Looking Forward to HOPE...

MTN Regional Meeting
Monday October 5th
Cape Town, South Africa
| 15 min | **Timeline and Operational Considerations**  
|        | Nyaradzo Mgodi, HOPE Protocol Co-chair  
|        | Ashley Mayo, FHI 360  
| 15 min | **Community Engagement for OLEs**  
|        | MU-JHU CRS, Kampala, Uganda  
| 15 min | **Adherence and Accountability**  
|        | Kalendri Naidoo, CAPRISA eThekwini CRS, Durban, South Africa  
| 15 min | **Q&A/Group Discussion** |
Out of ASPIRE, there is HOPE

HIV Open-label Prevention Extension
Out of ASPIRE, there is HOPE

Large Scale Implementation
From Research to Rollout

- **Post-trial access**: Intervention provided to trial participants and, sometimes, their communities, after the trial is over and before a product is available for widespread use.

- **Open label extensions**: Intervention made available in the context of a follow-on study protocol in which participants from the previous RCT know that they are receiving the active intervention.

- **Open label / implementation studies**: Research protocols similar to OLEs but enrolling new participants.

- **Demonstration projects**: “Road test” use of new option in real-world settings—not in trial site.

- **Product introduction**: Complex process of formally making new options widely available.

- **Scale-up**: Process of ramping up access to new options for all who need them.

Adapted from: AVAC Report 2013: Research & Reality
Open Label Extensions (OLEs)

- Ethical obligation to provide access to proven products in the immediate post-trial period to former participants
- Not full out delivery = has to incorporate being a regulated piece of research
- Partial step towards understanding what ring use would be like in a population with full access and knowledge about it’s then-proven effectiveness
OLEs are not the same as the trial

- Primary goal → provide **first access** to safe and effective product to participants who took part in ASPIRE
- OLEs are not to be confused with demonstration projects or full-scale product introduction *but they should move the field in that direction*
- But they are also not a continuation of the active arm of an RCT
Three examples

Trial results
- Partners PrEP Study
- iPrEx
- CAPRISA 004

Open label use
- Partners PrEP Study Extension
- iPrEx OLE
- CAPRISA 008
# Open Label Extensions

<table>
<thead>
<tr>
<th>Study Extension</th>
<th>Enrollment</th>
<th>Timeline to Implementation</th>
<th>Results</th>
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</thead>
<tbody>
<tr>
<td>Partners PrEP</td>
<td>89% of those eligible</td>
<td>3 months after results</td>
<td>High adherence and continued HIV protection</td>
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<tr>
<td>Study Extension</td>
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<tr>
<td>iPrEx OLE</td>
<td>65% of those eligible (of whom ~75% accepted PrEP [PrEP use was optional])</td>
<td>7 months after results</td>
<td>High adherence to open-label PrEP and high HIV protection with high adherence</td>
</tr>
<tr>
<td>CAPRISA 008</td>
<td>85% of those eligible</td>
<td>Protocol finalized 4 months after results; 2 year gap due to regulatory delays.</td>
<td>Pending</td>
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MTN-025 Design: Protocol v2.0

- Nonrandomized, open-label, phase III B trial, transitioning from a monthly to a quarterly visit schedule
Key scientific outcomes

• Important data on safety with open-label use, coincident with regulatory submission of this product
• Assessment of adherence, transitioning from monthly clinical trial visits to quarterly visits to mimic delivery settings
• Measurement of the key outcomes of HIV-1 incidence and resistance once efficacy is known
• Understanding declines of the ring (as one prevention tool is not for everyone)
HOPE Implementation Timeline

GOAL: Activation of HOPE in Q2 2016
Regulatory Approvals

• Priority: Timeliness in resubmission to IRBs
  – Recommend starting ICF translations now, to be able to submit quickly once ASPIRE results are released
  – GOAL: have supplemental materials that require IRB approval available at the same time as ICF resubmission
  – Be familiar with your IRB meeting dates/submission deadlines for Q1 2016
# HOPE Provisional Approvals

<table>
<thead>
<tr>
<th>Site</th>
<th>Primary IRB</th>
<th>Other IRB(s)</th>
<th>Drug Regulatory</th>
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<tbody>
<tr>
<td>MRC CTU</td>
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<tr>
<td>eThekwini</td>
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<td></td>
<td>Submitted</td>
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<td>Blantyre</td>
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<tr>
<td>Uganda</td>
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<td>Pending Submission</td>
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From Phase III to OLE

• What questions should we be asking now?
  – How do we best engage and educate communities about OLEs?
  – How to pace and manage accrual of an already identified study population?
  – What will our approach be to adherence support?
  – Are there concerns about product accountability and how do we manage these?
  – How to best retain participants on a quarterly schedule?
  – Others???
Thank you

Participants and communities
Acknowledgements

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