The Novartis Malaria Initiative
Committed to malaria control and elimination
With this in mind, we have set up a holistic program to fight malaria: the Novartis Malaria Initiative. Resting on four key pillars – treatment, access, capacity building, and research and development – the Novartis Malaria Initiative is tailored to best meet patient needs. It has become one of the largest access-to-medicine programs in the healthcare industry, measured by the number of patients reached annually.

Since 2001, working with a range of organizations, we have provided more than 750 million treatments for adults and children, without profit, to more than 60 countries, contributing to a dramatic reduction of the malaria burden in Africa.

Overall, from 2001 to 2015, an estimated 6.2 million lives have been saved and the upward disease spiral reversed thanks to a concerted international effort to scale up interventions. We are proud of the remarkable public health milestones these collaborations have helped to achieve.
The last 15 years have brought great progress in the fight against malaria. Of the 106 countries that had ongoing malaria transmission in 2000, some 102 have met the MDG target of reversing the incidence of malaria; 57 of those have reduced malaria incidence by more than 75% by 2015 while a further 18 countries have reduced malaria incidence by 50-75%. While we should celebrate these successes, we must also recognize and overcome key challenges that could slow down the current momentum.

First, emerging drug and insecticide resistance must be actively confronted. We must therefore continue our vigorous efforts to develop new drugs and insecticides to respond to emerging resistance. The work of Novartis in researching and developing the next generation antimalarials is an essential component of the successful fight against malaria.

Second, political commitment and high ambition must be sustained. Decreased political commitment at either the domestic or international level would derail momentum. History has proven that gains in reducing malaria can be fragile, and that success can be too easily reversed.

Finally, adequate financing for malaria is crucial. This funding must be available to the poorest African countries with the highest burden of disease, and also to the countries that have made great progress toward elimination, but still face potential malaria resurgence. Such resurgences will only be avoided through ongoing investment and vigilance.

We must build upon the extraordinary progress of the last 15 years. With effective strategies, excellent collaboration, smart research and adequate resources, we will maintain our momentum and continue to drive toward malaria elimination, country by country and region by region.

Our ultimate goal is nothing less than zero human malaria on planet earth. Let us all remain focused on this common objective and intensify the collective work we have begun to ensure we see it through to its end.

Professor Sir Richard Feachem, KBE, FREng, DSc(Med), PhD
Director of the Global Health Group at the University of California, San Francisco
Founding Executive Director of the Global Fund to Fight AIDS, TB and Malaria
Treatment – Malaria is preventable and curable, yet it is still one of the most deadly diseases in developing countries.

Although nations across Africa, where the incidence of malaria is the highest, have scaled up malaria control strategies, effective control and treatment present enormous logistical difficulties, as many at-risk populations live in extreme poverty in remote rural areas. Reaching remote communities with poor transport systems and ensuring drug supplies do not run out represent some of the greatest hurdles to malaria elimination.

The World Health Organization (WHO) emphasizes the importance of treating uncomplicated Plasmodium falciparum malaria, the most dangerous form of the disease, with artemisinin-based combination therapies (ACTs) as they represent the best treatment currently available.

ACTs are recommended over older treatments such as chloroquine, sulfadoxine-pyrimethamine and artemisinin monotherapies, as parasites have developed resistance to these drugs. The WHO estimates that the number of ACT treatment courses delivered to the public and private sectors have increased from 11 million in 2005 to 337 million in 2014 – of these, more than 66% were for the public sector.

Leading the path toward malaria elimination

Two decades of public health milestones

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<th>1994</th>
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<tr>
<td>License agreement signed between Novartis and Chinese partners</td>
<td>Novartis commits to make the fight against malaria a key aspect of the company’s access-to-medicine programs</td>
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</table>
The proportion of children under 5 years with *Plasmodium falciparum* malaria who were treated with an ACT is estimated to have increased from less than 1% in 2005 to 16% in 2014. This proportion falls substantially short of the target of universal access for malaria case management. A primary reason is that a high proportion of children with fever are not taken for care or use the informal private sector, where they are less likely to obtain ACTs for treatment.

**Pioneering a standard of care for millions of patients**

In 1999, Novartis was the first healthcare company to launch a fixed-dose ACT, and in 2009 the first dispersible ACT tailored to meet the needs of children, the most vulnerable to malaria.
“Novartis is in the fight against malaria for the long haul. We will continue to partner with the best institutions and companies and intensify our research efforts to develop efficient compounds against malaria to eventually eliminate the disease. But we cannot do this on our own, neither as a company nor as an industry. We need support from politics, technology and academia as well as the public at large, because we can only win this fight together.”

Joerg Reinhardt, Chairman of the Board of Directors of Novartis AG
In 2010, Novartis was awarded the Prix Galien USA award in the category of the “Best Pharmaceutical Agent” for its antimalarial treatment.

The Novartis antimalarial treatment has become a standard of care for millions of patients around the world:

- With a cure rate of over 95%6-10 and a demonstrated safety profile6-11, this was the first fixed-dose ACT brought to market, and prequalified by the WHO for its quality, safety and efficacy12.
- Approved in more than 60 countries, this was the first and only ACT approved by the US Food and Drug Administration in 200913.

Over the past three years, on average, a treatment was made available to approximately 200,000 malaria patients every day.

Evaluating safety and efficacy in pregnant women

Malaria during pregnancy remains a significant health risk to the mother and unborn child. Malaria can cause adverse outcomes, including abortion, anaemia and low infant birth weight14. Various studies to evaluate the efficacy and safety of ACTs, including artemether-lumefantrine (AL), in pregnant women have been conducted.

Two prospective studies in Zambia14 and Rwanda15, performed in collaboration with the WHO from 2004 to 2009, evaluated the safety of the Novartis ACT in more than 3,000 pregnant women with malaria. Results suggested that exposure to AL in pregnancy is not associated with particular safety risks in terms of perinatal mortality, malformations or developmental impairment14,15. The outcomes of these studies are aligned with the current WHO recommendations on the use of ACTs for the treatment of uncomplicated Plasmodium falciparum malaria during the second and third trimesters of pregnancy.

A multicenter, randomized, open label four-arm study in four African countries involving a total of 3,428 people evaluating the safety and efficacy of AL, amodiaquine-artesunate, mefloquine-artesunate and dihydroartemisinin-piperaquine, published in the New England Journal of Medicine in 2016, showed that all the drugs had acceptable cure rates. However, AL was associated with the fewest adverse effects, adding to the existing body of evidence of the safety profile of AL in pregnancy16.

Responding to the unmet medical needs of children

Children are the most vulnerable to malaria: in 2015, approximately 70% of all deaths from malaria occurred in children under the age of five1. Malaria remains a major killer of children, particularly in sub-Saharan Africa, taking the life of a child every two minutes.1

Yet, until a few years ago there was no child-friendly treatment for these vulnerable patients.

Ahead of the call from the WHO and UNICEF for “child-sized” medicines, the Novartis Malaria Initiative started developing, in collaboration with Medicines for Malaria Venture17, a sweet-tasting ACT specifically for children18.

The Novartis pediatric antimalarial treatment is the first:

- Dispersible ACT specifically tailored for infants and children (≥5 kg)
- Pediatric ACT approved by Swissmedic (2008)17
- Pediatric ACT prequalified by the WHO (2009)12 and recommended for use in the WHO treatment guidelines5
- Sweet-tasting antimalarial to mask the bitter taste of lumefantrine
Launched in 2009, this was the first ACT meeting WHO requirements for a pediatric antimalarial. The medicine contains the same concentration of active ingredients as the regular tablet, but in a dispersible formulation that is easier to give to babies and children weighing 5 kg and above, which helps to ensure that this population receives the correct dose. The sweet-tasting formulation disperses quickly in small amounts of water which enhances its use in young children.

Since its launch, more than 300 million treatments have been delivered without profit to more than 40 countries, mainly in Africa. This makes it the first pediatric ACT to have been delivered in such large quantities.

This development program has spanned about four years starting with a rigorous preliminary pharmaceutical evaluation and development, followed by a bioequivalence study. The new dosage strength was approved by Swissmedic in November 2013 and received WHO prequalification in July 2015 making it the first artemether-lumefantrine (AL) with a reduced pill burden available for public sector procurement. To date, the treatment has been launched in more than fifteen African countries in the private sector.

Supporting treatment adherence through packaging

We have developed innovative packaging for our antimalarial treatments to help patients take the medication properly. In addition to written instructions, the packaging uses pictograms that remind patients of how many tablets to take and when. The packaging is color-coded to help identify appropriate dosing regimens for different body-weights.

This is particularly important in areas with low levels of education, where illiteracy is common and the disease transmission high.

The packaging was further enhanced to support treatment adherence, with images of malaria parasites decreasing in number as the three-day course progresses.

We worked with PSI, a global health organization with programs targeting malaria, the Zambian Nurses Association, the University of Oslo, the KEMRI-University of Oxford-Wellcome Trust collaborative program, Medicines for Malaria Venture (MMV) and the World Health Organization (WHO) to develop this unique packaging – which received the “Drug Packaging Design Award” from the Healthcare Compliance Packaging Council-Europe in 2009.

“The story of the Novartis child-friendly ACT is proving that partnerships are key, not only to develop new, high-quality medicines for malaria but also to deliver these to vulnerable populations.”

David Reddy, Chief Executive Officer, Medicines for Malaria Venture

Reducing the pill burden for adults

We have developed a new dosage strength of our ACT for adult patients which reduces the number of tablets to be taken during the treatment course from 24 to 6 tablets, i.e. one tablet twice daily for three days instead of four tablets twice daily for three days. A 75% pill burden reduction has the potential to improve treatment adherence and clinical outcomes.

Start of best practice sharing workshops with national malaria control program managers

Driven by economies of scale, Novartis more than halves the price of its ACT

Healthcare Compliance Packaging Council Award
Through a partnership with the World Health Organization (WHO) in 2001, we were the first company in the healthcare industry to commit to the supply of antimalarial treatments to the public sector of malaria-endemic countries without profit. This joint effort has had immense health benefits, leading to the provision of more than 750 million treatments and contributing to a dramatic reduction of the malaria burden in Africa.

To further demonstrate its commitment, Novartis did not enforce the patent for artemether-lumefantrine (AL), opening the door to other manufacturers to supplement its efforts in increasing access to medicines. Currently, there are 8 WHO prequalified manufacturers of AL.

In 2011, the 10-year formal alliance with the WHO came to an end, but we entered a new phase, continuing to provide medicines on the same terms as before. Underscoring our long-term commitment, we work with a range of other partners involved in the procurement of treatment for public sector use. These include UNICEF, UNITAID, the Global Fund to fight AIDS, Tuberculosis and Malaria, the US President’s Malaria Initiative, the United Nations Development Program, Doctors Without Borders, international procurement agencies and national procurement partners.

Globally, the number of ACT treatment courses procured from manufacturers increased from 11 million in 2005 to 337 million in 2014 – Africa accounted for 98% of ACT deliveries in 2014 with more than half being doses for children. Today, AL accounts for the largest volume of ACTs delivered (73% in 2013).
Expanding access in the private sector of malaria-endemic countries

It is estimated that up to half of malaria patients in Africa do not have access to public health services and buy antimalarials from the private sector, at local market stalls and drug stores, where they often purchase sub-standard or counterfeit medicines because they are cheaper and available. This is particularly true for people living in urban townships and remote rural villages. We are therefore exploring novel distribution channels to improve access to high-quality antimalarials for people relying on the private sector. In particular, we are partnering with The Global Fund through an innovative financing mechanism, called the Private Sector Co-Payment Mechanism. Since 2010, more than 100 million Novartis treatments, including 58 million pediatric treatments, were provided through this channel.

In order to supplement these efforts and further expand access to ACTs in the private sector, we also launched an access program in 2012 in malaria-endemic countries. These countries were chosen based on multiple criteria including high unmet medical need; lack of access to quality ACTs in the private sector; or absence of Co-Payment Mechanism access programs. Importantly, this access program does not rely on donor funding, thus is more likely to be sustainable long-term. As part of this effort, we are also training staff in pharmacies and retail outlets in appropriate diagnosis and treatment of malaria.

“The progress that has been made toward significantly reducing the malaria burden in Africa will be quickly undermined if we do not tackle the endemic problem of poor quality antimalarials in the private sector. The issue urgently needs to be addressed through a collaborative effort between governments and the wider malaria constituency so we can ensure that all patients have access to the best antimalarials available.”

Professor Bob Snow, Chairman of the Malaria Public Health Department at the KEMRI-Wellcome Trust
In the private sector, our activities focus on four tracks:

- Collaboration with reputable local business partners in order to expand access to quality-assured ACTs and ensure effective local distribution channels
- Training of external field staff on the appropriate use of our antimalarial treatments, including provision of patient information and educational materials
- Distribution of appropriate dosage forms according to epidemiological data and patient needs, with a special emphasis on infants and children
- Monitoring of the availability, accessibility and retail prices of our antimalarial treatments

**Impacting lives with SMS**

Stock-outs of antimalarial medicines at the health facility level in rural sub-Saharan Africa are a major barrier to the effective management of the disease. Lack of visibility of stock levels largely contributes to this problem.

In many African countries, supply chain problems make it difficult to get malaria medicines to patients.

**Barriers include:**

- High stock-outs at rural health facilities, i.e. the point of care, where patients can get free drugs rather than having to pay for them at pharmacies or private clinics
- Limited visibility to district management on the medicine stock levels in their facilities
- Difficulty in forecasting demand for the drug, resulting in emergency orders that require ramping up production and transporting the drug by air
- Inconsistent reporting of consumption and sporadic, paper-based ordering

In an effort to tackle stock-outs of antimalarials in malaria-endemic countries, Novartis joined forces with private and public partners, including the Global Fund and various African health ministries. Called SMS for Life, the project uses mobile phones, tablet PCs and electronic mapping technology to track stocks of key antimalarials and other essential medicines in rural health facilities. The overall goal is to eliminate stock-outs, increase access to medicine and reduce the number of deaths from malaria.

What makes this solution unique is that it has demonstrated it works in the targeted environment by reducing and eliminating stock-outs. It is flexible, expandable and scalable to support any number of additional health facilities, countries and products. It can be deployed quickly (6,000 health facilities in 7 months) and at a total operational cost of less than USD 80 per health facility per year.

Novartis Malaria Initiative honored with the World Business and Development Award by the UN Development Program, the International Chamber of Commerce and the International Business Leaders Forum for its contribution to the MDGs
The system automatically sends an SMS to all health facilities on a regular basis asking for their current stock. Responses are collected and stored centrally on a website, and reports generated and sent to key health staff in the country including the National Malaria Control Program. Reports are also made available via the Internet or mobile phone.

SMS for Life 1.0, the phone- and SMS-based version, has been rolled out in more than 10,000 healthcare facilities in sub-Saharan Africa, including more than 3,000 facilities in Cameroon. Further, the solution is now being used to track bed nets, rapid diagnostic tests (RDTs) and health data, as well as antibiotics, leprosy and tuberculosis medicines and blood supplies.

An enhanced version called SMS for Life 2.0, based on tablet computers instead of text messages, can now track more stock items and more disease surveillance indicators. The platform will also be used to deliver high-quality training directly to health workers at their health facility.

SMS for Life 2.0 is currently under advanced discussions for implementation in Gabon, Nigeria and Zambia.

Since its inception, SMS for Life has received numerous awards and recognitions, including the 2012 Ethical Corporation Award for Best Corporate/NGO Partnership and Computerworld’s 21st Century Achievement Award in the Innovation IT category. Earlier recognitions include the Wall Street Journal’s Technology Innovation Award in the Health-Care IT category, being ranked #1 in Technology in the Health category in the GBC Business Action on Health Awards, and a catalytic grant from The Innovation Working Group, part of the UN Secretary-General’s Every Woman Every Child effort, and the mHealth Alliance.

As we are constantly looking for innovative ways to help improve access to medicines, in 2013, we joined forces with Malaria No More, a global charity, to support Power of One, a fund-raising campaign to help accelerate progress toward malaria elimination. Over three years, Novartis partnered with Malaria No More to deliver malaria treatments to children in Africa. Every dollar donated served to treat a child with a confirmed case of malaria and Novartis matched the number of treatments funded by Novartis associates and the public – translating into two treatments delivered for every dollar donated. Overall, the campaign led to the delivery of 3.6 million treatments for children with malaria in Africa.

“The reward for success is not just the lives impacted, but the fact that there are now a number of companies, large and small, realizing they may have a license to operate that requires them to commit to diseases in parts of the world where they do not typically focus.”

Dr. William Rodriguez, Research Associate, Harvard Medical School
Learning by sharing to better fight malaria

In 2006, the Novartis Malaria Initiative introduced workshops with managers of National Malaria Control Programs (NMCP) in Africa. NMCPs, a part of health ministries in African countries, are charged with overseeing malaria control interventions by setting national standards and providing guidelines and technical assistance.

The NMCP workshops, held once a year, are designed to share best practice and experiences between African countries, highlight successes and challenges, and discuss practical solutions to improve malaria control in endemic regions. To date, NMCP workshops have been held in Benin, Ethiopia, Kenya, Mali, Mozambique, Rwanda, South Africa, Tanzania, Uganda, and Zambia.

Topics discussed at the workshops range from case management and utilization of rapid diagnostic tests and ACTs to private sector engagement, awareness campaigns, forecasting, distribution, stock management, health impact measurement and innovative strategies to accelerate malaria elimination. A prime focus at these workshops has been the collection of data from the field to quantify the impact of new malaria policies.

Groundbreaking projects have emerged from these meetings. For instance, as a result of discussions with NMCP managers, Novartis substantially reduced the packaging size of its antimalarial treatment, making transport and storage more efficient.

It was also at NMCP workshops that participants raised the stock-out issue which led to the SMS for Life program to support more efficient stock management in rural health facilities.

Capacity building is a cost-effective and sustainable means of advancing health and development in developing countries.
The availability of an ACT specifically tailored to infants and children was also a key discussion topic during NMCP workshops as Novartis and Medicines for Malaria Venture collaborated to develop the dispersible pediatric formulation.

More recently, the Novartis Malaria Initiative’s program to expand access to affordable, quality-assured malaria treatments in the private sector of African countries was also a result from previous NMCP meetings.

Building capacity on the ground
We have more than a decade of experience in training endemic countries in international standards of Good Clinical Practice, in order for them to become self-reliant in the conduct of clinical trials.

As part of a large 14,000-patient study we undertook in Burkina Faso, we provided clinical research and pharmacovigilance training to a team of 220 healthcare personnel.

“...the greatest burden of the disease is felt at the household level since my daily income is generated almost entirely from agriculture. The debilitating nature of this disease puts our lives under constant threat.”

Angeline Nyandiko, grandmother, Kenya

Nigeria is the first country worldwide to launch the new Novartis ACT in the private market reducing the treatment course to 6 tablets (from 24)

SMS for Life wins Ethical Corporation Award for Best Corporate/NGO Partnership and is recognized among the top 100 innovative solutions at the forefront of sustainable transformation by Sustainia
“Malaria is one of the top ten diseases that we treat in our health district. About 50 percent of the patients come for malaria treatment. Depending on the season, we often treat up to 15-20 patients a day with ACTs.”

Dr. Zaina Mfouka, District Malaria Health Officer, Tanzania

The ALIVE study (Artemether-Lumefantrine In Vulnerable patients: Exploring health impact) on the safety monitoring of the Novartis ACT in rural Tanzania showed that by offering healthcare workers frequent training and refresher sessions on pharmacovigilance, safety monitoring and reporting is possible, even in rural settings where health services are limited.

Training healthcare personnel and communities

Training health professionals and workers in diagnosis and treatment, informing the public about treatment availability and measuring the impact of malaria policies are key elements for endemic countries to combat the disease.

In 2005, in collaboration with the WHO, Novartis built the capacity of extension health workers in the Tigray region, northern Ethiopia. This led to the rational use of medicines and huge cost savings for the Tigray Health Bureau. In the same year, Novartis carried out nationwide training of healthcare workers in Zambia to support knowledge dissemination on malaria treatment guidelines.

We have developed case management training for nurses and educational materials for healthcare workers to improve the diagnosis and treatment of malaria. Other initiatives have included workbooks to educate health workers about the disease, foster a dialogue with patients and train other co-workers.

Further, to support the introduction of our dispersible formulation for infants and children, we developed a workbook and educational poster for healthcare workers available in different languages. Several NMCPs in African countries have included these materials into their own training programs.

More recently, we have produced an educational story booklet for children and their families.

Using full color illustrations, it presents key information on how to prevent and treat malaria for readers with low literacy levels.

In Uganda, together with the Scort Foundation, The Football Club Social Alliance and the Ministry of Health, the Novartis Malaria Initiative is working to educate the young generation about malaria, the country’s leading cause of sickness and death.

Novartis awarded with Malaria No More’s Global Corporate Citizenship Award for its leading role in the fight against malaria

Novartis reaches milestone of providing 700 million treatments without profit to malaria-endemic countries, of which 250 million dispersible pediatric treatments since 2009
Booklets telling the story of a young girl named Tatu who is fighting malaria were distributed to “young coaches” to help them explain malaria prevention, symptoms, diagnosis and treatment to their communities. The Football Club Social Alliance counts world-renowned partner clubs including FC Basel 1893 in Switzerland. In another initiative in Mozambique with the Peace Corps Volunteers, we supported the distribution of Tatu booklets to more than 2,000 mothers and children as part of the Stomp Out Malaria program.

**Transferring technology and know-how**

In China and Madagascar, we are providing indirect support to local farmers in the cultivation of *Artemisia annua*, the source of artemisinin.

Support starts during the seed ordering of *Artemisia annua* in January where we forecast requirements and commit to certain volumes from the upcoming annual harvest. Farmers are provided with planting material and training in Good Agricultural Practice for *Artemisia annua* cultivation to ensure high-quality returns. In addition, a dedicated biomass manager provides seeds and technical support to farmers.

We also source the Active Pharmaceutical Ingredients (APIs) of our antimalarial treatments from China. As part of our collaboration, every year, we spend several weeks on the ground, training suppliers and transferring knowledge and technology on the latest manufacturing methods. This technology transfer has enabled them to meet international quality and health, safety and environment standards in the production of APIs, and allowed the registration of their facilities by drug regulatory authorities.

Our partners have played key roles in the scale-up of production and remain critical to our ability to satisfy demand.
Ever since we pioneered artemisinin-based combination therapies (ACTs) in 1999, we have continued to leverage both the expertise of our large research organization and our unique network of external partners to research and develop best-in-class compounds against malaria.

**Discovering next-generation treatments**

Since 2006, we have been working with various partners including the Genomics Institute of the Novartis Research Foundation, the Swiss Tropical and Public Health Institute, and the Biomedical Primates Research Center (Netherlands) to discover the next generation of antimalarial drugs. The discovery program is supported in part by the Wellcome Trust, the Singapore Economic Development Board and Medicines for Malaria Venture (MMV).

Research, conducted by an international team of scientists at the Novartis Institute for Tropical Diseases, the Genomics Institute of the Novartis Research Foundation and the Swiss Tropical and Public Health Institute (Swiss TPH) led in 2010 to a promising new drug candidate for drug-resistant malaria, which achieved Proof of Concept (PoC) in 2012. About 20 patients infected by one of the two main malaria-causing parasites took part in the PoC study conducted in Bangkok and Mae Sot near the Thailand/Burma border where first signs of resistance to current therapies had been reported. In just five years, this compound was moved into Phase 2 clinical trials.

This compound belongs to a new class called spiroindolones, the first true innovation since the launch of ACTs. It kills the blood stages of *Plasmodium falciparum* and *Plasmodium vivax* through a novel mechanism.
mechanism of action, including parasites that have developed drug resistance. It also appears to be effective against the sexual forms of the parasite, so could help prevent disease transmission.

In 2011, the same group of scientists announced the discovery of a second new dual-acting class of antimalarial compounds – called imidazolopiperazines – that act on both blood and liver infections\textsuperscript{2,3}. The malaria parasite first infects the liver before moving to red blood cells and causing symptoms.

Preventing the disease through seasonal chemoprophylaxis will require that future antimalarials work against both blood and liver stages to bring us closer to the goal of malaria elimination. The compound achieved PoC in 2013 and has also moved into Phase 2 clinical trials.

Further, our scientists are working on additional projects which include a back-up compound to one of the compounds now in Phase 2 clinical development, various blood and liver stage actives with novel mechanisms of action.

Setting a standard in treatment efficacy and safety

Over twenty Novartis-sponsored clinical studies, corroborated by more than sixty independent trials, spanning 15 years with more than 12,000 patients, have demonstrated the positive safety\textsuperscript{4-10} and efficacy\textsuperscript{4-8} profile of our ACT treatment across different populations and regions. Further, post-marketing surveillance, based on the delivery of more than 750 million treatments to date, has not identified any new safety concerns.

In an effort to address the unmet needs of pregnant women with malaria, together with the WHO, we conducted the largest prospective study in Zambia between 2004 and 2008 to evaluate the safety of our treatment in this specific patient population\textsuperscript{11}. The outcomes of the study were aligned with the current WHO recommendations on the use of ACTs for the treatment of uncomplicated \textit{Plasmodium falciparum} malaria during the second and third trimesters of pregnancy\textsuperscript{15}.

“I know many people who have lost family members due to malaria ... This is a disease that tears apart families and makes them poor. It makes me sad.”

Emis Mtonga, father, Zambia
The development of the dispersible formulation for infants and children weighing 5 kg and above consisted of four studies\textsuperscript{8,12}. Two pharmacokinetic studies were performed in healthy volunteers in Europe. The other two were carried out in sub-Saharan Africa, one in healthy schoolchildren to evaluate the medicine’s palatability – a key factor in aiding compliance in children's medicines – and one in infants and children with malaria. The dispersible formulation is as effective and well tolerated as the standard adult tablets\textsuperscript{10}, and encourages improved adherence to the drug regimen.

**How to counter drug resistance?**

Over the years, in many parts of the world, the malaria parasite has become resistant to conventional treatments, such as chloroquine, and other antimalarials when used on their own. As a consequence, the WHO changed its treatment guidelines to recommend the use of ACTs for *Plasmodium falciparum* malaria.

Yet, today, early signs of resistance to artemisinins have appeared in five countries of South-East Asia resulting in delayed parasite clearance from the blood\textsuperscript{13}. Even though ACTs may take longer to act in these areas, their overall efficacy is not affected as long as the partner drug to artemisinin remains effective\textsuperscript{14}.

“**It is very important to keep one step ahead of the parasite and provide innovative treatments to support malaria elimination efforts.**”

Thierry Diagana, Head of the Novartis Institute for Tropical Diseases

As the lumefantrine component in the Novartis treatment has never been used by itself to treat malaria\textsuperscript{15}, unlike the partner drugs of all other ACTs, the risk of resistance against the treatment may be lower compared to other ACTs. Yet, in an effort to anticipate any potential challenge to the effectiveness of its drug, Novartis is currently leading research to develop new drug candidates for drug-resistant malaria. These would be the first new antimalarials not belonging to the artemisinin class.
From 2000 to 2015, malaria mortality rates fell by 60% around the world. During this period, an estimated 6.2 million malaria deaths, of which 5.9 million among children under 5, were averted globally, primarily as a result of a scale-up of interventions.

These major achievements have substantially contributed to achieving the malaria-specific target of the Millennium Development Goal (MDG 6 target C) with a 37% decline in global malaria incidence since 2000. Vector control has been, and still is, instrumental in reducing malaria transmission at the community level. Long-lasting insecticide-treated nets (LLINs) and indoor residual spraying (IRS) with insecticides that kill the mosquitoes carrying malaria parasites are effective in a wide range of circumstances.

The World Health Organization (WHO) recommends LLIN coverage for all persons at risk of malaria. Indoor spraying remains effective for 3 to 6 months but requires at least 80% of houses in targeted areas to be sprayed to reach its full potential.

Prevention efforts have made a major difference. The proportion of the population having access to vector control (ITNs and/or IRS) in sub-Saharan Africa has increased from 2% in 2000 to 59% in 2014. In 2015, more than half of the population in sub-Saharan Africa (55%) is now sleeping under an insecticide-treated mosquito net, compared to 2% in 2000. Although this result represents a substantial increase since 2000, it falls short of universal coverage of this preventive measure.

Yet, the proportion of the population at risk that is protected by IRS has declined globally from a peak of 5.7% in 2010 to 3.4% in 2014.

Prevention alone is not sufficient. Treatment is needed to save lives and eliminate malaria parasites, preventing further transmission of the disease.

Patient impact – The combination of prevention and treatment to fight malaria is yielding unprecedented benefits for patients.
Since 2002, the WHO recommends the use of ACTs and as a result, most African countries have adopted the Novartis ACT as a first-line treatment. Rapid diagnostic tests (RDTs) also play a crucial role in fighting drug resistance as they help to ensure ACTs are only administered to patients who actually need them.

Beyond prevention and treatment, building capacity in malaria-endemic countries to strengthen their healthcare systems and deliver high-quality interventions is essential to ensuring long-lasting health impacts.

Importantly, malaria elimination requires sustained and aggressive efforts in the long term. This is why it is crucial that public donors and private companies alike continue to scale up funds and R&D toward malaria elimination.

“With a holistic approach including prevention and treatment, there’s a high potential to eliminate the disease in Zambia, but we need continued attention on the disease.”
Dr. Mabvuto Kanjo, former Case Management Specialist, Ministry of Health, Zambia

Combining interventions for maximum impact in Zambia, Ethiopia, Rwanda and Senegal

**Zambia**

The scaling up of malaria prevention strategies and vector control has dramatically reduced the disease burden in Zambia, the first African country to adopt the Novartis ACT as first-line therapy in 2003. An integrated malaria control program distributing ACTs and bed nets and applying indoor residual spraying was scaled up during 2003-2007. Following the program, malaria mortality and morbidity were dramatically reduced. In-patient malaria cases and deaths declined by 61% and 66%, respectively, in 2008 compared with the reference period (2001-2002) before the program. Under-five mortality was also reduced from 16.8% in 2002 to 7.5% in 2013. Although far below the recommended universal coverage rate, the proportion of children under 5 sleeping under a bed net has nearly doubled from 24% in 2006 to 41% in 2013.
Ethiopia
Similar positive outcomes were measured in Ethiopia, where 68% of the population lives in at-risk areas with an estimated 12 million suspected malaria cases each year. The Novartis ACT was launched as first-line therapy in 2004. As a result of combined interventions, including the delivery of ACTs in the public sector and more than 64 million LLINs between 2005 and 2014, the prevalence of malaria parasitemia in Ethiopia is now 1.3%, and the incidence of malaria deaths in children aged under 5 was 12.6% in 2010/2011, compared with 21.1% in 2003/2004. The country has also set up an elaborate health extension program involving around 38,000 volunteers who visit individual households, teach people about sanitation, do rapid diagnostic tests and treat positive cases.

Rwanda
Rwanda adopted the Novartis ACT as first-line therapy in 2006. It reported a significant decline in malaria incidence. Between 2005 and 2012, malaria morbidity decreased by 87%, while malaria mortality declined by 74%. This decrease is attributed to several measures including the distribution of LLINs, ACTs in all public health facilities and improved patient awareness. In spite of this, Rwanda has unfortunately experienced an upsurge in malaria cases in 2009, 2012 and 2013. Nonetheless, with the significant reduction in malaria cases over the past 10 years, the country aims to achieve malaria pre-elimination status by 2018.

Senegal
Large-scale deployment of the Novartis ACT and RDTs began in 2007 in Senegal and progressed rapidly, leading to a 3% prevalence of parasitologically-confirmed malaria cases in 2009 (from 36% clinical cases in 2001). The proportion of deaths attributable to malaria in children under 5 was also drastically reduced from 30% to 7% in the same timeframe, and by 2009, malaria accounted for 4% of all deaths in the country. To further reinforce the interventions and successes in the fight against malaria, in 2008, Senegal introduced a new type of health worker, the village malaria worker, who provides RDT testing and ACT treatment to patients in the household. This program is now active in almost 2,000 rural villages across 13 regions. Senegal, like Rwanda, hopes to achieve pre-elimination status by 2018.
Looking ahead

We have witnessed remarkable progress in the fight against malaria in the past 15 years – thanks to integrated strategies combining prevention and treatment, as well as efforts from endemic countries in malaria control.

Yet, the enormous progress achieved appears to have slowed down in recent years. International funding for malaria control has leveled off, and is projected to remain substantially below what is required to achieve universal coverage of malaria interventions.

To achieve the milestones and goals set out in the WHO’s Global Technical Strategy for Malaria 2016-2030, malaria investments will need to increase substantially above the current annual spending of USD 2.7 billion. The annual investment will need to reach an estimated USD 8.7 billion by 2030 to reduce malaria case incidence and mortality rates by at least 90% by 2030. Further, additional funding of USD 673 million will be required annually for R&D.

Key steps to malaria elimination

A sustained effort is required to continue to scale up access to treatment in order to reduce malaria mortality by 90% by 2030, as advocated by the WHO’s Global Technical Strategy for Malaria 2016-2030. While there are challenges, including a global funding gap partly due to declining donor financing, weak health systems and the potential emergence of drug and insecticide resistance, there is hope. Efforts must focus at all levels of the malaria “chain,” from quality of medicines to countering parasite resistance.

Quality

The use of monotherapies and sub-standard antimalarials should be stopped to prevent the development of parasite resistance. Quality-assured ACTs provide one way to slow the potential spread of drug resistance. Renewed international attention should also be given to deter counterfeits. Malaria is best fought using treatments with compounds that have never been deployed as a monotherapy, hence where no resistance has yet developed.

Affordability and accessibility

Effective treatments need to be made affordable to patients in the public and private sector alike. Initiatives such as the Private Sector Co-Payment Mechanism and the Novartis access program in the private sector can help bridge the gap.

Case management

Malaria elimination requires effective case management to scale up malaria diagnostic testing, treatment and surveillance systems.

Strengthening these three pillars presents significant challenges. Programs such as SMS for Life support these efforts by tracking surveillance data in addition to providing stock visibility of diagnostics and treatments.

Patient adherence

Continued information is necessary to maximize treatment adherence and successful health outcomes. Further, formulations tailored to the needs of patients, such as pediatric dispersible tablets or formulations that reduce pill burden, and user-friendly packaging can enhance treatment adherence. Fostering disease awareness and a timely treatment-seeking behavior among patients is also key to adherence.

Parasite resistance

Research and Development to discover the next generation of antimalarials is needed in case resistance to ACTs emerges. It is therefore important to develop new classes of treatment that are one step ahead of the parasite should resistance to current therapies occur. Efforts should also focus on radical cure, prevention and development of prophylactic treatments.

“Thanks to initiatives like the Novartis Malaria Initiative, people can have hope. We will be able to really tackle this disease and one day maybe, for the next generation, there will be a malaria-free world.”

Professor Awa Marie Coll-Seck,
Minister of Health, Senegal
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Pages 10-13: Access

Pages 14-17: Capacity building