FINAL

December 20, 2022

Letter of Amendment 3

Protocol

Version 1.0

HVTN 140 / HPTN 101

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 / HPTN 101 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 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 / HPTN 101 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 Updated in Section 8.3.2, *VRC07-523LS*: storage conditions for VRC07-523LS vials after thaw and prepared product in IV bags or syringes

The Investigator's Brochure for VRC07-523LS was recently updated. To align the protocol with the current Investigator's Brochure, the storage conditions for vials after thaw and prepared product in IV bags or syringes listed in Section 8.3.2 were updated as shown below.

Tracked revised text Section 8.3.2.1, #4

4. Thawed vials may be stored **cumulatively** for up to 24 hours at controlled room temperature (maximum 27°C) and~~/or~~ up to 2 weeks (14 days) at 2°C to 8°C. Product may not be stored in direct sunlight. If stored at 2 ºC to 8 ºC, vials must be equilibrated at controlled room temperature (maximum 27 ºC) for a minimum of 30 minutes and may be held at room temperature for up to 8 hours prior to product preparation.

Tracked revised text Section 8.3.2.2, #5

5. The prepared VRC07-523LS IV container may be stored **cumulatively** at 2°C to 8°C **for** up to 48 hours **and**~~or~~ at controlled room temperature (maximum 27°C) for a maximum of 4 hours total including the infusion time. Product may not be stored in direct sunlight. If stored at 2°C to 8°C, prepared product must be equilibrated at

controlled room temperature (maximum 27°C) for a minimum of 30 minutes prior to product administration.

Tracked revised text Section 8.3.2.3, #5

5. The prepared VRC07-523LS IV container may be stored **cumulatively** at 2°C to 8°C **for** up to 48 hours **and**~~or~~ at controlled room temperature (maximum 27°C) for a maximum of 4 hours total including the infusion time. Product may not be stored in direct sunlight. If stored at 2°C to 8°C, prepared product must be equilibrated at controlled room temperature (maximum 27°C) for a minimum of 30 minutes prior to product administration.

Tracked revised text Section 8.3.2.4, #5

5. The prepared VRC07-523LS syringe(s) may be stored **cumulatively** at 2°C to 8°C for up to 24 hours **and**~~or~~ at controlled room temperature (maximum 27°C) for a maximum of 4 hours, including the administration time. Product may not be stored in direct sunlight. If stored at 2°C to 8°C, prepared product must be equilibrated at controlled room temperature (maximum 27°C) for a minimum of 30 minutes prior to product administration.

Tracked revised text Section 8.3.2.5, #5

5. The prepared VRC07-523LS syringe(s) may be stored **cumulatively** at 2°C to 8°C for up to 24 hours **and**~~or~~ at controlled room temperature (maximum 27°C) for a maximum of 4 hours, including the administration time. Product may not be stored in direct sunlight. If stored at 2°C to 8°C, prepared product must be equilibrated at controlled room temperature (maximum 27°C) for a minimum of 30 minutes prior to product administration.

Item 2 Updated in Section 1.1, *Protocol Team*: HVTN Protocol Team leader

The HVTN Protocol Team leader for this study is Carmen Paez.

Tracked revised text:

HVTN Protocol Team leader~~s~~	~~Shelly Karuna~~ **Carmen Paez** HVTN LOC, Fred Hutch 206-667-~~4355~~**2881** ~~mkaruna~~ **cpaez**@fredhutch.org

Protocol modification history

Protocol modifications are made via clarification memos, letters of amendment, or full protocol amendments. The version history of, and modifications to, Protocol HVTN 140 / HPTN 101 are described below.

Date: December 20, 2022

Protocol version: Version 1.0
Protocol modification: Letter of Amendment 3

Item 1 Updated in Section 8.3.2, *VRC07-523LS*: storage conditions for VRC07-523LS vials after thaw and prepared product in IV bags or syringes

Item 2 Updated in Section 1.1, *Protocol Team*: HVTN Protocol Team leader

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 / HPTN 101

DAIDS Protocol Version: Version 1.0

Protocol Date: June 23, 2021