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**Two new studies in the *New England Journal of Medicine*
show malaria vaccine candidate advancing in Africa**

**Data in infants and young children reinforce
case for phase III trial of RTS,S/AS**

NEW ORLEANS, December 8, 2008—Results published online today in the *New England Journal of Medicine* revealed that the world’s most clinically advanced malaria vaccine candidate provides both infants and young children with significant protection against malaria. Two separate phase II trials reaffirmed earlier study results and support the ongoing efforts, pending regulatory approvals, to launch the phase III study of GlaxoSmithKline (GSK) Biologicals’ RTS,S/AS vaccine candidate across Africa.^{i,ii}

In infants, data show for the first time that the vaccine candidate can be administered as part of existing African national immunization programs. In children aged 5 to 17 months, the candidate RTS,S/AS01 reduced the risk of clinical episodes of malaria by 53 percent over an eight-month follow-up period and was shown to have a promising safety profile. The studies were conducted in Kenya and Tanzania and were presented today at the American Society for Tropical Medicine and Hygiene (ASTMH) annual meeting.

RTS,S/AS is the leading candidate in a global effort coordinated by the PATH Malaria Vaccine Initiative (MVI) to develop a malaria vaccine. Malaria kills almost one million people each year—most of them infants and young children in Africa, the intended recipients for this vaccine candidate.ⁱⁱⁱ

“Today’s study results strongly show that our investments in developing malaria vaccines are beginning to pay dividends,” said Christian Loucq, MVI director. “We are closer than ever before to developing a malaria vaccine for children in Africa. History has shown that vaccines are the most powerful tool to control and eliminate infectious diseases. Clearly, the world urgently needs a safe and effective vaccine to win the war against this terrible disease.”

The studies published today build on previous findings indicating the efficacy of

RTS,S/AS, including a phase 2 trial, published in *The Lancet* in 2007, that demonstrated “proof of concept” that RTS,S/AS could prevent malaria infection in infants.^{iv}

“The vaccine works alongside standard infant vaccines of WHO’s Expanded Program of Immunization (EPI), has a favorable safety profile, and has consistently shown a significant efficacy level. We can begin to foresee the difference this scientific breakthrough could make in the lives of millions of African children who suffer and die from this disease year after year,” said Joe Cohen, a co-inventor of the vaccine and vice-president of Research & Development, Emerging Diseases & HIV at GSK Biologicals. “The energy and motivation levels are at an all-time high, as the partnership finalizes preparations to launch the historic phase III trial early next year.”

Infant Study: Effective co-administration with EPI Vaccines¹

The infant study enrolled 340 infants under 12 months of age in Tanzania and found that RTS,S/AS02, when administered at 8, 12, and 16 weeks of age with a commonly used childhood vaccine, did not interfere with the protective immune responses to each of the vaccine components. The childhood vaccine contained antigens for Diphtheria (D), Tetanus (T), whole-cell pertussis (Pw) and *hemophilus influenzae* B (Hib). In countries where a malaria vaccine is needed most, the current immunization schedule for infants, called the WHO Expanded Program on Immunization (EPI), would provide an optimal delivery platform.

Researchers evaluated the safety and immune responses when administering the RTS,S/AS02 vaccine in conjunction with an EPI schedule. It was a randomized double-blind trial with participants simultaneously receiving either RTS,S/AS02 and DTP w/Hib as well as oral polio vaccine; or a hepatitis B vaccine and DTP w/Hib as well as oral polio vaccine.

Additionally, the study reported 65 percent reduction against first infection from malaria in those infants who received three doses of the RTS,S/AS02 vaccine and were followed over a six-month period. This study builds upon results published in October 2007 in *The Lancet*, which found a similar level of efficacy for RTS,S/AS02 when it was given in a staggered fashion with the administration of DTPw/Hib vaccine.⁴

“This finding has a very strong implication for protecting infants: RTS,S/AS efficacy data are very encouraging when administered alongside the childhood vaccines now widely in use and those vaccines maintain their desired efficacy alongside RTS,S,” said Salim Abdulla of the Ifakara Health Institute of the Tanzanian Ministry of Health. Abdulla led a team that included researchers from the Swiss Tropical Institute and the London School of Hygiene and Tropical Medicine, GSK Biologicals, and MVI.

Child study: 53% efficacy against clinical malaria in children²

The other trial enrolled 894 children 5-17 months old in both Kenya and Tanzania. It was designed to evaluate the safety and efficacy of the RTS,S/AS, combined with another GSK's proprietary Adjuvant System, coded AS01. The study was a double-blind randomized clinical trial in which children received either three doses of the RTS,S/AS01 vaccine candidate or a rabies vaccine.

It found that the RTS,S/AS01 formulation reduces clinical malaria episodes by 53 percent for up to an average of eight months. Earlier studies in Mozambique using RTS,S formulated with a different GSK Adjuvant System (AS02) demonstrated 35 percent efficacy against clinical disease for 18 months among children 1–4 years old. Researchers concluded that these study results support the use of RTS,S/AS01 for upcoming Phase 3 trials.

“These findings build a solid case for phase III testing, which the partners in this endeavor are looking forward to starting in the near future,” said Philip Bejon of Kenya Medical Research Institute (KEMRI)-Wellcome Collaborative Research Programme and the Centre for Tropical Medicine, University of Oxford, the study's lead author.

The team for the efficacy trial of RTS,S/AS01 in young children comprised researchers from the KEMRI-Wellcome Collaborative Research Programme (Kilifi, Kenya), the National Institute for Medical Research (Tanzania), the Joint Malaria Programme (Korogwe, Tanzania), and other institutions in collaboration with GSK and the MVI.

About RTS,S/AS

GSK and the PATH Malaria Vaccine Initiative signed a public-private partnership agreement in 2001 to pursue pediatric clinical development of RTS,S/AS in Africa. To advance the development program, African research centers in five countries, and collaborating institutions, joined with the partnership.

Pending approvals by national regulatory agencies and ethics committees, a multi-center phase III efficacy trial is on track to start in early 2009. The trial will seek to confirm and evaluate with precision the vaccine's efficacy, including duration, and will continue to closely monitor safety.

The vaccine was invented, developed and manufactured in laboratories at GSK Biologicals' headquarters in Belgium in the late 1980s and initially tested in US volunteers as part of a collaboration with the US Walter Reed Army Institute of Research.

Funding for the development of this vaccine candidate has been made possible through a US\$107.6 million grant from the Bill & Melinda Gates Foundation to the PATH Malaria Vaccine Initiative. GSK has invested approximately \$300 million to date and expects to invest another \$50-100 million before the completion of the project.

The clinical development of RTS,S/AS is led by the Clinical Trial Partnership

Committee, a collaboration of leading African research institutes, Northern academic partners, MVI and GSK with support from the Malaria Clinical Trial Alliance.

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About KEMRI-Wellcome Research Programme

The KEMRI-Wellcome Research Programme is an internationally renowned research centre tackling malaria and other important diseases in Kenya. Safeguarding the health of young African children and their families is the primary motivation of research. The Programme is fully integrated into the Kenyan research infrastructure, through its close relationship with KEMRI (Kenya Medical Research Institute). In Kilifi, the Programme is embedded within Kilifi District Hospital, building its research programmes around local medical infrastructure and contributing to healthcare delivery. Researchers are also committed to engaging with the local community, to discuss their research and why it is being carried out. The Programme is located at sites in Kilifi, an hour's drive north of Mombasa on the coast of Kenya, and in the capital Nairobi. For more information, please visit <http://www.kemri-wellcome.org>

About the Joint Malaria Programme, Tanzania

The Joint Malaria Programme (JMP) is a joint collaborative link between the National Institute for Medical Research (NIMR) in Tanzania, Kilimanjaro Christian Medical Centre (KCMC) in Tanzania, London School of Hygiene and Tropical Medicine (LSHTM) in the UK, and the Centre for Medical Parasitology (CMP) at the University of Copenhagen in Denmark. Its mission is to conduct health research to alleviate disease burden in Tanzania. The Korogwe trial site, established in 2002 under NIMR Tanga Centre, has a staff of around 70. The site aims to be a center of excellence in clinical and biomedical research. Korogwe is located in the Tanga region of Tanzania, an area that has seen a recent decline in malaria rates. Korogwe has a Demographic Surveillance System (DSS) under NIMR Tanga Centre for malaria intervention trials. For more information, please visit <http://196.45.36.203/Pages/projects/about.html>

About the Bagamoyo Branch of the Ifakara Health Institute

The Ifakara Health Institute (IHI), formerly IHRDC, is an autonomous, non-profit, district-based health research and resource institute headquartered in Ifakara, Tanzania. The Bagamoyo unit was established as an extension of the Ifakara Health Institute in 2005. It is dedicated to promoting effective solutions to important public health issues through research, training and service support for community development. It has distinguished itself in a short time period as a leading clinical trial site and has made a significant positive impact on the community through the improvements it has brought to the Bagamoyo District Hospital and the peripheral health facilities in the vicinity of the hospital.

IHI was registered as a Tanzanian Trust in 1996 under the leadership of the Board of Trustees chaired by Ministry of Health. Other members of the Board include National Institute for Medical Research, Swiss Agency for Development and Cooperation, Swiss Tropical Institute, Commission for Science and Technology, Regional Medical Officer for Morogoro, Managing Trustee of African Malaria Intervention Network, Muhimbili University College of Health Sciences, Economic and Social Research Foundation, INDEPTH, Representative of Regional Administration and Local Government. For more information, please visit <http://www.ihl.or.tz>

About GSK Biologicals

GlaxoSmithKline—one of the world's leading research-based pharmaceutical and healthcare companies—is committed to improving the quality of human life by enabling people to do more, feel better and live longer. For company information, please visit www.gsk.com/media.

GSK Biologicals (GSK Bio), one of the world's leading vaccine manufacturers, is headquartered in Rixensart, Belgium, where the majority of GlaxoSmithKline's activities in the field of vaccine research, development and production are conducted. In 2006, GSK Bio distributed more than 1.1 billion doses of vaccines to 169 countries. Of these doses, seventy-five percent of these went to the developing world. Approximately 136 million were doses of combination pediatric vaccines which protect the world's children from up to six diseases in one vaccine.

About the PATH Malaria Vaccine Initiative (MVI)

The PATH Malaria Vaccine Initiative (MVI) is a global program established at PATH through an initial grant from the Bill & Melinda Gates Foundation. MVI's mission is to accelerate the development of malaria vaccines and ensure their availability and accessibility in the developing world. MVI's vision is a world free from malaria. For more information, please visit www.malariavaccine.org. Founded in 1977, PATH is an international, nonprofit organization that creates sustainable, culturally relevant solutions, enabling communities worldwide to break longstanding cycles of poor health. By collaborating with diverse public- and private-sector partners, PATH helps provide

appropriate health technologies and vital strategies that change the way people think and act. PATH's work improves global health and well-being. For more information, please visit www.path.org.

ⁱ Abdulla S, Oberholzer R, Juma O, et al. Safety and immunogenicity of RTS,S/AS02D malaria vaccine in infants. *N Engl J Med* 2008;359:2533-44.

ⁱⁱ Bejon P, Lusingu J, Olotu A, et al. Efficacy of RTS,S/AS01E: clinical malaria in 5 to 17 month old children. *N Engl J Med* 2008;359:

ⁱⁱⁱ World Health Organization. World Malaria Report 2008, Sept 2008. <http://malaria.who.int/wmr2008>. Last accessed: Nov 2008

^{iv} Aponte JJ, Aide P, Renom M, et al. Safety of the RTS,S/AS02D candidate malaria vaccine in infants living in a highly endemic area of Mozambique: a double blind randomised controlled phase I/IIb trial. *Lancet* 2007 Nov 3;370(9598):1543-51. Epub 2007 Oct 18.

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