

2018 in review – a triumph of partnerships

Dear MMV Friends,

As MMV's 19th year comes to an end, we once again pay tribute to the power of partnerships and collaboration. Once again, as we follow the path outlined by our 5-year Business Plan, MMV's partnerships have had considerable impact on the lives of people living in malaria-endemic countries that we serve. Our unified efforts to make antimalarials available to the vulnerable continues to save countless lives. In parallel, we continue to progress next-generation medicines through our pipeline with the confidence that these, too, will one day have the same impact.

Facilitating access to quality antimalarials

Remote, rural communities are often left behind in terms of health coverage – this is particularly tragic in the case of severe malaria that can kill within 24 hours if left untreated. Two MMV-supported rectal artesunate suppository (RAS) products for this disease, produced by Cipla and Strides Pharma, were prequalified in 2018 by the WHO. RAS helps buy time for vulnerable children with severe malaria who live far from health care facilities, to be transported to referral centers where WHO-recommended treatment, injectable artesunate (Inj AS), is available to treat their disease.

A one-year pilot study in Serenje district, Zambia led by a consortium including Transaid, MMV, and the Zambian National Malaria Elimination Centre (NMEC), aimed to introduce and increase access to community-based management for severe malaria using pre-referral RAS for children aged 6 months to 6 years; and to reduce referral delays to appropriate health facilities. The study reported an impressive 96% reduction in [severe malaria case fatality](#) by increasing access to RAS and Inj AS, both co-developed by MMV, and using [bicycle ambulances](#) to take children to health facilities. This project saved the lives of children like one-year old [Alexandria](#) in Serenje, giving him a second chance at life.

The gains achieved by this project, has helped the consortium secure funding to help scale up the intervention for a further 2 years. The NMEC and Zambian Ministry of Health have also agreed to scale-up RAS at the community level with the aim of making it available nationwide, and ensuring no one is left behind. This is amazing success at all levels of partnership.

In addition, thanks to MMV and partners, 127 million vials of Inj AS have been delivered to malaria-endemic countries since 2010, estimated to have saved an additional 800,000 lives compared to treatment with quinine. Eighty percent of procured RAS is now prequalified, and 1.5 million deliveries are expected by end 2018.

Prioritizing children

Up-scaling of seasonal malaria chemoprevention to protect children from malaria in the rainy season is another success story – an estimated 60M children in the Sahel region of Africa have been protected, given the 250 million treatments of SP-amodiaquine (SP+AP) distributed since 2013, of which 70 million were shipped in Jul-Nov 2018. In addition, MMV has supported the submission of S. Kant's dossier for SP+AQ dispersible for WHO prequalification in July 2018.

From the very start MMV has focused on treatments for young children – the main victims of malaria. Since the launch 10 years ago of the MMV-Novartis co-developed Coartem® *Dispersible* for children, 385 million treatments have been delivered. A paediatric formulation of Pyramax, Pyramax® granules, has been developed with Shin Poong and approved by the EMA in 2017, while a paediatric formulation of Eurartesim® is currently in development with Alfasigma.

Traditionally, as was the case for these three paediatric formulations, new medicines are first developed for adults, after which child-friendly versions are pursued. MMV is working to change that, given that more than 70% of people dying from malaria are children under the age of 5 years. If the safety profile in adults allows it, we have begun to run studies to find the right dose for children using a staged-down strategy during early clinical development. Phase II studies begin in cohorts of adult patients, then progress down the age-scale to successively younger cohorts as tolerability is established. Using this approach in studies like the artefenomel + ferroquine Phase II 'FALCI' study with Sanofi and the KAF156 + lumefantrine study with Novartis, MMV and its partners hope to register new medicines for children sooner and without the need for extensive separate paediatric development programmes.

In October 2018, MMV hosted a Forum on Paediatric Drug Development bringing together formulation, drug development and regulatory experts from the public and private sectors. MMV is now documenting the outcomes to help guide best practice for future R&D efforts for children.

Tafenoquine approved to treat malaria relapse

In 2018, the long-standing MMV partnership with GSK successfully brought tafenoquine (*Krintafel/ Kozenis*) through the regulatory approval process in both the [US](#) and [Australia](#), making it the first new medicine for relapsing malaria in more than 60 years. More importantly, tafenoquine is a huge advance on the current 7-14 days therapy for *P.vivax*, which often suffers a significant lack of patient compliance and could result in resistance developing to the treatment. Single-dose tafenoquine overcomes this issue. Following these approvals by Stringent Regulatory Authorities, the first application seeking marketing authorization for *Kozenis* in a malaria endemic country, was submitted in Brazil. Work is now ongoing with pharma and country partners to file in other countries and thus help ensure that this radical cure is made available and accessible to all those who need it.

Developing next-generation antimalarials

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. We continue our collaborations on new combinations of antimalarials and, with Novartis, have progressed KAF156 combined with a new formulation of lumefantrine through Phase IIb. Interim analysis on 261 patients is promising and shows no safety signal; more than 90% of subjects show no recrudescence at 45 days. In addition, a promising long-acting atovaquone pro-drug with the potential to provide a month's protection with one injection has been selected for clinical development as a chemoprotectant.

Bringing forward new tools to contain resistance, cure relapse and eliminate malaria

For the second year in a row, the figures reported in the World Malaria Report 2018 showed no significant change in the number of malaria cases (~ 219 million) and malaria-related deaths (435,000) since 2016. Although an increasing number of countries are headed towards malaria elimination (e.g., Uzbekistan, too, joined the list of malaria-free countries in December 2018), the global gains made in the first 15 years of this century have plateaued. In fact, in some of the highest burden countries, e.g., Nigeria and Democratic Republic of Congo, the struggle to control malaria is losing ground.

MMV is striving to provide therapeutic solutions for this struggle. In parallel to further increasing access to the 11 antimalarials we have brought forward, particularly in high-burden areas where the fight against malaria is most complex and challenging, we are developing more effective and simpler tools to deepen impact. These include:

- KAE609, MMV048 and DSM265 – currently in Phase II development
- M5717 – a University of Dundee compound in development with Merck and currently in first-in-human studies
- SAR121 – with Sanofi will shortly progress into clinical development
- Two new chemical entities, MMV052, GSK701, active against drug resistant parasites, have joined the pipeline
- The first ever non-8 aminoquinoline project to prevent relapse achieved successful review from our Expert Scientific Advisory Committee and an early lead is expected in 2019.

New R&D platforms for integrated drug development

Developing a new medicine that can successfully treat patients and combat drug resistance ideally requires at least two drugs in combination, each with a different mechanism of action or different mechanism of resistance. Selecting the optimal combination is a complex scientific challenge and this has meant rethinking drug development to address the need for accelerated, efficient and appropriate pathways. As a result, MMV and partners have developed and implemented a series of platforms to gather data to feed into a tool that enables every compound pair to be compared in a

similar manner. These [new R&D platforms](#) allow unbiased prioritization of optimal drug combinations for further research via [human volunteer infection studies](#); SCID mouse models, expanded to include artemisinin-resistant parasites; and mouse models with humanized livers, a screening platform encompassing the full *P falciparum* lifecycle.

Leveraging drug discovery competencies and assets for wider global health impact

From 2011, MMV has been working on an initiative called *MMVopen* to share compounds with researchers and take drug discovery to the next level. To date, over 850,000 compounds have been made available to researchers via the Malaria Box and the Pathogen Box for screening against neglected tropical diseases. With partner DNDi, a Pandemic Response Box of compounds is now ready for delivery in 2019.

In addition, a new collaboration with IVCC on oral endectocides will identify compounds for membrane feeding as potential attractive targeted sugar bait options.

In conclusion:

As we enter our 20th year, it becomes increasingly apparent that our achievements are entirely due to dedicated partners, donors, advisors and Board members, working closely with the MMV team. As part of an enthusiastic global health community, we are keen to contribute to the drive towards malaria elimination with new, effective and affordable next-generation antimalarials, as well as with programmes to ensure equitable access to today's medicines. Beyond this, we will continue to push forward with our open innovation initiatives that we hope will contribute to drug research for other tropical diseases and to counter the growing threat of antimicrobial resistance.

We look forward to the year ahead, which will no doubt bring new challenges, new scientific solutions and, of course, new partners. Since the launch of our first partnership medicine, Coartem® *Dispersible* with Novartis in 2009, MMV co-developed antimalarials have saved the lives of almost 2 million children, like Alexandria, and they will continue to do so. On behalf of the MMV team, I would like to take this opportunity to express our deepest gratitude for your unstinting support. This year has demonstrated the triumph of partnerships. With our partners we will keep the pressure on malaria, until we defeat it altogether.

Yours sincerely,



David Reddy
CEO - MMV