

## Supplementary Information for: Rational Design and *in vivo* Characterization of mRNA-encoded Broadly Neutralizing Antibody Combinations Against HIV-1

**Table S1.** Neutralization antibody concentration inhibiting 80% of viral infection.

	<b>IgG</b>	<b>scFv-Fc.r1</b>	<b>scFv-Fc.r2</b>
<b>PGDM1400</b>			
Mean (SD)	3.75 (5.4)	21.05 (53.67)	31.76 (90.05)
Median (IQR)	1.17 (0.13, 6.75)	3.05 (0.38, 7.72)	1.64 (0.32, 12.56)
<b>10-1074</b>			
Mean (SD)	1.13 (2.46)	2.59 (7.45)	1.05 (2.14)
Median (IQR)	0.25 (0.07, 1.10)	0.14 (0.04, 0.45)	0.24 (0.07, 0.91)
<b>PGT121</b>			
Mean (SD)	3.67 (8.2)	2.72 (7.21)	2.54 (7.16)
Median (IQR)	0.13 (0.04, 0.56)	0.16 (0.07, 0.45)	0.12 (0.05, 0.42)
<b>3BNC117</b>			
Mean (SD)	3.23 (7.43)	13.15 (11.08)	3.58 (3.37)
Median (IQR)	0.55 (0.17, 1.61)	11.09 (1.02, 25.00)	2.21 (0.71, 5.97)
<b>N6</b>			
Mean (SD)	0.43 (0.51)		2.73 (3.00)
Median (IQR)	0.20 (0.05, 0.85)		1.33 (0.45, 5.24)
<b>NIH45-46</b>			
Mean (SD)	0.38 (0.41)		2.73 (3.00)
Median (IQR)	0.24 (0.06, 0.75)		1.33 (0.45, 5.24)

IQR, interquartile range (25% percentile, 75% percentile); SD, standard deviation.

**Table S2.** scFv-Sc Round 2 Variant Mutations.

<b>scFv-Sc Round 2 Variants</b>	<b>Mutations</b>
<b>PGDM1400</b>	
Var_7	Linker20 (GGGGS) 4
Var_8	L20 + H:K23R
Var_9	L20 + H:K23R + H:K94F
Var_10	L20 + H:K19R
Var_11	L20 + H:K19R + S82AN
Var_12	L20 + S39Y
Var_13	VH_VL + L20
<b>10-1074</b>	
Var_7	Linker20 (GGGGS)4
Var_8	L20 + H:S79Y
Var_9	L20 + H:S19R
Var_10	L20 + H:K81Q
Var_11	L20 + H:S18R + H:S79Y + H:K81Q
Var_12	L20 + H:S18R + H:S79Y + H:K81Q + H:V68T
Var_13	L20 + H:L80Y
Var_14	L20 + H:S23Q
Var_15	L20 + H:S40R
Var_16	L20 + H:K13R
Var_17	L20 + H:K13R + S23Q
Var_18	VH_VL + L20

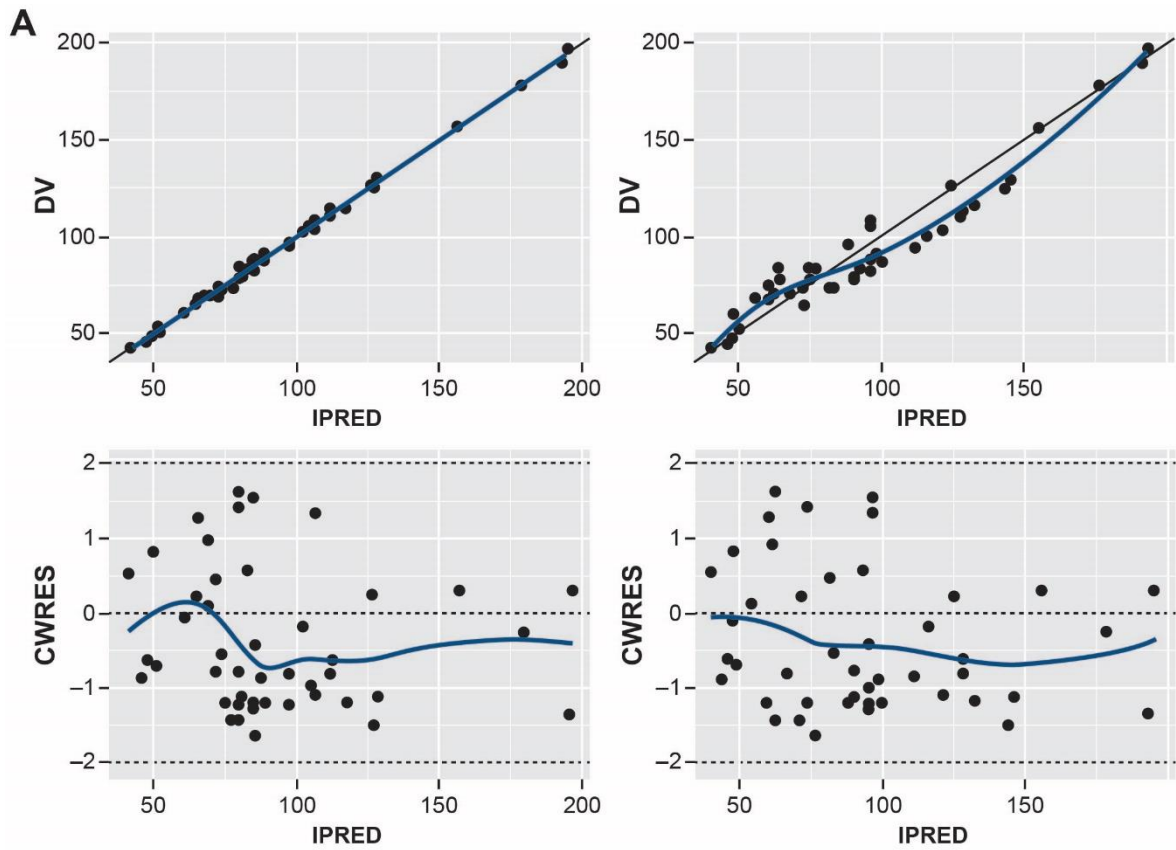
PGT121	
Var_7	Linker20 (GGGGS)4
Var_7a	L20 + 68N_Rev
Var_8	L20 + 68N_Rev + H:S79Y
Var_9	L20 + 68N_Rev + H:S19R
Var_10	L20 + 68N_Rev + H:S81Q
Var_11	L20 + 68N_Rev+ H:S19R + H:S79Y + H:S81Q
Var_12	L20 + H:S19R + H:S79Y + H:S81Q
Var_13	L20 + 68N_Rev + H:S81I
Var_14	L20 + 68N_Rev + H:S23Q
Var_15	L20 + 68N_Rev + L:S63M
Var_16	VH_VL + L20
N6	
Var_2	Linker20 (GGGGS)4
Var_3	L20 + H:A10Y
Var_4	L20 + H:K12R
Var_5	L20 + H:D81Q
Var_6	L20 + H:D81Q + H:R82AY

Var, variant.

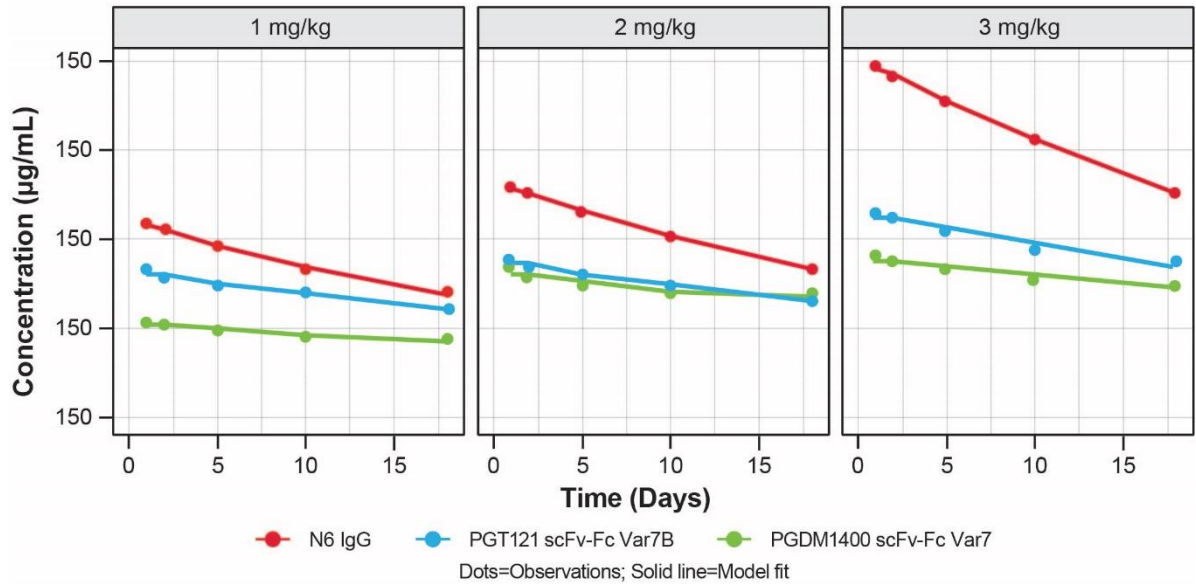
**Table S3.** Kinetic–Pharmacodynamic Model Parameters.

Parameter (unit)	Estimate		
	N6 IgG	PGT121 scFv-Fc Var7B	PGDM1400 scFv-Fc Var7
m	0.862	0.566	0.438
CL <sub>ab</sub> (mL/h)	0.00111	0.000719	0.000507
t <sub>1/2</sub> (days)	26.0	40.2	57.0

CL<sub>ab</sub>, the antibody clearance rate from the central compartment; Fc, crystallizable fragment; IgG, immunoglobulin G; M, linear slope parameter; scFv, single-chain variable fragment; t<sub>1/2</sub>, half-life.



**B** DV, Dependent variable; IPRED, Individual fit; PRED, Population Fit; CWRES, Conditional weighted residuals



**Figure S1.** Kinetic-pharmacodynamic model diagnostics. (A) Goodness-of-fit plots and (B) fits for individual groups.