MMV'S Update

RBM CRSPC meeting, Abidjan

November 22, 2023

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Director Access & Product Management

MMV
Medicines for Malaria Venture

What *is* MMV?

MMV is a product development partnership (PDP),
Swiss foundation and US charity

of

over 100 people
working towards one mission:
to reduce the burden of malaria
in disease-endemic countries by

discovering, developing and delivering
new, effective and affordable
antimalarial drugs

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MMV portfolio at inception (1999)

	Discover	Translational		Product development			Access
	Candidate profiling	Preclinical	Human volunteers	Patient exploratory	Patient confirmatory	Regulatory review	Approved/ERP
Treatments							
Medicines for prevention							
Elimination tools							

In 1999 there were **2 projects in lead optimization** (prior to candidate profiling): cysteine protease inhibitor and synthetic peroxide

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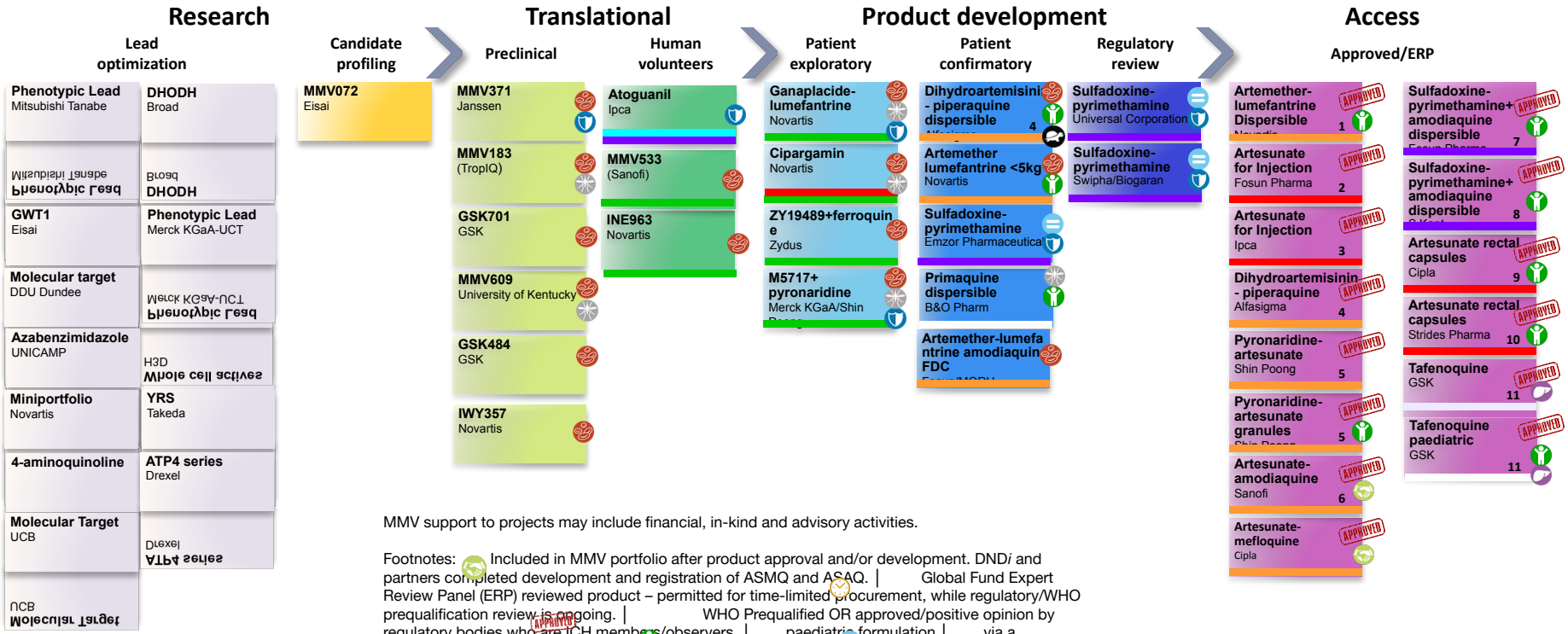
MMV-supported projects



MMV support to projects may include financial, in-kind and advisory activities.

Footnotes: Included in MMV portfolio after product approval and/or development. DND*i* and partners completed development and registration of ASMQ and ASAQ. | Global Fund Expert Review Panel (ERP) reviewed product – permitted for time-limited procurement, while regulatory/WHO prequalification review is ongoing. | WHO Prequalified OR approved/positive opinion by regulatory bodies who are ICH members/observers. | paediatric formulation. | via a bioequivalence study. Past partners are in brackets (-). Relapse prevention | No progress report in the last 2 years

Brand names 1: Coartem® *Dispersible*; 2: Artesun®; 3: Larinate® 60mg; 4: Eurartesim®; 5: Pyramax® tablets or granules; 6: ASAQ Winthrop®; 7: SPAQ-CO™; 8: Supyra®; 9: 100mg Artesunate Rectocaps; 10: Artecap™; 11: *Kozenis or Krintafel* (Trademarks owned or licensed by GSK)

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MMV's focus: addressing unmet medical needs

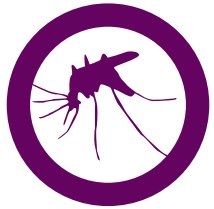
ARTEMISININ PARTIAL RESISTANCE

CHEMOPREVENTION FOR CHILDREN & PREGNANT WOMEN

1x

SINGLE DOSE CURES

PREVENTION OF RELAPSE



TRANSMISSION BLOCKING

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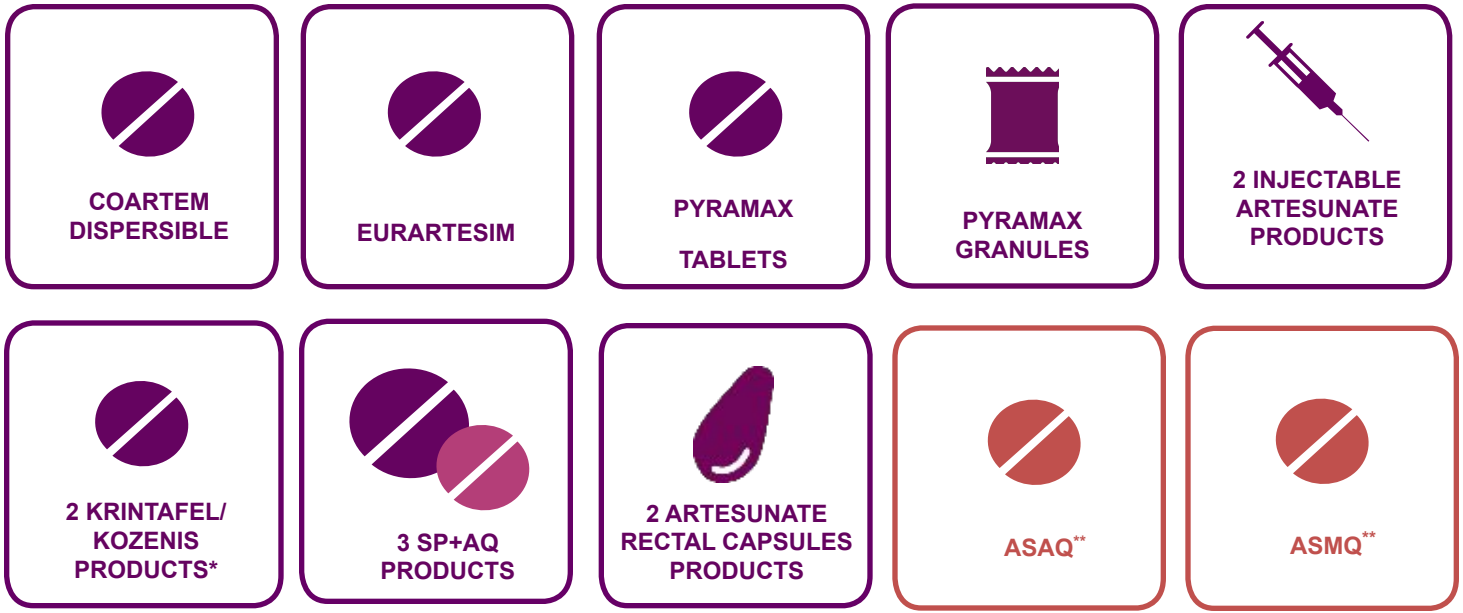
15 medicines launched
from 2009-2023



*Trademarks owned or licensed by GSK
**Transferred from DNDi-led partnership portfolio to MMV-led partnership portfolio 20th May 2015

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Key Achievements – Product Access

15 products launched

- **Covering key unmet medical needs**
  - medicines to treat uncomplicated malaria, severe malaria, and relapsing malaria
  - medicines that prevent malaria
  - medicines designed for vulnerable populations (children; pregnancy)
- **First pediatric ACT (AL-dispersible)**
- **First ACT (artemether-lumefantrine) recommended for use in 1st trimester of pregnancy**
- **First new therapy for relapsing malaria in over 60 years**
  - single dose tafenoquine
  - pediatric formulation approved in 2022
- **1.1 billion treatments distributed**
- **13.6 million deaths averted**
- **48 million children protected with MMV-supported SPAQ in 2022** ***(1 billion SPAQ in 2023)***

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Key Achievements – Product Access

- **MMV increasingly taking the lead on leading on product launch & implementation (tafenoquine)**
  - TRuST and ARCTIC studies
  - Effectiveness and cost effectiveness at different levels of healthcare system (Brazil CONITEC listing)
- **Sharing of best practices**
  - Severe Malaria Observatory – (a community of practice)
  - SMC Alliance – sharing best practices across implementing countries and partners
  - CoP PMC: gathering all pilot PMC implementers and countries for introduction of the new PMC
  - P. Vivax Information Hub – a one-stop shop for information on Plasmodium vivax malaria.
- **Social science**
- **Qualitative and quantitative market research (desired product attributes; barriers to uptake)**
- **Supply chain management**
  - Demand forecasting
  - Generic production
  - Manufacturing cost / price reduction
  - Local manufacturing : UCL (Kenya); EMZOR & SWIPHA (Nigeria)

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Key Achievements – Scientific Advances

- **First non-ACT combination for resistance management progressing to Phase III in 2023**
- **>9 million compounds screened; >20 novel targets identified**
- **Human and non-human platforms developed to expedite and de-risk clinical development**
  - MMV*sola* platform (machine learning) that predicts PK/PD and dose, including predictions for pregnant and lactating women
  - Non-clinical reproductive safety platforms
- **Tool for rapid assessment of drug combinations**
- **Advanced modeling and simulation capabilities established**

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Some sample projects

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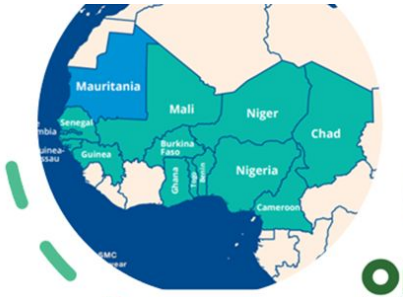
OPT-SMC Project

Strengthening the capacities of the NMPs implementing SMC:

- To define research priorities for **optimizing SMC effectiveness**
- To **conduct IR/OR projects** for improving SMC effectiveness:
- interpret and make use of malaria surveillance data
- target effectively (high risk or hard to reach populations, and periods of the year)
- monitor delivery, uptake and effectiveness

Promote inter-country collaboration, information sharing and expertise

Working with 13 SMC implementing countries



OPT-SMC
Optimizing Seasonal Malaria Chemoprevention in West and Central Africa

SMC Impact

- **Contributing to cover the remaining gaps for the current eligible target**

- **Contribute to the body of evidence about**
  - Efficacy and cost effectiveness of increasing SMC to 5-10 years old
  - Additional impact of adding one month of SMC coverage during the transmission season
- **Development of SPAQ line extension for 5-10 years old;** in anticipation of the eligibility of this target group to SMC

- **Contributing to increase knowledge about Pyramax® and introduction in malaria endemic countries** as an alternative therapeutic solution
- **5 countries: Nigeria, The Gambia, Niger, Mali, Guinea**

PROGRAMME NATIONAL DE LUTTE CONTRE LE PALUDISME PNLP

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MINISTRY OF HEALTH, THE GAMBIA

PROGRAMME NATIONAL DE LUTTE CONTRE LE PALUDISME

NATIONAL MALARIA ELIMINATION PROGRAMME
Federal Ministry of Health, Abuja

Global Disease Eradication Fund | KOREA

KOICA Korea International Cooperation Agency

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

CRS CATHOLIC RELIEF SERVICES

malaria consortium disease control, better health

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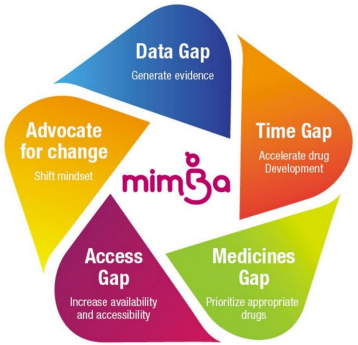
MiMBa strategy aims to address the gaps to better serve the needs of women



MMV will accelerate discovery, development and delivery of appropriate antimalarial options for women who are/could become pregnant and for women who are breastfeeding

1	2	3
Broaden access to currently used antimalarial medicines	**Invest in appropriate new molecules for the future**	**Accelerate population appropriate compounds in the current pipeline**
…by collecting evidence on the safety and efficacy of existing antimalarials in pregnancy and lactation and ensuring quality-assured supply of medicines	……by exploring new modalities and enriching the future pipeline with appropriate New Chemical Entities for medicines that serve all malaria populations from the start	…by intentionally addressing the needs of women who are - or could become – pregnant and breastfeeding women

4

Advocate for greater inclusion of women who are – or could become – pregnant and lactating across antimalarial R&D and access

…by leveraging MMV's position at the interface of academic, pharmaceutical industry, regulatory, and global health communities

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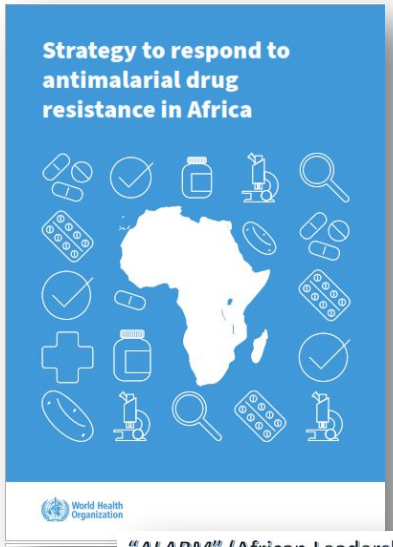
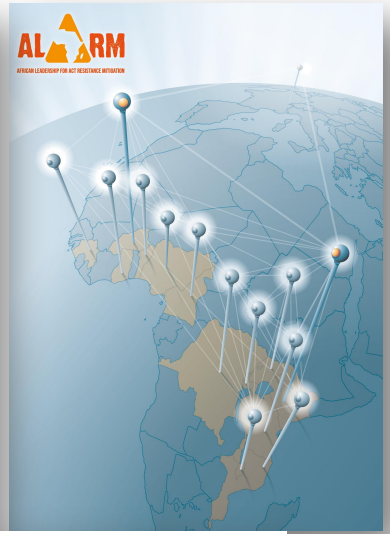
MMV, facilitator of the ALARM partnership / consortium



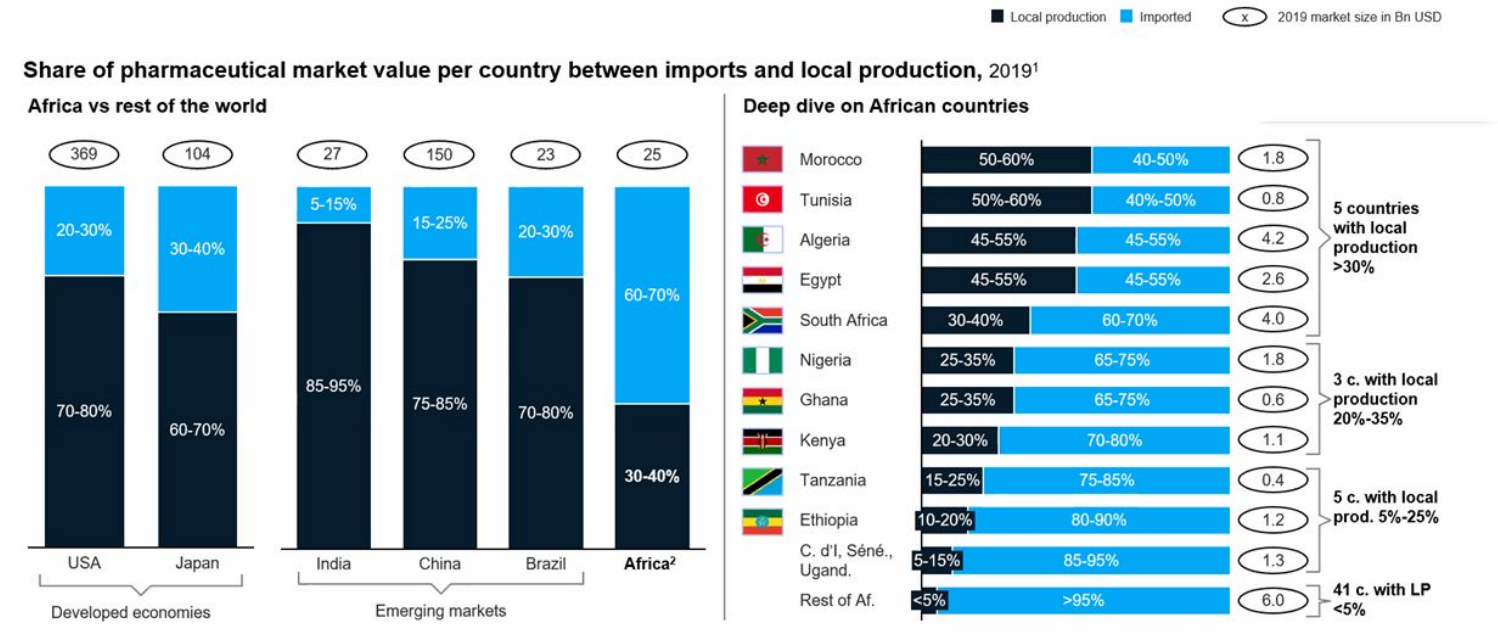


- The ALARM Partnership has been instituted with the aim of piloting / expanding then deploying at scale, MFT in 13 African countries
- It draws on the expertise and experience of Kenya and Burkina Faso, pioneer pilot countries
- Members include Uganda, Kenya, Rwanda, Mozambique, Tanzania, DRC, Malawi, Burkina Faso, Cameroon, Nigeria, Guinea, Ghana and Benin

ALARM
AFRICAN LEADERSHIP FOR ACT RESISTANCE MITIGATION

Supply security Situational analysis – Africa -

- **>95% of world's malaria cases and deaths occur in sub-Sahara Africa** and yet the continent imports **>90% of the drug needed**
- The continent overall has ~375 drug makers, to serve a population of around 1.3 bill people[1]
- African population set to triple by 2050.[2]
- **Top three African markets** (Kenya, South Africa, Nigeria) import significant pharma products



Notes: 1. https://www.mckinsey.com/industries/public-and-social-sector/our-insights/should-sub-saharan-africa-make-its-own-drugs
2. https://www.weforum.org/agenda/2020/01/the-children-s-continent/

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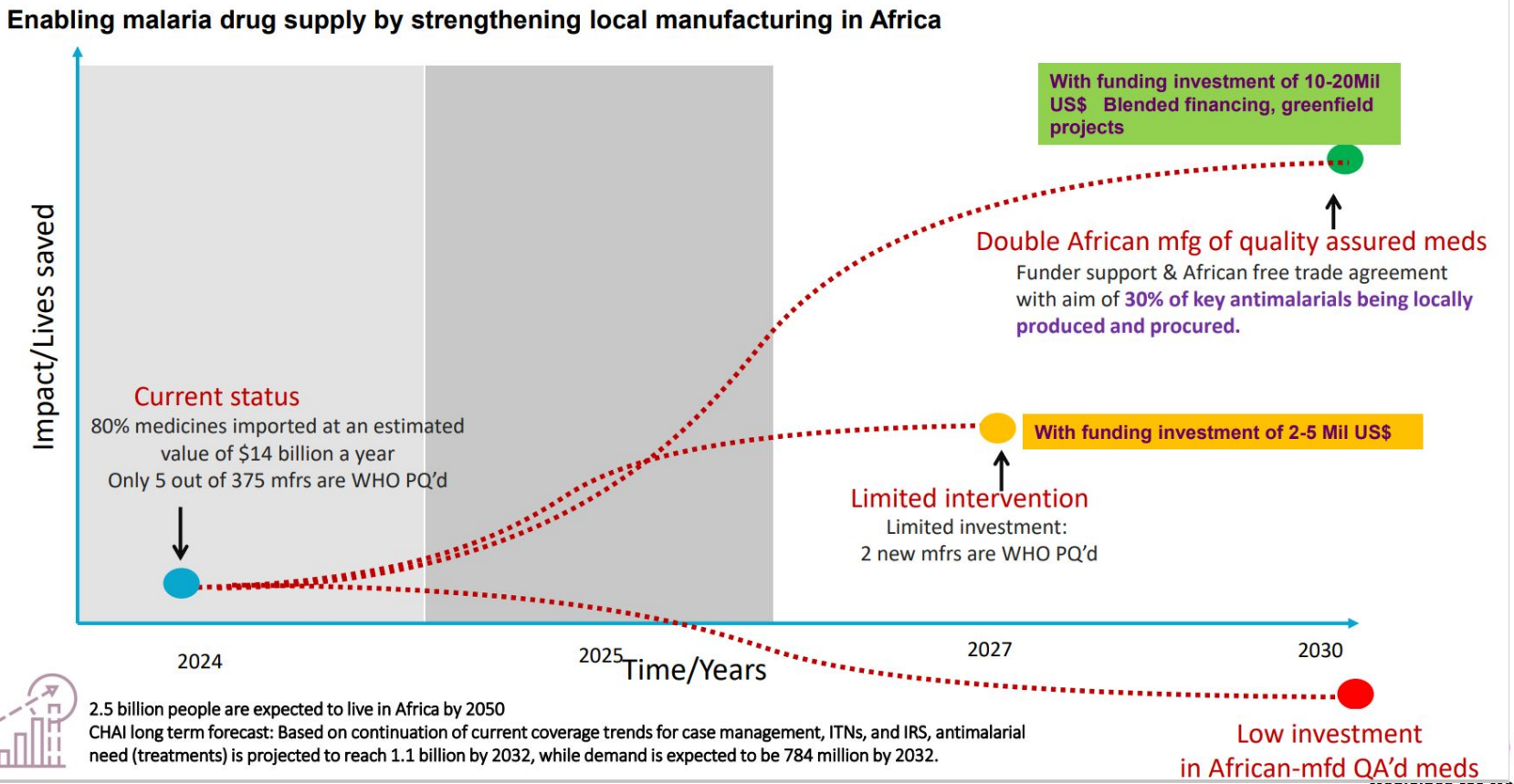
Supply security for essential medicines in Africa



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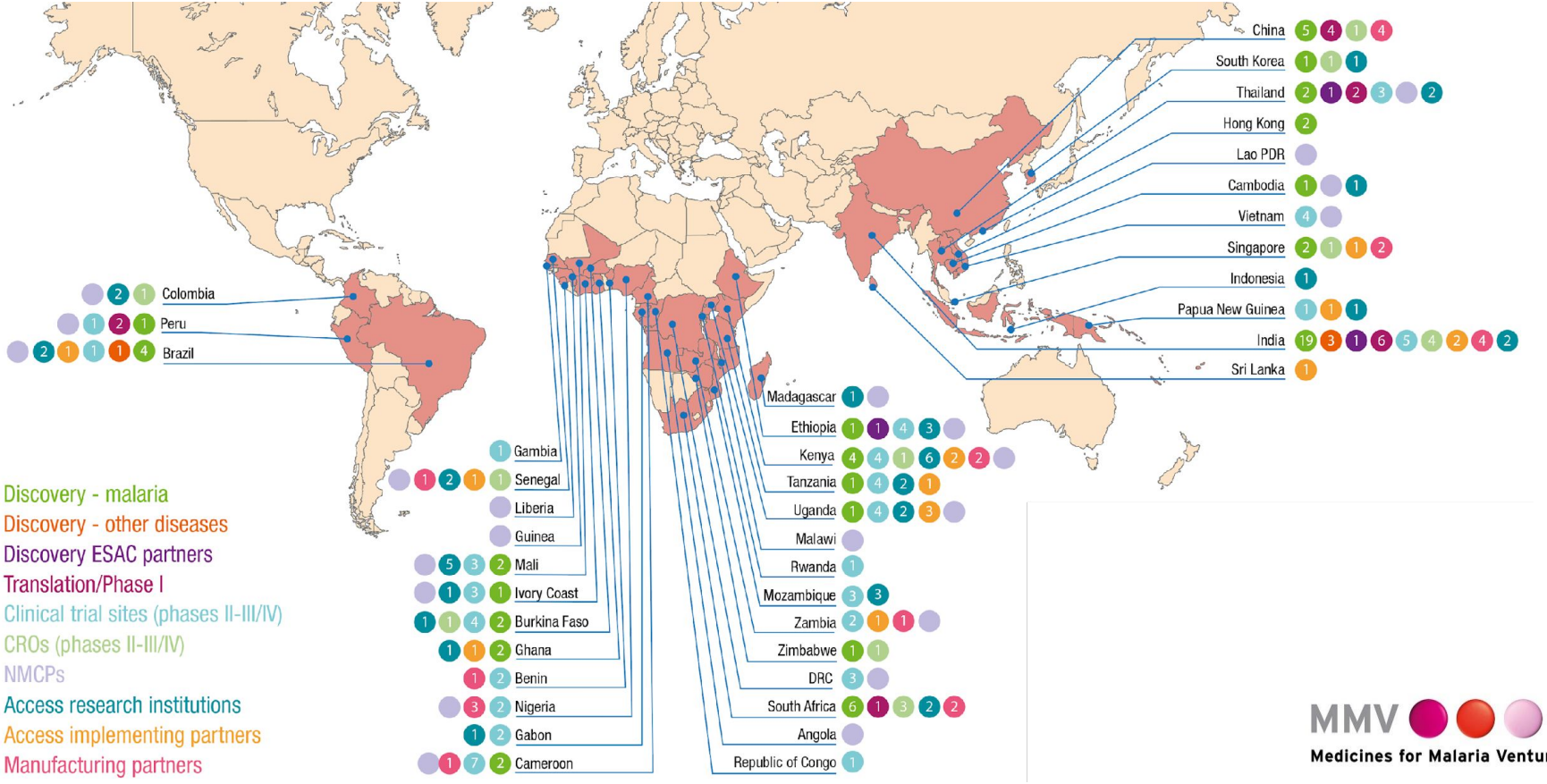
400+ strong partnership network – spanning more than 50 countries



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MMV | Guiding Principles of Equitable Partnership

Reduce death, suffering and hardship from malaria, by delivering…

Sustainable R&D and product access

that addresses key **unmet patient needs**

with **urgency** and clear **prioritization**

…in a manner that fosters **equity**, **inclusion**, **empowerment** & **shared leadership** with partners

THANK you to you and our committed funders

Back up slides

Key Projects, Uncomplicated Malaria

- **Anti-Malarial Drug Resistance (AMDR)**
  - Supporting deployment of Multiple First-Line Treatments (MFT)
  - Triple ACT combinations: approval and launch
  - Ganaplacide-Lumifantrine SDF (Gan-Lum) launch
  - ACT +sLDPQ
- **Coartem Baby (AL<5kg) launch**

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Multiple First-Line Treatment (MFT)

Background

- Markers of ACT resistance together with delayed parasite clearance have been detected in a growing number of African countries (Rwanda, Uganda, Eritrea, Tanzania, Burkina Faso)
- Proactive and pre-emptive intervention is needed to mitigate the emergence and spread of partial ACT resistance and to protect partner drugs (especially lumefantrine)
- WHO's strategy to respond to ACT resistance in Africa recommends ACT diversification as part of the toolkit to mitigate emergence and spread of resistance
- One way to achieve this is by deployment of MFT, which has been postulated in modelling studies to be highly effective in achieving this
- Pilot studies to demonstrate feasibility have been completed in Kenya and Burkina Faso

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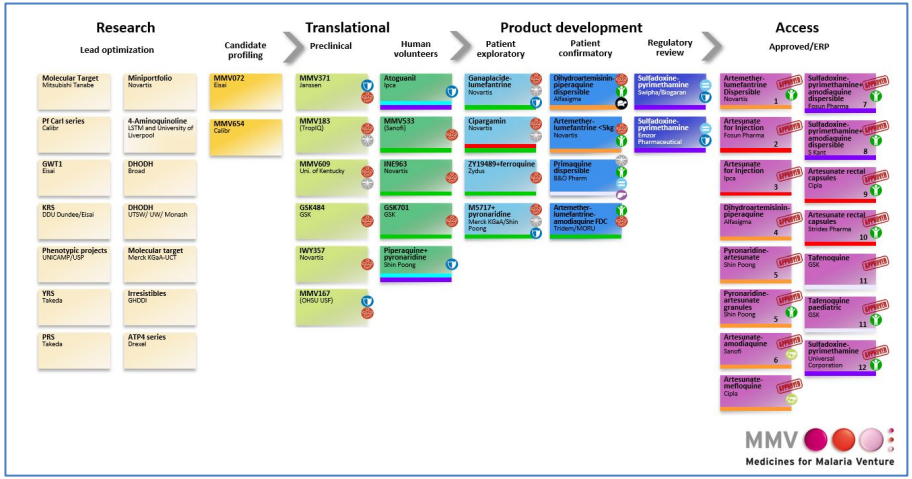
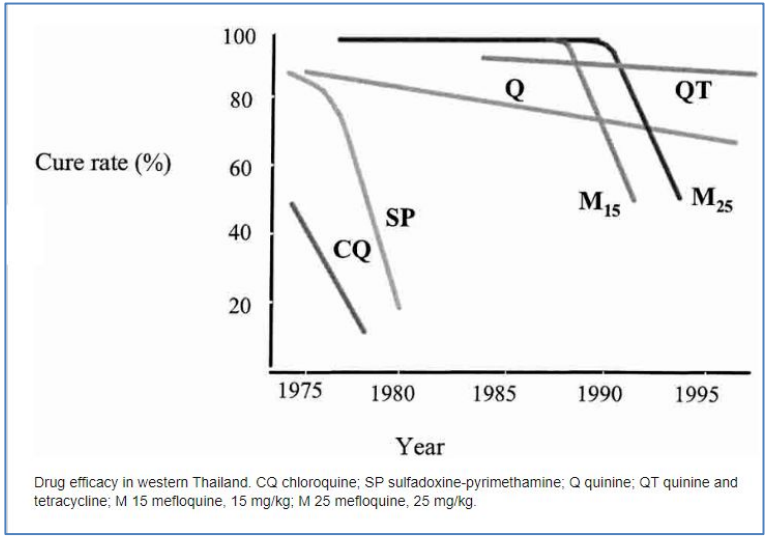
MMV's pipeline – our *raison d'être* – is a global "insurance policy" to defend against the devastating threat of drug resistance

The largest end-to-end pipeline for defeating malaria in the history of modern drug development



A grim reminder of how earlier medicines have been swept away by resistance [1]



Drug efficacy in western Thailand. CQ chloroquine; SP sulfadoxine-pyrimethamine; Q quinine; QT quinine and tetracycline; M 15 mefloquine, 15 mg/kg; M 25 mefloquine, 25 mg/kg.

[1] S. Yeung et al (2004). Antimalarial drug resistance, artemisinin-based combination therapy, and the contribution of modeling to elucidating policy choices. The American journal of tropical medicine and hygiene. 71. 179-86. 10.4269/ajtmh.2004.71.179.

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Expected impact

By the end of 2027, at least 10 countries will have implemented MFT as a resistance mitigation strategy on a partial or national basis

ALARM will help diversify ACT use through the following activities: 1) supporting new countries in deploying MFT strategies, based on learnings from the MMV-supported pilots in Kenya and Burkina Faso; 2) bolstering resistance monitoring in all ALARM countries; 3) supporting education, training, logistics management and stakeholder engagement; and 4) bundling and analyzing the combination of rotational, stratification and geographical approaches across all ALARM partners.

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Triple ACTs: development and introduction

Background

- Against a background of ACT partial resistance in South-East Asia and now sub-Saharan Africa, dual ACT combinations are under increasing pressure
- Adding a third drug has been shown in studies to date to be highly effective, even against resistant strains
- Triple ACTs (TACTs) have the advantage of using existing drugs which are already familiar to healthcare providers and patients
- Funding has just been granted by GHIT to Fosun Pharma, MORU, MMV and Marubeni to develop an affordable fixed-dose combination of AL+AQ including a child-friendly formulation – a Phase III study to support registration will commence in 2024

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Ganaplacide-Lumefantrine (Gan-Lum) development and launch

Background

- Despite interventions such as MFT and TACT, at some point ACTs will begin to fail as a class of antimalarials - in the absence of effective alternatives, a resurgence in malaria cases and deaths will ensue creating a potential public health catastrophe
- It is therefore crucial that alternative treatments are developed, approved and included in treatment guidelines before such a situation develops
- Ganaplacide-Lumefantrine (Gan-Lum), being jointly developed by Novartis and MMV, is expected to be the first modern non-artemisinin-based combination treatment (NACT) to be approved and launched
- First approval expected 2027

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Coartem Baby (AL<5kg) launch

Background

- No ACT is currently approved for very young infants (<5kg)
- Although AL dispersible is often used for malaria in this age group, the current ratio of artemether: lumefantrine raises the risk of overdosing and causing potential neurotoxicity
- Quantifying the potential number of patients is difficult as current surveys (eg WMR) do not differentiate infants and older children
- Novartis and MMV are co-developing a formulation with a different A:L ratio specifically intended to address this unmet need
- Launch currently expected in 2025

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