



Global Malaria Portfolio

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Medicines for Malaria Venture

MMV's Mission



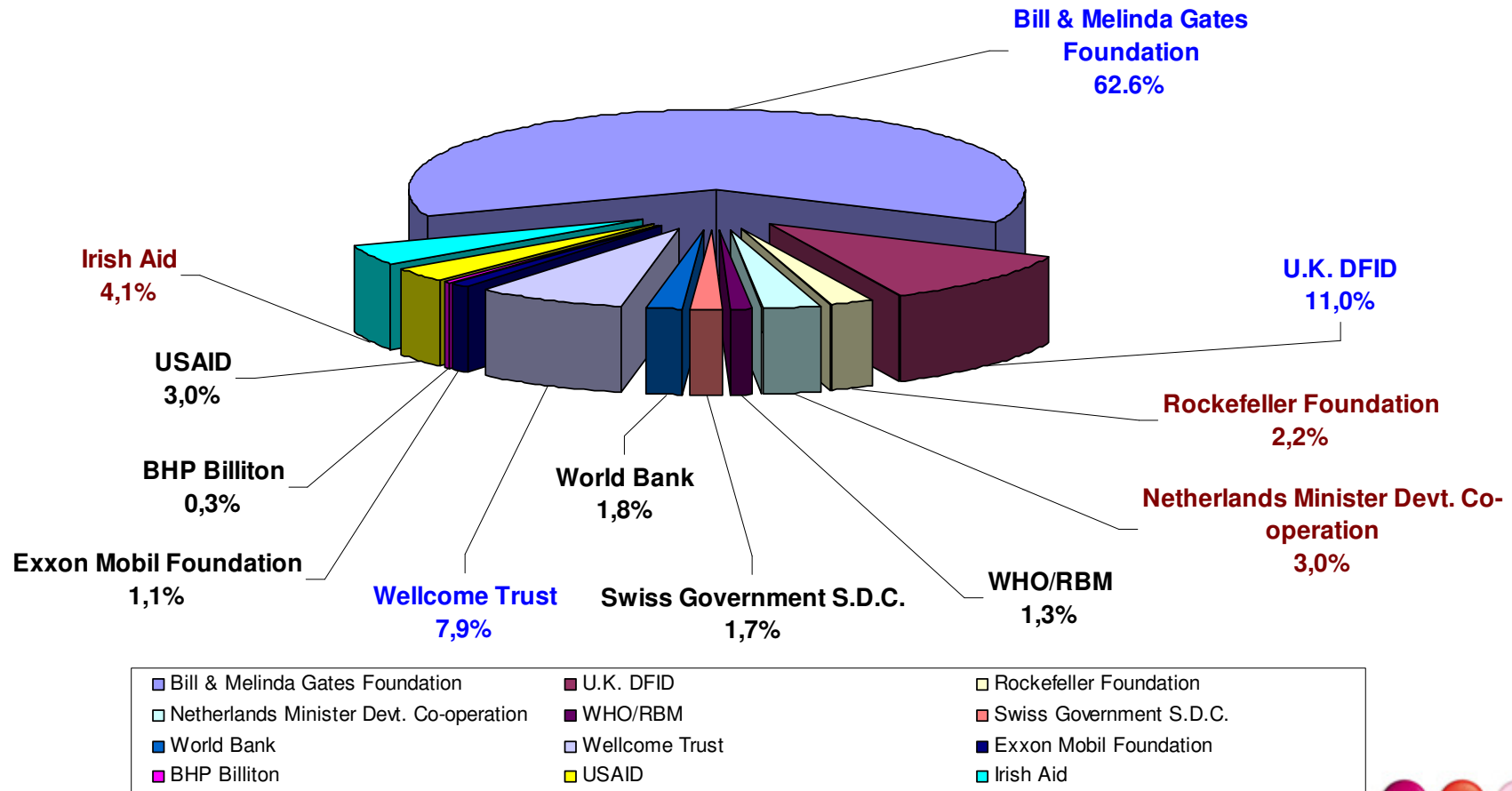
- Discover, develop and deliver safe, effective and affordable antimalarials to treat and protect people most at risk of malaria
- Provide the public health community with the most appropriate tools to achieve maximum public health impact

MMV has a wide panel of donors



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

(Total Received/Pledged \$263 Million)



Bill & Melinda Gates Foundation	U.K. DFID	Rockefeller Foundation
Netherlands Minister Devt. Co-operation	WHO/RBM	Swiss Government S.D.C.
World Bank	Wellcome Trust	Exxon Mobil Foundation
BHP Billiton	USAID	Irish Aid



MMV Portfolio Non Severe Malaria

March 2008



Research		Translational			Development	
Discovery	Lead Opt	Preclinical	Phase I	Phase II	Phase III	Registration
Novartis 9 projects	DHFR Thailand	Isoquine	Tafenoquine		Eurartesim	Coartem D
GSK 3 projects	DHFR NITD	MK 4815			Pyramax	
Broad/Genzyme 5 projects	Pyridones GSK	Pyridone 932121				
Others 6 projects	Macrolides GSK	OZ439				
	DHODH					
	Nat Product NITD					
	Immucillins Einstein					
	Biarthemides NITD					
Likelihood to Launch (CMR)	7%	14%	27%	38%	72%	

Global Portfolio: Non-severe malaria

March 2008



2016+	2016	2014	2013	2012	2010	2008
Novartis 9 projects	DHFR Thailand	Isoquine	Tafenoquine	Fosmidomycin Clindomycin	Eurartesim	Coartem D
GSK 3 projects	DHFR NITD	MK 4815	Blue AQ	Artesunate Ferroquine	Pyramax	Mefloquine Artesunate
Broad/Genzyme 5 projects	Pyridones GSK	Pyridone 932121	AQ13 Immtech		Azithromycin chloroquine	Amodiaquine Artesunate
Others 6 projects	Macrolides GSK	Ozonides				
Others 53 projects	DHODH	SAR116242 Trioxalanes				
	Nat Product NITD					
	Immucillins Einstein					
	Biartemides NITD					
	PS22 triazine Jacobus					

- MMV projects
- sanofi aventis projects
- Other projects

Source: iddb3 database search; MMV internal database

Coartem Dispersible



	2007				2008				2009			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Coartem D	Filing				Reg.				Launch			

- 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)



	2007				2008				2009			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Dacart	III				Filing							

- 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

Eurartesim (DHA-Piperaquine)



	2007				2008				2009			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Eurartesim	III								File			

- 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

Pyramax (Pyronaridine- Artesunate)



	2007				2008				2009			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Pyramax	III								Filing			

- 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

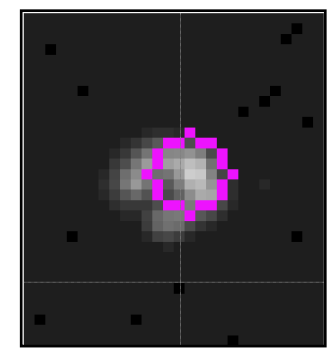
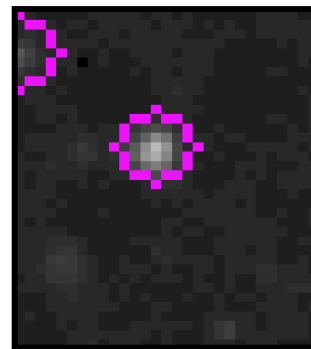
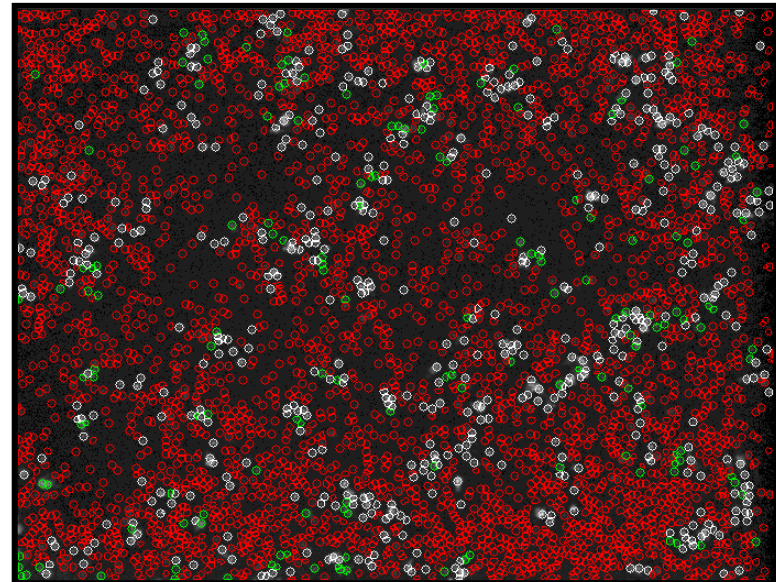


- Do our pipeline drugs work in ‘artemisinin refractory’ patients?
 - Although pipeline has other ‘ozonide’ drugs, chemically they are very different
 - Testing all the development candidates against primary patient samples
 - Include related negative controls, blind testing
- Rapid progression to clinical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