

INTERNATIONAL PARTNERSHIP FOR MICROBICIDES

## Dapivirine Vaginal Ring Programme

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#### **Presentation Outline**

- Video setting the scene
- More about the dapivirine vaginal ring
- What we learnt from the Phase III studies ASPIRE and The Ring Study
- What happens next
- Regulatory Pathway
- Discussion



# So what else do we know about the ring?



#### **Prior Research on Rings**

- Vaginal rings used safely and effectively for other medical purposes in Europe and US for nearly 20 years
- IPM research studies to date show dapivirine ring is safe and welltolerated
- Steady drug release and low systemic absorption





#### **Microbicide Vaginal Rings**

- Long-acting: monthly or longer
  - Could support improved adherence
  - Thus better effectiveness

#### Easy to use, comfortable

- Flexible ring, can be self-inserted
- Rarely felt by women or male partners
- High willingness-to-use
- Little or no impact on sexual experience
- Suitable for developing countries
  - Relatively low manufacturing cost
  - Good safety and acceptability data
- Potential for drug combinations



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Important potential new option for women

## Let's recap: Dapivirine Ring Phase III Studies





	The Ring Study (IPM 027)	ASPIRE (MTN-020)	
Objectives	Long-term safety and efficacy	Safety and effectiveness	
Study design	Double-blind, randomized (2:1), placebo-controlled	Double-blind, randomized (1:1), placebo-controlled	
Enrollment	Total: 1959 women, ages 18-45 Active arm: ~1300	Total: 2629 women, ages 18-45 Active arm: ~1315	
Research sites	7 IPM research center partners in South Africa and Uganda	15 MTN research centers in Malawi, South Africa, Uganda, Zimbabwe	





#### HE RING **HIV protection differed by age** Highest HIV-1 protection was seen in women aged 22 - 25 years old ≤ 21 years **22 – 25** years 26 – 45 years 15% 41% 33% reduction reduction reduction INTERNATIONAL PARTNERSHIP FOR MICROBICIDES

#### **HIV protection differed by age**



Women age 25 or older had substantial HIV protection while those younger than age 25 had no significant reduction in HIV incidence.



#### **Safety results**



ting for Extended Us



- Dapivirine vaginal ring was shown to be very safe
- No difference between dapivirine and placebo groups in:
  - Number of adverse events (side effects / health problems) experienced
  - Number of pregnancies
  - Number of sexually transmitted infections
- No significant HIV-1 drug resistance



#### **Phase III Results Summary**



- IPM's monthly dapivirine ring safely reduced HIV risk by approximately 30% overall
- Higher protection seen in women older than 21
- Higher efficacy seen with consistent use
- More research needed to understand prevention needs of younger women



11 | Month/Year

## Regulatory Pathway for Dapivirine Vaginal Ring



Path to Approval

Why do we need regulatory approval of medicines?

EMA, FDA, NDA, MCC? What are these?

What information do they need?





13 | Month/Year

#### But why does it take so long?

 For the dapivirine ring, IPM has organised 13 years of data and findings from nearly 250 studies into each application

> 260 000 pdf pages 1200 files 69000 links 4.4 terrabytes >10 hours to upload



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



#### **Regulatory Pathway**



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## **Regulatory Timeline**



#### Access



#### We need a strong partnership







# Phase IIIb Open-Label Extension: Status

LS1

IPM 027<br/>(n=1959)IPM 032DREEAN<br/>Depiring Rigg Extended Access and MonitoringEligibleScreenedEnrolledSouth Africa and Uganda\*:<br/>• 6 Research Centres1731<br/>at 7 RCs962876

\*Data as of 01 June 2017

	MTN-020 (n=2629)	MTN-025	
HIV Open-label Prevention Extension Out of ASPIRE, there is HOPE	Eligible	Screened	Enrolled
Malawi, South Africa, Uganda and Zimbabwe**: • 14 NIH Clinical Research Units	2448	1249	1134

\*\*Data as of 02 June 2017

## **Qualitative Component**

#### **In-depth interviews:**

- Decliner population
- Ring users
- Ring non-users
- Cases of interest
- Male partners
- Male community members

#### **DVR-naïve cohorts:**

Baseline behavioural assessment

#### ACCEPTABILITY AND INFLUENCERS OF RING USE

Behavioural data will support the potential introduction of a microbicide as a public health intervention and assist with future program development.



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#### DREAM (IPM 032): Ring-use Naïve Participant Cohorts

No HIV risk reduction was observed in younger women in the Phase III program, a protocol amendment includes:

- two additional cohorts of young women ≥18 to ≤21 years and
  >21 to <25 years who have not used the Dapivirine Vaginal Ring-004 previously
- 300 participants per cohort

#### BETTER UNDERSTANDING OF UNIQUE CHALLENGES

Additional data will be collected to gain a better understanding of younger women's unique challenges in using HIV prevention methods



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## **Dapivirine Ring Licensure Program**

**IPM 027** Long-term safety and efficacy study The Ring Study 1959 participants in Africa (2012-2016), in data analysis Safety and efficacy study **MTN-020** 2629 participants in Africa (2012-2015), completed ASPIRE Drug-drug interaction (one completed; one in data analysis) Extended use pharmacokinetic profile (completed) Condom functionality – male (completed); female (completed) Additional Safety in adolescents (data analysis) safety studies • Safety in women >45 (completed) Menses and tampon use PK (completed) PK in lactating women (ongoing) National Institute of NTERNATIONAL ARTNERSHIP FOR Allergy and MICROBICIDES Infectious Diseases