

# Medicines for malaria: setbacks and successes on the road to eradication



**Mr Per Wold-Olsen**  
Chairman of the  
Board



**Dr David Reddy**  
CEO

On right on this page  
**Inness Kalunga**  
and her mother

**W**e are at a critical juncture in the fight against malaria. After almost two decades of success in reversing the incidence of the disease, the World Health Organization (WHO) reports that progress is stalling. In 2016, around 216 million people fell ill from malaria, 445,000 of whom lost their lives. In comparison with 2015, that's almost 5 million more people who became ill.

Turning this setback around is the objective of entire malaria community. MMV's focus is to strengthen successful efforts to facilitate access to quality antimalarials while developing new medicines to meet unmet needs and counter the challenges ahead. This work includes the development of a new road map of the medicines needed to defeat malaria and the tools to realize it.

MMV's efforts to date have delivered seven new medicines, which have saved the lives of more than 1.5 million people. Let us start with just one of them. At the end of 2017, we learned of 16-month-old Inness's story of survival. MMV works with a consortium of partners led by the NGO Transaid, in Zambia, to provide access to severe malaria medicines. When Inness fell ill, her mother brought her to a community health volunteer who had been trained to recognize severe malaria danger signs. The volunteer quickly administered a rectal artesunate suppository (RAS), provided by the project for pre-referral management of severe malaria. She was then referred to a clinic and treated with injectable artesunate (Inj AS), followed by *Coartem® Dispersible* when she was able to hold down oral medicine. The combination of these medicines helped save her life.

For MMV, Inness's story has huge significance and, in particular, is a testament to the power of our partnerships to save lives. All the projects that enabled the medicines to reach Inness at the right time were conducted in partnership, harnessing the strength of numerous individuals and organizations. Our work with Cipla to get

RAS reviewed by The Global Fund in 2016 paved the way for the first-ever batch of around 500,000 quality-assured suppositories to be delivered to the field. In 2010, with Guilin, we obtained prequalification of Inj AS: to date, 100 million vials have been delivered. In 2009, MMV launched *Coartem Dispersible* with partner Novartis: to date, 350 million treatments have been delivered. We are moving deeper and deeper into the last mile with the medicines required to save the lives of people most vulnerable to malaria.

Our focus is not only on treating these at-risk populations, but also protecting them. MMV is working with partners to use medicines to protect pregnant women and young children from getting malaria in the first place. For example, seasonal malaria chemoprevention (SMC) administered to children under 5 in Africa's Sahel region during the rainy season has dramatically reduced disease incidence. As a member of the Unitaid-funded ACCESS-SMC consortium, MMV is supporting the scale-up of the intervention in 12 countries. In 2017, more than 68 million courses of sulfadoxine-pyrimethamine + amodiaquine (SPAQ) had been delivered to the Sahel, enough to protect 17 million children from malaria.

These consortium-based approaches to scale-up access draw on the strengths of different organizations to understand the issues, develop data-driven solutions, pilot these solutions and then run with them. The success of this approach has led us to explore how it could be applied to other projects in the pipeline. One such exciting project is the potential roll-out of tafenoquine. At the end of 2017, MMV partner GlaxoSmithKline (GSK) submitted tafenoquine to the US Food and Drug Administration (FDA) and the Australian Therapeutic Goods Administration (TGA) for regulatory assessment. This tremendous achievement was the result of decades





“MMV’s focus is to strengthen successful efforts to facilitate access to quality antimalarials while developing new medicines to meet unmet needs and counter the challenges ahead.”

of work by generations of scientists. We congratulate all those involved and eagerly await the verdict from the regulatory authorities, which could make tafenoquine the first single-dose medicine to cure relapsing malaria and the first for this indication since 1952.

With one eye on the shifting malaria landscape and another on the development of future antimalarials, MMV has taken a leadership role in coordinating the thinking of the antimalarial drug development community. We have helped define standards, target candidate profiles and target product profiles, contributing to a road map for product development: the update of the Malaria Eradication Research Agenda (malERA Refresh).<sup>1</sup>

Part of this planning also includes keeping a view on antimalarial drug resistance, particularly in the Greater Mekong Sub-region. As attempts are made to contain artemisinin-resistant malaria in Cambodia, we continue to see partner drugs succumbing to resistance in other parts of the world – another setback causing concern in our global efforts to defeat malaria. Thus, the deployment of newer artemisinin-based combination therapies, such as Shin Poong’s co-developed Pyramax® (pyronaridine-artesunate), remains critical.

We also need to be ready with new drugs should resistance gain a greater hold. We have two new combinations in phase II trials in adults and children: artefenomel plus ferroquine with Sanofi, and KAF156 in combination with a new formulation of lumefantrine with Novartis. In addition, we have three other new

medicines being tested in patients, as well as promising new compounds in human volunteer infection studies. Moreover, we are ready to accelerate development of these medicines through trials in patients with drug-resistant malaria should more cases occur and/or resistance emerge in Africa.

Aware of all these avenues that require our attention, we began implementation of a new business plan that charts MMV’s course for 2017–2021. Drug development for malaria will require a strategic commitment not just for the next 4 years but for the next decade and beyond. At MMV, we are committed to maintaining the focus that has already helped us successfully deploy our seven co-developed medicines.

We would particularly like to express our gratitude to the many organizations and individuals who make the work of MMV possible. In 2017, we were delighted that there was global recognition for the work of several of our partners, including Drs Elizabeth Winzeler and John Burke, and Professors Awa Marie Coll-Seck, James McCarthy and Peter Kremsner. We are honoured to be working with such partners, and with many others across the globe, as dedicated as MMV to the defeat of malaria. On behalf of patients like Inness, saved by our co-developed medicines, we thank you for your contribution and sustained support of our work. Together with you, we will do everything in our power to help turn recent setbacks to success on the road to malaria eradication. ●

<sup>1</sup> malERA Refresh Consultative Panel on Insecticide and Drug Resistance. “An updated research agenda for insecticide and drug resistance in malaria elimination and eradication.” *PLoS Med.* 30;14(11):e1002450 (2017).

**1.5 million lives saved by MMV co-developed medicines**



**1 donor dollar**

creates an estimated

**3.5 dollars**

of investment impact thanks to direct and in-kind support



**CANTAM** study

to investigate the real-life safety and tolerability of Pyramax<sup>®</sup> initiated in Central Africa and Ivory Coast, with 1,102 patients recruited by end of 2017



**Key achievements**

**Pyramax<sup>®</sup> and Pyramax<sup>®</sup> granules**

(pyronaridine-artesunate), the only ACT approved by a stringent regulatory authority for the treatment of both *P. falciparum* and *P. vivax* malaria, added to the WHO's Model List of Essential Medicines and Model List of Essential Medicines for Children



**160 active partners**

working to help defeat malaria – part of an overall network of 400 partners in 55 countries



**7 new drug candidates**

investigated, to date, against uncomplicated malaria in volunteer infection studies at QIMR Berghofer, Australia

## KAF156/ lumefantrine,

a promising new combination therapy in development with Novartis, entered phase IIb patient trials in nine countries in Africa and Asia



## Over 350 million

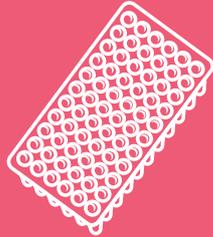
treatments of child-friendly Coartem® *Dispersible* (artemether-lumefantrine) distributed to more than 50 countries since 2009



## 10,000

compounds screened in *P. vivax* liver-stage assays and one potential anti-relapse series under evaluation

## Over 230 Pathogen Boxes



shipped free of charge to scientists around the world to boost drug discovery for neglected diseases

## Single-dose tafenoquine

for relapse prevention of *P. vivax* malaria submitted to US FDA and Australian TGA for regulatory approval



## 14

compounds now in preclinical and clinical development,

**9** with entirely novel mechanisms of action compared with compounds used in ACTs

## 68 million

courses of seasonal malaria chemoprevention delivered to countries in the Sahel in 2017, enough to protect 17 million children



## Two rectal artesunate

suppository products for pre-referral management of severe malaria (from Cipla and Strides Shasun) approved for procurement by international donors leading to the first order of ~500,000 suppositories being placed



## 100 million

vials of injectable artesunate for severe malaria delivered since 2010, saving the lives of an estimated 650,000 additional vulnerable children compared with quinine treatment



# Strategic focus

**MMV's** mission is to develop and deliver the medicines needed to support malaria-endemic countries in their quest to control and eventually eradicate malaria. In line with global frameworks from the World Health Organization and the United Nations, MMV is focused on three strategic areas of activity:

1. Facilitating equitable access to existing quality antimalarials to maximize health impact (pp. 14–23).
2. Developing easy-to-administer, next-generation medicines to improve case management, overcome drug resistance and protect vulnerable populations, such as children and pregnant women (pp. 24–35).
3. Bringing forward new tools to counter resistance, achieve elimination and reduce transmission to ultimately help eradicate malaria (pp. 36–41).

To facilitate access (1), MMV works with partners and key global and country-level stakeholders to gather data on the tolerability of new medicines, specifically in vulnerable populations and in “real-world” settings. This evidence supports their registration and adoption into relevant policies and guidelines. These efforts also include securing sustainable supply, by diversifying the manufacturing base of existing medicines, and scaling up use.

In its research and development (R&D) efforts (2 & 3), MMV has developed an integrated model that addresses the need for an accelerated, efficient and appropriate approach. Given the 12-to-15-year timeline from discovery to launch of a new medicine, it is important to invest in only those promising compounds that can potentially satisfy unmet medical needs. This is described by two target product profiles (TPPs).

**TPP 1** defines the characteristics of drugs for treatment, prevention and transmission-blocking, also known as a single-encounter radical cure and prophylaxis (SERCaP).<sup>1</sup> Drugs that meet TPP 1 would be effective against resistant strains of malaria, would cure clinical malaria, stop transmission and prevent relapse. They would also simplify case management and thus improve compliance.

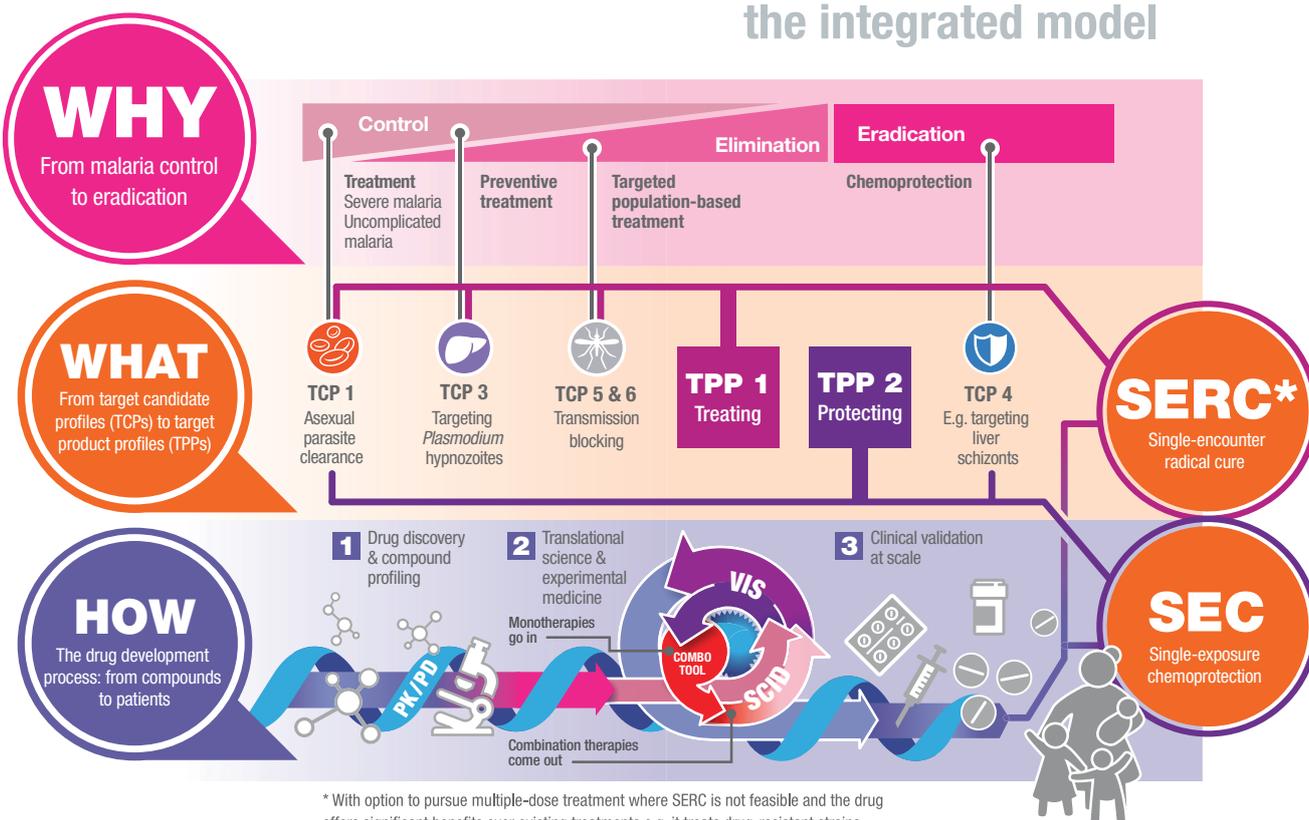
**TPP 2** describes drugs that can protect non-infected people entering an area of high malaria endemicity, also known as single-exposure chemoprotection (SEC). Compounds that meet this profile would need to provide a long duration of protection and have distinct mechanisms of action compared with those used by TPP 1 drugs.

The development of a new treatment (SERCaP) or new protection (SEC) requires the combination of at least two active candidate drugs. Thus, MMV has defined five target candidate profiles (TCPs) corresponding to different clinical attributes for compounds that will contribute to the TPPs (see figure below) and has built a strong portfolio of molecules with diverse or competing mechanisms to combat resistance.<sup>2,3</sup>

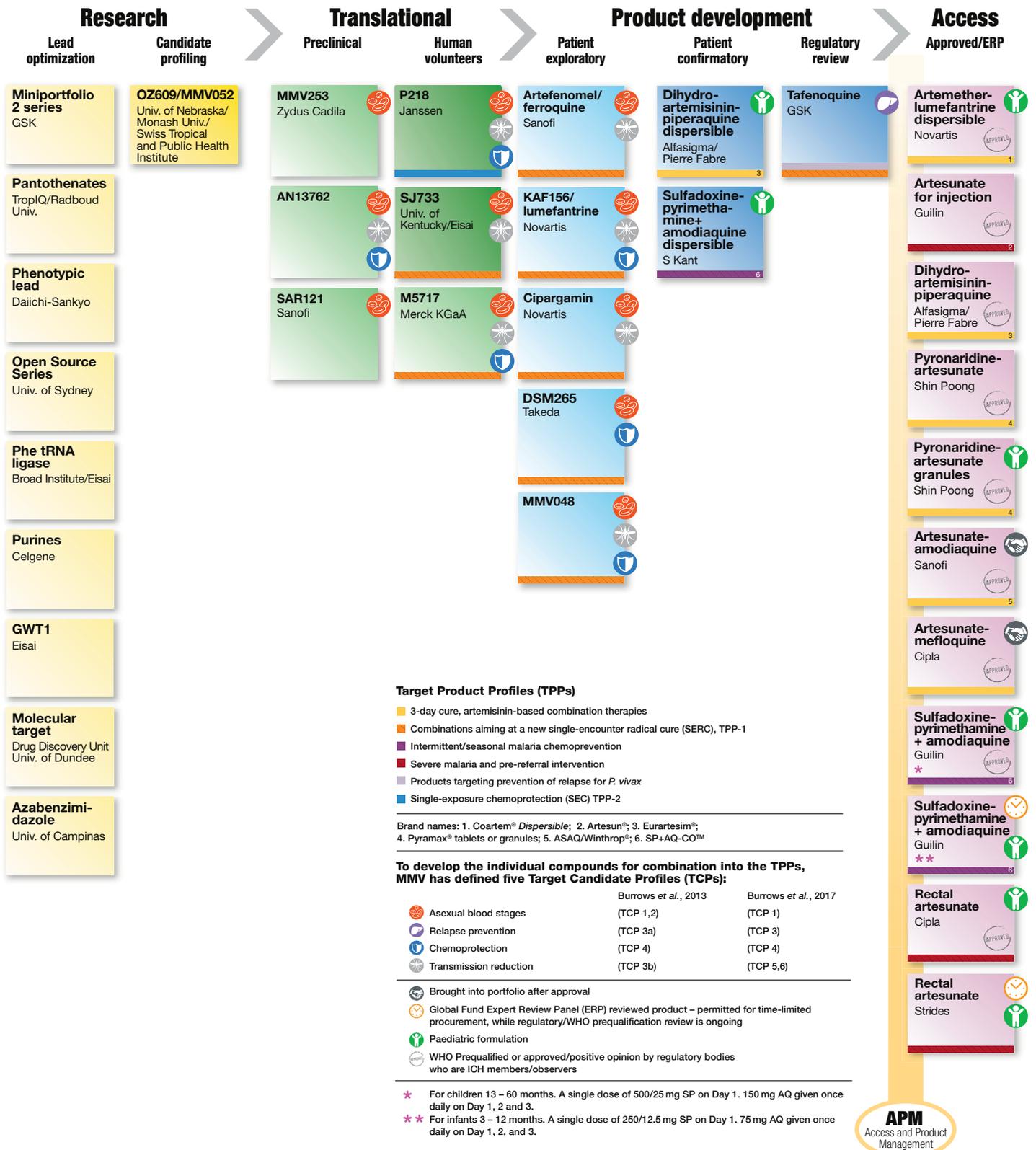
MMV is working with around 160 active partners around the world on R&D projects. Innovative approaches are being used to enhance speed and efficiency, including volunteer infection studies and the Combo tool (pp. 38–39). Together with our partners, we will continue to rethink and optimize the development of new antimalarials to help control and ultimately eradicate malaria. ●

- 1 As proposed 7 years ago by the malERA Consultative Group on Drugs. “A Research Agenda for Malaria Eradication: Drugs”. *PLoS Med.* 8(1): e1000402 (2011).
- 2 Burrows JN *et al.* “Designing the next generation of medicines for malaria control and eradication”. *Malar J* 12:187 (2013).
- 3 Burrows JN *et al.* “New developments in anti-malarial target candidate and product profiles”. *Malar J* 16:26 (2017).

## Rethinking drug development: the integrated model



# MMV-supported projects



**GOVERNANCE**

**ESAC** Expert Scientific Advisory Committee

**GSB**  
Global Safety Board

**APAC** Authorization for Phase III/Advancement Committee

**APMAC**  
Access and Product Management Advisory Committee

**MMV Board** of Directors/Executive Committee/Financial Audit Committee