Supporting a portfolio of three clinical studies, the MMV-led PAMAfrica consortium aims to develop new antimalarial medicines for the most at-risk populations, including newborns, patients with severe malaria and those with drug-resistant infections.

Malaria remains a global and national priority. Since 2000, the malaria community has made huge gains in reducing the burden of this disease. However, since 2018, the decline in malaria incidence and mortality has slowed. A child continues to die every 2 minutes from malaria and malaria-related deaths still exceed 400,000.

As corroborated by the WHO and the Lancet Commission on Malaria Eradication, defeating malaria will need new tools to address key unmet needs.

PAMAfrica’s portfolio will draw on the scientific expertise of consortium partners to progress three different therapies through the research pipeline over the next 5 years.

What is the PAMAfrica consortium?

A group of nine public and private sector research and development partners across Africa and Europe, led by Medicines for Malaria Venture (MMV).

It has been granted €21.9 million over 5 years by European & Developing Countries Clinical Trials Partnership (EDCTP) to implement an ambitious drug development project with an additional co-funding of €22m from the PAMAfrica consortium partners.

1 World Malaria Report, WHO (2019).
2 Ibid.
3 https://www.thelancet.com/commissions/malaria-eradication
The project is divided into four main work packages, each addressing a specific unmet medical need; and a fifth will oversee coordination.

Work Package 1: Next-generation drug combination for uncomplicated malaria
With the detection of artemisinin insensitive parasites in Africa in 2019, the malaria medicine chest needs new combination therapies, preferably in a single dose. Of several promising compounds from MMV’s portfolio known to be fully active against all drug-resistant strains, one or more promising combination of two or more will be selected that has the best profile and the most extensive clinical data supporting their activity. The combination will then be tested in a Phase II clinical study, initially in adults and then descending through the age ranges.

Work Package 2: New formulation of artemether-lumefantrine (AL) for infants < 5 kg in weight
Antimalarial medicines specifically designed for infants below 5kg is a critical unmet need. Currently, newborns or underweight infants infected with malaria are treated with either a whole tablet or half a tablet of Coartem® (artemether-lumefantrine/AL) or with quinine. However, this could lead to inappropriate dosing, and/or adverse reactions. The safety and efficacy of Novartis’ AL is well studied in children older than 6 months and over 5 kg. The PAMAfrica consortium will trial a new formulation of this gold-standard antimalarial and provide valuable support for a new dose ratio designed specifically for newborns.

Work Package 3: Back-up to the current standard of care for severe malaria
The WHO recommends injectable artesunate for the management of severe malaria. However, given evidence of prolonged parasite clearance times with artemisinin-derivatives in the Greater Mekong region, an alternative non-artemisinin-based therapy is vital, should this current standard of care be further compromised by resistance. Hence, a new intravenous (i.v.) formulation of the fast-acting compound cipargamin has been developed to treat severe, artemisinin-resistant *P. falciparum* malaria. The PAMAfrica consortium will assess the efficacy, safety and tolerability of up to three different dosing regimens of parenteral cipargamin in patients hospitalized with severe malaria at clinical centres in several African countries.

Work Package 4: Capacity building
To support the effective conduct of PAMAfrica’s three clinical programs the consortium’s goals include strengthening both research capacity at trial sites and research capability of next-generation African scientists from partnering institutions. Targeted workshops for site personnel will ensure that patients receive optimal care, and that both the implementation of clinical studies and the data generated are of the highest quality. Long-term academic training of PhD and MSc students will help develop future scientific leaders.

Work Package 5: Coordination and administration
A Grant Management Team (GMT) ensures the coordination and administration of the PAMAfrica project. It monitors the progression of the four work packages and dissemination of results, and ensures streamlined communication within the consortium, with external stakeholders and with EDCTP. It is also responsible for the production of annual technical and financial reports. The GMT liaises with the PAMAfrica Strategy & Management Committee (PSMC), which is chaired by MMV’s Chief Scientific Officer and has ultimate responsibility for the consortium’s scientific and technical decision-making.

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4 The ongoing CALINA study will expand to include paediatric population below 6 months and 5 kg
5 Cipargamin (KAE609) is a spiroindolone, originally discovered in 2008 as part of a Novartis-led consortium funded by MMV and the Wellcome Trust

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**PAMAfrica: Expected outcomes**

1. A next-generation drug combination for uncomplicated malaria
2. The first especially formulated malaria medicine for newborns under 5kg
3. A new, fast-acting injectable treatment for severe malaria
4. Increased research capacity and capability in sub-Saharan Africa.