CLARIFICATION MEMO #03 TO:

MATRIX-001

A Phase I Randomized, Placebo-Controlled, Double-Blind Study to Assess Safety, Pharmacokinetics, and Modeled Pharmacodynamics of a Vaginal Insert Containing Tenofovir Alafenamide and Elvitegravir

Cooperative Agreement #7200AA22CA00002

IND # 141,295

Version 1.0 / May 4, 2023

Clarification Memo Date: October 27, 2023

Section 1: Summary of Clarifications and Rationale

The procedures clarified in this Clarification Memorandum (CM) have been approved by the MATRIX Prime-Clinical Trials Hub, MATRIX-001 Protocol Co-Chairs, and MATRIX-001 Product Developer (PD)/Sponsor and are to be implemented immediately upon issuance. IRB/IEC approval of this CM is not required by MATRIX prior to implementation; however, investigators may submit the CM to the IRB/IEC overseeing the study at their site for the IRB/IEC's notification. This CM is official MATRIX-001 documentation and is effective immediately. A copy of this CM must be retained in the PD/Sponsor's and in each study site's Essential Documents file for MATRIX-001. No changes in the sample informed consent form or schedule of visits/procedures are included in this CM.

This document clarifies that Visits 3 and 5 should ideally be scheduled 10-14 days after Visits 2 and 4, respectively, but may be scheduled more than 14 days after to allow the participant's menstrual flow to cease prior to starting product use.

Section 2: Implementation

With the exception of updates to the protocol team roster, text to be deleted is noted below with a ~~strikethrough~~, text to be added is in **bold**, and text in ***bold italics*** is not to be added, but to serve as a clarification of the implementation item in question. This information will be included in the protocol the next time the protocol is updated.

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1. The following clarification applies to Sections 7.2.2 (Randomization Visit – Visit 3) and 7.3.2 (Fourth Dose Visit – Visit 5), which state "Visit 3 should be scheduled 10-14 days after Visit 2, not less than

10 days after biopsy. Visit 3 will be scheduled shortly after menstrual flow ceases for cycling participants to ensure the 3 days of product use do not occur during a menstrual cycle" and "Visit 5 should be scheduled 10-14 days after Visit 4, not less than 10 days after biopsy. Visit 5 will be scheduled shortly after menstrual flow ceases for cycling participants to ensure the 14 days of product use do not occur during a menstrual cycle", respectively.

Visit 3 should ideally be scheduled 10-14 days after Visit 2 but may be scheduled more than 14 days after Visit 2 to allow the participant's menstrual flow to cease prior to starting product use. Visit 5 should ideally be scheduled 10-14 days after Visit 4 but may be scheduled more than 14 days after Visit 4 to allow the participant's menstrual flow to cease prior to starting product use.

The above information will be incorporated into the next version of the protocol at a later time if it is amended.