



> malaria endemic areas

## MMV Project of the Year 2002 Protein farnesyltransferase inhibitors (Pf-PFT): from novel concept to potent new leads

The MMV Project of the Year 2002 Award was presented to key Pf-PFT project team members Wesley Van Voorhis and Michael Gelb of the University of Washington (Seattle), Andrew Hamilton of Yale University, and David M. Floyd of Bristol-Myers Squibb (BMS) during MMV's 3<sup>rd</sup> Annual Stakeholders' Meeting on 18 May 2003.



Team members (above) with their awards on the World Economic Forum's terrace overlooking Lake Geneva. From left to right: Andrew Hamilton, Professor and Chair of Chemistry, Yale University; Wesley Van Voorhis, Professor of Medicine, and Michael Gelb, Departments of Chemistry and Biochemistry, University of Washington (Seattle); David M. Floyd, Vice-President, Bristol-Myers Squibb (BMS), USA

Since its introduction into the MMV portfolio in 2001, the protein farnesyltransferase inhibitors (Pf-PFT) project has moved from strength to strength, earning it MMV's Project of the Year 2002 Award. In its first year, the project advanced from "lead discovery" to "lead optimization", a process which normally takes two years. Experts consider the Pf-PFT protein to be a novel target for the development of new antimalarial drugs. Having scanned more than 300 compounds known to inhibit PFT, the project team now has compounds that show great promise for drug therapy for malaria (*On-line news, University of Washington School of Medicine, Vol. 7, Number 20, May 23, 2003*).

Wes Van Voorhis and Mike Gelb of the University of Washington (Seattle) summed up reasons for the project's rapid progress in its first year:

- ▶ The availability of the *P. falciparum* genome as a facilitator of drug research and development
- ▶ "Piggy-backing" on the human-PFT inhibitors that Bristol-Myers Squibb (BMS) is developing for cancer chemotherapy
- ▶ Strong collaboration between private sector and academia
- ▶ Expert advice from MMV staff and Expert Scientific Advisory Committee (ESAC), and MMV funding.



**Mike Gelb** (left) presents background on the Pf-PFT project to MMV stakeholders during the 18 May meeting

**Wes Van Voorhis** (right) explains how the Pf-PFT project was able to rapidly develop from a novel concept to potent new leads

## Content

Cover page and inside

MMV Project of the Year 2002

2 World Economic Forum hosts MMV's 3<sup>rd</sup> Annual Stakeholders' Meeting

3 Transition: from Roche to Ranbaxy, from discovery to development  
Latest on the synthetic peroxide project

4 New partnership to fight malaria: GlaxoSmithKline and MMV announce agreement

New projects in MMV's portfolio

5 News...views

Back page

6 MMV stakeholders and friends meet in Geneva for an annual gathering

## World Economic Forum hosts MMV's 3<sup>rd</sup> Annual Stakeholders' Meeting

On 18 May 2003 in Geneva, José María Figueres, Senior Managing Director, World Economic Forum, warmly welcomed MMV stakeholders and friends to Forum headquarters, graciously made available to MMV for the occasion. Figueres, former President of Costa Rica, made pertinent reference to his struggles as President with the re-emergence of malaria in his home country in the mid-90s, and to the nationwide malaria control efforts he personally led. He congratulated MMV on its important work and hoped that MMV's relationship with the Forum would continue to strengthen.



1

Presentations by Chris Hentschel, MMV Chief Executive Officer, and Peter Potter-Lesage, MMV Chief Financial Officer, focused respectively on the "MMV business plan update" and "sustainable financing", and were followed by an update on MMV's portfolio by J Carl Craft, MMV Chief Scientific Officer.

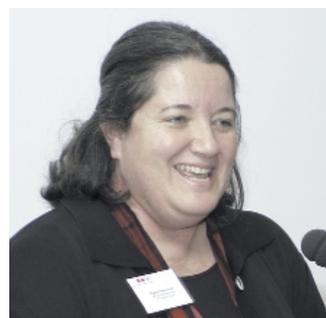
Regina Rabinovich, Director, Infectious Disease Program, Bill and Melinda Gates Foundation, the first ever representative from the Foundation to attend an MMV Stakeholders' Meeting, spoke on the important role groups such as MMV play in the fight against malaria.

The highlight of the day was the presentation of the Project of the Year 2002 Award to the Pf-PFT team by José María Figueres and Dame Bridget Ogilvie, Chair of the MMV Board (*see page 1*).

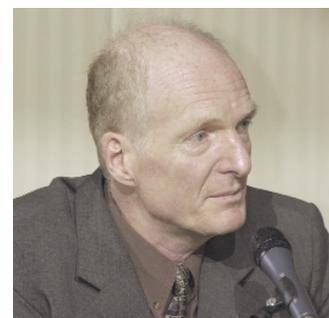
The handover from leading healthcare group Roche to Ranbaxy, India's largest pharmaceutical company, for further development of selected compounds resulting from MMV's synthetic peroxide project followed (*see page 3*).

Kate Taylor, Associate Director, Global Health Initiative (GHI), World Economic Forum, and Fatoumata Nafo-Traoré, Executive Secretary, Roll Back Malaria (RBM) Partnership Secretariat, World Health Organization, addressed the gathered participants. Both emphasized the mutual benefit of continued collaboration between MMV and their respective organizations.

Representation and significant input from many of MMV's major donors and friends, linked with the lovely setting of the World Economic Forum's headquarters, contributed to the meeting's success. MMV thanks all participants for giving up their weekend to attend what, for MMV, is its most important event each year.



2



3

**1. José María Figueres**, Senior Managing Director, World Economic Forum and former President of Costa Rica, gave a moving welcome to participants before presenting the Project of the Year Award to the Pf-PFT team

**2. Regina Rabinovich**, Director, Infectious Disease Program, Bill and Melinda Gates Foundation, delivers a message to MMV stakeholders on behalf of the Gates Foundation, one of MMV's major donors

**3. Nick White**, Chairman, Wellcome Trust SE Asian Tropical Medicine Research Units, Thailand, opened the MMV Stakeholders' Meeting on the evening of 17 May with a tongue-in-cheek, yet sobering look at "Malaria treatment – past mistakes, present opportunities". Dame Bridget Ogilvie, Chair of MMV's Board, introduced Nick White as one of her "oldest friends in malaria", from her days at the Wellcome Trust, where she ultimately served as Director. She commended him as "Mr Clinical Malaria" for his fieldwork since 1980 in clinical malaria, and for having elected to stay in SE Asia doing this crucial and important work.

# Transition: from Roche to Ranbaxy, from discovery to development

## Latest on the synthetic peroxide project

In the presence of MMV board members and stakeholders on 18 May 2003, F. Hoffmann-La Roche Ltd, a leading health-care group, handed over the role of main pharmaceutical partner with MMV's synthetic peroxide project to Ranbaxy Laboratories Ltd, India's largest pharmaceutical company. René Imhof, Head of Pharma Research at Roche Basel, Switzerland, symbolically "passed the baton" to Rashmi Barbhuiya, Ranbaxy's President of R&D, who took up the challenge: "Trust me, we are going to run as fast as we can and we are going to reach the finish line first."

The synthetic peroxide or OZ project has now advanced to the point where a new antimalarial compound can be proposed for further technical and clinical development. Based on Ranbaxy's R&D strengths in process chemistry, formulation development and other preclinical expertise, strong regulatory submission capabilities and cost-effectiveness, MMV's management team elected to partner with the Indian company to move the project to its next stages.

The OZ project, which was MMV's Project of the Year 2001, is one of the key projects in MMV's portfolio. The project team includes leading scientists from the University of Nebraska Medical Center, Monash University, the Swiss Tropical Institute (STI),



**René Imhof**, Head of Pharma Research, F. Hoffmann-La Roche Ltd, Switzerland and **Rashmi Barbhuiya**, President of R&D, Ranbaxy Laboratories Ltd, India, hold the baton symbolizing the handover to Ranbaxy for large-scale development of the OZ compounds

Roche, and now Ranbaxy. Ranbaxy's coming on board has not precluded Roche's continued support in ongoing preclinical evaluation and generation of OZ back-up compounds.

The "handover" was held at the World Economic Forum headquarters in Geneva, Switzerland. The story made the front page of the Wall Street Journal Europe on 19 May 2003. Full press release and selected press clippings are available at [www.mmv.org](http://www.mmv.org)

### MMV Project of the Year 2002 *(continued from page 1)*

In his presentation to stakeholders, Mike Gelb gave MMV kudos for its ability to not only foster projects but to terminate them when a dead end is reached, something which happens rarely in the academic world. He cited MMV's ESAC as a key force in getting the academic members of teams to "listen" and even admit that academics "don't really understand how to make a drug". Gelb also said that ESAC, which includes a number of people who have made drugs for a living, acted as the catalyst that pushed their project forward in the right direction.

“

**We always talk about how this is going to be hard to pull off...but this experience with MMV has been genuinely optimistic.**

”

*Mike Gelb, University of Washington (Seattle) addressing MMV stakeholders*

Solomon Nwaka, MMV Scientific Officer managing the project said, "This is a good project, a good team, a good partnership. It exemplifies how the MMV approach can facilitate development of new drugs for diseases of the poor". For more information on this project and to read the full press release, visit [www.mmv.org](http://www.mmv.org)

**Congratulations to the entire Pf-PFT project team:** University of Washington (Wes Van Voorhis, Mike Gelb, Pravin Bendale, Kohei Yokoyama, Laxman Nahlen, Kasey Rivas, Kevin Bauer, Fred Buckner, Christophe Verlinde); BMS (David Floyd, David Williams, Lou Lombardo); Yale University (Andy Hamilton, Erin Pusateri, Dora Carrico, Jeff Lockman, Zheng Zang); University of South Florida (Said Sebti); University of Central Florida (Debopam Chakrabarti, Shelly Patterson); Paragon Biomed (Marie Hanley); MMV (Solomon Nwaka, J Carl Craft).

# New partnership to fight malaria: GlaxoSmithKline and MMV announce agreement

On 13 June 2003 at the World Economic Forum's Africa Economic Summit in Durban, South Africa, MMV and GlaxoSmithKline (GSK) announced a strengthening in the collaboration between the two organizations, aimed at finding new treatments for malaria in the third world.

A portfolio of projects will be jointly managed by MMV and GSK, with GSK contributing funding, expertise in malaria drug discovery, and state-of-the-art facilities, in particular at its drug discovery unit in Tres Cantos, Spain.

MMV will fund the malaria drug discovery projects by subsidizing employment of additional scientists to join existing staff at Tres Cantos, and will provide expertise from its Expert Scientific Advisory Committee (ESAC) and MMV staff.

## Projects in the joint GSK/MMV portfolio

- **Falcipains** (*MMV project since 2001*)  
**Principal organizations:** University of California, San Francisco, USA; GSK in Tres Cantos, Spain and Philadelphia, USA.  
**Summary:** ongoing proof of concept studies in rodents will help to identify compounds for further testing and eventual entry into preclinical development; potential for a totally new antimalarial drug.  
**Public health impact:** new pharmacophore\* to treat malaria  
**Contact at MMV:** Solomon Nwaka  
nwakas@mmv.org
- **4(1H)-Pyridones** (*MMV project since 2003*)  
(see below)

## Following the ESAC meeting in March 2003, MMV has integrated the following projects into its portfolio:

- **Glyceraldehyde-3-phosphate dehydrogenase (GAPDH)**  
**Principal investigators/organizations:**  
Gerd Pluschke, Swiss Tropical Institute (STI), Switzerland  
Hugues Matile, F. Hoffmann-La Roche, Switzerland  
**Summary:** an exploratory project with an important new target for malaria drug development, which could lead to a totally new drug.  
**Public health impact:** could provide a new pharmacophore  
**Contact at MMV:** Solomon Nwaka  
nwakas@mmv.org
- **4(1H)-Pyridones**  
**Principal investigators/organizations:**  
Federico Gomez de las Heras, GlaxoSmithKline, Tres Cantos, Spain  
**Summary:** selective inhibitors of mitochondrial function. Most rapidly moving chemistry programme in GSK/MMV joint portfolio. Expect to have a candidate for development in 12 to 18 months.  
**Public health impact:** new class active against atovaquone-resistant *P. falciparum*  
**Contact at MMV:** Solomon Nwaka  
nwakas@mmv.org
- **DB289 – Phase II**  
**Principal investigators/organizations:**  
Richard R. Tidwell, University of North Carolina at Chapel Hill, USA (*in collaboration with Georgia State University, USA*)  
James Allen, Immtech International, USA  
Reto Brun, Swiss Tropical Institute (STI), Switzerland  
**Summary:** proof of concept trial which, if successful, will provide the first new malaria drug within this class of compound. Can also be successful if it validates follow-on discovery project.  
**Public health impact:** could provide a new pharmacophore  
**Contact at MMV:** Lise Riopel  
riopell@mmv.org
- **New dicationic molecules**  
**Principal investigators/organizations:**  
Richard R. Tidwell, University of North Carolina at Chapel Hill, USA (*in collaboration with Georgia State University, USA*)  
James Allen, Immtech International, USA  
Reto Brun, Swiss Tropical Institute (STI), Switzerland  
**Summary:** novel and more potent follow-up for DB289  
**Public health impact:** new pharmacophore to treat malaria  
**Contact at MMV:** Solomon Nwaka  
nwakas@mmv.org

\*pharmacophore - the group of atoms in a drug molecule which is responsible for the action of the compound.

# news...views...news...views...news...views...news...

## Malaria, the mostly forgotten killer

BusinessWeek Online Asia spoke with Dame Bridget Ogilvie, Chair of MMV's Board, during her recent trip to India. Highlighting the disproportionate reaction of the western world recently to the SARS outbreak, Dame Bridget reflected, "I understand that people are afraid of SARS...because it affects you and me," but "the people who have malaria have no money", and those of us fortunate enough to live outside malaria-endemic areas have largely forgotten the toll malaria takes.

Worldwide research on malaria last year amounted to just US\$100 million, a tiny amount compared to the vast sums spent on "higher profile" illnesses. As malaria has little pull for researchers, the article noted that MMV is "trying to exert some push", as evidenced by the 15 projects now in its pipeline, supported in large part by the Bill and Melinda Gates Foundation and western governments (from "Malaria, the Mostly Forgotten Killer," by Bruce Einhorn, BusinessWeek Online Asia, June 9, 2003). Full article at [www.mmv.org](http://www.mmv.org)

## Interest in malaria, it's catching

In summer 2002, MMV had the pleasure to welcome Megumi Itoh, a senior majoring in molecular biology at Princeton University, as an intern in its Geneva offices. MMV Board Member Leon Rosenberg, a professor at Princeton, recommended Meg. At MMV Meg created product profiles for all known antimalarials. Back at Princeton, Meg chose to focus her Bachelor of Arts thesis on medicines for malaria. "Medicines for Malaria: New Scientific and Policy Directions for Antimalarial Drug Development" highlights MMV's projects and dedicates an entire chapter to MMV, describing how MMV got started, its drug R&D process, and its success as well as challenges for the future. Many thanks to Meg and best wishes to her for the future.

## What do you know about malaria?

Caroline Loviat, a Swiss communications student at Polycom in Lausanne, Switzerland, was with MMV as an intern from March to June 2003. Caroline put together a survey which she distributed to English and French-speaking NGOs to determine how much they knew about MMV and malaria. Almost 45% of those surveyed had heard of MMV and nearly 72% of respondents had actually suffered or had a family member who had suffered from malaria. Many thanks to all those who responded, and to Caroline for her initiative and hard work at MMV.

## Dame Bridget Ogilvie, FRS

On 15 May 2003, the Royal Society (UK) named new Fellows and Foreign Members from the fields of science, engineering and technology. MMV was proud to have the Chair of its Board, Dame Bridget Ogilvie elected as a Fellow of the Royal Society. Fellows are elected for their contributions to science, both in fundamental research resulting in greater understanding, and in leading and directing scientific and technological progress in industry and research establishments. Congratulations Bridget!

## The Wider Context

► [swissinfo](http://www.swissinfo.org) ([www.swissinfo.org](http://www.swissinfo.org)), a Swiss news and information platform, published 13 on-line articles on malaria in April/May 2003. Interest generated by these articles lead [swissinfo](http://www.swissinfo.org) to produce an entire website in English dedicated to malaria entitled "**The Malaria Business**". You can find this informative website at <http://www.swissinfo.org/sen/Swissinfo.html?siteSect=670>

► The World Health Organization (WHO) and the United Nations Children's Fund (UNICEF) released the first ever **Africa Malaria Report 2003** on Africa Malaria Day (25 April). The report gives a continent-wide picture of the struggle against malaria, highlighting the urgent need to make effective antimalarial treatment available to those most at risk. The Africa Malaria Report 2003 is available on-line at [http://www.rbm.who.int/amd2003/amr2003/amr\\_toc.htm](http://www.rbm.who.int/amd2003/amr2003/amr_toc.htm)

► "**Valuing Industry Contributions to Public-Private Partnerships for Health Product Development**" by Hannah Kettler and Karen White in consultation with Scott Jordan, was published in April 2003 by the Initiative on Public-Private Partnerships for Health (IPPPH), Global Forum for Health Research. This important paper evaluates "contributions that private industry has made – both compensated and 'in-kind' – to public-private partnerships (PPPs) involved in the development of new treatments for diseases prevalent in the developing world" (p. 1), including malaria. The authors explain the ins and outs of transactions and provide case studies of partnerships between the pharmaceutical and biotech industries, and the nonprofit and public sectors, to develop needed drugs, vaccines, and other health products for poor countries. Copies of the paper are available free of charge from IPPPH at [info@ippph.org](mailto:info@ippph.org)

► Médecins Sans Frontières (MSF) Access to Essential Medicines Campaign's brochure **ACT NOW to get malaria treatment that works to Africa**, published in April 2003, is MSF's proposal for immediate action to tackle the malaria problem in Africa. Their argument hinges on artemisinin-based combination therapy (ACT) as "the prescription for Africa" (p. 10), citing ACT as the "only current option" (p. 16). MSF has decided to implement artemisinin-based combination therapy for first-line treatment of all its malaria patients by the end of 2003. The ACT NOW brochure is available on-line at <http://www.accessmed-msf.org/>

► Dr Solomon Nwaka, MMV Scientific Officer, gave a presentation about malaria and MMV at a press conference in New York on 26 June 2003 when Pfizer announced a **potential new malaria treatment**. MMV is in very early-stage discussions with Pfizer on possible collaboration.

The above links can also be accessed at [www.mmv.org](http://www.mmv.org) on the MMVnews page.

# MMV stakeholders and friends meet in Geneva for annual gathering



1



5



2



6



3

> 1  
Project of the Year 2002 team leaders Mike Gelb and Wes Van Voorhis of the University of Washington (Seattle) holding their award, with Dame Bridget Ogilvie, Chair of MMV's Board, and José María Figueres, Senior Managing Director, World Economic Forum

> 2  
Solomon Nwaka (*far left*), MMV Scientific Officer, and Simon Campbell (*far right*), founding Chair of MMV's Expert Scientific Advisory Committee, celebrate with the Pf-PFT Project of the Year team (*middle*)

> 3  
Melinda Moree, Executive Director, Malaria Vaccine Initiative, with MMV Board Member Francis Nkrumah, and Regina Rabinovich, Director, Infectious Disease Program, Bill and Melinda Gates Foundation

> 4  
MMV Scientific Officer Lise Riopel with Allan Schapira, Coordinator, Strategy and Operations, Roll Back Malaria (RBM), World Health Organization; David Alnwick, Director, Malaria Control Department, World Health Organization, and Hugues Matile, F. Hoffmann-La Roche Ltd

> 5  
David Ubben, MMV Scientific Officer, talks with Brian Greenwood, Director, Gates Malaria Partnership, and Professor, London School of Hygiene and Tropical Medicine

> 6  
Henk Schallig, Research Coordinator of Parasitology, Royal Tropical Institute (KIT), The Netherlands, with MMV Board Members Trevor Jones and Enriqueta Bond



4

## The following organizations were represented at the MMV Stakeholders' Meeting on 17/18 May 2003:

Bill and Melinda Gates Foundation; Mailman School of Public Health, Columbia University; DNDi (Drugs for Neglected Diseases Initiative); ExxonMobil Corporation; Films of Record Ltd; Foundation for Innovative New Diagnostics (FIND); Foundation Strategy Group; GlaxoSmithKline Pharma; Initiative on Public-Private Partnerships for Health (IPPPH); London School of Hygiene and Tropical Medicine; Wellcome Trust SE Asian Tropical Medicine Research Units; Malaria Vaccine Initiative (MVI); Management Sciences for Health (MSH)

Europe; Royal Tropical Institute (KIT), The Netherlands; Ministry of Foreign Affairs, The Netherlands; Ranbaxy Laboratories Ltd; F. Hoffmann-La Roche Ltd; Bio-Partnerships for Global Health; Sidley, Austin, Brown & Wood LLP; Swiss Agency for Development and Cooperation; World Economic Forum; Malaria Control Department, World Health Organization; External Relations and Governing Bodies, World Health Organization; Special Programme for Research and Training in Tropical Diseases (TDR), World Health Organization; Roll Back Malaria (RBM) Partnership, World Health Organization; World Intellectual Property Organization (WIPO).

Medicines for Malaria Venture (MMV) is a nonprofit foundation created to discover, develop and deliver new affordable anti-malarial drugs through effective public-private partnerships. Our vision is a world in which affordable drugs will help eliminate the devastating effects of malaria and help protect the children, pregnant women, and vulnerable workers of developing countries from this terrible disease.

MMVnews is published by the Medicines for Malaria Venture (MMV).

Subscriptions to MMVnews are free. Please direct inquiries to :

Medicines for Malaria Venture  
International Centre Cointrin  
Route de Pré-Bois 20  
PO Box 1826  
1215 Geneva 15  
Switzerland  
Tel. +41 22 799 4060  
Fax +41 22 799 4061  
www.mmv.org  
e-mail: communications@mmv.org

## MMV TEAM

**Chief Executive Officer**  
*Chris Hentschel*  
**Chief Scientific Officer**  
*J Carl Craft*  
**Scientific Officers**  
*Solomon Nwaka*  
*Lise Riopel*  
*David Ubben*  
**Chief Financial Officer**  
*Peter Potter-Lesage*  
**Director, International Operations**  
*P V Venugopal*  
**Human Resources and Administration Manager**  
*Diana Cotran*  
**Assistant to the CEO/Newsletter and Website Coordinator**  
*Erin Kimaoui*  
**Scientific Team Administration**  
*Marion Hutt*

© 2003 Medicines for Malaria Venture  
All rights reserved  
Photo credits: Thomas Hensinger



Medicines for Malaria Venture