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## **New *Lancet* Study: Malaria Vaccine Candidate Has Promising Safety, Tolerability Profile in Infants**

### **First “Proof of Concept” of World’s Most Advanced Malaria Vaccine Candidate in African Infants Shows Protection Against Malaria**

SEATTLE, 17 October 2007—The first study to test GlaxoSmithKline’s (GSK) investigational RTS,S/AS02 malaria vaccine in African infants serves as the first proof of concept in this population that the vaccine has a promising safety and tolerability profile and reduces malaria parasite infection and clinical illness due to malaria, according to a paper published today online in *The Lancet*.

The study reports that vaccine efficacy against new infections was 65 percent over a three-month follow-up period after the infants received all three doses of the vaccine. The results also showed that the vaccine reduced episodes of clinical malaria by 35 percent over a six-month follow-up period starting after the first dose.

This efficacy data is consistent with the estimate of 45 percent reduction in new infections reported in a 2004 trial in Mozambique among children one to four years old. However, the clinical malaria results from this study should be viewed in the context that the primary endpoint was safety. The secondary endpoints are efficacy against infection and against clinical malaria. Efficacy against severe disease was not included due to the smaller size of the safety study. Although a large-scale Phase III study will be required to definitively determine the efficacy of the vaccine, the data from this trial are encouraging.

The primary objective of the study was to assess whether RTS,S could be safely administered to the age group most vulnerable to severe disease and death from malaria. For the study, 214 infants between 10 and 18 weeks of age were enrolled. The vaccine candidate's safety and reactogenicity profiles were similar to those observed with standard EPI vaccines given to infants, including comparable local pain and swelling.

This Phase II trial was conducted by the Manhiça Health Research Centre (CISM) in Mozambique by scientists from the Hospital Clinic of the University of Barcelona and the Mozambique Ministry of Health. The PATH Malaria Vaccine Initiative, which is a key partner in the clinical development of RTS,S, provided funding for the trial based on a grant from the Bill & Melinda Gates Foundation. RTS,S was invented and first developed by GSK scientists in 1987 and the company has overseen its development ever since.

“We have shown for the first time that a vaccine can reduce the risk of malaria infection in young African infants exposed to intense *P. falciparum* transmission,” said CISM’s Pedro Alonso, MD, PhD, senior author of *The Lancet* article, principal investigator of the study, and head of the Barcelona Center for International Health Research (CRESIB) at the Hospital Clinic of the University of Barcelona. “These tantalizing and unprecedented results further strengthen the vision that a vaccine may contribute to the reduction of the intolerable burden of disease and death caused by malaria.”

“We have invested over US\$300 million in the development of this vaccine to make it as safe and effective as possible,” said Jean Stéphenne, president of GSK Biologicals, the vaccine division of GSK. “Our collaboration with the PATH Malaria Vaccine Initiative and CISM, which dates back to 2001, demonstrates how public-private partnerships can help overcome critical health problems in Africa. Anticipating licensure, we are already working with our partners and with international donors to ensure that this vaccine is affordable and available to all who need it.”

“While other Phase II studies of this vaccine candidate are underway, this study helps pave the way for a pivotal Phase III trial of what could be the first malaria vaccine for infants and young children in Africa,” added Christian Loucq, MD, director of the PATH Malaria Vaccine Initiative. “The world urgently needs a safe and effective vaccine to reduce the suffering malaria causes.”

The RTS,S vaccine uses a recombinant protein created by GSK scientists that fuses part of the *P.falciparum* circumsporozoite protein (CSP) with hepatitis B surface antigen. Combined with a proprietary GSK Adjuvant System, RTS,S induces the production of antibodies and T cells that interfere with the ability of the malaria parasite to infect humans. Early development of RTS,S was undertaken by GSK in close collaboration with the US Walter Reed Army Institute of Research (WRAIR).

RTS,S will require a few more years of clinical investigation. The trials are being implemented by an international public-private collaboration, including African research institutions and scientists in five countries, GSK, and the PATH Malaria Vaccine Initiative. PATH received a grant of \$107 million from the Bill & Melinda Gates Foundation in 2005 to expand clinical evaluation of RTS,S.

If the results continue to look promising, testing would move on to a Phase III trial, which is currently slated to begin in the second half of 2008. A successful Phase III trial could result in submission to regulatory authorities in 2011.

The trial was approved by Mozambican National Bioethics Committee, the Hospital Clinic of Barcelona Ethics Review Committee and the PATH Human Subjects Protection Committee. It was conducted with the oversight of an independent Local Safety Monitor and a Data Safety Monitoring Board.

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**About the Manhica Health Research Centre (Centro de Investigação em Saude da Manhica, CISM)**

The mission of CISM is to develop a centre of excellence in rural Mozambique which contributes to improved health and development through provision of health care, scientific and technical capacity strengthening and research in priority health problems. Founded in 1996, CISM was developed under a collaborative program between the Mozambique Ministry of Health, the Maputo School of Medicine (Universidade Eduardo Mondlane), and the Hospital Clínic of the University of Barcelona with core funding from the Spanish Agency for International Cooperation. Visit CISM's web site at [www.manhica.org](http://www.manhica.org).

**About the Center for International Health Research at Hospital Clínic of the University of Barcelona (CRESIB)**

The CRESIB is a new global health institute based at Hospital Clinic of the University of Barcelona, which is the leading Spanish biomedical research center. Research into poverty related diseases and building research capacity in Africa are two cornerstones of its mission. The center, with core funding from the Catalan Government, hosts one of the world's leading groups in the development and testing of malaria control strategies. For more information, visit [www.hospitalclinic.org/www.cresib.cat](http://www.hospitalclinic.org/www.cresib.cat)

**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](http://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 is a global program established at PATH through an initial grant of \$50 million from the Bill & Melinda Gates Foundation, which has since awarded it an additional \$207.6 million, including \$107.6 million to help complete development of the RTS,S vaccine. MVI's mission is to accelerate the development of promising malaria vaccines and ensure their availability and accessibility for the developing world. For information, visit [www.malariavaccine.org](http://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](http://www.path.org).

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