**Supplementary Material**

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## Supplementary Tables

**Supplementary Table 1. Full eligibility criteria.**

| |
|---|
| Age = 18 to 50 years |
| Access to CRS and willingness to be followed for the planned duration of the study |
| Ability and willingness to provide informed consent |
| Assessment of understanding |
| Agrees not to enroll in another study of an investigational research agent until study completion |
| Good general health as shown by medical history, physical exam, and screening laboratory tests |
| Willingness to receive HIV test results |
| Willingness to discuss HIV infection risks and amenable to HIV risk reduction counseling |
| At “low risk” for HIV infection and committed to maintaining low risk behavior |
| Hemoglobin: ≥11.0 g/dL for volunteers assigned female sex at birth, ≥13.0 g/dL for volunteers assigned male sex at birth |
| White blood cell (WBC) count = 2,500 to 12,000 cells/$mm^3$ |
| WBC differential either within institutional normal range or with site clinician approval |
| Platelets = 125,000 to 550,000/$mm^3$ |
| ALT <1.25 times the institutional upper limit of normal; creatinine ≤ institutional upper limit of normal |
| Negative HIV-1 and -2 blood test |
| Negative Hepatitis B surface antigen (HBsAg) |
| Negative anti-Hepatitis C virus antibodies (anti-HCV) or negative HCV PCR |
| Negative pregnancy test performed prior to study product administration for volunteers assigned female sex at birth: |
| Volunteers assigned female sex at birth agree to use contraception to prevent pregnancy |
| Volunteers assigned female sex at birth must also agree not to seek pregnancy |

**Supplementary Table 2. Pseudoviruses used to assess bnAb-specific neutralizing activity in the TZM-bl assay.**

| | | PGT121 | | PGDM1400 | | 10-1074 | | VRC07-523LS | |
|---|---|---|---|---|---|---|---|---|---|
| **Virus** | **Study Group** | **IC50** | **IC80** | **IC50** | **IC80** | **IC50** | **IC80** | **IC50** | **IC80** |
| T250-4 | **1-3** | **0.003** | **0.008** | **0.001** | **0.003** | **0.003** | **0.007** | >10 | >10 |
| CNE55.N160K | **1-4** | >10 | >10 | >10 | >10 | >10 | >10 | **0.042** | **0.168** |
| 6540.v4.c1 | **4** | >10 | >10 | **0.003** | **0.017** | >10 | >10 | >10 | >10 |
| CH505TF.N334S. N160A.N280D.1 | **4** | **0.005** | **0.011** | >10 | >10 | **0.007** | **0.017** | >10 | >10 |

**IC50 and IC80 values are ug/ml. Positive values are bolded.**

**Supplementary Table 3. Inhibitory concentrations of non-infused bnAbs against pseudoviruses used to assess combination effects of post-infusion bnAbs.**

| | Isolate | PGT121 | 10-1074 | VRC07-523LS | PGDM1400 |
|---|---|---|---|---|---|
| IC50 | 377.v4.c09 | 0.32 | 0.53 | 0.67 | 1.27 |
| | PVO.4 | 0.11 | 0.11 | 0.13 | 1.29 |
| | DU172.17 | 0.08 | 0.11 | 0.15 | 2.69 |
| | SC422661.8 | 0.05 | 0.06 | 0.06 | 0.99 |
| | AC10.0.29 | 0.05 | 0.04 | 0.39 | 0.12 |
| | TRO.11 | 0.02 | 0.04 | 0.17 | 0.92 |
| | Ce1176_A3 | 0.02 | 0.03 | 0.38 | 0.83 |
| | T263-8 | 1.38 | 0.63 | 0.06 | 0.02 |
| | RHPA4259.7 | 0.02 | 0.04 | 0.03 | 0.42 |
| | 0330.v4.c3 | 0.07 | 0.01 | 0.06 | < 0.01 |
| | DU156.12 | 0.01 | < 0.01 | 0.03 | 0.01 |
| | 3426.v5.c17 | 0.01 | < 0.01 | 0.08 | < 0.01 |
| IC80 | 377.v4.c09 | 1.14 | 1.72 | 2.1 | 6 |
| | PVO.4 | 0.38 | 0.35 | 0.42 | 4.55 |
| | DU172.17 | 0.9 | 0.47 | 0.72 | 10.29 |
| | SC422661.8 | 0.16 | 0.2 | 0.16 | 7.72 |
| | AC10.0.29 | 0.15 | 0.12 | 1.65 | 0.54 |
| | TRO.11 | 0.06 | 0.09 | 0.45 | 3.14 |
| | Ce1176_A3 | 0.05 | 0.07 | 1.38 | 12.36 |
| | T263-8 | 9.37 | 6.21 | 0.21 | 0.09 |
| | RHPA4259.7 | 0.06 | 0.15 | 0.09 | 1.38 |
| | 0330.v4.c3 | 0.23 | 0.18 | 0.2 | 0.01 |
| | DU156.12 | 0.03 | 0.07 | 0.08 | 0.02 |
| | 3426.v5.c17 | 0.03 | < 0.01 | 0.35 | < 0.01 |

Concentrations in μg/mL.

**Supplementary Table 4. Primary, secondary and exploratory objectives and endpoints of the trial.**

| Primary Objectives | Primary Endpoints |
|---|---|
| To evaluate the safety and tolerability of PGT121 or PGDM1400 or 10-1074 when administered in sequence via IV with VRC07-523LS (2-mAb combinations), and of PGDM1400, PGT121, and VRC07-523LS administered in sequence via IV (3-mAb combination) | Local and systemic Solicited AEs, laboratory measures of safety, Unsolicited AEs, and SAEs<br><br>Early discontinuation of administration and reason(s) for discontinuation and early study termination |
| To evaluate the serum concentrations and pharmacokinetics of PGT121, PGDM1400, 10-1074 and VRC07-523LS after a single 2-mAb administration and after each PGDM1400, PGT121, VRC07-523LS 3-mAb administration | Serum concentrations of PGT121, PGDM1400, 10-1074, and VRC07-523LS at prespecified timepoints among participants who received all scheduled product administrations |
| To evaluate the individual mAb-specific serum neutralizing activity of PGT121, PGDM1400, 10-1074 and VRC07-523LS after a single 2-mAb administration and after each PGDM1400, PGT121, VRC07-523LS 3-mAb administration | Magnitude of serum neutralizing activity measured with mAb-specific Env-pseudotyped viruses in TZM-bl cells at prespecified timepoints among participants who received all scheduled product administrations |
| Secondary Objectives | Secondary Endpoints |
| To correlate serum concentrations of PGT121, PGDM1400, 10-1074, and VRC07-523LS with corresponding virus neutralization titers in serum | Serum concentrations of PGT121, PGDM1400, 10-1074, and VRC07-523LS at prespecified timepoints for all participants in all groups regardless of how many product administrations and how much product they received<br>Magnitude of serum neutralizing activity measured with Env pseudotyped viruses in TZM-bl cells at prespecified timepoints for all participants in all groups regardless of how many product administrations and how much product they received |
| To determine whether the mAbs maintain their expected combined magnitude and breadth of serum neutralizing activity after a single 2-mAb administration (Groups 1-3) and after each 3-mAb administration (Group 4) as predicted by the known magnitude and breadth of neutralization of the corresponding mAb combinations as non-infused clinical products | Magnitude of neutralizing activity against a panel of Env pseudotyped reference viruses in TZM-bl cells at selected timepoints for all participants in all groups regardless of how many product administrations and how much product they received |
| To determine whether ADA are present and whether there is a correlation among PGT121, PGDM1400, 10-1074, and VRC07-523LS concentrations and ADA titers in serum samples | Serum PGT121, PGDM1400, 10-1074, and VRC07-523LS concentrations and ADA titers in each group measured at prespecified timepoints for all participants in all groups regardless of how many product administrations and how much product they received |
| Exploratory Objectives | |
| To determine whether any confirmed positive ADA samples have functional activity that impacts the neutralizing activity of PGT121, PGDM1400, 10-1074, and VRC07-523LS | |
| To further evaluate non-neutralizing antiviral activities, additional assays (eg, antibody dependent cell mediated cytotoxicity [ADCC], antibody dependent cellular phagocytosis [ADCP], virion capture) may be performed for activities that PGT121, PGDM1400, 10-1074, and VRC07-523LS are shown to exhibit in vitro | |
| To develop predictive population PK models and to assess PK, drug-drug interaction, and neutralization drug-drug interaction among PGT121, PGDM1400, 10-1074, and VRC07-523LS | |

| |
|---|
| To conduct analyses related to furthering the understanding of HIV, monoclonal antibodies, immunology, vaccines, and clinical trial conduct |

**Supplementary Table 5. Overall protocol status of enrolled participants.**

| | T1 (N=6) n (%) | T2 (N=6) n (%) | T3 (N=6) n (%) | T4 (N=9) n (%) | Total (N=27) n (%) |
|---|---|---|---|---|---|
| Status | | | | | |
| In SPA Phase | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| In FU, Completed SPA Phase | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| In FU, Discontinued SPA | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| Completed FU and SPA Phase | 6 (100.0%) | 3 (50.0%) | 2 (30.0%) | 6 (66.7%) | 17 (63.0%) |
| Completed FU, Discontinued SPA | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| Term. Early, Completed SPA Phase | 0 (0.0%) | 3 (50.0%) | 3 (50.0%) | 0 (0.0%) | 6 (22.2%) |
| Term. Early, Discontinued SPA | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (11.1%) | 1 (3.7%) |
| Unknown | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| Other | 0 (0.0%) | 0 (0.0%) | 1 (16.7%) | 0 (0.0%) | 1 (3.7%) |
| **Total** | **6 (100.0%)** | **6 (100.0%)** | **6 (100.0%)** | **9 (100.0%)** | **27 (100.0%)** |
| Reason for Discontinuation of SPA | | | | | |
| Other | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 3 (33.3%) | 3 (11.1%) |
| Reason for Early Termination | | | | | |
| Death | 0 (0.0%) | 1 (16.7%) | 0 (0.0%) | 0 (0.0%) | 1 (3.7%) |
| Participant unable to adhere to visit schedule | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 1 (11.1%) | 1 (3.7%) |
| Unable to contact participant | 0 (0.0%) | 1 (16.7%) | 3 (50.0%) | 0 (0.0%) | 4 (14.8%) |
| Participant incarcerated | 0 (0.0%) | 1 (16.7%) | 0 (0.0%) | 0 (0.0%) | 1 (3.7%) |
| Other | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| **Total** | **0 (0.0%)** | **3 (50.0%)** | **3 (50.0%)** | **1 (11.1%)** | **7 (25.9%)** |

**Supplementary Table 6. Observed serum concentrations for each bnAb by treatment arm and visit timepoint.**

| Antibody | Arm | Day | N | Median (µg/mL) | Min (µg/mL) | Max (µg/mL) |
|---|---|---|---|---|---|---|
| PGT121 | T1 | Day 3 | 6 | 196.48 | 145.27 | 307.19 |
| | | Day 6 | 6 | 129.26 | 102.94 | 139.80 |
| | | Day 14 | 6 | 80.07 | 68.39 | 88.27 |
| | | Day 28 | 6 | 44.41 | 39.64 | 62.21 |
| | | Day 56 | 6 | 22.03 | 14.01 | 34.57 |
| | | Day 112 | 6 | 3.98 | 2.94 | 14.17 |
| | | Day 168 | 4 | 1.65 | 0.62 | 5.59 |
| | | Day 224 | 1 | 0.26 | 0.26 | 0.26 |
| | | Day 336 | 4 | <0.01 | <0.01 | 0.38 |
| | T4 | Day 3 | 9 | 181.33 | 147.86 | 314.16 |
| | | Day 6 | 9 | 130.93 | 105.24 | 198.14 |
| | | Day 14 | 9 | 90.42 | 63.67 | 177.54 |
| | | Day 28 | 9 | 56.70 | 34.75 | 82.61 |
| | | Day 56 | 9 | 29.27 | 14.71 | 38.12 |
| | | Day 84 | 9 | 14.95 | 6.82 | 22.27 |
| | | Day 112/2nd infusion | 6 | 5.77 | 5.17 | 13.38 |
| | | Day 140 | 3 | 6.03 | 1.98 | 49.12 |
| | | Day 168 | 2 | 2.67 | 1.28 | 4.05 |
| | | Day 224 | 5 | 4.11 | 0.47 | 13.93 |
| | | Day 280 | 7 | 1.42 | 0.17 | 5.40 |
| | | Day 336 | 8 | 0.66 | 0.08 | 3.28 |
| | | Day 392 | 7 | 0.13 | <0.01 | 1.11 |
| | | Day 448 | 7 | <0.01 | <0.01 | 0.49 |
| PGDM1400 | T2 | Day 3 | 6 | 251.52 | 229.15 | 285.10 |
| | | Day 6 | 6 | 182.21 | 140.51 | 221.09 |
| | | Day 14 | 6 | 139.75 | 96.15 | 152.68 |
| | | Day 28 | 6 | 70.90 | 54.45 | 77.44 |
| | | Day 56 | 6 | 27.86 | 25.67 | 33.07 |
| | | Day 112 | 5 | 5.49 | 4.13 | 6.40 |
| | | Day 168 | 4 | 1.06 | 0.89 | 1.10 |
| | | Day 224 | 1 | 0.24 | 0.24 | 0.24 |
| | | Day 280 | 1 | 0.07 | 0.07 | 0.07 |
| | | Day 336 | 2 | <0.01 | <0.01 | <0.01 |
| | T4 | Day 3 | 9 | 231.31 | 184.14 | 409.83 |
| | | Day 6 | 9 | 173.79 | 139.74 | 225.87 |
| | | Day 14 | 9 | 126.54 | 88.81 | 233.94 |
| | | Day 28 | 9 | 71.58 | 47.84 | 104.45 |
| | | Day 56 | 9 | 33.68 | 13.64 | 40.92 |
| | | Day 84 | 9 | 12.24 | 5.60 | 22.07 |
| | | Day 112/2nd infusion | 6 | 4.97 | 3.39 | 12.50 |
| | | Day 140 | 3 | 3.47 | 1.17 | 46.05 |
| | | Day 168 | 2 | 1.49 | 0.75 | 2.23 |
| | | Day 224 | 5 | 2.19 | 0.20 | 11.98 |
| | | Day 280 | 7 | 0.48 | 0.05 | 3.70 |
| | | Day 336 | 8 | 0.24 | <0.01 | 1.59 |
| | | Day 392 | 7 | 0.02 | <0.01 | 0.40 |
| | | Day 448 | 7 | <0.01 | <0.01 | 0.13 |
| 10-1074 | T3 | Day 3 | 6 | 521.28 | 69.27 | 900.85 |
| | | Day 6 | 6 | 413.99 | 75.29 | 682.78 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | Day 14 | 6 | 287.54 | 78.17 | 469.94 |
| | | Day 28 | 5 | 237.78 | 114.61 | 259.30 |
| | | Day 56 | 5 | 98.06 | 26.67 | 130.22 |
| | | Day 112 | 5 | 23.75 | 4.80 | 46.41 |
| | | Day 168 | 4 | 8.39 | 0.75 | 12.77 |
| | | Day 280 | 4 | 0.39 | <0.01 | 1.09 |
| | | Day 336 | 2 | 0.11 | <0.01 | 0.23 |
| **VRC07-523LS** | T1 | Day 3 | 6 | 265.93 | 233.50 | 434.45 |
| | | Day 6 | 6 | 171.02 | 137.06 | 233.03 |
| | | Day 14 | 6 | 134.40 | 94.21 | 143.47 |
| | | Day 28 | 6 | 94.57 | 68.09 | 106.09 |
| | | Day 56 | 6 | 60.50 | 53.73 | 72.92 |
| | | Day 112 | 6 | 24.92 | 16.28 | 29.61 |
| | | Day 168 | 4 | 14.41 | 10.51 | 18.90 |
| | | Day 224 | 1 | 8.45 | 8.45 | 8.45 |
| | | Day 336 | 4 | 1.22 | 0.61 | 2.83 |
| | T2 | Day 3 | 6 | 239.32 | 204.18 | 278.39 |
| | | Day 6 | 6 | 176.51 | 144.43 | 205.83 |
| | | Day 14 | 6 | 139.17 | 98.25 | 160.87 |
| | | Day 28 | 6 | 96.16 | 80.78 | 117.03 |
| | | Day 56 | 6 | 56.91 | 25.22 | 59.54 |
| | | Day 112 | 5 | 31.64 | 10.36 | 36.35 |
| | | Day 168 | 4 | 12.56 | 9.93 | 14.26 |
| | | Day 224 | 1 | 11.23 | 11.23 | 11.23 |
| | | Day 280 | 1 | 3.87 | 3.87 | 3.87 |
| | | Day 336 | 2 | 1.30 | 1.00 | 1.61 |
| | T3 | Day 3 | 5 | 182.65 | 139.61 | 306.89 |
| | | Day 6 | 5 | 176.00 | 163.93 | 189.27 |
| | | Day 14 | 5 | 119.66 | 83.64 | 158.63 |
| | | Day 28 | 5 | 87.91 | 59.76 | 101.73 |
| | | Day 56 | 4 | 59.32 | 34.68 | 67.49 |
| | | Day 112 | 4 | 29.36 | 11.52 | 31.12 |
| | | Day 168 | 4 | 11.56 | 5.74 | 13.15 |
| | | Day 280 | 3 | 3.16 | 0.45 | 3.82 |
| | | Day 336 | 3 | 1.47 | 0.21 | 3.19 |
| | T4 | Day 3 | 9 | 230.05 | 178.13 | 421.63 |
| | | Day 6 | 9 | 169.53 | 142.89 | 283.07 |
| | | Day 14 | 9 | 133.01 | 114.41 | 254.92 |
| | | Day 28 | 9 | 96.51 | 65.06 | 123.47 |
| | | Day 56 | 9 | 60.23 | 36.79 | 80.51 |
| | | Day 84 | 9 | 41.63 | 24.23 | 54.12 |
| | | Day 112/2nd infusion | 6 | 26.05 | 13.38 | 48.39 |
| | | Day 140 | 3 | 13.93 | 12.22 | 76.01 |
| | | Day 168 | 2 | 9.97 | 8.93 | 11.01 |
| | | Day 224 | 5 | 22.65 | 5.43 | 44.71 |
| | | Day 280 | 7 | 14.83 | 2.78 | 19.52 |
| | | Day 336 | 8 | 7.48 | 1.49 | 14.98 |
| | | Day 392 | 7 | 2.73 | 0.88 | 6.61 |
| | | Day 448 | 7 | 1.08 | 0.48 | 3.07 |

Concentrations in µg/mL. Treatment arms: (T1) single dose of PGT121T1 and VRC07-523LS; (T2) single dose of PGDM1400 and VRC07-523LS; (T3) single dose of 10-1074 and VRC07-523LS; and (T4) two doses (at baseline and 4 months) of PGT121, PGDM1400, and VRC07-523LS.

**Supplementary Table 7. Estimates of key pharmacokinetics parameters for each bnAb.**

| | | Median distribution half-life, days (range) | Median elimination half-life, days (range) | AUC[1], day/mL*kg (range) |
|---|---|---|---|---|
| **PGT121** | T1 | 4·0 (3·1, 6·7) | 24·2 (21·9, 44·2) | 235·6 (176·1, 275·6) |
| | T4 | 7·0 (3·1, 8·6) | 32·4 (19·9,44·9) | 232·4 (176·1, 277·2) |
| | Overall | 6·0 (3·1, 8·6) | 32·2 (19·9, 44·9) | 233·2 (176·1, 277·2) |
| **PGDM1400** | T2 | 8·1 (7·7, 8·9) | 24·4 (21·5, 25·9) | 267·0 (244·5, 324·9) |
| | T4 | 9·8 (6·5, 12·5) | 27·5 (20·7, 34·2) | 311·1 (235·8, 371·2) |
| | Overall | 8·7 (6·6, 12·5) | 25·4 (20·7, 34·2) | 306·1 (235·8, 371·2) |
| **10-1074[2]** | T3 | 0·16 (0·14, 0·19) | 27·5 (18·1, 33·3) | 1761·7 (28·4, 2009·3) |
| **VRC07-523LS** | T1 | 6·6 (4·0, 7·7) | 53·2 (43·3, 65·1) | 521·3 (389·6, 609·6) |
| | T2 | 5·6 (4·5, 9·6) | 50·6 (46·2, 59·2) | 441·2 (404·0, 536·8) |
| | T3 | 7·4 (4·8, 8·1) | 51·8 (41·0, 61·2) | 492·0 (360·7, 556·3) |
| | T4 | 7·0 (4·9, 14·5) | 54·9 (47·0, 69·7) | 514·1 (389·6, 613·3) |
| | Overall | 6·4 (4·0, 14·5) | 52·9 (41·0, 69·7) | 508·3 (360·7, 613·3) |

[1] Dose- and weight-adjusted

[2] Dual combination in T3

The detailed PK parameter estimates are in Supplementary Table 4.

**Supplementary Table 8. Summary of fold differences and CCC estimates based on PGDM1400 + PGT121 + VRC07-523LS ID80 samples.**

| | | Fold Difference (Predicted vs. Observed) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Isolate** | **Model** | **Min** | **Max** | **Median** | **Mean** | **25%-tile** | **75%-tile** | **CCC (95% CI)** | **N (ppt*visit)** |
| 0330.v4.c3 | Maximum | 0.18 | 1.30 | 0.74 | 0.71 | 0.49 | 0.90 | 0.96 (0.93,0.98) | 41 |
| | Additivity | 0.19 | 1.65 | 0.89 | 0.84 | 0.52 | 1.17 | 0.96 (0.94,0.98) | 41 |
| | Bliss Hill | 0.23 | 2.51 | 1.15 | 1.17 | 0.63 | 1.74 | 0.94 (0.92,0.96) | 41 |
| 3426.v5.c17 | Maximum | 0.12 | 1.53 | 0.52 | 0.65 | 0.28 | 1.04 | 0.93 (0.9,0.96) | 41 |
| | Additivity | 0.13 | 1.99 | 0.57 | 0.77 | 0.30 | 1.22 | 0.93 (0.9,0.95) | 41 |
| | Bliss Hill | 0.16 | 3.05 | 0.73 | 1.08 | 0.37 | 1.80 | 0.92 (0.9,0.93) | 41 |
| 377.v4.c09 | Maximum | 0.21 | 1.16 | 0.36 | 0.42 | 0.28 | 0.50 | 0.81 (0.72,0.88) | 41 |
| | Additivity | 0.38 | 1.55 | 0.72 | 0.75 | 0.57 | 0.86 | 0.96 (0.92,0.98) | 41 |
| | Bliss Hill | 0.67 | 2.37 | 1.27 | 1.27 | 0.97 | 1.47 | 0.95 (0.92,0.97) | 41 |
| AC10.0.29 | Maximum | 0.21 | 0.71 | 0.39 | 0.42 | 0.33 | 0.47 | 0.89 (0.83,0.93) | 41 |
| | Additivity | 0.31 | 1.35 | 0.61 | 0.65 | 0.50 | 0.78 | 0.96 (0.94,0.98) | 41 |
| | Bliss Hill | 0.50 | 2.30 | 1.02 | 1.10 | 0.85 | 1.31 | 0.96 (0.95,0.97) | 41 |
| Ce1176_A3 | Maximum | 0.22 | 0.86 | 0.60 | 0.59 | 0.49 | 0.72 | 0.93 (0.89,0.96) | 41 |
| | Additivity | 0.23 | 1.00 | 0.65 | 0.65 | 0.54 | 0.80 | 0.95 (0.93,0.97) | 41 |
| | Bliss Hill | 0.28 | 1.40 | 0.81 | 0.81 | 0.64 | 0.98 | 0.98 (0.96,0.98) | 41 |
| DU156.12 | Maximum | 0.09 | 0.67 | 0.32 | 0.32 | 0.26 | 0.40 | 0.8 (0.71,0.86) | 41 |
| | Additivity | 0.17 | 1.43 | 0.65 | 0.67 | 0.49 | 0.87 | 0.93 (0.89,0.96) | 41 |
| | Bliss Hill | 0.31 | 2.65 | 1.19 | 1.23 | 0.86 | 1.58 | 0.94 (0.92,0.96) | 41 |
| DU172.17 | Maximum | 0.13 | 1.51 | 0.38 | 0.50 | 0.28 | 0.59 | 0.82 (0.73,0.88) | 41 |
| | Additivity | 0.21 | 1.70 | 0.56 | 0.66 | 0.44 | 0.79 | 0.91 (0.86,0.94) | 41 |
| | Bliss Hill | 0.36 | 2.26 | 0.92 | 1.00 | 0.68 | 1.26 | 0.95 (0.92,0.96) | 41 |
| PVO.4 | Maximum | 0.23 | 1.09 | 0.45 | 0.52 | 0.35 | 0.68 | 0.85 (0.78,0.9) | 41 |
| | Additivity | 0.43 | 1.29 | 0.72 | 0.78 | 0.58 | 0.96 | 0.96 (0.94,0.98) | 41 |
| | Bliss Hill | 0.73 | 2.14 | 1.20 | 1.24 | 0.97 | 1.51 | 0.96 (0.94,0.98) | 41 |
| RHPA4259.7 | Maximum | 0.15 | 0.98 | 0.34 | 0.39 | 0.27 | 0.46 | 0.75 (0.64,0.83) | 41 |
| | Additivity | 0.29 | 1.35 | 0.62 | 0.63 | 0.50 | 0.73 | 0.92 (0.88,0.95) | 41 |
| | Bliss Hill | 0.48 | 2.07 | 1.02 | 1.01 | 0.84 | 1.11 | 0.98 (0.96,0.99) | 41 |
| SC422661.8 | Maximum | 0.26 | 1.21 | 0.52 | 0.55 | 0.38 | 0.65 | 0.87 (0.8,0.91) | 41 |
| | Additivity | 0.45 | 1.31 | 0.74 | 0.78 | 0.61 | 0.88 | 0.96 (0.94,0.98) | 41 |
| | Bliss Hill | 0.73 | 1.92 | 1.18 | 1.19 | 0.98 | 1.35 | 0.97 (0.95,0.98) | 41 |
| T263-8 | Maximum | 0.24 | 1.16 | 0.41 | 0.49 | 0.33 | 0.68 | 0.89 (0.83,0.93) | 41 |
| | Additivity | 0.33 | 1.66 | 0.70 | 0.75 | 0.51 | 1.00 | 0.96 (0.94,0.98) | 41 |
| | Bliss Hill | 0.51 | 2.57 | 1.13 | 1.17 | 0.79 | 1.50 | 0.96 (0.95,0.98) | 41 |
| TRO.11 | Maximum | 0.30 | 0.69 | 0.48 | 0.49 | 0.39 | 0.58 | 0.91 (0.86,0.94) | 41 |
| | Additivity | 0.36 | 1.30 | 0.66 | 0.68 | 0.49 | 0.83 | 0.96 (0.93,0.97) | 41 |
| | Bliss Hill | 0.52 | 2.11 | 0.98 | 1.03 | 0.74 | 1.31 | 0.97 (0.96,0.98) | 41 |

CCC = concordance correlation coefficient

**Supplementary Table 9. Summary of PGT121 individual level PK parameter estimates, half-live, AUCadj, and Cmaxadj by treatment arm.**

| Parameter | Treatment Arm | N | Median | Min | Max | Mean | SD |
|---|---|---|---|---|---|---|---|
| CL | Overall | 15 | 0.31 | 0.19 | 0.48 | 0.32 | 0.08 |
| | T1 | 6 | 0.34 | 0.20 | 0.48 | 0.34 | 0.10 |
| | T4 | 9 | 0.28 | 0.19 | 0.38 | 0.30 | 0.06 |
| Vc | Overall | 15 | 5.90 | 4.63 | 9.05 | 6.43 | 1.43 |
| | T1 | 6 | 5.61 | 4.85 | 9.05 | 6.17 | 1.55 |
| | T4 | 9 | 6.74 | 4.63 | 8.70 | 6.60 | 1.41 |
| Q | Overall | 15 | 0.27 | 0.12 | 0.46 | 0.29 | 0.11 |
| | T1 | 6 | 0.35 | 0.21 | 0.46 | 0.35 | 0.10 |
| | T4 | 9 | 0.24 | 0.12 | 0.43 | 0.25 | 0.11 |
| Vp | Overall | 15 | 4.23 | 2.91 | 6.32 | 4.52 | 1.02 |
| | T1 | 6 | 4.80 | 3.79 | 5.36 | 4.66 | 0.60 |
| | T4 | 9 | 3.88 | 2.91 | 6.32 | 4.42 | 1.25 |
| Vz | Overall | 15 | 13.18 | 10.33 | 20.50 | 13.87 | 2.99 |
| | T1 | 6 | 13.07 | 10.33 | 16.57 | 13.35 | 2.42 |
| | T4 | 9 | 13.18 | 10.48 | 20.50 | 14.23 | 3.41 |
| k | Overall | 15 | 0.02 | 0.02 | 0.03 | 0.02 | 0.01 |
| | T1 | 6 | 0.03 | 0.02 | 0.03 | 0.03 | 0.01 |
| | T4 | 9 | 0.02 | 0.02 | 0.03 | 0.02 | 0.01 |
| $C_{maxADJ}$ | Overall | 15 | 13.13 | 9.21 | 21.72 | 14.00 | 3.91 |
| | T1 | 6 | 13.30 | 11.67 | 21.72 | 14.78 | 3.62 |
| | T4 | 9 | 11.57 | 9.21 | 21.08 | 13.48 | 4.21 |
| $AUC_{ADJ}$ | Overall | 15 | 233.17 | 176.10 | 277.20 | 234.19 | 36.53 |
| | T1 | 6 | 235.62 | 176.10 | 275.57 | 231.49 | 41.54 |
| | T4 | 9 | 232.36 | 176.10 | 277.20 | 236.00 | 35.32 |
| Elimination half-life | Overall | 15 | 32.24 | 19.87 | 44.99 | 31.79 | 8.55 |
| | T1 | 6 | 24.15 | 21.87 | 44.20 | 28.82 | 8.80 |
| | T4 | 9 | 32.43 | 19.87 | 44.99 | 33.77 | 8.27 |
| Distribution half-life | Overall | 15 | 5.96 | 3.08 | 8.60 | 5.61 | 1.92 |
| | T1 | 6 | 3.98 | 3.08 | 6.70 | 4.54 | 1.46 |
| | T4 | 9 | 6.96 | 3.12 | 8.60 | 6.32 | 1.93 |

ADJ: dose- and weight-adjusted.

**Supplementary Table 10. Summary of PGDM1400 individual level PK parameter estimates, half-lives, AUCADJ and CmaxADJ by treatment arm.**

| Parameter | Treatment Arm | N | Median | Min | Max | Mean | SD |
|---|---|---|---|---|---|---|---|
| CL | Overall | 15 | 0.23 | 0.17 | 0.31 | 0.23 | 0.04 |
| | T2 | 6 | 0.21 | 0.17 | 0.24 | 0.21 | 0.03 |
| | T4 | 9 | 0.25 | 0.17 | 0.31 | 0.25 | 0.04 |
| Vc | Overall | 15 | 4.76 | 3.17 | 7.87 | 5.13 | 1.28 |
| | T2 | 6 | 4.54 | 3.39 | 5.37 | 4.50 | 0.70 |
| | T4 | 9 | 6.12 | 3.17 | 7.87 | 5.55 | 1.44 |
| Q | Overall | 15 | 0.06 | 0.06 | 0.06 | 0.06 | 0.00 |
| | T2 | 6 | 0.06 | 0.06 | 0.06 | 0.06 | 0.00 |
| | T4 | 9 | 0.06 | 0.06 | 0.06 | 0.06 | 0.00 |
| Vp | Overall | 15 | 1.42 | 1.06 | 1.98 | 1.40 | 0.24 |
| | T2 | 6 | 1.20 | 1.06 | 1.45 | 1.23 | 0.14 |
| | T4 | 9 | 1.47 | 1.15 | 1.98 | 1.52 | 0.23 |
| Vz | Overall | 15 | 8.48 | 6.50 | 12.91 | 8.68 | 1.85 |
| | T2 | 6 | 6.98 | 6.50 | 8.88 | 7.33 | 0.88 |
| | T4 | 9 | 9.10 | 7.41 | 12.91 | 9.58 | 1.80 |
| k | Overall | 15 | 0.03 | 0.02 | 0.03 | 0.03 | 0.00 |
| | T2 | 6 | 0.03 | 0.03 | 0.03 | 0.03 | 0.00 |
| | T4 | 9 | 0.03 | 0.02 | 0.03 | 0.03 | 0.00 |
| $C_{maxADJ}$ | Overall | 15 | 11.82 | 9.21 | 21.08 | 13.18 | 3.29 |
| | T2 | 6 | 12.58 | 11.46 | 14.26 | 12.75 | 1.24 |
| | T4 | 9 | 11.57 | 9.21 | 21.08 | 13.48 | 4.21 |
| $AUC_{ADJ}$ | Overall | 15 | 306.11 | 235.81 | 371.18 | 299.56 | 45.46 |
| | T2 | 6 | 267.03 | 244.54 | 324.89 | 274.89 | 31.47 |
| | T4 | 9 | 311.13 | 235.81 | 371.18 | 316.01 | 47.29 |
| Elimination half-life | Overall | 15 | 25.36 | 20.67 | 34.17 | 26.02 | 3.92 |
| | T2 | 6 | 24.38 | 21.50 | 25.88 | 24.17 | 1.57 |
| | T4 | 9 | 27.50 | 20.67 | 34.17 | 27.24 | 4.59 |
| Distribution half-life | Overall | 15 | 8.68 | 6.57 | 12.53 | 8.98 | 1.55 |
| | T2 | 6 | 8.09 | 7.66 | 8.93 | 8.21 | 0.50 |
| | T4 | 9 | 9.84 | 6.57 | 12.53 | 9.50 | 1.81 |

ADJ: dose- and weight-adjusted.

**Supplementary Table 11. Summary of 10-1074 individual level PK parameter estimates, half-lives, AUCADJ and CmaxADJ by treatment arm.**

| Parameter | Treatment Arm | N | Median | Min | Max | Mean | SD |
|---|---|---|---|---|---|---|---|
| CL | T3 | 6 | 0.06 | 0.01 | 0.09 | 0.05 | 0.03 |
| Vc | T3 | 6 | 0.05 | 0.05 | 0.05 | 0.05 | 0.00 |
| Q | T3 | 6 | 0.14 | 0.14 | 0.14 | 0.14 | 0.00 |
| Vp | T3 | 6 | 1.39 | 0.20 | 1.85 | 1.25 | 0.60 |
| Vz | T3 | 6 | 2.18 | 0.26 | 2.77 | 1.84 | 0.93 |
| k | T3 | 6 | 0.03 | 0.02 | 0.04 | 0.03 | 0.01 |
| $C_{max}$ | T3 | 6 | 26.06 | 3.91 | 45.04 | 27.35 | 15.23 |
| $AUC_{ADJ}$ | T3 | 6 | 1761.72 | 28.41 | 2009.29 | 1478.48 | 755.67 |
| Elimination half-life | T3 | 6 | 27.51 | 18.10 | 33.34 | 27.04 | 5.78 |
| Distribution half-life | T3 | 6 | 0.16 | 0.14 | 0.19 | 0.17 | 0.02 |

ADJ: dose- and weight-adjusted.

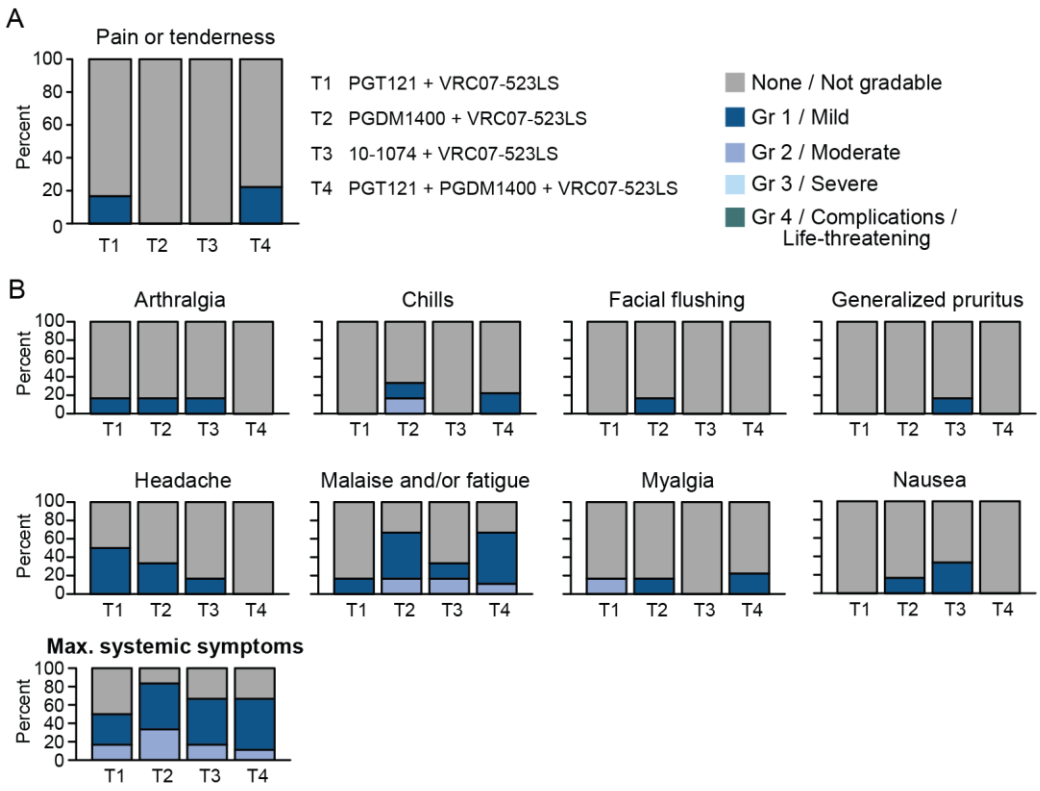
**Supplementary Table 12. Summary of 10-1074 individual level PK parameter estimates, half-lives, AUCADJ and CmaxADJ by treatment arm.**

| Parameter | Treatment | N | Median | Min | Max | Mean | SD |
|---|---|---|---|---|---|---|---|
| CL | Overall | 26 | 0.14 | 0.10 | 0.21 | 0.14 | 0.03 |
| | T1 | 6 | 0.14 | 0.11 | 0.17 | 0.14 | 0.02 |
| | T2 | 6 | 0.13 | 0.10 | 0.21 | 0.13 | 0.04 |
| | T3 | 5 | 0.15 | 0.10 | 0.21 | 0.15 | 0.04 |
| | T4 | 9 | 0.15 | 0.12 | 0.16 | 0.14 | 0.02 |
| Vc | Overall | 26 | 4.92 | 3.52 | 7.29 | 5.14 | 1.08 |
| | T1 | 6 | 4.52 | 4.09 | 6.45 | 4.92 | 0.92 |
| | T2 | 6 | 4.42 | 3.52 | 5.63 | 4.55 | 0.80 |
| | T3 | 5 | 6.01 | 4.16 | 7.29 | 5.77 | 1.18 |
| | T4 | 9 | 5.14 | 3.62 | 6.73 | 5.34 | 1.20 |
| Q | Overall | 26 | 0.19 | 0.09 | 0.33 | 0.21 | 0.06 |
| | T1 | 6 | 0.22 | 0.16 | 0.33 | 0.22 | 0.06 |
| | T2 | 6 | 0.21 | 0.12 | 0.30 | 0.21 | 0.06 |
| | T3 | 5 | 0.19 | 0.15 | 0.32 | 0.22 | 0.07 |
| | T4 | 9 | 0.18 | 0.09 | 0.30 | 0.19 | 0.07 |
| Vp | Overall | 26 | 4.02 | 3.43 | 4.68 | 4.02 | 0.29 |
| | T1 | 6 | 4.12 | 3.73 | 4.43 | 4.11 | 0.25 |
| | T2 | 6 | 3.86 | 3.43 | 4.10 | 3.79 | 0.30 |
| | T3 | 5 | 4.03 | 3.60 | 4.39 | 4.02 | 0.28 |
| | T4 | 9 | 4.14 | 3.81 | 4.68 | 4.10 | 0.28 |
| Vz | Overall | 26 | 10.35 | 8.41 | 16.12 | 10.77 | 1.74 |
| | T1 | 6 | 10.24 | 9.43 | 11.98 | 10.43 | 0.98 |
| | T2 | 6 | 9.16 | 8.41 | 13.72 | 9.88 | 2.04 |
| | T3 | 5 | 11.36 | 9.12 | 12.60 | 11.27 | 1.39 |
| | T4 | 9 | 10.55 | 9.31 | 16.12 | 11.32 | 2.04 |
| k | Overall | 26 | 0.01 | 0.01 | 0.02 | 0.01 | 0.00 |
| | T1 | 6 | 0.01 | 0.01 | 0.02 | 0.01 | 0.00 |
| | T2 | 6 | 0.01 | 0.01 | 0.02 | 0.01 | 0.00 |
| | T3 | 5 | 0.01 | 0.01 | 0.02 | 0.01 | 0.00 |
| | T4 | 9 | 0.01 | 0.01 | 0.01 | 0.01 | 0.00 |
| CmaxADJ | Overall | 26 | 13.40 | 9.21 | 45.04 | 17.18 | 9.16 |
| | T1 | 6 | 13.30 | 11.67 | 21.72 | 14.78 | 3.62 |
| | T2 | 6 | 12.58 | 11.46 | 14.26 | 12.75 | 1.24 |
| | T3 | 5 | 29.92 | 20.76 | 45.04 | 32.03 | 11.20 |
| | T4 | 9 | 11.57 | 9.21 | 21.08 | 13.48 | 4.21 |
| AUCADJ | Overall | 26 | 508.28 | 360.74 | 613.25 | 497.87 | 77.03 |
| | T1 | 6 | 521.26 | 389.60 | 609.64 | 512.13 | 91.90 |
| | T2 | 6 | 441.18 | 404.02 | 536.78 | 454.17 | 52.00 |
| | T3 | 5 | 492.04 | 360.74 | 556.26 | 489.59 | 79.75 |
| | T4 | 9 | 514.05 | 389.60 | 613.25 | 522.11 | 78.13 |
| Elimination half-life | Overall | 26 | 52.87 | 40.95 | 69.74 | 53.52 | 6.51 |
| | T1 | 6 | 53.20 | 43.28 | 65.05 | 52.86 | 7.17 |
| | T2 | 6 | 50.63 | 46.15 | 59.20 | 51.80 | 4.69 |
| | T3 | 5 | 51.80 | 40.95 | 61.21 | 52.87 | 8.31 |
| | T4 | 9 | 54.91 | 47.01 | 69.74 | 55.46 | 6.70 |
| Distribution half-life | Overall | 26 | 6.37 | 4.03 | 14.54 | 6.80 | 2.06 |
| | T1 | 6 | 6.57 | 4.03 | 7.72 | 6.28 | 1.35 |
| | T2 | 6 | 5.61 | 4.53 | 9.58 | 6.11 | 1.76 |
| | T3 | 5 | 7.35 | 4.76 | 8.11 | 6.84 | 1.31 |
| | T4 | 9 | 7.02 | 4.87 | 14.54 | 7.59 | 2.85 |

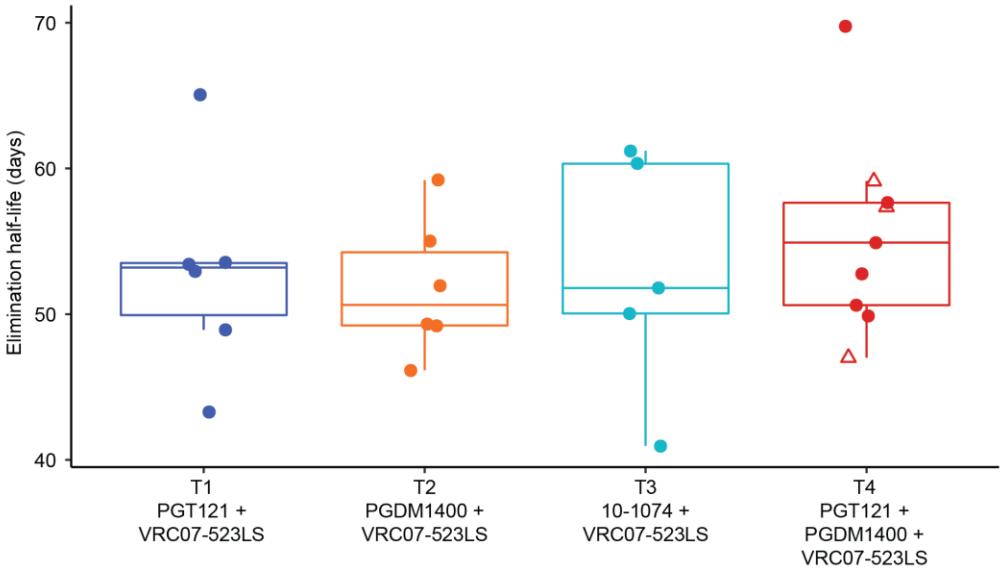
ADJ: dose- and weight-adjusted.

## Supplementary Figures

**Supplementary Figure 1. Frequency and maximum severity of local and systemic solicited AEs.** A. Local solicited AEs. B. Systemic solicited AEs. There were no instances of increased body temperature, non-exertional dyspnea, non-exertional tachycardia, unexplained diaphoresis, or urticaria in any treatment arm.

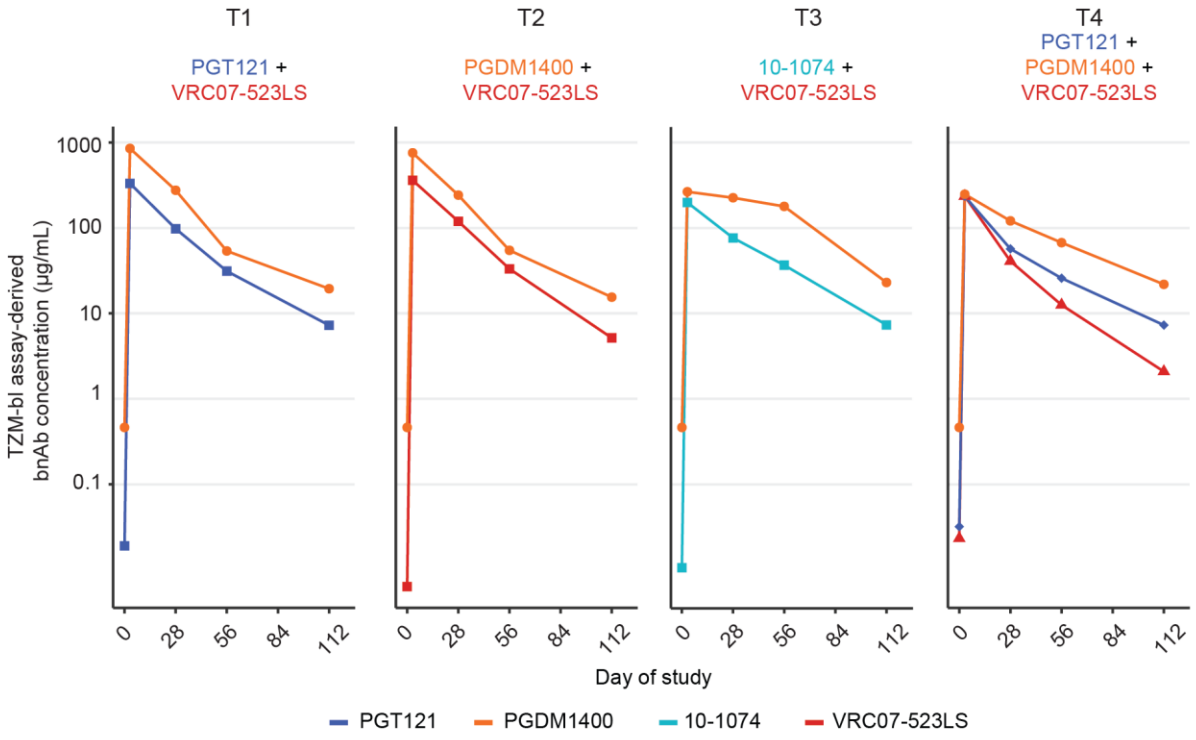


**Supplementary Figure 2. No Differences in Half-life Estimated Between any Dual- Compared to Triple- bnAb Combinations (VRC07-523LS).** Top) The estimated elimination half-lives (y axis; days) of VRC07-523LS in each treatment arm (x axis) are shown. Bottom) Table comparing the median VRC07-523LS half-lives between each dual and triple combination.

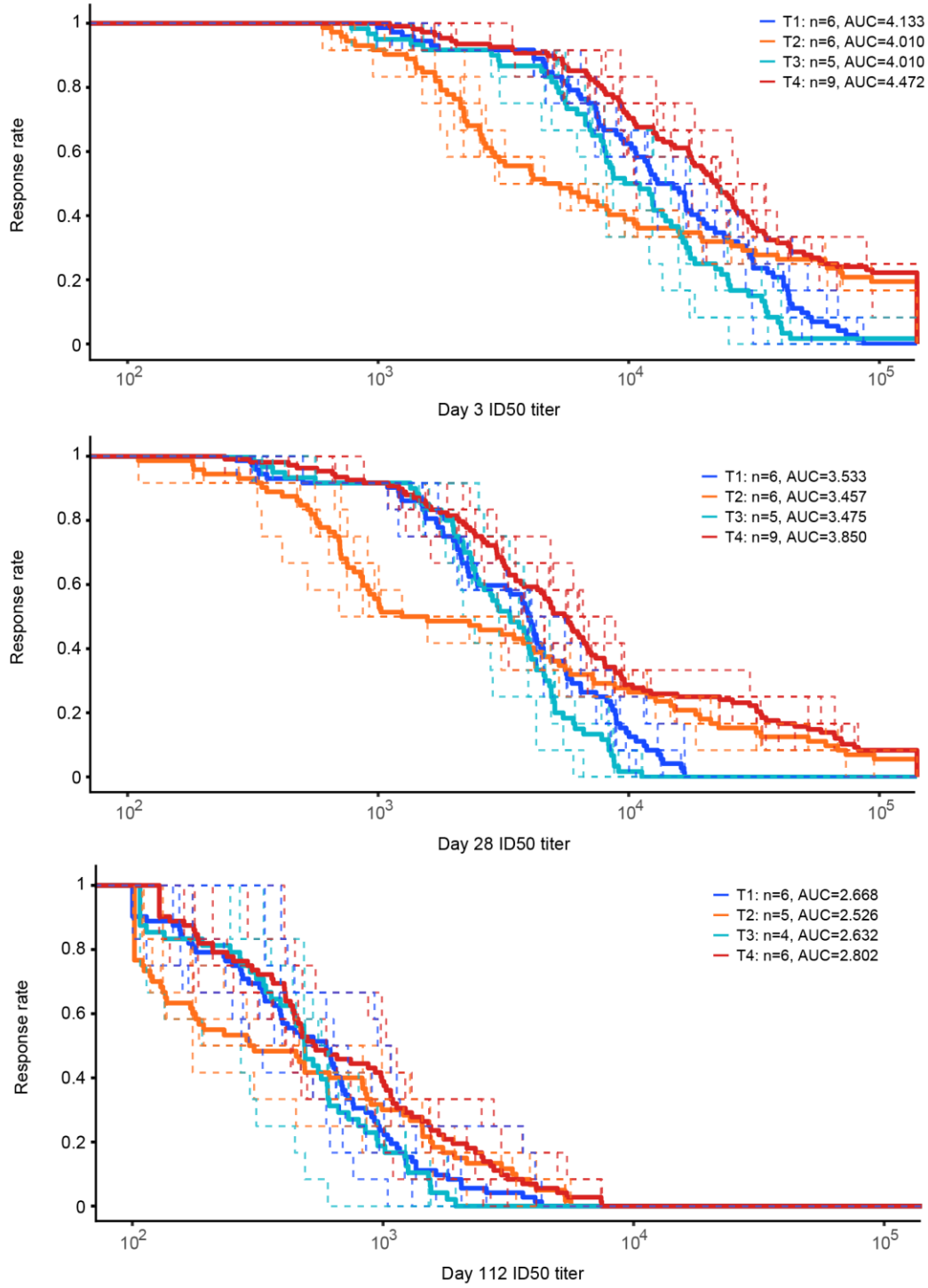



| | VRC07-523LS elimination half-life (days) | | |
|---|---|---|---|
| | **Dual** | **Triple** | **P value** |
| T1 vs T4 | 53.2 | 54.9 | 0.45 |
| T2 vs T4 | 50.6 | 54.9 | 0.25 |
| T3 vs T4 | 51.8 | 54.9 | 0.50 |

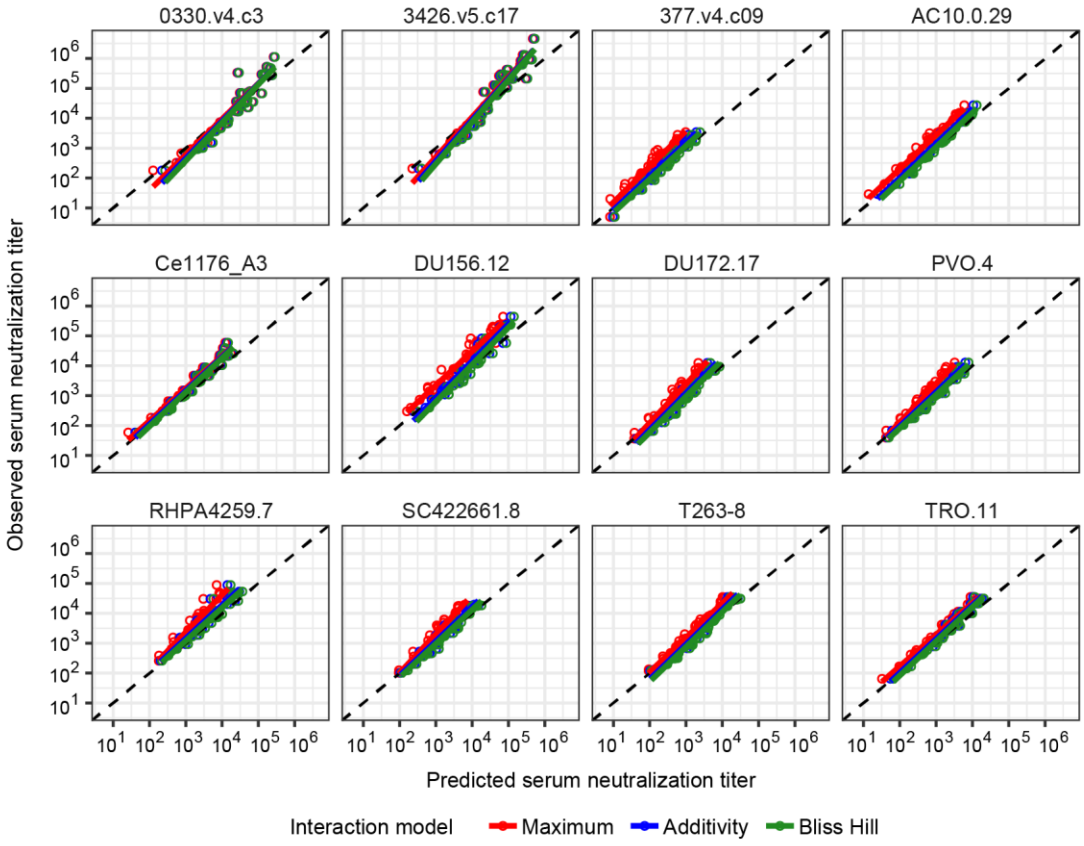
**Supplementary Figure 3. Similar ID50 neutralization-effective serum levels in dual and triple bnAb combinations are comparable to observed serum levels.**



**Supplementary Figure 4. Greater ID50 neutralization magnitude and breadth of triple compared to dual bnAb combinations against a 12 multi-clade virus panel.**



**Supplementary Figure 5. Combination bnAb neutralization ID50 titers can be predicted using individual titers.**



**Supplemental Figure 6. Anti-drug antibody levels.** 10-1074, PGDM1400, PGT121, or VRC07-523LS ADA titers at baseline (day 0) and post-treatment visits are plotted. Each line represents a single participant. Samples for which an ADA was not observed are plotted in the shaded grey region and the number of subjects for which no ADA was observed is noted at right. The subject IDs are listed for any subject with one or more ADA positive time points. Ppt = participant.