Looking to the future: MMV’s Discovery and Development Priorities in the Eradication Era

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Chief Scientific Officer
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MMV’s R&D priorities

- **Bring fixed-dose ACTs to the market**
  - Expand range for paediatric/pregnancy indications
- **Severe malaria: GMP supply of artemesunate for injection**
- **Next Generation of Treatments**
  - Compounds active against all resistant strains
  - Includes synthetic artemisinins
  - Activity on gametocytes important for eradication
- **Radical cure for *P. vivax* malaria**
  - Cell model, animal model, clinical model
## MMV Portfolio of New Medicines

Over 50 projects from Discovery to Delivery

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<thead>
<tr>
<th>Research Lead Gen</th>
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<th>Preclinical</th>
<th>Translational Phase I</th>
<th>Phase II</th>
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<tr>
<td>Novartis miniportfolio</td>
<td>Whole Cell Lead Novartis</td>
<td>MK 4815 (Merck)</td>
<td>GSK 932121 GSK</td>
<td>iv artesunate Quillin</td>
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<td>GSK miniportfolio</td>
<td>Pyridone GSK</td>
<td>KAE 609 Novartis</td>
<td>Tafenoquine GSK</td>
<td>Artemisone UHKST</td>
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<td>Broad/ Genzyme miniportfolio</td>
<td>DHODH UTSW/UW/Monash</td>
<td>P218 DHFR (BIOTEC/Monash/LSHTM)</td>
<td>OZ 439 (Monash/UNMC/STI)</td>
<td>(+) Mefloquine Treague</td>
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<td>sanofi aventis Orthologue screen</td>
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<td>Whole Cell Hits St Jude/Rutgers</td>
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<td>Other Projects 13 Projects</td>
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<th>Development Pivotal Study</th>
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<tr>
<td>Pyramax® Shin Poong/University of Iowa</td>
<td>Coartem®-D Novartis</td>
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<td>Coarsucam® sanofi aventis/DNDI</td>
<td>Eurartesim™ sigma-tau</td>
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☑️ Prequalified by WHO
Coartem® *Dispersible* (artemether/lumefantrine)
Already saving children’s lives

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- **Partner:** Novartis

- **Key advantages:**
  - new paediatric formulation (sweet, cherry)
  - tablet disperses easily

- **Current Status:**
  - Approved by Swissmedic, and by WHO Prequalification (2009)
  - Effectiveness Studies (with INESS network) 2010
  - Longitudinal Studies (with EDCTP) 2010
  - Asymptomatic Carrier studies for Eradication 2010
Eurartesim™ (DHA-piperaquine)
In review with EMEA – approval 2010

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• **Partners: Sigma-Tau, (Holley, Oxford University)**

• **Key advantages:**
  ✓ once-a-day,
  ✓ long half-life: better post-treatment prophylaxis

• **Current Status:**
  ✓ regulatory submission to EMEA,
  Next stage Disease Endemic Countries, and WHO Prequalification
  Longitudinal Studies (with EDCTP) 2010
  Effectiveness Studies (with INESS network) 2010
Pyramax® (pyronaridine-artesunate)  
Regulatory Submission in March 2010

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- **Partners:** Shin Poong, University of Iowa

- **Key advantages:** once a day, long half-life, paediatric formulation, *P. vivax* indication, 3 year shelf-life

- **Current Status:**
  - ✔ regulatory submission to EMEA -1Q 2010
Malaria Eradication
Key challenges for the next decade in Research

- **Single Encounter Radical Cure (SERC) targeting *P. falciparum***
  - Kills blood stages, and gametocytes

- **Single Encounter Radical Cure (SERC) targeting *P. vivax***
  - Kills blood stages, gametocytes, and hypnozoites

- **Long Term Protection against exposure**
  - Protected against resistance, safe in expectant mothers and infants
Artemisinin Resistance
How effective are the synthetic artemisinins?

• Clinical Proof of Concept
  • Parasite Clearance Time and *in vitro* resistance of artesunate and artemisone in Pailin and Mae Sot (Myanmar?)
  • Synthetic peroxides (Artemisone and Rbx11160) clinical test 2010
  • OZ439 (long acting synthetic artemisinin) in phase I – could be in tested in 2011

• Cell biology: Artemisinin Resistance Profiles
  • Testing all synthetic endoperoxides *ex vivo* – which ones are the best in five centres
OZ439 next generation synthetic trioxolane
Part of single dose cure for *falciparum* malaria

- **Partners:** Nebraska/STI/Monash; un-partnered development project

- **Current Status:**
  - Phase I studies completed successfully: half life >12h
  - Phase IIa Proof of Concept 1Q’10
  - Identify partner drug and dose
Mini-portfolios
Changing the face of Malaria Discovery

- Compounds can be tested against whole parasites in high content assays
- Using 384 and 1536-well systems 5 million compounds have now been tested
- Collaborations with over 20 companies – including all the top 5
- Over 20,000 submicromolar hits – elaborated in collaboration with Industry/academic centres
- Estimated 200 drugable targets, assays available for 100
- Screen to phase I in 4-5 years
Malaria Life-Cycle Fingerprints
Defining the medicines for eradication

- New chemical series from uHTS are profiled against key life cycle stages
  - Gametocyte assays
  - *P. cynomolgi* hypnozoite assay (2010)
- Compare *Life Cycle Fingerprint* with all molecules in *Malaria Portfolio Collection*
  - >50 molecules with distinct *in vivo* activities
Tafenoquine for *P. vivax* radical cure
Better compliance, better safety margin

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- **Partner:** GlaxoSmithKline
- **Key advantage:** Only needs 3 day therapy
- **Current status:**
  - Interaction studies: Chloroquine and Tafenoquine (ongoing)
  - Safety studies in G6PD volunteers and patients (and children)
  - Interaction studies: Pyramax and Tafenoquine (2010)
Partnerships for success

- Phase IV and capacity building: EDCTP, MCTA, INDEPHT, Wellcome Trust, WHO, TDR
- Pharmaceutical and Biotech Partners: from screen to phase IV
- Scientific and Clinical Partners ESAC, GSB, BMGF, Wellcome
- Financial Sponsors
- Clinical Trial Sites
- Our patients and their families
Conclusions

• MMV has a strong portfolio of new medicines from discovery to delivery

• Advances in technology (screens and genes) mean our discovery mini-portfolios are well supplied

• New development candidates are being pre-selected for their role in malaria eradication

• Collaboration at all levels is the key to our success