What a difference 20 years of partnership makes. In 1999, when MMV and its partners made a commitment to fill the empty malaria R&D pipeline, around one million people were losing their lives to the disease. Since then, as the global health community works towards the goal of eradication, the 10 medicines brought forward by MMV and partners have contributed to saving almost 2 million lives from malaria, mostly young children.

Yet the malaria parasite is fiercely tenacious. Despite a 60% drop in malaria deaths between 2000 and 2015, the World Malaria Report 2018 describes a slowing in progress to reduce malaria cases between 2015 and 2017. Around 435,000 people continue to lose their lives to malaria each year.

In light of this, in 2018, the malaria community, including MMV, reassessed their strategies to understand why progress is levelling off and what else can be done to win the fight against this disease. In response, in 2018 the World Health Organization (WHO) and partners launched the “High burden to high impact” initiative, a country-led approach which aims to accelerate much-needed progress against malaria focusing on 11 countries that account for approximately 70% of the global malaria burden, 10 on the African continent plus India.

A focus on children – the most vulnerable

Seven out of every ten malaria deaths are those of a child under the age of 5. We want all children in eligible malaria-endemic areas to benefit from seasonal malaria chemoprevention (SMC). Last year, 81 million monthly courses of SMC (sulfadoxine-pyrimethamine plus amodiaquine) were shipped – enough to reach more than 20 million children. MMV has also launched a new programme known as SEAMACE (SEASONAL MAliaria Chemoprevention Extension) to explore smarter ways of reaching even more children living at risk of malaria.

Furthermore, we are working to ensure that no child faces disability or death from severe malaria because they were unable to reach a healthcare facility in time. Two MMV-supported rectal artesunate suppositories (RAS) products, from Cipla and Strides Shasun, both prequalified by the WHO last year, are being rolled out in programmes designed to ensure their timely and correct use. In this context, RAS is buying valuable time for afflicted children to receive the follow-on care they need.

New medicines

Meanwhile, 2018 saw 10 years of development work, in partnership with GlaxoSmithKline (GSK), bear fruit – tafenoquine (Krintafel/Kozenis), was approved both by the US Food and Drug Administration (FDA) and the Australian Therapeutic Goods Administration (TGA).
With these approvals, tafenoquine became the first new medicine for the radical cure of relapsing Plasmodium vivax malaria in more than 60 years. For endemic countries, for example in Southeast Asia and Latin America, this marks a major milestone on the road to malaria eradication.

Behind this, our portfolio of next-generation medicines – designed to meet the unmet medical needs of malaria patients in the highest burden countries – is robust and growing stronger. Ten compounds or combinations are in clinical trials today. In one example, MMV in partnership with Novartis have progressed ganaplacide combined with a new formulation of lumefantrine through Phase IIb and results of the interim analysis are promising. Furthermore, the combination is already being formulated to address the needs of children.

New drug discovery

Meanwhile, MMV’s drug discovery engine delivered a steady stream of new potential product candidates. New tools, from liver assays to volunteer infection studies and preclinical models, are providing us with a breadth and depth of information on these new previously inaccessible candidates. Armed with this information, we can get smarter not only in our efforts to identify new compound series for the treatment of malaria but also in the selection of compounds for combinations. Furthermore, these tools and data guide the identification of compounds for relapse prevention, transmission blocking and the protection of vulnerable populations – essential characteristics of the medicines needed for elimination and eradication.

Looking ahead

Twenty years ago, we laid an important cornerstone in the foundation to build a world free from malaria. The next 20 years will be just as critical as some countries move towards elimination and the malaria community works to turn the tide for high burden countries. As WHO Director-General Dr Tedros Adhanom Ghebreyesus told the 71st World Health Assembly: “We must act with a sense of urgency in everything we do, because every moment we lose is a matter of life and death.” It is with this urgency that MMV will pursue the parallel tracks of facilitating access to antimalarials for high burden countries today while developing the tools needed tomorrow for the elimination and eventual eradication of malaria.

We would like to thank all our partners – past, present and future – who join us in this mission. We thank, too, the board and donors for their unstinting support, and our staff for their passion, commitment and hard work. And we urge you all to continue with us on our journey to destination eradication.

MMV will pursue the parallel tracks of facilitating access to antimalarials for high burden countries today while developing the tools needed tomorrow.
Key achievements 2018

1.9 million lives saved by MMV-supported antimalarials since 2009

96% reduction in severe malaria case fatality demonstrated in a pilot project to expand access to life-saving medicine in Zambia led by a consortium of partners including Transaid, the Zambia National Malaria Elimination Center and MMV

10th MMV-supported medicine: Strides Pharma Science’s rectal artesunate product (Artecap®) received WHO prequalification

1st new medicine for the radical cure of relapsing P. vivax malaria in more than 60 years, tafenoquine developed with GSK, approved by the US FDA (Krintafel) and the Australian TGA (Kozenis)

2nd manufacturer of injectable artesunate secured – Ipca received WHO prequalification in Dec 2018 for Larinate® 60

10 compounds in clinical development with the potential to become medicines for children, pregnant women and people suffering from drug-resistant malaria

1 donor dollar creates an estimated 3.5 dollars of investment impact thanks to direct and in-kind support from our partners
Artesun® (injectable artesunate) delivered by Fosun Pharma since 2010 for severe malaria, saving an estimated 840,000 additional lives compared with quinine treatment.

385 million treatments of child-friendly ACT Coartem® Dispersible (artemether-lumefantrine, developed with Novartis) distributed to more than 50 countries since 2009 – a volume MMV estimates to have saved around 825,000 lives.

128 million vials of Artesun® (injectable artesunate) delivered by Fosun Pharma since 2010 for severe malaria, saving an estimated 840,000 additional lives compared with quinine treatment.

84% of patients recruited in CANTAM* study to investigate the real-life safety and tolerability of Pyramax® (pyronaridine-artesunate, developed with Shin Poong) in Central Africa and Ivory Coast.

81 million courses of seasonal malaria chemoprevention shipped to countries in the Sahel in 2018, enough to protect 20 million children.

40 chemical series being optimized towards preclinical candidates and 3 new antimalarial candidates delivered in 2018.

319 Pathogen Boxes shipped to scientists around the world free of charge by year end – catalysing drug discovery for neglected diseases.

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

30,000 compounds screened in P. vivax liver-stage assays led to the identification of several potential radical cure hits, with one series currently undergoing early optimization.

* CANTAM: Central African Network on Tuberculosis, HIV/AIDS and Malaria.
**Strategic focus**

In line with global frameworks from the WHO and the United Nations, MMV is focused on facilitating access to current antimalarials, particularly in high-burden countries, while researching and developing the next generation of medicines needed for the elimination and eventual eradication of malaria.

To facilitate access, 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 adoption into relevant national 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, MMV focuses on the need for accelerated, efficient and appropriate drug discovery and development using a range of supportive research tools, including assays (p. 27), models and platforms (pp. 30–32). 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 identified unmet medical needs. This is described by two target product profiles (TPPs).

**TPP1** defines the characteristics of drugs for treatment of uncomplicated malaria by targeting the blood-stage infection. The ultimate goal is to overcome resistance and shorten the treatment course. Such a drug may also provide post-treatment protection and block transmission. In the best case it would be what is known as a single exposure radical cure and prophylaxis (SERCaP). Simplifying case management would thus help improve compliance. MMV also reviews all molecules for potential to provide new injectable treatments for severe malaria.

**TPP2** describes drugs to protect vulnerable populations, such as non-infected people entering an area of high malaria endemicity, or children already living in areas of high endemicity. This is described as single exposure prophylaxis and would always include one molecule active against the liver stages of malaria. To reduce the risk of drug resistance emerging, for a given geographic area, combinations used for protection should have different active ingredients from those used to cure malaria.

The development of a new treatment for uncomplicated malaria or a new prophylactic regimen requires the combination of at least two active candidate drugs. MMV has defined five target candidate profiles (TCPs) corresponding to different clinical attributes needed for combination to meet the TPPs (Figure 1).

MMV is currently working with more than 150 partners around the world on its portfolio of R&D and access projects. Together with partners, MMV will continue to optimize the discovery, development and delivery of new antimalarials to help control and ultimately eradicate malaria.

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**Figure 1: Linking the TPPs to the TCPs**

NB: TCP 2 has been retired and incorporated into TCP 1.
### MMV-supported projects

<table>
<thead>
<tr>
<th>Research</th>
<th>Translational</th>
<th>Product development</th>
<th>Access</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lead optimization</strong></td>
<td><strong>Candidate profiling</strong></td>
<td><strong>Preclinical</strong></td>
<td><strong>Human volunteers</strong></td>
</tr>
<tr>
<td>Miniportfolio</td>
<td>Pantothenates</td>
<td>MMV253 Zydus Cadila</td>
<td>P218 Janssen</td>
</tr>
<tr>
<td>Phenotypic lead</td>
<td>Dalichi-Sankyo</td>
<td>SAR121 Sanofi</td>
<td>SJ733 Univ. of Kentucky/Eisai</td>
</tr>
<tr>
<td>Open Source Series</td>
<td>Purines</td>
<td>MMV370 MMV371</td>
<td>M5717 Merck KGaA</td>
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<td>Global Fund</td>
<td></td>
<td></td>
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<td>GSB Global Safety Board</td>
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<td></td>
</tr>
<tr>
<td>MMV Board of Directors/Executive Committee/Financial Audit Committee</td>
<td>MMV-supported projects</td>
<td></td>
<td></td>
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</tbody>
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**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 prophylaxis TPP-2

**Brand names:**

**To develop the individual compounds for combination in the TPPs, MMV has defined five target candidate profiles (TCPs):**
- Blood-stage killers (TCP 1)
- Hypnozoite killers (anti-relapse) (TCP 3)
- Prophylaxis (TCP 4)
- Transmission blockers (TCP 5)
- Paediatric formulation

**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
- WHO-prequalified or approved/positive opinion by regulatory bodies who are ICH* members/observers

* International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use