The global malaria portfolio: where we stand today

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Defeating Malaria Together
Public health imperative

- 3.3 billion people at risk
- Low-economy countries
- Children and women disproportionately affected
- Resistance to current interventions
MMV strategic priorities 2015-2018
from control to eradication

Maximize health impact of launched antimalarial medicines

Introduce better medicines to enhance malaria control and reduce morbidity/mortality

Single-dose cures to facilitate elimination & eradication
376 partners spanning the world

including:

- 28 pharmaceuticals companies
- 13 biotech companies
- 56 universities
- 38 research institutes
- 72 clinical sites
- 50 government agencies
5 (+2) medicines launched from 2009-2015

COARTEM DISPERSIBLE
EURARTESIM
PYRAMAX
ARTESUN INJECTED
SP-AQ

AS-AQ*
AS-MQ*

* Transferred from DNDi-led partnership portfolio to MMV-led partnership portfolio 20th May 2015
SERCaP

Fast killing

Long-acting

Radical cure

Transmission blocking

single encounter radical cure and prophylaxis
### 9 new medicines in clinical development

<table>
<thead>
<tr>
<th>Name</th>
<th>Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pyramax-granules</td>
<td>Filed</td>
</tr>
<tr>
<td>Eurartesim-dispersible</td>
<td>Phase III</td>
</tr>
<tr>
<td>Rectal artesunate</td>
<td>Phase IIIb</td>
</tr>
<tr>
<td>Tafenoquione</td>
<td>Phase III</td>
</tr>
<tr>
<td>OZ439/PQP</td>
<td>Phase IIb</td>
</tr>
<tr>
<td>KAE609</td>
<td>Phase IIa</td>
</tr>
<tr>
<td>KAF156</td>
<td>Phase IIa</td>
</tr>
<tr>
<td>DSM265</td>
<td>Phase IIa</td>
</tr>
<tr>
<td>MMV048</td>
<td>Phase I</td>
</tr>
</tbody>
</table>
**Novel chemotypes and new targets**

<table>
<thead>
<tr>
<th>Chemotype and related series</th>
<th>Biological Target</th>
<th>Number of molecules</th>
</tr>
</thead>
<tbody>
<tr>
<td>4-aminoquinolines</td>
<td>Active against CQ-resistant malaria</td>
<td>1 (FQ)</td>
</tr>
<tr>
<td>Semi- or fully synthetic peroxides</td>
<td>Active against ART resistance</td>
<td>1 (OZ439)</td>
</tr>
<tr>
<td>Diaminopyrimidine</td>
<td>Active against all DHFR resistance</td>
<td>1 (P218)</td>
</tr>
<tr>
<td>8-aminoquinoline</td>
<td>Unknown</td>
<td>1 (tafenoquine – single dose)* studies in C21st!</td>
</tr>
<tr>
<td>Multiple diverse series</td>
<td>New - ATP4</td>
<td>4 (KAE609, SJ733, GSK030, PA92)</td>
</tr>
<tr>
<td>Triazolopyrimididine</td>
<td>New – DHODH</td>
<td>1 (DSM265)</td>
</tr>
<tr>
<td>Aminopyridine</td>
<td>New - PI4K</td>
<td>1 (MMV048)</td>
</tr>
<tr>
<td>Quinoline</td>
<td>New - to be disclosed</td>
<td>1 (MMV121)</td>
</tr>
<tr>
<td>Triaminopyrimididine</td>
<td>New - V-type H+ ATPase</td>
<td>1 (MMV243)</td>
</tr>
<tr>
<td>Quinolone</td>
<td>New – bc1 Qi inhibitor</td>
<td>1 (ELQ-300)</td>
</tr>
</tbody>
</table>

New modes of action, overcome historical resistance or single dose
**Target Product Profiles (TPPs) for medicines to make eradication achievable: TPP1:**
- 3-day cure/artemisinin-based combination therapies
  - Artemether-lumefantrine dispersible (Coartem® Dispersible), generic by Ajanta
  - Dihydroartemisinin-piperaquine (Eurartesim®)
  - Dihydroartemisinin-piperaquine paediatric (Eurartesim®)
  - Pyronaridine-artesunate (Pyramax®)
  - Pyronaridine-artesunate paediatric (Pyramax®)
  - Artesunate-amodiaquine (Coarsucam™, ASAQ/Winthrop®) FDC generics by Ajanta, Ipca, Guilin and co-blistered generics by Strides & Cipla
  - Artesunate-mefloquine, co-blistered generic by Acino/Mepha

**Potential single-dose agents:**
- OZ439/FQ
- OZ439/PQP
- KAE609
- KAF156
- Tafenoquine

**Target Candidate Profiles (TCPs):**
- Fast clearance (TCP1)
- Long duration (TCP2)
- Relapse prevention (TCP3a)
- Transmission blocking (TCP3b)
- Chemoprevention (TCP4)

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**Research**
- Novartis
  - Miniportfolio
  - 1 project
- GSK
  - Miniportfolio
- AstraZeneca
  - Miniportfolio
- Celgene
  - Heterocycles
- Univ. Campinas
  - Heterocycles
- Daiichi-Sanyo
  - Screening
- Takeda
  - Screening
- Eisai
  - Screening
- MMV
  - Pathogen Box
- Other projects
  - 15 projects

**Translational**
- Preclinical
  - P218 DHFR
    - Biotec/monash Univ./London School of Hygiene & Trop Med
  - SJ733
    - National Institutes of Health (Nihy)/St Jude/Rutgers Univ
  - DDD498
    - Merck Serono/Univ. Dundee
  - PA02
    - Imperial Kering / Univ. Washington/Genomics Institute of the Novartis Research Foundation
  - MMV253
    - Astrazeneca

**Human volunteers**
- MMV048
  - Univ. Cape Town/Technology Innovation Agency

**Patient exploratory**
- OZ439/PQP
  - Sanofi
- OZ439/FQ
  - Sanofi
- KAE609
  - Novartis
- KAF156
  - Novartis
- DSM265
  - Takada/NIH

**Patient confirmatory**
- Tafenoquine
  - GSK
- Palmarone
  - Pfizer

**Development**
- Rectal Artesunate
  - Cipla/Strides/WHO-TDR
- Pyronaridine-artesunate paediatric
  - Shin Poong/Univ. Iowa
- Artemether-lumefantrine dispersible
  - Novartis
- Artesunate for injection
  - Guitin
- Pyronaridine-artesunate
  - Shin Poong
- Artesunate-amodiaquine
  - Sanofi/DNDi
- Artesunate-mefloquine
  - Cipla/DNDi
- SP+SAP
  - (Sulododine+Pyremethamine + Amodiaquine)

**APM**
- Post approval

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**Notes:**
- Bioequivalence studies planned in preparation for WHO prequalification
- Included in MMV portfolio post registration
- First review or approval by WHO Prequalification, or by regulatory bodies who are ICH members or observers

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**Images:**
- Project overview diagram
- Table showing lead optimization and project status
MMV strategic framework to 2018
portfolio | pipeline

Key Unmet Needs
- Facilitating Access to ACTs
- Single-Dose Cure
- Medicines for Children
- Medicines for Expectant Mothers
- Treatment for Severe Malaria
- Transmission Blocking
- Relapse Prevention
- Chemoprotection

2015
Registered as of May

2015-2018
Filing

2018+
Filing
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- Unitaid
- UKaid
- Wellcome Trust
- USAID