

Partnering for HIV Prevention — The Case of Maraviroc

Maraviroc, sold under the trade name Selzentry™/Celsentri®, is the first in a new class of oral medicines for HIV. Pfizer discovered the molecule and mechanism of action in 1997 and after several years of clinical trials, the medication was put on fast-track review for approval by the U.S. Food and Drug Administration. Approved in 2007, maraviroc approaches HIV in a unique way. The new class of drugs, known as CCR5 blockers, slow HIV infection by preventing the virus from entering uninfected cells.

Microbicides and the Worldwide HIV Epidemic

According to the Joint United Nations Programme on HIV/AIDS women make up half of the HIV cases worldwide. In sub-Saharan Africa, women and girls account for 61% of the cases. More than two in three adults infected worldwide live in this region, and more than 75% of global deaths from AIDS occur in sub-Saharan Africa highlighting the need for prevention and treatment options.¹

Major risk factors for infection are being female, married and poor, especially in sub-Saharan Africa. The ABC approach (Abstinence, Being faithful and using Condoms) does not sufficiently meet women's prevention needs. "Among young women surveyed in Harare (Zimbabwe), Durban and Soweto (South Africa), 66% report having one lifetime partner, and 79% had abstained from sex at least until the age of 17. Yet, 40 % of these young women were HIV-positive." Even women faithful to one partner are often infected. "Female-initiated" prevention options, such as microbicides, are critically needed.²

"Microbicides are a development priority. I can think of no other technology that has the potential to dramatically improve the health of women in developing countries. Moreover, I do not see how we can meet the MDGs [Millenium Development Goals] without safe and effective microbicides."

--Stephen Lewis, former UN Special Envoy for HIV/AIDS in Africa

¹ UNAIDS. AIDS Epidemic Update: December 2007, page 7.

² UNAIDS. AIDS Epidemic Update: December 2005, page 9.

Pfizer Partners with IPM

“The International Partnership for Microbicides (IPM) is a non-profit product development partnership established in 2002 to prevent HIV transmission by accelerating the development and availability of a safe and effective microbicide for use by women in developing countries.”



“IPM is committed to providing women with an affordable and self-initiated HIV- prevention strategy to reduce the cycle of infection which has led to the deaths of more than 25 million people worldwide and orphaned more than 15 million children since 1981. Like the promise of a future AIDS vaccine, microbicides represent an essential component of an integrated and comprehensive global response to the HIV/AIDS epidemic.”³

In early 2008, Pfizer and IPM signed a licensing agreement to develop a microbicide from maraviroc. The agreement marks only the second time a pharmaceutical company has licensed an already approved HIV therapy to be developed as a microbicide. Given maraviroc’s mechanism of action blocking entry of HIV into healthy cells, the possibility of its use as a microbicide is exciting.

The Partnership Process

Microbicides are products that can be applied vaginally by women to impede sexual transmission of HIV. A variety of formulations are possible, including gels, films, vaginal tablets, and intravaginal rings.

“The development of microbicides is a long and complicated process, with many hurdles that are unique to this class of product, including challenges in product design, in the conduct and design of clinical trials, and in obtaining licensure of a new class of products intended for use almost exclusively in developing countries.”⁴

Pfizer began discussions with IPM while the compound now known as maraviroc was still in the registration phase. Negotiations needed to resolve several important questions regarding the development process, funding and licensing. Because maraviroc is currently on the market as a treatment for HIV infection, the prospect of simultaneously developing maraviroc as a microbicide for use in prevention presents a number of challenges. The results of IPM’s preclinical and

³ http://www.ipm-microbicides.org/about_ipm/english/index.htm

⁴ Nuttall, J et al., “The future of HIV prevention: prospects for an effective anti-HIV microbicide,” *Infect Dis Clin North Am*. 2007 Mar;21(1):219-39.

clinical studies of maraviroc, as well as IPM's efforts to obtain regulatory approval, could potentially have an impact on the status of maraviroc as a therapeutic. However, these challenges did not deter Pfizer from making a commitment to the development of maraviroc as a microbicide.

Development

IPM is responsible for the design and implementation of the development program and anticipates initial Phase 1 safety trials of a maraviroc microbicide will be initiated in 2010. Pfizer has provided valuable preclinical and clinical data concerning maraviroc to IPM, and IPM and Pfizer communicate regularly concerning the progress of the development effort.

Development of maraviroc as a microbicide will require a full range of drug development activities, from preclinical formulation and testing through manufacture of clinical trial material and clinical trials through Phase III. IPM's scientific, manufacturing and clinical staff based in the U.S. and South Africa will have primary responsibility for these activities. IPM will also engage its development partners in the U.S., Europe and Africa, and will contract with qualified organizations for development and clinical services.

IPM has prepared a written development plan for the project which IPM shares with Pfizer on a regular basis. IPM holds regular meetings with Pfizer and engages in frequent informal communication with Pfizer to keep Pfizer updated about the progress of the project.

Funding

In the development effort to use maraviroc as a microbicide, IPM will be responsible for all costs. IPM receives funding from foundations, including the Bill and Melinda Gates Foundation and the Rockefeller Foundation, multilateral organizations such as the European Commission, and from 12 national governments. The Bill and Melinda Gates Foundation has a particular interest in the development of microbicides as a mechanism to combat HIV worldwide and made the largest grant ever to support research efforts in 2003 to IPM.

The chief executive officer of IPM, referred to the new approach as a sort of "'venture capital fund' for microbicides."⁵

Licensing

The collaboration between IPM and Pfizer is governed by a Development and License Agreement. Under the agreement, Pfizer has licensed maraviroc to IPM

⁵ IPM Press Release, "Gates Foundation makes \$60 million grant to accelerate HIV/AIDS microbicide research," March 21, 2003. http://www.ipm-microbicides.org/news_room/english/press_releases/2003/2003_0431_gates.htm

for the development and manufacture of microbicides for prevention of HIV/AIDS and distribution on an affordable basis in resource poor countries. The license is non-exclusive and royalty free.

In the negotiation of the License Agreement equitable resolutions were reached on issues such as supply and manufacture of the active compound, and access to maraviroc for partners and contractors providing development services to IPM. IPM and Pfizer are pleased that the time and effort invested in negotiating the terms of their relationship has resulted in arrangements that are beneficial to both.

Pfizer's Contributions to New Approaches to HIV

Pfizer is proud to contribute to the effort to develop a safe and effective microbicide with the potential to give women around the world new ways to protect themselves from HIV. In addition to developing new drugs to treat AIDS, and in line with the expectations of the international development community, Pfizer is committed to searching for ways in which its drugs can be used to slow down or stop this epidemic. The Bill and Melinda Gates Foundation considers stopping AIDS its top priority and believes the participation of pharmaceutical companies to be a key component in this battle. Melinda Gates addressed the XVI International AIDS Conference in 2006 and explained:

*"Pharmaceutical companies can make a powerful contribution by spending more on research and development for preventive tools, including microbicides. But there is another exciting way in which they can contribute. Drug companies have developed medicines to treat people with HIV. They should do more to share these drugs with researchers who want to test whether they can also be effective for prevention."*⁶

In the next few years IPM will conduct clinical trials as part of this collaboration, and IPM is hopeful Pfizer's safety and efficacy data for maraviroc as a therapeutic will speed its development as a microbicide. A crucial factor in successfully implementing this partnership has been Pfizer's confidence in IPM's ability to undertake drug development in a professional manner, and in IPM's understanding of Pfizer's perspective and drug development generally. Without this threshold level of trust the collaboration would probably not have been possible.

⁶ Gates, M., Keynote Address XVI International AIDS Conference, August 13, 2006.

**XVI International AIDS Conference Keynote Speech
Melinda Gates, August 13, 2006⁷**

“...Governments should make the search for new prevention tools, such as microbicides, a bigger priority in their budgets. If they can, they should host clinical trials, and use their influence to help the trials run smoothly.

Pharmaceutical companies can make a powerful contribution by spending more on research and development for preventive tools, including microbicides. But there is another exciting way in which they can contribute. Drug companies have developed medicines to treat people with HIV. They should do more to share these drugs with researchers who want to test whether they can also be effective for prevention.

Researchers can help test the drugs more quickly by developing novel trial designs, finding faster ways to analyze data, and coming up with biomarkers that can help test a hypothesis without needing a clinical trial of 10,000 patients. They should also make sure that when clinical trials are run, they benefit those who are in greatest need.

The WHO, UNAIDS, and other organizations should help develop common ethical standards for clinical trials so they can start faster and run without interruption.

If all these players do their part, we will move forward, as fast as science can take us, to discoveries that can help block the transmission of HIV. This goal is worth our greatest efforts; it could very well be the turning point that leads to the end of this disease.”

⁷ Video available at: <http://www.gatesfoundation.org/speeches-commentary/Pages/melinda-french-gates-2006-international-aids.aspx>

Discussion Questions

1. What issues must be resolved for private entities and public groups to work together to address public health epidemics such as HIV/AIDS?
2. How can microbicides be used as a tool against HIV infections?
3. Who should be responsible for developing innovative treatments for public health crises in resource-poor countries?
4. Are there ways non-profits and governments could encourage pharmaceutical manufacturers to develop treatments and preventions for diseases like HIV? How could it be done? Should it?
5. Should private companies develop products for diseases with limited commercial viability? Why or why not?