PRESS RELEASE

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GSK and MMV announce positive headline phase III results showing single-dose tafenoquine reduces risk of relapse in patients with *Plasmodium vivax* malaria

GSK and Medicines for Malaria Venture (MMV) today announced positive results from two phase III studies of tafenoquine, an investigational 8-aminoquinoline, for the prevention of relapse of *Plasmodium vivax* (*P.vivax)* malaria.

The headline results, presented today at the International Conference on *Plasmodium vivax* Research (ICPVR) in Manaus, Brazil, show that a single-dose of 300mg tafenoquine, when given with a 3-day blood-stage chloroquine treatment, reduced the risk of relapse in patients with *P.vivax* malaria significantly more than placebo when given with chloroquine.

P. vivax is one of several species of *Plasmodium* parasite known to cause malaria. After an infected mosquito bite, the parasite has the ability to lie dormant in the liver and periodically reactivate causing relapses of *P. vivax* malaria. These relapses can occur weeks or even years after the initial infection. The disease is estimated to cause around 8.5 million clinical infections every year.[1] Each of these infections keeps a child or adult from school or work for at least 3 days.[2] Studies have shown that beyond lost time, malaria can also have adverse effects on cognitive ability.[3,4]

Since 2008, GSK and MMV have been working together to develop single-dose tafenoquine as an alternative to the existing standard of care, primaquine, which must be taken for 14 days for patients with the relapsing form of malaria. The two phase III randomised, double-blind studies, “DETECTIVE” and “GATHER”, were conducted in malaria-endemic countries covering South America, Asia, and Africa.

DETECTIVE (TAF112582): This was a double-blind, double-dummy phase III study evaluating the efficacy, safety and tolerability of tafenoquine in 522 patients with *P.vivax* malaria. Patients were randomised to receive either a single-dose (1-day) of tafenoquine (300mg), a 14-day course of primaquine (15mg), or placebo, with all patients also receiving a 3-day course of chloroquine to treat the acute blood stage of the infection.

The study met its primary endpoint, showing that a statistically significant greater proportion of patients treated with tafenoquine (60%) remained relapse-free over the 6-month follow-up period than patients on placebo (26%), with an odds ratio for risk of relapse vs placebo given with chloroquine of 0.24, $p<0.001$.[5]

Further, a statistically significant greater proportion of patients treated with 14-days of primaquine (64%) were relapse-free over the 6-month follow-up period than patients on placebo (26%), with an odds ratio vs. placebo when given with chloroquine of 0.20, $p<0.001$.

The frequency of adverse events was 63% for the tafenoquine group, 59% for the primaquine group and 65% for the chloroquine group, and the frequency of serious adverse events was 8% for the tafenoquine group, 3% for the primaquine group and 5% for the chloroquine group.

GATHER (TAF116564): This was a study in 251 patients investigating a single-dose of 300mg tafenoquine on levels of haemoglobin (a protein in red blood cells that carries oxygen) when compared to a 14-day course of 15mg primaquine, with all patients also receiving a standard 3-day course of chloroquine. The incidence of decline in haemoglobin (the primary endpoint) was very low and similar between the two treatment groups (2.4% for patients receiving tafenoquine and chloroquine vs. 1.2% for patients receiving primaquine with chloroquine), with the difference in proportions (95% CI) of 1.23% (-4.16%, 4.98%). No patient required a blood transfusion.

The frequency of adverse events was 72% for the tafenoquine group and 75% for the primaquine group and the frequency of serious adverse events was 4% for the tafenoquine group and 1% for the primaquine group.

Adverse events from the headline data from both studies were consistent with the known safety profile of tafenoquine. The proportion of patients experiencing adverse events and serious adverse events during the 6-month study was similar for tafenoquine, primaquine and chloroquine alone.

Patrick Vallance, President, GSK R&D said: "One of the greatest challenges for patients with *P. vivax* malaria is preventing relapses. Being able to treat patients with a single dose of medicine would be an important step forward in ensuring efficacious treatment, thereby reducing the risk of relapse, particularly in areas with very limited healthcare infrastructure. We are grateful to the dedication and commitment from the patients, investigators and community workers who took part in this study, some of whom live in remote areas with little or no access to healthcare. Malaria remains a leading cause of death and disease in many developing countries and at GSK we are committed to play a role to support the World Health Organization's goal to end malaria for good. As part of these efforts, our aim is to make tafenoquine available and affordable as a single-dose medicine in malaria-endemic countries."

David Reddy, CEO of Medicines for Malaria Venture said, "The positive results of the phase III trials for single-dose tafenoquine provide great hope that a new, effective drug to stop the relapse of *P. vivax* malaria is in sight. Relapsing malaria places a heavy burden on the world, infecting over 8.5 million people a year. Without treatment to eliminate the dormant form of the parasite, patients live with the disease, never knowing when it will relapse and when its debilitating symptoms will return. Not only could single-dose tafenoquine help to put a stop to the relapse for individual patients but it could also help make malaria elimination a real possibility in *P. vivax* endemic countries. Our successful partnership with GSK on the development of this important medicine is the product of joint commitment to eliminate this terrible disease."

Tafenoquine is currently not approved for use anywhere in the world. GSK plans to progress regulatory filings for the prevention of relapse of *P. vivax* malaria later in 2017.

Full results from both studies will be submitted for publication in peer-reviewed journals.

[1] World Health Organization. World Malaria Report 2016 (2016): http://www.who.int/malaria/publications/world-malaria-report-2016/report/en/

[2] Price RN *et al.* "Vivax malaria: neglected and not benign." *Am J Trop Med Hyg* 77:79–87 (2007).

[3] Vitor-Silva S *et al.* "Malaria is associated with poor school performance in an endemic area of the Brazilian Amazon." *Malar J.* 8:230 (2009).

[4] Fernando SD *et al.* "The impact of repeated malaria attacks on the school performance of children." *Am J Trop Med Hyg.* 69(6):582–8 (2003).

[5] Using the FDA preferred categorical analysis.

About *Plasmodium vivax* malaria
Malaria is caused by a parasite known as *Plasmodium*. Five different species of *Plasmodium* parasites cause malaria in different regions of the world: *P. vivax, P. falciparum, P. malariae, P. ovale and P. knowlesi*.

The parasite is a complex organism with a lifecycle spanning both humans and mosquitoes. In *P. vivax*, the parasite lifecycle includes a dormant liver stage, the hypnozoite. Hypnozoites are formed immediately after infection of the human host, and their activation leads to the re-appearance of clinical symptoms of malaria up to several weeks or even years after the initial infection. Hence, a single *P. vivax* infection can give rise to multiple episodes of malaria, in absence of a new mosquito bite. This is known as 'relapse', which represents an important biological difference to infection caused by *P. falciparum*.

P. vivax malaria has a significant public health and economic impact primarily in South and South East Asia, Latin America and the horn of Africa.

About tafenoquine
Tafenoquine was first discovered by scientists at the Walter Reed Army Institute of Research in 1978 and is now being developed in collaboration by GSK and MMV for the treatment of relapsing malaria in patients infected with *P. vivax*.

It is an investigational 8-aminoquinoline derivative with activity against the *P. vivax* lifecycle, including hypnozoites. It was granted Breakthrough Therapy designation by the U.S. Food and Drug Administration (FDA) in December 2013. Breakthrough Therapy designation is the newest of the FDA's programmes aimed at expediting the development and review times of drugs for serious or life-threatening conditions.

Medicines from the 8-aminoquinoline class are associated with haemolytic anaemia in individuals with inherited glucose-6-phosphate dehydrogenase (G6PD) deficiency. Plans are in progress to develop a point-of-care diagnostic as a mandatory test to identify individuals with G6PD deficiency to support well-tolerated and effective use of medicines for the treatment of relapsing malaria in patients infected with *P. vivax*.

GSKs commitment to malaria
Malaria is one of the greatest global healthcare challenges of today. While great progress has been made in the fight against malaria, still every minute a child dies from this treatable and preventable disease. GSK is committed to challenge malaria and to drive change. Our legacy of fighting malaria stretches back more than a century, beginning with Sir Henry Wellcome pioneering organised research of tropical diseases. Our ultimate goal, in collaboration with the wider malaria community, is to help end malaria for good and we are committed to playing our part in making this happen. In support of our goal to help achieve a world free of malaria, GSK commits to work with our partners to fight this disease in four ways. Firstly, we will continue to invest in research to discover new medicines and vaccines for malaria; secondly, we will make these tools available to as many people who need them as possible; thirdly, we will work in collaboration with communities to help build core skills and improve healthcare services; and, fourthly, we will advocate in support of the global malaria community to ensure there are sufficient resources to combat malaria.

GSK – 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.

PRESS RELEASE

MMV – a leading product development partnership (PDP) in the field of antimalarial drug research and development – has the mission to reduce the burden of malaria in disease-endemic countries by discovering, developing and delivering new, effective and affordable antimalarial drugs.
Since its foundation in 1999, MMV and partners have developed and brought forward six new medicines that are now treating patients. In addition, MMV has taken over the stewardship of two approved artemisinin combination therapies (ACTs) developed by Drugs for Neglected Diseases initiative (DND*i*) and partners. Since 2009, these MMV-supported medicines have saved the lives of an estimated one million people.

MMV and partners manage a portfolio of 65 projects, the largest portfolio of antimalarial R&D and access projects ever assembled. The portfolio includes nine new drugs in clinical development addressing unmet medical needs in malaria, including medicines for children, pregnant women and relapsing malaria, and drugs that could support the elimination/eradication agenda. MMV's success in research and access & product management comes from its extensive partnership network of over 400 pharmaceutical, academic and endemic-country partners in more than 55 countries.

MMV's vision is a world in which innovative medicines will cure and protect the vulnerable and under-served populations at risk of malaria, and ultimately help to eradicate this terrible disease.

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GSK cautionary statement regarding forward-looking statements

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. Such factors include, but are not limited to, those described under Item 3.D 'Principal risks and uncertainties' in the company's Annual Report on Form 20-F for 2016.

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