CONTACT: Lisa Rossi
PHONE: +1- 412- 916-3315 (mobile)
E-MAIL: rossil@upmc.edu

HIV Prevention Trial of ARV-Based Strategies to Begin Next Month

Women are focus of VOICE Study testing both a vaginal gel and ARV tablets

CAPE TOWN, SOUTH AFRICA, JULY 20, 2009 – A large-scale clinical trial looking to prevent HIV infection in women, an especially vulnerable population in sub-Saharan Africa, is expected to launch in Zimbabwe next month, say researchers from the Microbicide Trials Network (MTN) who are leading the study .

The VOICE Study — Vaginal and Oral Interventions to Control the Epidemic — will help determine whether some of the same antiretroviral (ARV) medications used to treat HIV can also be used to prevent it when they are given as a vaginal microbicide gel or as an oral tablet taken once a day, an approach called pre-exposure prophylaxis (PrEP). VOICE is the first HIV prevention trial that will evaluate two different approaches in the same study and the first effectiveness trial of a microbicide in which women will use the gel every day instead of only at the time of sex. The U.S. National Institutes of Health is funding the study.

Nearly 5,000 women will be enrolled in VOICE, which will take about three and a half years to complete with results expected in 2012. Three sites in Zimbabwe, operated by the University of Zimbabwe-University of California-San Francisco (UZ-UCSF) Clinical Trials Unit in Harare, will begin enrolling women in the coming weeks. Makerere University-Johns Hopkins University Research HIV Clinical Trial Unit in Kampala, Uganda, is expected to start the study shortly thereafter.

VOICE will also be conducted in Lusaka, Zambia, and at multiple sites in South Africa affiliated with the South African Medical Research Council, the Reproductive Health & HIV Research Unit (RHRU) and the Centre for the AIDS Programme of Research in South Africa (CAPRISA). Pending government approval, the study may be conducted in Malawi as well.

Women represent nearly 60 percent of adults living with HIV in sub-Saharan Africa. In most cases, women acquire HIV through sexual intercourse with an infected male partner. Although correct and consistent use of male condoms has been shown to prevent HIV infection, women often cannot control if or when condoms are used by their male partners. Moreover, women are twice as likely as their male partners to acquire HIV during unprotected sex, due in part to biological factors that make them more susceptible to infection.

"ARVs have made a tremendous difference in the treatment of HIV, and we have a good indication of their potential in the prevention arena as well. What's unique about VOICE is that we'll be able to evaluate two different ARV-based prevention approaches, each with great promise as a method for preventing the sexual

- more -

transmission of HIV in women. Women throughout the world, but especially here in Africa, stand to benefit if we find either one is safe and effective," said Mike Chirenje, M.D., associate professor and consultant gynecologist in the department of obstetrics and gynecology at the University of Zimbabwe in Harare and co-chair of the VOICE Study.

Two ARV tablets are being tested in VOICE: tenofovir and Truvada.® Tenofovir, short for tenofovir disoproxil fumarate (TDF), is also known by the brand name Viread®, while Truvada is the brand name for a combination drug that contains tenofovir and another active ingredient called emtricitabine (FTC). Both are approved for treating HIV as part of antiretroviral therapy (ART). While at least three ARVs are typically used for ART, a single ARV tablet taken once a day is the regimen being tested for HIV prevention in current PrEP trials, including VOICE.

The vaginal microbicide being evaluated in VOICE, tenofovir topical gel, contains the activated form of the same ingredient in the oral tablet. It is among a newer class of candidate microbicides – substances intended to reduce or prevent the sexual transmission of HIV and other sexually transmitted infections when applied topically inside the vagina or rectum – with specific activity against HIV.

Women in VOICE will be randomly assigned to one of five study groups. Two groups will apply gel every day – either tenofovir gel or a placebo gel with no active ingredient. Three groups will be assigned to daily tablet regimens, with either tenofovir, Truvada or a placebo tablet as the drug under study. Because the study is blinded, neither the participants nor the researchers will know who is in which gel or tablet group. Women will use the same product every day the entire time they are in the study, which is expected to be an average of 22.5 months. All participants will receive ongoing HIV risk-reduction counseling, condoms, and diagnosis and treatment of sexually transmitted infections (STIs).

To determine the approach that women are more likely to use consistently, researchers will ask participants a series of standard questions about sexual activity, product use, product use adherence, male condom use and product sharing. Participants will also answer the same kinds of questions privately with the help of a computer, an approach that is thought to be a better way to collect information about sensitive behaviors.

"We're focusing this research in a part of the world where it really needs to work, but for any approach to be truly effective, women have to use it. So, a major question that we will also address in VOICE is which of the two – the tablet or the gel – will women actually be more inclined to use," said Jeanne Marrazzo, M.D., M.P.H., associate professor of medicine in the division of allergy and infectious diseases at the University of Washington in Seattle, U.S.A., and VOICE Study co-chair with Dr. Chirenje.

VOICE researchers also plan to conduct a companion study at RHRU's Tshireletso Clinic in Soweto looking specifically at household and community factors that might influence adherence to products. Another companion study, VOICE B, or the Bone Mineral Density Sub-study, is being conducted at the Uganda and Zimbabwe sites. VOICE B will involve about 300 women who have been randomized to the oral tablet groups to determine the potential effects, if any, that oral ARVs may have on bone health in HIV-negative women.

- more -

Including VOICE, there are seven ongoing trials of oral PrEP in different at-risk populations. Some of these are being conducted in Africa.

One other trial is evaluating tenofovir gel. Unlike VOICE, this study, called CAPRISA 004, is testing a regimen in which women insert gel before and after sexual intercourse.

Earlier this year, researchers from the MTN reported the results of a study called HPTN 035 showing that a microbicide called PRO 2000 gel was 30 percent effective. Although this fell short of statistical significance, the results demonstrated for the first time the promise of a vaginal microbicide for preventing HIV in women. Results of a larger study of PRO 2000 sponsored by the Medical Research Council and the Department for International Development of the United Kingdom will be reported later this year.

“VOICE is entering the HIV prevention landscape at a time of renewed hope and optimism. Could tenofovir gel or oral PrEP be powerful tools that will slow the rate of new infections? We think so. There is no magic bullet, but both gel and tablets could make a difference in the lives of people by helping to prevent women from getting infected,” commented Sharon Hillier, Ph.D., vice chairman and professor, department of obstetrics and gynecology and reproductive sciences at the University of Pittsburgh School of Medicine, and MTN principal investigator.

The VOICE Study is being funded by the National Institute of Allergy and Infectious Diseases (NIAID) 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.

Truvada and the oral and topical formulations of tenofovir were developed by Gilead Sciences, Inc., of Foster City, California, USA, which assigned a royalty-free license for the topical gel to the International Partnership for Microbicides of Silver Spring, Maryland., and CONRAD, of Arlington, Virginia., in December 2006. As co-sponsors of VOICE, Gilead is providing tenofovir and Truvada tablets free of charge, and CONRAD is providing both the gel and gel applicators at no cost.

# # #

More information about the VOICE Study can be found at http://www.mtnstopshiv.org/news/studies/mtn003

About the MTN

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.