

# Beyond ASPIRE



# ASPIRE results

- November 2015, the data disclosure meeting will be held in Seattle, WA.
- ASPIRE is powered to detect effectiveness of at least 60% and to rule out effectiveness of 25% or lower.
- Press release likely in January 2016
- Paper submission shortly after November meeting and possible CROI abstract



# MTN-025 (HOPE)

- Our work is not complete!
- Open-label extension of ASPIRE
- Women from ASPIRE will be offered enrollment into HOPE to provide access to the unlicensed dapivirine VR
  - Assumption of ~80% wanting to use the VR
- HOPE will continue to provide safety data along with several other objectives.
  - Women will be seen monthly for the first 3 months and then once every 3 months for up to 12 months

# MTN-025 (HOPE)

- Primary Objectives
  - To characterize the **safety** profile associated with open label use
  - To characterize **adherence** to open label use
- Secondary Objectives
  - To assess the **incidence** of HIV-1 infection
  - To assess the frequency of HIV-1 **drug resistance**
- Exploratory Objectives
  - To explore **participant understanding of efficacy, ring acceptability, and delivery feasibility**
  - To characterize MTN-020 participants who choose not to enroll in MTN-025 (**decliner population**)

# MTN-025 lab testing

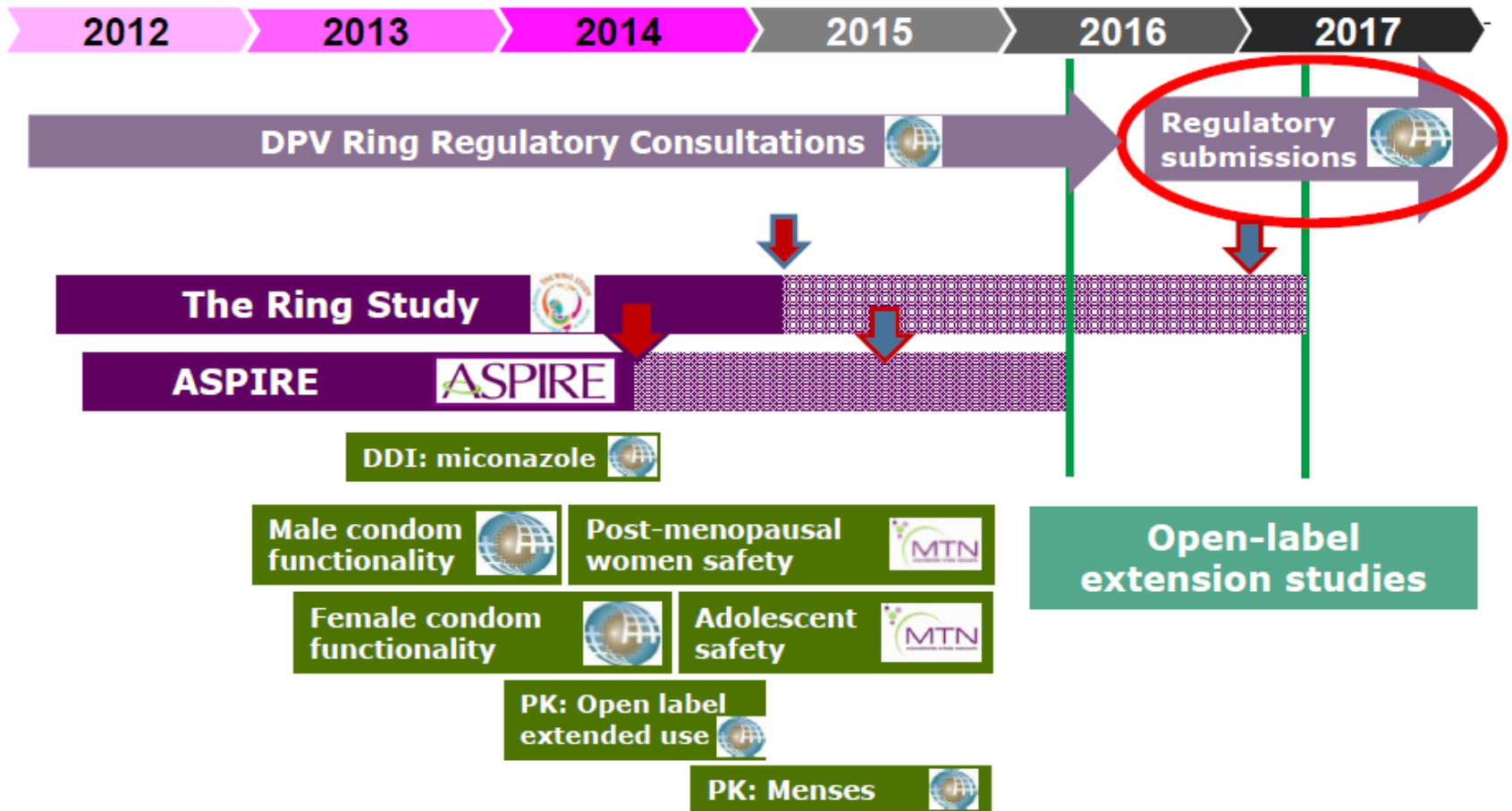
## Local Lab

- Urine
  - hCG
  - NAAT for GC/CT
  - urine culture (per local standard of care)
- Blood
  - Plasma archive; blood for PK
  - Syphilis serology
  - HIV-1 serology
  - CBC with platelets
  - Chemistries (AST/ALT/Creatinine)
- Pelvic
  - Rapid test for Trichomonas
  - Vaginal fluid

## MTN LC

- Blood
  - Drug concentration in blood
  - HIV-1 confirmatory testing as needed
  - HIV drug resistance
- Pelvic
  - Vaginal fluid for candidate biomarkers of safety, adherence and efficacy, HIV exposure and antiretroviral resistance, and/or genital microflora, as needed
- Vaginal Ring
  - Residual drug analysis at designated laboratory

# But what else needs to be done?



# For the Dapivirine VR licensure

- Use in other populations
  - Breast feeding women (MTN-029), to begin shortly at two sites in the US (first study)
  - Pregnant women; in the US (concept)
- Use in other age ranges
  - Post-menopausal women (MTN-024)
    - 96 women evaluated VR for 3 months at 3 US sites
    - Study complete and results to be presented at CROI 2016
  - Adolescent women (MTN-023)
    - 96, 16-17 yo women evaluating VR for 6 months
    - Study ongoing at six US sites



# And MTN-034

- ~300 adolescents enrolled from CAPRISA (eThekweni), MRC (Veralum), MU-JHU, and Zimbabwe
- Randomized, cross-over trial of 12 weeks using the **dapivirine VR** and 12 weeks taking oral **Truvada**
- Should anticipate a “real-time” PK testing → frequent shipments
- Protocol development meeting will be Thursday Oct 8

	N	Period 1 (12 Weeks)	Off- Product	Period 2 (12 Weeks)	Follow-up (~1 Week)
Sequence A	150	Vaginal (dapivirine 25 mg VR)	~1 week	Oral (Daily FTC/ TDF tablet)	
Sequence B	150	Oral (Daily FTC/ TDF tablet)	~1 week	Vaginal (dapivirine 25 mg VR)	

# MTN-034 objectives

- Primary objectives
  - To evaluate **safety** and **adherence** of oral tablets and VRs in adolescent women
- Secondary objective
  - To determine **acceptability** of tablets and VRs in an adolescent population
- Exploratory objectives
  - To define changes to the vaginal microenvironment
  - To assess the frequency of **HIV drug resistant** virus and **HSV1/2 acquisition**

# MTN-034 current lab testing

## Local Lab

- Urine
  - hCG
  - NAAT for GC/CT
  - Dipstick UA and/or urine culture (per local standard of care)
- Blood
  - Plasma archive Blood for PK
  - Syphilis serology
  - HIV-1 serology
  - CBC with platelets
  - Chemistries (AST/ALT/Creatinine)
  - Creatinine clearance
  - **HBsAG and Hep C antibody**
- Pelvic
  - Vaginal pH
  - Vaginal Gram stain
  - Rapid test for Trichomonas
  - Herpes culture (fluorescent antibody or PCR)
  - Saline wet mount for BV
  - Wet prep/KOH wet mount for candidiasis/BV

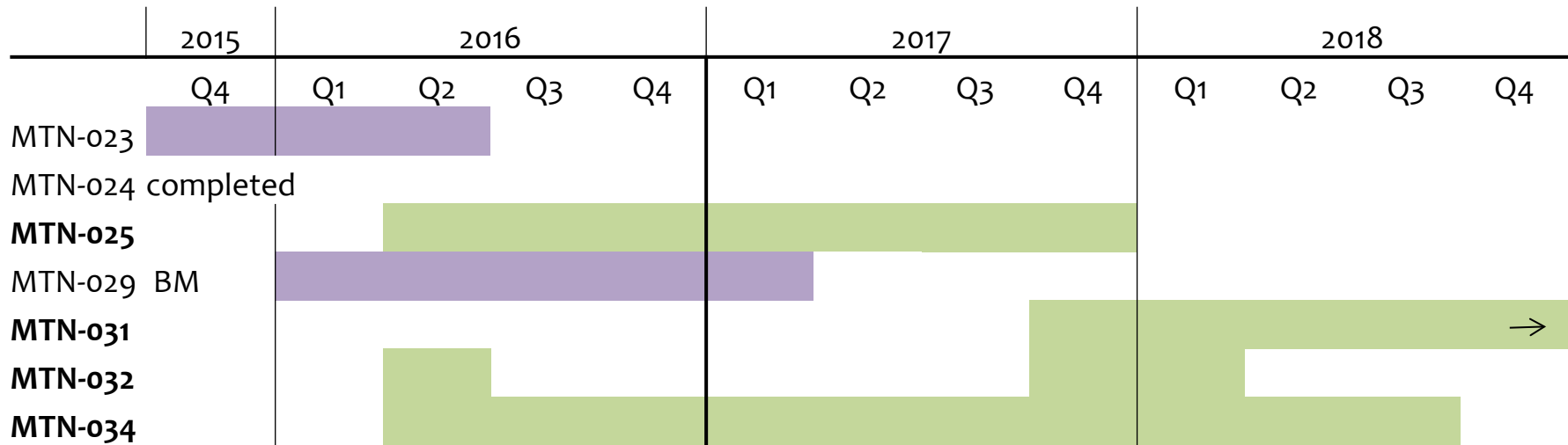
## MTN LC

- Blood
  - Drug concentration in blood
  - HIV-1 confirmatory testing as needed
  - HIV drug resistance
- Pelvic
  - Drug concentration in vaginal fluid
  - Vaginal qPCR for microflora
  - Vaginal swabs for biomarkers
- Vaginal Ring
  - Residual drug analysis
  - At designated laboratory

# What about adherence?

- MTN-031, an incentive based adherence study
  - Enroll women from SA and Malawi post-HOPE
  - Involve lab testing for STI/HIV testing and real time blood / VR for PK
- MTN-032, assessment of ASPIRE and HOPE adherence (AHA)
  - Much like VOICE D, this will be in-depth interviews of women with their PK data presented to them

# When should we anticipate their start?



These are the **estimated** start dates and follow-up for the current and new trials

# Final thoughts

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- You've done a tremendous amount of work for ASPIRE.
- Maintain positive thoughts while we wait for ASPIRE data release!
- We still have lots to do...