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**FOR IMMEDIATE RELEASE**

# Study Comparing Tenofovir Gel and Oral Tablet Finds Gel Provides More Drug to Tissue

## Preferences for HIV prevention products differ among U.S. and African women

**BOSTON, Feb. 28, 2011 –** In the first study to make head-to-head comparisons between tenofovir gel and oral tenofovir – two promising approaches for preventing HIV in women – researchers found that daily use of the vaginal gel achieved a more than 100-times higher concentration of active drug in vaginal tissue than did the oral tablet, while, compared to the gel, the tablet used daily was associated with a 20-times higher active drug concentration in blood.

Results of the Phase II trial, which examined differences in drug absorption as well as women's preferences for each daily regimen, were reported today at the 18th Conference on Retroviruses and Opportunistic Infections (CROI). The study, known as MTN-001, did not assess the effectiveness of each approach.

MTN-001 involved 144 women, evenly divided between the U.S., and Uganda and South Africa. All women in the study used each product daily for six weeks, as well as the two together, allowing for direct comparisons between the oral tablet and vaginal gel formulations of tenofovir, an antiretroviral (ARV) drug commonly used in the treatment of HIV.

Most of the women in the U.S. favored the oral tablet over the vaginal gel, while African women who participated in the study favored the gel and tablet equally. Many of the African women said they liked the gel because it enhanced sexual pleasure, reported Craig Hendrix, M.D., who led the U.S. National Institutes of Health (NIH)-funded study for the Microbicide Trials Network (MTN).

"It's important, but not surprising, to learn that women's preferences differ. It's also encouraging to know that there is a clear interest in both formulations, because although we saw much higher drug concentrations in vaginal tissue with the gel, how the differences between the gel and the tablet will translate in terms of protective effect, we can't say just yet. We don't know for certain where the drug needs to be or how much of the drug is needed to be most effective against HIV," explained Dr. Hendrix, a professor of medicine and pharmacology and molecular sciences in the Division of Clinical Pharmacology, Johns Hopkins University School of Medicine in Baltimore, Md., U.S.

MTN-001's findings will be better understood in the context of VOICE results, which are expected in 2013, Dr. Hendrix said. This includes understanding which approach – and at what dose – may be optimal for preventing HIV. VOICE – Vaginal and Oral Interventions to Control the Epidemic – is MTN's flagship study, a large-scale effectiveness trial of tenofovir gel, oral tenofovir and Truvada®, enrolling 5,000 women in southern Africa. Researchers designed MTN-001 and VOICE as complementary studies.

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Women in sub-Saharan Africa continue to be among the hardest hit by HIV. Six out of 10 new HIV infections in adults occur in women, primarily through unprotected sex with an infected male partner. Male condoms are effective in preventing HIV, but women can't always control their use. In contrast, a vaginal gel and an oral tablet are approaches that women could decide to use, independent of their husband or partner.

MTN-001 found all three daily regimens (vaginal gel, oral tablet and the two combined) were well tolerated by the women in the study. Nausea occurred in 15 percent of the women when using the tablet and 14 percent when the gel and tablet were used together. Vaginal itching and irritation were the most common side effects with the gel. According to self-reports, women were able to follow each regimen equally well. When asked if they would consider using any of the products in the future, 93 percent of the participants said they would be likely to use the oral tablet and 83 percent said they would be likely to use the gel. Among only U.S. women, 87 percent said they would be likely to use the oral tablet and 64 percent, the gel. Interestingly, when African participants were asked about the gel and the tablet, the response was the same for each approach– 100 percent said they would be likely to use either product if it became available. As for which approach they preferred, 72 percent of the U.S. women said they liked taking the tablet, compared to 14 percent who preferred using the gel. The African women liked both products: 42 percent favored the gel, 40 percent preferred the tablet and 14 percent said they liked them both equally.

"We have to be cognizant that there will be women who prefer using a gel and others who will want to take an oral tablet, and that the reasons will vary from individual to individual and that preferences may change as circumstances change. Quite simply, no one approach is going to be suitable to all women," explained Alexandra Minnis, Ph.D., M.P.H., an epidemiologist with RTI International in San Francisco and a co-author of the study.

Pharmacokinetic studies analyzed concentrations of tenofovir in vaginal tissue and blood in both its inactive and active states. To work against HIV, tenofovir must be activated by the addition of two molecules called phosphates, a process that takes place inside the cell. Using a unit of measure called a femtomole (fmol), researchers calculated 2,352 fmol of activated drug per milligram (mg) of vaginal tissue after vaginal gel use, whereas, with the tablet, the concentration achieved in tissue was less than 17 fmol/mg – a more than a 100-fold difference. The concentration of activated drug in blood cells with the oral tablet was 52 fmol/million cells and less than 5 fmol/million cells with the vaginal gel – more than a 20-times difference.

Oral tenofovir (tenofovir disoproxil fumarate), known by the brand name Viread®, and Truvada, a combination tablet that contains tenofovir and emtricitabine, are both approved for the treatment of HIV when used in combination with other ARVs. Viread and Truvada are registered trademarks of Gilead Sciences, Inc., of Foster City, Calif., U.S. Both are being evaluated in clinical trials to determine if they also can prevent HIV in people who are HIV-negative, an approach known as oral pre-exposure prophylaxis, or PrEP. A recent trial called iPrEx found that daily use of Truvada reduced the risk of HIV by 44 percent among men who have sex with men.

Tenofovir gel is a vaginal microbicide that contains the same active ingredient as the oral tablet formulation of tenofovir. Microbicides are products designed to prevent or reduce the sexual transmission of HIV when applied topically on the inside of the vagina or rectum. In CAPRISA 004, there were 39 percent fewer infections among women who used tenofovir gel before and after sex compared to women who used a placebo gel. In VOICE, women are using gel daily, regardless of when they have sex. The U.S. Food and Drug Administration (FDA) has indicated that it will consider approving tenofovir gel as an HIV prevention method for women depending on the results of VOICE. The FDA has also granted the gel Fast Track designation, which allows for its expedited review.

In the U.S., MTN-001 was conducted at Case Western Reserve University in Cleveland; the University of Pittsburgh; University of Alabama Birmingham (UAB); and Bronx Lebanon Hospital, Columbia University, in New York. In Africa, the study was conducted at Makerere University-Johns Hopkins University (MU-JHU) Research Collaboration in Kampala, Uganda; and at the Umkomaas and Botha's Hill clinical research sites affiliated with the Medical Research Council (MRC) of South Africa in Durban. The three African sites are among 15 currently conducting VOICE.

In addition to Drs. Hendrix and Minnis, other authors of the study are Vijayanand Guddera, Ph.D., from the MRC, South Africa; Sharon Riddler, M.D., M.P.H., University of Pittsburgh; Robert A. Salata, M.D., from Case Western; Clemensia Nakabiito, MBChB, MMed, from MU-JHU; Uganda; Craig Hoesley, M.D., UAB; Jessica Justman, M.D., Columbia University; Lydia Soto-Torres, M.D., M.P.H., National Institute of Allergy and Infectious Diseases (NIAID) Division of AIDS (DAIDS); and Barbra Richardson, Ph.D., from the Statistical Center for HIV/AIDS Research & Prevention, University of Washington.

MTN-001 was funded by NIAID/DAIDS, a component of the NIH. The study products were provided free of charge by Gilead Sciences, which donated the oral tenofovir tablets, and by CONRAD, of Arlington, Va., U.S., which donated both the gel and gel applicators.

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Additional information about MTN-001 is available at http://www.mtnstopshiv.org/news/studies/mtn001

*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 who are devoted to preventing or reducing the sexual transmission of HIV through the development and evaluation of products applied topically to mucosal surfaces or administered orally.*

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