

The Ring Study

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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

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

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

DESMOND TUTU
HIV FOUNDATION



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

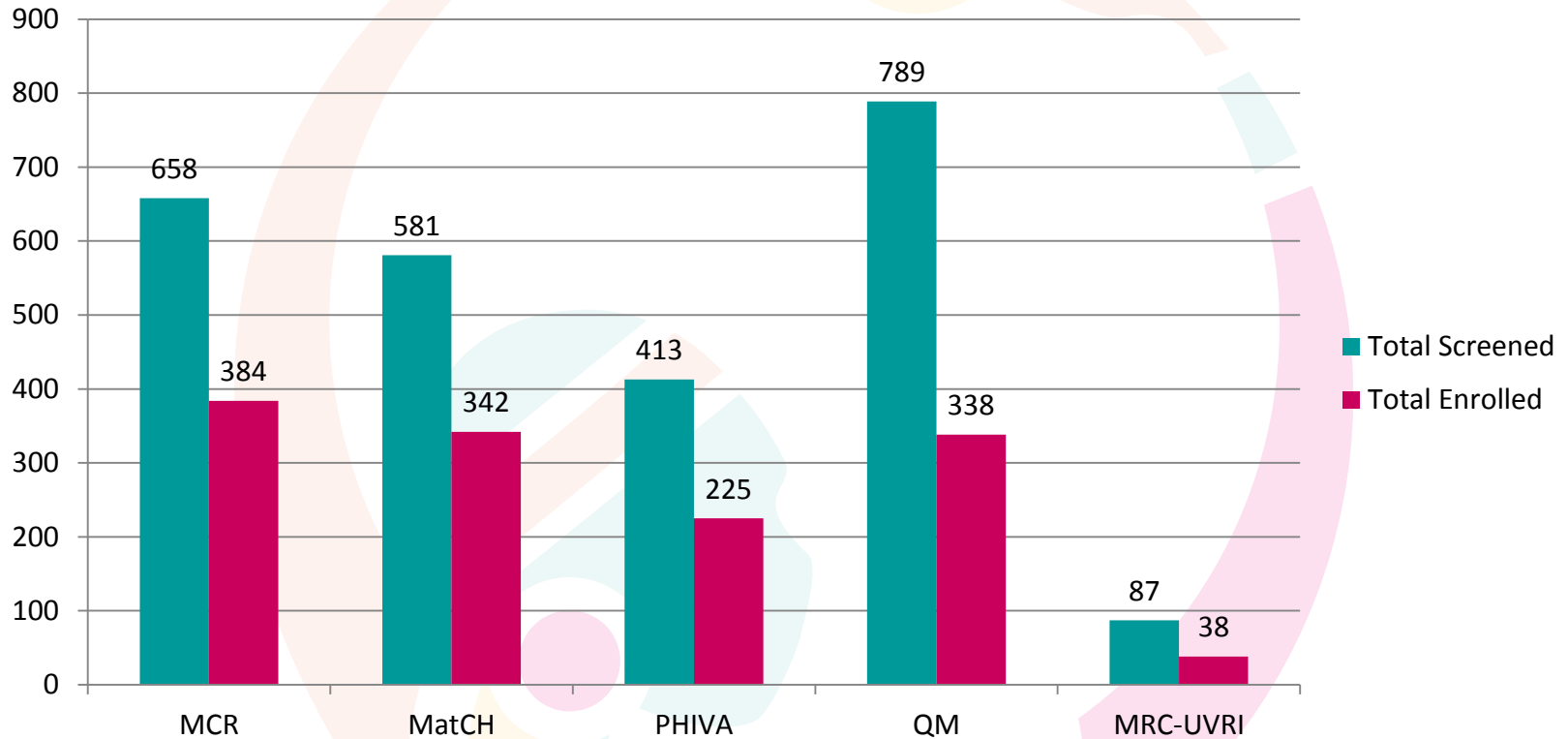
- Estimated LPI: Q4 `14
- Estimated LPO: Q4 `16 / Q1 '17

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



Recruitment



Total	Screened 2528	Enrolled 1327
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Screened : Enrolled is 2:1
Average enrolled/week is 1-2/site

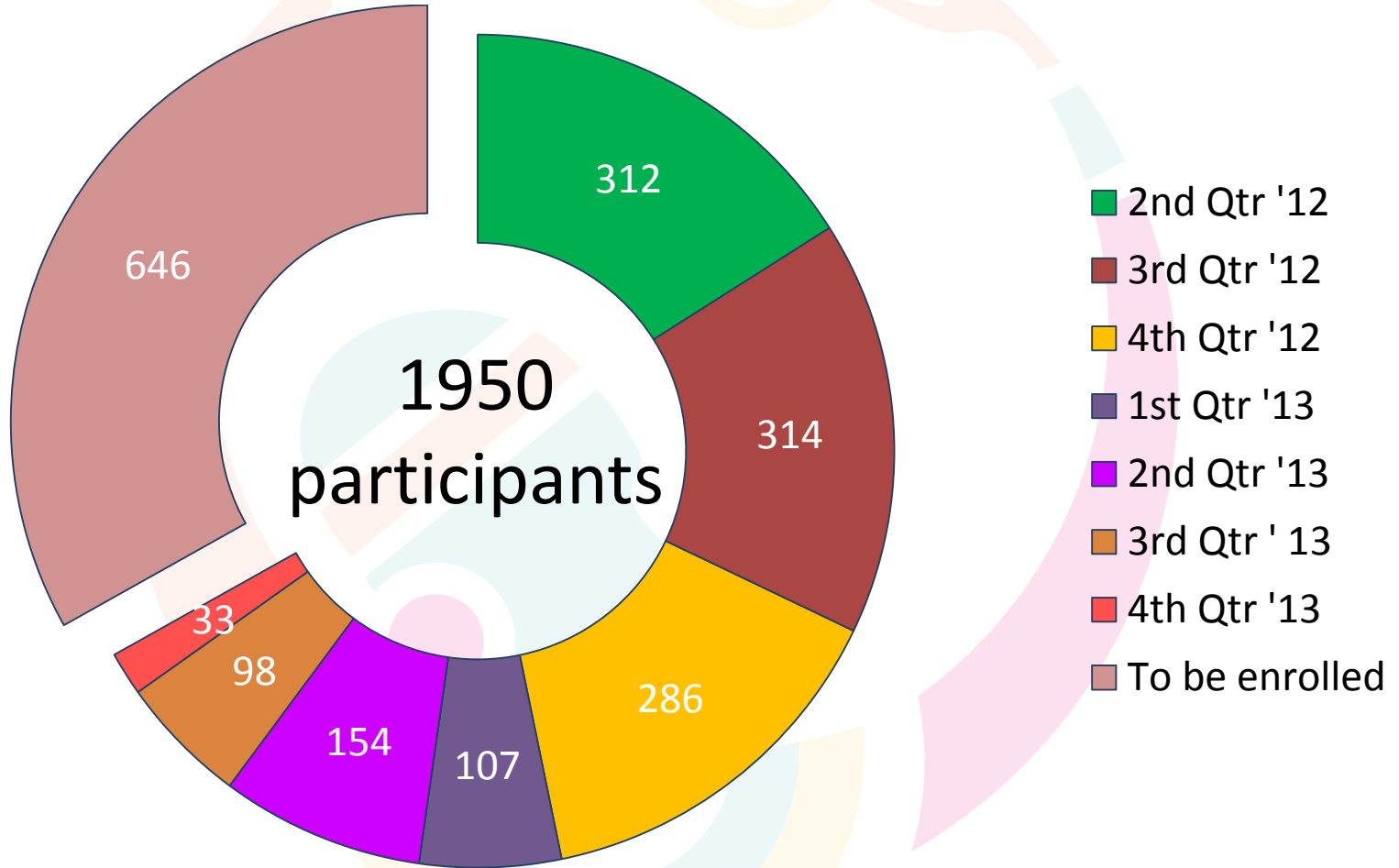
Snapshot: 24 October '13

Use Only - Not for

Screen Failures

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

Quarterly Recruitment



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:
 - Number of participants contributing to protocol non-adherence
 - Missed Visits
 - Delayed Visits > 35 days (ring dispensing <35 days)
- Adherence questionnaires: Real-time review

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Retention for Ongoing Participants

IPM 027 All research centres	Week 4	Week 8	Week 12	Week 16	Week 20	Week 24	Week 28	Week 32	Week 36	Week 40	Week 44	Week 48	Week 52	Week 56	Week 60	Week 64	Week 68	Week 72	Week 76	Ave	
% Attended - May '12	99%																				99%
% Attended - June 2012	100%	97%																			99%
% Attended - July 2012	96%	99%	99%																		98%
% Attended - August 2012	94%	93%	95%	97%	100%																96%
% Attended - September 2012	94%	90%	97%	95%	96%	100%															95%
% Attended - October 2012	92%	92%	89%	94%	91%	93%	89%														91%
% Attended - November 2012	95%	91%	95%	94%	92%	90%	90%	87%													92%
% Attended - December 2012	89%	93%	89%	92%	91%	89%	84%	88%	100%												91%
% Attended - January 2013	99%	97%	93%	93%	98%	91%	98%	94%	96%	97%											96%
% Attended - February 2013	97%	97%	97%	97%	95%	97%	98%	96%	96%	95%	96%										96%
% Attended - March 2013	100%	97%	95%	98%	100%	96%	96%	98%	97%	99%	95%	100%									98%
% Attended - April 2013	100%	100%	94%	98%	98%	99%	94%	97%	98%	95%	96%	97%	98%								97%
% Attended - May 2013	100%	98%	100%	100%	100%	97%	99%	98%	98%	95%	96%	97%	94%	94%							97%
% Attended - June 2013	98%	100%	95%	100%	100%	100%	95%	99%	94%	99%	95%	97%	95%	96%	93%	100%					97%
% Attended - July 2013	100%	95%	98%	98%	97%	100%	98%	95%	97%	97%	100%	96%	96%	94%	96%	98%	100%				97%
% Attended - August 2013	100%	100%	97%	100%	97%	97%	100%	100%	94%	94%	97%	98%	95%	93%	95%	98%	100%	100%			98%
% Attended - September 2013	100%	100%	100%	98%	100%	100%	100%	100%	97%	98%	96%	98%	99%	96%	98%	99%	99%	98%	100%		99%
Average	97%	96%	96%	97%	97%	96%	95%	96%	97%	97%	97%	98%	96%	95%	95%	99%	100%	99%	100%		96%

*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

Use Only - Not for



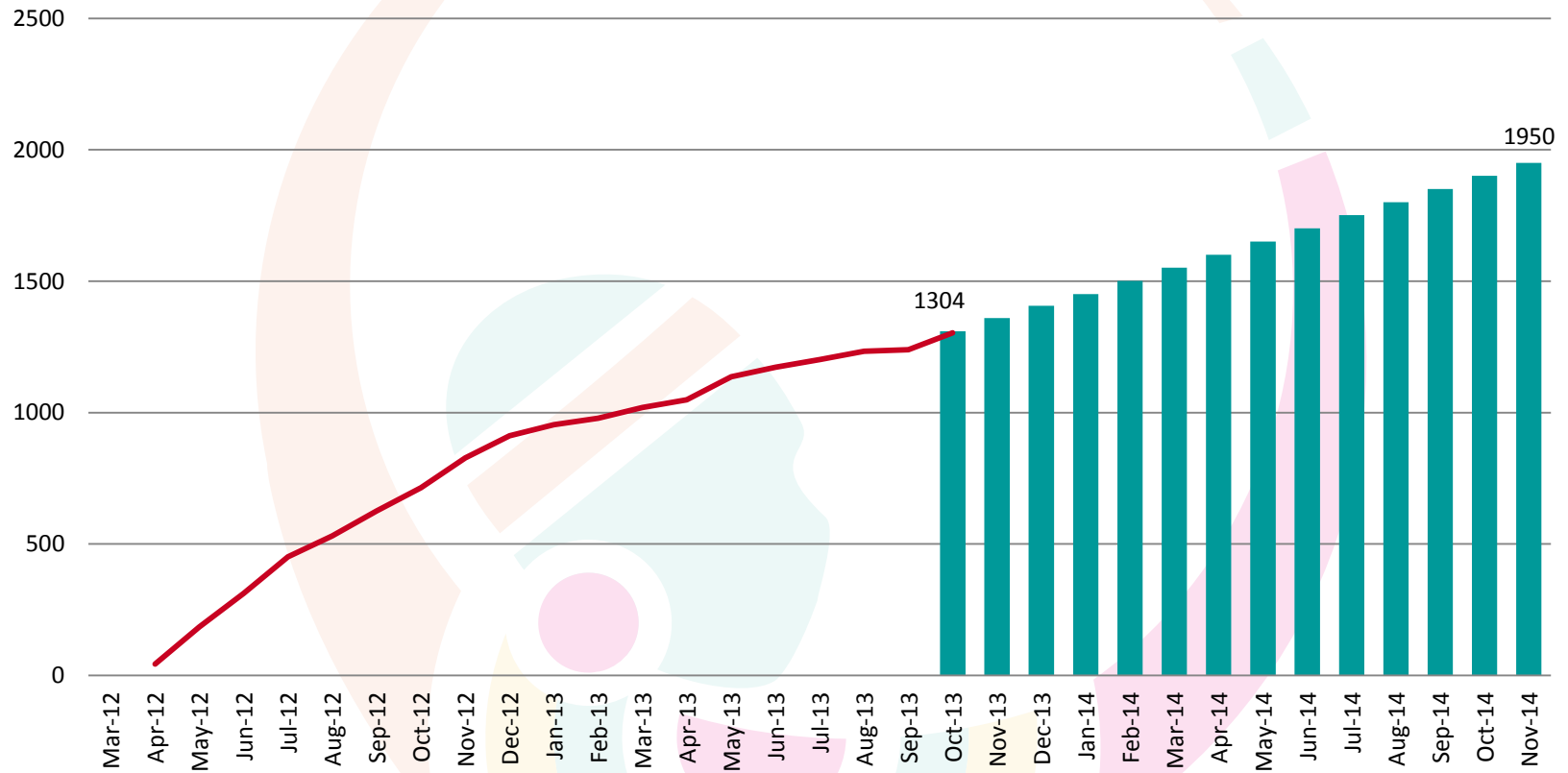
Objective Adherence Measurable

4-weekly Pharmacokinetic sampling for:

- Dapivirine Residual levels
- Dapivirine Plasma levels
- Dapivirine Vaginal Fluid levels

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Estimated Recruitment Timelines



Planned - IPM 027 Cumulative Revised Enrolment Forecast (November 2014 - 1950 participants)

IPM 027 Actual Enrolment - 17 October 2013

Currently:

3 Research Centers currently screening

To start:

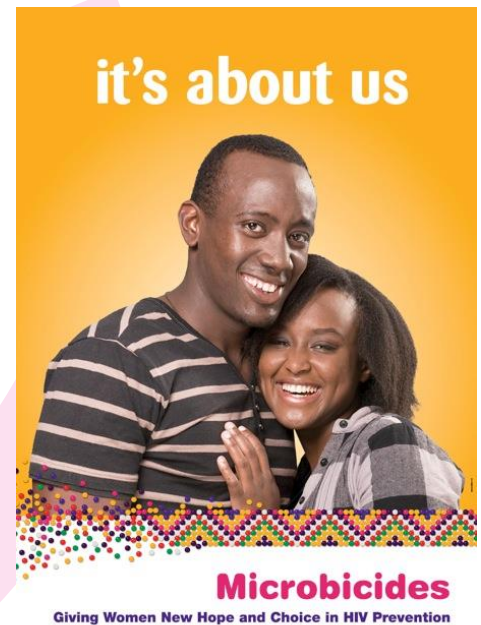
Masi estimate screening start date **Nov '13**

Ndlovu estimate screening start date Jan/Feb '14

Use Only - Not for

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*