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THE MEDICINES OF TOMORROW

Born out of an urgent need to counter the looming threat of drug resistance and the prolonged production period for novel treatments, Medicines for Malaria Venture is striving towards a world free of malaria. Dr David Reddy lays out the initiative’s ambitious short-term goals, and outlines the projects that are bringing new antimalarial drugs to those most in need.
You have a background in the development and commercialisation of medicines for infectious diseases. How does this help you in your role as CEO of Medicines for Malaria Venture (MMV)?

Nearly 20 years in the pharmaceutical industry prior to MMV gave me an in-depth understanding of drug development; the process and importance of assembling the information needed to assess the benefits and risks of potential medicines; and, above all, the underlying importance of quality. Working on infectious diseases brought into sharp relief the global disparities in access between developed and developing nations, and the problems that can only be solved through partnerships between the public and private sectors.

How did you come to be involved with MMV, and what does your role entail?

I was asked to join MMV as CEO, and the role seemed extremely appealing. Clearly, the case for addressing malaria is compelling, and the role lies at the intersection of my areas of expertise: developing new medicines, forging partnerships to facilitate development and bringing medicines to those who need them. My role at MMV is to ensure that the organisation remains focused on key unmet needs in the field of malaria; to ensure that MMV continues to add unique value in the global fight against the disease; and to act as a facilitator, removing roadblocks so that MMV’s talented people can get their job done with minimal constraints.

You have over 300 partners in 50 countries. What key competencies do they represent and how do they help further the work of MMV? What are the advantages of working with MMV?

Almost 80 per cent of MMV’s core work is in the R&D of new medicines for malaria, and in our 14 years of existence we have built this robust network that covers all of our R&D needs, from early science through drug development, to access and delivery. Currently we are working with our partners on 65 different drug projects.

We benefit from their compound libraries, which we can screen for molecules with antimalarial potential; laboratory facilities to conduct optimisation and preclinical tests of candidate molecules; clinical sites to assess the safety and efficacy of candidate medicines; and members who have experience working in the field with healthcare workers or in advocacy to keep donors engaged.

In their turn, by sharing the risk inherent in R&D, scientists from pharma and academia are given the exciting opportunity to engage in research for diseases they would have been unable to do independently, and have free access to our worldwide network of scientific excellence.

MMV was founded in 1999 – how has the malaria epidemic changed since then, and how has the organisation evolved in this time?

In 1999, the world faced a rising malaria burden among neglected populations; growing resistance to the most commonly used antimalarial medicines; and virtually empty drug pipelines. A global public health crisis threatened to ensue. The urgent need for a new approach to develop therapies for this disease and the lack of commercial incentives to undertake malaria R&D led to the creation of MMV, an innovative product development partnership (PDP).

MMV started out modestly with US $4 million in seed finance from five motivated donors and just three early-stage projects in our portfolio. Strongly supported over the years by 17 committed public and private sector donors, today MMV and its partners have launched four products and manage a portfolio of over 65 projects targeting unmet medical needs in malaria, including medicines for children, pregnant women and patients who suffer from severe malaria; and drugs that could potentially contribute to the eventual eradication of malaria.

The malaria landscape is changing and the burden falling. Given the roll-out of effective control measures such as insecticide-treated bed nets, rapid diagnostic tests and indoor residual spraying, an estimated 3.3 million deaths were averted between 2001 and 2012, and 86 per cent of these were children under five. This is an exceptional achievement for the malaria community, but we cannot stop there – an estimated 627,000 people continue to die each year, largely in sub-Saharan Africa.

In addition, the spectre of drug resistance looms close. To ensure that we do not fall into the trap of complacency, as the world did in the 1950s, MMV will continue to work with partners to discover and develop more effective medicines.

Apart from resistance, what are the other major challenges associated with malaria drug development and delivery, and how can they be surmounted?

Another major challenge facing R&D is the length of time it takes for a compound to become a drug (normally 10-15 years), and the amount it costs (the figure varies between $1.2 and $1.7 billion). To accelerate the R&D process, MMV has a number of exciting initiatives that it has put into practice, such as mathematical modelling and the human challenge model. These new tools
MMV’s primary goal is to discover, develop and deliver new, affordable and effective antimalarial medicines to cure and protect vulnerable populations across the world. We bring together the multifarious strengths of our partners from the private sector (the pharmaceutical industry) and the public sector (academic research organisations) to collaborate on antimalarial drug projects, and our vision is to ultimately help eradicate this terrible disease.

Scientists can request an open access ‘Malaria Box’ free of charge, which contains 400 antimalarial compounds. How can this be used to promote new discoveries in malaria research?

The Malaria Box was assembled by MMV in a bid to catalyse a virtual cycle of malaria and neglected disease drug discovery and research.

Researchers normally have to pay for the physical compounds they wish to work on. The Malaria Box compounds, selected from around 20,000 ‘hits’ generated from an extensive screening campaign of around 4 million compounds that St Jude Children’s Research Hospital, Novartis and GlaxoSmithKline have provided free of charge to researchers. In return, they are asked to publish the resulting data and place it in the public domain to help continue the virtuous cycle of research in the hope that potential new therapies will be developed.

Since 2011, 160 Malaria Boxes have been dispatched to 27 countries. From this treasure trove of compounds, researchers from the Drugs for Neglected Diseases initiative have identified two potential drug series for sleeping sickness and one for leishmaniasis that will strengthen their research pipeline.

How does the MMV bring together academia and pharmaceutical companies? Could you provide some insight into your PDP model?

Although the specific objectives of individual PDPs vary, they all share a basic mission: to work with partners and develop medical products as a public good that will address the health needs of underserved populations in the developing world.

As a ‘virtual’ pharmaceutical organisation, MMV contributes funding and expertise, but rather than establishing facilities from scratch, we draw on existing laboratories, technologies and know-how from partner organisations. The value of this input from pharmaceutical partners exceeds the funding received from our donors, sometimes even tripling the value – making this approach incredibly cost-effective. The PDP model also offers a strategic overview of the entire antimalarial pipeline. This means that we can prioritise effectively, avoid replication of effort and benefit from the capabilities of others.
Project of the Year Award

• The Medicines for Malaria Venture (MMV) Project of the Year award recognises the most exciting drug discovery and development projects in the MMV portfolio.

• The 2012 winner was a novel antimalarial compound from the aminopyridine class called MMV390048.

• This chemical series was initially identified by Griffith University scientists in Australia as part of MMV’s extensive malaria screening campaign of around 6 million compounds.

• A team of scientists from the University of Cape Town, led by Professor Kelly Chibale, further explored the antimalarial potential of the series, and in July 2012, this compound was selected for preclinical development.

• It shows potent activity against multiple developmental stages of the malaria parasite’s life cycle, with potential for transmission blocking. The compound is currently undergoing safety studies in preparation for Phase I trials in early 2014.

• The 2013 Project of the Year will be announced at the next stakeholders’ meeting.

MMV supports the ‘Fight the Fakes’ campaign, which aims to raise awareness of the dangers of false antimalarials. How serious is this problem, and how can false medications be eradicated?

Fake drugs can not only endanger the lives of patients but also undermine entire public health initiatives. A significant proportion of drugs in the market are fake and we believe that if those drugs were removed we could save more lives.

MMV strongly believes that all malaria patients, rich or poor, deserve the best and safest treatment possible. All new antimalarial medicines co-developed by MMV must meet high international standards. MMV-supported drugs are developed to the highest clinical and manufacturing standards, and meet stringent regulatory approval and/or WHO prequalification. We are, therefore, firmly against fake drugs and support any activity that aims to reduce their presence and eliminate them altogether. The only way to vanquish this public health threat is by ensuring coordination among all actors involved in the approval, manufacturing and distribution of medicines, as well as by tightening and implementing national regulations and enforcement measures.

12 million vials of artesunate, a life-saving medicine, have been delivered thanks to the work of the MMV. Is there any other achievement which you have been involved in of which you are particularly proud?

I am most proud of our focus on children. Although this vulnerable population is disproportionately affected by malaria, it is often neglected in terms of having appropriate and palatable medicines. MMV and its partners have changed that. Since 2009, over 200 million treatments of a sweet-tasting dispersible formulation of the antimalarial Coartem, developed with our partner Novartis, have been delivered to 50 malaria-endemic countries, and countless children have been treated and cured by this medicine.

MMV has the largest-ever antimalarial drug portfolio. How do you decide which projects to include in the portfolio, and how is the MMV working to reduce clinical development costs?

MMV works within the framework built by WHO’s Global Malaria Programme and the objectives of our respective donors. We work with our partners to define profiles for the candidate drugs we seek to develop and jointly agree on the criteria used to select medicines that are worthy of progressing into clinical studies. We utilise standard assays to evaluate different compounds from our various collaborations, encouraging unprecedented pre-competitive collaboration between pharmaceutical companies, wherein they screen one another’s compounds and pass on the most promising ones to MMV. An independent Expert Scientific Advisory Committee comprising renowned scientists from across the world annually review MMVs drug projects as well as data emerging from the assays to ensure transparent progression and selection of the most promising compounds.

The time taken to develop a new medicine and make it available to those who desperately need it is as important a factor as how much it costs. We therefore spend some time understanding how our drug development candidates work, how quickly they kill the malaria parasites and which doses will be most effective. This is exemplified by novel approaches such as the Human Challenge Model, developed in collaboration with Professor James McCarthy at the Queensland Institute of Medical Research, Brisbane, Australia, which tests candidate molecules in healthy volunteers inoculated with minute amounts of the malaria parasite under very controlled conditions, without putting patients at risk. The aggregated raw data are then used to make predictions about the optimal dose and how a compound will behave in patients. This approach can help accelerate the drug development process by several years and help us to generate more data in less time and at lower development costs.

Could you provide some insight into the medicines you currently have in development?

MMV is working to develop medicines for key unmet medical needs in the field of malaria. This includes appropriate medicines suitable for the broadest use across populations affected by malaria, including children, pregnant women and patients suffering from severe malaria. We are also working towards ‘medicines of tomorrow’: simple, easy-to-take, ideally single-dose formulations with characteristics that can overcome resistance and cure all forms of malaria in the body.

MMV’s project portfolio has made significant progress. Six medicines are currently in clinical development with our partners, covering a number of these target attributes. These molecules could become part of the next-generation medicines to cure malaria in a single dose and revolutionise the treatment landscape.

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