Breaking the cycle

Dr David Reddy, CEO of Medicines for Malaria Venture

“We should all be concerned about the future because we have to spend the rest of our lives there.”

Charles F Kettering, American engineer

Malaria and poverty are inextricably linked. The disease hinders economic development in many regions, trapping others in a seemingly endless cycle of poverty. We witness the link whenever we travel in endemic countries. In a mountain village in Cambodia, a soya bean farmer explained he had suffered from malaria five times in 2014 and was sick yet again. As the main breadwinner, when he has malaria, he can’t work and struggles to put food on the table for his wife and children. The story was similar on the other side of the world, on the banks of the Amazon in Peru. A mother explained she could not earn her daily living selling chicken broth when her young children have malaria; she has to stay at home and care for them.

Malaria affects not just individuals and families, but communities and economies. People living an already precarious existence are struggling against this debilitating disease, not just in Cambodia and Peru, but in 97 countries – half of all countries in the world.

Each of us committed to ending malaria is fuelled by a vision of a better world, one where no child dies before his or her fifth birthday because of a mosquito bite; where no parents lose the ability to provide for their children because they are too ill to work; and where development is not hindered by disease.

MMV, a leading product development partnership (PDP) in the field of antimalarial drug research, is committed to playing its part in the fight against malaria. Thanks to our committed donors and alongside our network of over 375 pharmaceutical, academic and endemic-country partners in 50 countries we are working to discover, develop and deliver new and better medicines to help break the cycle of malaria and poverty. The good news is that we are making extraordinary progress.

Managing the largest portfolio of antimalarial R&D projects ever assembled, of over 65 projects, we have nine new drugs in clinical development addressing unmet medical needs in malaria, including medicines for children, pregnant women and relapsing malaria, and drugs that could support the elimination and eradication of malaria. Each holds the promise of a new medicine that could improve the quality of life and future of those most affected.

Working with our partners we have taken giant strides towards a single-exposure cure for both uncomplicated and relapsing malaria. OZ439, a molecule MMV has progressed discovery for the treatment of uncomplicated malaria is currently in a phase IIb trial with Sanofi, while tafenoquine, for the liver-stage of relapsing malaria, is in phase III trials with GSK and progressing ever closer to regulatory filing.

Today, we are also reaping the benefits of extensive screening efforts, with many novel antimalarial compounds progressing through the portfolio. This allows us to select...
only those that meet stringent target profiles. In addition, together with our partners, we have established innovative enabling technologies such as the Controlled Human Malaria Infection Model. This model provides us with a granularity of data previously inaccessible, allowing us to quickly understand whether a compound will work in humans and so make decisions regarding which molecules to take forward quickly and cost-effectively.

With increased understanding of the malaria parasite’s biology, we have been able to identify new junctures at which to break the parasite’s lifecycle (Figure 1. The lifecycle of the malaria parasite). In addition to conventional blood-stage assays or tests, new assays recapitulating the biology at these points leading to infection and transmission have been developed and are being used to screen increasing numbers of compounds for new attributes. In this way, we are advancing the science of malaria elimination and eradication. Piecing together emerging data from these assays could help us find a molecule active against all lifecycle stages.

Meanwhile, the five medicines MMV and partners have developed to date are already treating people across the globe from Cambodia to Nigeria to Peru, and saving lives: Coartem® Dispersible (artemether-lumefantrine), a child-friendly formulation developed with Novartis; Guilin’s artesunate injection Artesun® for the treatment of severe malaria (see box below, Saving Precious); Eurartesim® (dihydroartemisinin-piperaquine) with Sigma-Tau; Pyramax®, (pyronaridine-artesunate) co-developed with Shin Poong; and Guilin’s sulphadoxine-pyrimethamine + artesunate amodiaquine (SP+AQ) for seasonal malaria chemoprevention, which received WHO prequalification with MMV’s support. In total, more than 255 million treatments have been delivered since 2009 – the vast majority to children.

The availability of these life-saving treatments, alongside vector control measures, has undoubtedly assisted the global community to achieve Millennium Development Goal 6.C, to halt and begin to reverse the incidence of malaria by 2015. Owing to the increased and effective delivery and use of malaria interventions since 2000, the incidence of the disease has fallen by 30% globally with a 47% decline in global mortality. Step by step, we are getting closer to breaking the cycle of malaria and poverty.

This achievement deserves acclaim. Yet, we must remember that the past is a springboard, not a hammock. We have no time to rest on...
Getting medicines to Precious

“On Sunday 3rd of May, 2015, Precious started vomiting and had diarrhoea. He had a high temperature and within a short time became very weak. I had to rush him to the hospital. I was so afraid that I left him in God’s and the doctors’ hands,” said Mrs Bosede Adebayo, whose son, 11-month-old Precious, was admitted to the General Hospital Okeho, Ibadan, Oyo State, Nigeria, on confirmation of severe malaria.

The first dose of injectable artesunate (Artesun® 60 mg, manufactured by Guilin Pharmaceutical) was immediately administered and after 3 days Precious was well enough to be discharged.

“The response to treatment was very encouraging and amazing,” said Dr Olusola Ayeleke the treating physician. “Precious responded quickly. Following the first dose there was significant improvement and by the time the second and third doses had been administered, he began eating well, taking oral medications and was good to go.”

Dr Ayeleke attributed the positive outcome to the use of injectable artesunate provided to the hospital through the Improving Severe Malaria Outcomes (ISMO) project, supported by UNITAID, MMV and the Malaria Consortium in collaboration with the Oyo State Government.

“Before the MMV-led ISMO project, treating severe malaria was really challenging because we were using intravenous quinine,” said Dr Ayeleke. “There was increased mortality due to malaria. Intravenous quinine is associated with side effects and must be administered more frequently. Injectable artesunate makes the management of severe malaria easier and more fruitful.”

“After the ISMO training, health workers can use injectable artesunate to treat severe malaria patients,” said Dr Campbell Ibijoke Oluyomi, the Consultant Paediatrician in charge of Oni Memorial Children’s Hospital. “It is very fast acting and so patients recover from the condition faster and are no longer dying from severe malaria.”

our laurels while people continue to die of malaria and global development continues to be hindered. Moreover, as we progress towards elimination and eradication, the demands placed on medicines will change; for example, immunity will start to decline and the need for new types of chemopreventive medicines will grow.

As the MDGs transition to the Sustainable Development Goals (SDGs) in 2016, MMV’s priorities too are evolving. We will focus less on developing artemisinin combination therapies and more on next-generation antimalarials. These future medicines will break the cycle of relapsing malaria, overcome the challenges of compliance and drug resistance, and protect vulnerable populations. In doing so, they will support the realization of the proposed SDG 3 – to ensure the sustainability of healthy lives and wellbeing for all, at all ages.

And while the goals have yet to be finalized, we, the global health community must advocate for health to feature high on the agenda. Health is after all, the foundation of all sustainable development.

Our goal to break the cycle of malaria and poverty by developing and delivering new medicines is certainly ambitious and MMV is but a small organization of 55 individuals. Yet, thanks to our ever-growing network of partners and donors, who are as committed as MMV to the fight against malaria and as concerned about the future of global health, we are stronger, more effective and more resolute. Together we are determined to build a better, healthier future for our children; a future where malaria is a disease of the past.
From molecule to medicine - MMV manages the largest portfolio of antimalarial drug projects ever assembled. Of the 65 projects, nine are in clinical development and five have been launched and are contributing to saving lives today.
Malaria kills a child every minute

New medicines can save their lives

Medicines for Malaria Venture and partners develop:

→ better medicines for uncomplicated malaria

→ medicines for children and pregnant women

→ new medicines to help eradicate malaria

We are grateful to our donors and partners whose support and expertise make this vital work possible.

www.mmv.org
250 million treatments of child-friendly Coartem® Dispersible
(artemether-lumefantrine, co-developed with Novartis) distributed to 50 countries since launch in 2009.

36 million vials of Artesun®
(Guilin Pharmaceutical’s MMV-supported injectable artesunate) for severe malaria delivered since 2010 – saving approximately 200,000-240,000 additional lives compared to treatment with quinine.

Defeating Malaria Together

4 molecules in clinical development as potential single-encounter cures:
OZ439 (Sanofi), KAE609 (Novartis), DSM265 (Takeda) and MMV048 (University of Cape Town).

1st single dose cure for relapsing malaria (tafenoquine) in large-scale phase III trials in partnership with GSK.

5th medicine brought forward:
(Guilin Pharmaceutical’s MMV-supported sulphadoxine-pyrimethamine-artesunate amodiaquine; SP+AQ) for seasonal malaria chemoprevention, receives WHO prequalification.

9 new medicines in clinical development targeting malaria eradication by aiming to stop relapse, block transmission, cure drug-resistant strains and serve the needs of as many patients as possible.

USD 1 = USD 3.50

Direct and in-kind support from our pharma partners more than triples the value of each donor dollar for R&D.

5th new medicine brought forward: (Guilin Pharmaceutical’s MMV-supported sulphadoxine-pyrimethamine-artesunate amodiaquine; SP+AQ) for seasonal malaria chemoprevention, receives WHO prequalification.