



from
SCIENCE to
SOLUTIONS

Developing new **HEALTH**
TECHNOLOGIES for **WOMEN**

DEAR FRIENDS AND COLLEAGUES:

In 2012, IPM saw years of research come together in a significant achievement — the start of the first efficacy study of a long-acting HIV prevention option for women, IPM's monthly dapivirine ring.

From the start, our goal has been to develop products that merge science with the social, cultural and behavioral complexities that shape the lives of women who are in urgent need of new health solutions. The Ring Study, along with additional studies that make up IPM's Dapivirine Ring Licensure Program, is a seminal step forward in the development of new, self-initiated HIV prevention options for women.

With last year's US FDA approval of the antiretroviral-based drug Truvada for use as pre-exposure prophylaxis, or PrEP, HIV prevention research has surged forward. The approval was based on the results of multiple clinical trials showing that ARVs can substantially reduce the risk of HIV infection when used consistently. These studies made clear an important lesson: the need for products that are not only efficacious but also easy to integrate into one's lifestyle.

IPM also recognizes that making HIV prevention work for women means taking into account other sexual and reproductive health issues that can threaten a woman's well-being, such as unintended pregnancy. That is why IPM is applying its experience in HIV prevention to the development of new multipurpose prevention technologies that could address multiple health risks in a single product.

We also continue to partner with pharmaceutical and academic partners to evaluate cutting-edge ARVs with different mechanisms of action, develop alternative formulations, and build upon current research with additional new products like combination microbicides, to potentially increase the breadth of protection against HIV.

IPM is motivated by the work we accomplished in 2012 and prepared for the challenges ahead as we lead the Dapivirine Ring Licensure Program while advancing the important products in our pipeline. It is through the strength of our many partnerships that this work is not only possible but within our reach.

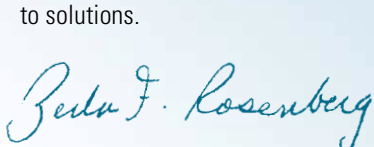
We extend our deepest gratitude to our global partners for making IPM's work possible: governments, foundations, private corporations, community research groups and advocates — and especially to the individuals who volunteer for our studies. To our donors around the world, we thank you for your continued commitment to moving health technologies for women forward, from science to solutions.



Dr. Zeda F. Rosenberg
Chief Executive Officer



Dr. Peter B. Corr
Chair of the Board


DR. ZEDA F. ROSENBERG


DR. PETER B. CORR

from **SCIENCE** to **SOLUTIONS**

IN 2012 IPM moved microbicide development forward with the start of **The Ring Study**, the first Phase III efficacy study of a vaginal ring for HIV prevention. Now, two parallel Phase III studies are evaluating the monthly **dapivirine ring** across 20 sites in Africa: IPM's Ring Study and the ASPIRE study, being conducted by our partner the Microbicide Trials Network (MTN). These sister studies, along with other supporting safety studies, make up the **Dapivirine Ring Licensure Program**. Pending results in 2016, this broad package of clinical studies is designed to provide the evidence needed to secure regulatory approvals and licensure for this potentially new lifesaving tool — an important step toward delivering on IPM's mission.

The Dapivirine Ring: Advancing the Promise of Prevention

IPM developed the monthly dapivirine vaginal ring to provide women with a discreet and easy-to-use tool they could use to protect themselves against HIV infection — the leading cause of death among women of reproductive age worldwide. The long-acting ring slowly releases the antiretroviral (ARV) drug dapivirine over the course of one month. Because women would only need to replace the ring monthly, it may encourage consistent use and help ensure effectiveness.

The ring's active ingredient

Dapivirine is a potent non-nucleoside reverse transcriptase inhibitor, or NNRTI, which works by preventing HIV from replicating inside healthy cells. IPM acquired a royalty-free license to develop dapivirine as a microbicide for use in developing countries in 2004 through a landmark public-private collaboration with Janssen R&D Ireland.

The Licensure Program At-a-Glance

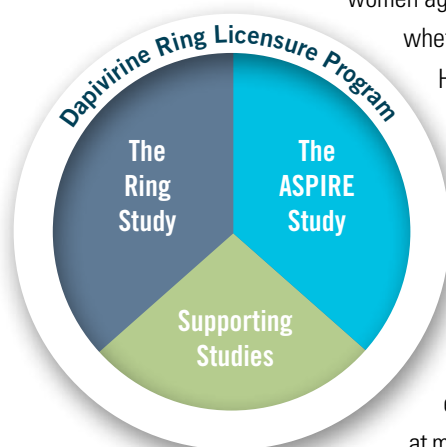
The Dapivirine Ring Licensure Program is the culmination of years of clinical development demonstrating the product's safety, long-acting duration, and acceptability to women and their male partners — and its potential to expand women's HIV prevention options with an affordable, self-initiated tool. Results are expected by 2016.

Joining forces — Phase III sister studies

Because at least two Phase III efficacy trials are generally needed for a product to be eligible for regulatory approval,

IPM designed the Dapivirine Ring Licensure Program with two efficacy studies running concurrently to keep the time line to approval as short as possible. Given the ring's promise, the MTN, which is funded by the US National Institutes of Health, partnered with us on this effort. Together, The Ring Study and MTN's ASPIRE study will evaluate the dapivirine ring among more than 5,000

women ages 18-45 to determine whether it helps to prevent HIV infection and is safe for long-term use. The Ring Study is expected to include 1,650 women across six sites in South Africa and Uganda when fully enrolled. ASPIRE is expected to enroll nearly 3,500 women at more than 15 sites in Malawi, South Africa, Uganda and Zimbabwe.




Supporting studies

IPM is also leading at least seven smaller safety studies needed to help secure regulatory approval for the ring. Among them is a study that began in 2012 looking at possible drug interactions, and studies evaluating ring use with male and female condoms that started in 2013. Studies on the effect of menses and tampon use as well as extended use of the ring are being planned for 2014. MTN, in partnership with IPM, is planning two additional studies for 2014 that will evaluate the dapivirine ring's safety in adolescents and women over 45.

Promoting Adherence

In a clinical study, *product adherence* (use of the study product as directed) is critical to determining whether the product works — in the case of the dapivirine ring, to prevent HIV. We know from several earlier HIV prevention studies that achieving robust product adherence can be a challenge, but that ARV-based methods can protect against infection when used consistently. We are taking a number of steps to measure and encourage adherence in both Phase III studies of the dapivirine ring.

Assessing Adherence



The Ring Study and ASPIRE will collect used rings each month to measure the amount of drug left in the product, which will tell us whether it was used for all or just part of the month. The studies also evaluate drug concentrations in plasma and vaginal fluid samples, and are using qualitative measures such as interviewer-led questionnaires, diary cards, focus groups and in-depth interviews to understand how women are using the product. Adherence counseling and education is a focus of regular visits, and community engagement activities highlight the importance of adherence.

Offering Options

It is hoped that the ring's monthly duration may help women use it consistently. As the contraceptive field has taught us, no single prevention product will be acceptable or appropriate for everyone. An array of safe and effective HIV prevention tools will be needed to meet women's needs and preferences.

Laying the Groundwork for Licensure

IPM continues to actively prepare for the dapivirine ring's potential licensure so that the product may be distributed quickly at low cost to women most at risk for HIV. In 2012, IPM worked with regulatory



authorities in Africa to define country-specific requirements for rapid regulatory submission and marketing approval. IPM also continues to receive scientific and regulatory advice from the US Food and Drug Administration (FDA), the European Medicines Agency (EMA) and the World Health Organization (WHO), to help expedite future marketing authorization.

This includes EMA review of the ring under Article 58, which will provide an opinion on the product's use in developing country settings, followed by WHO drug prequalification. Both mechanisms are key steps toward accelerating the ring's availability in countries with high rates of HIV where women urgently need new prevention tools.

Partnering on the Path to Access

Successful introduction and rollout of microbicides will require collaboration across sectors, including governments, industry, communities, NGOs and advocates. IPM is working alongside other HIV prevention partners to align access activities and develop paths to commercialization that will be customized on a country basis across sub-Saharan Africa and beyond. As a key element of our access strategy, these activities leverage partnerships at each point in the value chain — from marketing and product launch to ongoing pharmacovigilance and program implementation. Other strategies to enhance access include efforts to reduce costs to the user in a number of ways, including potentially extending the ring's duration of use for multiple months at a time.

Manufacturing advances

IPM scientists worked with QPharma in Malmö, Sweden, in 2012 to further optimize the ring production process for the Phase III trials, which led to more than a doubling of yields as it shortened time lines — and will help keep costs as low as possible at scale-up.



Forging Public-Private Partnerships to Improve Women's Health

Since IPM was founded as a nonprofit product developer in 2002, we have leveraged public, philanthropic and private sector funding and scientific ingenuity to spur development of safe and effective lifesaving technologies for women. For example, IPM's partnerships with major pharmaceutical companies in the HIV prevention effort have led to six non-exclusive, royalty-free licensing agreements which allow IPM to develop and manufacture eight different ARV compounds as microbicides or multipurpose prevention technologies (MPTs) for use by women in developing countries. These agreements ensure that IPM's products will be made as affordable and accessible as possible where they are needed most.



From Promise to Products

In just seven years since IPM acquired dapivirine from Janssen, we took the monthly ring from scientific concept to our Dapivirine Ring Licensure Program now under way. We are also building on our ring

technology with an MPT ring that contains both dapivirine and the contraceptive levonorgestrel to help reduce the dual risks women face from HIV and unintended pregnancy.



Safety Study Results Are In

High adherence and acceptability

A microbicide, no matter how effective, will not prevent HIV unless women find it easy to incorporate into their varying lifestyles. As IPM reported in 2012, results from a safety study of the dapivirine ring among 280 HIV-negative women in Kenya, Malawi, South Africa and Tanzania showed the ring was safe, well-tolerated and used regularly during the study. Nearly all participants found the ring acceptable and said they would use it if it is shown to prevent HIV, supporting previous IPM findings on the ring's acceptability.

Low systemic absorption: The same study showed that only low levels of dapivirine were detected systemically, which could minimize potential side effects and reduce the possible risk for drug resistance.

Right drug, right amount, right place: Results of one smaller safety study released in 2012 showed that, in vaginal fluid samples, dapivirine reached high concentration levels and remained active against HIV, further supporting advancement of the dapivirine ring.

Gels are safe and acceptable

Results presented in 2012 from a safety study evaluating two dapivirine gel formulations among 128 women in the United States showed both products to be safe and well-tolerated. In addition, dapivirine was released at high levels and retained anti-HIV activity in vaginal fluid samples. Two-thirds of participants in the United States said they would use the gel if it were proven effective against HIV. Also, a joint IPM and MTN male tolerance study of dapivirine gel showed it to be safe, adding to the body of data supporting dapivirine.

Building Capacity

IPM worked closely with the research center partners leading our trials in Africa to build local capacity through infrastructure improvements, regular trainings for research staff on clinical and laboratory compliance, workshops on adherence and counseling, scientific meetings for center staff, and support for community engagement and communications outreach. These collaborations have contributed to more HIV awareness, men's involvement in HIV prevention efforts, women's empowerment through education and counseling, employment opportunities and professional development, as well as improved access to health services in high-risk communities.



IPM in 2012 helped procure freezers, generators and temperature monitoring systems for research center partners conducting The Ring Study, which saved the time and expense of transporting samples to a lab for storage, and expanded partners' capacity to conduct future research (funded by OFID).



IPM's CEO Dr. Zeda Rosenberg with NIAID Director Dr. Carl Dieffenbach (far left), Ring Study Protocol Chair Dr. Saidi Kapiga, MTN Principal Investigator Dr. Sharon Hillier and ASPIRE Protocol Chair Dr. Jared Baeten at a joint press briefing on the dapivirine ring at the 2012 International AIDS Conference in Washington, DC.

Progress in the Pipeline

IPM's leading-edge pipeline responds to women's urgent need for tools that can prevent HIV, and address other sexual and reproductive health concerns. Bringing the global HIV epidemic to an end will require a diverse toolkit of products women can fit into their varying

lifestyles and that meet the need for increasingly effective methods that will prevent HIV over time. To that end, IPM is developing multiple ARVs with different mechanisms of action in single and combination rings, gels, films and tablets. IPM is also advancing a multipurpose prevention technology (MPT) that could protect women against the dual risks of HIV and unintended pregnancy.



Confronting dual risks with an MPT Ring

Integrated solutions like a long-acting MPT ring could help reduce the high rates of both HIV infection and maternal and newborn deaths associated with unintended pregnancy. In 2012, through a grant from USAID, IPM continued work on a 60-day MPT ring, which provides sustained release of the ARV dapivirine and the contraceptive hormone levonorgestrel. Building on our existing dapivirine ring technology, IPM, in collaboration with our partners Particle Sciences, Inc. (US) and Queens University Belfast (UK), is evaluating several lead prototypes of the ring, with clinical studies planned for 2015. IPM researchers are also investigating the potential of the MPT ring to be used for up to one year.

Dapivirine-maraviroc ring for added protection

In 2012, IPM and MTN completed a Phase I safety trial of the first combination microbicide, IPM's dapivirine-maraviroc ring, as well as a maraviroc-only ring, with results expected in 2013. Combining the ARV maraviroc, an entry inhibitor that acts early in the HIV life cycle, with dapivirine, which acts later in the virus' life cycle, could broaden protection against HIV and increase the product's potency. IPM is working to further optimize this product, and a second safety study is planned for 2015.

Other maraviroc products: IPM is also studying maraviroc as a film, alone and in combination with other ARVs, in partnership with the Magee Women's Research Institute at the University of Pittsburgh, with funding from NIH.



DS003 — new mechanism of action

A potent gp120-binder licensed to IPM by Bristol Myers-Squibb, DS003 (also known as BMS 793) works by binding to a protein on the surface of HIV to prevent its entry into a healthy cell. Because the drug targets HIV itself, it has the potential to render the virus non-infectious when it enters the body with few possible side effects.

Why DS003? DS003 is also an important candidate for development because its mechanism of action has yet to be used for HIV treatment or prevention, which means it would be unlikely to interfere with therapeutic regimens or result in resistance to other ARVs. IPM has formulated the drug as a vaginal tablet and conducted work in 2012 that supports advancing the compound's development as a vaginal ring, either alone or in combination with another ARV.

Partnering on pipeline expansion

IPM supplies other nonprofit product developers with compounds and regulatory support for several products in the field, including dapivirine and DS003 vaginal films and maraviroc-based rectal gels, both under NIH-funded programs, as well as dapivirine-darunavir gel and rings under the European Commission-funded CHAARM consortium.

Looking ahead

IPM continually surveys emerging data and consults with pharmaceutical partners to source new compounds. These include novel drugs that target specific enzymes such as integrase and protease inhibitors, which may have benefits for HIV prevention.



Partners in Advocacy

Awareness-raising is crucial to building broad political, public and financial support for microbicides, and other tools women need to protect their sexual and reproductive health. In 2012, IPM worked with a network of civil society partners across sub-Saharan Africa, Europe and North America — from local and national NGOs to professional medical societies. With women's health and the promise of an AIDS-free generation at the top of their agendas, these influential advocacy coalitions partnered with IPM to host stakeholder roundtables, brief policymakers, and engage communities and media to help ensure government and public policy support for microbicides and MPTs.

Scientific Contributions

IPM continued to make scientific contributions to the field in 2012 by publishing in peer-reviewed journals and presenting at major international conferences, including the International AIDS Conference, the Conference on Retroviruses and Opportunistic Infections and Microbicides 2012. IPM conducted or supported studies on dapivirine safety, acceptability and pharmacokinetics, along with work on combination microbicides and MPTs, all of which were featured in more than 45 presentations and publications.



IPM co-hosted five sessions at the 2012 International AIDS Conference in July in Washington, DC, including this one with Women Deliver called "Advancing the Integration of Sexual and Reproductive Health."



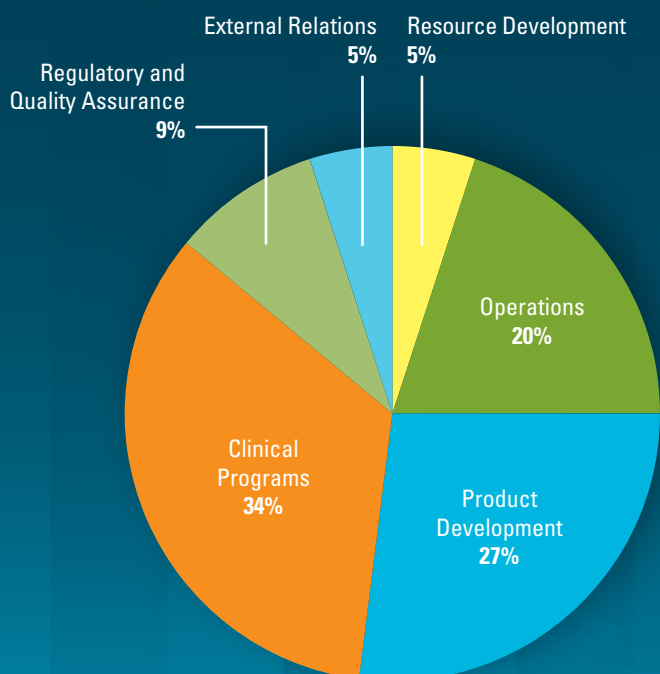
2012 Financial Considerations

IPM's cash, cash equivalents and short-term investments as of December 31, 2012 were \$37.2 million. As a result of the ongoing tightening of the global economy, IPM continues to adjust its financial and operating model to ensure the organization maximizes and efficiently allocates donor funds to address program needs and carry out IPM's mission. These activities have focused on streamlining personnel and making various system improvements, including introducing an Enterprise Resource Planning (ERP) system.

During 2012, IPM increased clinical research center expenditures in Africa in anticipation and support of the start of The Ring Study, the first Phase III clinical trial of the dapivirine ring. Research center costs included the purchase of laboratory equipment, and the hiring and training of personnel to support the trial. In addition, IPM made infrastructure investments across the organization to ensure accurate and timely reporting of clinical trial, financial and operating data.

IPM also continued to advance the product pipeline in 2012, though at a slower pace than the previous year due to the limited availability of donor funds allocated to product development. However, new funding received in 2013 will allow IPM to expedite pipeline development in the coming year, 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

Cash and cash equivalents	\$7,913,596
Short-term investments	\$29,356,232
Accounts receivable	\$2,416,907
Prepaid expenses and other assets	\$1,575,408
Property and equipment	\$2,219,180
Total Assets	\$43,481,324

DEC. 31, 2012

LIABILITIES AND NET ASSETS

Liabilities

Accounts payable and accrued expenses	\$2,740,137
Grant advances and deferred revenue	\$20,002,490
Total Liabilities	\$23,754,899

Net Assets

Unrestricted	\$19,726,425
Temporarily restricted	\$0
Total Net Assets	\$19,726,425

TOTAL LIABILITIES AND NET ASSETS \$43,481,324



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