

## GLAXOSMITHKLINE'S CONTRIBUTION TO FIGHTING HIV/AIDS & IMPROVING HEALTHCARE IN THE DEVELOPING WORLD

### *Introduction*

There are no easy solutions to the challenge of providing access to sustainable healthcare in developing countries. Poverty is the single biggest barrier. In many countries people do not have enough food, access to a clean water supply, hospitals or clinics in which to receive treatment, and healthcare professionals to care for them.

Often the governments of these countries simply do not have the resources needed to address the healthcare needs of their people. The WHO recommends a minimum spend on health of £17 per person per year to provide the most basic health services. Yet the average spend in sub-Saharan Africa is just £5. The African Region of the WHO suffers more than 24 percent of the global burden of disease, but has only 3 percent of the world's health workers. Significant additional funding from new national and international sources must be mobilised to really make a difference.

However, lack of resources can be no excuse for lack of action. AIDS is robbing communities and nations of their greatest asset - their people. That is why providing HIV treatment is so critical. By keeping people alive, existing capacities can be preserved. Treatment for people already living with HIV/AIDS should not be seen as a cost; but as an investment. We believe that it is the responsibility of governments and intergovernmental agencies, supplemented by the work of many NGOs, to work in partnership to deliver the healthcare needed in these countries. However, the pharmaceutical industry can play a significant role in supporting their work.

### *Our Approach*

GlaxoSmithKline is committed to playing a full part in addressing the healthcare challenges of the developing world by taking an innovative, responsible and, above all, sustainable approach. Our core business activity of developing and launching new medicines and vaccines significantly improves health. However, we do not have the mandate, expertise or resources to deliver healthcare unilaterally, GSK is making a vital contribution to developing country healthcare through action in four areas<sup>1</sup>: **preferential pricing** of our antiretrovirals, anti-malarials and vaccines; investing in **research and development** (R&D) that targets diseases particularly affecting the developing world; **community investment** activities and partnerships that foster effective healthcare; and, **innovative partnerships** and solutions.

We believe that our response is not only the right thing to do but makes good business sense. Companies that respond sensitively and with commitment by changing their business practices to address such challenges will be the leaders of the future.

A number of basic principles underpin GSK's contribution to improving healthcare in the developing world. Fundamental to these is the need for our approach to be sustainable. This means long-term for patients and viable for GSK. We also have a duty to try to ensure our products are used in a clinically appropriate way in all countries where they are available. This is particularly important in the case of communicable diseases, where inappropriate use of products can speed the development of resistance to treatment. Our activities are undertaken in partnership with organisations that have relevant specialised knowledge, such as governments, international agencies, charities, other private sector organisations and academic institutions. And we support intellectual property protection because it stimulates and underpins the continued R&D of new and better medicines.

### *Preferential Pricing*

**GSK has offered sustainable preferential pricing for ARVs since 1997 and for vaccines for over 20 years.**

Our AIDS medicines and anti-malarials are available at not-for-profit (n-f-p) prices to public sector customers and not-for-profit organisations in 64 countries - all the Least Developed Countries (LDCs) and all of sub-Saharan Africa (SSA). In addition, all private employers in sub-Saharan Africa who provide care and treatment to their uninsured staff can purchase our ARVs at n-f-p preferential prices. All CCM projects fully funded by the Global Fund to Fight AIDS TB and Malaria, are also eligible, which means that our not-for-profit prices are now available in over 80 countries, including projects run by the US President's Emergency Plan for AIDS Relief (PEPFAR). Our prices are sustainable – we do not make a profit on them, but we do cover our costs. This means that we can sustain supply of these high-quality products for as long as they are needed. Our n-f-p prices include insurance and freight costs and are applicable to orders of any size and are not dependent on large order quantities.

For middle-income developing countries we continue to negotiate public sector prices on a case-by-case basis to improve affordability.

**In Feb 2008 we introduced significant new price reductions averaging 21% across the range of our ARVs.** This reduction was the fifth time we have reduced prices as part of our pioneering preferential pricing policy originally introduced in 1997. The most significant reduction, of almost 40 per cent, was on Ziagen oral solution (abacavir), which is recommended by the World Health Organization (WHO) for use in first-line and second-line regimens within resource-limited settings, particularly for children. **Combivir was reduced by 17% to 54 cents per day.**

**In 2007 we shipped 13 million tablets of n-f-p-priced Combivir and 72 million tablets of n-f-p Epivir to the developing world** compared with 27 million and 59 million tablets respectively in 2005. This decrease was expected and is primarily due to more customers purchasing ARVs from generic manufacturers, including those licensed by GSK. In many ways this a positive indication that our licensing policy is working. **In 2007 our licencees supplied**

<sup>1</sup> For more information, please see <http://www.gsk.com/responsibility/cr-review-2006/access-to-medicines.htm>

**183 million tablets** of their versions *Epivir* and *Combivir*, compared to 120 million in 2006, making a total of 268 million shipped compared to 206m in 2006 and 126m in 2005.

It is difficult to estimate the number of patients treated as a result of our preferential pricing agreements, since GSK does not control healthcare provision. A report from the AAI, suggests that by **June 2007, some 694,400 patients in developing countries were receiving at least one ARV treatment supplied by the eight pharmaceutical companies in the AAI.** This includes 458,700 patients in Africa. Overall shipments and patient numbers are still low given the scale of the AIDS epidemic in Africa but the growth is encouraging.

With regard to vaccines, it is widely acknowledged that global immunisation is one of the most successful public health initiatives ever undertaken. It has led to the eradication of smallpox, the potential eradication of polio, and it is estimated to save the lives of up to three million children world-wide each year. GSK has played a key role in this effort as one of the primary suppliers of vaccines to major international organisations such as WHO, the United Nations Children's Fund (UNICEF) and the Pan-American Health Organisation (PAHO). **Consequently, typically 75-90% of all the vaccines we sell go to the developing world.**

**In June 2007, we announced our intention to donate 50 million doses of pre-pandemic flu vaccine to the WHO's stockpile for distribution to the world's poorest countries at short notice.**

#### ***R&D for tomorrow's medicines and vaccines***

As well as helping the developing world today, we are committed to its future by investing in the R&D that will produce the new treatments and vaccines for tomorrow. **GSK has the industry's most extensive portfolio of R&D projects for diseases of the developing world, with 12 clinical programmes, seven of which are for diseases that disproportionately affect developing countries. For HIV/AIDS, GSK is supporting 20 collaborative studies in developing countries, including 16 in Africa.** These studies involve more than 19,700 patients, including children. **We believe that we are the only company undertaking R&D into the prevention and treatment of all three of the World Health Organisation's priority diseases in the developing world – HIV/AIDS, tuberculosis and malaria.**

For diseases of the developing world, a dedicated group, based in the UK, US and Spain, has been created within GSK's pharmaceutical R&D organisation to ensure a focus on these diseases. For this group, drug development projects are prioritised primarily on their socio-economic and public health benefits rather than their commercial returns. There are over 100 GSK scientists at Tres Cantos half of whom are subsidised by our partner organisations - the Medicines for Malaria Venture (MMV) and the Global Alliance for TB Drug Development (TB Alliance). A similar group exists in our vaccines organisation based in Belgium.

In February 2008, GSK and the Medicines for Malaria Venture (MMV) received data from two Phase III clinical trials assessing use of the artemisinin-based combination therapy *Dacart*, we were developing together. One of the trials included our existing ant-malarial *Lapdap*. A key safety finding from these trials were that patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency were found to be more at risk of anaemia after taking either *Dacart* or *Lapdap*. Consequently, given the haematological profile of *Dacart*, and the fact that 10-25% of the population in sub-Saharan Africa is G6PD deficient, GSK and MMV decided to terminate the further development of *Dacart*. For the same reasons, GSK also decided to withdraw *Lapdap* from the market. This disappointment highlights the highly risky and complex nature of pharmaceutical research and development. However, GSK remains committed to working with partners such as MMV to seek solutions for patients suffering from this devastating disease.

**In January 2008, we announced a new collaboration with MMV** to identify novel drugs for the treatment of malaria. Research will focus on macrolide antibiotics, based on azithromycin, which may have promise as an antimalarial treatment. Under the new agreement, MMV will provide funding for research to be performed at GSK. This is in addition to our ongoing pyridone, falcipain and isoquine projects with MMV which are investigating new classes of compounds for use against malaria.

**In March 2008 we announced a new collaborative research effort with the Drugs for Neglected Diseases initiative (DNDi).** Research will focus on the most neglected diseases of visceral leishmaniasis, African sleeping sickness and Chagas disease.

**RTS,S/AS, our candidate malaria vaccine for children is currently in phase II clinical trials. We have been working on this vaccine for over 20 years and have invested over US\$300m.** In 2004 a clinical trial conducted in Mozambique showed unprecedented results in protecting a significant percentage of children against uncomplicated malaria, malaria infection, and even severe forms of the disease. In 2005, we published new data showing that the vaccine remained efficacious over an extended 18 month period.

**In 2007 the Lancet published results of a study that provided the first proof of concept of RTS,S in infants, the most vulnerable age group for malaria in Africa.** It demonstrated for the first time that African infants exposed to malaria transmission (*P. falciparum*) can be protected by a vaccine. These landmark results substantially advance the vision that a vaccine will be capable of protecting young African children and infants against malaria and therefore will contribute to reducing the burden and deaths caused by the disease. **We will now be moving into a full Phase III trial which if successful could result in submission to regulatory authorities in 2011.**

**GSK is also developing sitamaquine a potential new once-a-day oral treatment for visceral leishmaniasis,** which affects half a million people a year in the developing world and is usually fatal if untreated. GSK is providing all the funding for this project. Sitamaquine has shown good efficacy in phase II trials. The low cost of goods suggests that sitamaquine could be the first truly accessible treatment for visceral leishmaniasis which affects the poorest of the poor.

**In 2005, Rotarix, our vaccine for the prevention of gastroenteritis, was launched in Mexico.** Rotavirus infection is the leading cause of severe diarrhoea and vomiting (gastroenteritis) in children under two and kills around 600,000 children each year - one child every minute - mostly in developing countries. It has now been approved in 90 countries world-wide, and children in some 50 countries are already benefiting from the vaccine. **Early in 2007, GSK received prequalification status for its rotavirus vaccine from the World Health Organisation (WHO).** This is required before UN organisations and GAVI (formerly known as the Global Alliance for Vaccines and Immunisation) can purchase a vaccine. **In 2007 we supplied 14m doses of the vaccine,** the vast majority to the developing world

**In January 2008 GSK and the TB Alliance announced the renewal of its joint drug discovery partnership,** which commenced in 2005 adding several novel classes of compounds to the world's TB pipeline. The agreement stipulates that any resulting medicines will be affordable and accessible to those most in need.

**In 2005 GSK and the Aeras Global TB Vaccine Foundation announced a partnership to develop GSK's tuberculosis candidate vaccine.** In 2006 GSK began additional trials involving adults previously infected with TB or vaccinated with BCG. We plan to conduct further studies in Africa and other locations to test the safety and efficacy of the vaccine candidate in populations highly affected by TB.

**We are working on new HIV medicines in several different drug classes, including an integrase inhibitor in phase 1, and a number of pre-clinical projects.** For children, we have developed scored tablets for our key ARVs (*EpiVir*, *Ziagen*, and *Combivir*) so they can be broken into two smaller doses to simplify treatment. **We received approval from the European Commission for these versions in Q3 2007.**

**In 2005, GSK and the Institut Pasteur announced a new European collaboration to develop an AIDS vaccine** by fusing genes from the human immunodeficiency virus (HIV) onto an existing measles vaccine. The initial project is being supported by a €5.5 million grant from the European Union. Clinical studies will begin in the third year of the four to five year collaboration.

**Also in 2005, GSK announced a collaboration with the International AIDS Vaccine Initiative (IAVI) to develop an AIDS vaccine.** The collaboration – the first-ever in AIDS vaccine research between IAVI and a major vaccine company – will facilitate early research and development of GSK's non-human primate adenovirus vaccine vector as an enabling component of an effective AIDS vaccine. The IAVI-GSK collaborative research will initially focus on vaccines against variants of HIV that circulate predominantly in Africa. GSK Biologicals also has two in-house AIDS vaccine development projects using the company's proprietary adjuvant technology. A successful AIDS vaccine might need to combine several of these approaches.

### **Community Investment**

Through our Global Community Partnerships programme, GSK funds community-led initiatives in over 100 countries around the world. We have a wide range of partnerships, with a focus on health and education programmes for under-served communities. **During 2007 we donated life-saving medicines valued at £16m to support relief efforts in over 100 countries.** In the developing world, GSK's activities span four major developing world diseases (lymphatic filariasis, HIV/AIDS, malaria and diarrhoeal disease), a number of regional health initiatives, health education, product donations, and employee involvement. The examples below are indicative of our activities in the developing world.

Lymphatic Filariasis (LF) - in 2007, through GSK's partnership with the WHO's Global Alliance to Eliminate Lymphatic Filariasis, we donated 150 million treatments of albendazole to 19 countries to prevent transmission of one of the world's most disabling tropical diseases. LF currently affects 120 million people and threatens over 1 billion in 80 countries. **The company has provided free of charge almost 750 million albendazole treatments since 1998. Over 130 million people have been treated at least once and many millions have received multiple rounds of treatment.** In 2005 we expanded our manufacturing site in Cape Town, South Africa, to produce albendazole tablets and help us deliver enough treatments to support elimination efforts in all at-risk countries. **Over the anticipated 20 year life of the programme, our donations will build to an estimated six billion tablets, valued at \$1 billion. We also gave £1 million in grants during 2007 to support the Global Alliance** and a team of dedicated GSK employees helps in its advocacy, research, community mobilisation and education initiatives.

HIV/AIDS – 2007 marked the 15th anniversary of Positive Action, GSK's programme to support the communities most affected by HIV/AIDS. Positive Action has pioneered building capacity and support for community organisations who are frequently the only source of HIV/AIDS education, treatment literacy and care for people living with HIV/AIDS in developing countries. **During 2007 Positive Action supported 17 programmes in 19 countries, many focused on countering the ignorance and stigma of AIDS.**

Malaria – Our first African Malaria Partnership supported education and behaviour change programmes in eight African countries, through partnerships with three non profit organisations. This was followed by a second £0.9m grant to the Malaria Consortium to raise awareness of malaria in Europe and throughout Africa and bring greater resources to bear against the disease, **In 2007 Innovation Grants for Malaria Advocacy were awarded to four organisations in Africa, working in Nigeria, Congo, Senegal and Uganda.**

Diarrhoeal Disease - Every year more than two million people die of diarrhoea-related disease, mostly children in developing countries. These deaths can often be easily prevented through better hand washing and sanitation. PHASE, established by GSK in 1998, is an education programme helping to reduce diarrhoea-related disease by encouraging school children to wash their hands. **In 2007 GSK committed three year funding of \$1.8 million to extend PHASE to Indonesia and Bolivia in partnership with Save the Children USA.** PHASE currently operates in ten countries and will reach over a million children by 2010. The programme has had impressive results. **For**

**example, studies show that diarrhoea rates have fallen by 40% following the introduction of PHASE to schools in the Kenyan community of Ongiello.**

### ***Innovative Partnerships***

GSK wants to be at the heart of the global response to the HIV/AIDS pandemic. We are constantly looking for creative ways and partnerships to help countries improve access to medicines. These can include the granting of voluntary licences (VL).

To reflect the gravity of the HIV/AIDS crisis in sub-Saharan Africa, we granted our first licence in October 2001 to Aspen Pharmacare, sub-Saharan Africa's largest generics company, for the manufacture and sale of versions of *Combivir*, *Epivir* and *Retrovir*. The licence now covers both the public and private sectors across all of sub-Saharan Africa. **In 2006 we granted our 8<sup>th</sup> voluntary licence** for our antiretrovirals (ARVs) in Africa, where HIV/AIDS is having a devastating impact. This includes six VLs in South Africa and two in Kenya. Some cover just parts of Africa and others all of sub-Saharan Africa. **In 2008 our licencees supplied over 180 million tablets of their versions *Epivir* and *Combivir* to Africa, more than we shipped ourselves.**

We are prepared, in appropriate circumstances, to grant other voluntary licenses. It is, however, important to be realistic about the challenges and benefits of VLs. It is vital to choose the right partners. Licensees must be able to ensure, inter alia - sustainability of supply of quality products; that the medicines are used safely; and that they can protect products against diversion (i.e. ensure those patients who need the medicines, get the medicines). We do not believe, therefore, that voluntary licencing is a universal solution to the HIV/AIDS crisis. We also recognise compulsory licencing (CL) as one of the flexibilities in the TRIPs agreement, as well as the 31f solution to allow CL for export. In this regard, **in August 2007, GSK was the first company to grant consent for a generic company to manufacture an ARV fixed dose combination containing GSK's molecules under the 31f agreement for supply to Rwanda.**

### ***The Role of Others***

Access to medicines in the developing world remains a complex issue. It presents a unique challenge to the global community. Welcome new resources are coming through from the Global Fund to Fight AIDS, TB and Malaria, the World Bank, the Gates Foundation, the US Government and others. Nevertheless, funding remains inadequate. Wealthy nations must give more. We must also stop the illegal diversion of discounted medicines from patients in the world's poorest countries to richer markets.

Developing world countries also have their part to play. Middle Income countries must accept their responsibilities and not seek the lowest prices offered to the world's poorest countries. Others need to show genuine political commitment of the kind shown by Uganda and Botswana. This means addressing stigma; it means removing import tariffs that raise prices; and it means prioritising healthcare in national budgets. Countries must also drive out inefficiencies in the procurement, storage, prescribing and use of drugs. The World Bank estimates that some African countries get the benefits of only \$12 worth of medicines for each \$100 spent on drugs by the public sector.

Resources are needed to provide the infrastructure – hospitals, clinics, distribution networks – which will ensure that medicines reach patients. The African Region of the WHO suffers more than 24% of the global burden of disease, but has only 3% of the world's health workers. Resources are needed to discourage the migration of healthcare workers.

Generic companies have an important role in addressing the AIDS crisis. But it would be counter-productive to ignore or undermine the role of the research-based industry. There is a fundamental truth about AIDS – we need new medicines and vaccines. We do not yet have a cure for AIDS. We do not have a vaccine for AIDS. Existing medicines are less and less effective as resistance to them grows. Intellectual property protection is of critical importance to the R&D-based industry. If there is no intellectual property protection, there will be no R&D. And if there is no R&D, there will be no new medicines and vaccines.

Too many people see local manufacturing, and tearing up intellectual property (IP) rules, as a panacea. This is simplistic and counter-productive. If that were the answer, India would deal with AIDS better than any country in the developing world. Until recently, India had no IP protection for pharmaceutical products, and has the most developed generics industry in the world, and yet access to ARVs for those who need them is arguably no better than in Africa. Additionally, of the 325 medicines on the WHO's Essential Medicines List, over 95% are off patent and yet the WHO state that a third of the world's population have no reliable access to them. Clearly, lack of healthcare infrastructure and resources are the problems, and where the focus should be, rather than on IP.

### ***Conclusion***

It is 10 years since GSK pioneered donation programmes and sustainable preferential pricing for antiretrovirals (ARVs) to prevent mother-to-child transmission of the HIV/AIDS virus. Since then we have learned many lessons. We have learned that stigma and discrimination are real barriers that limit access to treatment. We have learned that donations are not a sustainable way to address chronic diseases. And we have learned that without the necessary healthcare infrastructure, access to treatment will always be denied to those who need it, no matter how low price medicines become. Most importantly, we have learned that only an holistic approach embracing both prevention and treatment will work - one in which medicines play a supporting role in a comprehensive programme of prevention, health education, screening diagnosis and treatment, community care and support.

The global community must provide political will, a significant mobilisation of additional resources and a spirit of partnership if we are to see an improvement in healthcare and quality of life across the developing world. At GSK, we believe we are playing our part. We will continue with our efforts, improving our initiatives by applying lessons learned and looking for opportunities to do more.