MMV at a Glance

10th ANNIVERSARY

10 years of successful malaria drug research

Medicines for Malaria Venture is a not-for-profit organization dedicated to reducing the burden of malaria in disease-endemic countries by discovering, developing and facilitating delivery of new, high-quality, affordable antimalarial drugs through public–private partnerships. Our vision is a world in which these innovative medicines will cure and protect the vulnerable and under-served populations at risk of malaria, and help to ultimately eradicate this terrible disease.

In 1999, MMV was a pioneering newcomer to the world of antimalarial drug research. More people were dying from malaria than ever before. The malaria parasite had become resistant to widely-used drugs, including two inexpensive medications, chloroquine and sulphadoxine-pyrimethamine (SP). In addition, due to cost, poor health systems, inadequate distribution networks and policy challenges, existing drugs were too often not reaching malaria's main victims, the rural poor and in particular, children. New medicines were desperately needed as malaria continued to afflict and take the lives of countless millions across the world.

While the antimalarial market is huge in terms of those in need, it is small in terms of profit. By 1999, this had led to a virtually empty pipeline of new antimalarial drugs. Motivated by this glaring inequity, and the need to act in the face of a projected public health disaster fueled by escalating drug resistance, a group of dedicated organizations launched MMV. It started out modestly with only USD 4 million in seed finance and three early-stage projects in its portfolio. However, MMV was already brimming with ambition.

MMV aspired to discover and develop at least one new safe, effective and affordable antimalarial drug before the end of 2010. Not just any drug but one that met the highest standards – as validated by the world's most stringent regulators. Today, in our 10th year, MMV has exceeded its initial goal, with one artemisinin combination therapy (ACT), especially formulated for children, already launched and two further ACTs being prepared for launch; "In this respect, MMV must be considered a success[1]".

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Although heartened by the milestones reached along the challenging path towards eradication, MMV recognizes the obstacles ahead. Not least of these is the need to ensure that the products emerging from the R&D pipeline reach those who need them most. In response to this need, in 2006, a deliver component was added to MMV's well-established discover and develop core functions. MMV is now working with its partners to ensure that its products, starting with Coartem® Dispersible, swiftly reach patients and have the much needed health impact.

With the largest-ever pipeline of antimalarials in development, MMV is set to discover, develop and deliver further new medicines to tackle the malaria parasite from all sides. These medicines will be an essential component of our global multi-pronged attack to ultimately eradicate malaria once and for all. ■

1. Global Program Review on MMV, Independent Evaluation Group, The World Bank, May 2007.

Curing Malaria Together

Medicines for Malaria Venture

R&D partnership model

MMV has nurtured and developed productive partnerships with clinicians and scientists from both the public and private sectors. The strength of this public–private partnership model and rigorous portfolio management make MMV a highly cost-effective and productive research and development (R&D) organization. The success of this operational model creates a virtuous circle that brings in new donors and stakeholders.

Today, MMV works in partnership with more than 80 research institutions and companies across the world. Each partner brings expertise, enabling technologies and research facilities. Funding from private foundations and governments is used to leverage further private sector assets.

MMV has created the largest, most successful and diverse portfolio of antimalarial drug discovery and development projects in history. After 10 years of dedication to our initial goals, the products of the MMV R&D pipeline are now emerging – with the launch of one new ACT especially formulated for children in early 2009, a second submitted for stringent regulatory approval and a third now being prepared for submission. Furthermore, our pipeline contains at least 19 completely new classes of compounds.

Apart from innovative individual projects, efficient mini-portfolios enable us to leverage cutting-edge technology that can accelerate the discovery of new compounds effective against the malaria parasite.

Meticulous selection processes are coupled with support for the most promising candidates and quick termination of those that miss milestones or do not meet MMV's demanding product profiles.

This industry-style portfolio management is not easy to execute but is essential if MMV's growing R&D expenditure is to be aligned effectively to its highly-focused mission.

MMV firmly believes in developing medicines to international standards and in being transparent and accountable. All of MMV's clinical development projects are conducted to ICH[2] guidelines and clinical trials conducted in malaria-endemic countries meet GCP standards and adhere to national regulations. ■

2. International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use

A world without malaria

A future without malaria is possible and MMV is playing a leading role in making it happen.

Elimination and eradication of malaria are now at the top of MMV's agenda. With this in mind, both innovation and the increased and combined use of the best existing tools are essential if we are to achieve our goal – banishing the world's deadliest parasite to the history books forever.

We have reprioritized our research accordingly and are now placing greater emphasis on the urgent need to fill MMV's portfolio with promising, wholly new compounds that could be developed into highly effective drugs to treat malaria. We are working with our partners to research and develop compounds that not only treat *Plasmodium falciparum* but also *Plasmodium vivax*. In addition, we are working to develop treatment tailored to the needs of vulnerable groups, such as children and pregnant women, as well as medicines to tackle emerging resistance and stop malaria transmission.

We have also increased our work in access and delivery (see p. 5) to ensure that effective ACTs are available to the poorest populations in malaria-endemic countries. ■

Malaria costs lives

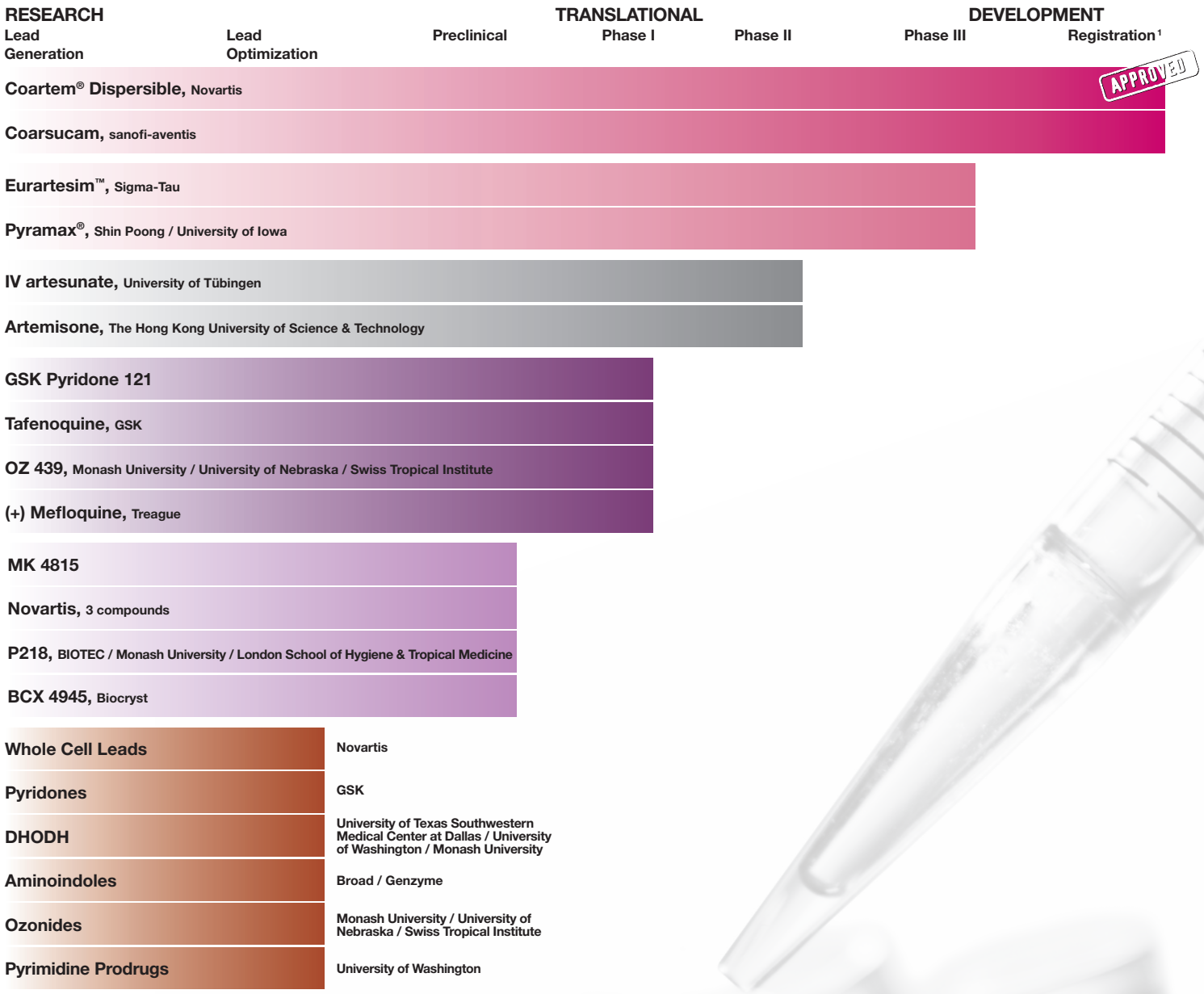
- A child dies from malaria every 30 seconds
- Almost 1 million people die each year
- 91% of those who die are from Africa
- 85% of those who die are children under 5
- An acute infection can kill a child within 48 hours
- Over 250 million cases of malaria occur annually
- Around 3.3 billion people are at risk – mostly in the poorest countries
- Malaria costs Africa USD 12 billion in lost GDP every year
- It accounts for 40 % of all public health spending in Africa
- Malaria is present in 109 countries around the world

MMV Project Portfolio – 2nd Quarter 2009

MMV's target is a one-dose cure for malaria

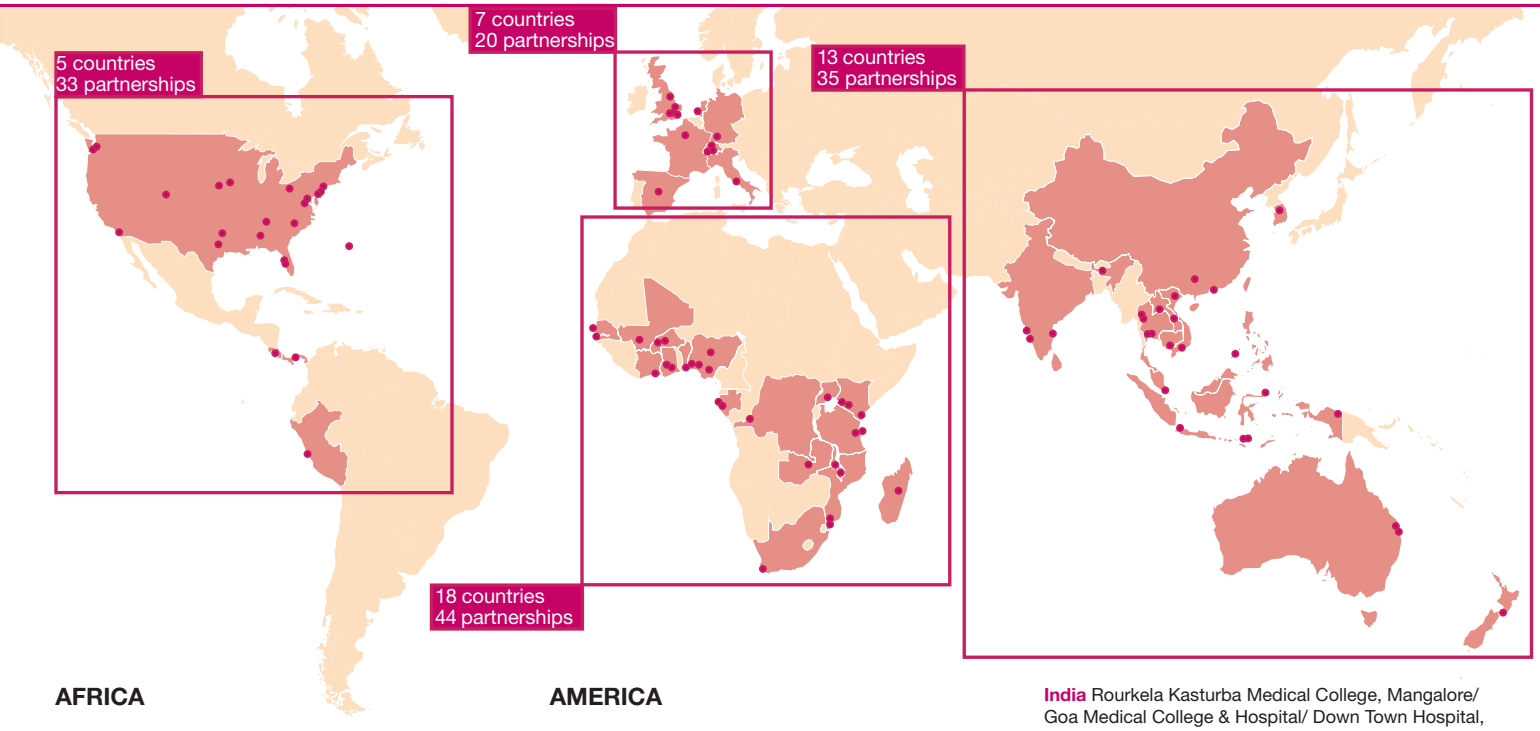
MMV's portfolio focuses on delivering efficacious medicines that are affordable, accessible and appropriate for use in malaria-endemic areas. Specifically, the goal is to develop products that will provide:

- Efficacy against drug–resistant strains of *Plasmodium falciparum*
- Potential for intermittent treatments (infants and pregnancy)
- Safety in small children (< 6 months old)
- Safety in pregnancy
- Efficacy against *Plasmodium vivax* (including radical cure)
- Efficacy against severe malaria
- Transmission-blocking treatment



[1] With stringent international regulatory authority

Working in Partnership



AFRICA

Benin Centre de Recherche Entomologique de Cotonou
Burkina Faso IRSS-DRO Centre Muraz, Bobo-Dioulasso/ Centre National de Recherche et de formation sur le Paludisme, Ouagadougou/ Nanoro Medical Centre, Ouagadougou
Democratic Republic of the Congo Université de Kinshasa, Ecole de Santé Publique
Gabon Université des Sciences de la Santé, Libreville/ Albert Schweitzer Hospital, Lambaréné
Ghana Kintampo Health Research Centre, Kintampo/ Komfo Anokye Teaching Hospital, Kumasi
Ivory Coast Institut Pasteur, Abidjan
Kenya Moi University, Eldoret/ Kenya Medical Research Institute/ Wellcome Trust Collaborative Centre, Kifili/ Centre for Clinical Research – Kenya Medical Research Institute, Kisumu – Malaria Branch Centre for Disease and Control and Prevention, Kisumu/ University of Nairobi Institute of Tropical & Infectious Diseases, Nairobi/ Siaya District Hospital, Siaya/ The Steadman Group, Nairobi
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Malawi Queen Elizabeth Central Hospital, Blantyre/ Ministry of Health and College of Medicine, Lilongwe
Mali University of Bamako, Malaria Research and Training Centre, Bamako
Mozambique Instituto Nacional de Saúde, Maputo/ Manhiça Research Centre, Maputo
Nigeria University of Calabar Teaching Hospital, Calabar/ University of Nigeria, Enugu/ University of Ibadan, Ibadan/ Obafemi Awolowo University Teaching Hospital, Ile-Ife/ Plateau State Specialist Hospital, Jos/ Jos University Teaching Hospital, Jos/ Lagos State University Teaching Hospital, Lagos
Senegal University Cheikh Anta Diop/ Université Cheikh Anta Diop, Laboratoire de Bactériologie Virologie/ Ministry of Health and National Malaria Control Program
South Africa University of Cape Town
Tanzania DIfakara Health Institute, Bagamoyo/ Malaria Research Unit of the Karolinska Institute, Zanzibar
The Gambia MRC Laboratories, Fajara
Uganda Epicentre – Médecins Sans Frontières, Mbarara/ Surgipharm, Kampala/ Uganda Ministry of Health and National Malaria Control Program/ National Drug Authority, Kampala/ Program for Accessible Health Communication and Education (formally PSI), Kampala
Zambia Tropical Diseases Research Centre, Ndola

AMERICA

Bermuda Novartis International Pharmaceutical, Hamilton
Costa Rica National Biodiversity Institute (INBio), Santo Domingo de Heredia
Panama Instituto Conmemorativo Gorgas de Estudios de la Salud, Panama
Peru Asociación Benéfica PRISMA, Lima
United States BioCryst Pharmaceuticals, Inc., Birmingham, AL/ Harvard Medical School, Biological Chemistry and Molecular Pharmacology, Boston, MA/ Harvard School of Public Health, Boston, MA/ Genzyme Corporation, Cambridge, MA/ The Broad Institute, Inc., Cambridge, MA/ Magellan Biosciences, Inc., Chelmsford, MA/ Texas AgriLife Research of the Texas A&M University System, College Station, TX/ University of Texas Southwestern Medical Center at Dallas, Dallas, TX/ Mycosynthetix, Inc., Hillsborough, NC/ University of Iowa, Iowa City, IA/ Geneva Foundation, Lakewood, WA/ St. Jude Children's Research Hospital, Memphis, TN/ Rutgers, The State University of New Jersey, New Brunswick, NJ/ Albert Einstein College of Medicine of Yeshiva University, New York, NY/ Clinton Foundation, New York, NY/ Columbia University, New York, NY/ University of Nebraska Medical Center, Omaha, NE/ Drexel University College of Medicine, Philadelphia, PA/ University of Pittsburgh, Pittsburgh, PA/ Oregon Health and Science University, Portland, OR/ Portland VA Research Foundation, Portland, OR/ North Carolina State University, Raleigh, NC/ Sanaria Inc., Rockville, MD/ Genomics Institute of the Novartis Research Foundation, San Diego, CA/ University of California, San Diego, CA/ Seattle Biomedical Research Institute, Seattle, WA/ University of Washington, Seattle, WA/ Walter Reed Army Institute of Research, Silver Spring, MD/ University of South Florida, Tampa, FL

ASIA & OCEANIA

Australia Eskitis Institute for Cell and Molecular Therapies, Griffith University, Brisbane, QLD/ Queensland Institute for Medical Research, Brisbane, QLD/ Australian Army Malaria Institute, Enoggera, QLD/ Monash University, Parkville, VIC
Cambodia Pailin Referral Hospital, Phnom Penh
China Guilin Pharmaceutical Co., Ltd., Guilin City
Hong Kong City University of Hong Kong, Kowloon/ Hong Kong University of Science and Technology, Kowloon
India Rourkela Kasturba Medical College, Mangalore/ Goa Medical College & Hospital/ Down Town Hospital, Guwahati
Indonesia Ministry of Health, Jakarta/ Jayapura General Hospital, Jayapura/ RSUD TC Hillers, Maumere/ Bethesda Hospital, Tomohon
Laos Phalanxay District Hospital, Phalanxay/ Xepon District Hospital, Xepon
New Zealand Industrial Research Limited, Lower Hut
Philippines Hospital of Palawan, Palawan
Singapore Novartis Institute for Tropical Diseases Pte Ltd, Singapore
South Korea Shin Poong Pharmaceutical Co. Limited, Seoul/ Eulji General Hospital, Seoul/ Ilsan Paik Hospital, Seoul/ Seoul National University, Seoul
Thailand Armed Forces Research Institute of Medical Sciences, Bangkok/ Mahidol University, Bangkok/ Mahidol–Oxford Tropical Medicine Research Unit, Bangkok/ Mae Sot Hospital, Bangkok/ Mae Ramat Hospital, Bangkok/ Mahidol University, Bangkok/ Thailand National Center for Genetic Engineering and Biotechnology, Pathumthani/ Suan Phung Hospital, Ratchaburi/ The Shoklo Malaria Research Unit, Shoklo
Vietnam National Institute of Malariology, Parasitology and Entomology, Hanoi/ Choray Hospital, Ho Chi Minh City

EUROPE

France Sanofi-aventis Recherche & Développement, Chilly-Mazarin/ Institut National de la Santé et de la Recherche Médicale (INSERM), Paris
Germany Universität Tübingen, Institut für Tropenmedizin, Tübingen
Italy Sigma-Tau Industrie Farmaceutiche Riunite S.p.A., Rome
Spain GlaxoSmithKline Investigacion y Desarrollo, S.L., Tres Cantos
Switzerland World Health Organization, Geneva/ TDR, Geneva/ The Global Fund to Fight AIDS, Tuberculosis and Malaria, Geneva/ Roll Back Malaria Partnership, Geneva/ Novartis Pharma AG, Basel/ Swiss Tropical Institute, Basel/ Drugs for Neglected Diseases Initiative, Geneva
The Netherlands Biomedical Primate Research Centre, Rijswijk/ i+solutions, Woerden
United Kingdom GlaxoSmithKline Research & Development Limited, Brentford/ Treague Ltd., Cambridge/ University of Dundee, Dundee, Scotland/ Glaxo Group Limited, Greenford, Middlesex/ Imperial College of Science, Technology and Medicine, London/ London School of Hygiene and Tropical Medicine

This list includes all the institutions, organizations and companies whom we are currently collaborating with in our science and access work, in addition to those with whom we have conducted clinical trials.

Ensuring access to MMV's medicines

In 2006, MMV broadened its original mission to include Access and Delivery in response to the recognition that our exclusive commitment to developing new innovative anti-malarials would not help reduce the global burden of malaria unless we also became involved in facilitating patients' access to them.

The challenges encountered in our work to assure access to antimalarials are numerous. They range from the frequency of artemisinin-based combination therapy (ACT) stock-outs in the public sector, due to weak procurement and distribution systems; the need to displace unaffordable, unsafe or untested drugs in the private sector; to the lack of market information to measure the impact of new therapies.

With the launch of Coartem® Dispersible in 2009 and two additional product launches expected in 2010 (Eurartesim™) and 2011 (Pyramax®), MMV's Access team is working with pharmaceutical partners, national health officials, and international funders and policy makers to assure broad access to these much-needed drugs.

MMV's Access work is based on a foundation of market intelligence and conducted in the spirit of our partnership model alongside national and international players. Information gleaned from numerous in-country sources is channelled into three main activities: supporting the adoption of effective antimalarials; extending their reach through public and private partners; and feeding information back from the field to shape MMV's future R&D agenda. With our partners, MMV works to do all that is required to achieve these goals so that ultimately new medicines reach endemic countries as quickly as possible and start saving lives. Specifically, this work involves:

- Providing requisite information on new therapies to be evaluated for inclusion in the WHO Standard Treatment Guidelines and the Model Essential Medicines List.
- Informing key decision makers, clinicians and patients about the importance of quality ACTs.
- Assuring correct, safe use of MMVs products through patient-friendly packaging, and effective education and training materials for healthcare professionals.
- Promoting the need for a confirmed diagnosis of malaria before treatment begins, thereby reducing inappropriate use.
- Making MMV's medicines more affordable for countries and for patients who purchase the drugs in the private sector.
- Making MMV's medicines more widely available through current and new channels of treatment delivery, including via community healthcare workers.
- Supporting efforts to strengthen pharmacovigilance systems that help monitor the safety of antimalarials used in the public sector.
- Rigorously measuring the reach and impact of MMV's drugs on patients from both urban and rural areas, in both public and private sectors.

Unfortunately, 60% of patients cannot access medicines via the public health system, and are forced to turn to the private sector. Accordingly, MMV supports initiatives to make medicines in the private sector more affordable. The Affordable Medicines Facility-malaria (AMFm) is the most significant effort to-date to develop an international subsidy mechanism that aims to dramatically reduce the cost of ACTs in malaria-endemic countries.

In September 2008, a year before the AMFm's anticipated roll-out, MMV and the Ministry of Health launched a pilot study in Uganda with the Consortium for ACT Private Sector Subsidy (CAPPS). The study was designed to demonstrate the rapid impact of subsidized quality ACTs on increasing uptake and displacing older, ineffective therapies as well as artemisinin monotherapy. The 6-month preliminary results of this trial have been promising. The study demonstrated that providing affordable ACTs through the private sector in combination with ACT awareness campaigns and appropriate dispenser training, has a dramatic impact.

Ultimately, increasing access to life-saving antimalarial treatments remains a multi-dimensional challenge, and MMV will work as closely as possible with decision-makers in malaria-endemic countries to help coordinate an efficient national response to malaria control. ■

Focus on Finances

Medicines for Malaria Venture receives funding and support from government agencies, private foundations, international organizations, corporations and corporate foundations. These funds are used to finance the MMV portfolio of R&D projects to provide and facilitate the delivery of new, effective and affordable medicines to treat malaria. Significant new funding commitments from the governments of Spain, UK Department for International Development and the Bill & Melinda Gates Foundation have augmented the amount of funds pledged to 2015, from USD 273 million to over USD 470 million. Since 1999 to the end of December 2008, MMV has spent USD 255 million building the largest-ever pipeline of antimalarial drugs.

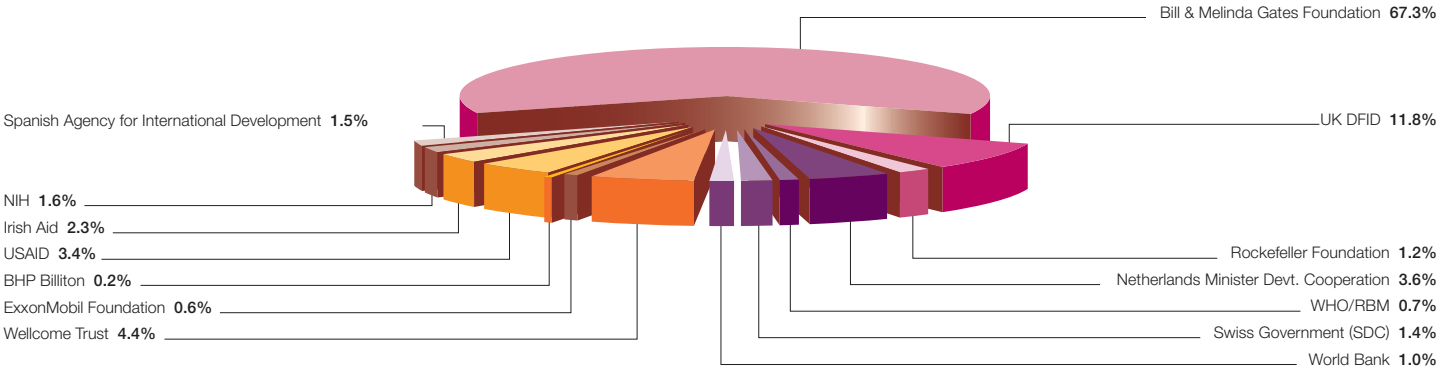

Figure 1 Funding from 2000–2015 as of 30 September 2009 – USD 470 million received and pledged

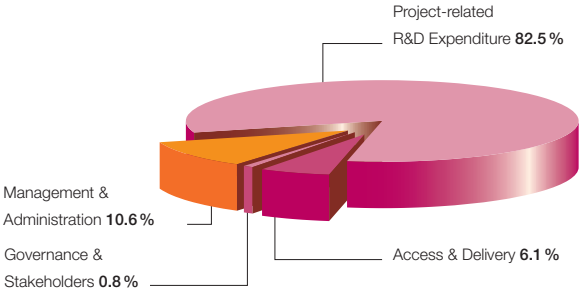

Figure 2 MMV Expenditure 2008
USD 55.8 million

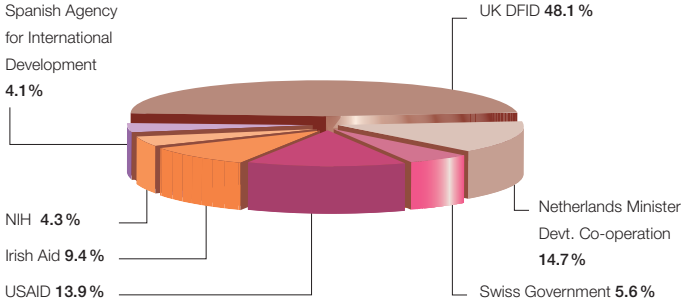

Figure 3 Funding from 7 Government Agencies
from 2000–2015 as of August 2009
USD 115 million received and pledged

Remarkably, in contrast to the subdued global economic environment, 2008 was a very successful financial year for MMV, which ensured sustained progress of the full R&D portfolio.

MMV's R&D expenditure increased by 11%, as did overall expenditure, which reached USD 55.8 million compared to USD 47.9 million in 2007. Also, encouragingly, the expenditure on recently implemented activities to facilitate Access & Delivery of MMV's new medicines more than doubled, from USD 1.6 million in 2007 to USD 3.4 million in 2008 (6.1% of total spending).

Nonetheless, cashflow issues faced by some donors in 2009 are now beginning to have an effect on MMV, as on other PDPs. In these turbulent financial times, MMV is actively striving to expand and develop current and new donor partnerships, solicit more in-kind input from pharmaceutical partners, negotiate better terms with CROs, universities and research institutes, and build networks. This also means dynamic management of cashflow against potential expenditures on a day-to-day basis in order to prioritize the principle needs over the 2009–2010 time period. ■

MMV Team
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