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Dapivirine Ring Development: Next Steps

Dr. Zeda Rosenberg, IPM

MTN Annual Meeting, March 20, 2017

Developing HIV Prevention Products for Women worldwide

What's Next for the Dapivirine Ring?

REGULATORY PATHWAY

Applications for regulatory approval will be submitted starting mid-2017

PUBLIC HEALTH PATHWAY

Two open-label extension studies and adherence studies to support consistent use

Potential Access

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Regulatory
Pathway
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Path to Regulatory Approval

IPM's role: regulatory sponsor

- Hold worldwide rights to dapivirine
- Ensure all preclinical, clinical and pharmaceutical quality/chemistry, manufacturing and controls (CMC) data meet regulatory requirements
- Formally apply for dapivirine ring approval through European, US and African regulatory authorities

Approval pathway for new HIV prevention drug can be more complex than for a drug already approved for treatment (e.g., oral Truvada)

Regulatory Submission Plans

As of 3/20/17

European Medicines Agency (EMA)

- Article 58 eligibility reconfirmed 2016
- (Co) Rapporteur meetings Jan 2017
- Pre-submission meeting Feb 2017
- Target submission Q2 2017

World Health Organization (WHO)

- Article 58 process facilitates WHO prequalification (PQ)

US Food and Drug Administration (FDA)

- Target submission mid-2018

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Why WHO Prequalification?

- **Process to evaluate whether a drug meets global standards**
  - Quality
  - Safety
  - Efficacy

- **Many African regulatory agencies use WHO prequalification to determine which new products to approve, and review EMA decisions**

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Regulatory Submission Plans (cont.)

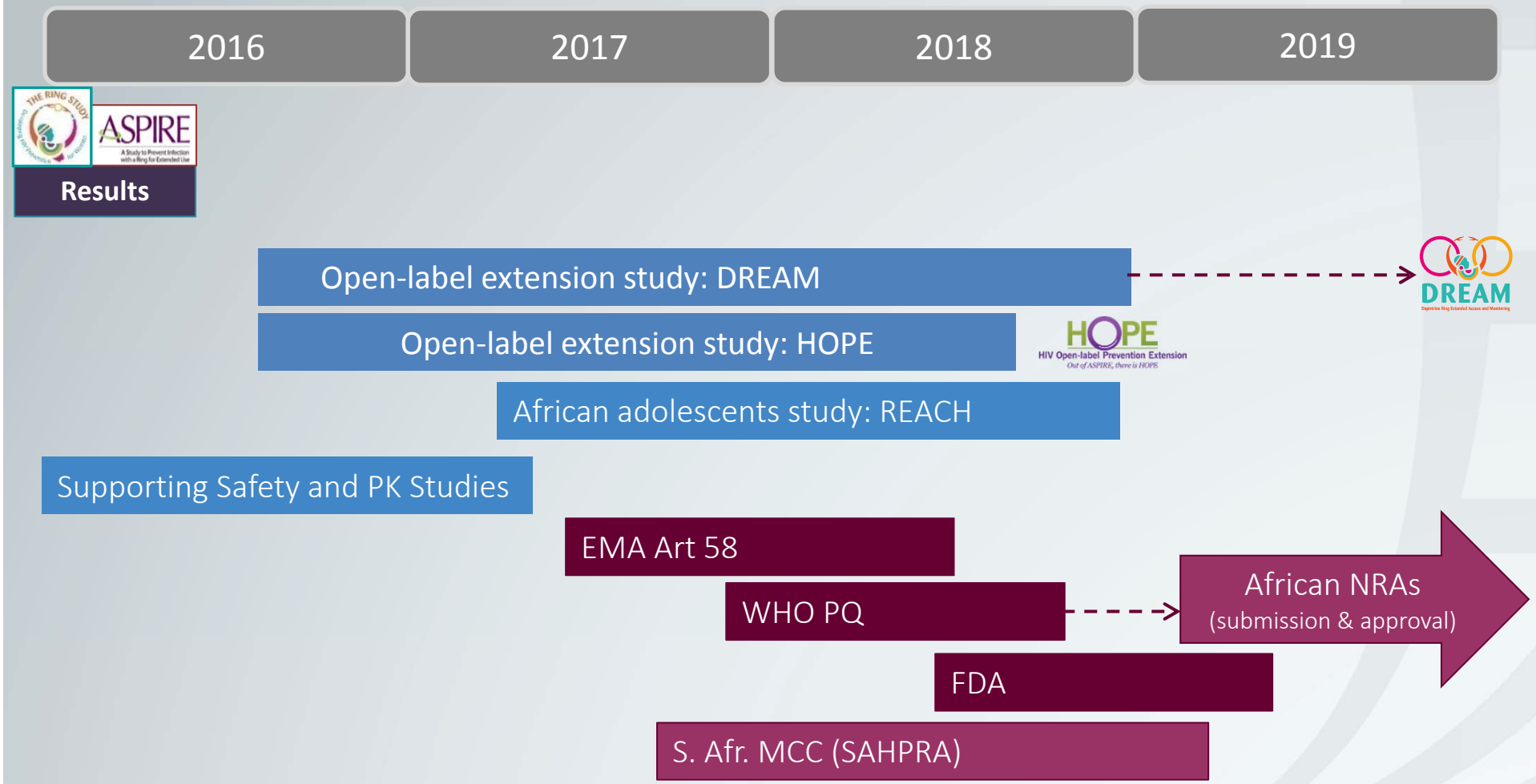
As of 3/20/17

African National Regulatory Authorities

- Target submission to South African Medicines Control Council in Q4 2017
- Following WHO PQ, first round of submissions to Kenya, Malawi, Rwanda, Tanzania, Uganda, Zambia and Zimbabwe

Regulatory Timeline

As of 3/20/17



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Public Health
Pathway

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Public Health Pathway

- **Open-label extension studies:** DREAM *(IPM 032)* and HOPE *(MTN-025)* launched in July 2016 for former Phase III participants
- **Assessment of ring adherence** in ASPIRE and HOPE *(MTN-032)*
- **REACH adolescent study planned for 2017:** Assess safety of and adherence to dapivirine ring and oral PrEP among 300 young women 16-21 in South Africa, Uganda, Zimbabwe *(MTN-034/IPM 045)*

DREAM
Dapivirine Ring Extended Access and Monitoring

HOPE
HIV Open-label Prevention Extension
Out of ASPIRE, there is HOPE

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DAPIVIRINE RING EXTENDED ACCESS AND MONITORING

A FOLLOW-ON, OPEN-LABEL TRIAL TO ASSESS CONTINUED SAFETY OF AND ADHERENCE TO THE DAPIVIRINE (25 MG) VAGINAL RING-004 IN HEALTHY, HIV-NEGATIVE WOMEN

Trial Design	Phase III, Open-label, Multi-Centre Trial
Primary Objective	• Assessment of Long-term Safety profile • Adherence to the Dapivirine Vaginal Ring use
Trial Population	Up to approximately 1400 former IPM 027 participants will be enrolled
Treatment Regimen	25 mg Dapivirine Vaginal Ring, replaced monthly
Follow-up Regimens	Follow-up visit one month after enrolment – up to three months 3-monthly visit schedule: • three rings dispensed to the participant • two additional to take home, or • dispensing will take place as arranged with the participant
Study Duration	Each participant will engage in the screening process for up to 45 days prior to enrolment Dapivirine Vaginal Ring-004 use cont. for a period of up to 12 months, with an option to extend

DAPIVIRINE RING EXTENDED ACCESS AND MONITORING

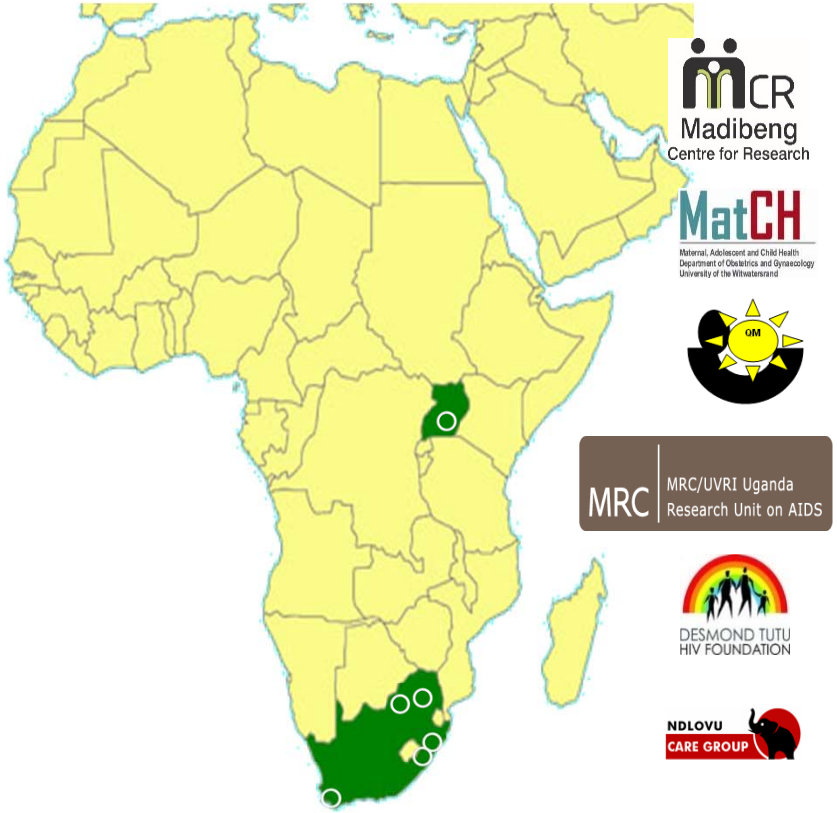
IPM 032 PROTOCOL_V2.0, AMENDMENT 2 DATED 16 JAN 2017*

SUMMARY OF CHANGES

Decliner Population	Behavioral Questionnaire
Ring Naïve Cohorts	Two additional DVR-naïve cohorts • ≥18 to ≤21 years and >21 to <25 years • 300 participants each
Enrolled Participants	• Option to not use the vaginal ring (ring non-users) after initial 3 months' of ring use • Initiate ring use again at any time
Qualitative Component	In-depth interviews: • Decliner population/Ring users/Ring Non-users/Cases of Interest/Male partners/and or male community members DVR-naïve cohorts: • Baseline behavioural assessment

*Awaiting final NRA/IEC approval

Accrual Status



Activation	Screened	Screen Failed	Enrolled	Discontinued
21 Jul 2016	245	15	211	2
23 Aug 2016	168	10	152	2
11 Jul 2016	224	25	196	6
30 Jan 2017	119	6	82	0
16 Aug 2016	61	1	60	2
22 Jul 2016	89	3	86	2
Total*	**906**	**60**	**787**	**14**

**16 March 2017*

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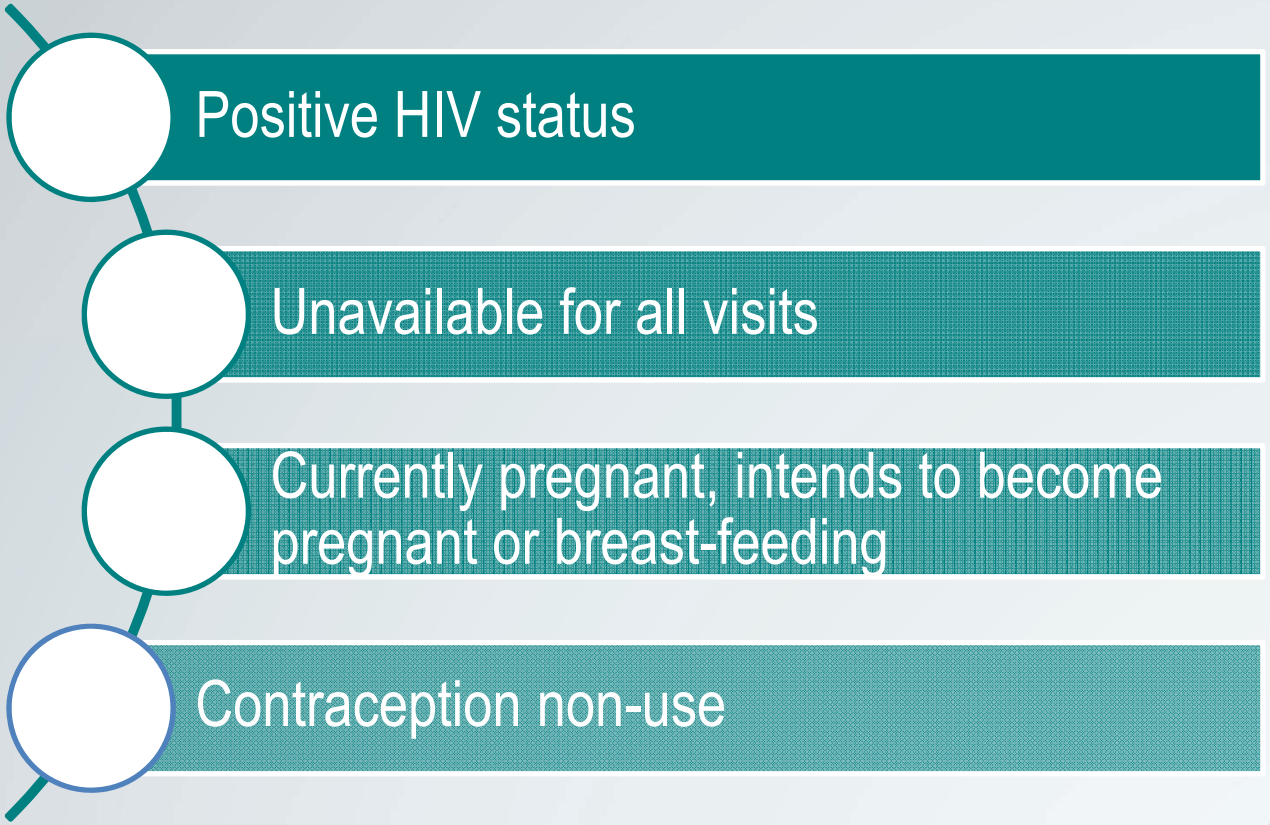
Main Reasons for Screening Failures



Main Reasons for Declining Trial Participation

- Family influences
- Working / school / studies
- Planning a family / getting married
- Relocation
- Not interested

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Preparing for **Access**

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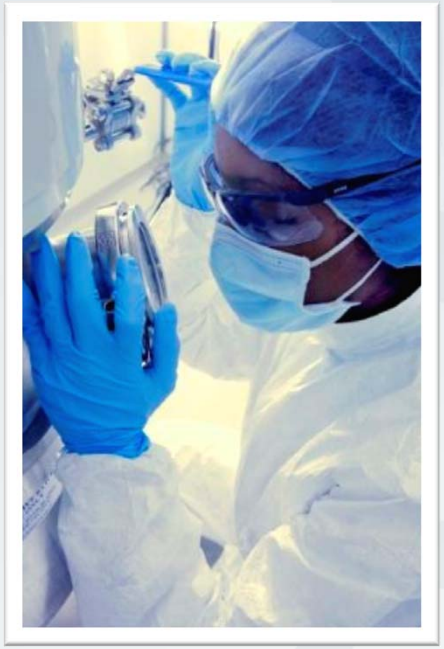
Meeting Manufacturing Demands

- **2005**: IPM built a clinical trials manufacturing facility for gels, helping to shorten time lines to clinical trials
- **2007**: Initiated expansion for ring manufacturing
- **2010**: Scaled up by transferring technology to partner QPharma (Sweden)



Commercial Manufacturing Summary

- QPharma will be commercial launch partner
- Capacity in place to meet commercial demand with ability to scale up
- Cost at current scale: ~$7/ring
- Target cost at advanced scale-up: ~$2-3/ring

Market Introduction: IPM Activity Tracker

	Task	2017	2018	2019	2020
Understanding the Market	**Demand Forecasting**				
	Stakeholder Mapping				
	Value Chain Situation Analysis				
	Market Research *Country studies on the target market's providers and end-users, for use in DVR packaging and informational materials*				
	Brand Development				

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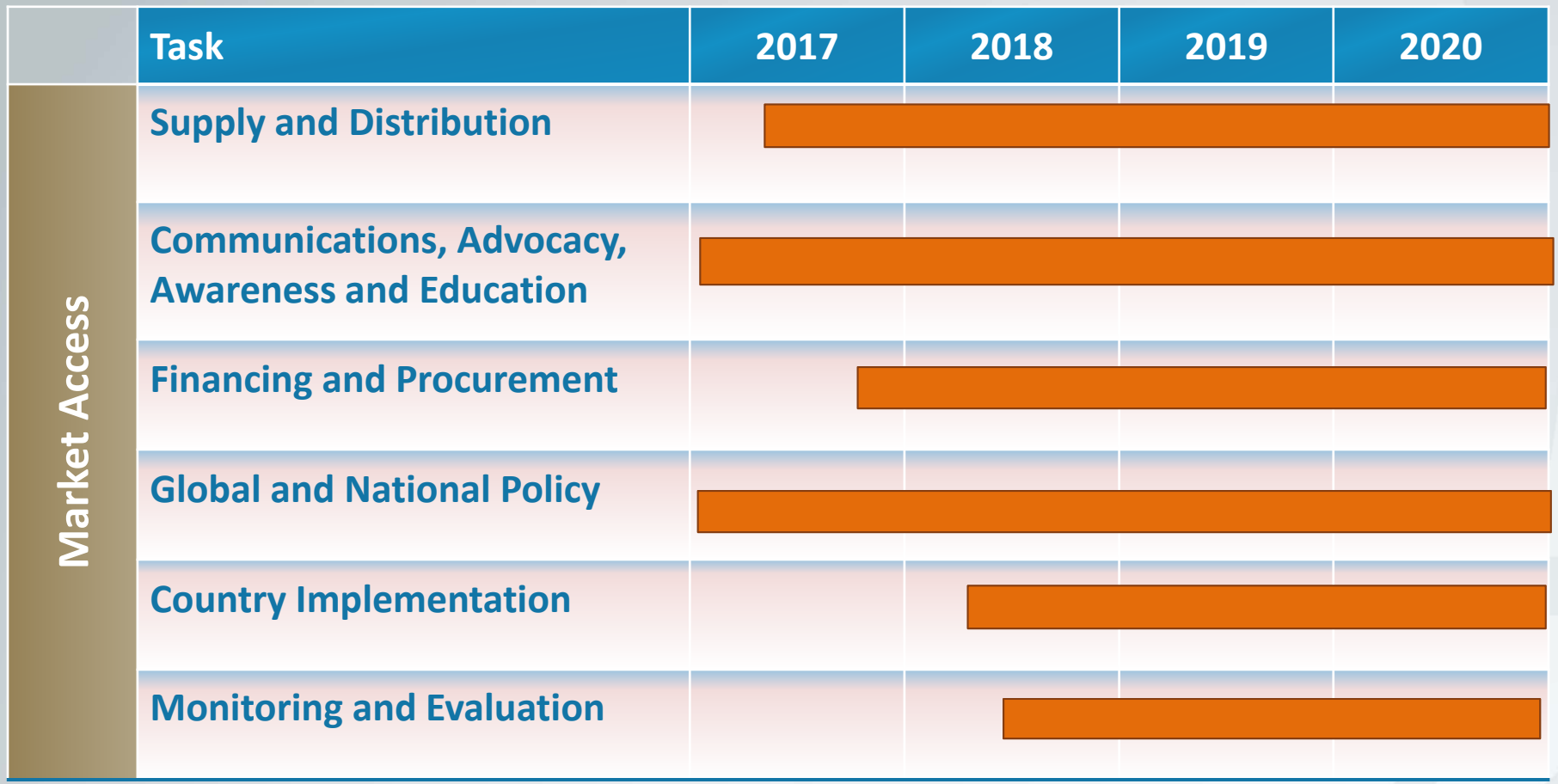
Market Introduction: IPM Activity Tracker (cont.)



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Brand Name Development

- **Conducted safety, market research on 22 names**
  - With Brand Institute/Drug Safety Institute
  - Research topics: fit-to-concept, attribute evaluations, memorability, exaggeration/appropriateness, similarity to current product names or medical terms, prescription simulation
  - Risk scores determined for each name
- **Eight candidates with lowest risk scores advanced**
  - Focus groups with 300+ women in Phase III countries
  - Janssen conducting trademark research
  - Results expected mid-2017
  - *Lead and backup candidate names expected 2017 for SA MCC submission*

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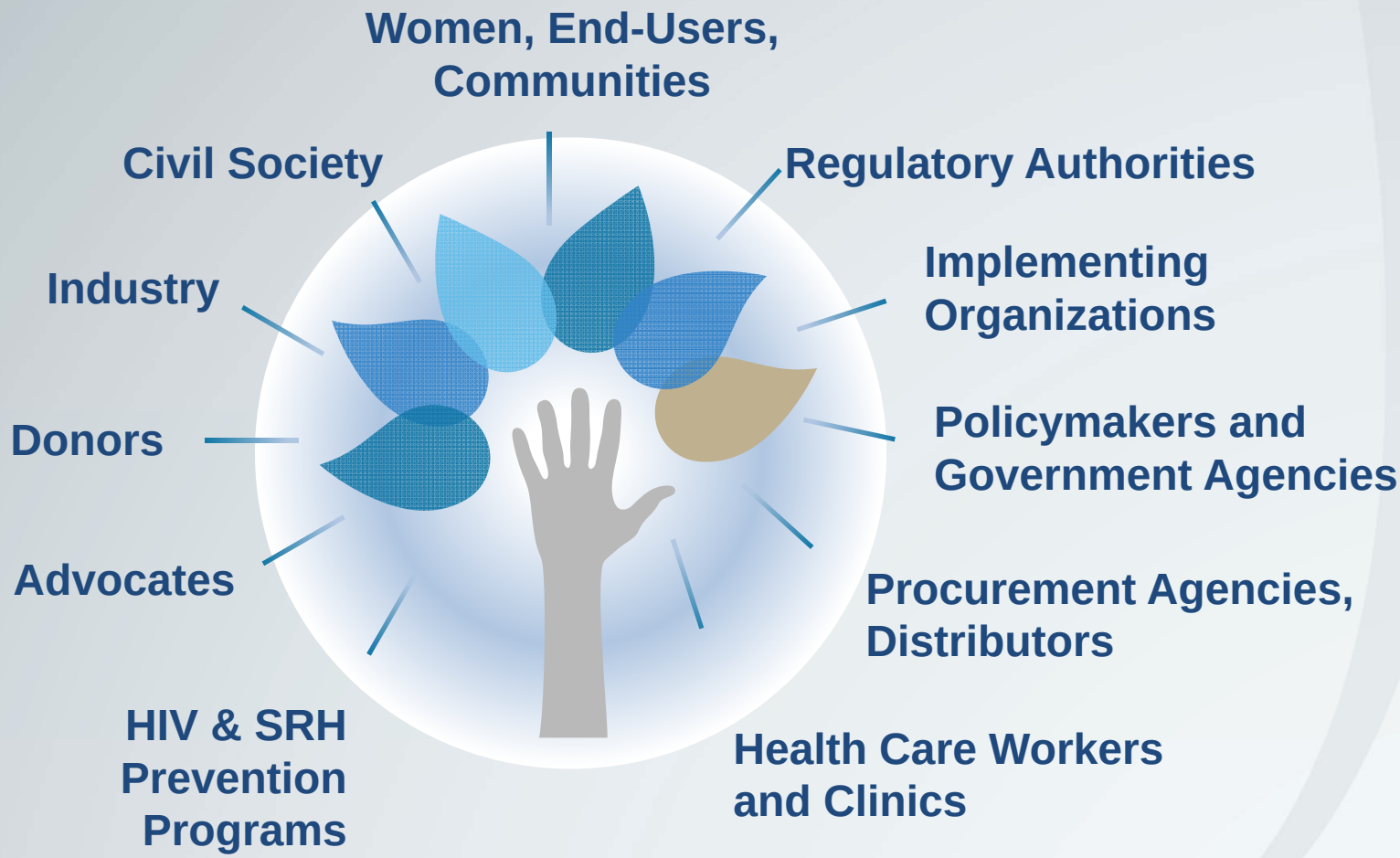
It Takes a Village



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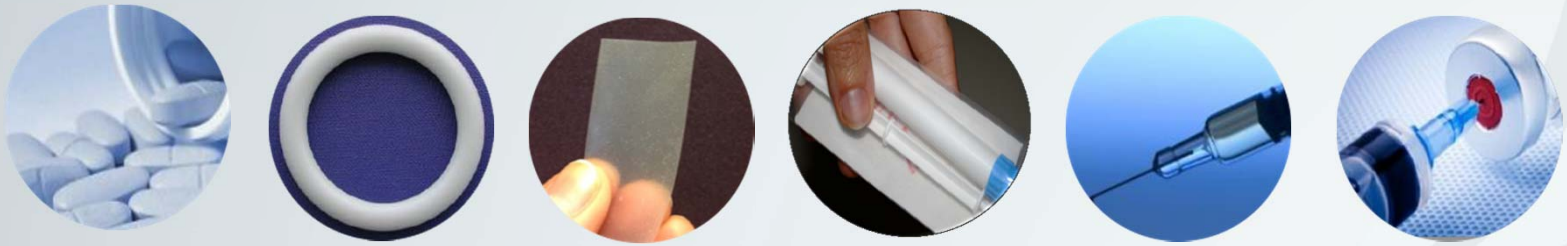
Women Need Multiple Options

- Women-initiated technologies are a key component of a comprehensive prevention package
- No one option will suit everyone
- To end the epidemic, women need multiple options that meet their various needs, including daily oral PrEP, long-acting vaginal rings and one day rectal microbicides, injectables and vaccines



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