Global Malaria Portfolio

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Chief Scientific Officer

Curing Malaria Together www.mmv.org

Medicines for Malaria Venture
MMV’s Mission

• Discover, develop and deliver safe, effective and affordable antimalarials to treat and protect people most at risk of malaria
• Provide the public health community with the most appropriate tools to achieve maximum public health impact
MMV has a wide panel of donors

MMV - Medicines for Malaria Venture
funding from Foundation to 2010 (May 2006)

(Total Received/Pledged $263 Million)
# MMV Portfolio Non Severe Malaria March 2008

<table>
<thead>
<tr>
<th><strong>Research</strong></th>
<th><strong>Translational</strong></th>
<th><strong>Development</strong></th>
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<tbody>
<tr>
<td><strong>Discovery</strong></td>
<td><strong>Preclinical</strong></td>
<td><strong>Phase III</strong></td>
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<tr>
<td>Novartis</td>
<td>Isoquine</td>
<td>Eurartesim</td>
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<td>GSK</td>
<td>Tafenoquine</td>
<td>Coartem D</td>
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<td>Broad/Genzyme</td>
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<td>Others</td>
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<td>DHFR Thailand</td>
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<td></td>
<td>DHFR NITD</td>
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<tr>
<td></td>
<td>Pyridones GSK</td>
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<td>Macrolides GSK</td>
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<td>Nat Product NITD</td>
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<td>Immucillins</td>
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<td>Biartemides NITD</td>
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<tr>
<td><strong>Likelihood to Launch (CMR)</strong></td>
<td>7%</td>
<td>14%</td>
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- **Novartis**: 9 projects
- **GSK**: 3 projects
- **Others**: 6 projects
- **Broad/Genzyme**: 5 projects
- **Likelihood to Launch (CMR)**: 7% for Novartis, 14% for GSK, 27% for Others, 38% for Broad/Genzyme, 72% for Others
Global Portfolio: Non-severe malaria March 2008

Source: iddb3 database search; MMV internal database
Coartem Dispersible

- Partner: Novartis
- Key advantage: new Pediatric formulation (cherry) – tablet disperses easily
- Current Status: Phase III trial non-inferiority of crushed tablet (890 pediatric patients)
- Next Steps: Launch. Submitted to Swissmedic December 2007
DACART (Chlorproguanil-Dapsone-Artesunate)

- Partners: GSK, WHO/TDR, Liverpool University
- Key advantage: once-a-day, short half-life, non-4 aminoquinoline
- Current Status: Phase III trials complete
  - Chlorproguanil-Dapsone (900) May’07
  - Artemether-Lumefantrine (1394) June’07
- Key issue: Comparison with Artemether-Lumefantrine showed
  - Larger drop in hematocrit in G6PD- patients
  - Higher number of AE for G6PD- patients in DACART group
- Decision not to file DACART made by GSK in March 2008

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<tr>
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<th>2007</th>
<th>2008</th>
<th>2009</th>
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<tbody>
<tr>
<td></td>
<td>Q1</td>
<td>Q2</td>
<td>Q3</td>
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<td>Dacart</td>
<td>III</td>
<td>Filing</td>
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Eurartesim (DHA-Piperaquine)

- Partners: Sigma-Tau, Holley, Oxford University
- Key advantage: Once-a-day, prophylactic effect
- Current Status: Databases locked
  - African children (1533) vs; Artemether/ Lumefantrine
  - Asia adults (1150) vs Artesunate/ Mefloquine (still blinded)
- Next Steps: Regulatory submission to EMEA 4Q’08
- Partner: Shin Poong, University of Iowa
- Key advantage: 3 year shelf life, pediatric formulation
- Current Status: Completing four Phase IV trials
  - Artesunate-Mefloquine
  - Artemether-Lumefantrine
  - Chloroquine (*P. vivax*)
  - Paediatric
- Next Steps: Completion of Phase III and filing to EMEA (article 58)
Lessons from Phase III

• MMV has eight Phase III studies completed, or completing in 2007-2008

• Lessons learned
  • Safety and efficacy have to be considered in parallel
  • ICH quality is not a luxury, but is essential for credible decisions based on data
  • Comparable endpoints result from close coordination

• MMV plays a key role ensuring the smooth interfaces
MMV’s Phase IV Objectives

• Quality data on effectiveness and safety
  • ICH quality in the evidence base for policy makers

• Addressing the gaps in the product profiles
  • Small infants (less than 5kg)
  • Pregnant and lactating mothers
  • *P. vivax* and mixed infections
  • Malnutrition status, coinfections

• New treatment paradigms in the eradication era
MMV Partnerships
Addressing the gaps with evidence

- District Level studies Effectiveness and Safety (INDEPTH)

- Strengthening the Pediatric Knowledge Base (EDCTP co-funding) <5 kg and Age/weight correlations studies

- ACTi: longitudinal studies with repeated doses

- ACT in pregnancy: extending the role of Eurartesim – through safety and efficacy in pregnancy to IPTp

- ACT in Infants – safety and PK in small infants bridging to IPTi
MMV tailoring the portfolio to address resistance

• Do our pipeline drugs work in ‘artemisinin refractory’ patients?
  • Although pipeline has other ‘ozonide’ drugs, chemically they are very different
  • Testing all the development candidates against primary patient samples
  • Include related negative controls, blind testing

• Rapid progression to clinical proof of concept
  • How much can we afford to trust the cell biology?

• Close co-ordination with WARN
Parasite biology: high content screening goes beyond life and death

- Biology in 1536 well plates
  - Image the parasite growing inside erythrocytes
  - Eliminate false positives
  - Biology: distinguishes different stages
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