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**RTS,S malaria candidate vaccine reduces malaria by approximately one-third in African infants**

- Results from ongoing Phase III clinical trial announced

International African Vaccinology Conference, Cape Town, South Africa—Results from a pivotal, large-scale Phase III trial, published online today in the *New England Journal of Medicine*, show that the RTS,S malaria vaccine candidate can help protect African infants against malaria. When compared to immunization with a control vaccine, infants (aged 6-12 weeks at first vaccination) vaccinated with RTS,S had one-third fewer episodes of both clinical and severe malaria and had similar reactions to the injection. In this trial, RTS,S demonstrated an acceptable safety and tolerability profile.

Eleven African research centres in seven African countries are conducting this trial, together with GlaxoSmithKline (GSK) and the PATH Malaria Vaccine Initiative (MVI), with grant funding from the Bill & Melinda Gates Foundation to MVI.

**Dr. Salim Abdulla, a principal investigator for the trial from the Ifakara Health Institute, Tanzania, said:** "We’ve made significant progress in recent years in our battle against malaria, but the disease still kills 655,000 people a year—mainly children under five in sub-Saharan Africa. An effective malaria vaccine would be a welcome addition to our tool kit, and we’ve been working toward this goal with this RTS,S trial. This study indicates that RTS,S can help to protect young babies against malaria. Importantly, we observed that it provided this protection in addition to the widespread use of bed nets by the trial participants.”

**Efficacy**

When administered along with standard childhood vaccines, the efficacy of RTS,S in infants aged 6 to 12 weeks (at first vaccination) against clinical and severe malaria was 31% and 37%, respectively, over 12 months of follow-up after the third vaccine dose. Insecticide-treated bed nets were used by 86% of the trial participants, which demonstrated that RTS,S provided protection beyond existing malaria control interventions. The efficacy observed with RTS,S last year in children aged 5-17 months of age against clinical and severe malaria was 56% and 47%, respectively. Follow-up in this Phase III trial will continue and is expected to provide more data for analyses to better understand the different findings between the age categories.

**Dr. Abdulla added:** “The efficacy is lower than what we saw last year with the older 5-17 month age category, which surprised some of us scientists at the African trial sites. It makes us even more eager to gather and analyze more data from the trial to determine what factors might influence efficacy against malaria and to better understand the potential of RTS,S in our battle against this devastating disease. We were also glad to see that the study indicated that RTS,S could be administered to young infants along with standard childhood vaccines and that side effects were similar to what we would see with those vaccines.”
Safety
There was no increase in overall reporting of serious adverse events\(^5\) (SAEs) between the infants vaccinated with the RTS,S malaria vaccine candidate and infants in the control group, which received a comparator vaccine. Side effects primarily included local injection site reactions, which were less frequent following RTS,S vaccinations compared to the DTP-HepB/Hib vaccine. Fever was reported more frequently following RTS,S vaccinations than the control vaccine group (30.6% versus 21.1% of vaccine doses, respectively).

Two new cases of meningitis were reported in the 6-12 week-old infant age category in addition to the 9 reported last year; one in the RTS,S group and one in the control vaccine group. Further analysis revealed a bacterial cause of the meningitis in 7 of the 11 cases.

Sir Andrew Witty, CEO, GSK said: “While the efficacy seen is lower than last year, we believe these results confirm that RTS,S can help provide African babies and young children with meaningful protection against malaria. They take us another important step forward on the journey towards having a new intervention available against this disease, which is a huge burden on the health and economic growth of Africa. We remain convinced that RTS,S has a role to play in tackling malaria and we will continue to work with our partners and other stakeholders to better understand the data and to define how the vaccine could best be used to provide public health benefit to children in malaria endemic areas in Africa.”

David Kaslow, Director of the PATH Malaria Vaccine Initiative, said: “Determining the role of RTS,S in Africa will depend on analyses of additional data. We are now an important step closer to that day. Success in developing malaria vaccines depends on many factors: at the top of the list are partnerships and robust evidence, coupled with an understanding that different combinations of tools to fight malaria will be appropriate in different settings in malaria-endemic countries. My congratulations go out to the team at GSK and to the African research centres for their exemplary conduct of this trial.”

“This is an important scientific milestone and needs more study,” said Bill Gates, co-founder of the Bill & Melinda Gates Foundation. “The efficacy came back lower than we had hoped, but developing a vaccine against a parasite is a very hard thing to do. The trial is continuing and we look forward to getting more data to help determine whether and how to deploy this vaccine.”

The vaccine is being developed in partnership by GSK and MVI, together with prominent African research centres\(^*\). The collaborators are represented on the Clinical Trials Partnership Committee, which oversees the conduct of the trial. An extended team of organisations work on RTS,S, including scientists from across Africa, Europe, and North America. Major funding for clinical development of RTS,S comes from a grant by the Bill & Melinda Gates Foundation to MVI.

Looking ahead
Follow-up in this Phase III trial will continue to provide more data for analyses to better understand the different findings between the age categories. These data and analyses should also provide insights into the vaccine candidate’s efficacy in different malaria parasite transmission settings. More data on the longer-term efficacy of the vaccine during 30 months of follow-up after the third dose, and the impact of a booster dose are expected to be publicly available at the end of 2014.

The data and analyses will inform the regulatory submission strategy and, if the required regulatory approvals are obtained and public health information, including safety and efficacy data from the Phase III programme, is deemed satisfactory, the World Health Organization (WHO) has indicated that a policy recommendation for the RTS,S malaria vaccine candidate is possible as early as 2015, paving the way for decisions by African nations regarding large-scale implementation of the vaccine through their national immunisation programmes. An effective vaccine for use alongside other measures such as bed nets and anti-malarial medicines would represent a decisive advance in malaria control.
GSK and MVI are committed to making this vaccine available to those who need it most, should it be approved and recommended for use. In January 2010, GSK announced that the eventual price of RTS,S (also known as Mosquirix™) will cover the cost of manufacturing the vaccine together with a small return of around 5% that will be reinvested in research and development for second-generation malaria vaccines or vaccines against other neglected tropical diseases.

Notes to Editors

About RTS,S
RTS,S is a scientific name given to this malaria vaccine candidate and represents the composition of this vaccine candidate. RTS,S aims to trigger the immune system to defend against Plasmodium falciparum malaria parasite when it first enters the human host’s bloodstream and/or when the parasite infects liver cells. It is designed to prevent the parasite from infecting, maturing, and multiplying in the liver, after which time the parasite would re-enter the bloodstream and infect red blood cells, leading to disease symptoms. In the Phase III efficacy trial, RTS,S is administered in three doses, one month apart. A booster dose administered 18 months after the third dose is also being studied in the trial.

The vaccine, based on a protein first identified in the laboratory of Drs Ruth and Victor Nussenzweig at New York University, was invented, developed, and manufactured in laboratories at GSK Vaccines 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.

In 2001, the MVI entered into partnership with GSK to study the vaccine candidate’s ability to protect young children in sub-Saharan Africa. Over time, the partnership expanded to include the 11 African research centres and, in some instances, associated scientific institutions from Europe and the United States.

With more than US$200 million in grant monies from the Bill & Melinda Gates Foundation, MVI contributes financial, scientific, managerial, and field expertise to the development of RTS,S. GSK takes the lead in the overall development of RTS,S and has invested more than $300 million to date and expects to invest more than $200 million before the completion of the project.

About the study
The first complete set of results in children aged 5 to 17 months and combined data for severe malaria in the first 250 cases from those aged 6 weeks to 17 months were published in the New England Journal of Medicine in November 2011. The Phase III trial has been designed in consultation with the appropriate regulatory authorities and the WHO. It is conducted in accordance with the highest international standards for safety, ethics, and clinical practices and is overseen by an independent data safety monitoring committee.

About GSK Vaccines
GlaxoSmithKline Vaccines is active in vaccine research and development. Headquartered in Belgium, GSK Vaccines has 14 manufacturing sites strategically positioned around the globe. Of the 1.1 billion doses of our vaccines we distributed in 2011, over 80% went to developing countries, which include the least developed, low- and middle-income countries.

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 further information, please visit www.gsk.com.
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.

PATH is an international nonprofit organization that transforms global health through innovation. PATH takes an entrepreneurial approach to developing and delivering high-impact, low-cost solutions, from lifesaving vaccines and devices to collaborative programs with communities. Through its work in more than 70 countries, PATH and its partners empower people to achieve their full potential. For more information, please visit www.path.org.

1 Burkina Faso – Nanoro, Institut de Recherche en Science de la Santé (IRSS) / Centre Muraz
Gabol – Lambaréné Albert Schweitzer Hospital, Medical Research Unit
Ghana – Agogo/Kumasi: School of Medical Sciences, Kwame Nkrumah University of Science and Technology; Kumasi Centre for Collaborative Research, Agogo Presbyterian Hospital
Ghana – Kintampo: Kintampo Health Research Centre, Ghana Health Service
Kenya – Kílifi, KEMRI-Wellcome Trust Research Program
Kenya – Kombewa (Kisumu), KEMRI-Walter Reed Project Kenya Medical Research Institute
Kenya – Siaya (Kisumu), KEMRI-CDC Research and Public Health Collaboration
Malawi – Lilongwe, University of North Carolina Project at the Tidziwe Centre
Mozambique – Manhica, Centro de Investigação em Saúde de Manhiça
Tanzania – Bagamoyo, Ifakara Health Institute
Tanzania – Korogwe, National Institute for Medical Research, Tanzania, Kilimanjaro Christian Medical Centre

2 Standard childhood vaccines used were the combined diphtheria-tetanus-whole-cell-pertussis, hepatitis B, and Haemophilus influenzae type b vaccine (DTPwHepB/Hib) and the oral polio virus vaccine (OPV).

3 Based on According To Protocol (ATP) statistical methodology.

4 Average risk for malaria in the control group was 0.9 clinical episodes per child per year and 2.3% of the children experienced at least one episode of severe malaria.

5 A serious adverse event refers to any medical event that occurs during the course of a clinical trial and that results in death, is life threatening, requires inpatient hospitalization, or results in a persistent or significant disability or incapacity needs, regardless of whether the event is considered by the investigator to be caused by the study vaccination. All SAEs are reported to regulatory authorities.

6 Contains QS-21 Stimulon® adjuvant licensed from Antigenics Inc, a wholly owned subsidiary of Agenus Inc. (NASDAQ: AGEN), MPL and liposomes

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Under the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995, GSK cautions investors that any forward-looking statements or projections made by GSK, including those made in this announcement, are subject to risks and uncertainties that may cause actual results to differ materially from those projected. Factors that may affect GSK’s operations are described under ‘Risk factors’ in the ‘Financial review & risk’ section in the company’s Annual Report 2011 included as exhibit 15.2 to the company’s Annual Report on Form 20-F for 2011.