Impact

The conclusion of the proposed studies with their high prospect of success will provide fosmidomycin with a number of therapeutic options.

In combination with piperaquine, it will serve as Non-Artemisinin-based Combination Therapy (NACT) in circumstances where the current first line therapies based on the Artemisinin-based Combination Therapies (ACTs) are becoming less effective as the result of the unremitting spread of artemisinin resistance in South-East Asia and the prospect of it extending to sub-Saharan Africa.

In combination with piperaquine, it will be available as **'stand-by treatment' for travellers** to sub-Saharan Africa in conjunction with a rapid diagnostic test.

Also in combination with piperaquine, it will provide seasonal malaria chemoprevention and intermittent preventive therapy in pregnancy, thereby addressing the therapeutic needs of the two most vulnerable populations - **young children and pregnant women.**

In combination with clindamycin and artesunate, it will cover the spectrum of antimicrobial activity for the **treatment of severe malaria** complicated by co-existing bacterial infections.

DMG Deutsche Malaria GmbH

is a privately owned company, based in Hamburg and funded by an interdisciplinary group of private and institutional shareholders coming from science, economy, law and politics.

It has a track record of more than 18 years in drug development.

Its lean structure under the direction of its CEO, Dr David Hutchinson, in collaboration with centres of excellence forms the basis for its highly flexible and cost-efficient drug development strategy: more than 90% of all invested funds are spent directly into drug development projects.

DMG is closely collaborating with the Medicines for Malaria Venture, the World Health Organisation as well as the majority of the German research groups in this field, including those at the Universities of Tübingen, Heidelberg, Erlangen and the Bernhard-Nocht-Institute for Tropical Medicine. It keeps close ties with many African countries and their research institutes as well as hospitals. To mention in particular Gabon, Mozambique, Benin, Uganda and Ghana.

DMG shares its goal of minimising deaths of children in Africa from severe malaria with the Bill and Melinda Gates Foundation.

DMG is actively pursuing partnership deals to maximise its performance.

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Our Vision

No more children

dying from malaria due to the lack of safe and effective therapy.

No more children
dying from malaria in the absence of safe and effective therapy.

No more pregnant women
losing their unborn or their own lives to malaria.

No more victims of severe malaria
sacrificed to the disease without hope of rescue.

Is That Possible?

Our aim is to make our vision come true.

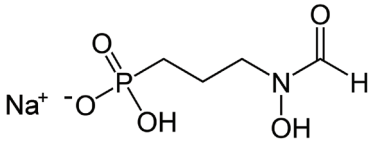
We are dedicated to the development of the novel antimalarial agent **fosmidomycin** as a component of combination therapies unaffected by existing resistance:

- ‘Stand-by treatment’ **for travellers** to endemic areas –
  in conjunction with a rapid diagnostic test
- Safe and efficient treatment **for children**
- Intermittent preventive therapy **in pregnancy**
- Acute therapy **for severe malaria**
  complicated by bacterial co-infections.

Why Fosmidomycin?

Fosmidomycin was created by *Streptomyces* microorganisms through evolution as a protective mechanism from other competing bacteria invading their habitat.

The compound can be chemically synthesized. It has no biochemical target in the human body and therefore no measurable side effects.



Instead, it blocks an essential metabolic pathway absent in humans, but vitally important for survival and growth of certain bacteria – and also of the malaria parasite *Plasmodium* species.

Fosmidomycin is selectively entering the parasites residing inside red blood cells via a unique, but highly efficient mechanism. Once inside the *plasmodial* organelle, the apicoplast, it rapidly kills the parasite.

Used in a combination therapy, parasite clearance times of less than 50 hours are achieved and the fever resolved within 40 hours.

Drug Resistance

The ability of the parasite to develop resistance to antimalarial drugs has undermined their effectiveness particularly when they have been used as monotherapy.

Strenuous efforts are being made to control the spread of resistance to artemisinin, the essential component of current first line therapies.

Therefore, the development of new therapies based on novel modes of action within the concept of combination therapy have gained high priority to delay resistance.

The Solution to Recrudescence

As monotherapy, fosmidomycin proved to be highly effective in the initial clearance of parasitaemia when administered orally.

However, its overall efficacy was compromised by susceptibility to recrudescent infections. Such an outcome may be expected when antimalarials are given singly.

Again, the solution is the concept of combination therapy. It provides for the co-administration of two or more agents with differing modes of action and different biochemical targets.

For our ‘stand-by treatment’ for travellers to endemic areas, we have addressed the problem of recrudescence by selecting piperaquine as the preferred partner drug on the grounds of its prolonged post-treatment prophylactic effect.

Clinical Data

This combination is a well tolerated and safe therapy as evidenced by the **100% cure rate** that was achieved in a proof of concept study.

Recently conducted in Gabon, the study provided for the enrolment of 100 adults and children from the **age of one year** with acute uncomplicated *Plasmodium falciparum* malaria.

The 100% cure rate on Day 28 was maintained in all evaluable subjects on Day 63 in the absence of any safety concerns.

Such an outcome is unsurpassed and warrants the further evaluation of this combination with the aim of substantiating a fully compliant, highly efficacious, well tolerated and safe therapy based on an optimised dosing regimen administered over three days.