CONTACT: Lisa Rossi
rossil@mwri.magee.edu
+1-412-916-3315

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"On-demand" HIV prevention method for women being tested in second early phase trial

Phase 1 study of the TAF/EVG fast-dissolving vaginal insert – intended for use at the time of sex – begins at US and African sites

PITTSBURGH – December 7, 2023 – A fast-dissolving vaginal insert that women would use at or around the time of sex as an "on-demand" HIV prevention method is being evaluated in a new early phase study being conducted by MATRIX, a United States Agency for International Development (USAID)-funded project focused on the early research and development of innovative HIV prevention products for women.

The insert, which resembles a bullet-shaped tablet, contains the antiretroviral (ARV) drugs tenofovir alafenamide (TAF) and elvitegravir (EVG). Once inside the vagina, it would begin to dissolve, and in doing so, release the two drugs. Animal and laboratory studies suggest the insert would provide protection against HIV for up to three days.

The MATRIX study is only the second Phase 1 trial of the TAF/EVG fast-dissolving insert used vaginally and the first to evaluate its use in multiple doses as well as in African women. The TAF/EVG fast-dissolving insert is the only on-demand HIV prevention product for use by women currently being evaluated in clinical trials.

The insert is being developed by CONRAD, a nonprofit research organization affiliated with Eastern Virginia Medical School (EVMS) in Norfolk, Va., U.S.A., for its use both vaginally and rectally. CONRAD-146, a first-in-human study conducted in the U.S. of its use as a vaginal insert, found that single administration was safe and acceptable among 16 women.

In the MATRIX study, known as MATRIX-001, researchers are evaluating the safety of the vaginal insert when used multiple times over several days, as well as user acceptability and how and where the two drugs are taken up in the body. The study, which will enroll 60 women at three sites in Kenya, South Africa and the United States, will help determine whether the product should advance to Phase 2 studies of its safety and acceptability when used as designed, i.e. at or around the time of sex.

Such a method could appeal to women who don't want or are unable to use oral pre-exposure prophylaxis (PrEP), which requires taking an ARV tablet every day, or long-acting products like the monthly dapivirine vaginal ring or cabotegravir injections given every two months. It may be especially appealing to women who have infrequent or clustered sex and want only to use a product when needed, with local delivery (in the vagina) and with little drug going elsewhere in the body.

"Existing methods aren't enough to meet women's varying needs and lifestyles. A product that's intended to be used at the time of sex, like the fast-dissolving TAF/EVG vaginal insert, would fill an important gap as alternative approach for women wanting protection only when they feel they need it," said Nelly Mugo, MBChB, Mmed, MPH, MATRIX-001 protocol co-chair and investigator of record of the Kenya Medical Research Institute (KEMRI) Centre for Clinical Research Thika clinical research site (CRS), one of the three sites conducting the MATRIX-001study.

"Granted, the TAF/EVG insert is early in development, which is why the MATRIX-001 study is so critically important, especially for African women. This study will help determine the way forward for this product, and potentially get us one step closer to it being a viable option for women in this region," added Leila Mansoor, PhD, protocol co-chair and the investigator of record at the Centre for the AIDS Programme of Research in South Africa (CAPRISA) eThekwini CRS, also a MATRIX-001 study site.

The TAV/EVG fast-dissolving insert contains 20 mg of TAF and 16 mg of EVG. TAF belongs to a class of ARVs called nucleoside reverse transcriptase inhibitors (NRTIs) that prevent HIV from making copies of itself inside human cells, therefore, preventing the spread of HIV inside the body. TAF has been approved by the U.S. Food and Drug

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Administration (FDA) for the treatment of chronic hepatitis B and for the treatment and prevention of HIV in men who have sex with men when used in combination with emtricitabine. Similarly, EVG has been approved by the U.S. FDA for the treatment of HIV in combination with other ARVs. EVG belongs to a class of ARV drugs known as integrase inhibitors that block HIV from being able to integrate its genetic code into human cells – a step that occurs later in the HIV lifecycle. Both TAF and EVG are being provided by Gilead Sciences for CONRAD's development in the insert product.

Women in the study will be randomly assigned to use either the TAF/EVG fast-dissolving insert or a placebo insert with no active drugs. Each participant will use a total of 10 inserts – at first, every day for three consecutive days, and then every other day (every 48 hours) for two weeks. Participants will insert the products themselves, the first time in the clinic, with guidance from study staff. During the two to three months women are in the study, they will undergo different tests and procedures and will be asked questions about product acceptability prior to, during and following insert use. In addition, laboratory tests of tissue samples will be conducted to assess its potential activity against HIV, as well as herpes simplex virus (HSV), because pre-clinical laboratory and animal studies have shown that TAF acts against HSV in addition to HIV.

The study enrolled its first participants this week at the U.S. site, the EVMS CRS in Norfolk, Va, and the CAPRISA eThekwini CRS in South Africa has started screening potential participants. The study should be underway at the KEMRI Thika CRS in Kenya by early January. MATRIX-001 is expected to take approximately one year to conduct, with results anticipated mid-2025.

The TAF/EVG fast-dissolving insert is one of nine HIV prevention products being developed under MATRIX, and the only product to have previously been evaluated in clinical trials. In addition to the CONRAD-146 first-in-human study of its use vaginally, researchers have also conducted the MTN-039 first-in-human study of its use as a rectal insert, which found single use and two inserts used together posing no safety concerns. In both studies, results of laboratory tests of tissue and fluid samples showed drug levels compatible with protection against HIV.

According to UNAIDS, women and girls accounted for 63 percent of all new HIV infections in sub-Saharan Africa in 2022, versus 46 percent globally. In much of Africa, daily oral PrEP is the only biomedical prevention method available, and daily pill-taking has been especially challenging for adolescent girls and young women. Both the monthly dapivirine ring and cabotegravir long-acting injectable (CAB-LA) have been recommended by the World Health Organization and approved for use in several African countries, though neither method is yet to be made widely available. Even so, women have different preferences and needs, and at different times in their lives, which is why additional options are needed.

MATRIX is a five-year program funded by USAID in 2021 that aims to expedite the research and development of HIV prevention products for women – including products designed to protect against both HIV and pregnancy – that in addition to being safe and effective, will be acceptable, affordable, scalable and deliverable in the settings where they are needed most. MATRIX activities are focused on the early research and development of products, which involves both pre-clinical research and the first clinical trials of products. Through its North-South partnerships, MATRIX also aims to strengthen the capacity of African investigators to facilitate full and sustainable ownership of this work into the future. MATRIX is being implemented by Magee-Womens Research Institute (MWRI) in collaboration with partner organizations based in Kenya, South Africa, the United States and Zimbabwe. Leading the project is Sharon Hillier, Ph.D., of MWRI and the University of Pittsburgh School of Medicine, with Thesla Palanee-Phillips, Ph.D., from the Wits RHI and University of Witwatersrand, South Africa, serving as deputy director.

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To learn about MATRIX go to www.matrix4prevention.org. Click here to read a QA about the TAF/EVG fast-dissolving vaginal insert and MATRIX-001 study. Additional information about MATRIX-001 can also be found at https://www.matrix4prevention.org/activity-hubs/clinical-trials/matrix-001.

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