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 (eThekwini), 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

<table>
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<th>N</th>
<th>Period 1 (12 Weeks)</th>
<th>Off-Product</th>
<th>Period 2 (12 Weeks)</th>
<th>Follow-up (~1 Week)</th>
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<td>Vaginal (dapivirine 25 mg VR)</td>
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<td>Sequence B</td>
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<td>Vaginal (dapivirine 25 mg VR)</td>
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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?

<table>
<thead>
<tr>
<th>Year</th>
<th>MTN-023</th>
<th>MTN-024 completed</th>
<th>MTN-025</th>
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These are the estimated start dates and follow-up for the current and new trials.
Final thoughts

• 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...