Final

September 19, 2022

Letter of Amendment 2

Protocol

Version 1.0

HVTN 140/ HPTN101

A phase 1 dose-escalation clinical trial to evaluate the safety, tolerability, and pharmacokinetics of PGDM1400LS alone and in combination with VRC07-523LS and PGT121.414.LS in healthy, HIV-uninfected adult participants

DAIDS-ES ID 38723

IND #154188—HELD BY DAIDS

HIV Vaccine Trials Network (HVTN) and HIV Prevention Trials Network (HPTN) Clinical Research Site (CRS) filing instructions

The following information impacts the HVTN 140/ HPTN101 study and must be forwarded to your Institutional Review Board (IRB)/Ethics Committee (EC) and any other applicable Regulatory Entity (RE) as soon as possible for their information and review. Their approval is required before implementation.

Upon receiving final IRB/EC and any other RE approval(s) for this LOA, CRSs must implement the LOA immediately.

Upon receiving final IRB/EC and any other applicable RE approval(s), CRSs are required to submit LOA registration documents to the DAIDS Protocol Registration Office (PRO) at the

Regulatory Support Center (RSC). CRSs will receive an LOA Registration Notification once the DAIDS PRO verifies that all the required LOA registration documents have been received and are complete. A Registration Notification from the DAIDS PRO is not required prior to implementing the LOA. A copy of the LOA Registration Notification, along with this LOA and any IRB/EC and RE correspondence, should be retained in the CRS's regulatory files.

For additional information on the registration process and specific documents required for LOA registration, refer to the current version of the DAIDS Protocol Registration Manual.

The following information does not affect the sample informed consent. The CRS's IRB/EC is responsible for determining the process of informing study participants of the contents of this LOA.

List of changes

The changes described herein will be incorporated in the next version of Protocol HVTN 140/ HPTN101 if it undergoes full protocol amendment at a later time. Added text is shown in **bold underline** and deleted text is shown with ~~strikethrough~~.

Item 1 Added in Section 7.2, *Exclusion criteria*; and Section 7.3.1, *Delaying study product administrations for a participant (Part B only)*: considerations for timing of receipt of vaccines for Monkeypox

This information has been added to provide guidance to CRSs on the timing of receipt of a vaccine for Monkeypox relative to study product administrations.

Two new exclusion criteria have been added, as number 8 and 9, in Section 7.2; subsequent criteria have been renumbered accordingly. Two new bullets have been added following the bullet regarding receipt of SARS CoV-2 vaccine in Section 7.3.1. Added text is shown below.

Added text in Section 7.2:

8. Jynneos vaccine for Monkeypox received within 14 days prior to HVTN 140/HPTN 101 enrollment or planned within 14 days after enrollment.

9. ACAM2000 vaccine for Monkeypox received within 28 days prior to HVTN 140/HPTN 101 enrollment or, if ACAM2000 received greater than 28 days prior to enrollment, vaccination scab still present; or planned within 14 days after enrollment.

Added text in Section 7.3.1:

- **Within 14 days of study product administration (ie, within 14 days prior to study product administration, or planned within 14 days after study product administration)**
  - **Receipt of Jynneos vaccine for Monkeypox**
- **Within 28 days prior to study product administration or, if ACAM2000 received greater than 28 days prior to study product administration, vaccination scab still present; or planned within 14 days after study product administration**
  - **Receipt of ACAM2000 vaccine for Monkeypox**

Protocol modification history

Protocol modifications are made via clarification memos, letters of amendment, or full protocol amendments. HVTN protocols are modified and distributed according to the standard HVTN procedures as described in the HVTN Manual of Operations (MOP).

The version history of, and modifications to, Protocol HVTN 140/ HPTN101 are described below.

Date: September 19, 2022

Protocol version: Version 1.0
Protocol modification: Letter of Amendment 2

Item 1 Added in Section 7.2, *Exclusion criteria*; and Section 7.3.1, *Delaying study product administrations for a participant (Part B only)*: considerations for timing of receipt of vaccines for Monkeypox

Date: July 7, 2022

Protocol version: Version 1.0
Protocol modification: Clarification Memo 2

Item 1 Corrected in Letter of Amendment 1 dated February 24, 2022, and Clarification Memo 1 dated March 28, 2022: date of original protocol

Date: March 28, 2022

Protocol version: Version 1.0
Protocol modification: Clarification Memo 1

Item 1 Corrected in Appendix G, *Laboratory procedures for Part B*: CBC/differential and Chemistry panel added to visit 2

Date: February 24, 2022

Protocol version: Version 1.0
Protocol modification: Letter of Amendment 1

Item 1 Added in Section 1, *Overview*: HPTN Leadership and Operations Center

Item 2 Updated in Section 1.1, *Protocol Team*: team members

Item 3 Added in Section 8.3.3.3, *PGT121.414.LS fixed-dose intravenous infusion* preparation: information regarding storage times and temperatures

Item 4 Corrected in Appendix F, *Laboratory procedures for Part A*: Ab reaction maximum blood volume in footnote 13

Item 5 Corrected in Appendix G, *Laboratory procedures for Part B*: formatting

Item 6 Corrected in Appendix F, *Laboratory procedures for Part A* and Appendix G, *Laboratory procedures for Part B*: visit number referenced in footnote 7

Item 7 Corrected in Appendix I, *Procedures at HVTN CRS for Part B*: remote documentation of diary in footnote 3

Item 8 Added in Section 8.4.1, *General considerations for subcutaneous infusion study product administration*: reference to HVTN140/HPTN101 Study-Specific Procedures (SSP) manual) for additional details on anatomic locations for infusions

Item 9 Revised in Section 8.3.1.1, *Thawing instructions*: PGDM1400LS vial storage time conditions

Date: June 23, 2021

Protocol version: 1.0
Protocol modification: not applicable

Original protocol

Protocol signature page

A phase 1 dose-escalation clinical trial to evaluate the safety, tolerability, and pharmacokinetics of PGDM1400LS alone and in combination with VRC07-523LS and PGT121.414.LS in healthy, HIV-uninfected adult participants

I will conduct the study in accordance with the provisions of this protocol and all applicable protocol-related documents. I agree to conduct this study in compliance with United States (US) Health and Human Service regulations (45 CFR 46); applicable US Food and Drug Administration regulations; standards of the International Conference on Harmonization Guideline for Good Clinical Practice (E6); Institutional Review Board/Ethics Committee determinations; all applicable in-country, state, and local laws and regulations; and other applicable requirements (eg, US National Institutes of Health, Division of AIDS) and institutional policies.

Investigator of Record Name (print)	Investigator of Record Signature	Date

DAIDS Protocol Number: HVTN 140/ HPTN101

DAIDS Protocol Version: Version 1.0

Protocol Date: June 23, 2021