CONTACT: **Lisa Rossi**
+1- 412-641-8940
+1- 412- 916-3315 (mobile)
rossiL@upmc.edu

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HIV prevention dapivirine vaginal ring found safe and acceptable in US adolescent girls

Results presented at IAS 2017 pave way for study in African girls and young women

PARIS, July 25, 2017 – A vaginal ring that researchers are hopeful will be approved as a method for preventing HIV in women was found to be safe and acceptable in teen girls, according to results of a study conducted in the United States and reported at the 9th IAS Conference on HIV Science (IAS 2017) today in Paris. The study is the first to evaluate the ring, which contains an antiretroviral (ARV) drug called dapivirine and is used for a month at a time, in girls under age 18.

The dapivirine ring has already been shown to be both safe and to help protect against HIV among women ages 18-45 in two Phase III trials – ASPIRE , which was conducted by the National Institutes of Health (NIH)-funded Microbicide Trials Network (MTN), and The Ring Study, led by the International Partnership for Microbicides (IPM), a non-profit organization that also developed the dapivirine ring. Together, the two trials enrolled more than 4,500 women from four African countries. IPM is seeking regulatory approval of the ring for adult women of the same age.

If approved, the dapivirine ring would be the first biomedical prevention product exclusively for women. The new study, known as MTN-023/IPM 030, was designed to provide the kind of information about safety and tolerability that regulatory authorities would need to expand approval of the ring to also include girls under age 18.

MTN-023/IPM 030 was conducted by the MTN in collaboration with the Adolescent Medicine Trials Network for HIV/AIDS Interventions (ATN), which is also funded by the NIH. MTN is planning to launch a second trial later this year, called REACH, that will collect safety data among adolescent girls and young women in Africa, who are among the most vulnerable population at risk of acquiring HIV.

"If the ring is approved for women older than age 18, it's imperative that we have the data in hand to show that the ring is safe to use in younger women as well," explained Sharon Hillier, Ph.D., principal investigator of the MTN, and professor and vice chair of the department of obstetrics, gynecology and reproductive sciences at the University of Pittsburgh School of Medicine. "HIV doesn't distinguish between a 16-year-old and an 18-year-old. Access to safe and effective HIV prevention shouldn't either. Young women of all ages deserve to be protected."

MTN-023/IPM 030 enrolled 96 girls ages 15-17 at six U.S. sites: two affiliated with the MTN (University of Pittsburgh and the University of Alabama at Birmingham) and four affiliated with the ATN (St. Jude Children's Research Hospital in Memphis; The Fenway Institute in Boston; Children's Hospital at

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Montefiore Medical Center, Bronx, N.Y.; and University of Colorado Denver School of Medicine). The study was conducted between July 2014 and July 2016, as ASPIRE and The Ring Study were underway.

Participants were randomly assigned to use either the dapivirine ring or a placebo ring that looked and felt the same but contained no active drug; 73 participants were in the dapivirine ring group and 23 were assigned to use the placebo ring. Participants were asked to use their assigned ring for a month at a time for a total of six months.

The study found no differences in safety outcomes between the dapivirine ring and the placebo ring, reported Katherine Bunge, M.D., at IAS 2017. Dr. Bunge, an assistant professor of obstetrics and gynecology at the University of Pittsburgh School of Medicine, was MTN-023/IPM 030 protocol co-chair. The study's protocol chair was Kathleen E. Squires, M.D., W Paul and Ida H Havens Professor of Infectious Diseases and director, Division of Infectious Diseases, Thomas Jefferson University in Philadelphia.

Adherence to ring use was also high. By self-report, 42 percent of participants said they had never removed the ring except to replace it monthly. In the dapivirine group, 87 percent of plasma samples had detectable levels of drug suggestive of the ring being used the previous day; 95 percent of the rings returned after use had drug levels that suggested consistent use during the previous month. Questions asked of participants three months into the study and after six months indicated the ring was highly acceptable, with 95 percent saying the ring was easy to use and 74 percent indicating they were not aware of the ring during daily activities. Some were worried that their partner would feel the ring during sex, but overall, the majority of participants (93 percent) said they liked the ring.

In the REACH study, investigators will collect information on the safety of both the monthly ring and Truvada as daily PrEP, and explore whether biological or physiological factors affect product efficacy or HIV susceptibility in adolescent girls and young women. In addition, REACH, also known as MTN-034/IPM 045, will evaluate how adolescent girls and young women use the ring and PrEP and their preferences for either or both approaches. Approximately 300 girls and young women ages 16-21 will be enrolled at five MTN-affiliated sites in Kenya, South Africa, Uganda and Zimbabwe. Pending ethics committee and in-country approvals, the study is expected to start late 2017.

Results of ASPIRE and The Ring Study, which were reported in February 2016, found the ring reduced women's risk of acquiring HIV by about 30 percent overall (by 27 percent in ASPIRE and by 31 percent in The Ring Study). Higher levels of protection were seen in women 21 and older, who used the ring more regularly. Results of an exploratory analysis of ASPIRE data reported at AIDS 2016 found the level of HIV protection was at least 56 percent with consistent use and as high as 75 percent or more with near perfect use.

Adolescent girls and young women (ages 15–24) accounted for 20 percent of new HIV infections among adults globally in 2015, yet represent just 11 percent of the adult population. In sub-Saharan Africa, adolescent girls and young women accounted for 25 percent, or one out of every four, new infections, with nearly 1,000 being infected every day.

MTN-023/IPM 030 was funded by jointly by the National Institute of Allergy and Infectious Diseases, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development and the National Institute of Mental Health, all part of the NIH.

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Safety and acceptability trial of the dapivirine vaginal ring in U.S. adolescents (Abstract TUAC0206LB) will be presented during the oral abstract session, Prevention and Adolescents, 11-12:30 p.m. CEST, Tuesday 25 July. The research team is also presenting a poster, Acceptability of a dapivirine vaginal ring among US adolescent females in Phase 2a safety trial (MTN 023) (Abstract WEPEC0933)

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About the Microbicide Trials Network

The Microbicide Trials Network (MTN) is an HIV/AIDS clinical trials network established in 2006 by the National Institute of Allergy and Infectious Diseases with co-funding from the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development and the National Institute of Mental Health, all components of the U.S. National Institutes of Health. Based at Magee-Womens Research Institute and the University of Pittsburgh, the MTN brings together international investigators and community and industry partners whose work is focused on the rigorous evaluation of promising microbicides – products applied inside the vagina or rectum that are intended to prevent the sexual transmission of HIV – from the earliest phases of clinical study to large-scale trials that support potential licensure of these products for widespread use. More information about the MTN is available at http://www.mtnstopshiv.org.

About the dapivirine ring

The dapivirine ring is made of a flexible material, and women can insert and replace it themselves. It sits high inside the vagina where it slowly releases the active drug over the course of a month. The ring was developed by the International Partnership for Microbicides (IPM), a nonprofit with offices in the United States, South Africa and Europe. IPM holds an exclusive worldwide license for dapivirine from Janssen Sciences Ireland UC, part of the Janssen Pharmaceutical Companies of Johnson & Johnson (Janssen), which is designed to ensure that women in low-resource settings have affordable access to any dapivirine-based microbicide. Dapivirine, also known as TMC-120, belongs to a class of ARVs called non-nucleoside reverse transcriptase inhibitors that bind to and disable HIV's reverse transcriptase enzyme, a key protein needed for HIV replication.

IPM is seeking regulatory approval of the dapivirine ring for women ages 18-45, the same age group in the ASPIRE and The Ring Study Phase III safety and efficacy trials. IPM is hopeful that the first regulatory approvals in African countries could be received as soon as early 2019.

For more information about the dapivirine ring, go to www.ipmglobal.org.

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