



INTERNATIONAL
PARTNERSHIP FOR
MICROBICIDES

RESPONDING to WOMEN'S NEEDS

Developing HIV and Multipurpose Prevention Products



2013 ANNUAL REPORT



Dr. Zeda F. Rosenberg
Chief Executive Officer



Dr. James McIntyre
Chair of the Board

Dear friends and colleagues,

Since our founding in 2002, the International Partnership for Microbicides (IPM) has dedicated itself to reducing the devastating toll that HIV has taken on women by developing new products that would enable them to protect their sexual and reproductive health on their own terms. Today, we are closer than ever to finding out whether the monthly dapivirine vaginal ring could be one such option.

Two Phase III trials of the ring, the IPM-led Ring Study and the Microbicide Trials Network (MTN)-led ASPIRE trial, are ongoing at over 20 sites in Malawi, South Africa, Uganda and Zimbabwe. With these two studies running in parallel and with smaller supporting studies of the ring, IPM has built a strong foundation from which to seek regulatory approval for the product should the studies show safety and efficacy in 2016.

Pending results and regulatory approval, the ring could be available to women in sub-Saharan Africa as early as 2017. If the results of the FACTS 001 trial expected early next year confirm the effectiveness of tenofovir gel, women could potentially benefit from multiple products that meet their unique needs.

We recognize that HIV is but one among a constellation of threats to women's sexual and reproductive health. IPM is actively developing new products in multiple formulations, including a 90-day vaginal ring that would protect women against both HIV and unintended pregnancy. We anticipate that this multipurpose prevention technology (MPT) will enter Phase I trials in 2015. Given our recently expanded partnership with Janssen R&D Ireland granting IPM exclusive worldwide rights to dapivirine, we could one day make our MPT ring available to women everywhere.

Staying on the front lines of prevention science is critically important if we are to overcome the constantly changing HIV epidemic. IPM is also pioneering the development of products that combine two types of antiretroviral drugs (ARVs) with different mechanisms of action to help ensure that a next generation of products will be available to combat the epidemic in the future.

This work could not occur without the efforts of the women who volunteer for clinical trials, the support of communities where the trials take place, research partners who conduct our trials, pharmaceutical companies who grant us licenses for their ARVs, civil society groups that build political will for global health R&D, and our donors, whose investment in the promise of a world where women can protect their own health renews our momentum every day. Each of these commitments sustains the research that is responding to the most pressing sexual and reproductive health issues affecting women today.

A handwritten signature in black ink that reads "Zeda F. Rosenberg".

Dr. Zeda F. Rosenberg

A handwritten signature in black ink that reads "James McIntyre".

Dr. James McIntyre

Around the world, **women face complex challenges to their sexual and reproductive health**. Issues such as HIV and unintended pregnancy have devastating effects on women, their families and their communities. IPM is designing a product pipeline to overcome these challenges by using cutting-edge science to respond to the complexity of the HIV epidemic and the diversity of individual needs. **Here are five highlights from 2013:**



Dapivirine Ring: Progress on the Path to Licensure

Women of reproductive age are the most at-risk for HIV infection. In sub-Saharan Africa, where the epidemic has hit hardest and is driven mainly by unprotected heterosexual sex, women make up nearly 60 percent of HIV-positive adults. Globally, young women ages 15-24 are twice as likely to be infected as young men of the same age. Women urgently need new prevention options they can initiate themselves.

IPM's discreet, easy-to-use monthly vaginal ring is designed to protect women from HIV infection during sex. The long-acting ring slowly releases an antiretroviral drug called dapivirine, a non-nucleoside reverse transcriptase inhibitor, or NNRTI, that prevents the virus from replicating in healthy cells. Because women can insert the ring and leave it in place for one month, it could help encourage consistent use.

Taking Phase III Trials to Scale

IPM brought the dapivirine ring from concept to Phase III clinical trials in just seven years. To minimize the time between research and regulatory approval, which generally requires replicated results from at least two late-stage trials, IPM's Dapivirine Ring Licensure Program includes two parallel Phase III trials. These two studies — The Ring Study, led by IPM, and its sister study called ASPIRE, led by the MTN (a National Institutes of Health-funded program), together will determine the ring's efficacy and long-term safety. The Ring Study and ASPIRE are the first Phase III trials of a microbicide ring and expanded rapidly in 2013, with enrollment at over 20 sites in Malawi, South Africa, Uganda and Zimbabwe. The two studies together are expected to include more than 4,500 women volunteers ages 18-45, with results expected by 2016.

Supporting studies

In 2013, five smaller safety studies of the dapivirine ring were conducted to support a robust data package for regulatory approval and eventual licensure. Studies that assessed interactions between dapivirine and a drug commonly used to treat vaginal yeast infections, and the use of the ring with male condoms both concluded in 2013. Results will be available in 2014. Studies initiated in 2013 are evaluating:

- use of the ring with female condoms
- extended use of the ring
- safety of the ring in postmenopausal women over 45 (in partnership with MTN)

Studies planned for 2014 will assess:

- effects of ring use during menses and with tampons
- sociobehavioral factors of adherence
- safety of the ring in adolescents (in partnership with MTN)



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Clinical Trial Success Factors

Prioritizing Adherence

Previous IPM studies have found the ring technology to be highly acceptable and well-tolerated by women and male partners. Yet the success of any prevention product depends on whether it is used consistently and correctly. HIV prevention research has shown that ARV-based methods can be effective when used as directed. That is why IPM focuses on promoting adherence in its clinical trials and identifying factors that encourage adherence.

How is adherence measured? The Ring Study and ASPIRE are using objective methods to monitor participant adherence to the monthly ring such as the amount of dapivirine remaining in used rings as well as drug levels in plasma and vaginal fluid samples. We are also collecting qualitative data from questionnaires and in-depth interviews.

How are we promoting adherence? IPM worked closely with research centers in 2013 to offer in-depth counseling training, refine adherence messaging and plan local events that engage communities in supporting trial participants to maintain adherence.



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Shaping the HIV Prevention Landscape

Turning research into on-the-ground benefits for women is a challenge for any organization. IPM is pursuing a comprehensive strategy to shorten the time line between clinical trial results for the dapivirine ring and its potential licensure, manufacturing and distribution.

Building a Case for Licensure

As the regulatory sponsor for the dapivirine ring, IPM continues to consult with regulatory authorities to understand country dossier requirements, and help streamline the regulatory submission and approval process. IPM met with national regulatory authorities in Kenya, Tanzania, Uganda, Zambia and Zimbabwe in 2013 to discuss country-specific requirements. In 2014, IPM will continue to engage with regulatory bodies in African countries where we hope the ring will be made available, including the Medicines Control Council of South Africa.

In addition, IPM has sought and received scientific advice at every step in the process from the European Medicines Agency (EMA), the US Food and Drug Administration (FDA) and the Medical Products Agency in Sweden, where the ring is manufactured. These consultations are key to expediting future marketing approvals and review under EMA Article 58 and FDA, both of which will inform the determination of drug prequalification by the World Health Organization.

Assembling a Regulatory Dossier

To request regulatory approval for the dapivirine ring, IPM is building a dossier of complete historical data on the product's ingredients; data from over 200 chemistry, manufacturing and control, and preclinical studies; and results from approximately 40 clinical studies. Because dapivirine is a new chemical compound not yet reviewed by regulators, our data would serve as reference for future dapivirine-based product submissions.

Moving Toward Access

IPM is leveraging its cross-sector collaborations and drawing on lessons learned from the global health community's experiences with product introduction in developing countries to plan for providing the dapivirine ring to women most at risk of HIV infection as quickly as possible upon regulatory approval.

In 2013, to prepare for the ring's roll-out, IPM began identifying potential partners for the ring's financing, commercial manufacturing, distribution, marketing and health service use.

IPM will continue to refine its access strategy in consultation with its donors and partners in 2014, including efforts to minimize the costs of the dapivirine ring to governments and end users, and to support country implementation through possible small-scale demonstration projects and studies.

Fostering Local Research Capacity

In 2013, IPM worked closely with research center partners to build skills and jointly develop solutions to potential challenges. IPM hosted trainings on topics such as good clinical practices, data management and quality control, interview techniques and study procedures. These ongoing collaborations help ensure the successful implementation of The Ring Study and other microbicide trials, while helping to build the capacity of the cadre of skilled African clinicians and researchers who are committed to turning the tide of the HIV epidemic.



In 2013, IPM's ring manufacturing partner, QPharma, produced the thousands of rings needed to meet the demands of both Phase III trials. Manufacturing for the Phase III trials and supporting studies was recently completed.

Spotlight on Scale-up

In anticipation of the ring's potential licensure, IPM is exploring various options that would enable higher product yields and drive costs down. For example, increasing automation and adding new equipment that would produce multiple batches of rings simultaneously could save time and translate to efficiencies of scale.

Planning for Efficacy

Should both The Ring Study and ASPIRE show the dapivirine ring to be safe and effective in preventing HIV, IPM and its partner MTN will invite former participants to enroll in follow-on trials that provide early access to the dapivirine ring. These Phase IIIb trials — now being designed — would allow former Ring Study and ASPIRE participants who remained HIV-negative to continue using the dapivirine ring while regulatory approval is pending.

In 2014, IPM and MTN are meeting with civil society advocates to seek input on the designs of the two follow-on studies in the four countries where the Phase III trials are now under way. These meetings also examine the realities of HIV prevention efforts on the ground and inform preparations for future access to the ring.

Raising the Ring's Profile Among Health Workers

It is essential that health policymakers and health care providers — who will have influence in determining the ring's accessibility and use — have a clear understanding of what microbicides are and the role they can play in overall HIV prevention efforts. To this end, in 2013, IPM embarked on a qualitative study of health workers' knowledge and perceptions of microbicides in Kenya, Malawi and Zimbabwe. IPM is conducting in-depth interviews and focus group discussions with health workers to assess knowledge gaps and factors that can promote or slow the introduction of the dapivirine ring. In 2014, the results will be used to inform the development and dissemination of educational materials about microbicides in general and the dapivirine ring specifically.





Staying One Step Ahead of HIV

Microbicides will prevent HIV only if women use them in their everyday lives. Women need multiple and complementary prevention tools that fit their needs — from oral ARVs to vaginal rings and gels to a future vaccine and beyond. A diverse product pipeline, including products containing multiple classes of ARVs that are used solely for HIV prevention, may increase efficacy and help prevent the acquisition of drug-resistant HIV over time.

Because it takes more than a decade for prevention technologies to go through clinical trials and reach regulatory approval, research and development on additional drugs must happen now. Through our six royalty-free licensing agreements with pharmaceutical partners for eight different ARV compounds, IPM is developing a range of products to address the urgent health risks that women face every day.

Harnessing the Potential of Dapivirine

IPM's first royalty-free licensing agreement was signed in 2004 with Janssen R&D Ireland, one of the Janssen Pharmaceutical Companies of Johnson & Johnson, granting IPM the right to develop dapivirine as a microbicide for use in developing countries. This license has since been expanded to a worldwide rights agreement. A highly potent NNRTI, dapivirine is not used for treatment and has been shown to be safe and well-tolerated in all 26 clinical studies to date. Recognizing dapivirine's potential, IPM is also evaluating other dapivirine formulations alone and with other ARVs.

A Multipurpose Prevention Ring for Broad Sexual and Reproductive Health Needs

Given the dual threats women worldwide face from HIV and unintended pregnancy, IPM is building on its ring technology with a long-acting multipurpose ring that contains both dapivirine and the contraceptive levonorgestrel. Because many women's perceived risk of HIV is low compared to their perceived risk for pregnancy, combined technologies may one day be more widely used than a product that targets HIV alone.

Protection for 90 days: In 2013, IPM worked with Particle Sciences, Inc. (US) and Queens University Belfast (QUB) (UK) to design and evaluate several prototypes of this multipurpose ring. IPM selected a silicone matrix formulation developed at QUB that released the two drugs at stable levels over 90 days. This long-acting feature would increase the ring's convenience and decrease its overall cost to women.

IPM is collaborating with QUB to develop the multipurpose ring, which is anticipated to enter Phase I trials in 2015.

Combination ARV Ring Shown to be Safe

Combining ARVs that use different mechanisms of action may offer increased protection against HIV compared to a single drug alone. In 2013, IPM's dapivirine-maraviroc ring was found to be safe, well-tolerated and acceptable in an MTN-led Phase I trial — the first combination ARV microbicide to go to clinical trials. IPM is now optimizing the formulation to increase maraviroc levels released from the ring over the course of one month. The reformulated ring is expected to be ready for preclinical testing in 2015.

Advancing Promising ARV Compounds

A potent gp120-binder licensed to IPM from Bristol-Myers Squibb called DS003 presents a new mechanism of action that has not yet been used in HIV prevention or treatment — greatly increasing the chance it will be active against drug-resistant HIV. Acting on that promise, IPM continued the development of prototype DS003 vaginal tablets in 2013 and conducted early preclinical assessments to help establish DS003's safety profile. Additional preclinical studies will be conducted in 2014. IPM is working to identify manufacturing partners for an anticipated Phase I clinical trial in 2015. A ring formulation is also being planned.

The Ring Study gives hope for women to have peace of mind in preventing HIV/AIDS. We hope our community will be among the first to start using the ring when licensed.

— Rose Masilo, Madibeng Centre for Research, South Africa

Partnering for a Diverse Pipeline

Through collaborations with other product developers, IPM leverages resources and scientific know-how to advance IPM-licensed compounds and help expand the broader field's product pipeline.

IPM is providing clinical supplies and regulatory support to collaborators to develop:

- **Dapivirine vaginal film** (NIH-funded Magee Womens Research Institute FAME program), which was found to be safe and acceptable in a 2013 Phase I safety study.

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Raising Microbicide Awareness

Community Engagement

Successful clinical research responds to the issues affecting the communities in which it is conducted. IPM places a high priority on community awareness and support, working with research center partners to deliver educational materials and hold local events and trainings. Strengthening research literacy in communities helps to increase awareness of HIV and other health issues, a benefit that can continue long after IPM's studies have concluded.



The South African National AIDS Council's (SANAC) Women's Sector held its biennial Women's HIV Prevention Summit in September 2013. IPM supported the summit, which brought together multiple sectors to focus on key issues in HIV prevention among women.

- **Maraviroc vaginal film** (FAME program), plans for which are under way.
- **Maraviroc-based rectal gel** (NIH-funded CHARM program at the University of Pittsburgh), which showed protection against HIV in a 2013 preclinical study in macaques. A Phase I trial is planned for 2014.
- **Dapivirine-darunavir ring and gel** (European Commission-funded CHAARM consortium) was evaluated in preclinical studies in 2013, with a Phase I trial expected in 2014.

Influencing Policy

IPM conducts outreach with national, regional and global decision-makers who will have key roles in influencing future access to microbicides and other tools women can use to protect their health. In 2013, IPM worked with its network of partners, including the Southern African AIDS Trust (SAT) and Kenya Medical Women's Association (KMWA), to offer research briefings for policymakers and advocates that take into account the evolving political and social contexts that affect HIV prevention and health care policy decisions. These coalitions are critical to building the support needed to effectively deliver new sexual and reproductive health products to the women who need them most.

Scientific Leadership

In 2013, IPM continued to share its scientific research at several major conferences, presenting on topics such as multipurpose prevention ring development at the 2013 Women Deliver Conference in Kuala Lumpur and at the annual Controlled Release Society meeting in Hawaii, sociobehavioral aspects of microbicide studies at the 11th International AIDS Impact Conference in Barcelona, and clinical trial ethics at the 6th annual South Africa AIDS Conference in Durban.

In addition, IPM's published or supported work appeared in a range of peer-reviewed journals in 2013, including articles in the *Journal of the International AIDS Society* on participant adherence in clinical trials and in *Antiviral Research* on the dapivirine ring's development and pharmacokinetics.



IPM led a panel on the role of global health partnerships and presented on microbicides and MPTs at the Women Deliver conference.

What gives me hope is knowing that we are working toward a product — a microbicide for women — that may help give women and their families a better future.

– Dr. Cynthia Gama, Maternal, Adolescent and Child Health, Wits University, South Africa

IPM Donors

Current Donors

Bill & Melinda Gates Foundation
Irish Aid, Department of Foreign Affairs
Ministry of Foreign Affairs of Denmark
Ministry of Foreign Affairs, the Netherlands
Norwegian Agency for Development Cooperation
Norwegian Ministry of Foreign Affairs
OPEC Fund for International Development, the development finance institution of OPEC Member States
United Kingdom Department for International Development
United States Agency for International Development through the United States President's Emergency Plan for AIDS Relief

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M•A•C AIDS Fund
Magee-Womens Research Institute and Foundation
Ministry for Foreign Affairs, Sweden
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Executive Vice President, Chief Medical Officer, Clinical Programs

Brid Devlin, PhD
Executive Vice President,
Product Development

Christopher Camut, MBA
Chief Financial Officer

2013 Financial Considerations

IPM's cash, cash equivalents and short-term investments as of December 31, 2013, were \$38.2 million. During 2013, IPM continued to increase clinical research center expenditures in Africa in support of The Ring Study, one of two parallel Phase III clinical trials of the dapivirine ring. In addition to the existing four research centers, IPM added three new centers to support the ongoing clinical study.

In 2013, IPM received grant awards from: M•A•C AIDS Fund (USD 50,000); Norwegian Agency for Development Cooperation (NOK 20 million); OPEC Fund for International Development (USD 300,000); United Kingdom Department for International Development (GBP 15 million); and United States Agency for International Development through the United States President's Emergency Plan for AIDS Relief (two awards totaling USD 40 million). In addition, IPM continues to receive extraordinary support from our other donors. IPM is in compliance with all financial

reporting requirements from all domestic and international government and private donors.

With new funding received in 2013, IPM also advanced its product pipeline, an integral component of the organization's strategy beyond our broader Dapivirine Ring Licensure Program. IPM will continue to apply a highly disciplined approach to product prioritization that advances only the most promising self-initiated HIV prevention tools, and other sexual and reproductive health technologies for women.

IPM's Board of Directors, management team and staff are committed to capably delivering on our mission for women around the world, and for the donors whose support fuels our progress. Sustained funding for IPM's success is essential, and we continue to advocate for increased funds from existing donors and pursue new sources of support to efficiently achieve our goals.

ASSETS

	DEC. 31, 2013
Cash and cash equivalents	\$14,544,424
Investments, at market	\$23,638,665
Accounts receivable	\$182,413
Prepaid expenses and other current assets	\$702,396
Property and equipment, net	\$1,469,510
Total Assets	\$40,537,408

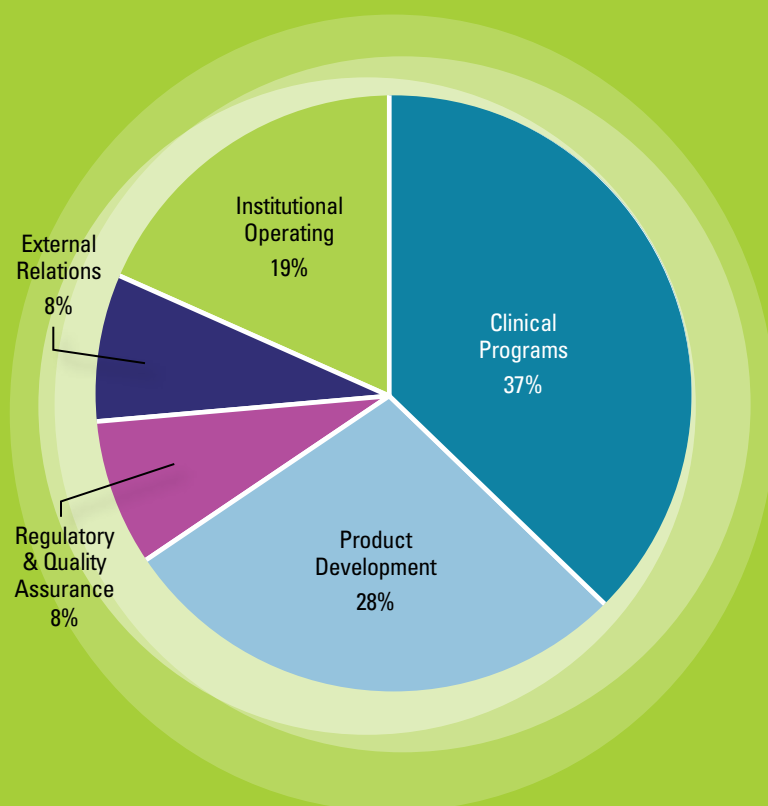
LIABILITIES AND NET ASSETS

Liabilities

Accounts payable and accrued expenses	\$4,396,442
Grant advances and deferred revenue	\$19,024,833
Total Liabilities	\$23,421,275
<i>Net Assets - unrestricted</i>	\$17,116,133

TOTAL LIABILITIES AND NET ASSETS	\$40,537,408
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EXPENSES BY DEPARTMENT





**INTERNATIONAL
PARTNERSHIP FOR
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