Project Brief: HVTN 140/HPTN 101

Full Title of Study/Programme	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.
Technical Focus Area/Key Words	HIV Prevention
Rationale	The HVTN 140/HPTN 101 study wants to understand how the body's immune system responds to a new lab-made antibody against HIV (Human Immunodeficiency Virus). The antibodies will be delivered directly into the body through Subcutaneous and Intravenous infusion (under the skin on your abdomen, arm, hand, or thigh). We are hoping that if this new HIV Prevention method is approved, we will have more options for HIV Prevention and treatment.
Primary Objectives	Primary objective 1: To evaluate the safety and tolerability of PGDM1400LS when administered via intravenous (IV) or subcutaneous (SC) routes (Part A) and of PGDM1400LS, VRC07-523LS and PGT121.414.LS when administered in sequence IV or SC (Part B) Primary objective 2: To evaluate the serum concentrations and pharmacokinetics of PGDM1400LS after a single administration (Part A) and of PGDM1400LS, VRC07-523LS, and PGT121.414.LS after each three-mAb administration (Part B) Primary objective 3: To evaluate the individual mAb-specific serum neutralizing activity after single product administration of PGDM1400LS (Part A) and after each three-mAb administration of PGDM1400LS, VRC07-523LS and PGT121.414.LS (Part B)
Primary Endpoint/Outcome	Primary endpoints 1: • Local and systemic Solicited AEs, laboratory measures of safety, Unsolicited AEs, and SAEs • Early discontinuation of administration and reason(s) for discontinuation and early study termination Primary objective 2: To evaluate the serum concentrations and pharmacokinetics of PGDM1400LS after a single administration (Part A) and of PGDM1400LS, VRC07-523LS, and PGT121.414.LS after each three-mAb administration (Part B) Primary endpoint 3: Magnitude and breadth of neutralizing activity measured with Env pseudotyped viruses specific for either PGDM1400LS, VRC07-523LS or PGT121.414LS in TZM-bl cells at prespecified timepoints among participants who received all scheduled product administrations
Study Design	Multicenter, randomized, open-label study
Study arms	Part A Group 1: PGDM1400LS 5 mg/kg to be administered via IV infusion at Month 0 Group 2: PGDM1400LS 20 mg/kg to be administered via IV infusion at Month 0 Group 3: PGDM1400LS 20 mg/kg to be administered via SC infusion at Month 0

	Group 4: PGDM1400LS 40 mg/kg to be administered via IV infusion at Month 0 Group 5: PGDM1400LS 40 mg/kg to be administered via SC infusion at Month 0 Part B Group 6: PGDM1400LS 20mg/kg + VRC07-523LS 20mg/kg + PGT121.414.LS 20 mg/kg to be administered via IV infusion sequentially in this order at Month 0 and Month 4 Group 7: PGDM1400LS 20mg/kg + VRC07-523LS 20mg/kg + PGT121.414.LS 20 mg/kg to be administered via SC infusion sequentially in this order at Month 0 and Month 4 Group 8: PGDM1400LS 1.4gram + VRC07-523LS 1.4gram + PGT121.414.LS 1.4gram to be administered via IV infusion sequentially in this order at Month 0 and Month 4 Group 9: PGDM1400LS 1.4gram + VRC07-523LS 1.4gram + PGT121.414.LS 1.4gram to be administered via SC infusion sequentially in this order at Month 0 and Month 4 Group 10: PGDM1400LS 40mg/kg + VRC07-523LS 40mg/kg + PGT121.414.LS 40 mg/kg to be administered via IV infusion sequentially in this order at Month 0 and Month 4
Study population	Healthy, HIV-1–uninfected volunteers aged 18 through 50 years
Study sample size	95
Follow up/duration	14 months (includes enrolment, planned safety holds, and follow-up)
Study/Programme sites	Bridge HIV CRS CAPRISA eThekwini CRS George Washington University School of Public Health Groote Schuur HIV CRS HIV Research Branch, KEMRI/CDC CTU Milton Park CRS New Jersey Medical School Clinical Research Center CRS Seke South CRS Soweto HVTN CRS Spilhaus CRS The Hope Clinic of the Emory Vaccine Center CRS Vanderbilt Vaccine (VV) CRS Ward 21 CRS Related Publications
Intervention	PGDM1400LS, VRC07-523LS and PGT121.414LS
Investigators	IOR: Prof Sinead Delany-Moretlwe Sub Investigators: Dr Carrie-Anne Mathew, Dr Juliet Vimbai Rundogo

Other Partners & Collaborators	Study product providers: • PGDM1400LS: DAIDS, NIAID, NIH, DHHS (Bethesda, Maryland, USA) • PGT121.414.LS: DAIDS, NIAID, NIH, DHHS (Bethesda, Maryland, USA) • VRC07-523LS: Dale and Betty Bumpers Vaccine Research Center (VRC), NIAID, NIH, DHHS (Bethesda, Maryland, USA)
Sponsors/Donors	DAIDS, NIAID, NIH, DHHS (Bethesda, Maryland, USA)
Linked Sub Studies and post grad projects	None
Publications/key presentations to date	None
Progress Update as of 08 April 2024	Screened: 28 participants Enrolled: 9 All 9 participants were followed up to completion and exited the study. Last participant visit occurred 06 July 2023. Study currently in close-out phase.
Frequency of donor narrative report	Annually
Overall Study/Project Contact	Dr Carrie- Anne Mathew
Briefing owner and date	Zulfa Baker 08 April 2024