

# A Ring to Protect Women Against HIV



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**IPM**'s most advanced product is a monthly vaginal ring that slowly releases the antiretroviral (ARV) drug dapivirine to prevent HIV. The novel ring adapts a common medical technology — a vaginal ring — to be used in the fight against HIV.

## IPM's Monthly Dapivirine Ring

The ring would address a critical gap in current prevention strategies by offering long-acting female-initiated protection against HIV. This is particularly important for women in developing countries, where the epidemic has hit hardest, and especially for young women, who are at least twice as likely to be infected as young men.

IPM's dapivirine ring is easy to use, and is designed to remain in place for a month at a time to provide sustained protection against HIV. Given the ring's promise, the US National Institutes of Health-funded Microbicide Trials Network (MTN) partnered with IPM to advance this important product into parallel late-stage clinical trials.



IPM and MTN, IPM's clinical trial partner, are each studying the ring in concurrent Phase III studies that together evaluate the ring's efficacy and long-term safety in women in four African countries. Efficacy results are expected as soon as early 2016. Because two Phase III trials are required for regulatory approval, conducting them simultaneously may help shorten the time line to approval for this urgently needed product.

### Benefits of the Ring: Discreet and Long-acting

The ring has tremendous potential as a new HIV prevention method. It could offer discreet and long-acting protection against HIV. Because the monthly ring is convenient and easy-to-use, it may be easier for women to use it consistently.

Efforts are under way to ensure that future manufacturing costs of the ring are kept as low as possible. Affordability, along with the product's known acceptability among women and their partners, could make the ring a practical HIV prevention option for women in developing countries and around the world.

### Ring Technology: Slow-release and Locally Acting

Vaginal rings provide controlled release of drugs over extended periods of time.

IPM's microbicide ring is a novel formulation. It is made of a flexible silicone material with the ARV drug dapivirine dispersed uniformly throughout a matrix ring. In clinical studies to date, the dapivirine ring has demonstrated a good safety profile and has been well-tolerated among study populations. Studies also show that the ring successfully delivers the drug locally for a month or longer, with low systemic absorption, which can help minimize side effects.

### The Active Ingredient: Dapivirine

Dapivirine belongs to the same class of ARVs used successfully to treat HIV/AIDS and prevent mother-to-child transmission. Dapivirine is a type of ARV drug known as a non-nucleoside reverse transcriptase inhibitor (or NNRTI), and works by preventing HIV from replicating inside a healthy cell.

Janssen Sciences Ireland UC, a Janssen pharmaceutical company of Johnson & Johnson, first tested dapivirine in oral formulations in 11 safety studies before 2004 and later partnered with IPM, which has since tested dapivirine as a vaginal ring or gel in 19 safety studies. In all clinical studies to date, dapivirine has been found safe and well-tolerated in healthy, HIV-negative women in Africa, Europe and the

United States. A joint 2012 study by IPM and MTN found the gel formulation to be acceptable to men as well.

IPM began developing dapivirine as a microbicide in 2004 through a royalty-free licensing agreement with Janssen Sciences Ireland UC. This license has since been expanded to a worldwide rights agreement.

### The Ring: Acceptability and Safety

ARVs can prevent HIV in women when they are used consistently. No matter how well-designed a product may be, it is essential that it fits women's needs and lifestyles so it is used consistently. IPM takes women's preferences into account from the earliest stages of product development.

- *High acceptability:* To ensure the ring would meet the needs of women who are at greatest risk of HIV, IPM conducted a study in 2010 to assess the acceptability and safety of a placebo ring (containing no active drug) among women in South Africa and Tanzania. Results showed the ring is acceptable to women, and nearly all women expressed interest in using the ring if proven effective against HIV. While some indicated interest in using it discreetly, the majority of women preferred to involve their partner. Male partners who were interviewed also supported use of the ring.

- *Safe for use:* The results from an additional safety and acceptability study conducted in four countries in Africa in 2011 showed the dapivirine ring to be safe and well-tolerated by women in the trial. Women overwhelmingly found the ring acceptable to use and expressed interest in using it for HIV prevention. IPM has completed 10 additional safety studies of different ring formulations, all of which support the ring's safety and tolerability.

### Phase III Results by 2016: The Ring Study & ASPIRE

IPM's Dapivirine Ring Licensure Program initiated in 2012 with the launch of two Phase III clinical trials — the culmination of years of research demonstrating the ring's safety, acceptability and long-acting duration. This program includes two parallel late-stage trials: IPM's Ring Study (IPM 027) and MTN's ASPIRE study (MTN-020), which together are designed to evaluate the ring's ability to prevent new HIV infections in women and its long-term safety.

The studies involve thousands of women across Africa, with efficacy results expected as soon as early 2016. The program also includes several smaller studies to examine the ring's safety in adolescents and women over 45, functionality with condom use, possible drug interactions, and effects of men- ses and tampon use.

Pending study results, IPM, as the ring's developer and regulatory sponsor, will seek regulatory approval for its licensure, and collaborate with key partners to help ensure

the ring is made available to women in developing countries at low cost as soon as possible.

The ring would address a critical gap by offering long-acting female-initiated protection against HIV.

### What's Next: The Ring as a Platform Technology

IPM is applying its expertise in ring development to create a multipurpose prevention technology that combines an ARV with a contraceptive hormone to address women's HIV prevention and reproductive health needs. This 90-day dapivirine-contraceptive ring is set to enter a Phase I trial in early 2016. IPM is also adapting the ring to deliver multiple ARVs that target HIV at different points in its life cycle, which could potentially provide greater protection than a single drug alone.

### Offering Hope with New Prevention Technologies

HIV/AIDS is one of the greatest threats to women's health globally, which is why women urgently need self-initiated, practical prevention tools they can and are willing to use. IPM's monthly dapivirine ring offers promising advantages, including its long-acting duration, affordability and the ability to deliver the drug where it is needed locally, with low systemic absorption. New ring technologies promise to empower women to protect their health — and, in turn, that of their families and communities.

