Novartis and collaborators discover new dual-acting class of antimalarial compounds with potential to both prevent and treat malaria infections

- A new class of antimalarial drug candidates inhibits malaria parasite liver and blood stages in malaria models
- Most current malaria treatments target blood infections but researchers believe both liver and blood infections need to be treated to eliminate malaria
- Data made publicly available to facilitate global discovery efforts
- Over the past decade, Novartis has delivered over 400 million doses of its antimalarial treatment Coartem® without profit, to more than 60 malaria-endemic countries for public sector use

Basel, November 17, 2011 – The discovery of a new class of dual-acting antimalarial compounds - the imidazolopiperazines (IZPs) – was published in the journal Science online, at the Science Express website today¹. The findings report on compounds that target both liver and blood infections, attacking the Plasmodium parasite at both stages in its reproduction cycle.

The findings describe how scientists developed a novel assay to determine liver stage activity of candidate small molecules, then used the assay and other tools to identify and optimize a chemical scaffold with activity on both blood- and liver-stage parasites in malaria mouse models. Several other compound classes, also with dual activity, are described and released by Novartis through ChEMBL – Neglected Tropical Disease at https://www.ebi.ac.uk/chemblintd.

“For over a decade, Novartis has engaged in the front ranks of combating malaria, pioneering the not-for-profit supply of our antimalarial treatment Coartem® to the public sector of endemic countries,” commented Joseph Jimenez, CEO of Novartis. “These new findings further demonstrate our innovative and sustainable research commitment in this important area which has become integral to our corporate strategy for social responsibility.”

Scientists from the Novartis Institute for BioMedical Research, through the Genomics Institute of the Novartis Research Foundation (GNF) and the Novartis Institute for Tropical Diseases (NITD), collaborated with the Scripps Research Institute and Swiss Tropical and Public Health Institute. Research was supported by the Wellcome Trust, Singapore Economic Development Board, and Medicines for Malaria Venture. This is the second new class of antimalarials discovered by the same group in the last two years and holds promise as a next-generation treatment for malaria if confirmed.

“Novartis is committed to the elimination of malaria. Programs with our current antimalarial treatment have helped save more than one million lives² to date, but there remains much to be done,” said Mark Fishman, NIBR President. “Concerns of potential future resistance to current medicines, and the need to treat liver forms of malaria, propel
our scientists to devise new medicines. The chemical data from this successful study, and the methods of chemical analysis, have all been released to the public domain. Hopefully, such sharing will facilitate broad-based discovery efforts across the globe towards elimination of this disease."

Researchers believe that future antimalarials will need to work against both blood and liver stages to bring us closer to the goal of eliminating malaria globally. The malaria parasite first infects the liver before moving to red blood cells and causing symptoms. However, after clearance in the blood, reservoirs of parasites can linger in the liver causing relapse and hampering efforts toward complete elimination of the disease. Each year there are about 250 million cases of malaria and nearly one million deaths – mostly among children living in Africa.

It is important to develop new classes of treatment that are one step ahead of the parasite should parasite resistance to current therapies occur, according to researchers. In collaboration with research partners, NIBR is working on developing a pipeline of potential new treatment candidates for drug-resistant malaria. Last year’s development of the spiroindolone class, represented by NITD609, is now in Phase I human clinical trials, with Phase II expected to commence in early 2012.

“Compounds with dual activity are rare among current antimalarials,” said Martin Seidel, GNF Institute Director. “The activity of the IZP compound class on liver-stage parasites, if it can be confirmed in clinical trials, gives promise to this class as a first-line therapy for the prevention and treatment of malaria.”

According to Elizabeth Winzeler, GNF Department Head and lead investigator, “Little was known about malaria liver stages when we started this work and as a consequence, we didn’t have a good idea about how to approach the problem. Eventually we decided to develop an automated microscopy method to look for compounds that would alter the appearance of the developing liver stages. We are excited that by publishing the full set of compounds active in both blood and liver stages, new targets might be identified.”

Broader commitment to fighting malaria: Novartis Malaria Initiative
This research is part of a broader commitment by Novartis in the fight against malaria. The Novartis Malaria Initiative is one of the pharmaceutical industry’s largest access-to-medicines programs, focused on treatment, access, capacity-building and research & development. Over the last decade, the initiative has delivered over 400 million treatments without profit to the public sector, in more than 60 countries, has helped save more than one million lives. Novartis believes that increasing access to medicines in developing countries is not just a matter of buying medicines and distributing them, it also requires bringing together good clinical practice, logistics management and other expertise to ensure a long-term sustainable approach to improving health. For more information visit www.malaria.novartis.com.

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The foregoing release contains forward-looking statements that can be identified by terminology such as "potential," "promise," "committed," "future," "will," "expected," "might," "commitment," "strategy," or similar expressions, or by express or implied discussions regarding the potential development of new antimalarial medicines, or potential future revenues from such antimalarial medicines. You should not place undue reliance on these statements. Such forward-looking statements reflect the current views of management regarding future events, and involve known and unknown risks, uncertainties and other factors that may cause actual results to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that any new antimalarial medicines will be developed and brought to market, or that Novartis will earn any revenues from any such medicines. In particular, management’s expectations could be affected by, among other
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Novartis Institutes for BioMedical Research (NIBR) is the global pharmaceutical research organization for Novartis. NIBR's research network is comprised of more than 6,000 scientists, physicians and business professionals working together across more than ten locations to discover innovative medicines to treat diseases with high unmet medical need. GNF is located in San Diego, CA; NITD is in Singapore. For more information, please visit http://www.nibr.com

Headquartered in Cambridge, MA, NIBR is an affiliate of Novartis AG, which provides innovative healthcare solutions that address the evolving needs of patients and societies. Headquartered in Basel, Switzerland, Novartis offers a diversified portfolio to best meet these needs: innovative medicines, eye care, cost-saving generic pharmaceuticals, preventive vaccines and diagnostic tools, over-the-counter and animal health products. Novartis is the only global company with leading positions in these areas. In 2010, the Group’s continuing operations achieved net sales of USD 50.6 billion, while approximately USD 9.1 billion (USD 8.1 billion excluding impairment and amortization charges) was invested in R&D throughout the Group. Novartis Group companies employ approximately 121,000 full-time-equivalent associates and operate in more than 140 countries around the world. For more information, please visit http://www.novartis.com.

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References
1. Imaging of Plasmodium liver stages to drive next generation antimalarial drug discovery. Science Express, Nov. 17, 2011. Copies of paper available to reporters through scipak@aaas.org
2. Estimate based on the ratio between annual malaria cases and deaths published in the WHO World Malaria Report, a distribution analysis of the cumulatively supplied artemether-lumefantrine treatments over time and the efficacy rate of artemether-lumefantrine as per published clinical trial data.
4. http://www.sciencemag.org/content/329/5996/1175.abstract

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