PRESS RELEASE

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GSK and MMV present positive data on treatment for *Plasmodium vivax* malaria in children from 6 months up to 15 years of age

GSK and Medicines for Malaria Venture (MMV) today presented positive data from the TEACH study of tafenoquine, an 8-aminoquinoline, for the prevention of relapse (radical cure) of *Plasmodium vivax* (*P. vivax)* malaria in children and adolescents.

The results of the Tafenoquine Exposure Assessment in Children (TEACH) study were presented during the American Society of Tropical Medicine & Hygiene 2020 virtual annual meeting.

TEACH evaluated dosages of tafenoquine based on weight in children and adolescents between the age of 6 months and up to 15 years. The safety profile was consistent with previous clinical studies with the exception of early post-dose vomiting. Ninety-five percent of the study's 60 subjects had no recurrence of *P. vivax* malaria during four months of follow-up.

The current standard of care for prevention of *P. vivax* relapse requires a 7- or 14-day course of treatment and at present there is no age-specific paediatric formulation. Tafenoquine is a single dose treatment for radical cure and is already licensed in people aged 16 and older. TEACH investigated the use of a novel 50 mg dispersible tablet, which was developed to facilitate use in children. The study also used the approved 150 mg tablet.

Pauline Williams, Head of Global Health R&D, GSK, said: "The results presented today represent an encouraging step forward in the fight against *P. vivax* malaria in children, providing evidence to support a paediatric formulation of tafenoquine. Poor compliance with the current standard of care can allow *P. vivax* malaria to relapse from its dormant stage, causing terrible suffering in the young people disproportionately affected by the disease and enabling ongoing malaria transmission, undermining malaria elimination efforts. These data underscore GSK's dedication to combatting infectious disease, especially in children, and our commitment to discover and develop interventions to tackle malaria."

David Reddy, MMV's Chief Executive Officer, said, "Children are particularly at risk of *P. vivax* malaria infections, which is why the development of a paediatric formulation of tafenoquine was critical. At MMV we aim to deliver treatments for the most vulnerable populations, and are proud to have worked together with GSK to meet this unmet need with a single-dose treatment for the prevention of relapse for children from 6 months of age."

The TEACH study evaluated tafenoquine in children and adolescents with *P. vivax* malaria weighing at least 10 kilograms. All subjects received a single dose of tafenoquine and a course of chloroquine administered per local or national treatment guidelines to treat the acute blood stage of the illness.

Different doses of tafenoquine were administered depending on weight. Data from TEACH show that subjects weighing between 10 kg and 20 kg should receive 100 mg in dispersible tablets; and those between 20 kg and 35 kg should receive 200 mg in dispersible tablets. Those weighing over 35 kg should receive 300 mg in the form of two, 150 mg tablets, currently approved for older populations. Although no subjects were recruited into the lowest weight band (≥6 months to <2 years, weighing ≥5 kg to ≤10 kg), the pharmacokinetic (PK) modelling data from TEACH indicate a child in that weight band should receive a 50 mg dose of tafenoquine.

The relapse-free efficacy rate of 95 percent at four months is in line with studies of tafenoquine in adults and older adolescents. The safety profile was consistent with previous clinical studies, with the exception of early post-dose vomiting. No drug-related, serious adverse events were reported.

Data from TEACH will support regulatory filings in Australia and malaria-endemic countries.

About TEACH (TAF113577)
This was an open-label, non-comparative, multi-centre Phase 2b study to assess the pharmacokinetics (PK), safety, and efficacy of single-dose tafenoquine in the treatment of paediatric subjects with *P. vivax* malaria.

The primary objective was to evaluate the PK of tafenoquine in children and adolescents aged ≥2 years to <16 years with *P. vivax* in order to identify appropriate doses that achieve a similar exposure to that of the tafenoquine adult dose of 300 mg. Secondary objectives were to assess the safety of tafenoquine when administered to paediatric subjects with *P. vivax* malaria; to assess the clinical and parasitological efficacy of tafenoquine as a radical cure for paediatric subjects with *P. vivax* malaria when co-administered with chloroquine. Another secondary objective was to assess the PK of tafenoquine in infants aged ≥6 months to <2 years (weighing ≥5kg) with *P. vivax* (if data permitted).

In all, 60 paediatric subjects were recruited (median age 10 years [range 2 – 15 years]) and dosed at three sites in Vietnam and one in Colombia. There were no unexpected safety findings. The overall percentage of subjects reporting adverse events was similar to adult studies [37/60 (62%)], with the highest frequency adverse event being vomiting in 12 (20%) subjects. Five subjects vomited within the first hour after dosing and two spat out their doses. Two who had a repeat of vomiting following a second dose were excluded from the PK analyses.

All subjects were screened for glucose-6-phosphate dehydrogenase (G6PD) deficiency prior to receiving tafenoquine and excluded from the study if they had <70% G6PD enzyme activity levels.

About *P. vivax* malaria
P. vivax malaria has a significant public health and economic impact, primarily in South-Asia, South-East Asia, Latin America and the horn of Africa. The disease is estimated to cause around 7.5 million clinical infections every year.[1] The clinical features of *P. vivax* malaria include fever, chills, vomiting, malaise, headache and muscle pain, and in some cases, can lead to severe malaria and death.[2] The prevalence of *P. vivax* peaks in children aged 2-6 years old. Further, children are four times as likely as adults to be affected.[3]

The *Plasmodium* parasite is a complex organism with a lifecycle spanning both humans and mosquitoes.[4] After an infected mosquito bite, the *P. vivax* parasite infects the blood and causes an acute malaria episode. It also has the ability to lie dormant in the liver (in a form known as hypnozoite) from where it periodically reactivates to cause relapses of *P. vivax* malaria. Hence, a single *P. vivax* infection can give rise to multiple episodes of malaria, in the absence of a new mosquito bite. These relapses can occur weeks, months or even years after the initial infection. The dormant liver forms of the parasite cannot be treated with most antimalarial treatments active against the blood-stage parasite.

The use of a medicine that targets the dormant liver forms of the *P. vivax* parasite, co-administered with currently available blood stage antimalarials such as chloroquine is known as radical cure. Up to

1 World Health Organization. World Malaria Report 2018 (2018): http://www.who.int/malaria/publications/world-malaria-report-2018/report/en/

2 Price RN et al. Vivax malaria: neglected and not benign. Am J Trop Med Hyg 2007; 77:79–87.

3 Howes, R.E et al. Am J Trop Med Hyg 2016; 95(6 Suppl): 15-34

4 Lima Jr JC, Pratt -Riccio LR. Major Histocompatibility Complex and Malaria: Focus on Plasmodium vivax Infection. Frontiers in Immunology 2016; 7(13): 1 -14

recently, the 8-aminoquinoline primaquine, was the only medicine approved to target the dormant liver stage to prevent relapse.[5] However, primaquine's 14-day treatment regimen is often associated with poor compliance, resulting in reduced effectiveness.[6, 7, 8]

About tafenoquine
Tafenoquine, developed by GSK and MMV, was first approved by the US Food and Drug Administration for the radial cure of *P. vivax* malaria in July 2018 for use in adults and adolescents ≥16 years old. It was subsequently approved by regulators in Australia, Brazil and Thailand.

Regulatory applications are being progressed in other malaria-endemic countries. All approvals were based on efficacy and safety data from a comprehensive global clinical development programme for *P. vivax* radical cure, conducted in nine malaria-endemic countries, which supported an overall positive benefit–risk profile for the use of the product.

Tafenoquine needs to be co-administered with chloroquine to treat both the blood and liver stages of acute *P. vivax* malaria infections (known as radical cure). Before taking tafenoquine or primaquine, patients must be tested for deficiency of a specific enzyme known as glucose-6-phosphate dehydrogenase (G6PD), which helps protect red blood cells. Patients with a G6PD enzyme deficiency could have severe adverse reactions, like hemolytic anemia, during treatment with radical cure drugs and only those with >70% G6PD enzyme activity should receive tafenoquine.

About the partners
Medicines for Malaria Venture (MMV) is a leading product development partnership (PDP) in the field of antimalarial drug research and development in its 22nd year. Its mission is to reduce the burden of malaria in disease-endemic countries by discovering, developing and facilitating delivery of new, effective and affordable antimalarial drugs. Since its foundation in 1999, MMV and partners have built the largest portfolio of antimalarial R&D and access projects ever assembled, have brought forward eleven new medicines and have assumed the access stewardship of a further two. An estimated 2.2 million lives have been saved by these co-developed medicines.

MMV's success is based on its extensive partnership network of around 150 active partners including from the pharmaceutical industry, academia and endemic 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 help to ultimately eradicate this terrible disease.
www.mmv.org

About GSK
GSK is a science-led global healthcare company with a special purpose: to help people do more, feel better, live longer. For further information please visit www.gsk.com/about-us.

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5 Wells TNC et al. Targeting the hypnozoite reservoir of Plasmodium vivax: the hidden obstacle to malaria elimination. Trends Parasitol 2010; 26:145-151.

6 Takeuchi R et al. Directly-observed therapy (DOT) for the radical 14-day primaquine treatment of malarial on the Thai-Myanmar border. Malar J 2010;9:308

7 Abreha A et al. Comparison of artemether-lumefantrine and chloroquine with and without primaquine for the treatment of Plasmodium vivax infection in Ethiopia: A randomized controlled trial. PLoS Med 2017;14:e1002299.

8 Douglas NM et al. Unsupervised primaquine for the treatment of Plasmodium vivax malaria relapses in southern Papua: a hospital-based cohort study. PLOS Med 2017;14: e1002379.

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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. Such factors include, but are not limited to, those described under Item 3.D "Risk Factors" in the company's Annual Report on Form 20-F for 2019 and as set out in GSK's "Principal risks and uncertainties" section of the Q3 Results and any impacts of the COVID-19 pandemic.

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