

## **New study finds Coartem® (artemether-lumefantrine) is the most effective malaria treatment in areas of high resistance to conventional anti-malarials**

- *USD 170 million financing commitment from Global Fund will help secure the majority of 2005-2006 Coartem supply*
- *Novartis continues unprecedented production scale-up to meet rapidly increasing demand estimates*

**Basel, April 26, 2005** – A new study published in *The Lancet* suggests that the combination of artemether and lumefantrine, available from Novartis under the brand name Coartem®, is the most effective available treatment for malaria in children in areas of Africa where resistance to conventional anti-malarial drugs is high. Developed and produced by Novartis and its Chinese partners, Coartem is currently the only fixed-dose artemisinin-based combination therapy pre-qualified by the World Health Organization (WHO) for procurement by United Nations agencies.

Recently, the Global Fund to Fight HIV/AIDS, Tuberculosis and Malaria approved a grant of USD 170 million to seven African nations for the procurement of Coartem over the next two years.

"These new clinical data confirm that Coartem is the current gold standard to treat malaria in areas of high resistance to conventional anti-malarials and is as such a life-saving drug," said Dr. Daniel Vasella, Chairman and CEO of Novartis. "When combined with the most recent financing commitment from the Global Fund, these results underpin our efforts to rapidly ramp up the production of Coartem."

Since 2001, Novartis has supplied more than six million treatments of artemether-lumefantrine on a non-profit basis for distribution to the public sector in malaria-endemic developing countries. Production of Coartem, currently the leading artemisinin-based combination therapy (ACT), has increased from 100,000 treatments in 2002 to a projected 30 million treatments in 2005. The original 2001 agreement between Novartis and the WHO forecast demand for Coartem at just over two million treatments in 2005. Since then, non-binding demand forecasts provided by WHO have continuously increased, including a six-fold jump in the 2005 demand forecast between December 2003 and March 2004. In this three month period, the WHO demand forecast surged from 10 million to 60 million treatments.

### **Results of new study by the London School of Hygiene and Tropical Medicine**

In the April 23, 2005 edition of *The Lancet*, Dr. T. K. Mutabingwa and colleagues at the London School of Hygiene and Tropical Medicine reported on a randomised trial of anti-malarial drug combinations for children (aged 4–59 months) with uncomplicated malaria in Muheza, Tanzania. This area has a high prevalence of resistance to sulfadoxinepyrimethamine and chloroquine. Children were randomly allocated three days of amodiaquine (n=270),

amodiaquine+sulfadoxine-pyrimethamine (n=507), amodiaquine+artesunate (n=515), or a three-day six-dose regimen of artemether-lumefantrine (n=519). Drugs were taken orally, at home, unobserved by medical staff. The primary endpoint was parasitological failure by day 14 assessed blind to treatment allocation. Secondary endpoints included day 28 follow-up and gametocyte carriage.

Analysis was by intention to treat. Of 3,158 children screened, 1,811 were randomly assigned treatment and 1,717 (95%) reached the 14-day follow-up. The amodiaquine group was stopped early by the data and safety monitoring board because it reached a pre-determined stopping rule of more than 40% parasitological failure by day 14. By day 14, the parasitological failure rates were 103 of 248 (42%) for amodiaquine, 97 of 476 (20%) for amodiaquine+sulfadoxinepyrimethamine, 54 of 491 (11%) for amodiaquine+artesunate, and seven of 502 (1%) for artemether-lumefantrine. By day 28, the parasitological failure rates were 182 of 239 (76%), 282 of 476 (61%), 193 of 472 (40%), and 103 of 485 (21%), respectively. The difference between individual treatment groups and the next best treatment combination was significant ( $p<0.001$ ) in every case. Recrudescence rates by day 28, after correction by genotyping, were 48.4%, 34.5%, 11.2%, and 2.8%, respectively.

The authors concluded that there are few options for treating malaria where there is a high level of resistance to sulfadoxinepyrimethamine and amodiaquine.

### **Unprecedented scale-up underway**

The rapid scale-up underway at Novartis to meet public sector demand for Coartem is unprecedented in commercial drug production for a new chemical entity. The effort will require operation of two large scale manufacturing plants to produce more than 1.9 billion Coartem tablets – which equates to 120 million treatments – in 2006.

“We have already significantly increased our investments in Coartem production, including in the cultivation of *Artemisia annua* and the extraction of artemisinin, which is currently in short supply due to the annual planting cycle,” Dr. Vasella added. “We are confident that we will succeed in increasing the available volumes to 30 million treatments by the end of the year and to 120 million treatments in 2006. While we provide Coartem at cost, our efforts would be in vain without the Global Fund's financial aid allowing governments of malaria endemic countries to purchase the drug.”

Novartis said its investments are focused on expanding manufacturing infrastructure, increasing and diversifying the supplier base for the production of raw material and transitioning a largely wild crop to commercial plantation cultivation. For the first time, significant volumes of artemisinin will be produced in Africa following the 2005 harvest.

Novartis said its ability to meet 2005 Coartem production goals remains dependent upon the availability of sufficient supplies of the key natural raw material *Artemisia annua* and the extraction product artemisinin, and, most importantly, the timely receipt of firm Coartem orders from affected countries.

“Firm financing commitments for the purchase of ACTs is perhaps the highest return investment in improving public health that donor organizations can make today,” said Professor Bob Snow, a leading scientist in the field of malaria research and public health, from Kenya Medical Research Institute, Nairobi and University of Oxford, UK. “Millions of lives can be saved through swift and decisive action that bridges the gap between enormous public demand and the realities of commercial supply for artemether-lumefantrine and other ACTs.”

Novartis communicated its 2006 production goal of 120 million treatments to leading representatives of the WHO, the Global Fund for HIV/AIDS, Tuberculosis and Malaria,

African health ministries and other key stakeholders in the battle against malaria at its annual Coartem Advisory Board meeting held last month in Dakar, Senegal.

### **About Coartem**

Coartem is a highly effective and well tolerated anti-malarial that achieves cure rates of up to 95%, even in areas of multi-drug resistance. It is indicated for the treatment of falciparum malaria, the most dangerous form of malaria. Coartem is the only pre-qualified, fixed-dose ACT combining artemether, an artemisinin derivative, and lumefantrine. This fixed-dose combination is of great benefit to patients as it facilitates treatment compliance and supports optimal clinical effectiveness.

Artemisinin is a compound extracted from the sweet wormwood plant and has been used for centuries in traditional Chinese medicine to treat fever. An artemisinin-based combination therapy is a combination of two or more drugs (one of which is an artemisinin derivative) with different modes of action and different targets. Studies have shown that using two or more drugs in combination has the potential to delay the development of resistance in areas of low transmission. Artemisinin-based combination therapies in particular have been found to be highly effective treatments for malaria and their potential to delay resistance in areas of intense transmission is under investigation.

Coartem was co-developed by Novartis in collaboration with Chinese partners who also supply the active ingredients (artemether and lumefantrine). The final Coartem tablets are produced in China by Novartis. Coartem is currently registered in 79 countries worldwide and more than six million patients have benefited from this innovative treatment since its first registration in October 1998. Coartem has been extensively studied in multi-center clinical trials involving more than 3,000 patients.

This release contains certain forward-looking statements that can be identified by the use of forward-looking terminology, such as “continues”, “will help secure”, “projected”, “will require”, “will succeed”, “would be”, “will be”, “has the potential”, or similar expressions, or by express or implied discussions regarding Novartis’ ability to meet its projected production goals of Coartem. Such forward looking statements reflect the current views of the Company regarding future events, and involve known and unknown risks, uncertainties and other factors that may cause the actual results with Coartem to be materially different from any future results, performance, or achievements expressed or implied by such statements. There can be no guarantee that Novartis will be able to achieve any particular level of Coartem production in the future. Any such results can be affected by, among other things, the ability to obtain the necessary raw materials, uncertainties relating to regulatory actions or government regulation generally, as well as factors discussed in the Company's Form 20-F filed with the US Securities and Exchange Commission. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those described herein as anticipated, believed, estimated or expected. 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 AG (NYSE: NVS) is a world leader in pharmaceuticals and consumer health. In 2004, the Group's businesses achieved sales of USD 28.2 billion and a pro forma net income of USD 5.6 billion. The Group invested approximately USD 4.2 billion in R&D. Headquartered in Basel, Switzerland, Novartis Group companies employ about 81 400 people and operate in over 140 countries around the world.

Novartis was recently honored with the 2005 Excellence in Corporate Philanthropy Award from the Committee to Encourage Corporate Philanthropy. In 2004, over 4.25 million

patients around the world benefited from Novartis programs valued at USD 570 million. These initiatives range from drug donation and research programs to combat neglected diseases like malaria, tuberculosis and leprosy in developing nations to patient assistance programs that help cancer patients receive the most innovative and effective treatments available. For further information please consult <http://www.novartis.com>.

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