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New Findings In Malaria Vaccine Development Announced At International Malaria Conference

ARUSHA, TANZANIA (19 November 2002) – The largest and most comprehensive malaria conference in the world, the Third Pan-African Malaria Conference of the Multilateral Initiative on Malaria (MIM), opened here Sunday. Organized by the Fogarty International Center of the U.S. National Institutes of Health, the conference brings together over 900 malaria research and control experts from across Africa and around the world. Global progress in malaria vaccine development is one of the major themes of the conference.

Presentations at the conference confirm that malaria vaccine research and development is advancing rapidly. Leading scientists are discussing key advances and challenges—from the results of clinical trials, to novel vaccine candidates that prompt unprecedented immune responses, to the issues involved in establishing clinical trial sites.

"The crucial difference between the situation today and several years ago is the increase in the number of malaria vaccine clinical trials in Africa with industry sponsorship," said speaker W. Ripley Ballou, MD, of MedImmune, a biotechnology company in Maryland. "The combined efforts of industry, researchers, and public health experts working in Africa are finally paving the way to a successful malaria vaccine."

Besides bringing news of important progress, the conference also calls attention to the need for much greater investment in vaccines against one of the world's deadliest diseases. Many malaria vaccine candidates are progressing slowly toward clinical trials because of inadequate funding and lack of industrial partnerships needed to prepare them for testing.

While the effort progresses, malaria kills an estimated 2.7 million people every year. Seventy-five percent of these deaths are of African children under the age of five. More than two billion people worldwide are at risk, with 300 to 500 million clinical cases occurring annually. Malaria also causes a staggering economic burden, costing Sub-Saharan Africa billions of dollars in health care and lost productivity.

"Key players in malaria vaccine development are coming together in Africa, which bears the brunt of the disease," said Regina Rabinovich, MD, director of the Malaria Vaccine Initiative, Program for Appropriate Technology in Health (PATH), a conference co-sponsor. "The synergy created by this information exchange will help inform the global malaria vaccine development

effort. We can report that more is being done today than ever before. However, much more remains to be done."

Highlights from malaria vaccine clinical trials reported on at the conference include:

- ***Promising vaccine candidate, RTS,S/AS02A, is reported safe in its first pediatric clinical trial in Africa.*** A Phase 1 pediatric trial in The Gambia showed RTS,S/AS02A to be safe in both six-to-eleven-year-old and one-to-five-year-old children. In addition, all doses of the vaccine induced good immune responses. GlaxoSmithKline Biologicals (GSK Bio) developed the vaccine, and the Malaria Vaccine Initiative supported the trials. Following on these encouraging results, a Phase 1 study in children is underway in Mozambique to prepare for trials to examine vaccine efficacy.

"The vaccine was well-tolerated in children and generated an immune response similar to what we have seen in adults," reported Kalifa Bojang, an investigator with the Medical Research Council in The Gambia. "The results were reassuring."

- ***U.S. Army's MSP-1 vaccine candidate is reported safe in its first adult clinical trial in Africa.*** José Stoute, U.S. Army Medical Research Unit (USAMRU) in Kisumu, Kenya, reported that the vaccine—previously tested in adults in the U.S.—is thus far safe in its first clinical trial in Africa.

If these preliminary results bear out, Stoute indicated that they will begin a Phase 1 safety trial in children next year, followed a year later by a larger trial to assess efficacy. The trials are a collaboration of Walter Reed Army Institute of Research (WRAIR), the Kenya Medical Research Institute, USAMRU, the U.S. Agency for International Development, GSK Bio (whose AS02 adjuvant is part of the vaccine), and the Malaria Vaccine Initiative.

- ***Two novel "prime boost" vaccine candidates show enhanced immune response.*** The prime-boost vaccine approach seeks to increase the body's natural resistance through a two-stage regime that primes the immune system with one vaccine, then boosts the response with another.

Commander Judith Epstein, U.S. Naval Medical Research Center (NMRC), reported on a prime-boost clinical trial recently completed in the U.S. It is the first human trial to use a DNA vaccine "boosted" by GSK Bio's RTS,S/AS02A. **Vical, Inc. produced the DNA vaccine.**

The regime was safe and well-tolerated, and it successfully stimulated production of several types of immune cells. "Although the number of volunteers was small, the results indicate that a vaccine strategy that utilizes a combination approach might provide a much broader and potentially more protective immune response than either of the individual components on its own," said Epstein.

NMRC and WRAIR executed the study in collaboration with GSK Bio and Vical, with

support from **the Office of Naval Research and the Military Infectious Disease Research Program.**

Vasee Moorthy, an Oxford University investigator working with the Medical Research Council (MRC), reported on a prime-boost trial completed in 29 adult men in The Gambia. A DNA vaccine was used to prime the immune system, while a weakened vaccinia virus vaccine known as MVA was used to boost. "The combination was safe and had a profound impact on the immune system," Moorthy said. "We believe we've found a way of inducing higher levels of T-cell activity than seen with any other vaccine."

The project has already followed up on the initial trial, applying the DNA/MVA regime in a randomized controlled efficacy trial with 372 adult male volunteers, also in The Gambia. If the results are favorable, Oxford and MRC will conduct a clinical trial of the complete regime in children ages 1-5. Funding for the trials comes from the Gates Malaria Partnership and the Wellcome Trust.

- ***Two "long synthetic peptide" (LSP) vaccine candidates prove safe and induce good immune responses.*** LSP vaccines are made by chemically assembling a protein in the laboratory. It is hoped that the immune system will target the synthetic protein just as it would a natural one.

Robert Sauerwein, of the University of Nijmegen, the Netherlands, reported on one LSP clinical trial in Europe. The vaccine candidate is based on a malaria parasite protein known as GLURP. Sauerwein's group compared the effect of the vaccine at different doses and in two different formulations. He reported that the vaccine was safe, side effects were mild, and both combinations induced pronounced immune responses, including specific antibodies to the natural GLURP protein.

"This may be the first time a blood-stage malaria vaccine has been shown effective in inducing the right antibodies using such a long synthetic peptide," Sauerwein said, adding that the manufacture of LSPs can be closely controlled and relatively inexpensive. The European Malaria Vaccine Initiative supported the trial.

Pierre Druilhe of the Pasteur Institute in Paris reported results of a clinical trial in Switzerland of another LSP vaccine candidate—based on the malaria protein MSP-3. "In addition to demonstrating safety, the trial had a remarkable result: the human immune response was markedly higher than that found in mouse and primate studies," said Druilhe. "The MSP3 LSP vaccine is safe, well-tolerated, and elicits in humans antibodies able to kill *P. falciparum*."

The vaccine theme of the conference was coordinated by Soren Jepsen, EMVI; Wen Kilama, African Malaria Vaccine Testing Network; and Regina Rabinovich, Malaria Vaccine Initiative. The vaccine abstracts can be found at <http://www.malariavaccine.org/files/0211-MIM-Vaccine-Abstracts.pdf>. For the entire conference program, visit http://www.mim.su.se/english/events/3rd_mim_conf/program.html.

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The Multilateral Initiative on Malaria (MIM) is an international alliance of research and public health agencies and African scientists, established in 1997. MIM seeks to stimulate and support collaborative research to address the needs of public health programs in malaria-endemic countries and to strengthen research capacity in malaria-endemic countries. The Arusha conference is convening sessions on cutting-edge research on malaria drug development and resistance, vector control, pathogenesis, vaccines, and issues that cut across the various aspects of malaria control, such as financing. The Fogarty International Center of the National Institutes of Health serves as the MIM Secretariat and organized the conference on behalf of the MIM partners. Following the conference, Sweden's Karolinska Institute will take on the Secretariat role for a three-year term. For more information about MIM and to view a full list of MIM partners, visit <http://www.mim.su.se/>.

The Malaria Vaccine Initiative (MVI) was created with an initial US\$50 million grant from the Bill & Melinda Gates Foundation to Program for Appropriate Technology in Health (PATH). MVI seeks to accelerate the development of promising malaria vaccine candidates and ensure their availability for the developing world. For more about MVI, visit www.MalariaVaccine.org. PATH (www.path.org) is dedicated to improving health, especially the health of women and children.

Information on organizations and companies mentioned in this release can be found at the following sites:

African Malaria Vaccine Testing Network: <http://www.amvtn.org>

European Malaria Vaccine Initiative: <http://www.emvi.org>

Fogarty International Center: <http://www.nih.gov/fic>

GlaxoSmithKline Biologicals : <http://www.gsk-bio.com>

Malaria Vaccine Initiative, PATH: <http://www.malariavaccine.org/>

Medical Research Council, The Gambia: <http://www.mrc.gm>

MedImmune: <http://www.medimmune.com/>

Naval Medical Research Center: <http://www.nmrc.navy.mil>

Pasteur Institute: <http://www.pasteur.fr/>

University of Nijmegen, Netherlands: <http://www.ncmls.kun.nl>

University of Oxford Malaria Vaccine Trials: <http://www.malaria-vaccines.org.uk>

USAID Malaria Vaccine Development Program:
http://www.usaid.gov/pop_health/id/malaria/techareas/vaccine.html

U.S. Army Medical Research Institute-Kenya: <http://www.usamrukenya.org/>

U.S. Naval Medical Research Center: <http://www.nmrc.navy.mil/>

Walter Reed Army Institute of Research (WRAIR): <http://wrair-www.army.mil/>

Wellcome Trust: <http://www.wellcome.ac.uk/>