

A woman with braided hair is shown in profile, looking down at a young child. The child has braids decorated with colorful beads. The background is a soft-focus outdoor setting.

10th
ANNIVERSARY

Partnering for success: MMV's long term view of Clinical Development

Stephan Duparc

Arusha, 14 October 2009

Curing Malaria Together
www.mmv.org



Medicines for Malaria Venture




MMV's Objectives

- **Bring fixed dose ACTs to the market**
 - Expand range for pediatric/pregnancy indications
- **Radical cure for *P. vivax* malaria**
 - Cell model, animal model, clinical model
- **Severe malaria: GMP supply of artesunate for injection**
 - (review next generation strategy in December?)
- **Uncomplicated malaria**
 - Compounds active against all resistant strains
 - No new 4-aminoquinolines or similar without significant advantage
 - Activity on gametocytes an advantage



MMV Portfolio: August 2009

Significant progress on key objectives

Research		Translational			Development	
Lead Gen	Lead Opt	Preclinical	Phase I	Phase II	Phase III	Registration ¹
Novartis 3 projects	KAC776 Novartis	MK 4815	Pyridone 121 GSK	IV artesunate Guilin	Pyramax® Shin Poong/University of Iowa	 Coartem® sanofi-sintelabo
GSK 3 projects	Pyridones GSK	KAC470 Novartis	Tafenoquine GSK	Artemisone UHKST		Coarsucam® sanofi-sventis
Broad/ Genzyme 3 projects	DHODH UTSW/UW/Monash	P218 BIOTEC/Monash/LSHTM	OZ 439 Monash/UNMC/STI			Eurartesim™ sigma-tau
Immucillins Albert Einstein 	Aminoindoles Broad/ Genzyme		(+)Mefloquine Treague			
Myosin Motor Drexel/UW 	Ozonide Monash/UNMC/STI					
Quinolones USF						
ELQs Portland						
Other Screening 18 Projects						

Eurartesim submitted on July 3rd 2009 to EMEA
Pyramax to be submitted March 2010 to EMEA
Tafenoquine, OZ439, GSK 932121 and
(+)Mefloquine started phase I



Confidential- MMV
internal use only



Medicines for Malaria Venture

Development of Coartem[®]-Dispersible

**Collaboration
with
Novartis**

Phase I palatability study in 30 healthy volunteer children (7-10y/Tanzania) to choose between cherry, orange and strawberry flavour

Bioavailability study in 48 healthy volunteers to bridge between Coartem tablets (given as crushed) and new dispersible tablet. Jan-May 2006

Phase III efficacy study in 890 patients (5-35 kg, <12y) in sub-Saharan Africa to compare safety and efficacy of Coartem dispersible tablets vs. coartem tablets (given as crushed) Jun 2006 – Oct 2007

Bioequivalence study in 60 healthy volunteers to compare bioavailability of dispersible tablets manufactured at commercial site with material similar as used in clinical studies. Jan – Aug 2008

**Approval
End of
2008**



internal use only



Medicines for Malaria Venture

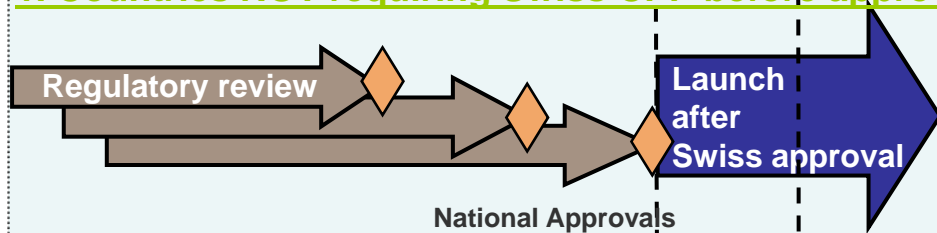
Registration of Coartem-D Launched Feb '09

Collaboration
with
Novartis

| 1Q08 | 2Q08 | 3Q08 | 4Q08 | 1Q09 | 2Q09 | 4Q09



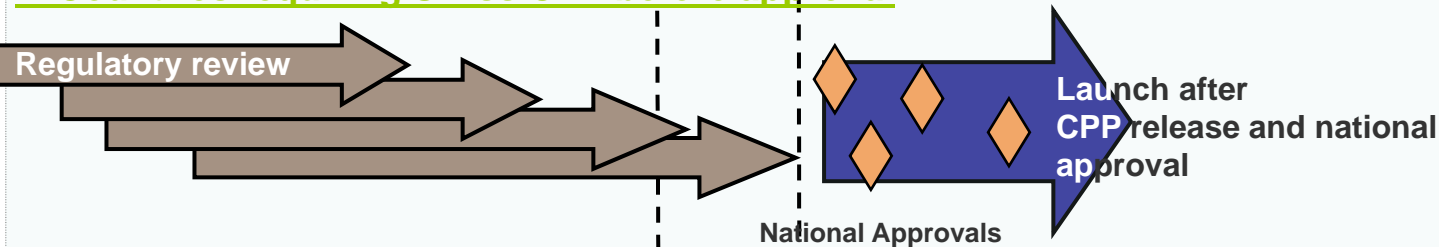
1. Countries NOT requiring Swiss CPP before approval



Countries in this group:

Benin, Burkina Faso, DRC, Gabon, Ghana, Guinea, Ivory Coast, Madagascar, Mauritania, Niger, Nigeria, Senegal, Togo
Cameroon, Central African Republic, Congo

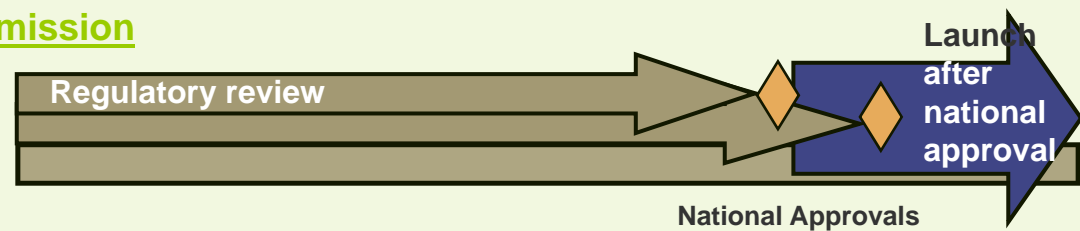
2. Countries requiring Swiss CPP before approval



Countries in this group:

Ethiopia, Kenya, Tanzania, Uganda, Zambia

3. Countries requiring Swiss CPP before submission



Eurartesim™ (DHA-piperaquine)

	2008				2009				2010				2011				
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	
Eurartesim									Reg.								Launch

Product Profile:

P. falciparum malaria

three days once daily dosage

treatment cost: <1 USD

GMP co-formulation

expected shelf-life of 3 years

Pediatric formulation development



**Collaboration
with
Sigma tau and
Pfizer**

Registration:

EMA (orphan drug): **Submitted 3 July '09**

Endemic Countries: after approval by EMA

US-FDA (orphan drug): Q4-2009

Confidential- MMV
internal use only



Medicines for Malaria Venture



Clinical development plan

five clinical trials carried out

**Collaboration
with
Sigma tau and
Pfizer**

Study	Indication (when pts included)	Population
PK (Swtz)	-	Healthy Subjects
PK Thailand	Acute, uncomplicated falciparum malaria	Adults patients
PK Burkina Faso	Acute, uncomplicated falciparum malaria	Pediatric patients
Phase III Africa (vs Coartem)	Acute, uncomplicated falciparum malaria	1500 pediatric patients
Phase III Asia (vs AS+MQ)	Acute, uncomplicated falciparum malaria	1150 adults and pediatric patients



Confidential- MMV
internal use only



Medicines for Malaria Venture

PYRAMAX[®]

(pyronaridine/artesunate)

	2008				2009				2010				2011			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
<i>Pyramax</i>	Phase III				+ filing				Reg.				Launch			

Product Profile:

P. falciparum and *P. vivax* blood stage malaria

three days once daily dosage

treatment cost: <1 USD

GMP co-formulation

expected shelf-life of 3 years

paediatric formulation under development



**Collaboration
with
Shin Poong**

Registration:

EMA (article 058) + Endemic Countries: March-2010

K-FDA and US-FDA (orphan drug): End of 2010



Confidential- MMV
internal use only



Medicines for Malaria Venture

Pyramax Phase III Clinical Trial Programme

**Collaboration
with
Shin Poong**

<p>SP-C-004-06 N=1272 PYRAMAX Tablets</p>	<p>Phase III comparative, open-label, randomised, multi-centre, study PYRAMAX[®] versus MEFLOQUINE (250 mg tablet) plus ARTESUNATE (100 mg tablet) in children and adult patients with acute uncomplicated <i>Plasmodium falciparum</i> Oral presentation at MIM, Nairobi 2009</p>
<p>SP-C-005-06 N=1272 PYRAMAX Tablets</p>	<p>Phase III comparative, double-blind, double-dummy, randomised, multi-centre, study PYRAMAX[®] versus COARTEM[®] (artemether/lumefantrine) in children and adult patients with acute uncomplicated <i>Plasmodium falciparum</i> Oral presentation at MIM, Nairobi 2009</p>
<p>SP-C-006-06 N=456 PYRAMAX Tablets</p>	<p>Phase III comparative multi-centre, randomised, double-blind, double-dummy, study PYRAMAX[®] versus CHLOROQUINE in children and adult patients with acute <i>Plasmodium vivax</i></p>
<p>SP-C-007-07 N=534 PYRAMAX Granules</p>	<p>Phase III comparative, open-labelled, randomised, multi-centre clinical study to PYRAMAX[®] granules versus COARTEM[®] (artemether/lumefantrine) crushed tablets in infants and children with acute uncomplicated <i>Plasmodium falciparum</i> Oral presentation at MIM, Nairobi 2009</p>
<p>SP-C-008-07 N=40 PYRAMAX Tablets</p>	<p>Phase III randomised, double-blind, double-dummy, comparative clinical study to PYRAMAX[®] versus CHLOROQUINE in children and adult patients in Korea with acute <i>Plasmodium vivax</i> Results in 2010</p>



**Confidential- MMV
internal use only**



Medicines for Malaria Venture

Pharmacovigilance: Monitoring Drug Safety

Collaboration
with
sanofi-aventis

MMV looks to WHO as policy lead on pharmacovigilance

MMV seeks to provide evidence to respond to countries' questions

- **Example: Phase IV field program to determine safety & effectiveness of ASAQ/Coarsucam in a pilot sanitary district of Côte d'Ivoire**

MOU between Sanofi-Aventis and MMV signed in September 2008

WHO Prequalification granted for Coarsucam on October 19, 2008

- **Implementation study** in 15,000 patients to enable, with a 95% likelihood, the detection of an adverse event occurring with a rate of 1/5000 (classified as-“rare” adverse event): Open-labeled study to assess the clinical safety, compliance and impact on malaria epidemiology of the implementation of ASAQ fixed-dose in the treatment of suspected uncomplicated *P. falciparum* malaria episodes
- **Pre- and post-studies** with 290 patients at each of the 2 time points: Nested open-labeled study to compare the effectiveness and safety of ASAQ fixed-dose in the treatment of uncomplicated *P. falciparum* malaria episodes at 2 year-intervals



Confidential- MMV
internal use only



Medicines for Malaria Venture



10th
ANNIVERSARY

THANK YOU
MERCI

Curing Malaria Together
www.mmv.org



Medicines for Malaria Venture

