Malaria vaccine candidate reduces disease over 18 months of follow-up in late-stage study of more than 15,000 infants and young children

- Malaria is a significant public health burden, claiming 660,000 lives a year - mostly children in sub-Saharan Africa
- Data support plan to submit regulatory application in 2014

Multilateral Initiative on Malaria Pan African Conference, Durban, South Africa — Results from a large-scale Phase III trial, presented today in Durban, show that the most clinically advanced malaria vaccine candidate, RTS,S, continued to protect young children and infants from clinical malaria up to 18 months after vaccination. Based on these data, GSK now intends to submit, in 2014, a regulatory application to the European Medicines Agency (EMA). The World Health Organization (WHO) has indicated that a policy recommendation for the RTS,S malaria vaccine candidate is possible as early as 2015 if it is granted a positive scientific opinion by EMA.

These latest results demonstrated that over 18 months of follow-up, RTS,S was shown to almost halve the number of malaria cases in young children (aged 5-17 months at first vaccination) and to reduce by around a quarter the malaria cases in infants (aged 6-12 weeks at first vaccination).

Vaccine efficacy was also assessed separately at each of the trial sites, which represent a wide range of malaria transmission settings; efficacy was found to be statistically significant at all sites in young children and at four sites in infants.

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.

"In Africa we experience nearly 600,000 deaths annually from malaria, mainly children under five years of age," says Halidou Tinto, Principal Investigator from the Nanoro, Burkina Faso trial site and chair of the Clinical Trials Partnership Committee (CTPC), which oversees the RTS,S Phase III programme. "Many millions of malaria cases fill the wards of our hospitals. Progress is being made with bed nets and other measures, but we need more tools to battle this terrible disease."

Efficacy and cases prevented
The efficacy and public health impact of RTS,S were evaluated in the context of existing malaria control measures, such as insecticide treated bed nets, which were used by 78% of children and 86% of infants in the trial. In these latest results over 18 months of follow-up, children aged 5-17 months at first vaccination with RTS,S experienced 46% fewer cases of clinical malaria, compared to children immunised with a control vaccine. An average of 941 cases of clinical malaria were prevented over 18 months of follow-up for every 1,000 children vaccinated in this age group, noting that a child can contract more than one case of malaria. Severe malaria cases were reduced by 36%; 21 cases of severe malaria were prevented over 18 months of follow-up for every 1,000 children vaccinated. Malaria hospitalisations were reduced by 42%.
Infants aged 6-12 weeks at first vaccination with RTS,S had 27% fewer cases of clinical malaria. Over 18 months of follow-up, 444 cases of clinical malaria were prevented for every 1,000 infants vaccinated. The reduction of severe malaria cases and malaria hospitalisations by 15% and 17%, respectively, were not statistically significant.

“It appears that the RTS,S candidate vaccine has the potential to have a significant public health impact,” says Tinto. “Preventing substantial numbers of malaria cases in a community would mean fewer hospital beds filled with sick children. Families would lose less time and money caring for these children and have more time for work or other activities. And of course the children themselves would reap the benefits of better health.”

Overall, vaccine efficacy declined over time: Previous results from one year follow-up of the Phase 3 trial showed that efficacy of RTS,S was 56% against clinical malaria and 47% against severe malaria for the 5-17 month-old age group and 31% against clinical malaria and 37% against severe malaria in the 6-12 week-old age group.

Safety
RTS,S continued to display an acceptable safety and tolerability profile during the 18 month follow-up. Apart from the meningitis signal previously reported, no other safety signal was identified. The occurrence of meningitis will be followed closely during the remainder of the trial.

Next year
Further data from 32 months follow-up and the impact of a fourth ‘booster’ dose given 18 months after the initial three doses are expected to become available in 2014.

Comments on results
Sir Andrew Witty, CEO of GSK, said: “We’re very encouraged by these latest results, which show that RTS,S continued to provide meaningful protection over 18 months to babies and young children across different regions of Africa. While we have seen some decline in vaccine efficacy over time, the sheer number of children affected by malaria means that the number of cases of the disease the vaccine can help prevent is impressive. These data support our decision to submit a regulatory application for the vaccine candidate which, if successful, would bring us a step closer to having an additional tool to fight this deadly disease. We are grateful to the scientists across Africa and GSK and to our partners who have worked tirelessly for almost 30 years to bring us to this point.”

Dr David C. Kaslow, vice president of product development at PATH, said: “Given the huge disease burden of malaria among African children, we cannot ignore what these latest results tell us about the potential for RTS,S to have a measurable and significant impact on the health of millions of young children in Africa. While we want to be careful about not getting ahead of the data, this trial continues to show that a malaria vaccine could potentially bring an important additional benefit beyond that provided by the tools already in use.”

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 that also contains the AS01 adjuvant system. RTS,S aims to trigger the immune system to defend against the *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 has been administered in three doses, one month apart. 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 $350 million to date and expects to invest more than $260 million until development is completed.
Looking ahead
These new data support GSK’s plans to submit, in 2014, an application for a scientific opinion by the Committee for Medicinal Products for Human Use (CHMP) on RTS,S through the EMA Article 58 procedure. The EMA, in the context of cooperation with the WHO, will evaluate data on the quality, safety, and efficacy of the RTS,S vaccine candidate. A positive CHMP scientific opinion would facilitate the registration of RTS,S by national regulatory authorities in Africa. Furthermore, if the EMA gives a positive opinion, and the public health information is satisfactory, including safety and efficacy data from the Phase III programme, the 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 positive advance in malaria control.

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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 catalyse timely access in endemic countries. 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 take an entrepreneurial approach to developing and delivering high-impact, low-cost solutions, from lifesaving vaccines, drugs, diagnostics, 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.

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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 Item 3D ‘Risk factors’ in the company’s Annual Report on Form 20-F for 2012.

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13 The GSK proprietary AS01 adjuvant system contains QS-21 Stimulon® adjuvant licensed from Antigenics Inc, a wholly owned subsidiary of Agenus Inc. (NASDAQ: AGEN), MPL and liposomes.