Towards a malaria-free world

Medicines for Malaria Venture (MMV) and partners discover, develop and deliver new, effective and affordable antimalarials to give populations at risk a better chance to achieve good health and wellbeing.

The success of the malaria community in reversing the incidence of malaria from 2000 to 2015 has been a major public health victory. According to the WHO, however, progress is stalling. Around 219 million people fell ill from malaria in 2017, 435,000 of whom lost their lives. In comparison with 2015, that’s almost 8 million more people who became ill.

Reversing this setback and accelerating progress towards malaria elimination is the objective of the entire malaria community. MMV’s focus is to work with partners to provide access to quality antimalarials while developing new medicines that will meet unmet needs and address future challenges, such as drug resistance.

Within the broader context of rising antimicrobial resistance, multidrug resistant malaria in the Greater Mekong Subregion is resulting in high levels of treatment failure with some artemisinin-based combination therapies.\textsuperscript{1,2} Should such resistance emerge in Africa where the majority of malaria deaths occur, the consequences could be devastating. MMV’s mission to bring forward next-generation antimalarials and ensure their availability and accessibility is aimed at both addressing this perpetual threat of resistance and reducing the malaria burden.

MMV’s focus is not only malaria treatment, but also prevention. We are working with partners to use medicines to protect pregnant women and young children from malaria in the first place. For example, seasonal malaria chemoprevention (SMC) administered to children under five in Africa’s Sahel region during the rainy season has dramatically increased access to chemoprotection for vulnerable children. In 2018, 81 million courses of SMC were delivered to countries in the Sahel, sufficient to protect over 20 million children. MMV is supporting the scale-up of this intervention in 12 countries.

MMV is committed to working in partnership to ensure no one is left without effective treatment. Since its foundation in 1999, MMV and its public and private partners have brought forward 10 new antimalarials and 2 more have been transferred to MMV to support improved access. To date, an estimated 1.9 million lives have been saved by the medicines we have supported.

Our antimalarial portfolio (see p. 3) is the largest ever assembled and comprises 11 compounds in clinical development targeting unmet medical needs, including medicines for children, pregnant women and people suffering from drug-resistant malaria. These antimalarials hold the promise of contributing to the global drive towards malaria eradication as well as Sustainable Development Goal 3 to achieve good health and wellbeing for all.

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Malaria

- Takes a child’s life every 2 minutes
- Kills an estimated 435,000 people each year – the vast majority are children
- Can kill within 24 hrs of symptom onset
- Can infect an African child up to 13 times a year
- Drug resistance has repeatedly emerged in Southeast Asia, where it is estimated that more than 11 million annual cases occur
- Is both a cause and consequence of poverty

1. WHO. Malaria Fact Sheet, 2018.

Quality medicine at an affordable price

MMV strongly believes that all malaria patients, rich or poor, deserve treatments that are high quality, efficacious and well tolerated. In order to ensure that is the case, all new medicines supported by MMV must meet internationally accepted standards from stringent regulatory authorities and/or WHO prequalification.

All development projects conducted by MMV and partners follow ICH guidelines every step of the way – from GLP standards for preclinical work to GCP standards for clinical trials in malaria-endemic countries that also adhere to national regulations. This is underpinned by strict adherence to GMP requirements for both investigational and registered products.

When MMV and a partner enter into a contractual relationship, they commit to developing a product together that will be accessible and affordable for endemic populations.

To keep the development costs, and, in turn, the final cost of our quality co-developed medicines, as low as possible, MMV benchmarks costs and follows a robust procurement process when engaging with research service providers. We also aim to contain production costs by working with our partners to seek the most efficient routes of synthesis for our medicines – beyond reductions expected from economies of scale.

In this way, MMV is able to maximize the value of every donor dollar to our highly focused mission and develop high-quality medicines that are affordable for vulnerable populations.

1. International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH)
2. Good Laboratory Practice (GLP)
3. Good Clinical Practice (GCP)
4. Good Manufacturing Practice (GMP)

MMV’s Product Development Partnership (PDP) continues to bear fruit. Combining the technical skills of our network of partners from industry, academia and endemic regions, with our in-house expertise, MMV remains a highly productive and cost-effective research and development organization.

Each partner brings technical know-how, enabling technologies, research facilities and funding. MMV brings a wealth of malaria and R&D knowledge together with industry-style portfolio management. Our Target Product Profiles and Target Candidate Profiles (see p. 3) provide a clear framework for research and development. With this in mind, support is provided for the most promising drug candidates, while those that do not meet the target profile are quickly terminated. This rigorous candidate selection and management enables us to maximize value while accelerating the progress of compounds through the pipeline.

MMV’s PDP model – The innovative route to neglected disease drug development

A network of over 400 dedicated partners over 19 years

224 years of in-house malaria experience

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

Goal:

50 cents or less to treat a child

1. USD 1 = 3.50 USD

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MMV-supported projects

Antimalarial drug discovery and development projects scientifically and/or financially supported by MMV.

### Research
- **Lead optimization**
- **Candidate profiling**
- **Preclinical**
  - **Miniporfolio**
    - GSK
    - Pantothanates: TropI/Q/Radboudu Univ.
  - **Phenotypic lead**
    - Daiichi-Sankyo
    - **Phe tRNA ligase**
      - Broad Institute/Eisai
  - **Open Source Series**
    - Univ. of Sydney
  - **Phe tRNA ligase**
    - Broad Institute/Eisai
  - **Purines**
    - Celgene
  - **GWT1**
    - Eisai
  - **Molecular target**
    - Drug Discovery Unit
    - Univ. of Dundee
  - **Azabenzimidazole**
    - UNICAMP (Univ. of Campinas)
  - **Miniporfolio**
    - Novartis
  - **SJ733 backup**
    - Kentucky
  - **Phenotypic lead**
    - Sanofi
  - **DHODH**
    - Univ. of Texas Southwestern/Univ. of Washington/Univ. of Monash
  - **Phenotypic lead**
    - Univ. of Cape Town
  - **Intra-muscular**
    - Calibr

### Translational
- **Human volunteers**
- **Patient exploratory**
- **Patient confirmatory**
- **Regulatory review**
  - **Artemether-lumefantrine dispersible**
    - Novartis
  - **Artesunate for injection**
    - Fosun (Guilin)
  - **Dihydroartemisinin-piperine**
    - Artasigma
  - **Pyronaridine-artesunate**
    - Shin Poong
  - **Pyronaridine-artesunate granules**
    - Shin Poong
  - **Artesunate-amoqua**
    - Sanofi
  - **Artesunate-mefloquine**
    - Cipla
  - **Sulfadoxine-pyrimethamine + amodiaquine**
    - Fosun (Guilin)
  - **Rectal artesunate**
    - Cipla
  - **Rectal artesunate**
    - Strides Pharma
  - **Tafenoquine**
    - GSK
  - **Artesunate for Injection**
    - Ipca

### Product development
- **3-day cure, artemisinin-based combination therapies**
- **Uncomplicated malaria treatments aiming at a new single-exposure radical cure (SERC) TPP-1**
- **Intermittent/Seasonal Malaria Chemoprevention**
- **Severe malaria treatment/ pre-referral intervention**
- **Products targeting prevention of relapse for P. vivax**
- **Single-exposure chemoprotection (SEC) TPP-2**

### Access

#### Target Product Profiles
- **3-day cure, artemisinin-based combination therapies**
- **Uncomplicated malaria treatments aiming at a new single-exposure radical cure (SERC) TPP-1**
- **Intermittent/Seasonal Malaria Chemoprevention**
- **Severe malaria treatment/ pre-referral intervention**
- **Products targeting prevention of relapse for P. vivax**
- **Single-exposure chemoprotection (SEC) TPP-2**

To develop the individual compounds for combination into the TPPs, MMV has defined five Target Candidate Profiles (TCPs):
- **Asexual blood stages**
- **Relapse prevention**
- **Chemoprotection**
- **Transmission reduction**

- **Brought into portfolio after approval and/or development**
- **Global Fund Expert Review Panel reviewed product – permitted for time-limited procurement, while regulatory/WHO prequalification review is ongoing**
- **Pediatric formulation**
- **WHO Prequalified or approved/positive opinion by regulatory bodies who are ICH members/observers**

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Working in partnership

Since its inception in 1999, MMV has successfully worked in over 50 countries with more than 400 partners from:
- the public and private sectors
- NGOs and non-profit organizations
- clinical trial sites

Today, over 150 active partners are working on MMV projects in 30 countries.

More than 400 partners

...over 50 countries

The road to health impact

Discovering and developing new life-saving antimalarials are not enough to ensure health impact, which is why MMV is also committed to delivering these medicines to those most in need. There are numerous obstacles along the road to health impact; here is how we work to overcome some of them.

During product development, we listen to the “voice of the malaria patient” to refine our Target Product Profiles (see MMV-supported projects, page 3). This focus often requires social and market research to document patient and health provider needs and to refine our understanding of product acceptability.

All MMV-supported medicines are prequalified by the WHO and/or receive approval from a stringent regulatory authority (see page 2). In addition, each country’s regulatory authorities must register new medicines for national use. By engaging with regulators and ensuring our pharma partners expedite submissions of drug dossiers, MMV supports faster introduction of innovative antimalarials.

To get a product ready for market delivery, we agree on affordable pricing with our pharma partners. This enables countries to offer the medicines for free or at heavily subsidized rates, often with support from international donors. In addition, we develop user-friendly packaging and training materials by field-testing them in “real-life” settings.

National malaria control programmes (NMCPs) consider scientific evidence and WHO guidance before changing their policy and reallocating finances in favour of a new treatment. MMV works closely with the WHO and NMCPs to disseminate evidence that may help inform policy and guideline decisions. In certain cases, MMV also collaborates on post-launch studies to generate additional safety data and operational research about new medicines.

To maximize their life-saving impact, highly effective antimalarials normally should be accessible to patients within 24 hours of initial symptoms. Thus, helping to address distribution challenges is critical to our mission. We focus on improving the suitability of our medicines for last-mile settings, where patient uptake and health impact occur. This includes ensuring product ease-of-use by community health workers and developing packaging that is appropriate for remote delivery via rural supply chains. MMV also recognizes that there are ongoing efforts to strengthen the performance of primary healthcare systems in many countries; as a result, we also select innovation partners who are developing better ways to ensure timely access to essential medicines and to quality medical care in rural settings.

Today, an estimated 435,000 people still die from malaria every year. Remedy this unacceptable situation is MMV’s raison d’être. By developing next-generation medicines and advancing access to those quality treatments that are already available, we are working with our partners in pursuit of a future where no one will suffer or die from malaria.
Focus on finances

Medicines for Malaria Venture receives sustained funding and support from government agencies, private foundations, international organizations, corporations, corporate foundations and private individuals. These funds are used to finance MMV’s portfolio of R&D projects as well as specific, targeted access and delivery interventions that aim to make it easier for vulnerable populations to access MMV products.

Since its foundation in 1999, MMV has established the world’s largest R&D portfolio of new and innovative antimalarial medicines. With partners, MMV has brought forward ten new antimalarials and taken over the access stewardship of two more. Together, these medicines have saved an estimated 1.9 million lives. Our 2017-2021 business plan estimates the need for a minimum of USD 340 million over the period 2018–2021 to sustain this work.

Progress in research is dependent on funding. With approximately USD 190 million available at the end of 2017 (USD 53 million cash and USD 137 million committed pledges over the 2018-2021 period), the organization is currently tracking a project-budget gap of approximately USD 150 million up to the end of 2021. To overcome this, we are striving to expand and develop current and new donor relationships and negotiate the best terms with our partners.

Figure 1  Donations received/pledged 1999–2021

- Bill & Melinda Gates Foundation: 53.4%
- United Kingdom (Department for International Development (DFID) and the Department of Health): 20.7%
- US Government: 4.3%
- Netherlands Ministry for Development Co-operation (OTA): 3.3%
- Welcome Trust: 2.9%
- Swiss Agency for Development and Cooperation (SDC): 2.5%
- UNITAID: 2.0%
- Irish Aid: 2.1%
- Global Health Innovative Technology Fund (GHIT): 1.7%
- Australian Government Department of Foreign Affairs and Trade (DFAT): 1.2%
- Spanish Agency for International Development (AECID): 1.1%
- German Federal Ministry for Education and Research (BMBF): 0.8%
- World Bank: 0.8%
- ExxonMobil Foundation: 0.7%
- Newcrest Mining Limited: 0.6%
- Rockefeller Foundation: 0.6%
- World Health Organization/Roll Back Malaria Partnership (WHO/RBM): 0.5%
- Norwegian Agency for Development Cooperation (NORAD): 0.3%
- Malaria Consortium: 0.1%
- Johnson & Johnson Corporate Citizenship Trust: 0.1%
- BHF Billiton: 0.1%
- Individual donors: 0.1%
- Direction de la Coopération Internationale, Principauté de Monaco (CIC): 0.04%
- CRIMALDII Consortium: 0.01%

Figure 2  MMV expenditure 2017 Total: USD 74.5 million

- Research & development: 72%
- Access & product management: 10%
- General & administration: 8%
- External relations & advocacy: 5%
- Funding reimbursements: 4%
- Foundation board: 1%
Key achievements

127 million vials of Artesun®
(Fosun Pharma’s MMV-supported injectable artesunate) for severe malaria delivered since 2010 – saving an estimated 800,000 additional lives compared to treatment with quinine.

385 million treatments of child-friendly Coartem® Dispersible
(artemether-lumefantrine, co-developed with Novartis) distributed in over 50 countries since launch in 2009.

Over 300 Pathogen Boxes shipped free of charge to scientists around the world to boost neglected diseases drug discovery.

An estimated 1.9 million lives saved by MMV-supported medicines since 2009.

1st child-friendly medicine approved via article 58. Pyramax® Granules (pyronaridine-artesunate, co-developed with Shin Poong) received EMA positive scientific opinion in Nov 2015. Added to the WHO List of Prequalified Medicinal Products in 2016 and to its Model List of Essential Medicines in 2017.

1st single dose cure for relapsing malaria (tafenoquine) approved by the US FDA and Australian TGA.

250 million courses of SP + AQ shipped to countries in West Africa’s Sahel region since 2013, by MMV’s partner Fosun Pharma, enough to provide an estimated 60 million children with Seasonal Malaria Chemoprevention.