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World's largest malaria vaccine trial now underway in seven African countries

Pivotal testing of RTS,S is on track for target enrollment of 16,000 children

NAIROBI, Kenya November 3, 2009 — A pivotal efficacy trial of RTS,S, the world's most clinically advanced malaria vaccine candidate, is now underway in seven African countries: Burkina Faso, Gabon, Ghana, Kenya, Malawi, Mozambique and Tanzania. The trial, which is expected to involve up to 16,000 children, is on schedule, with more than 5,000 children already enrolled, researchers announced Tuesday at the Fifth Multilateral Initiative on Malaria Pan-African Malaria Conference.

Developing a vaccine against malaria, a scientific challenge for decades, is critical to defeating the disease. A vaccine would complement existing interventions, such as bed nets and effective drug therapies. GlaxoSmithKline Biologicals' (GSK Bio) RTS,S is the first malaria vaccine candidate to demonstrate significant efficacy during early development to warrant Phase 3 testing. It is the leading vaccine candidate in the global effort by the PATH Malaria Vaccine Initiative (MVI) to develop a malaria vaccine.

"A malaria vaccine could help save countless lives and redefine the future for Africa's children," said Dr. Patricia Njuguna, RTS,S principal investigator (KEMRI-Wellcome Trust, Kilifi, Kenya) and chair of the Clinical Trials Partnership Committee, a collaboration of African research institutions, MVI, and GSK Bio that is leading the clinical development of RTS,S. "Communities all across Africa are dedicated to this future and are participating to ensure that we develop a vaccine with an acceptable safety and efficacy profile."

RTS,S is the first vaccine designed primarily for use in Africa, where malaria kills more than 800,000 people every year, the majority of them children under the age of five. By conducting the trial in seven different countries across sub-Saharan Africa, researchers will be able to evaluate the vaccine candidate's efficacy in a variety of settings, with diverse patterns of malaria transmission. For example, some trial sites are located in areas where there is a year-round threat of malaria, while others experience only seasonal transmission.

All of the research centers were chosen for their track record of world-class clinical research, strong community relations, and commitment to meeting the highest international ethical, medical, clinical and regulatory standards.

"This is a tremendous moment in the fight against malaria and the culmination of more than two decades of research, including ten years of clinical trials in Africa," said Dr. Joe Cohen, co-inventor of RTS,S and

Vice President of R&D, Vaccines for Emerging Diseases and HIV, at GSK Biologicals. “The Phase 3 trial is a huge undertaking that depends on effective coordination between researchers, regulators, families and communities. Everyone involved has invested significant energy and resources to pave the way for what could become the world’s first malaria vaccine.”

Recent Phase 2 studies showed that RTS,S reduced clinical episodes of malaria by 53 percent over an eight-month follow-up period. Findings from a Phase 2 trial initiated in 2002 and conducted with more than 2,000 children in southern Mozambique, published in the medical journal *The Lancet* in 2004 and 2005, showed that RTS,S was efficacious for at least 18 months in reducing clinical malaria by 35 percent, and severe malaria by 49 percent.^{i,ii} In addition, RTS,S was shown to have a promising safety and tolerability profile when used alongside the World Health Organization’s (WHO) standard infant vaccines.

“This historic trial could lead to the availability of a vaccine with the potential to save the lives of hundreds of thousands of African children, if the data are positive,” said Dr. Christian Loucq, director of MVI. “But development is only half the mission; MVI and its partners are committed to ensuring this vaccine reaches those who need it most. We hope the international community will respond by starting to prepare for the day when—if all goes well—this vaccine will be available for distribution and use.”

The Phase 3 trial

The Phase 3 trial will evaluate the vaccine’s efficacy in two groups of children. One group, aged 6 to 12 weeks, will be vaccinated as part of their regular schedule of infant immunizations; the second group includes children aged 5 to 17 months. The vaccine profile is intended primarily for infants, as they and children under the age of five are the most vulnerable to malaria.

“This is the largest trial ever conducted in Africa of a vaccine specifically designed for use with African children. We have great appreciation for the families and children participating,” said Dr. Salim Abdulla, director of the Ifakara Health Institute, Tanzania, which is participating in the Phase 3 trial. “Development of RTS,S across Africa has strengthened our research capacity, a legacy that will far outlast the trials.”

Each country hosting a study site has undertaken independent reviews to ensure the trial meets national safety, ethical and legal standards for medical research. In addition, an independent data and safety monitoring board oversees the entire trial with support from local safety monitors. The trial has been designed in consultation with appropriate regulatory authorities in the European Union, the United States and African countries, in conjunction with the WHO.

Looking ahead

If the Phase 3 program progresses as expected, RTS,S could be submitted for regulatory review under Article 58 as early as 2012. Article 58 is a special review procedure that allows the European Medicines Agency, in close collaboration with the WHO, to issue a scientific opinion regarding the quality, the efficacy and the safety of a medical product that is intended for use exclusively outside the European Union.

Under current plans, the RTS,S vaccine candidate would be submitted to regulatory authorities in 2012 based on efficacy in children 5 to 17 months of age. Additional safety and immunogenicity data from the infant population will be submitted soon thereafter, followed by efficacy data for infants once available. Depending on the final clinical profile of the vaccine and the timetable of the regulatory review process, the first vaccine introduction could take place over the next three to five years.

“GSK’s approach is to make every effort possible to accelerate the availability of this life-saving vaccine,” said Mr. Jean Stéphenne, President and General Manager, GSK Bio. “Ever conscious of the burden of malaria, we have no time to lose and we will exhaust every avenue at our disposal. This is our commitment as a company.”

MVI, the WHO and US Agency for International Development developed the Malaria Vaccine Decision-Making Framework to help countries prepare to make decisions related to future adoption of a malaria vaccine and thereby avoid unnecessary delay between the recommendation for use of a vaccine and its availability in low-income countries. GSK and MVI are already working with malaria-affected countries and international institutions to ensure that, if successful, a malaria vaccine will be readily available and affordable to those who need it most.

About RTS,S

GSK and MVI signed a collaboration agreement in 2001 to pursue the pediatric clinical development of RTS,S in Africa. To advance the development program, African research centers in five countries, and collaborating institutions, joined the partnership. Centers in two additional African countries have joined for the Phase 3 trial.

The vaccine was invented, developed, and manufactured in laboratories at GSK Bio’s headquarters in Belgium, with the research starting in the late 1980s. The vaccine was initially tested in US volunteers, in the mid-1990’s, as part of a collaboration with the Walter Reed Army Institute of Research.

Funding for the development of this vaccine candidate has been made possible through the support of the Bill & Melinda Gates Foundation, which has provided more than \$200 million in grant monies to MVI for this project since 2001. GSK has invested more than \$300 million to date and expects to invest at least another \$100 million before the completion of the project.

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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.

About PATH

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.

About GlaxoSmithKline Biologicals (GSK Bio)

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, 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 2008, GSK Bio distributed more than 1.1 billion doses of vaccines to 176 countries. Close to 80 percent of these doses went to developing countries.

ⁱ Alonso PL, Sacarlal J, Aponte JJ, et al. Efficacy of the RTS,S/AS02A vaccine against *Plasmodium falciparum* infection and disease in young African children: randomized controlled trial. *The Lancet*. 2004; 16-22;364(9443):1411-1420.

ⁱⁱ Alonso PL, Sacarlal J, Aponte JJ, et al. Duration of protection with RTS,S/AS02A malaria vaccine in prevention of *Plasmodium falciparum* disease in Mozambican children: single-blind extended follow-up of a randomised controlled trial. *The Lancet*. 2005; 10;366(9502):2012-2018.