IPM 027 Current Status

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ASPIRE Team Meeting
MTN Regional Meeting
Westin Cape Town Hotel, Cape Town South Africa
04 October 2014
Two Studies, One Product
The Ring Study

<table>
<thead>
<tr>
<th>Objective</th>
<th>Information</th>
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<tbody>
<tr>
<td>Objectives</td>
<td>Long-term Safety and Efficacy</td>
</tr>
<tr>
<td>Study design</td>
<td>Double-blind, Randomized (2:1), Placebo-controlled</td>
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<tr>
<td>Investigational product</td>
<td>Vaginal rings inserted every 4 weeks ± 7 days</td>
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<tr>
<td>Power</td>
<td>81% power to detect 50% treatment effect</td>
</tr>
<tr>
<td>Targeted enrollment</td>
<td>1950 women, ages 18-45</td>
</tr>
<tr>
<td></td>
<td>1300 on Ring-004</td>
</tr>
<tr>
<td>Sites in Africa</td>
<td>7 IPM research center partners in 2 countries</td>
</tr>
<tr>
<td>Participant follow-up</td>
<td>2 years + 6 weeks following ring discontinuation</td>
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</table>
The Ring Study: timelines

**Madibeng Center for Research**
Brits, South Africa

**Maternal, Adolescent and Child Health (MatCH)**
Edendale, South Africa

**Prevention of HIV/AIDS Project (PHIVA)**
Pinetown, South Africa

**Qhakaza Mbooks**
Ladysmith, South Africa

**Desmond Tutu HIV Foundation (DTHF)**
Masiphumelele, South Africa

**Uganda Virus Research Institute (UVRI)**
Masaka, Uganda

**Ndlovu Care Group**
Groblersdal, Limpopo, South Africa

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<table>
<thead>
<tr>
<th>First Participant Enrolled</th>
<th>Apr ‘12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Last Participant Enrolled</td>
<td>Nov ‘14</td>
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<tr>
<td>Final Visit</td>
<td>Dec ‘16</td>
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The Ring Study: key priorities

Adherence:
- 25% Participants still active → significant impact

Retention
- 97% for ongoing participants → significant impact

Clinical and Laboratory Safety
- No safety concerns or laboratory disconcerns

Data Quality
- 99% clean database
- Real time data entry & cleaning

Inspection Readiness
- Ready at any time
Two Studies, Different Timelines

Both studies started enrolling in 2012, but are designed differently:

**ASPIRE**
- Followed participants for minimum 1 year
- Study completed June 2015
- ASPIRE results expected early 2016

**The Ring Study**
- Following participants for 2 years for long-term safety
- Completion December 2016 after last participant completes safety follow-up
- Ring Study efficacy results scheduled for early 2017
  - Possibly 2016 pending DSMB recommendation
IPM 027: Results Scenarios pending ASPIRE Results

**SAFETY + EFFICACY**
- DSMB recommends – Amend Ring Study to Open-label and/or Initiate DREAM study
- Submit dossier for regulatory approval
- Consult Regulators

**CONTINUE AS PLANNED**
- DSMB recommends – Study continue as planned to ensure robust results and provide comprehensive data on the ring’s efficacy and long-term safety
- Consult Regulators

**SAFETY + INSUFFICIENT EFFICACY**
- DSMB recommends - Stop The Ring Study Terminate dapivirine ring program
- Results show the dapivirine ring is safe but not efficacious or has limited efficacy
- Consult Regulators
### IPM 032: Open-Label Ring Follow-on

<table>
<thead>
<tr>
<th><strong>DREAM</strong></th>
<th>Dapivirine ring Extended Access and Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary Objectives</strong></td>
<td>Long-term Safety and Adherence</td>
</tr>
<tr>
<td><strong>Design</strong></td>
<td>Follow on IPM 027; Open-Label</td>
</tr>
<tr>
<td><strong>Treatment Follow-up Regimen</strong></td>
<td>Vaginal rings inserted monthly&lt;br&gt;1-monthly (no additional rings)&lt;br&gt;3-monthly (optional: 2 additional rings)</td>
</tr>
<tr>
<td><strong>Targeted enrollment</strong></td>
<td>Approximately 1400 women</td>
</tr>
<tr>
<td><strong>Product use period</strong></td>
<td>Approx. 1-year follow-up with option to extend</td>
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<tr>
<td><strong>Expected start</strong></td>
<td>Pending outcome Phase III trials</td>
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Regulatory preparation is real time

2015
- IPM 027 / The Ring Study
- MTN-020/ASPIRE

2016
- Results?

2017
- Open-label extension studies: IPM 032 & MTN-025

2018
- Supporting Safety and PK Studies
- Dapivirine Ring Regulatory Consultations
- EMA Art 58
- WHO PQ
- US FDA
- S. Afr. MCC

2019
- African NRAs (submission & approval)
The Ring Study
Adherence is Still Everything

- The Ring Study participants are still ongoing
- Keep focus on retention and adherence
- Results of The Ring Study are scheduled early 2017
  - Available sooner pending ASPIRE results and IPM DSMB recommendation
- If both Phase III studies find the dapivirine ring safe and effective, it would be a pivotal moment for the future of microbicides
Acknowledgements

- Participants
- Research Centre Teams
- Community Members and Stakeholders
- MTN / NIH / DAIDS colleagues
- Vendors and Partners
- IPM Colleagues and Friends
- Donors

It takes a village to raise the child: Dapivirine Ring-004
We are closer to making the Dapivirine Ring-004 an important new HIV prevention option for Women
Current IPM Donors

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