

AVAC

Global Advocacy for HIV Prevention

# What's New; What's Next

## *A Quick Overview of the Px Pipeline*

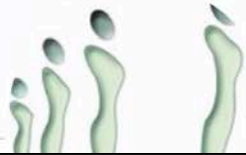
Mitchell Warren, Executive Director  
*11 February 2019, MTN Annual Meeting*

# Outline

- Why
- Where we are now
- What next – near-term
- What next – medium-term
- How

Today is...

# International Day of Women and Girls in Science



February 11

# THE LANCET

Volume 393 · Number 10121 · Pages 493-610 · February 9-15, 2019

[www.thelancet.com](http://www.thelancet.com)

Advancing women in science,  
medicine, and global health



*I read the news today; Oh, boy*

## Five African Countries Approach Control of Their HIV Epidemics as U.S. Government Launches Bold Strategy to Accelerate Progress

September 19, 2017

# PEPFAR

U.S. President's Emergency Plan for AIDS Relief

## Strategy for Accelerating HIV/AIDS Epidemic Control (2017-2020)

*The New York Times*

In Africa, a Glimpse of Hope for Beating H.I.V.

VOA search text ... [social media icons: f, t, y, i, g+, A]

HOME WORLD EDITOR'S PICKS TECHNOLOGY SCIENCE & HEALTH US POLITICS SOUTH CHINA SEA MORE LISTEN

SCIENCE & HEALTH

November 27, 2017  
2:54 AM  
Carol Pearson

# We Have the Tools to End AIDS Now

# Easy to Say; Hard to Do

## Trajectories to fast-track prevention targets: The present state of HIV prevention



People on ART



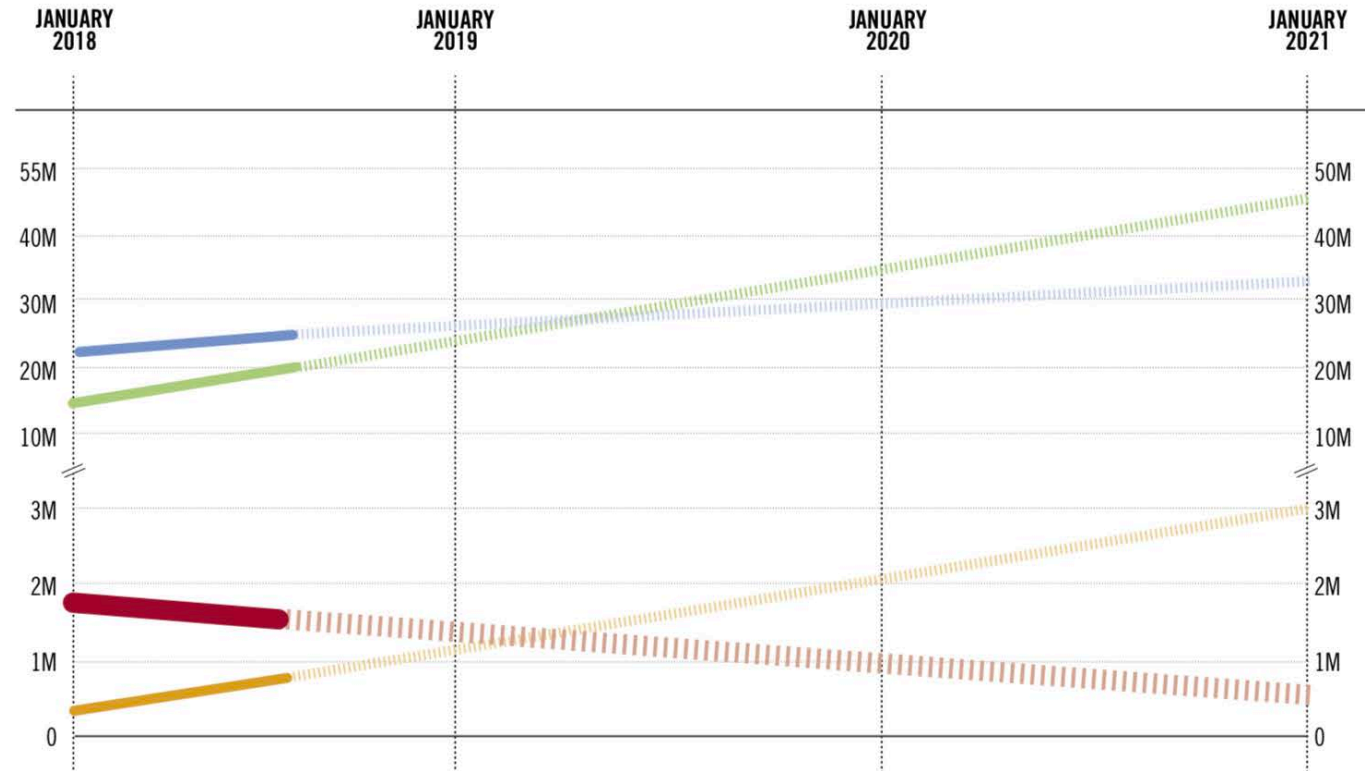
VMMCs performed



New HIV infections

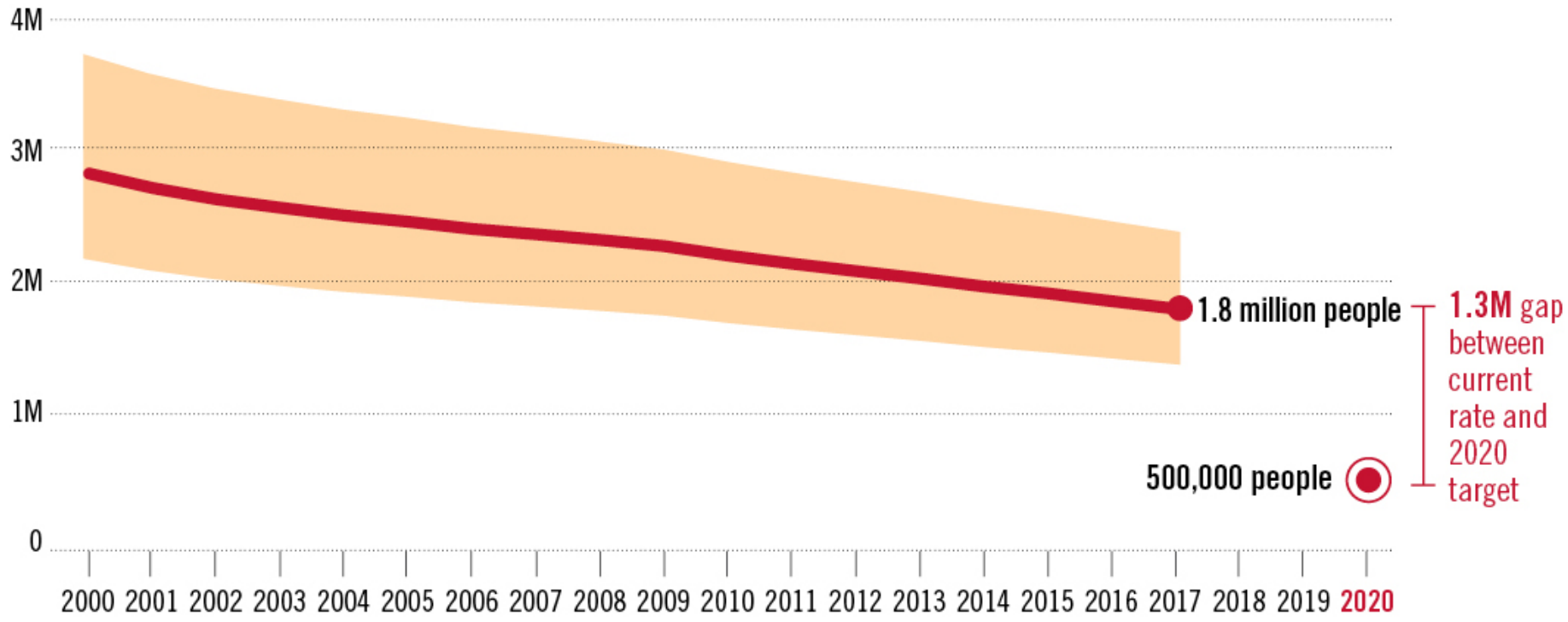


Oral TDF/FTC PrEP users



# And We're Missing the Target – Badly

## Global Number of New HIV Infections, 2000-2017 and 2020 Target



Source: UNAIDS. *Miles to Go—Closing gaps, breaking barriers, righting injustices*. July 2018. Accessible at: [www.unaids.org/en/resources/documents/2018/global-aids-update](http://www.unaids.org/en/resources/documents/2018/global-aids-update).

AVAC Report 2018: *No Prevention, No End*  
[www.avac.org/report2018](http://www.avac.org/report2018)

# New Biomedical Approaches

## Upcoming efficacy trial results: The future of HIV prevention



Vaginal ring



Oral PrEP



Long-acting injectable



Antibody



Preventive HIV vaccine

JANUARY  
2018

JANUARY  
2019

JANUARY  
2020

JANUARY  
2021

Dapivirine (HOPE/MTN 025)

Dapivirine (DREAM/IPM 032)



F/TAF (DISCOVER)

Cabotegravir (HPTN 083)

Cabotegravir (HPTN 084)

VRC01 (HVTN 704/HPTN 085)

VRC01 (HVTN 703/HPTN 081)

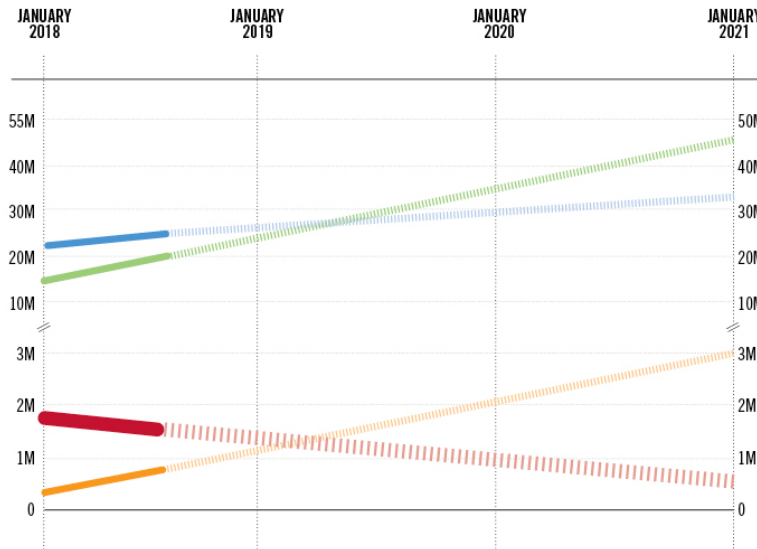
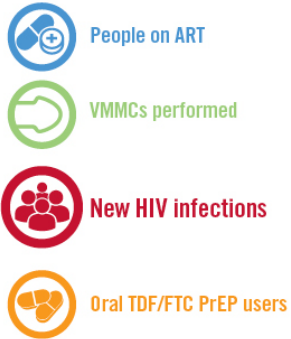
ALVAC (HVTN 702)

Ad26 (HVTN 705)

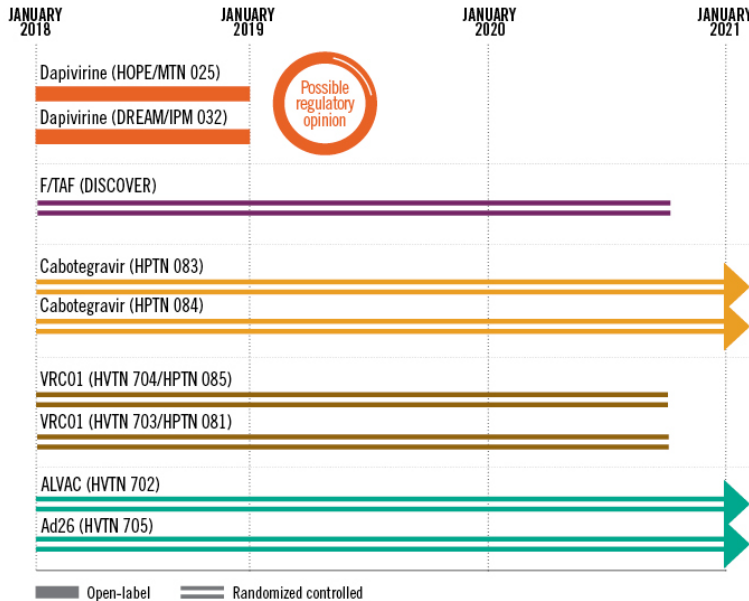
Visit [www.avac.org/pxrd](http://www.avac.org/pxrd) for trial status updates.

— Open-label    == Randomized controlled

**Trajectories to fast-track prevention targets: The present state of HIV prevention**



**Upcoming efficacy trial results: The future of HIV prevention**



Visit [www.avac.org/pxrd](http://www.avac.org/pxrd) for trial status updates.

# One Timeline, Two Stories, One Message

- With the current trajectory, we will miss targets for incidence reduction & scale up of primary prevention
- At the same time, we will see key trial results
- Need to tell these two stories, and support an evidence-based narrative
- Preparing for this is key!



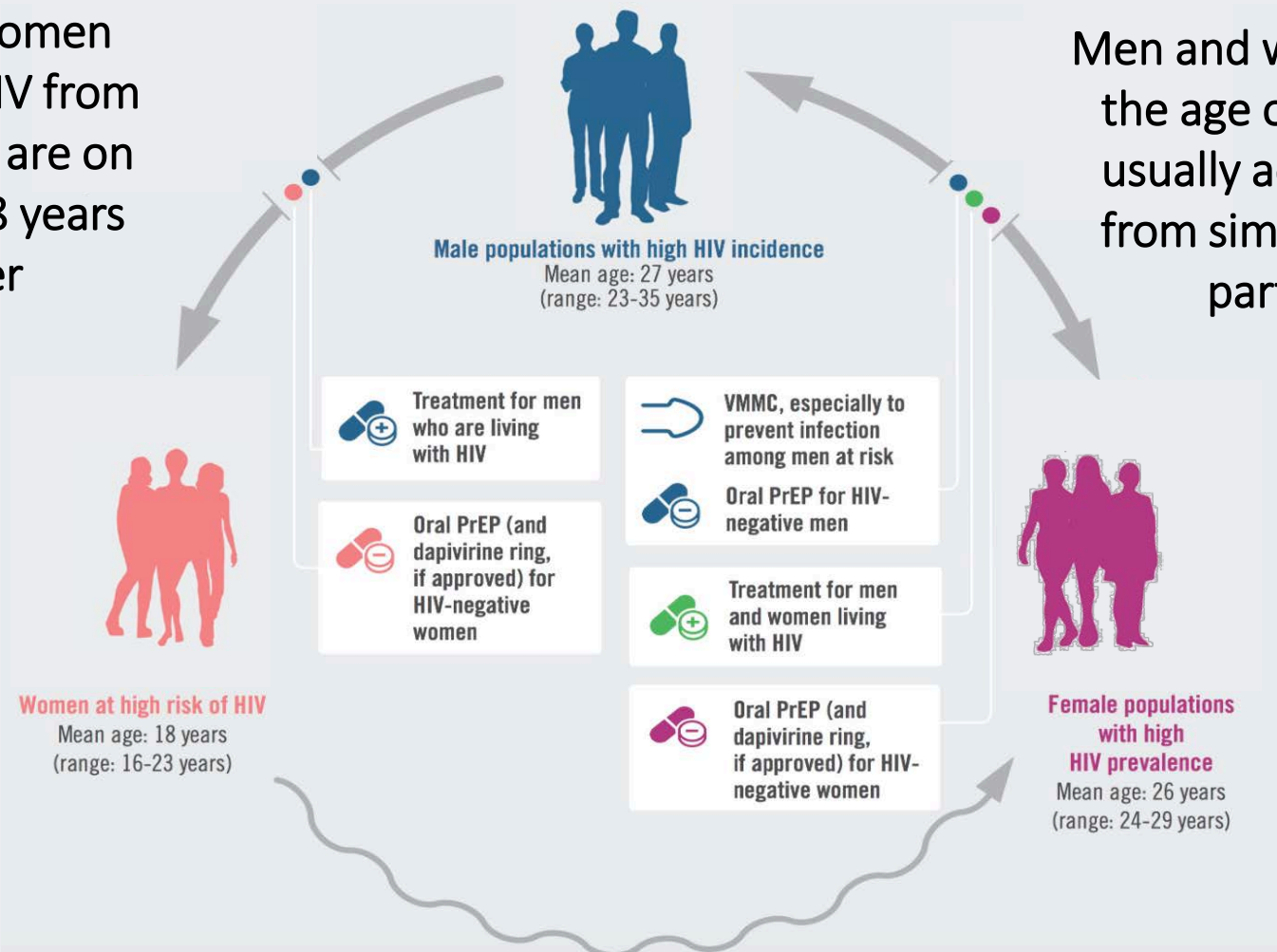
# To Think About Now

- Where is the greatest unmet need for prevention?
- What products will people want AND use?
- What trial designs can best answer the questions fastest and ethically?
- How will we deliver next generation PrEP?
- How to best “balance our portfolio”?
- How do we keep R&D part of the “ending AIDS” narrative?

# Breaking the Cycle of Heterosexual Transmission

Young women acquire HIV from men who are on average 8 years older

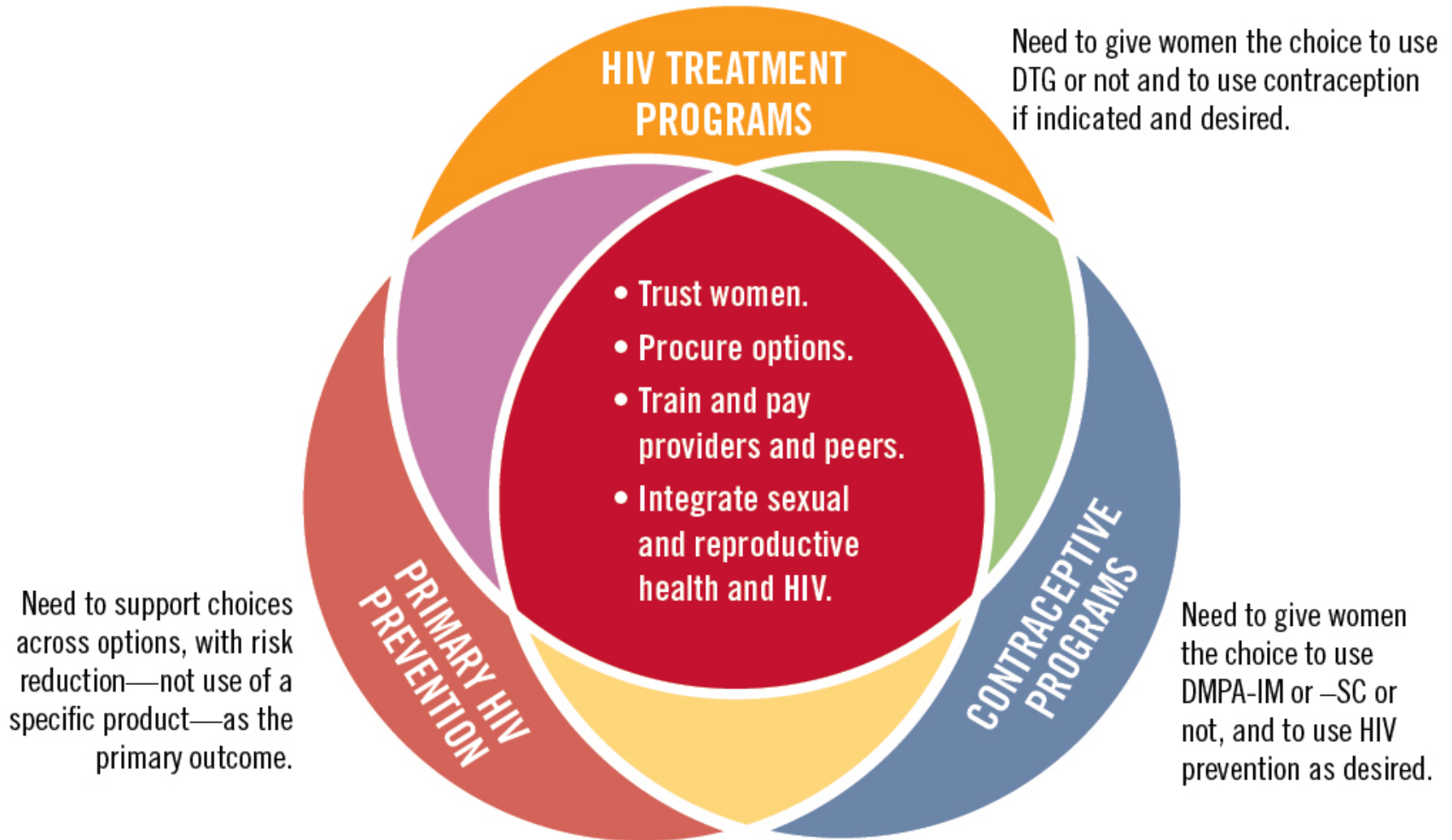
Men and women over the age of 24 years usually acquire HIV from similarly aged partners



When teen women with HIV reach their mid-20s, if they aren't on effective ART, then they may transmit to partners of the same age—and vice versa

Adapted from: Dellar R, Tanser F, Abdool Karim Q, et al. Manuscript in preparation. / Abdool Karim Q. *HIV infection in young women in Africa: An overview*. Presentation at AIDS 2016. <http://programme.aids2016.org/Programme/Session/1257>. <http://www.avac.org/infographic/breaking-cycle-heterosexual-transmission>

# Putting Women\* at the Center: Informed choice in 2018 and beyond



\* This graphic uses issues of primary relevance to cisgendered women and does not reflect diversity within those communities. The principles at the center could be adapted to apply to every category of person affected by HIV, including but not limited to transgender women, gay men and other men who have sex with men, heterosexual men and migrants. We also stand firm in the belief that the needs and issues of cisgendered women must be continually and specifically foregrounded as central to any epidemic response.

# Prevention Paradigm 2018 & beyond

## Different Strokes for Different Folks

Method	Contraception	HIV Prevention
Behaviour	✓	✓
Barrier Methods	✓	✓
Gels	✓	✓ – not registered
Rings	✓	✓ – with regulatory body
Oral pill	✓	✓
Injectables	✓	? – 1 ARV, 1 bNAb, 2 vax in phase 3; others in development
Implants	✓	? – multiple in preclinical
Surgical procedures	✓	✓
Treatment		✓

# 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



Dapirine 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

# 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

- Davipirine vaginal ring

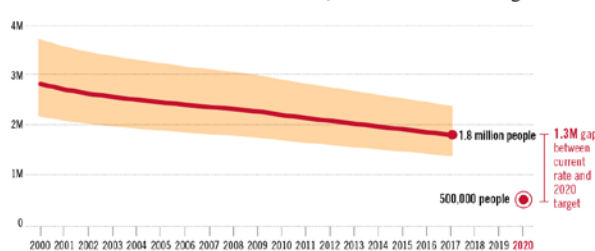
## In development: Efficacy trials Under way

- 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

Global Number of New HIV Infections, 2000-2017 and 2020 Target

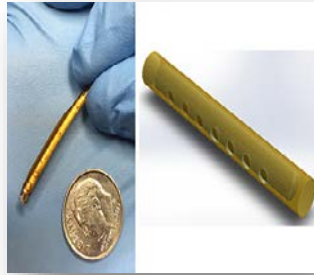


Source: UNAIDS. *Miles to Go—Closing gaps, breaking barriers, righting injustices*. July 2018. Accessible at: [www.unaids.org/en/resources/documents/2018/global-aids-update](http://www.unaids.org/en/resources/documents/2018/global-aids-update).

AVAC Report 2018. *No Prevention, No End*. [www.avac.org/report2018](http://www.avac.org/report2018)



# Next Up – Implant Devices



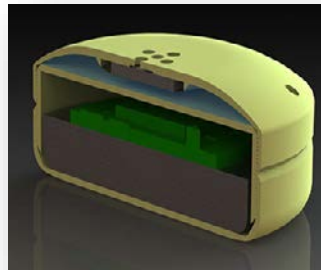
**IRTI**  
INTERNATIONAL

**OAK CREST**  
INSTITUTE  
OF  
SCIENCE

 **CAPRISA**  
CENTRE FOR THE AIDS PROGRAMME OF RESEARCH IN SOUTH AFRICA

  
**Intarcia**  
Therapeutics, Inc.

- Active Drugs**
- TAF (Gilead)
  - EFdA/MK-8591 (Merck)
  - Cabotegravir (ViiV)
  - bNAbs (multiple)



 **Northwestern**  
University

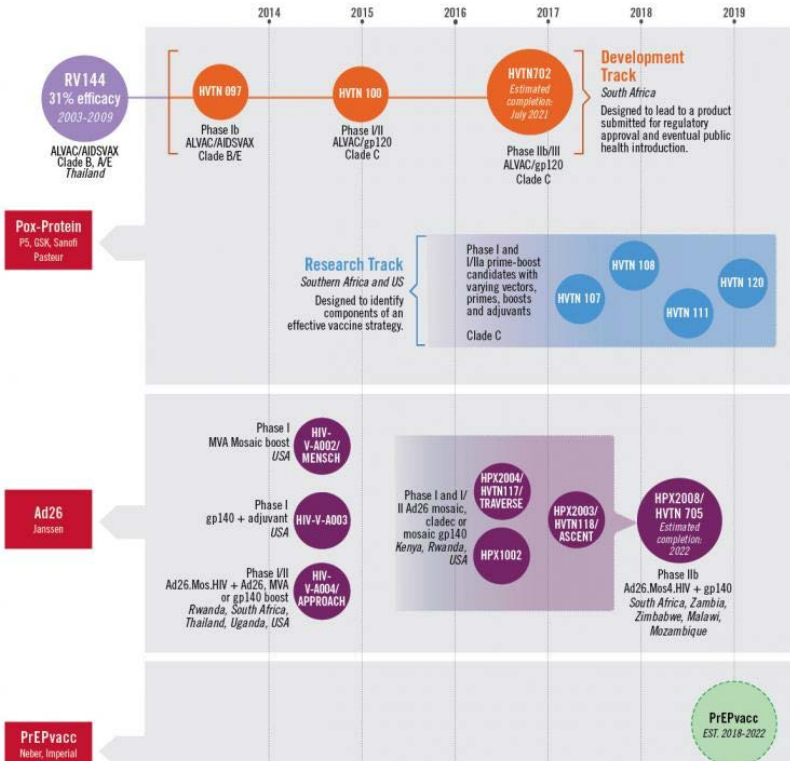
**HOUSTON**  
**Methodist**  
LEADING MEDICINE

 **MERCK**

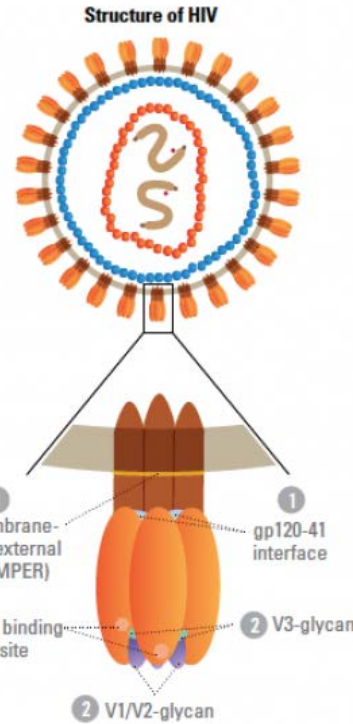


# Next-Gen Vax & bNAb

## VACCINE EFFICACY TRIALS PIPELINE



## HIV-SPECIFIC NEUTRALIZING ANTIBODIES: Targets and research status



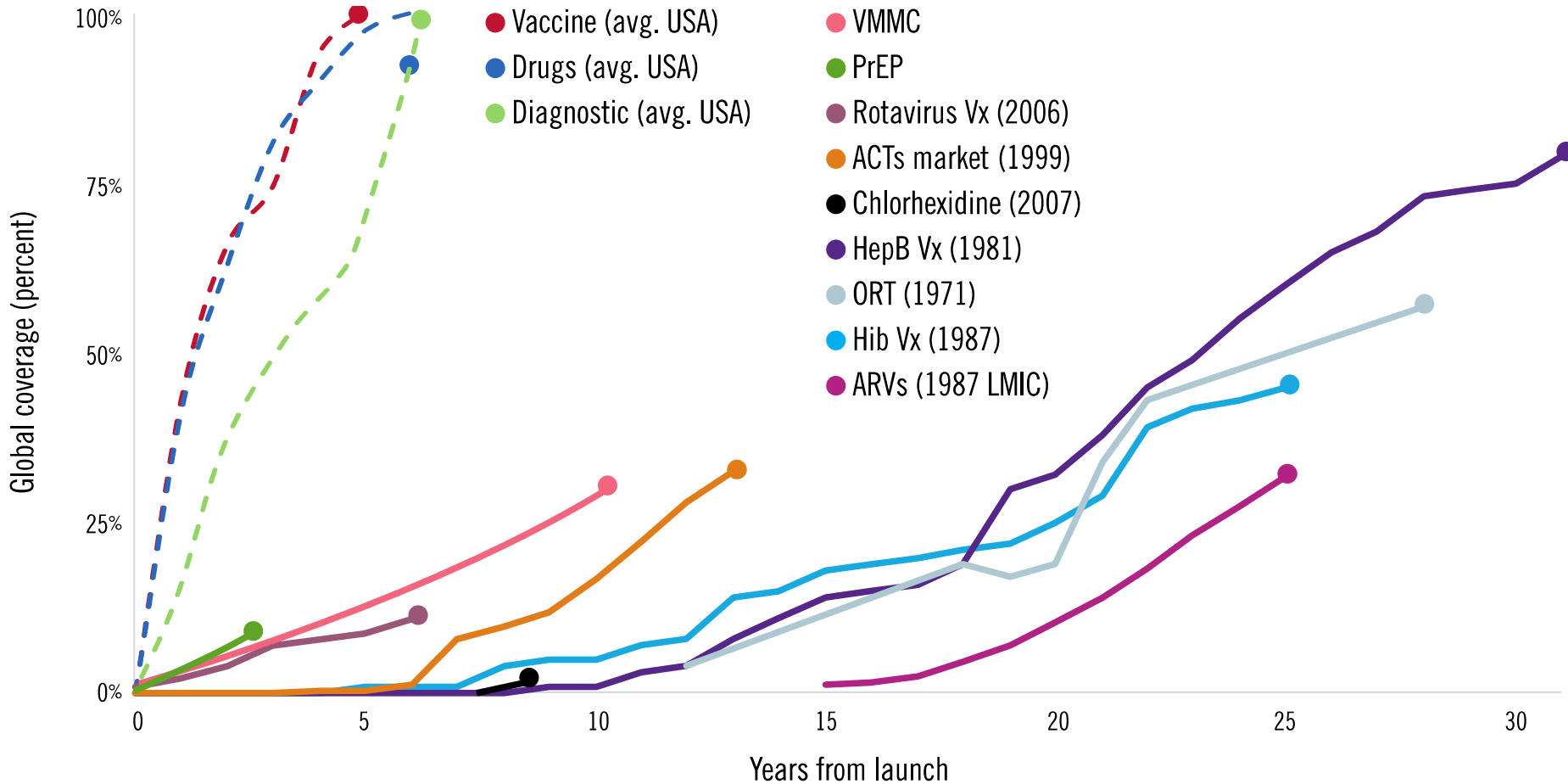
HIV envelope target	Antibody	Status			
		Pre-clinical	Phase I	Phase II	Phase I/II/III
CD4 binding site	3BNC117		Y		
	VRC01		Y		Y
	VRC07-523		Y		
gp41 membrane proximal external region (MPER)	N6		Y		
	10e8	Y			
gp120-41 interface	4e10		Y		
	8ANC195	Y			
V1/V2-glycan	PGT151	Y			
	CAP256-VRC26		Y		
V3-glycan	PGDM1400		Y		
	PG9		Y		
	CH01	Y			
CD4 binding / V3-glycan	PGT121		Y		
	PGT128	Y			
	PGT135	Y			
CD4 binding site	10-1074		Y		
	3BNC117+10-1074		Y		
	CAP256-VRC26+PGT121			Y	
CD4 binding site	CAP256-VRC26+VRC07		Y		

KEY: Y Ongoing Trials Y Planned Trials

## Vaccine Strategies in the Pipeline

Vaccine Component				Delivery Mechanism		
<b>DNA</b> DNA + MVA DNA + AIDSVAX	<b>Adenovirus vectors</b>	<b>Lipopeptides</b>	<b>Proteins</b>	<b>Electroporation</b>	<b>Oral</b>	<b>Intradermal</b>
Variations on the only strategy to show efficacy to date.	Vectors carry synthetic fragments of HIV. "Ad" vectors help prompt strong T-cell responses.	A molecular hybrid (amino acid plus lipid) that is used to generate T-cell responses.	Viruses make proteins that the immune system responds to. These can be used in vaccines.	A delivery method using an electrical field to increase the permeability of cells to the vaccine.	A delivery strategy that could prompt strong mucosal responses.	Delivery into the skin rather than the muscle; uses a much smaller needle.

# But What If It Works?



Product launch year is shown in parentheses.  
LMIC = Lower- and middle-income countries

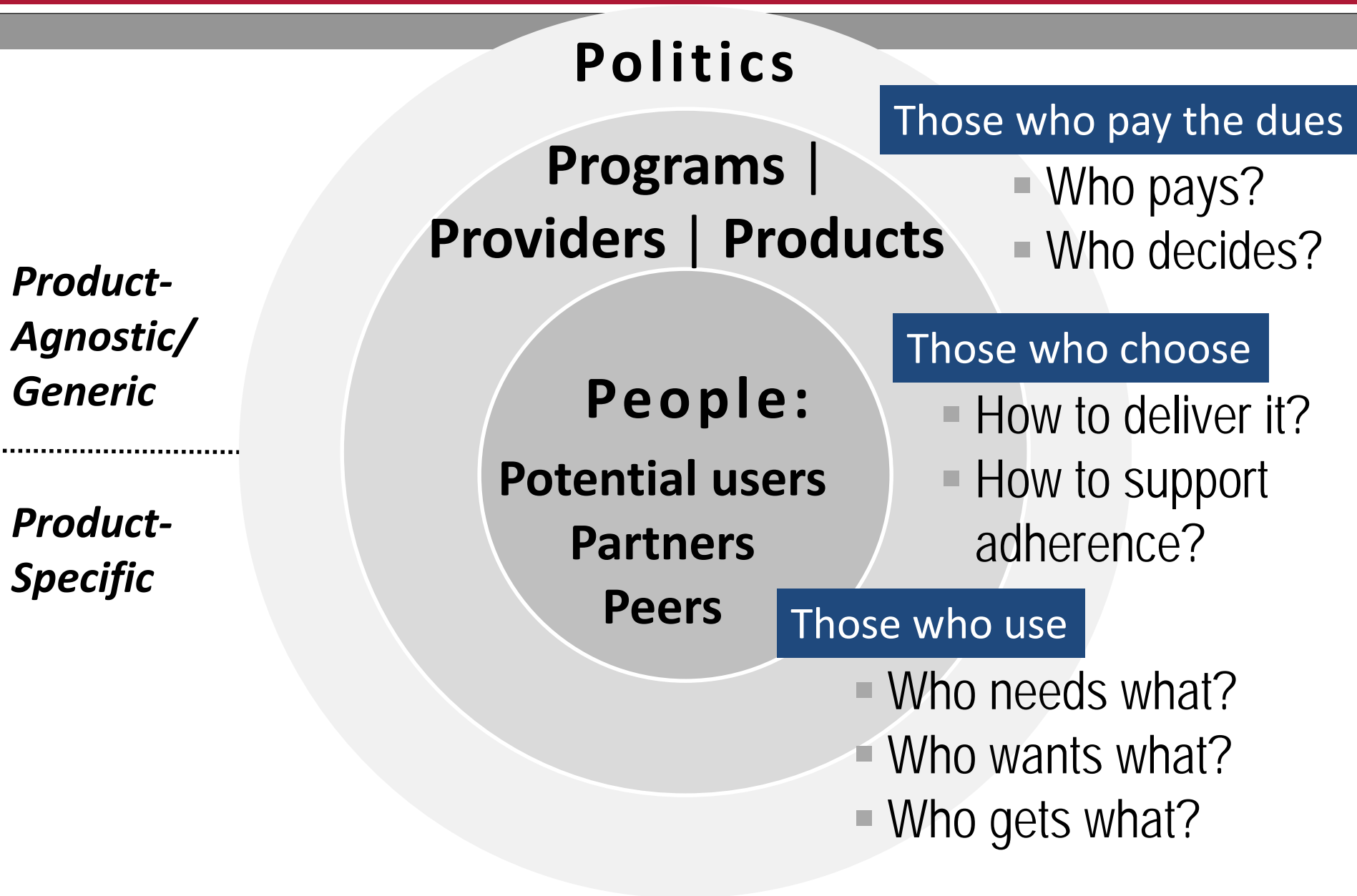
Figure courtesy of Dana Hovig, Bill & Melinda Gates Foundation.

# Avoiding Historic Delays with Intro

Full impact of recent advances—including VMMC & oral PrEP—delayed by years because of limited advance planning for roll-out:

- Limited research to identify & understand potential users
- Lack of coordinated plans for demonstration projects – e.g., many small studies; not big or consistent enough to draw conclusions
- Few tools for country-level decision makers e.g., estimated costs or impact of investments
- Slow recognition of importance of and investments in strategic demand creation

# Product Introduction & Access



# Product Considerations

For each product, understand and balance:

## Clinical

- Biologic efficacy
- Dosing
- Reversibility
- Side effect profile
- Systemic/Topical

## Policy & Programs

- Delivery channel(s)
- Health system burden
- Product cost
- Program cost
- Provider training

## Personal

- User effectiveness
- User preference
- User burden
- Discretion of use
- Contribution to stigma

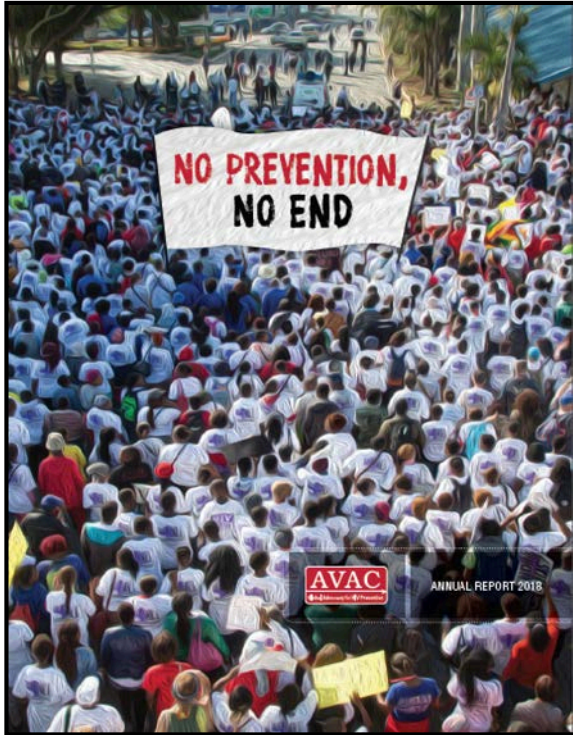
# The Months Ahead

- NIAID Clinical Trial Network announcement
- REACH trial launch
- PEPFAR COP review
- PopART/HPTN 071 results
- Dolutegravir and possible neural tube defects?
- Appointment of new UNAIDS director
- DISCOVER oral F/TAF results – *possible*
- EMA opinion on dapivirine ring Article 58 – *possible*
- ECHO Trial Results – *possible*
- IAS 2019
- Global Fund replenishment
- Ad26 Phase 3 launch – *possible*
- Early indication of CAB-LA efficacy – *possible*
- Early indication of VRC-01 efficacy – *possible*

# Bottom line(s)

- Oral TDF/FTC is the PrEP we have now
- Oral F/TAF results due in 2019/20 – BUT currently only being studied for efficacy in men and transgender women who have sex with men
- Dapivirine ring could enter the market by 2020 – possible multi-purpose product could follow (ring as well as oral combo)
- Fast Track targets (90-90-90+++) due in 2020
- Earliest injectable px to market in 2022 – one possible product
- Earliest vax or bNAb to market in 2024 – multiple products
- Earliest implant px to market in 2025 – multiple devices; two active drugs
- Fast Track targets (95-95-95+++) due in 2030

# Acknowledgements



Thank you!

- [www.avac.org](http://www.avac.org)
- [www.PrEPWatch.org](http://www.PrEPWatch.org)
- [mitchell@avac.org](mailto:mitchell@avac.org)

**HIV Prevention Market Manager** | Accelerating Product Introduction  
Informing Product Development  
Reducing Time to Impact

**AVAC** | CLINTON HEALTH ACCESS INITIATIVE  
Global Advocacy for HIV Prevention

Supported by the Bill & Melinda Gates Foundation

**BILL & MELINDA GATES** foundation

**OPTIONS**  
OPTIMIZING PREVENTION TECHNOLOGY INTRODUCTION ON SCHEDULE

**fhi360** THE SCIENCE OF IMPROVING LIVES | **WITS RHI** | **AVAC** Global Advocacy for HIV Prevention | **PZAT** (PILGICAL ZEPHRAE AIDS TRUST) | **lvct health** healthy systems

**FSG** REIMAGINING SOCIAL CHANGE | **McCANN** GLOBAL HEALTH | **Avenir Health** | **LONDON SCHOOL OF HYGIENE & TROPICAL MEDICINE**

**USAID** FROM THE AMERICAN PEOPLE | **PEPFAR**

**Coalition to Accelerate & Support Prevention Research (CASPR)**

**USAID** FROM THE AMERICAN PEOPLE | **PEPFAR** U.S. President's Emergency Plan for AIDS Relief | **AVAC** Global Advocacy for HIV Prevention

**APHIS** | **Avenir Health** | **fhi360** THE SCIENCE OF IMPROVING LIVES | **tavi** International AIDS Vaccine Initiative

**Internews** Local voices. Global change. | **UNIVERSITY OF KWAZULU-NATAL** (SCHOOL OF HEALTH, BEHAVIOUR & SOCIETY) | **Waci Health** Empowering Health for All in Africa | **WITS RHI**

Cooperative Agreement No. AID-OAA-A-16-00031  
HIV Vaccine and Biomedical Prevention Research Project—Objective 3



# Acknowledgements

