The Ring Study: the road we travelled...

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SA National PI: Linda-Gail Bekker

1 October 2012, Cape Town, South Africa
The Ring Study

IPM 027

Protocol Version 1.0 Amendment 1.0 Dated 23 January 2012

A MULTI-CENTRE, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED SAFETY AND EFFICACY TRIAL OF A DAPIVIRINE VAGINAL MATRIX RING IN HEALTHY HIV-NEGATIVE WOMEN
# The Ring Study

**IPM 027**

Protocol Version 1.0 Amendment 1.0 Dated 23 January 2012

<table>
<thead>
<tr>
<th>Study design</th>
<th>Double-blind, Randomized (2:1), Placebo-controlled</th>
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<tbody>
<tr>
<td><strong>IP</strong></td>
<td>Vaginal rings inserted every 4 weeks ± 7 days</td>
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<tr>
<td><strong>Endpoints</strong></td>
<td>Approx 80 endpoints; 2 year on IP</td>
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<tr>
<td><strong>Power</strong></td>
<td>83.2% power to detect 50% treatment effect</td>
</tr>
<tr>
<td><strong>Targeted enrollment</strong></td>
<td>1650 women, ages 18-45</td>
</tr>
<tr>
<td><strong>Sites in Africa</strong></td>
<td>5-6 IPM research center partners in 2-3 countries</td>
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<tr>
<td><strong>Participant follow-up</strong></td>
<td>2 years + 6 weeks following ring discontinuation</td>
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IPM 027: Clinical Research Center Partners

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

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

**Qhakaza Mbokodo**
Ladysmith, South Africa

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

**Projet Ubuzima**
Kigali, Rwanda
Regulatory & IRB Approval Status

- **V1.0 (Long-term safety)**
  - MCC: Full approvals in South Africa 02 Nov 2011 for 4 research centres
  - Ethics/District: All approvals by Jan ’12

- **V1.0, Amendment 1 (Long-term safety and efficacy)**
  - MCC, South Africa submitted 26 Jan `12, final approval 05 June ’12 & Ethics/District approvals by Mar ‘12
  - Rwanda submitted 28 Feb `12, final approval 06 July ‘12
  - Malawi submitted to COMREC 20 Mar `12 - Pending
IPM 027: Timelines

- Investigator Meeting: 14-16 Feb ‘12
- SIVs: 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
- Rwanda SIV: 21-24 Aug ’12
  estimated FPI Nov ‘12
- Estimated LPI: Q1/2 `13
- Estimated LPO: Q2 `15
IPM 027: Screening & Enrollment

As of 27 September 2012

<table>
<thead>
<tr>
<th></th>
<th>Screened</th>
<th>Enrolled</th>
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<tbody>
<tr>
<td>MCR</td>
<td>318</td>
<td>162</td>
</tr>
<tr>
<td>MatCH</td>
<td>318</td>
<td>175</td>
</tr>
<tr>
<td>QM</td>
<td>311</td>
<td>134</td>
</tr>
<tr>
<td>PHIVA</td>
<td>285</td>
<td>153</td>
</tr>
<tr>
<td>Projet Ubuzima</td>
<td>Expected FPI Nov '12</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1232</td>
<td>624</td>
</tr>
</tbody>
</table>
Screen Failures

- HIV positive at Screening
- Unstable form of Contraception
- Cervical Cytology Abnormalities
- Symptomatic for Genital Infections
- Grade 2 or higher abnormal lab values
- Investigator Opinion
Early Discontinuations

- Relocation out of district
- Partner Pressure
- Withdrew of informed consent
- Medical reasons
Accumulative Participant Enrollment/Month

- Mar-12: 0
- Apr-12: 44
- May-12: 186
- Jun-12: 312
- Jul-12: 451
- Aug-12: 531
- Sep-12: 666
- Oct-12: 624
- Nov-12: 881
- Dec-12: 1053
- Jan-13: 1163
- Feb-13: 1314
- Mar-13: 1482
- Apr-13: 1650

27 September 2012
Upscaling....

- Infrastructure & Equipment
- Optimization of resources & space allocation
- Revisit clinic flow
- Research staff composition
- Increase community mobilisation & innovative recruitment
......weeks to come

- Focus on Retention
- Re-align Recruitment Strategy
- Environmental Factors
- Operational Challenges
- Male Partner Involvement
- Dispense Family Planning
- Per Participant strategy for relocation out of the area
- Proactive planning for festive season...
Months to come.....

- Getting to 1650
- Data Quality is Important
- Cost-Efficiency Matters
- Adherence is Key
- Retention is Adherence
- Plan for Success
Ordinary people can achieve Extraordinary things as a TEAM