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# Staying true to our malaria mission in a time of global uncertainty

## Message from the Chairman and CEO

It is 2021, and the world is still striving to emerge from the long, dark shadow of SARS-CoV-2, searching, as American poet Amanda Gorman[1] says to find "find light in this never-ending shade".

In 2020, Medicines for Malaria Venture (MMV) joined that search wholeheartedly. While keeping a strong focus on our core mission to discover, develop and deliver effective antimalarials for underserved populations, we expanded our work to include efforts to respond to COVID-19 in areas where we could make a unique contribution.

### All hands on deck: contributing to the global pandemic response

Six years after the launch of the Global Health Security Agenda[2] the world was nonetheless caught off guard by the rapid spread of SARS-CoV-2. At MMV, we contributed our core R&D and access strengths to the global effort (pp. 10-11). In response to supply chain issues, raised initially by our drug manufacturing partners, and given the intense interest in existing antimalarials as potential treatments for COVID-19, we joined forces with the World Health Organization (WHO), partners and major suppliers, advising on linkages with industry and coordinating efforts to monitor the supply chain and safeguard access to critical malaria commodities.

In addition, we swiftly sent antimalarial compound collections with potential SARS-CoV-2 activity to testing centres and distributed our open access compound collections to researchers free of charge. Since initiating the distribution of these compound collections, 125 copies of the Pandemic Response Box and 50 of the newly launched COVID Box, have been distributed, and shipments continue. We also supported clinical studies to repurpose existing medicines, including launching a Phase II clinical study in South Africa (p. 11).

### Coming at malaria from all sides: prevention, treatment, radical cure

All the while, more than 400,000 people continue to lose their lives from malaria each year. As such, our core malaria work remains top priority, and together with our partners we continue to focus on expanding access to therapies that prevent, treat and cure both *Plasmodium falciparum* and *Plasmodium vivax* malaria.

#### Prevention

Young children urgently need protection from malaria, as they are the hardest hit by this disease. Despite challenges brought on by the COVID-19 pandemic, we helped ensure that the seasonal malaria chemoprevention (SMC) (pp. 25-28) programme for young children stayed on track in 13 implementing countries, helping protect 30 million children.

COVID-related disruptions did not unduly delay the distribution of this lifesaving intervention thanks to the exceptional effort of healthcare workers, government officials and political leadership. It is heartening that this success has also encouraged the expansion of SMC into new areas in the Sahel – in one example, three times as many children were reached in Nigeria in 2020 than in 2019.

#### Management of severe malaria

In Malawi, a study led by MMV on artesunate rectal capsules (ARC) generated important evidence demonstrating the role of toolkits and a formalized referral slip protocol in increasing the likelihood of a positive treatment outcome for patients. ARC is a pre-referral, lifesaving intervention for the very young with severe malaria. It halts the progression of the disease, giving time for patients to be transported to a health facility where they can be treated with injectable artesunate. Another exciting development on the horizon is the novel injectable compound *KAE609 (cipargamin)*, which is in Phase II trials in collaboration with Novartis as an alternative

1 Amanda Gorman was America's first National Youth Poet Laureate (2017) – this phrase is from her poem The Hill We Climb that she read out at President Biden's inauguration on 20 January 2021.

2 www.ghsagenda.org: a group of 70 countries and public and private sector organizations whose vision "is to achieve a world safe and secure from infectious disease threats" by improving country capacity and leadership to prevent, detect and effectively respond to infectious diseases.

treatment for severe malaria. This is particularly important in view of the recent identification of partial artemisinin resistance in Rwanda and several other African countries.

### Radical cure

Our work to introduce and support the integration of tafenoquine (TQ)[3] into *P. vivax* clinical management bore fruit – the first country in South East Asia to grant TQ marketing authorization approval, Thailand, also marked the first step to open up access to TQ across the Asia-Pacific, where *P. vivax* is becoming the more dominant malaria species. TQ was also submitted for approval in Myanmar, Vietnam, Philippines and Peru, while the paediatric dossier was submitted to the Australian Therapeutic Goods Administration (TGA).

## Preparing for the next big global health crisis — Antimicrobial Resistance (AMR)

In 2020, reports of *de novo* artemisinin resistance in Rwanda were an urgent reminder of the need to step up surveillance for antimalarial drug resistance indicators both in the lab and the field. Although the artemisinin-based combination therapies (ACTs) AL and DHA-PQP[4] continued to show cure rates of > 95%, it is likely only a matter of time before ACTs, too, begin to lose their effectiveness as a treatment for uncomplicated *P. falciparum* malaria in the endemic regions of sub-Saharan Africa.

As with all forms of antimicrobial resistance, three things are required to prevent its rapid spread: to protect existing treatments, monitor their efficacy, and accelerate the development of next-generation medicines (pp. 12-17).

In the race against resistance, MMV's strategy is to work with partners to develop simpler, effective, high-quality, patient-friendly medicines for adults and children that improve treatment adherence. Ganaplacide–lumefantrine is a leading combination currently in Phase IIb with Novartis for uncomplicated malaria. Behind that we have a healthy pipeline of compounds being assessed in various combinations, including for chemoprevention, through our Malaria Drug Development Catalyst. The Catalyst provides a legal and scientific platform to promote effective collaboration between industry partners, to facilitate decision-making on the most appropriate compounds for combination therapies and to accelerate the development of new drug combinations.

When it comes to finding ways to accelerate the discovery of new compounds, MMV continues to be a pioneer. We have established discovery networks and assay platforms to expedite identification of the most promising compounds against malaria as well as drug-resistant strains of other pathogens. In 2020, we developed two new tools to support the selection and dosage of compounds for combination therapies (pp. 38-39): the ACPR28 mathematical model and a mathematical application, MMVSola, named after the late Suresh Solapure, an MMV partner and an early champion of using pharmacokinetic/pharmacodynamic modelling to predict dosage, who tragically passed away in 2020.

## Redressing the fatal gender imbalance

This year, MMV shone a stronger light on the unmet needs of pregnant women. Each year, malaria causes over 10,000 maternal and 200,000 newborn deaths. MMV and partners have committed to exploring innovative R&D strategies to identify new medicines that serve the needs of this population. As a first step, we designed a far-sighted strategy, 'MiMBa',[5] (p. 22) to generate more data on the impact of existing antimalarials on pregnant women, enrich the R&D pipeline with appropriate new drugs deemed low risk to mother and foetus, and advocate for earlier inclusion of pregnant and breastfeeding women in clinical trials than currently practiced. In 2020, this led to the launch of MMV and LSTM's[6] pregnancy registry (pp. 22-23) in three African countries to capture safety and exposure data on the real-life use of ACTs during all stages of pregnancy. Its aim is to support policy change through robust data, thereby improving treatment options for pregnant women suffering from malaria.

## Prepared for an uncertain future…

2020 was an unprecedented year for global health. The MMV team, our Board, donors, indispensable partners and stakeholders demonstrated exemplary agility and adaptability at every level. We are grateful and inspired by their commitment and support.

As the SARS-CoV-2 virus continues to disrupt the economic, political, social and health systems of the world, the critical value of scientific research to global health security, and the preparedness, resilience and flexibility of the partnership model have been recognized. Both will continue to be needed.

Since 2009, the 13 malaria therapies that we have brought forward, together with our partners, have saved an estimated 2.7 million precious lives. While we remain resolute in our commitment to a malaria-free world, we also commit to sharing our expertise and experience when global health crises occur in the future. In this hyper-connected 21st century, we will work with partners to pursue the end of malaria and help ensure preparedness for the next impending global health crisis, for it will affect us all. ■

> ***"The MMV team, our Board, donors, indispensable partners and stakeholders demonstrated exemplary agility and adaptability at every level."***

**Dr David Reddy**
CEO
(left)

**Mr Per Wold-Olsen**
Chairman of the Board
(right)

3 The single-dose radical cure (prevention of relapse) for *P. vivax* malaria co-developed by MMV and GSK.
4 Artemisinin-based combination therapies: Artemether–lumefantrine (AL) and Dihydroartemisinin–piperaquine (DHA–PQP).
5 Malaria in Mothers and Babies – MiMBa means pregnancy in Swahili.
6 LSTM: Liverpool School of Tropical Medicine.

# Milestones 2020

## The WHO Global Technical Strategy for Malaria 2016–2030[1] provides a framework and key targets for all malaria-endemic countries working towards control and elimination. Reaching these targets will contribute to achieving Sustainable Development Goal 3 'Ensure healthy lives and promote well-being for all at all ages'.[2] In 2020, MMV and key partners made important strides towards meeting these targets by:

## Accelerating efforts towards elimination and attainment of malaria-free status

**Marketing authorization application of tafenoquine paediatric** submitted to Australian Therapeutic Goods Administration

**Ganaplacide–lumefantrine (frontrunner new combination therapy)** progressed to Part B of the Phase IIb trial, with an additional paediatric study (KALUMI) starting in 2021

**Cipargamin new formulation** for intravenous administration completed Phase I with Phase II expected to start in 2021

To date, **6,500 new data points** have been generated from transmission-blocking assays performed in collaboration with Imperial College London

**Investigation of next-generation combinations for uncomplicated malaria** through the Malaria Drug Development Catalyst

**Two potent compounds against *P. vivax* liver stages** identified through screening

**Three new regulatory approvals** for *Krintafel/Kozenis* (tafenoquine),[3] including in Thailand, the first South East Asian country to grant marketing authorization approval

**3.8 million** doses of **artesunate rectal capsules** delivered to date with registration in 17 countries, saving an estimated 443,000 lives

**209 million vials of injectable artesunate** delivered since launch, estimated to have saved **1.36 million additional lives** compared to treatment with injectable quinine[4]

**A new pregnancy registry** has been established to monitor the impact of different antimalarials on mother and child, inform policymakers and strengthen healthcare systems

**Over 100 Pandemic Response Boxes** shipped in 2019–2020 to facilitate drug discovery in other disease areas

**Two compounds active against *Plasmodium cynomolgi* liver stages** identified through screening

## Ensuring universal access to malaria prevention and treatment

**2.7 million lives** estimated to have been saved to date through MMV-supported medicines

**536 million** courses of SPAQ delivered since its launch in 2014 for **seasonal malaria**, protecting over **30 million** children in 2020. Six new combinations of licensed molecules have been evaluated and ranked as alternatives to SPAQ for SMC.

**430 million** paediatric treatment courses of **Coartem® *Dispersible*** (artemether–lumefantrine) distributed to over 50 countries since 2009, saving an estimated **926,000 lives**

**7.9 million Eurartesim®** (dihydroartemisinin–piperaquine) treatments distributed since approval with registration in 24 countries

**1.73 million** patients treated with **Pyramax®** (pyronaridine–artesunate); tablets approved in 29 countries and granules in 19 countries

**Four new late leads** approved in 2020

**New candidate selected for development**: ELQ331

## Strengthening the enabling environment

**European and Developing Countries Clinical Trials Partnership (EDCTP)-funded PAMAfrica training** to strengthen research capacity at trial sites and research capability of next-generation African scientists

## Harnessing innovation and expanding research

**11 compounds in preclinical and clinical development** including 10 with novel biological pathways compared with existing ACTs

## Working beyond our scope:

## Response to the COVID-19 pandemic

**Implemented measures to support supply chains** for chloroquine to treat malaria in *P. vivax*-endemic countries and mitigate stockouts

**Promoted healthcare awareness in rural communities** adapting existing malaria educational initiatives, e.g. training community health volunteers on danger signs and protocols around COVID-19

**Safeguarded continued SMC campaigns**, protecting 30 million children in 2020

**Over 50 COVID Boxes** shipped to enable standardization of testing results across various laboratories

**Worked with partners on COVID-19 clinical studies**, including the ReACT and ANTICOV studies

1 WHO Global Technical Strategy for Malaria 2016–2030: https://www.who.int/docs/default-source/documents/global-technical-strategy-for-malaria-2016-2030.pdf?sfvrsn=c82afcc_0

2 UN Sustainable Development Goals (SDGs): https://www.who.int/health-topics/sustainable-development-goals#tab=tab_1

3 Tafenoquine is marketed as *Kozenis* in Australia and *Krintafel* in the USA. Trademarks are owned by or licensed to the GSK group of companies.

4 Assuming that patients would have received injectable quinine in the absence of injectable artesunate.