The Ring Study

Annalène Nel, CMO
On behalf of the IPM 027 Team

28 October 2013, Cape Town, South Africa
### The Ring Study

**IPM 027**  
Protocol Version 3.0 Amendment 1.0 Dated 12 September 2013

<table>
<thead>
<tr>
<th>Objectives</th>
<th>Long-term Safety and Efficacy</th>
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<tr>
<td>Study design</td>
<td>Double-blind, Randomized (2:1), Placebo-controlled</td>
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<td>IP</td>
<td>Vaginal rings inserted every 4 weeks ± 7 days</td>
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<td>Endpoints</td>
<td>Approx 96 endpoints; 2 year on IP</td>
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<td>Power</td>
<td>81% power to detect 50% treatment effect</td>
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<td>Targeted enrollment</td>
<td>1950 women, ages 18-45</td>
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<td>1300 on Ring-004</td>
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<td>Sites in Africa</td>
<td>7 IPM research center partners in 2 countries</td>
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<td>Participant follow-up</td>
<td>2 years + 6 weeks following ring discontinuation</td>
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Clinical Research Centres

Madibeng Center for Research
Brits, South Africa
First enrolled participant – 11 April ’12

Maternal, Adolescent and Child Health (MatCH)
Edendale, South Africa
First enrolled participant – 26 April ’12

Prevention of HIV/AIDS Project (PHIVA)
Pinetown, South Africa
First enrolled participant – 23 April ’12

Qhakaza Mbokodo
Ladysmith, South Africa
First recruited participant – 16 April ’12

Desmond Tutu HIV Foundation (DTHF)
Masiphumelele, South Africa
Awaiting approval

Uganda Virus Research Institute (UVRI)
Masaka, Uganda
First enrolled participant – 12 September ’13

Ndlovu Care Group
Groblersdal, Limpopo, South Africa
Awaiting approval
Timelines

- Investigator Meeting: 14-16 Feb ‘12
- SIVs for 4 SA sites: 19-29 Mar ‘12
- IXRS activated: 23 Mar ‘12
- 1st SA Participant Screened: 27 Mar ‘12
- IP at SA Research Center: 10 Apr ‘12
- 1st SA Participant Enrolled: 11 Apr ‘12
- MRC-URVI, Uganda: FPI 12 Sep ‘13
- DTHF, Masiphumelele: Estimate FPI Q4 ‘13
- Ndlovu Care Group: Estimate FPI Q1 ‘14
- DSMB: Nov ‘12 and May ‘13
  19 November 2013
- Estimated LPI: Q4 ‘14
- Estimated LPO: Q4 ‘16 / Q1 ‘17
Since October 2012.....

- exceeded 1300 enrolled participants
- first enrolled participants >18 months on The Ring Study
- >95% visit retention per ongoing participants
- faxed in >170,000 CRF pages
- >99% clean records in database
- >95% data queries resolved
- <6% data query rate per 100 CRF pages per research centre
- no safety signals or laboratory trends
What matters

- Retention
- Adherence
- Endpoints
- Data Quality
- Participant Safety
Recruitment

Screened : Enrolled is 2:1
Average enrolled/week is 1-2/site

Snapshot: 24 October ‘13
Screen Failures

- HIV positive at Screening
- Unavailable for all visits and procedures
- Investigator Opinion
- Exceed 28-day Screening
- Cervical Cytology Abnormalities
Quarterly Recruitment

1950 participants

- 2nd Qtr '12: 312 participants
- 3rd Qtr '12: 314 participants
- 4th Qtr '12: 286 participants
- 1st Qtr '13: 154 participants
- 2nd Qtr '13: 107 participants
- 3rd Qtr '13: 98 participants
- 4th Qtr '13: 646 participants
- To be enrolled: 33 participants
Adherence Measurable

• Research staff observations: anecdotal feedback
• Feedback from participant and male engagement events
• Listening to the community voices
• Feedback after group ring adherence discussions
• Protocol adherence:
  o Number of participants contributing to protocol non-adherence
  o Missed Visits
  o Delayed Visits > 35 days (ring dispensing <35 days)
• Adherence questionnaires: Real-time review
## Retention for Ongoing Participants

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*Note Missed Visits are conducted on retrospective data and may change as participants are discontinued or reach end of product dates.

Snapshot : 26 Sept ‘13
Objective Adherence Measurable

4-weekly Pharmacokinetic sampling for:

- Dapivirine Residual levels
- Dapivirine Plasma levels
- Dapivirine Vaginal Fluid levels
Estimated Recruitment Timelines

Currently:
3 Research Centers currently screening

To start:
Masi estimate screening start date Nov '13
Ndlovu estimate screening start date Jan/Feb '14
Key Messages

• Retention is Key
• Ring Adherence is Everything
• Participant Care matters
• Male and Community Involvement is Essential
• Data Quality is Important
• Cost-Efficiency Counts
• Proactive planning for festive season
• Plan for Success
Many small things –
together their effect is massive....
- Derek Arbuckle