PRESS RELEASE

Pyronaridine-artesunate demonstrates high real-life safety, tolerability and effectiveness in the treatment of uncomplicated malaria in large multi-country study in Africa

Study run in partnership with the CANTAM network and published in PLoS Medicine supports further uptake of antimalarial in Africa

Geneva, Switzerland and Seoul, South Korea 17 June 2021. MMV and Shin Poong Pharmaceutical Co. Ltd., announce the publication of the largest real life study of Pyramax® (pyronaridine-artesunate) for the treatment of uncomplicated malaria to date, with over 8,500 malaria episodes across five African countries.[1] The study, conducted in partnership with the Central Africa Network on Tuberculosis, HIV/AIDS and Malaria (CANTAM)[2], the University of Agboville, Cote d'Ivoire and the University of Tübingen, reported high effectiveness (D28 PCR-adjusted cure rate of 98.6%) and safety and tolerability under conditions similar to everyday clinical practice.

Completion of this 2-year study fulfils Shin Poong and MMV's post-approval commitment to the European Medicines Agency (EMA), following a positive scientific opinion for the use of *Pyramax* under the Article 58 procedure for both tablets and the child-friendly granule for suspension presentation. The EMA requested this large study to provide supplementary assurance regarding the real-life safety – in particular, liver safety – and tolerability of *Pyramax* in populations not assessed in the previous studies, given that it would be used outside of the EU and in malaria-endemic countries where pharmacovigilance systems may not be fully developed.

The study demonstrated high real-life safety, tolerability and effectiveness even in patients who had pre-existing hepatic impairment. The study population included patients with acute hepatitis, in addition to those with HIV, malnourished patients, children under 1 year of age and women who were unknowingly pregnant; overall, this was a much broader population than that of the previous phase 3 programme and WANECAM study.

"Through the CANTAM study, we have demonstrated the real-world utility of *Pyramax* while also providing access to an approved quality-assured artemisinin-combination therapy, to malaria patients in some of the most remote areas in Africa," said Prof. Francine Ntoumi,

1 Gabon: Albert Schweitzer Hospital (CERMEL), Lambaréné, Côte d'Ivoire: Health Center of Azaguié & Health Center of Agboville, Cameroon: Biotechnology Center, University of Yaoundé & Mfou District Hospital, Congo: Congo foundation for the Medical Research, Brazzaville, Makélélé Hospital, Health Center of Madibou, DR of Congo: Faculty of Medicine, University of Kinshasa, Mont-Amba Hospital, Kinshasa, Evangelic Medical Institute of Kimpesé

2 For more information about CANTAM, please visit: https://www.cantam.org/index.php/cantam-about-us

CANTAM Coordinator. “The collaboration with MMV and Shin Poong Pharmaceutical Co. Ltd. has strengthened the Central African clinical research network by supporting our need to conduct a multicentric clinical trial. This major study provided the opportunity to implement all the skills that have been acquired by staff since the creation of CANTAM in 2009. This successful endeavour with MMV and Shin Poong Pharmaceutical Co. Ltd. allows CANTAM to stand as a competitive group for conducting relevant clinical trials in the region.”

“*Pyramax* has been a joint development with MMV since 2001, and we are very proud that its utility, efficacy and safety in clinical practice have been confirmed in this huge real-life study, proving that Pyramax is an optimal ACT, even in challenging real-life settings. The study results reinforce its use as a powerful and well-tolerated first line ACT. We will continue to produce this high-quality product to meet the demand to support malaria elimination and eradication efforts,” said Mr Won June Chang, CEO of Shin Poong Pharmaceutical Co. Ltd.

“Malaria continues to kill more than 400,000 lives a year, mostly African children under 5 years old, often in remote rural settings,” said George Jagoe, MMV’s EVP of Access and Product Management. “These positive results from the CANTAM study confirm that Pyramax may be used widely in community settings to help save the lives of adults and children with malaria. MMV is committed to working with Shin Poong and in-country partners to make Pyramax as accessible as possible.”

Notes for editors

Background on the malaria burden

According to the latest World malaria report, released on 30 November 2020, there were 229 million cases of malaria in 2019 compared to 228 million cases in 2018. The estimated number of malaria deaths stood at 409 000 in 2019, compared with 411 000 deaths in 2018.

The WHO African Region continues to carry a disproportionately high share of the global malaria burden. In 2019, the region was home to 94% of all malaria cases and deaths.

In 2019, 6 countries accounted for approximately half of all malaria deaths worldwide: Nigeria (23%), the Democratic Republic of the Congo (11%), United Republic of Tanzania (5%), Burkina Faso (4%), Mozambique (4%) and Niger (4% each).

Children under 5 years of age are the most vulnerable group affected by malaria; in 2019 they accounted for 67% (274 000) of all malaria deaths worldwide.

Background of Pyramax®

Pyramax, a fixed-dose combination of pyronaridine and artesunate co-developed by MMV and Shin Poong Pharmaceutical Co. Ltd., South Korea, is the newest ACT combination to be approved by a Stringent Regulatory Authority and recommended by WHO.

It is the only ACT to be granted a positive scientific opinion under the European Medicines Agency's (EMA) Article 58 procedure and is also the only ACT to be registered by a stringent regulatory authority for the blood-stage treatment of both of the two main strains of malaria: *P. falciparum* and *P. vivax*.

This once-daily, 3-day therapy is indicated for the treatment of acute uncomplicated malaria in adults and children over 20 kg (Pyramax® tablets) and in children and infants between 5 and 20 kg (Pyramax® granules).

After a restricted label was granted in 2012, via the EMA's Article 58 procedure, *Pyramax* was assessed in a phase IIIb/IV safety and efficacy study in West Africa (WANECAM) over 4 years to increase the availability of safety data after repeat dosing. The safety profile of *Pyramax* is similar following re-treatment to that seen with initial treatment.[3]

This positive data was instrumental in informing the EMA's decision to grant a revised label for *Pyramax* tablets in 2015, removing restrictions on repeat dosing, on use only in areas of high resistance and low transmission, and on requirements for liver-function monitoring. In addition, a positive scientific opinion was granted for *Pyramax* granules, a child-friendly paediatric formulation. The CANTAM study is a Phase IIIb/IV Cohort Event Monitoring study to evaluate, in a real-life setting, the safety, tolerability and effectiveness in malaria patients of the fixed-dose Artemisinin-based Combination Therapy pyronaridine-artesunate.

About the partners

The CANTAM network - The Central Africa Network on Tuberculosis, HIV/AIDS and Malaria (CANTAM) was created in 2009 with the major aim to build capacity in seven institutions in the three countries Cameroon, Gabon and the Republic of Congo (RoC) for the conduct of clinical trials.

The strategy for achieving this goal was to select institutions with the lowest capacities to conduct clinical research in Cameroon and RoC and to drive them to a higher level through participation in multicentre clinical research involving the highly experienced center in Gabon. Thus, during the past 5 years, baseline data on HIV/AIDS, tuberculosis and malaria have been collected. A dynamic training platform for academic and non-academic training has been developed involving regional partners like WHO/AFRO, UNICEF, Ministries of Public Health and Ministries of Science and Technology.

For more information, please visit https://cantam.tghn.org/

Shin Poong Pharmaceutical Co. Ltd. – Shin Poong Pharm Co., Ltd was founded in 1962 with headquarters based in Seoul, Korea. Shin Poong is one of the largest pharmaceutical companies in Korea that produces both active pharmaceutical ingredient and finished pharmaceutical product in facilities, to which European Union Good Manufacturing Practices

[3] The West African Network for Clinical Trials of Antimalarial Drugs (WANECAM),Pyronaridine–artesunate or dihydroartemisinin–piperaquine versus current first-line therapies for repeated treatment of uncomplicated malaria: a randomised, multicentre, open-label, longitudinal, controlled, phase 3b/4 trial, The Lancet 2018 Apr 7;391(10128):1378-90. https://www.mmv.org/access/products-projects/pyramax-pyronaridine-artesunate-treatment-acute-uncomplicated-malaria

(EU GMP) certification was granted in 2012 for its flagship antimalarial product Pyramax® (pyronaridine tetraphosphate and artesunate).

'For the health of the people' is the driven corporate philosophy of the Company. Shin Poong Pharm contributed largely to eradicate parasitic diseases from Korea during 1970s and 80s and from other countries in Africa, China, and South East Asian countries through strong collaboration with the World Health Organization (WHO).

Shin Poong with its partners were pioneers in Public Development Partnership' access providing a healthcare model to end global epidemics of infectious diseases and to work for end-to-end execution from early discovery to field implementation for endemic infections.

For more information, please visit https://shinpoong.co.kr/en/

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, have brought forward eleven new medicines and have assumed the access stewardship of a further two. An estimated 2.7 million lives have been saved by these MMV 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.

For more information, please visit http://www.mmv.org

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We ask you not rely unduly on these statements. Such forward-looking statements reflect the current views of Medicines for Malaria Venture (MMV) and its partner(s) regarding future events and involve known and unknown risks and uncertainties.

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