

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

FOR IMMEDIATE RELEASE

Understanding the Results of CAPRISA 004

The results of CAPRISA 004 provide the first evidence that a vaginal microbicide –specifically, tenofovir gel – can help prevent HIV in women. The study represents an exciting milestone in HIV prevention, but more research is needed to confirm these results and to see if there are ways that tenofovir gel can be made to be even more effective. Research also needs to continue exploring similar approaches involving the use of antiretroviral drugs for HIV prevention.

The CAPRISA 004 study results are to be presented at the International AIDS Conference (AIDS 2010) in Vienna, July 20, and published online by the journal *Science* the same day.

SUMMARY

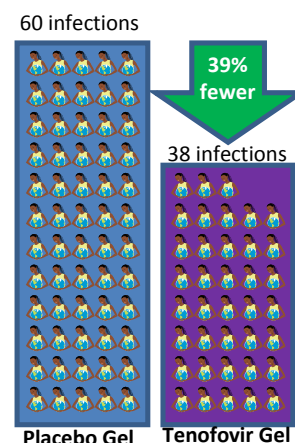
- **CAPRISA 004 is the first completed effectiveness study of an antiretroviral (ARV)-based prevention approach.** ARV-based prevention approaches incorporate some of the same ARV medicines used successfully for treatment of HIV, and the hope is that they will also be safe and effective for HIV prevention. A microbicide is one approach. Another is oral pre-exposure prophylaxis (PrEP), which involves the use of oral ARV tablets. There are 11 ongoing trials of ARV-based prevention in different at-risk populations; additional studies are being planned.
- **Researchers conducting CAPRISA 004 tested a vaginal microbicide containing the ARV tenofovir** to determine whether women at risk of HIV can be protected against infection by following a specific dosing regimen timed before and after sexual intercourse. Tenofovir is a drug that is commonly used as part of a multi-drug regimen to treat HIV in people who are already infected.
- **At the end of the study, there were 39 percent fewer HIV infections among women who used tenofovir gel before and after sex than among those who used a placebo gel with no active ingredient,** researchers reported at AIDS 2010. These findings provide proof of concept that ARV-based microbicides, in particular tenofovir gel, can help protect women against HIV.
- **CAPRISA 004 evaluated tenofovir gel when used in a certain way – before and after sex. The study involved about 900 women from South Africa. Additional studies are needed to test the promise of tenofovir gel in more women and with different dosing strategies .** More research is needed to confirm these results in diverse populations of women and to answer additional questions about the safety and effectiveness of tenofovir gel for preventing HIV.
- **VOICE– Vaginal and Oral Interventions to Control the Epidemic – is an ongoing study evaluating daily use of tenofovir gel, regardless of when participants have sex. Moreover, VOICE is also testing daily use of two different oral ARV tablets, tenofovir and Truvada[®],** an important approach to help determine how well each product works compared to its control (placebo gel or placebo tablet) and which approach – gel or tablet – women prefer to use. VOICE will enroll approximately 5,000 women at sites in four countries in southern Africa. About 1,000 women are enrolled in the study so far.
- **CAPRISA 004 and VOICE are complementary studies.** Each is critical for advancing understanding about the safety and effectiveness of tenofovir gel using different strategies among different populations of African women. Taken together, the studies can provide a much more reliable scientific assessment of tenofovir gel than either alone.

- more

BACKGROUND

CAPRISA 004

- CAPRISA 004 was a Phase IIb (proof of concept) trial conducted by the Centre for the AIDS Programme of Research in South Africa (CAPRISA) to assess the safety and effectiveness of tenofovir gel for preventing HIV infection in women when applied within 12 hours prior to sex and as soon as possible within 12 hours after sex.
- The study enrolled 889 sexually active HIV-uninfected women at two sites in South Africa: the CAPRISA eThekweni clinical research site, located in central Durban, and the Vulindlela clinical research site, located in a rural setting approximately 90 minutes by car outside of Durban.
- Women were randomized to one of two study groups – 445 to the tenofovir gel group and 444 to the placebo gel group – and instructed to use the study product before and after sex, but not to exceed two doses over 24 hours, regardless of the frequency of intercourse. All participants received condoms, intensive counseling and other routine interventions for reducing HIV risk throughout the time they were in the trial, which averaged 18 months. The trial started in late May 2007 and enrollment was completed in early January 2009. Study exit visits were completed at the end of November 2009.
- The study found tenofovir gel was safe when used before and after sex and 39 percent more effective than placebo gel for protecting against HIV. In other words, there were 39 percent fewer HIV infections among women using tenofovir gel. Of the 444 women who used a placebo gel, 60 acquired HIV during the study, whereas 38 out of the 445 women in the tenofovir gel group became infected. While this finding meets the definition for statistical significance, a measure used to judge the credibility of a result, the 39 percent level of protection found in the study remains only an *estimate* of the gel's true effect in a broader population. The confidence interval, which is expressed as a range with a lower and upper bound, helps to understand the strength and reliability of a result. The confidence interval for the CAPRISA 004 result indicates the true level of effectiveness of tenofovir gel – when used before and after sex – could be anywhere between 6 and 60 percent.
- The CAPRISA 004 study was a collaboration involving CAPRISA at the University of KwaZulu-Natal in Durban; FHI; and CONRAD, which holds the license for tenofovir gel. It was funded by USAID and the Technology Innovation Agency, formerly known as LIFElab, in South Africa.



There were 39 percent fewer HIV infections in the tenofovir gel group

VOICE

- VOICE is a Phase IIb trial designed to evaluate both the safety and effectiveness of two approaches for preventing the sexual transmission of HIV: daily use of an ARV tablet (tenofovir or Truvada) and daily use of an ARV-based gel (tenofovir gel). VOICE is the first effectiveness study of a microbicide that women use every day. It is also the only trial evaluating both a tablet and a gel in the same study, which will help determine which approach women are more likely to use.
- The VOICE Study is being conducted at multiple clinical research sites in South Africa (including the CAPRISA eThekweni site) and at sites in Malawi, Uganda and Zimbabwe. The study began in September 2009 and is expected to be completed in 2012 with results available some time in 2013.
- Women in VOICE are randomized into one of five study groups, either to one of the three tablet groups: tenofovir, Truvada, or oral placebo; or to one of the two gel groups: tenofovir gel or placebo gel. About 5,000 women will be enrolled, 1,000 in each group. Participants use their assigned study product every day for the

- more -

duration of the study, about two years on average. As with CAPRISA 004, trial participants in VOICE receive ongoing HIV risk-reduction counseling, condoms, and diagnosis and treatment of STIs – proven measures for reducing the risk of HIV.

- VOICE is the flagship study of the Microbicide Trials Network (MTN), an HIV/AIDS clinical trials network established and funded in 2006 by the Division of AIDS (DAIDS) at the National Institute of Allergy and Infectious Diseases (NIAID) with co-funding from the National Institute of Mental Health and the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, all components of the U.S. National Institutes of Health (NIH). As co-sponsors of the trial, CONRAD of Arlington, Virginia, USA; and Gilead Sciences, Inc., of Foster City, California, USA, are providing the study products free of charge.

Tenofovir Gel

- Tenofovir gel belongs to a newer class of candidate microbicides with specific activity against HIV. The gel contains the same ingredient that is in the oral tablet, which is approved as a treatment for HIV infection in combination with other drugs. Laboratory and animal studies have demonstrated that tenofovir gel acts on certain cells of the vagina and cervix that are the primary targets for HIV infection. Safety studies performed to date have found the gel to be well tolerated and safe in humans. An expanded safety and acceptability trial called HPTN 059 found daily use of the gel over six months by sexually active HIV-negative women was safe and well-tolerated.
- Tenofovir gel was initially developed by Gilead Sciences, Inc., of Foster City, California, USA, which assigned a royalty-free license to the International Partnership for Microbicides of Silver Spring, Maryland, and CONRAD, of Arlington, Virginia, in December 2006. The ARV tablets tenofovir (known by the brand name Viread®) and Truvada, a combination of both tenofovir and a second ARV called emtricitabine, are Gilead products.

OTHER NEWS AHEAD

Also to be presented at AIDS 2010 are preliminary findings from the U.S. PrEP Safety Study among men who have sex with men. Two other studies expect to report results early next year.

- The **U.S. PrEP Safety Study** is a U.S. Centers for Disease Control and Prevention (CDC) study that assessed the safety of and adherence to daily oral tenofovir in 400 HIV-negative men who have sex with men (MSM) The study was conducted in San Francisco, Atlanta and Boston. Participants were randomly assigned to one of four study groups. Two groups received either tenofovir or placebo as soon as they were enrolled into the study, while the other two groups received either tenofovir or placebo nine months after enrollment. Results (which are being presented at AIDS 2010 as a late breaker abstract on 23 July) will assess whether a daily PrEP regimen is associated with changes in risk behaviors among MSM.
- **iPrEx**, the Pre-Exposure Prophylaxis Initiative, is a large-scale trial designed to assess whether daily use of Truvada can help prevent HIV in gay men and other men who have sex with men. The study, which is funded by NIAID, enrolled 2,499 participants at 11 sites in Peru, Ecuador, the United States, Brazil, South Africa and Thailand. Enrollment into the study began in June 2007 and ended in December 2009. Results are expected to be reported in early 2011.
- **MTN-001** is a Phase II trial that directly compared the oral tablet and vaginal gel preparations of tenofovir, looking at differences in how and where the drug is absorbed in the body and differences in women's adherence to and acceptability of each dosing approach separately and in combination. The study, which was conducted by the MTN, involved 168 sexually active, HIV-negative women who enrolled at one of seven sites in the United States, Uganda and South Africa. Results of MTN-001, which are expected early 2011, will help researchers understand how the drug penetrates the cells in tissue where infection typically occurs when delivered as either a tablet or a vaginal gel. MTN-001 also will provide important insight about women's preferences for and their ability to adhere to each daily regimen.

WHY WOMEN NEED HIV PREVENTION METHODS

- Women make up half of the more than 33 million people living with HIV/AIDS worldwide. In sub-Saharan Africa, six of ten new HIV infections in adults happen in women. In several southern African countries, young women aged 15 to 24 are at least three times more likely than their male peers to be infected with HIV.
- Among women, unprotected sex with an infected male partner remains the primary risk factor for HIV infection, and in many parts of the world, heterosexual intercourse is the driving force of the epidemic. Women are twice as likely as their male partners to acquire HIV during sex, due in part to biological factors that make women more vulnerable. Although correct and consistent use of male condoms has been shown to prevent HIV infection, often women do not have a choice if they are used. Women need prevention tools that they can decide to use on their own.

#

More information about the VOICE Study can be found at <http://www.mtnstopshiv.org/news/studies/mtn003>
More information about the results of CAPRISA 004 can be found at www.caprisa.org

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 (NIAID), part of the U.S. National Institutes of Health (NIH). The MTN brings together international investigators and community and industry partners who are devoted to reducing the sexual transmission of HIV through the development and evaluation of products applied topically or administered orally, working within a unique infrastructure specifically designed to facilitate the research required to support licensure of these products for widespread use.

Based at the University of Pittsburgh and Magee-Womens Research Institute in Pittsburgh, Pennsylvania, USA, MTN's core operations are supported by a network laboratory at the University of Pittsburgh, a statistical and data management center housed within the Statistical Center for HIV/AIDS Research & Prevention (SCHARP) at the Fred Hutchinson Cancer Research Center, and Family Health International, a global organization with expertise conducting clinical protocols. MTN conducts its trials at clinical research sites located in seven countries and spanning three continents. MTN receives its funding from three NIH institutes: NIAID, the National Institute of Mental Health and the Eunice Kennedy Shriver National Institute of Child Health and Human Development. Among the groups developing and evaluating microbicides for HIV prevention globally, the MTN is the only one funded by NIH.

20-July-10