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MEDIA & INVESTOR RELEASE

Novartis and Medicines for Malaria Venture announce positive efficacy and safety data for a novel treatment for babies <5 kg with malaria

- *There is currently no evidence-based treatment for the smallest babies with malaria*
- *The CALINA study tested a new ratio and dose of Coartem® (artemether-lumefantrine) to account for metabolic differences in babies under 5 kg*
- *The CALINA trial indicated that the new formulation has good efficacy and safety, and the data have been submitted for regulatory review*

Basel, April 24, 2024 – Novartis and Medicines for Malaria Venture (MMV) announce positive data from their phase II/III CALINA study, demonstrating that a novel formulation of Coartem® (artemether-lumefantrine) developed for babies weighing less than 5kg with malaria has the required pharmacokinetic profile and good efficacy and safety. The trial was conducted in several African countries. The data, which will be presented this week at the Multilateral Initiative on Malaria (MIM Society) 8th Pan-African Malaria Conference in Kigali, have been submitted for regulatory review.

Malaria exerts a massive burden on public health across the world, particularly in Africa[1]. Huge strides have been made in recent decades in the treatment of malaria. However, to date, little data has been generated in the smallest children – babies less than 5 kg.

“We are pleased with the positive outcomes from our CALINA study and to be one step closer to bringing an effective malaria treatment to all age groups, including vulnerable newborn babies," said Shreeram Aradhye, President, Development and Chief Medical Officer at Novartis. “We have been committed to the fight against malaria for more than two decades, and this successful trial represents another milestone towards ensuring that all people have access to an appropriate antimalarial therapy.”

The CALINA study is led by Novartis, with the scientific and financial support of Medicines for Malaria Venture (MMV), and as part of the PAMAfrica consortium, which is funded by the European & Developing Countries Clinical Trials Partnership (EDCTP2). It is the first evidence-based trial conducted to evaluate a new antimalarial dose and regimen for all infants weighing under 5 kg with acute uncomplicated malaria. If approved, Novartis and MMV aim to make the treatment available as soon as possible to the youngest infants, who currently lack access to evidence-based treatment options.

The new formulation, known as Coartem <5 kg Baby, uses a new ratio and dose of artemether-lumefantrine to account for metabolic differences in babies under 5kg.

Infants under 5 kg can be affected by placental malaria, leading to poor birth outcomes, or contract malaria from the bite of an infected mosquito. The prevalence of the disease in this age and weight group is poorly understood, and it is therefore often misdiagnosed.

Current antimalarials have not been developed specifically for infants weighing under 5 kg. There is no approved treatment available for them, and they are treated with tablets meant for children above 5 kg adjusted by weight[2]. Yet, these tiny patients handle drugs differently due to the immaturity of their metabolizing organs, which can lead to overdose and toxicity. Coartem <5 kg Baby provides optimized dosing specifically tailored to the needs of these vulnerable patients. If approved, the treatment will close a significant treatment gap.

“Infants below 5 kg make up a critical neglected group, and developing antimalarials specifically suited to their needs is essential to malaria control efforts,” said Wiweka Kaszubska, Executive Vice President, Head of Product Development, MMV. “The success of the CALINA trial brings us one step closer to ensuring that all patients have access to appropriate and effective treatments.”

“The CALINA trial is an example of the type of Europe-Africa collaboration we need to close malaria treatment gaps for vulnerable groups, and EDCTP is proud to be part of this endeavor,” said Pauline Beattie, Operations Manager and Scientific Advisor, EDCTP Association.

This year's theme for World Malaria Day – Health Equity, Gender, and Human Rights – serves as a stark reminder of our collective responsibility to protect every child from malaria. It underscores the need to ensure that the youngest and most vulnerable among us also have access to the right treatment.

About the CALINA study
Pharmacokinetics, Safety, Tolerability and Efficacy of a New Artemether-lumefantrine Dispersible Tablet in Infants and Neonates <5 kg Body Weight With Acute Uncomplicated Plasmodium Falciparum Malaria (CALINA) is an open-label, single-arm, multicenter phase II/III study in young infants < 5 kg with uncomplicated *Plasmodium falciparum* malaria, which evaluated the PK, safety, tolerability and efficacy of a new dose regimen (5mg:60mg). The study consists of a core segment (treatment and follow-up for 43 days) and long-term follow-up at 12 months of age to assess neurodevelopmental status. The trial was conducted in Burkina Faso, DRC, Kenya, Mali, Nigeria, and Zambia.

The primary PK endpoint of the study was met for patients > 28 days of age. For neonates <= 28 days of age, although the sample size was too small for a conclusive statistical evaluation, the required value of the PK endpoint was also within the calculated interval.

The key secondary endpoint of lumefantrine C168 concentration was also met for cohort 1 and within range for cohort 2. This indicates that the new dose regimen/formulation delivers exposures to artemether and lumefantrine proven to be safe and effective in paediatric patients of higher body weight.

More information about the trial can be found here.

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are based on our current beliefs and expectations regarding future events, and are subject to significant known and unknown risks and uncertainties. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those set forth in the forward-looking statements. There can be no guarantee that the investigational or approved products described in this press release will be submitted or approved for sale or for any additional indications or labeling in any market, or at any particular time. Nor can there be any guarantee that such products will be commercially successful in the future. In particular, our expectations regarding such products could be affected by, among other things, the uncertainties inherent in research and development, including clinical trial results and additional analysis of existing clinical data; regulatory actions or delays or government regulation generally; global trends toward health care cost containment, including government, payor and general public pricing and reimbursement pressures and requirements for increased pricing transparency; our ability to obtain or maintain proprietary intellectual property protection; the particular prescribing preferences of physicians and patients; general political, economic and business conditions, including the effects of and efforts to mitigate pandemic diseases; safety, quality, data integrity or manufacturing issues; potential or actual data security and data privacy breaches, or disruptions of our information technology systems, and other risks and factors referred to in Novartis AG's current Form 20-F on file with the US Securities and Exchange Commission. Novartis is providing the information in this press release as of this date and does not undertake any obligation to update any forward-looking statements contained in this press release as a result of new information, future events or otherwise.

About Novartis
Novartis is an innovative medicines company. Every day, we work to reimagine medicine to improve and extend people's lives so that patients, healthcare professionals and societies are empowered in the face of serious disease. Our medicines reach more than 250 million people worldwide.

Reimagine medicine with us: Visit us at **https://www.novartis.com** and connect with us on **LinkedIn**, **Facebook**, **X/Twitter** and **Instagram**.

About MMV
MMV is a leading product development partnership (PDP) in the field of antimalarial drug development and delivery. 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 15 medicines that are treating patients. An estimated 15.4 million deaths have been averted by these MMV co-developed medicines.

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.

References

1. World malaria report 2023 (who.int)
2. WHO guidelines for malaria - 16 October 2023 (magicapp.org)

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