CONTACT: **Clare Collins** **Lisa Rossi**
+1-412-641-7299 **+1-412-641-8940**
+1-412-770-8643 (mobile) **+1-412-916-3315 (mobile)**
collcx@upmc.edu **rossil@upmc.edu**

BACKGROUNDER

MTN-039
Phase 1 Safety and Pharmacokinetic Study of a Rectally-Administered Tenofovir & Elvitegravir Insert

Summary

- MTN-039 is a Phase I study evaluating whether a fast-dissolving insert containing the antiretroviral drugs tenofovir alafenamide (TAF) and elvitegravir (EVG) is safe to use in the rectum. The study will include approximately 20 HIV-uninfected individuals at two sites in the United States. It will help determine whether further testing on the safety and acceptability of a TAF/EVG rectal insert for preventing HIV from anal sex can be conducted in a larger population. Results are anticipated by late 2020.

- MTN-039 is a study of the Microbicide Trials Network (MTN), 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. The TAF/EVG insert being studied in MTN-039 was developed by CONRAD, a nonprofit, non-governmental organization that conducts research on contraception and HIV prevention based in Arlington, Va. The protocol chair for the study is Sharon Ridder, M.D., of the University of Pittsburgh School of Medicine.

- MTN-039 is part of a research agenda at the MTN focused on the development and testing of HIV prevention products for individuals who engage in condomless anal sex, a major risk factor for HIV infection.

Why this Study is Important

Microbicides are products used inside the vagina or rectum that are intended to protect against HIV infection acquired through sex. Products currently being tested in clinical trials contain antiretroviral (ARV) drugs, many of which are commonly used to treat people with HIV. Although the majority of microbicide research has focused on products to prevent HIV infection associated with vaginal sex, important strides are being made in research aimed at addressing the need for rectal microbicides.

Anal sex is a common sexual behavior practiced by people of all genders and sexualities around the world. According to some estimates, the risk of becoming infected with HIV during anal sex is 20

-more-

times greater than vaginal sex because the rectal lining is thinner and more fragile than the vaginal lining.

While condoms are an effective method to prevent HIV infection through anal sex, many people can't or don't want to use them every time they have sex. Similarly, oral pre-exposure prophylaxis (PrEP) – an HIV prevention strategy in which people take a daily pill to prevent infection – has been shown to be highly effective, however, not all individuals vulnerable to HIV may be willing or able to access it. Just as there are multiple contraception options for people who choose to prevent pregnancy, a rectal microbicide could give people who practice anal sex an additional choice for HIV prevention. And, importantly, one that is non-systemic, short-acting and could be used around the time of sex (on-demand).

Rectal microbicides are being developed and tested in several formulations including gels, douches, suppositories and inserts. Several rectal microbicide studies have been completed to-date, with others currently underway. One study, MTN-035, or DESIRE (Developing and Evaluating Short-acting Innovations for Rectal Use), is comparing acceptability, tolerability and adherence to three placebo rectal products: a douche, suppository and insert. MTN-039 is an important complement to DESIRE by evaluating a rectal insert that contains an active product.

How the Study is Designed

MTN-039 is a Phase I trial designed to evaluate the safety of a TAF/EVG insert used rectally, as well as determine the degree that drug concentrates in the blood, rectal and/or vaginal fluid and rectal tissue. The study will enroll approximately 20 HIV-uninfected individuals who will be administered a single dose of the insert in the clinic, followed by safety testing and tissue sampling. After a period of up to seven weeks in which participants will not receive product, they will be administered two doses of the insert, followed by additional safety testing and tissue sampling.

The study will be conducted at the University of Pittsburgh, site investigator Ken Ho, M.D., and the University of Alabama at Birmingham, site investigator Craig Hoesley, M.D. Tests and procedures performed as part of MTN-039 will determine the safety of the products, and how much drug is absorbed in blood, rectal and/or vaginal fluid and rectal tissue. To explore the acceptability of the insert, study participants will be asked about any side effects they may have experienced and their likes and dislikes about the product overall. All participants will receive HIV risk reduction counseling and condoms, and be tested for HIV and sexually transmitted infections.

The Products Being Studied

Inserts are fast-dissolving tablets applied into the vagina or rectum as a delivery method for HIV prevention drugs. Originally developed by CONRAD for vaginal use, they are now being tested in the rectum for HIV prevention from anal sex. In addition to being low-cost, inserts are portable and discreet, which may make them particularly suited to on-demand use.

The insert being studied in MTN-039 is comprised of tenofovir alafenamide (TAF) and elvitegravir (EVG). TAF is a nucleotide reverse transcriptase inhibitor (NRTI) used in the treatment of HIV infection and chronic hepatitis B. NRTIs work against HIV by blocking reverse transcriptase, an enzyme the virus needs to make copies of itself. EVG is an integrase inhibitor – a class of ARVs

designed to block the action of integrase, an enzyme that causes HIV and other viruses to spread. Combining these two different classes of drugs into a rectal insert could produce a more potent response to HIV.

MTN-039 is the first clinical study to explore rectal use of the TAF/EVG insert.

# # #

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 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 development and 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 www.mtnstopshiv.org.

12-December-2019