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## US FDA Advisory Committee endorses the effectiveness and safety of single-dose tafenoquine for the radical cure of *P. vivax* malaria

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GSK and Medicines for Malaria Venture (MMV) today announced that the Antimicrobial Drugs Advisory Committee (AMDAC) of the United States Food and Drug Administration (FDA) voted that there is substantial evidence of the effectiveness (13 for; 0 against) and adequate evidence of the safety (12 for; 1 against) of single-dose tafenoquine for the radical cure (prevention of relapse) of *Plasmodium vivax* (*P. vivax*) malaria in patients 16 years of age and older.

Pauline Williams, Head of Global Health R&D, GSK said: "After extensive efforts to develop a new treatment for patients with *P. vivax* malaria, working in collaboration with Medicines for Malaria Venture, we welcome this endorsement. If approved, tafenoquine would be the first new medicine for this indication in more than 60 years. Together with our partners, we look forward to the final decision by the FDA."

David Reddy, CEO of Medicines for Malaria Venture said: "MMV welcomes the outcome of today's Advisory Committee meeting. Our 12-year collaboration with GSK on this project has resulted in the development of a medicine with the potential to improve the management of *P. vivax* malaria, offering a single-dose radical cure. The positive vote is an important step towards tafenoquine becoming a significant addition to the global anti-malaria arsenal."

The AMDAC is convened to provide the FDA with independent expert advice on a broad range of issues related to infectious diseases and disorders. The committee provides non-binding recommendations for consideration by the FDA, with the final decision on regulatory approval made by the FDA. *Krintafel* is the proposed US proprietary name for tafenoquine.

Tafenoquine is not approved for use anywhere in the world. The new drug application (NDA) was submitted by GSK to the FDA in November 2017. A regulatory submission was also made to the Australian Therapeutic Goods Administration (TGA) in December 2017 with a decision anticipated in the next few months. Approvals of tafenoquine by the FDA and TGA would help support registrations in countries where *P. vivax* malaria is endemic, and would be first steps on the path to global adoption of the new medicine.

### **About *Plasmodium vivax* malaria**

The *Plasmodium* parasite is a complex organism with a lifecycle spanning both humans and mosquitoes. 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, even in the absence of a new mosquito bite. These relapses can occur weeks, or months or even years after the initial infection. The dormant liver forms of the parasite cannot be readily treated with most anti-malarial treatments active against the blood stage parasite. The 8-aminoquinoline, primaquine, is currently the only FDA approved medicine.



Primaquine must be taken for 14 days to show efficacy for the dormant liver stage and therefore prevent relapse.

The use of a medicine that targets the dormant liver form of the parasite, co-administered with currently available anti-malarials such as chloroquine or artemisinin-based combination therapies (ACTs) is known as radical cure.

*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 8.5 million clinical infections every year. 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 be fatal.

#### **About tafenoquine**

Tafenoquine is an investigational 8-aminoquinoline derivative with activity against all stages of the *P. vivax* lifecycle, including hypnozoites. It was first synthesised by scientists at the Walter Reed Army Institute of Research in 1978. GSK's legacy in the research and development of tafenoquine as potential medicine for malaria commenced over 20 years ago. In 2008, GSK entered into a collaboration with the not-for-profit organisation, MMV, to develop tafenoquine as an anti-relapse medicine for patients infected with *P. vivax*. The tafenoquine clinical program is part of GSK's global health program aimed at improving healthcare for underprivileged populations.

#### **About the regulatory submission**

The regulatory submission included efficacy and safety data on tafenoquine from a comprehensive global clinical development program, designed in agreement with the FDA, comprising thirty-three studies in healthy volunteers and patients, of which more than 4000 trial subjects were exposed to tafenoquine.

Thirteen of these studies directly support the *P. vivax* radical cure program. The primary evidence for the clinical efficacy and safety of the 300mg single-dose, of which more than 800 subjects were exposed, was provided by three randomised, double-blind studies: DETECTIVE Part 1 and Part 2 (TAF112582) and GATHER (TAF116564). The results of the two phase 3 studies were announced in June 2017.

#### **GSK's commitment to malaria**

Malaria remains one of the greatest global healthcare challenges. Whilst good progress has been made in the fight against malaria this progress is fragile. GSK supports the WHO target to cut malaria cases and deaths by 90% by 2030 and believes that with renewed global commitment from all stakeholders working together, this goal can be met. GSK is playing its part by building on its 40-year commitment to work with partners to fight malaria in the lab and on the ground.

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**Medicines for Malaria Venture (MMV)** - MMV is a leading product development partnership (PDP) in the field of antimalarial drug research and development. 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, and brought forward seven new medicines that are already saving lives. MMV's success is based on 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 help to ultimately eradicate this terrible disease.



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**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 2017.

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