ready?

- Oral PrEP is highly effective for those who can adhere; for those who cannot, there is an unmet need
- Robust prevention pipeline for alternatives to oral PrEP
- Could F/TAF (Descovy) have added value in Europe?
- Long-acting injectable PrEP results in 2022
- Vaginal ring EMA opinion for Africa in 2020
- Mosaic vaccine efficacy trial in Europe, starts this year
- Trial design and advancing new products in age of PrEP—what designs are efficient and ethical?
- How to keep R&D on the HIV agenda?

Shout Out

- Greater Involvement of People who use PrEP in practice, advocacy and policy.

The logo for Prepster, featuring the word "Prepster" in a black, cursive script font with a thick black underline.

- AVAC website: www.avac.org
- PrEPWatch: Clearinghouse for PrEP data, research, cost, access, etc. www.prepwatch.org