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PUBLIC-PRIVATE PARTNERSHIP LEADS TO SCIENTIFIC BREAKTHROUGH IN MALARIA VACCINE DEVELOPMENT

Encouraging Results from Largest Pediatric Safety and Efficacy Clinical Trial of Malaria Vaccine in Africa to be Published in *The Lancet*

LONDON, Friday 15 October 2004 – In a proof-of-concept study to be published this week in *The Lancet*, researchers report that GlaxoSmithKline (GSK) Biologicals' RTS,S/AS02A malaria vaccine candidate protected a significant percentage of children against uncomplicated malaria, infection, and even severe forms of the disease for at least six months. This largest malaria vaccine efficacy trial ever conducted in Africa also re-confirmed the vaccine's safety in one-to-four year old children. Further efficacy studies will be needed before consideration for licensure.

The results will be published on a fast-track basis in the October 16 issue of the journal. The double-blind, controlled trial involved 2,022 children in southern Mozambique and was conducted by the Centro de Investigação em Saude da Manhica (CISM). GSK Biologicals and PATH's Malaria Vaccine Initiative (MVI) co-sponsored the trial, which was approved by Mozambique's Ministry of Health.

"Our results demonstrate the feasibility of developing an efficacious vaccine against malaria," wrote CISM's Pedro Alonso, MD, Ph.D., lead author of the *Lancet* article, adding that "...malaria vaccines could greatly contribute to reducing the intolerable global burden of this disease." Dr. Alonso was the principal investigator of the study and heads the Center for International Health of the Hospital Clinic at the University of Barcelona.

Mozambique's Minister of Health, Dr. Francisco Songane, said his nation was proud to be a part of such a groundbreaking study. "Malaria is the number one killer of African children. We did this not only for the people of Mozambique, but for the people all over Africa whose health and development suffer greatly from this terrible disease."

"It will still take some years before this vaccine becomes a reality, but the commitment is certainly there," said Jean Stéphenne, president and general manager of GSK Biologicals, one of the world's largest vaccine companies. "We are very encouraged by these results. They demonstrate that a *Plasmodium falciparum* malaria vaccine based on the circumsporozoite protein is feasible. Such a vaccine could have a major impact on public health. This project demonstrates the power of collaboration between the public and private sectors," he added.

"These findings represent a breakthrough in the science of malaria vaccines," offered Dr. Melinda Moree, Ph.D., director of MVI, a global program created to overcome barriers to malaria

vaccine development. "They provide convincing evidence that a vaccine could become part of the world's efforts to spare children and families from the devastating effects of this disease. This brings us another step closer to a licensed vaccine." In 2000, GSK Biologicals and MVI entered into a partnership to develop the vaccine for children. MVI was started in 1999 with a grant from the Bill & Melinda Gates Foundation, which made this collaboration possible.

According to the study, vaccine efficacy against clinical malaria attacks was 30 percent. Efficacy against primary infection with *Plasmodium (P.) falciparum* was 45 percent, and efficacy against severe disease was 58 percent. *P. falciparum* is the parasite that causes the greatest number of cases of malaria in Africa.

"The results of this trial represent a significant scientific advance and an important step forward. In contrast to the previous trials of this vaccine in adults, which suggested that vaccine efficacy was short-lived, protection in these children has lasted at least six months," Dr. Alonso added. Follow-up with the children continues.

A recombinant protein that fuses a part of the *P. falciparum* circumsporozoite (CS) protein with the hepatitis B surface antigen molecule, RTS,S, has been under development by GSK Biologicals for more than 15 years.

"There was a lot of skepticism about our approach in the scientific community," recalled Joe Cohen, Ph.D., director, Emerging Diseases, HIV & Therapeutic Vaccines R&D at GSK Biologicals, who is co-inventor of the vaccine. "We're dealing with a very complex parasite that goes through different life stages in the human host. But we were highly committed and kept at it for over 15 years."

The vaccine is directed against the form of the *P. falciparum* parasite that is injected by mosquitoes. This form is known as the sporozoite. After immunization, antibodies and white blood cells are produced which can prevent the sporozoite from surviving or from further development in the liver. The vaccine is delivered in a three-dose regimen.

Among infectious diseases, malaria is one of the world's biggest killers. It is estimated that malaria kills between one and three million people in the world's poorest countries every year, and more children in sub-Saharan Africa than any other infectious disease.

Due to the need for further studies, a licensed malaria vaccine is not expected to be available before 2010, by when it is projected that half the world's population, or 3.5 billion people, will be living in areas in which malaria is transmitted. The economic costs of the disease for Africa alone are equivalent to US\$12 billion annually.

Editors' notes:

An audio conference media briefing will report the results of this trial at 1000 Hours London Time (1100 Hours Central European Summer Time), Thursday, 14 October 2004. Media around

the world can access the audio conference by calling +44 207 081 9432. Please contact Preeti Singh or Ellen Wilson at +1-301-652-1558, ext. 108 or +1 301 922 4969 or psingh@burnesscommunications.com to RSVP and receive the URL for the embargoed online press kit.

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Mozambique's Ministry of Health has as its mission to promote and preserve the health of the Mozambican population and to promote and provide quality and sustainable health care services, gradually increasing its accessibility to all Mozambicans with equity and efficiency.

The Centro de Investigação em Saude da Manhica (CISM) is the first peripheral health research centre in Mozambique to undertake medical research into the key health problems in that country. Founded in 1996, CISM was developed under a collaborative programme between the Mozambique Ministry of Health, the Maputo School of Medicine (Universidade Eduardo Mondlane), and the Hospital Clinic of the University of Barcelona (www.hospitalclinic.org) with core funding from the Spanish Agency for International Cooperation. Visit CISM's web site at www.manhica.org.

GlaxoSmithKline Biologicals (GSK Biologicals), one of the world's leading vaccine manufacturers, is located in Rixensart, Belgium. In 2003, GSK Biologicals distributed more than 850 million doses of vaccines to 152 countries in both the developed and the developing world – an average of 27 doses per second. For information, visit GSK Biologicals' vaccines website site at www.gsk-bio.com. 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.

PATH's Malaria Vaccine Initiative (MVI) is a global program established through an initial grant of \$50 million from the Bill & Melinda Gates Foundation, which awarded it an additional \$100 million in 2003. MVI's mission is to accelerate the development of promising malaria vaccines and ensure their availability and accessibility for the developing world. MVI's vision is a world where vaccines protect children from death and severe disease caused by malaria. For information, visit www.malariavaccine.org. PATH is an international, non-profit organization that creates sustainable, culturally relevant solutions enabling communities worldwide to break longstanding cycles of poor health. For more information, please visit www.path.org.