Figure 1a.

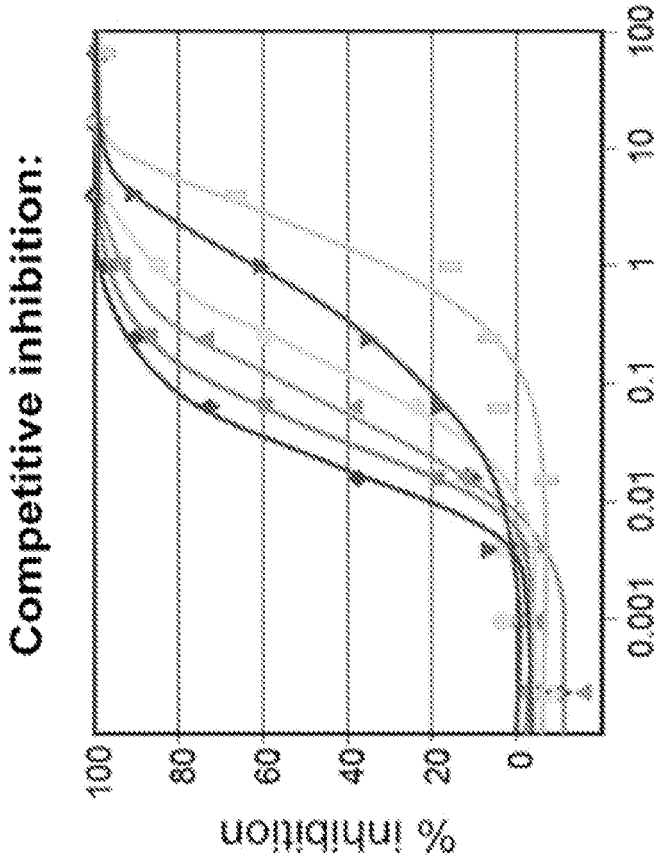


Figure 1b.

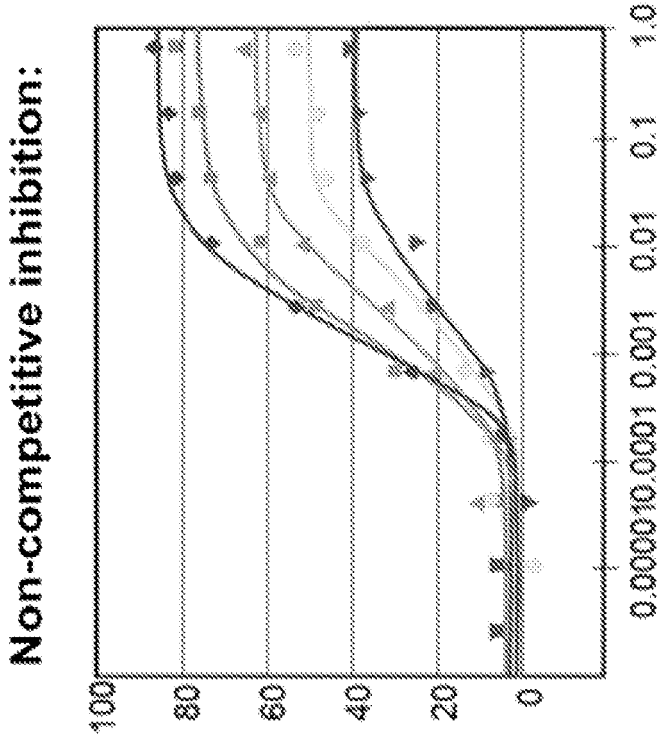


Figure 2.

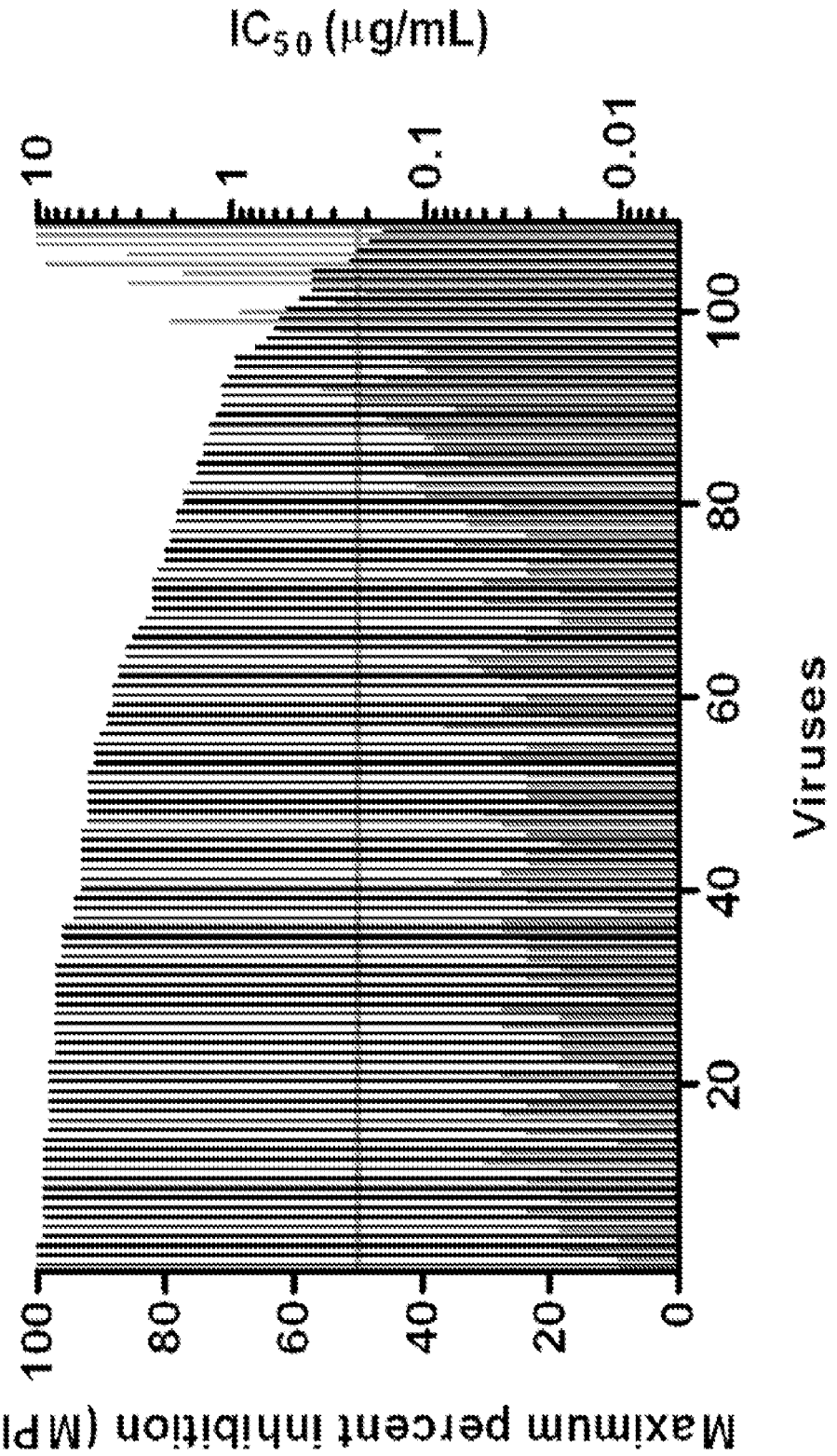

IC50 (µg/mL)
10
1
0.1
0.01
100
80
60
40
20
0
Maximum percent inhibition (MPI)
100
80
60
40
20
0
Viruses

Figure 3.

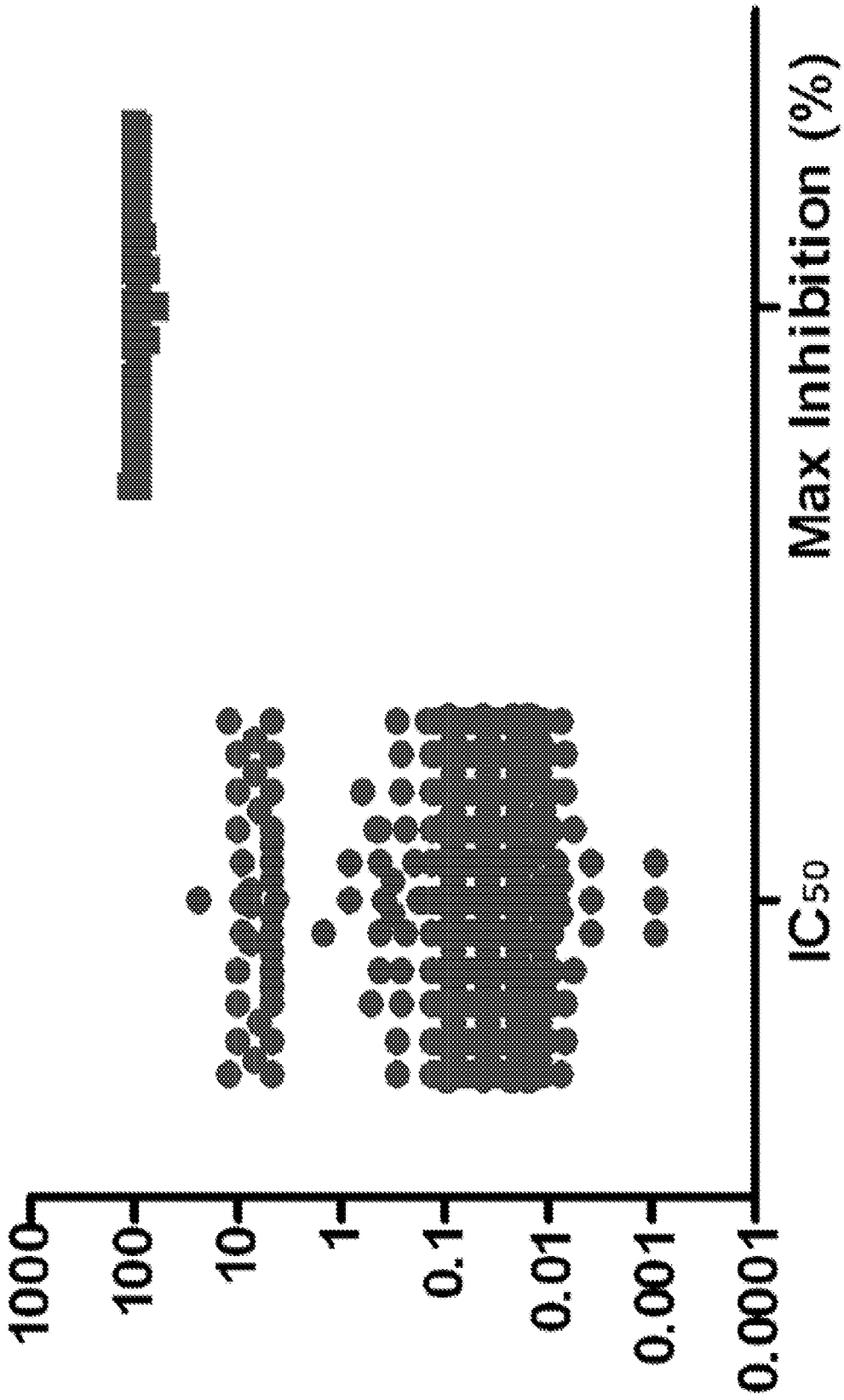


Figure 4.

Full Heavy Chain Fv Region of mAb dB4C7/UB-421 (SEQ ID NO: 7):

Figure 5.

Full Light Chain Fv Region of mAb dB4C7/UB-421 (SEQ ID NO: 8):

DIVLTQSPASLAVSLGQRATITCKAGQSVDYDGDSYMNWYQQKPGQPPKLLIYYASNLESGIPARFSGSG

CDR2

GTDFTLNIHPVEEDAATYYCQQSYKDPLTFGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNN

CDR1

CDR3

FYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKLYACEVTHQGLSSPVTKSF

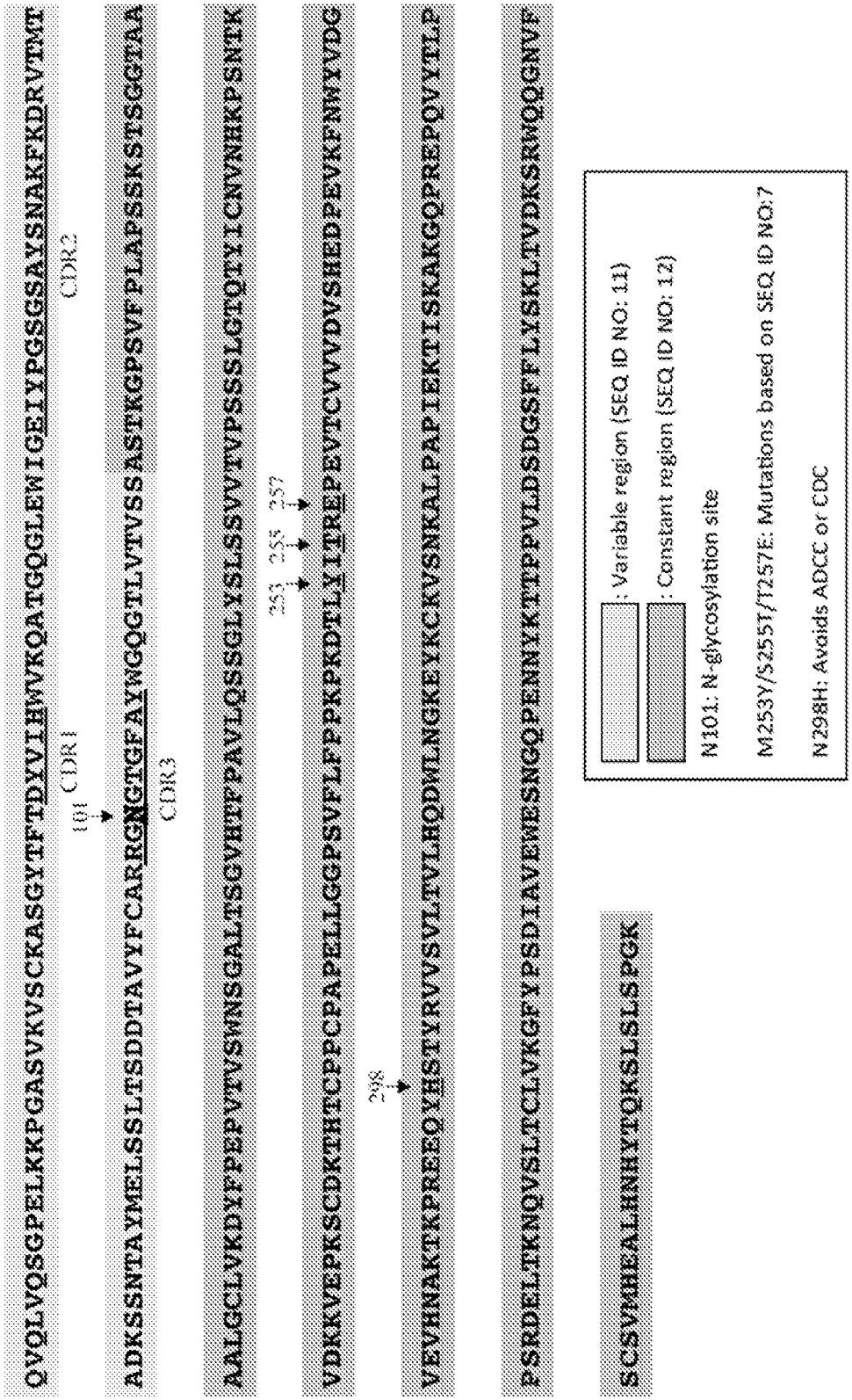
NRGEC

: Variable region (SEQ ID NO: 13)

: Constant region (SEQ ID NO: 14)

Figure 6.

Full Heavy Chain Fv Region of Improved Humanized Antibody (SEQ ID NO: 9):



: Variable region (SEQ ID NO: 11)

: Constant region (SEQ ID NO: 12)

N101: N-glycosylation site

M253Y/S255T/T257E: Mutations based on SEQ ID NO:7

N298H: Avoids ADCC or CDC

Figure 7.

Full Heavy Chain Fv Region of mAb dB4 (SEQ ID NO: 10):

QVQLVQSGPELKKPGASVKVSCKASGYTFTDYVIHWVKQATGQGLEWIGEIYPGSGSAYSNAKFKDRVTMT

CDR1 101 CDR2

ADKSSNTAYMELSSLTSDDTAVYFCARRGNGTGFAYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAA

CDR3

ALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTK

253 255 257

VDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLXIXRTPEVTCVVVDVSHEDPEVKFNWYVDG

298

VEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLP

PSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVF

SCSVMHEALHNHYTQKSLSLSPGK

: Variable region (SEQ ID NO: 11)

: Constant region (SEQ ID NO: 12)

N101: N-glycosylation site

X253: M (SEQ ID NO: 7) or Y (SEQ ID NO: 9)

X255: S (SEQ ID NO: 7) or T (SEQ ID NO: 9)

X257: T (SEQ ID NO: 7) or E (SEQ ID NO: 9)

X298: N (native IgG_1) or H (SEQ ID NOs: 7 and 9)

N298H: Avoids ADCC or CDC

Figure 8.

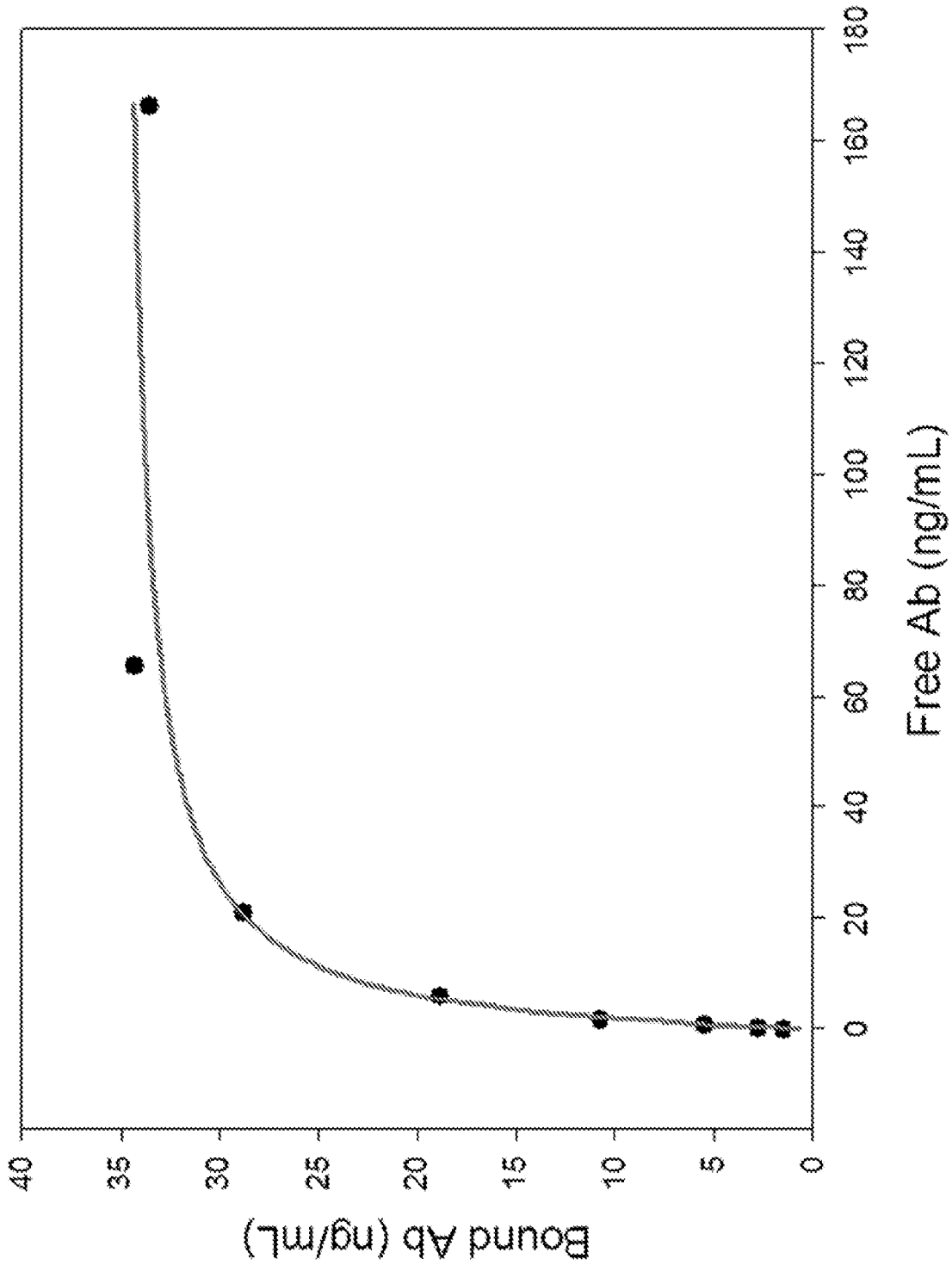

Bound Ab (ng/mL)
0
5
10
15
20
25
30
35
40
Free Ab (ng/mL)
0
20
40
60
80
100
120
140
160
180

Figure 9.

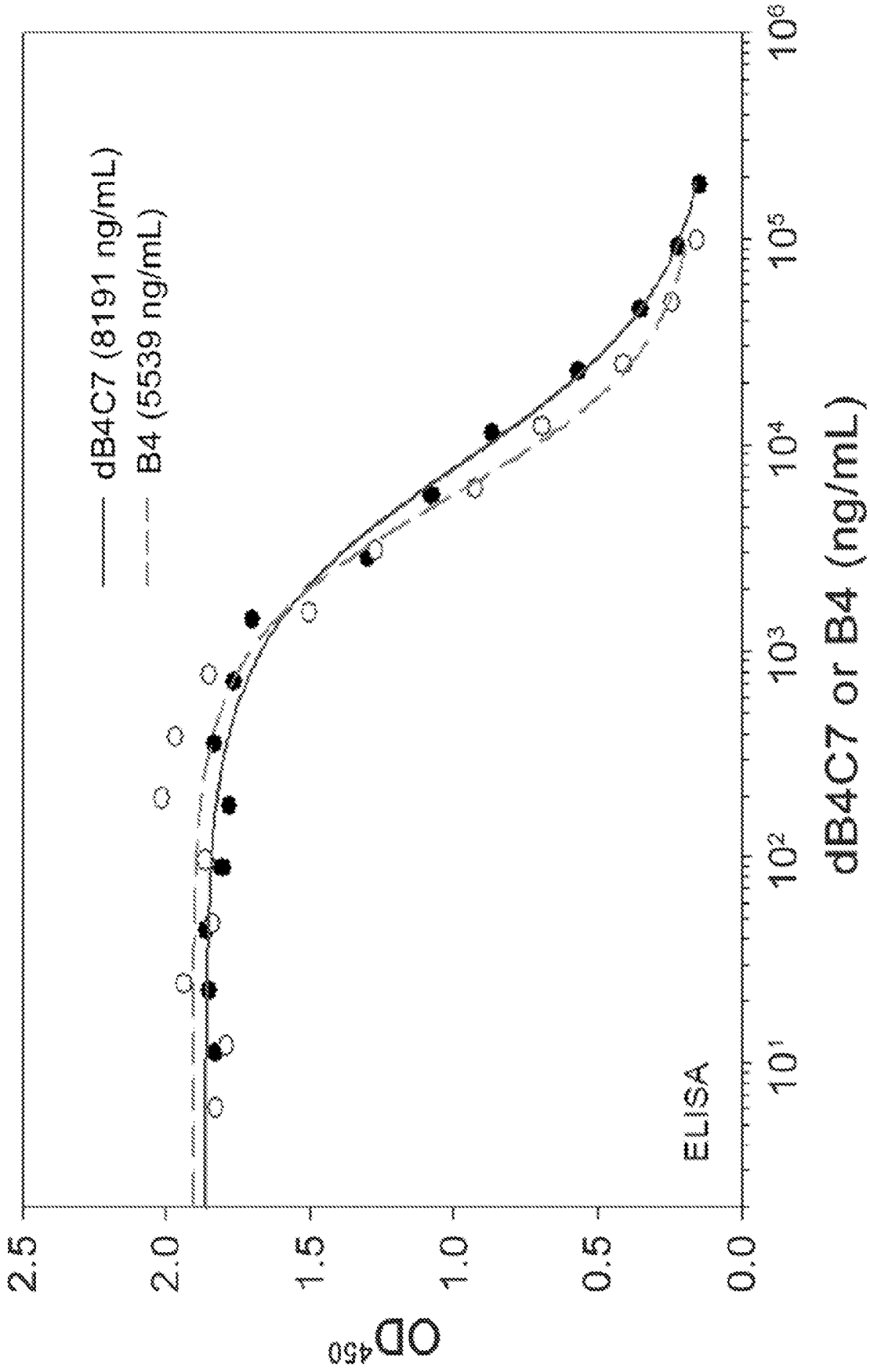

dB4C7 (8191 ng/mL)
B4 (5539 ng/mL)
ELISA
OD450
dB4C7 or B4 (ng/mL)
0.0
0.5
1.0
1.5
2.0
2.5
10¹
10²
10³
10⁴
10⁵
10⁶

Figure 10.

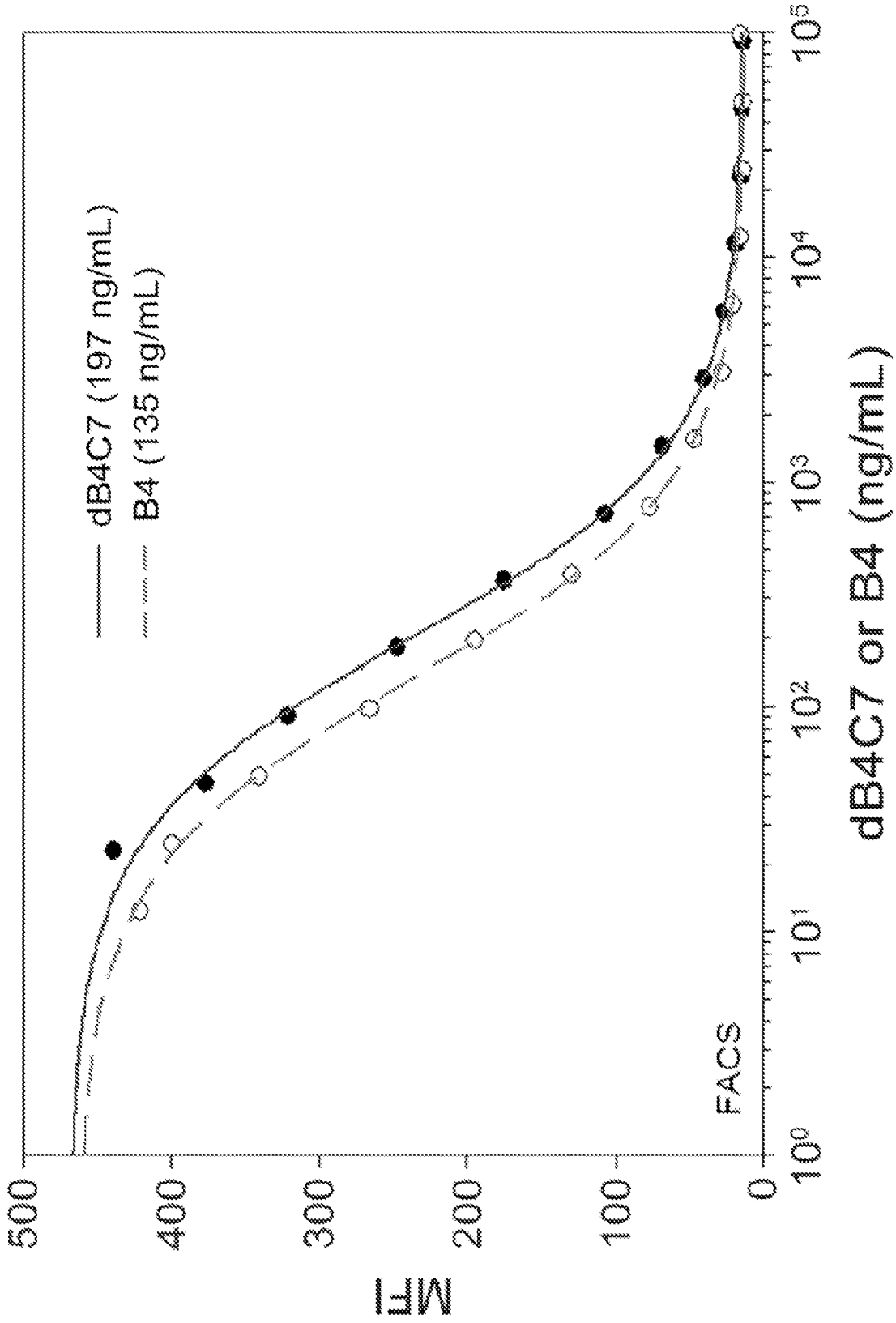

dB4C7 (197 ng/mL)
B4 (135 ng/mL)
FACS
MFI
dB4C7 or B4 (ng/mL)
0
100
200
300
400
500
10^0
10^1
10^2
10^3
10^4
10^5

Figure 11.

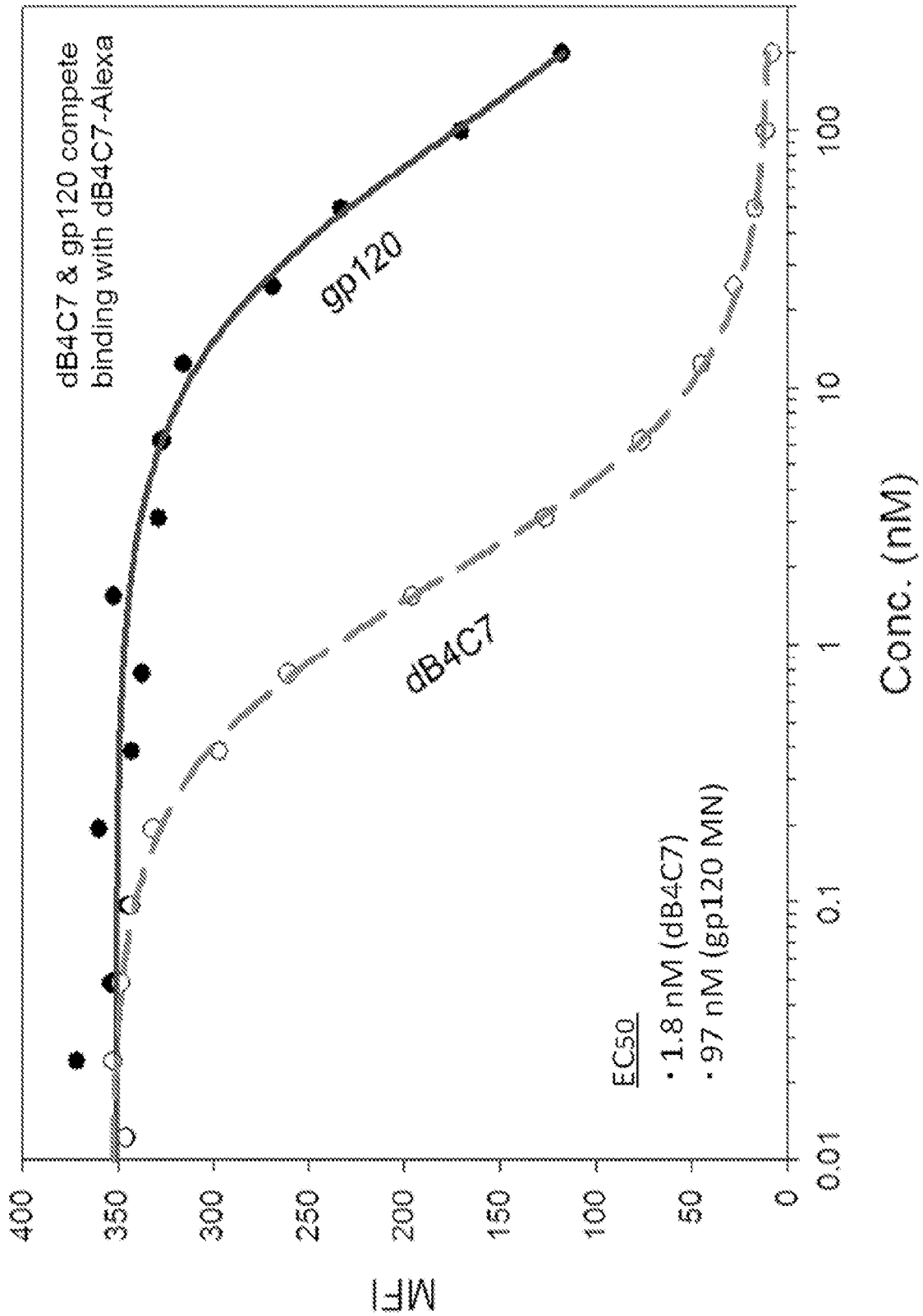

dB4C7 & gp120 compete
binding with dB4C7-Alexa
gp120
dB4C7
EC50
• 1.8 nM (dB4C7)
• 97 nM (gp120 MN)
MFI
Conc. (nM)
400
350
300
250
200
150
100
50
0
0.01
0.1
1
10
100

Figure 12.

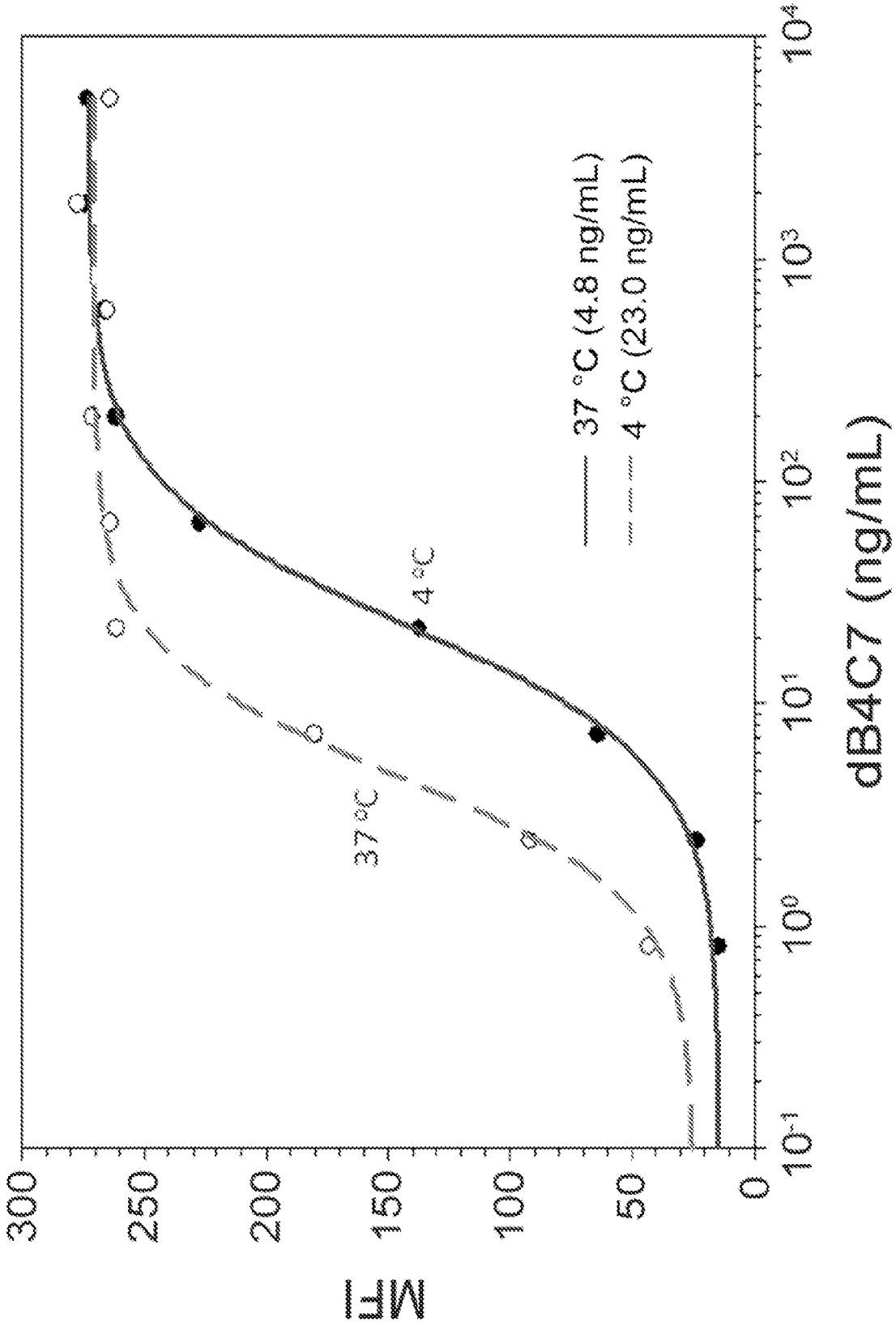

MFI
300
250
200
150
100
50
0
10^{-1}
10^{0}
10^{1}
10^{2}
10^{3}
10^{4}
dB4C7 (ng/mL)
37 °C (4.8 ng/mL)
4 °C (23.0 ng/mL)
4 °C
37 °C

Figure 13.

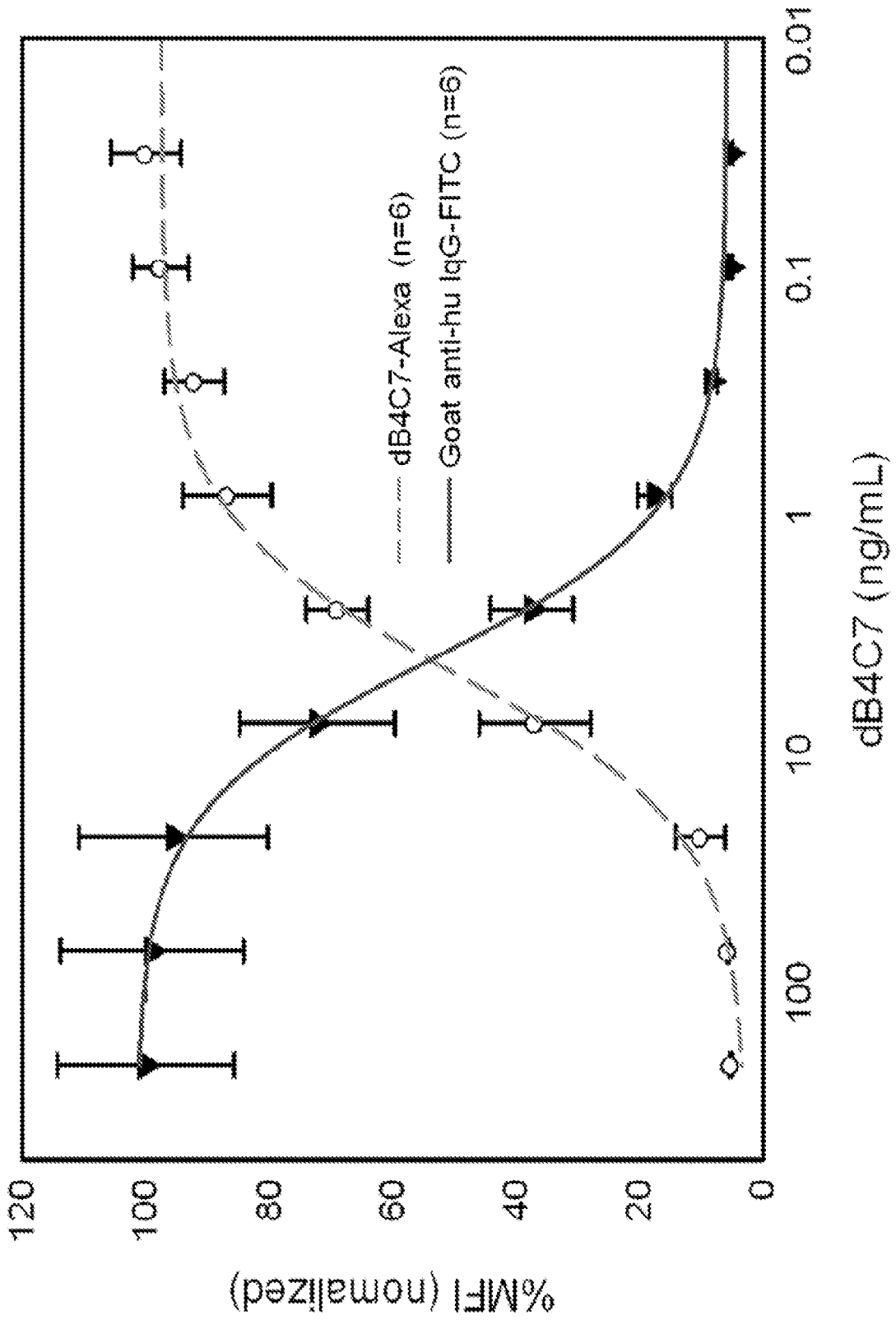

%MFI (normalized)
120
100
80
60
40
20
0
100
10
1
0.1
0.01
dB4C7 (ng/mL)
dB4C7-Alexa (n=6)
Goat anti-hu IgG-FITC (n=6)

Figure 14.

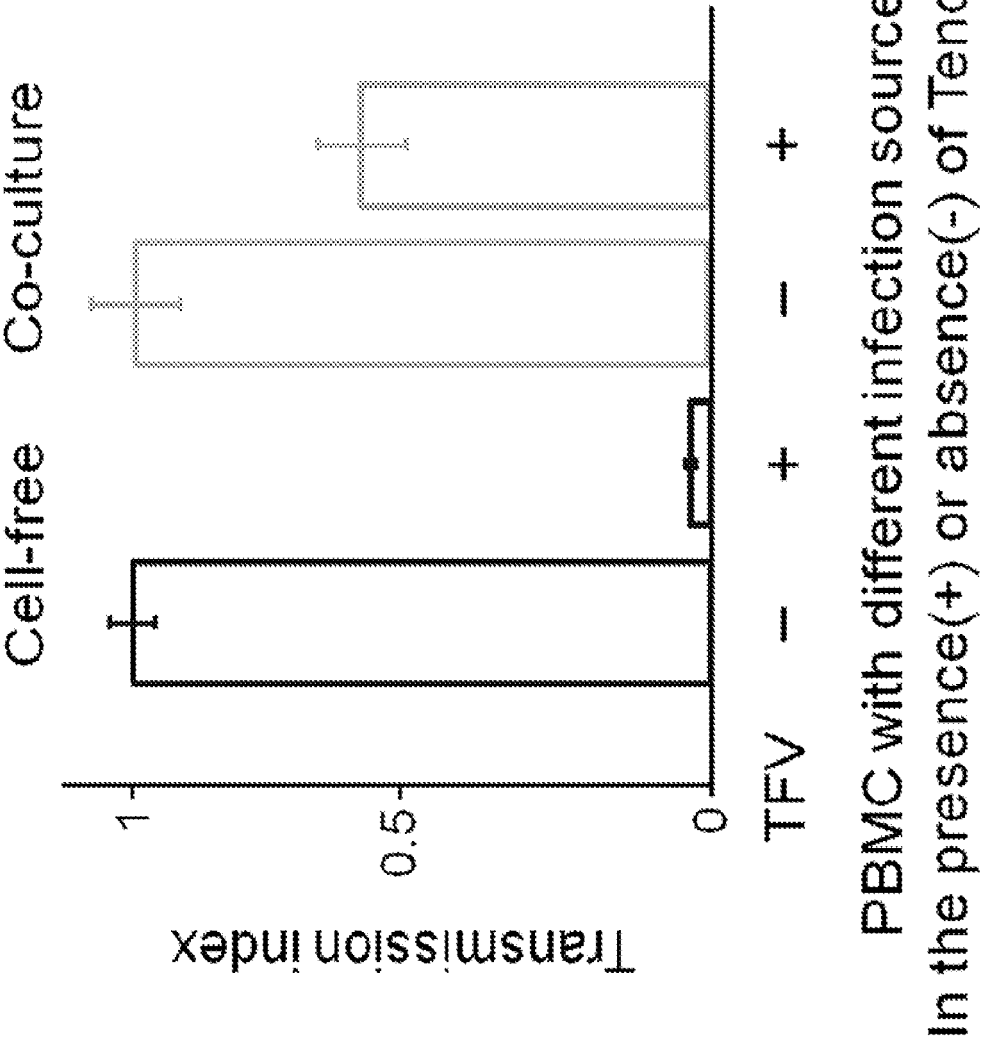

Cell-free
Co-culture
Transmission index
1
0.5
0
TFV
–
+
–
+
PBMC with different infection sources
In the presence(+) or absence(-) of Tenofovir.

Figure 15.

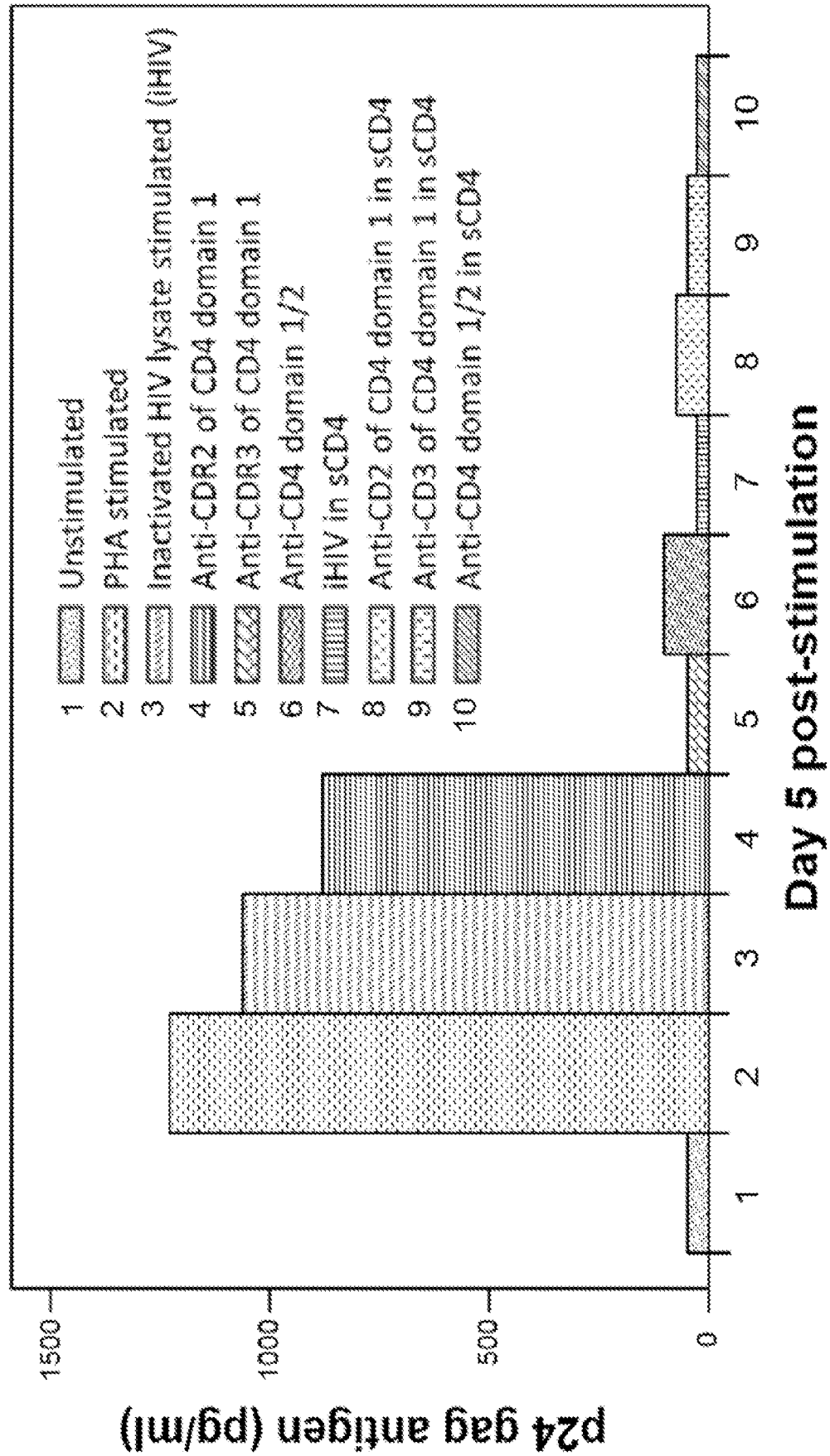

1 Unstimulated
2 PHA stimulated
3 Inactivated HIV lysate stimulated (iHIV)
4 Anti-CDR2 of CD4 domain 1
5 Anti-CDR3 of CD4 domain 1
6 Anti-CD4 domain 1/2
7 iHIV in sCD4
8 Anti-CD2 of CD4 domain 1 in sCD4
9 Anti-CD3 of CD4 domain 1 in sCD4
10 Anti-CD4 domain 1/2 in sCD4
1500
1000
500
0
1
2
3
4
5
6
7
8
9
10
Day 5 post-stimulation
p24 gag antigen (pg/ml)

Figure 16.

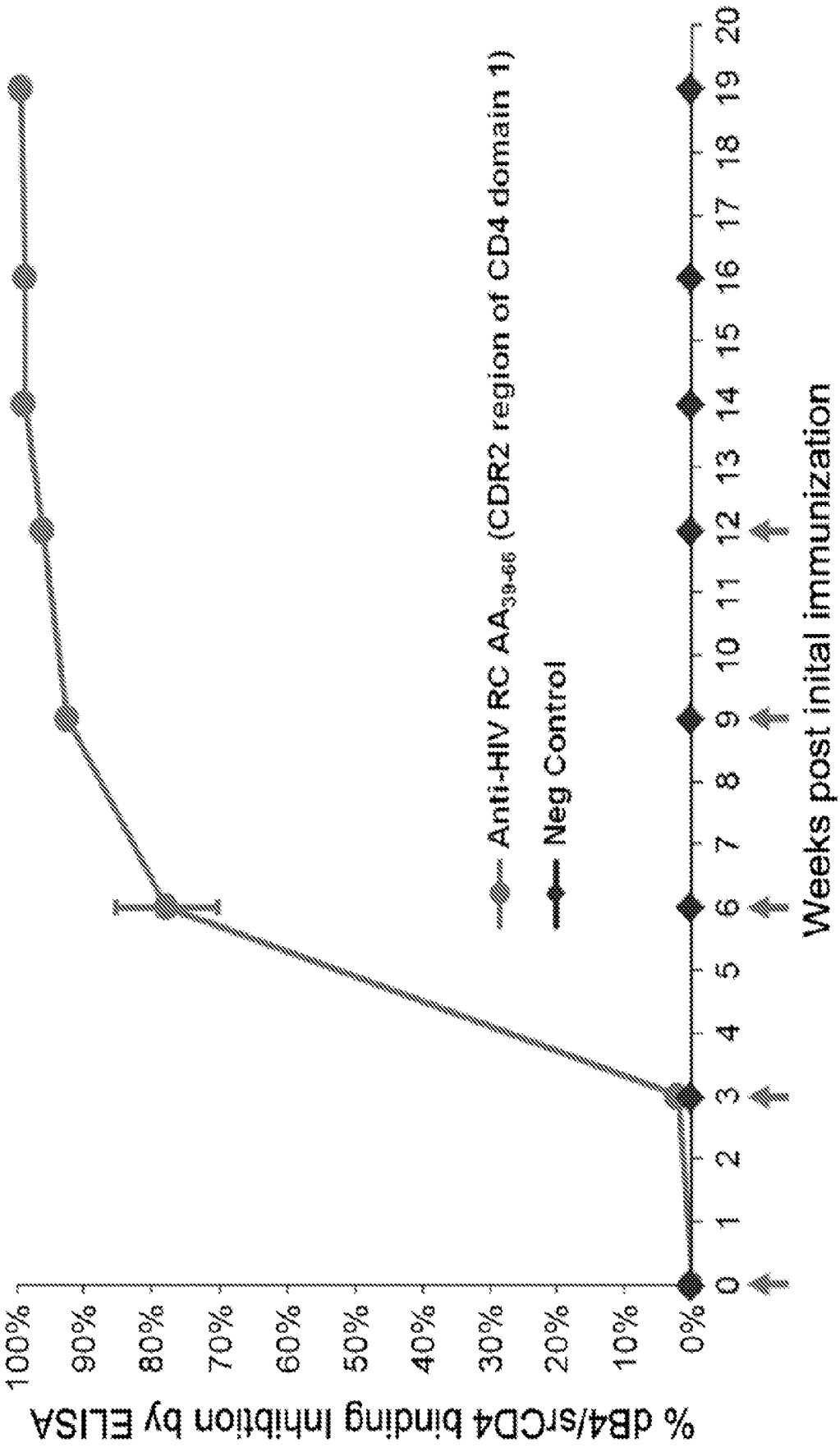
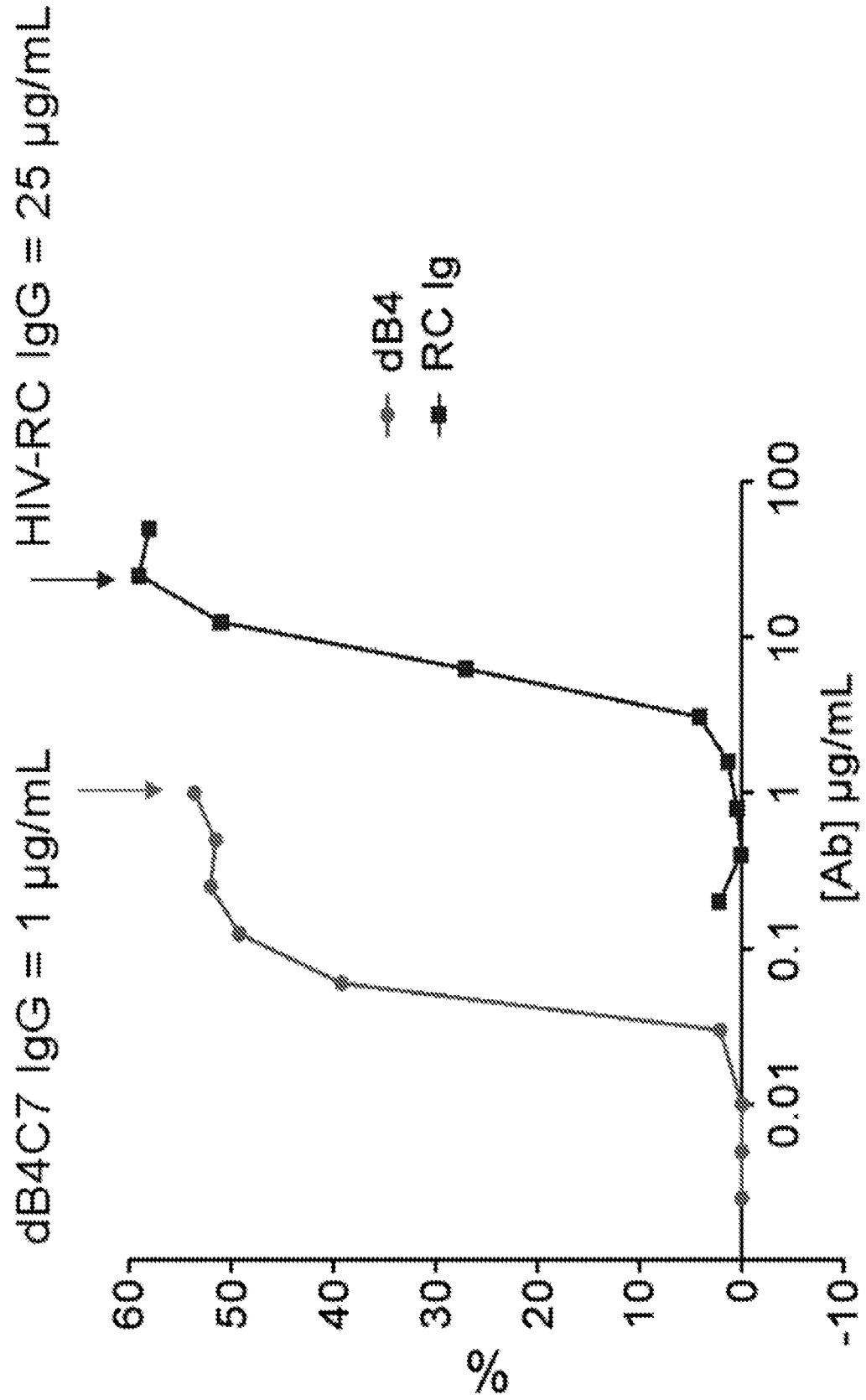

% dB4/srCD4 binding Inhibition by ELISA
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
Weeks post inital immunization
Anti-HIV RC AA39-68 (CDR2 region of CD4 domain 1)
Neg Control

Figure 17.


HIV-RC IgG = 25 µg/mL
dB4C7 IgG = 1 µg/mL
dB4
RC Ig
60
50
40
30
20
10
0
-10
%
0.01
0.1
1
10
100
[Ab] µg/mL

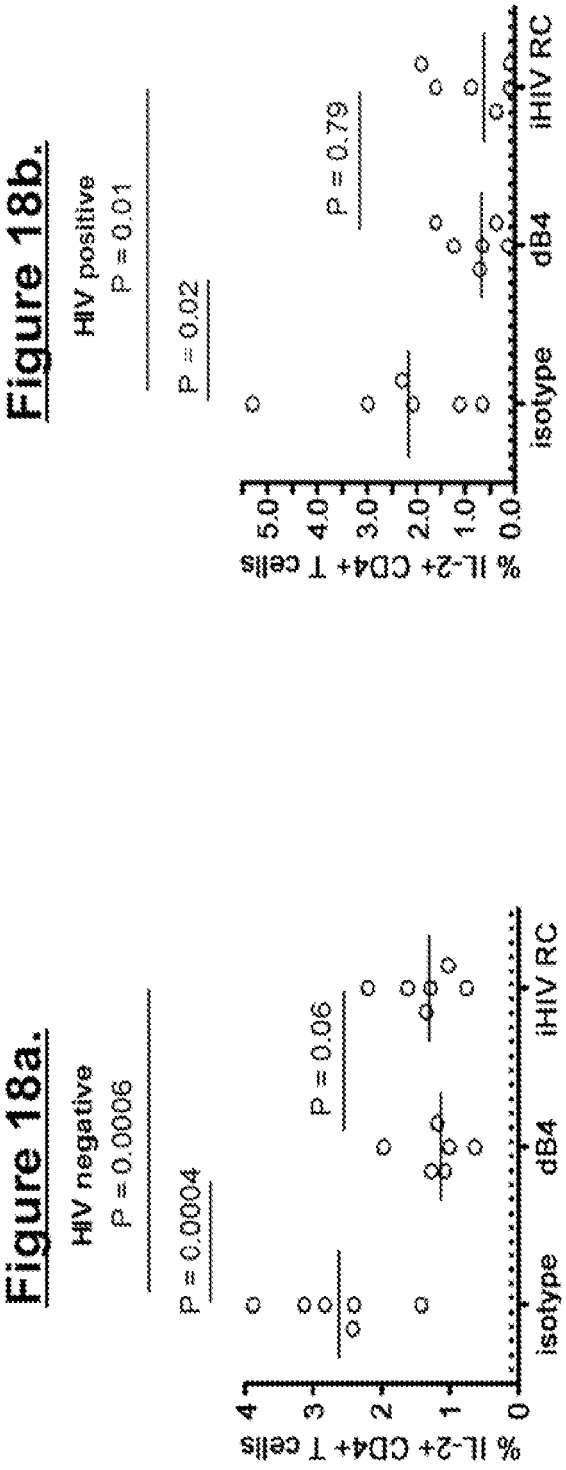

Figure 18a.
HIV negative
P = 0.0006
P = 0.0004
P = 0.06
% IL-2+ CD4+ T cells
4
3
2
1
0
isotype
dB4
iHIV RC

Figure 18b.
HIV positive
P = 0.01
P = 0.02
P = 0.79
% IL-2+ CD4+ T cells
5.0
4.0
3.0
2.0
1.0
0.0
isotype
dB4
iHIV RC

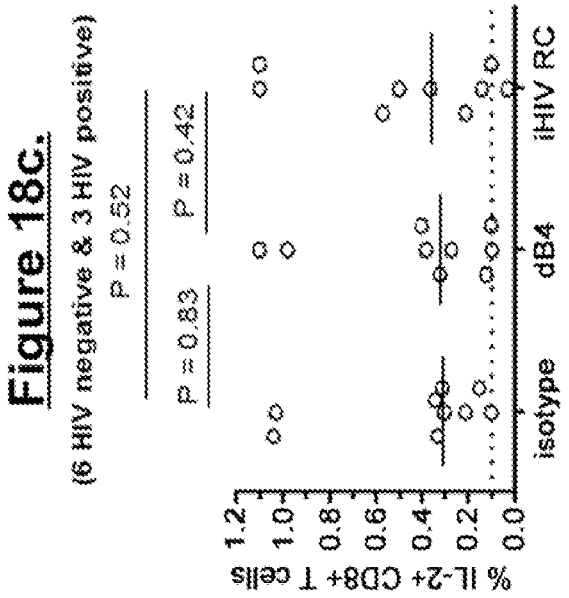

Figure 18c.
(6 HIV negative & 3 HIV positive)
P = 0.52
P = 0.83
P = 0.42
% IL-2+ CD8+ T cells
1.2
1.0
0.8
0.6
0.4
0.2
0.0
isotype
dB4
iHIV RC

Figure 18e.

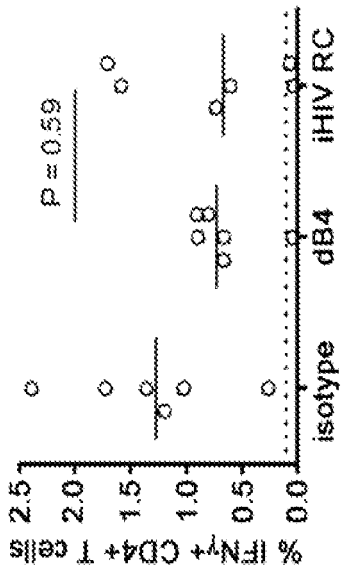


Figure 18g.

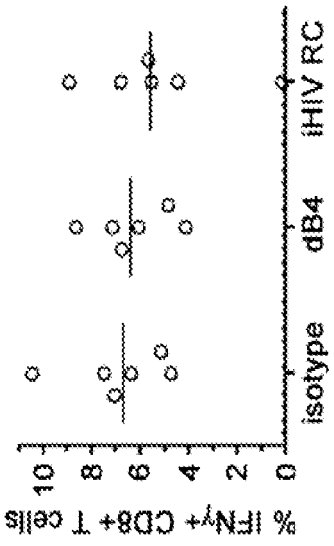


Figure 18d.

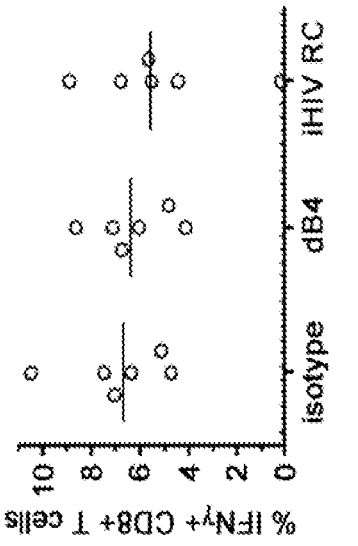


Figure 18f.

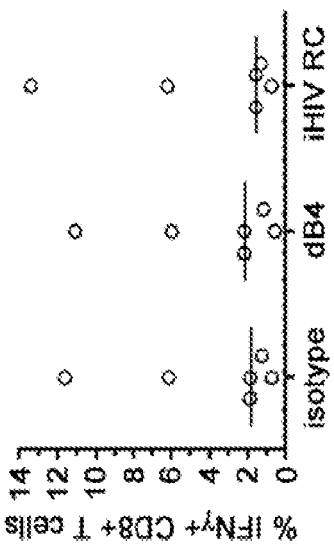


Figure 19a.

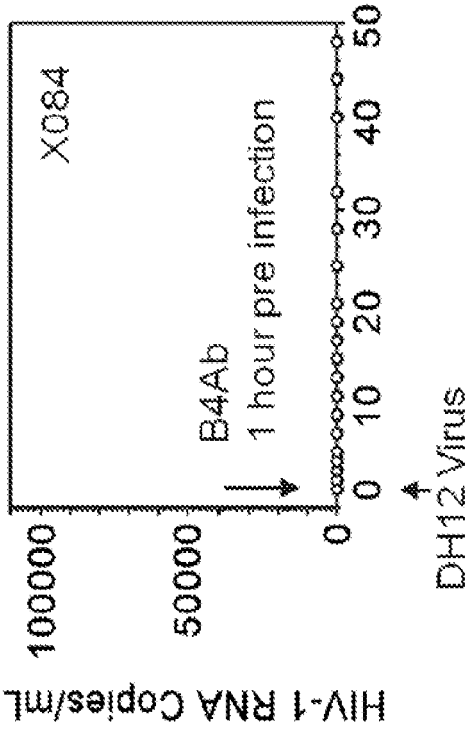


Figure 19b.

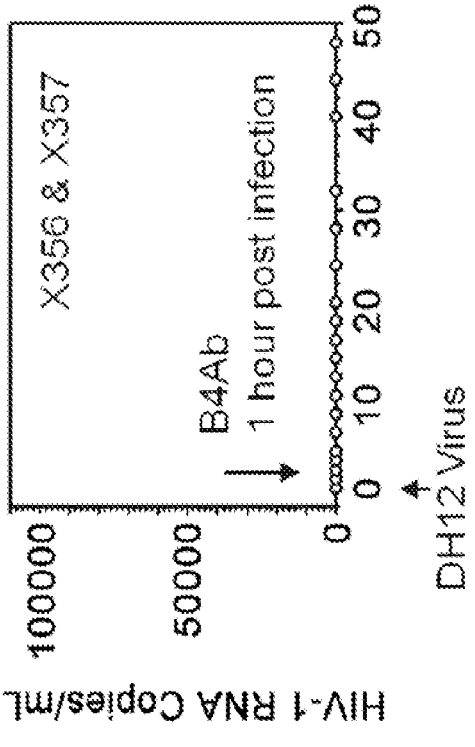


Figure 19c.

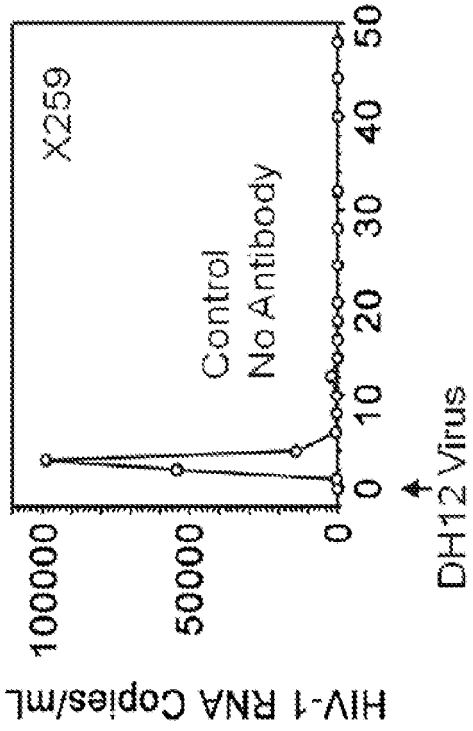


Figure 20b.

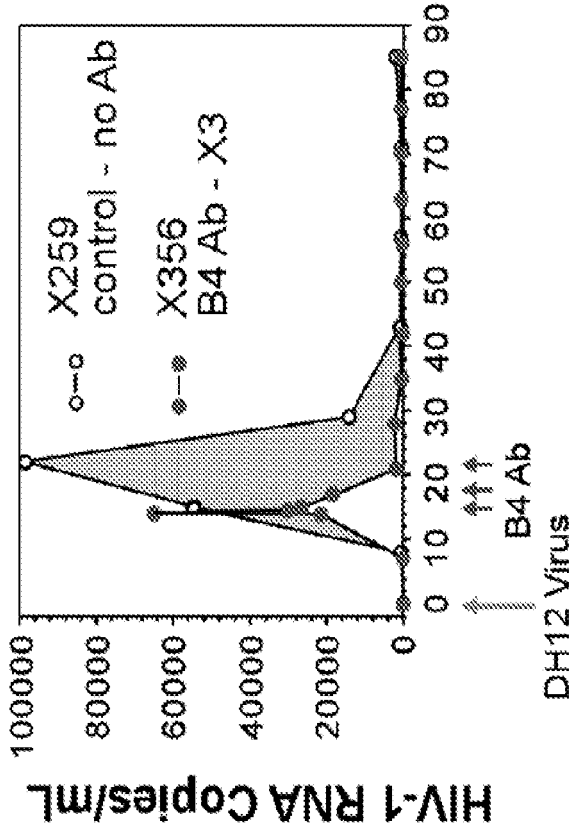


Figure 20a.

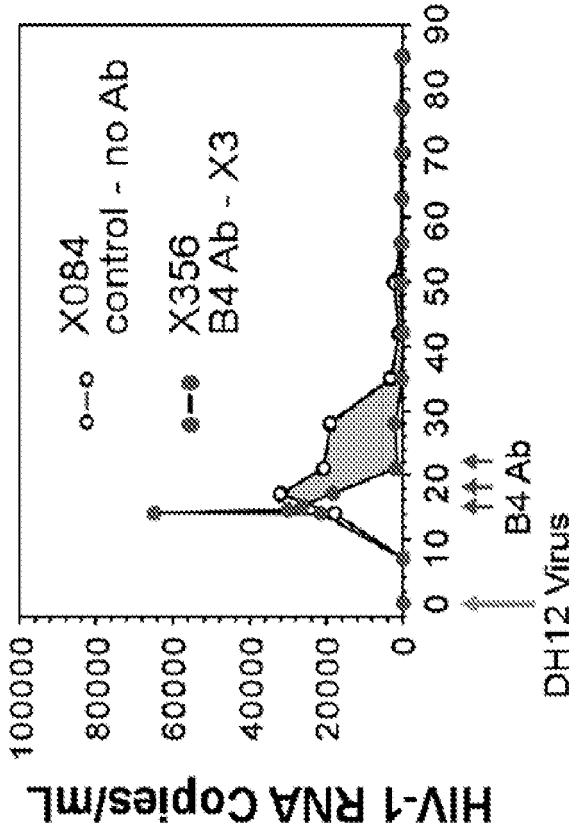


Figure 21.

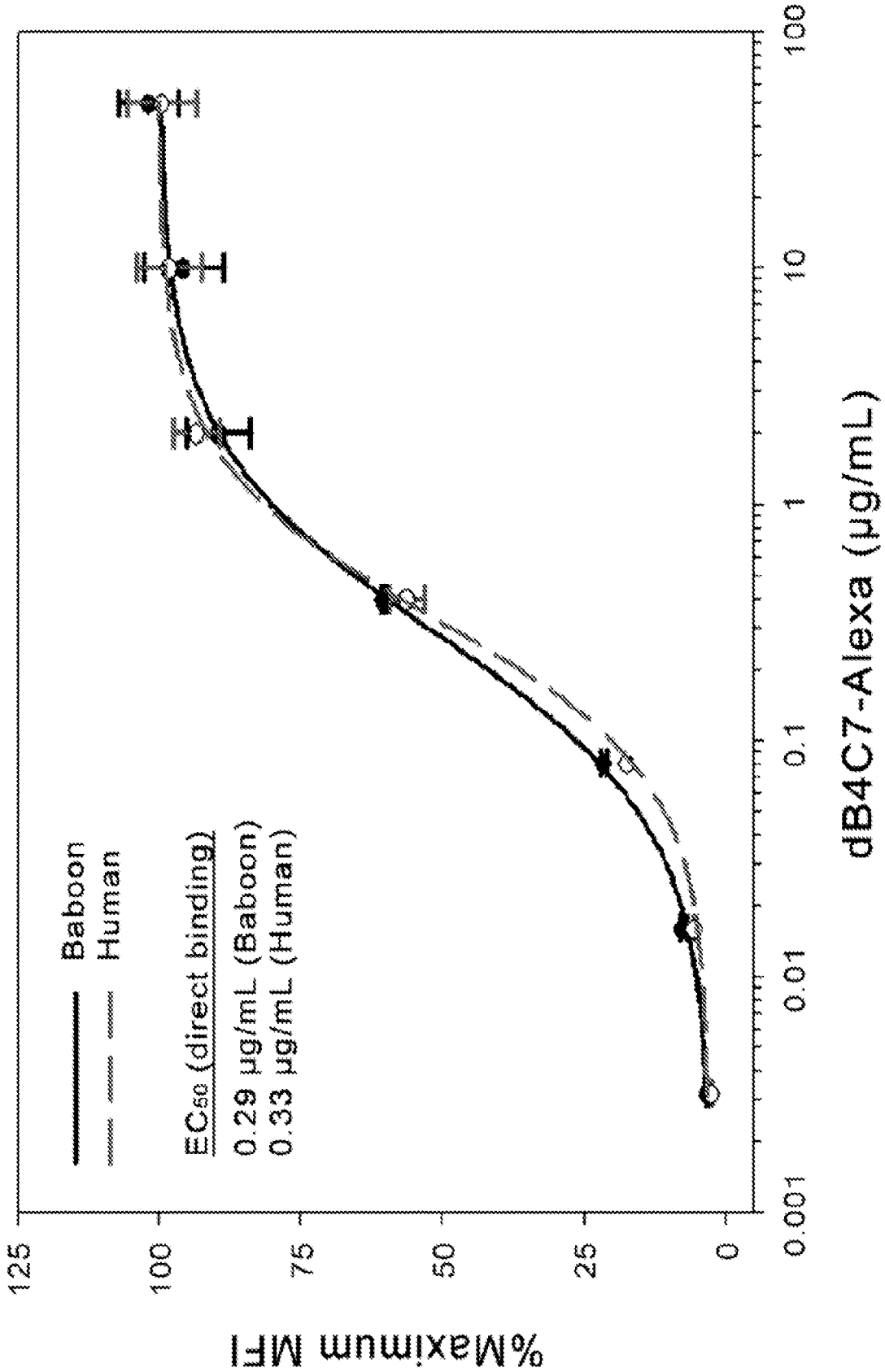

%Maximum MFI
125
100
75
50
25
0
0.001
0.01
0.1
1
10
100
dB4C7-Alexa (µg/mL)
Baboon
Human
EC50 (direct binding)
0.29 µg/mL (Baboon)
0.33 µg/mL (Human)

Figure 22b.

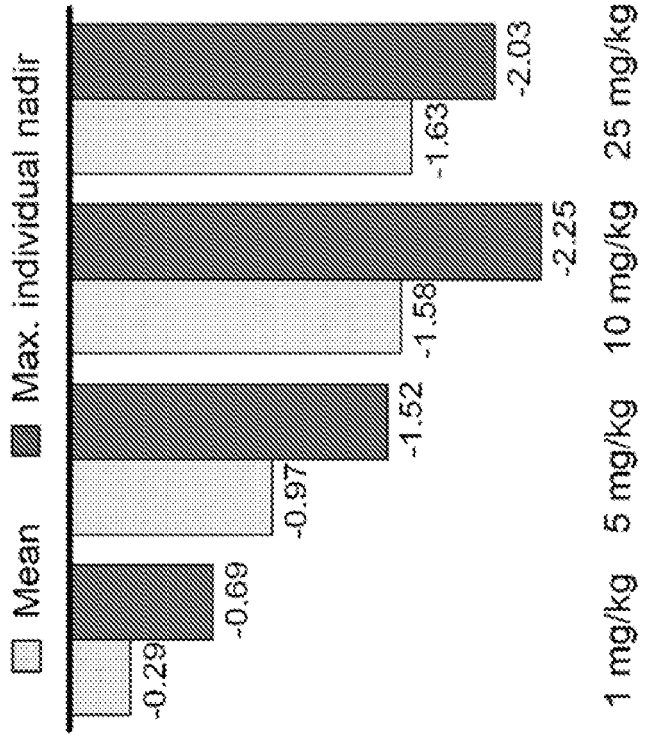


Figure 22a.

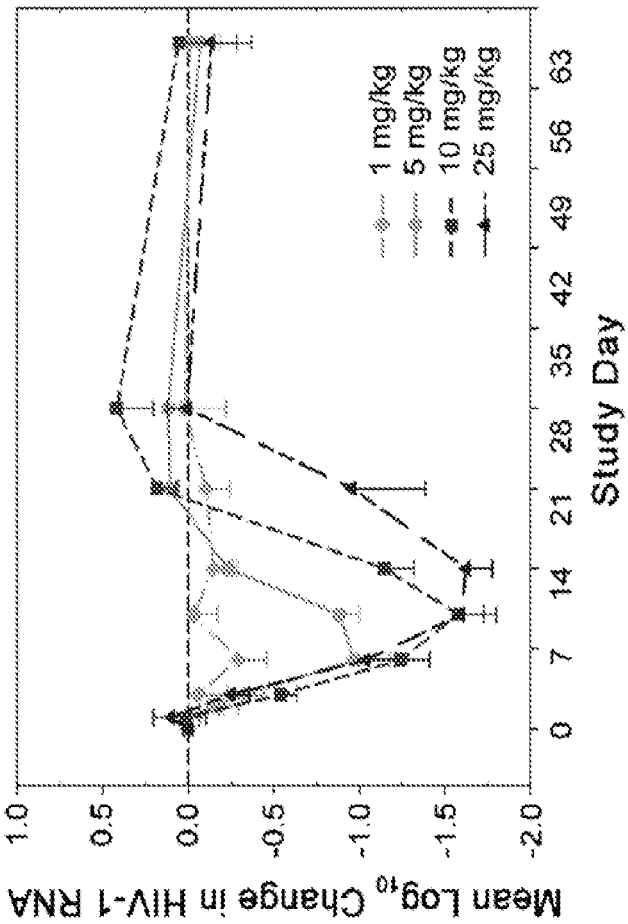


Figure 23a.

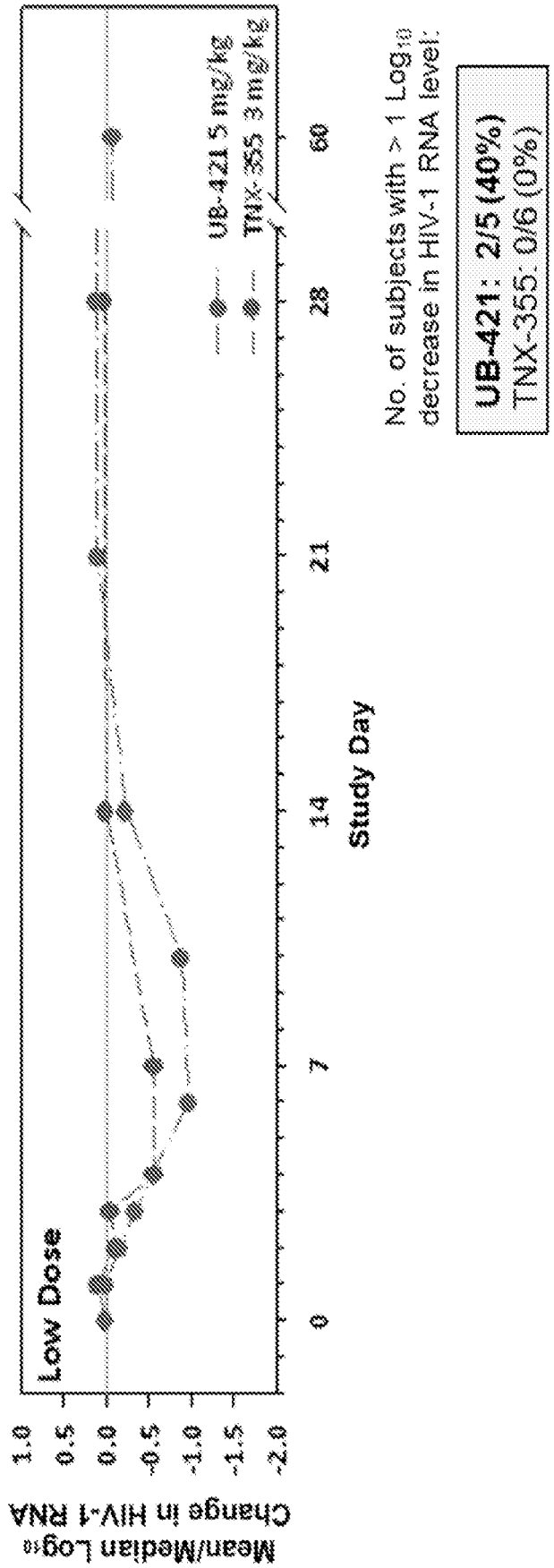

Low Dose
UB-421 5 mg/kg
TNX-355 3 mg/kg
Mean/Median Log10 Change in HIV-1 RNA
1.0
0.5
0.0
-0.5
-1.0
-1.5
-2.0
0
7
14
21
28
60
Study Day
No. of subjects with > 1 Log10 decrease in HIV-1 RNA level:
UB-421: 2/5 (40%)
TNX-355: 0/6 (0%)

Figure 23b.

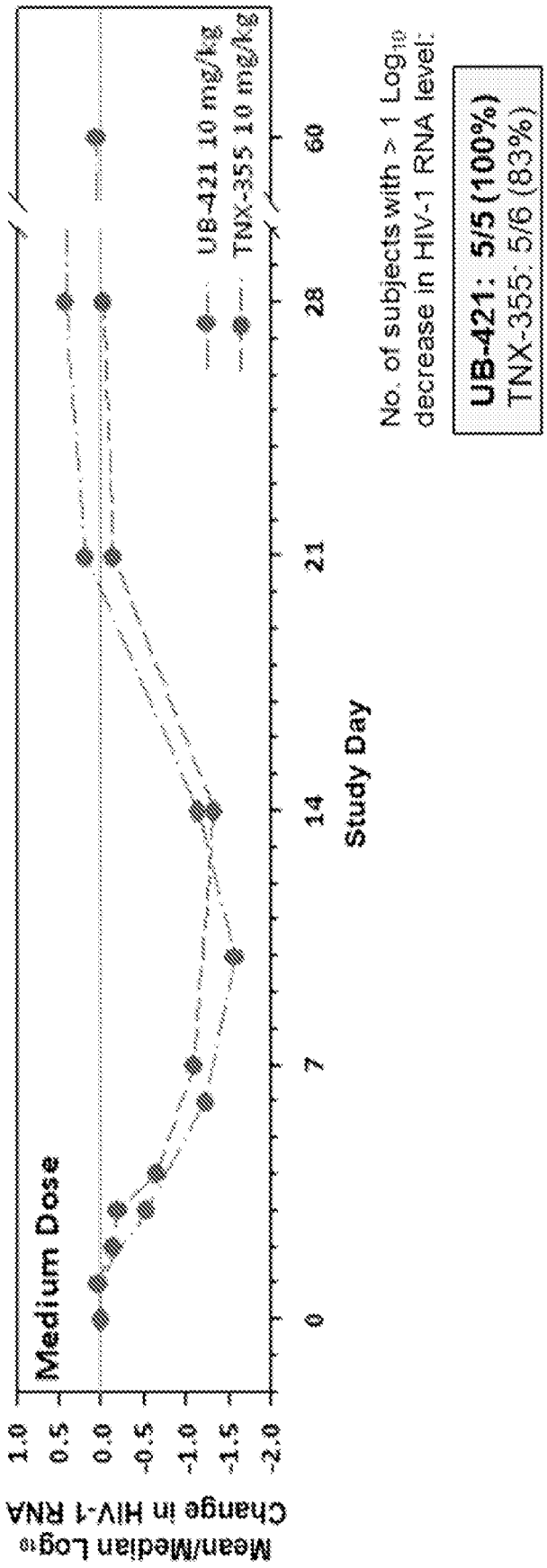

Mean/Median Log10 Change in HIV-1 RNA
1.0
0.5
0.0
-0.5
-1.0
-1.5
-2.0
Medium Dose
0
7
14
21
28
60
Study Day
UB-421 10 mg/kg
TNX-355 10 mg/kg
No. of subjects with > 1 Log10 decrease in HIV-1 RNA level:
UB-421: 5/5 (100%)
TNX-355: 5/6 (83%)

Figure 23c.

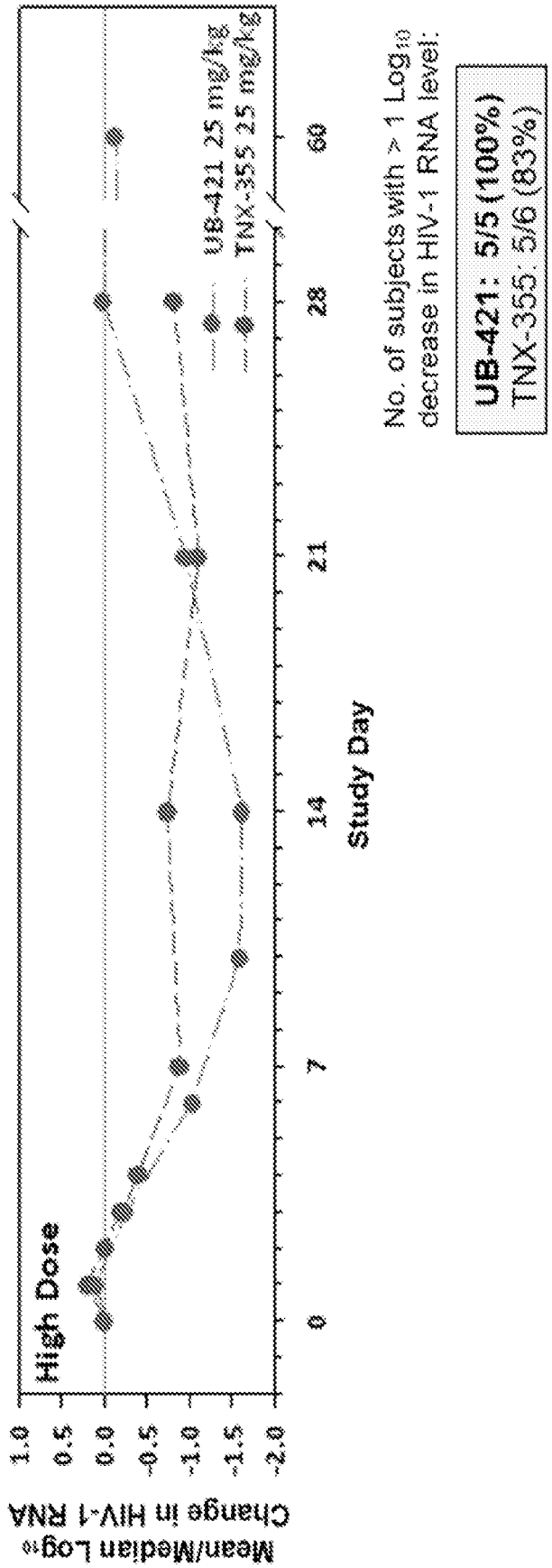

High Dose
Mean/Median Log10 Change in HIV-1 RNA
1.0
0.5
0.0
-0.5
-1.0
-1.5
-2.0
0
7
14
21
28
60
Study Day
UB-421 25 mg/kg
TNX-355 25 mg/kg
No. of subjects with > 1 Log10 decrease in HIV-1 RNA level:
UB-421: 5/5 (100%)
TNX-355: 5/6 (83%)

Figure 24a.

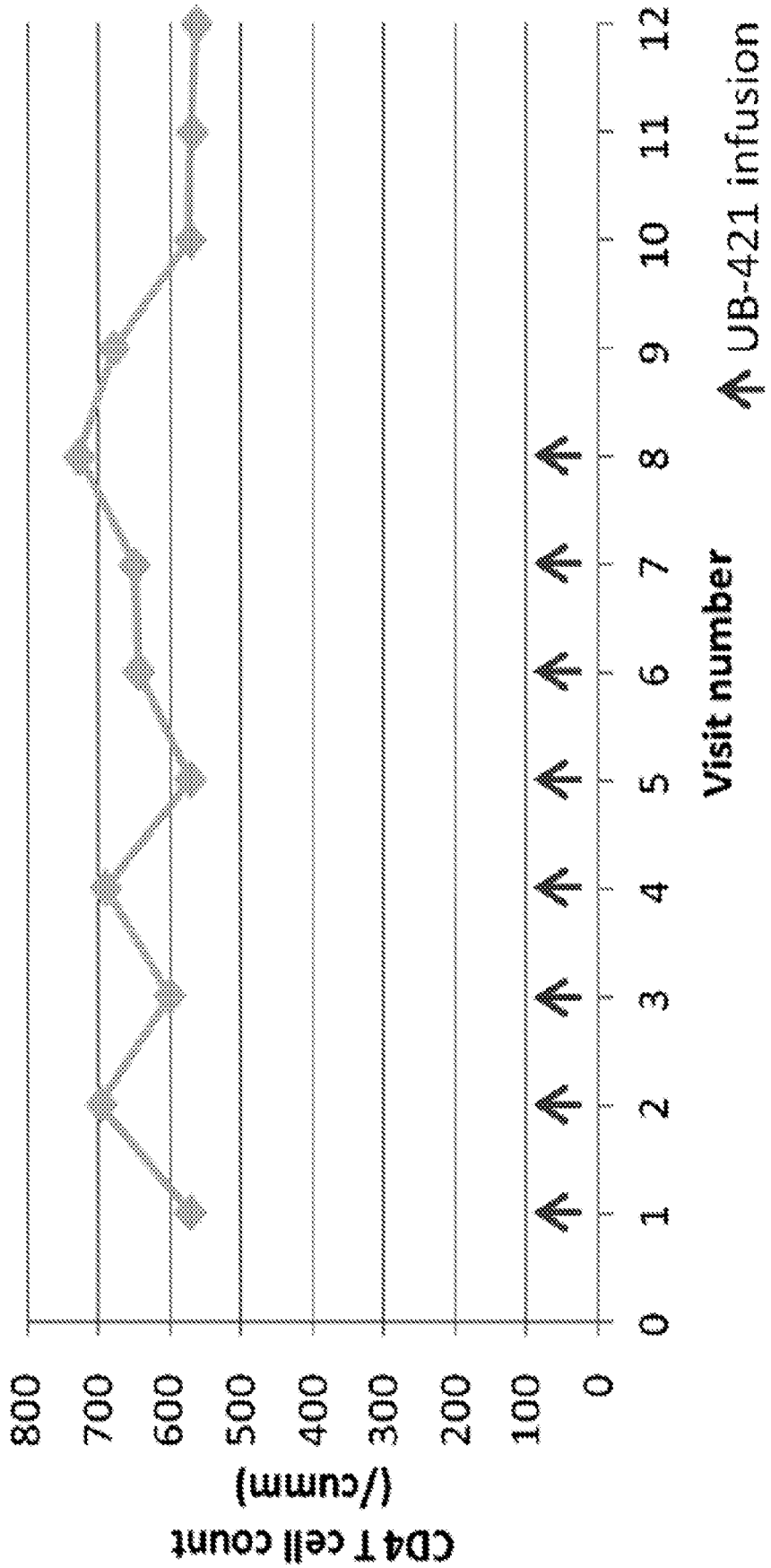

Mean CD4 T cell count
CD4 T cell count (/cumm)
800
700
600
500
400
300
200
100
0
0 1 2 3 4 5 6 7 8 9 10 11 12
Visit number
UB-421 infusion

Figure 24b.

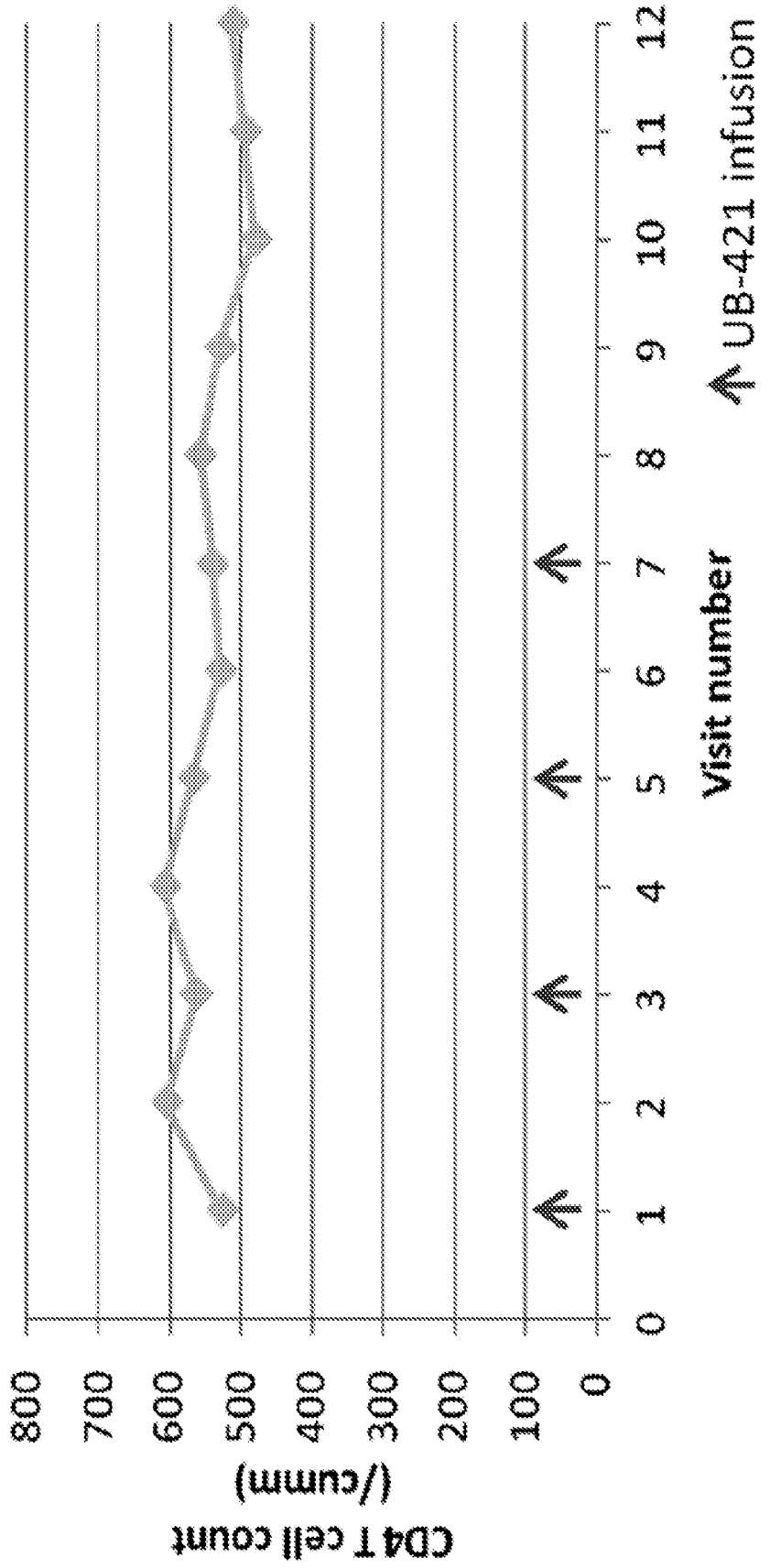

Mean CD4 T cell count
CD4 T cell count (/cumm)
800
700
600
500
400
300
200
100
0
0 1 2 3 4 5 6 7 8 9 10 11 12
Visit number
UB-421 infusion

Figure 25a.

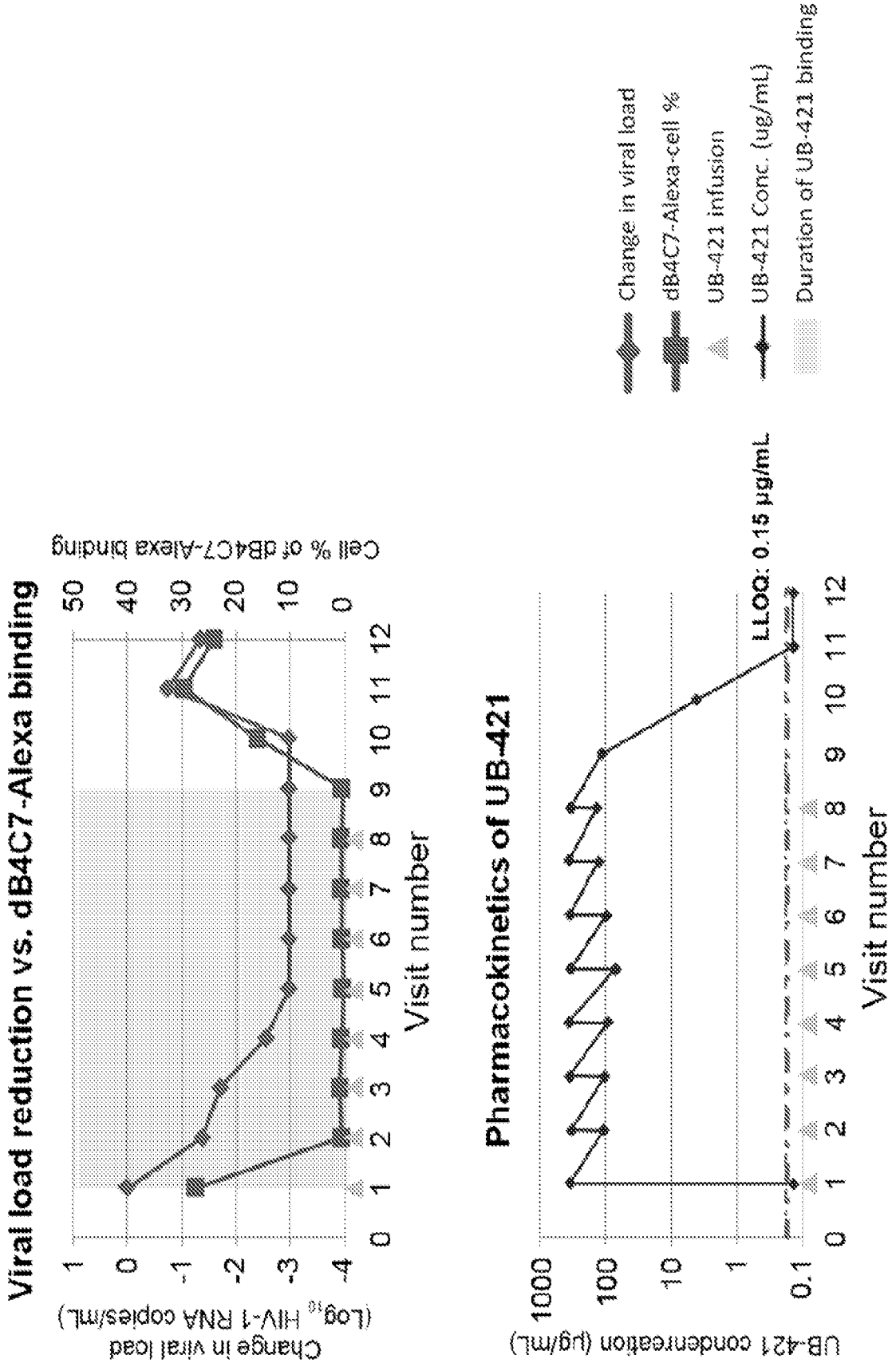

Viral load reduction vs. dB4C7-Alexa binding
Change in viral load (Log10 HIV-1 RNA copies/mL)
Cell % of dB4C7-Alexa binding
Visit number
Pharmacokinetics of UB-421
UB-421 condenreation (µg/mL)
LLOQ: 0.15 µg/mL
Visit number
Change in viral load
dB4C7-Alexa-cell %
UB-421 infusion
UB-421 Conc. (ug/mL)
Duration of UB-421 binding

Figure 25b.

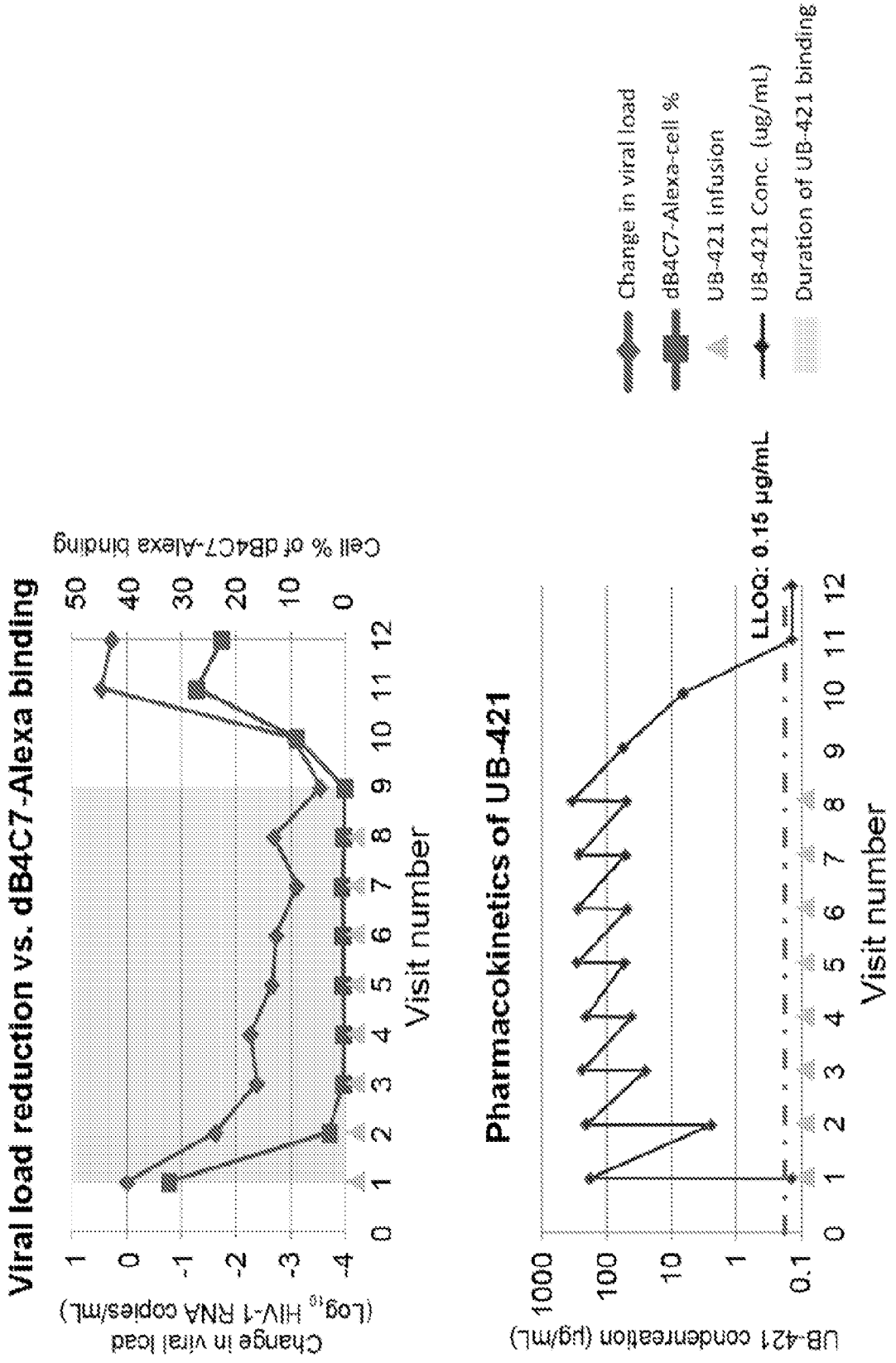

Viral load reduction vs. dB4C7-Alexa binding
Change in viral load (Log10 HIV-1 RNA copies/mL)
Cell % of dB4C7-Alexa binding
Visit number
Pharmacokinetics of UB-421
UB-421 condenreation (µg/mL)
LLOQ: 0.15 µg/mL
Visit number
Change in viral load
dB4C7-Alexa-cell %
UB-421 infusion
UB-421 Conc. (ug/mL)
Duration of UB-421 binding

Figure 25c.

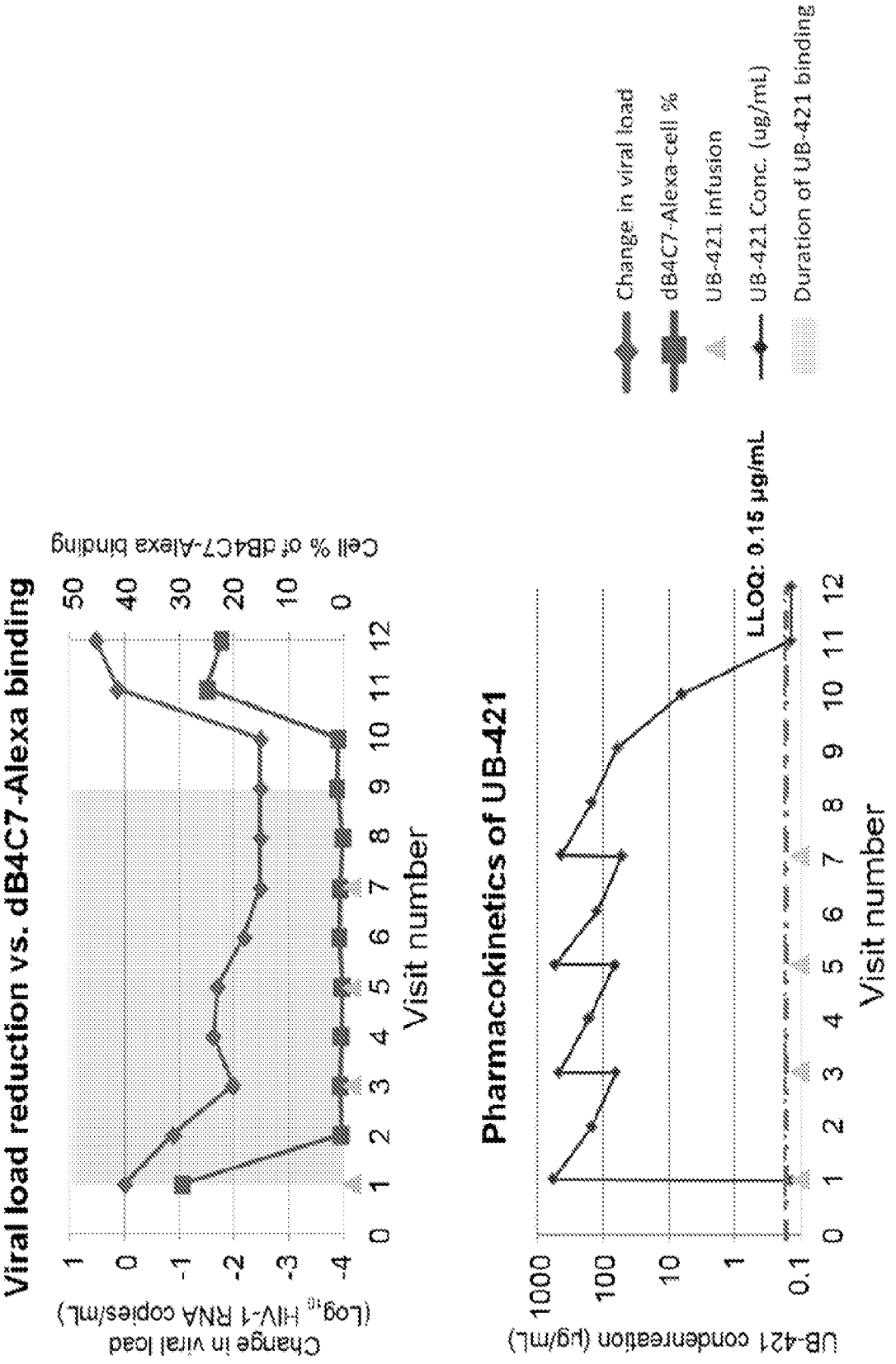

Viral load reduction vs. dB4C7-Alexa binding
Change in viral load (Log10 HIV-1 RNA copies/mL)
Cell % of dB4C7-Alexa binding
Visit number
Pharmacokinetics of UB-421
UB-421 condenreation (µg/mL)
LLOQ: 0.15 µg/mL
Visit number
Change in viral load
dB4C7-Alexa-cell %
UB-421 infusion
UB-421 Conc. (ug/mL)
Duration of UB-421 binding

Figure 25d.

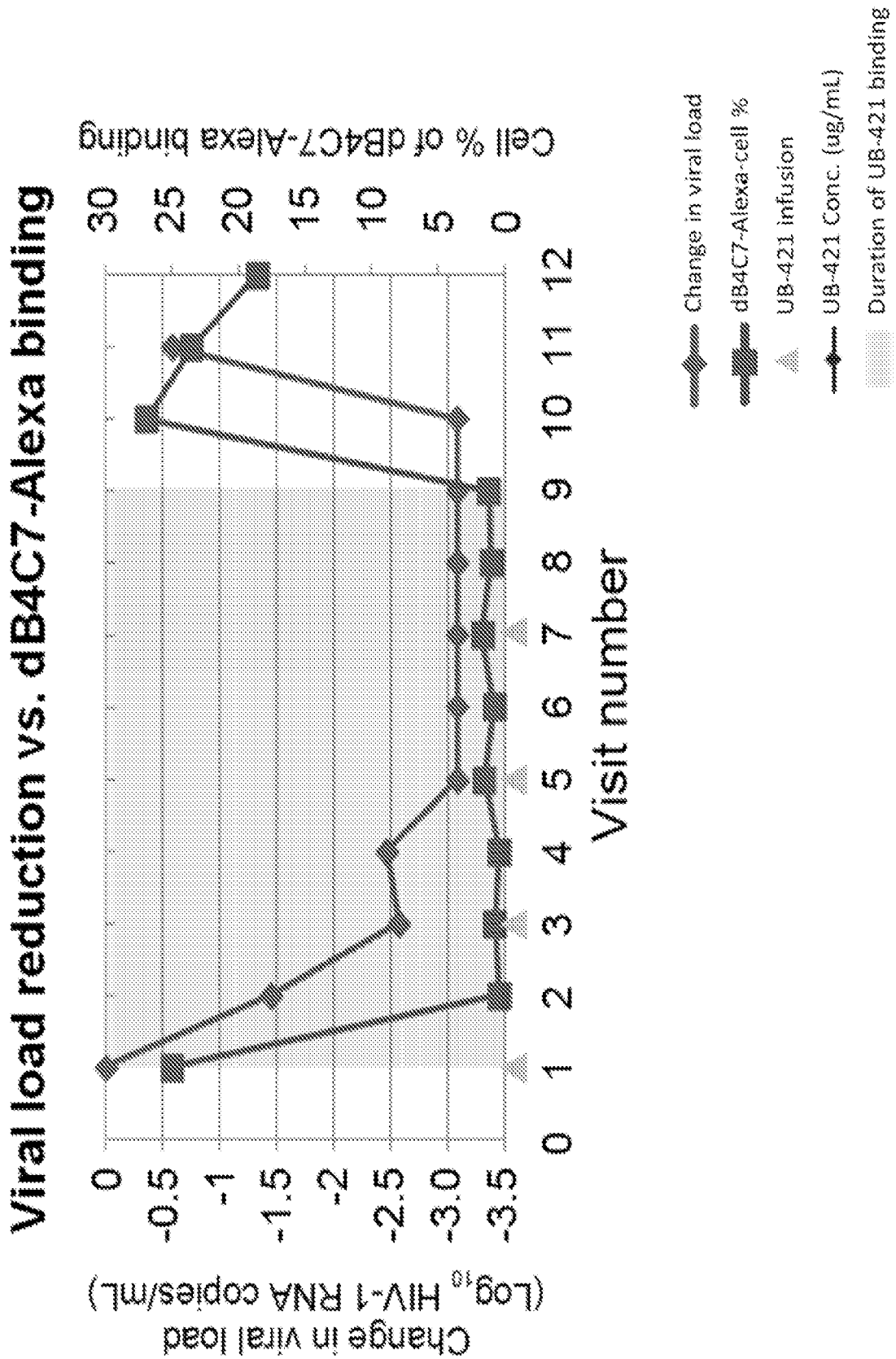

Viral load reduction vs. dB4C7-Alexa binding
Change in viral load (Log10 HIV-1 RNA copies/mL)
0
-0.5
-1
-1.5
-2
-2.5
-3.0
-3.5
Visit number
0 1 2 3 4 5 6 7 8 9 10 11 12
Cell % of dB4C7-Alexa binding
30 25 20 15 10 5 0
Change in viral load
dB4C7-Alexa-cell %
UB-421 infusion
UB-421 Conc. (ug/mL)
Duration of UB-421 binding

Figure 26a.

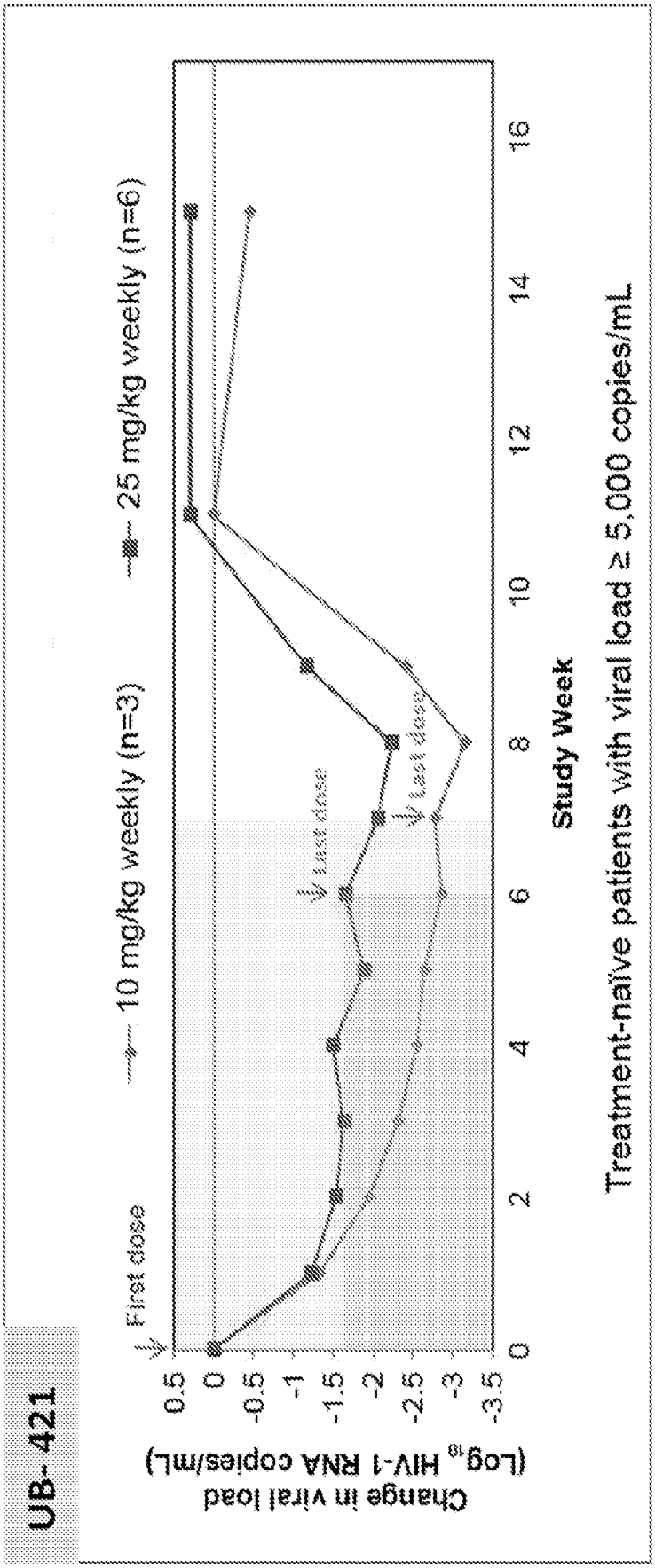

UB- 421
10 mg/kg weekly (n=3)
25 mg/kg weekly (n=6)
First dose
Last dose
Last dose
Change in viral load
(Log10 HIV-1 RNA copies/mL)
0.5
0
-0.5
-1
-1.5
-2
-2.5
-3
-3.5
0
2
4
6
8
10
12
14
16
Study Week
Treatment-naïve patients with viral load ≥ 5,000 copies/mL

Figure 26b.

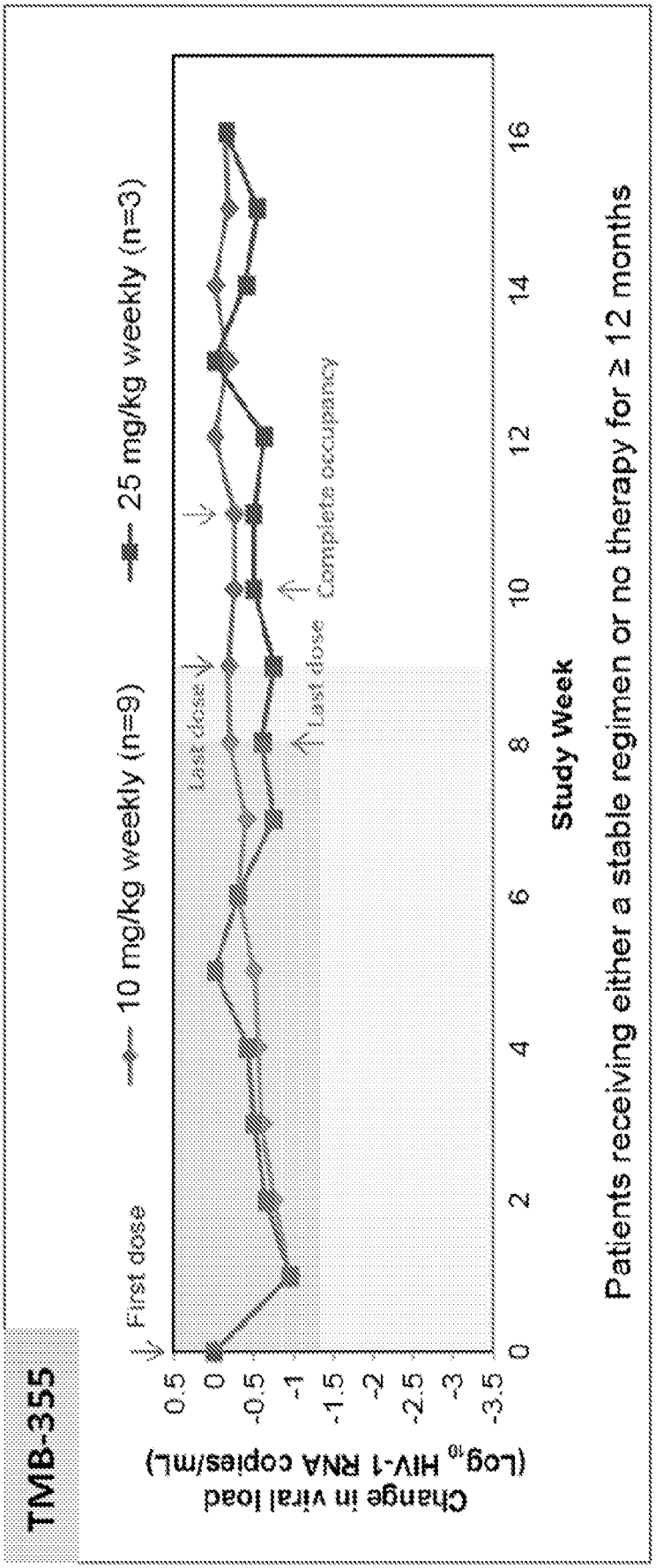

TMB-355
Change in viral load
(Log10 HIV-1 RNA copies/mL)
0.5
0
-0.5
-1
-1.5
-2
-2.5
-3
-3.5
0
2
4
6
8
10
12
14
16
Study Week
First dose
10 mg/kg weekly (n=9)
25 mg/kg weekly (n=3)
Last dose
Last dose
Complete occupancy
Patients receiving either a stable regimen or no therapy for ≥ 12 months

Figure 27. UB421 monotherapy as HAART Replacement Therapy

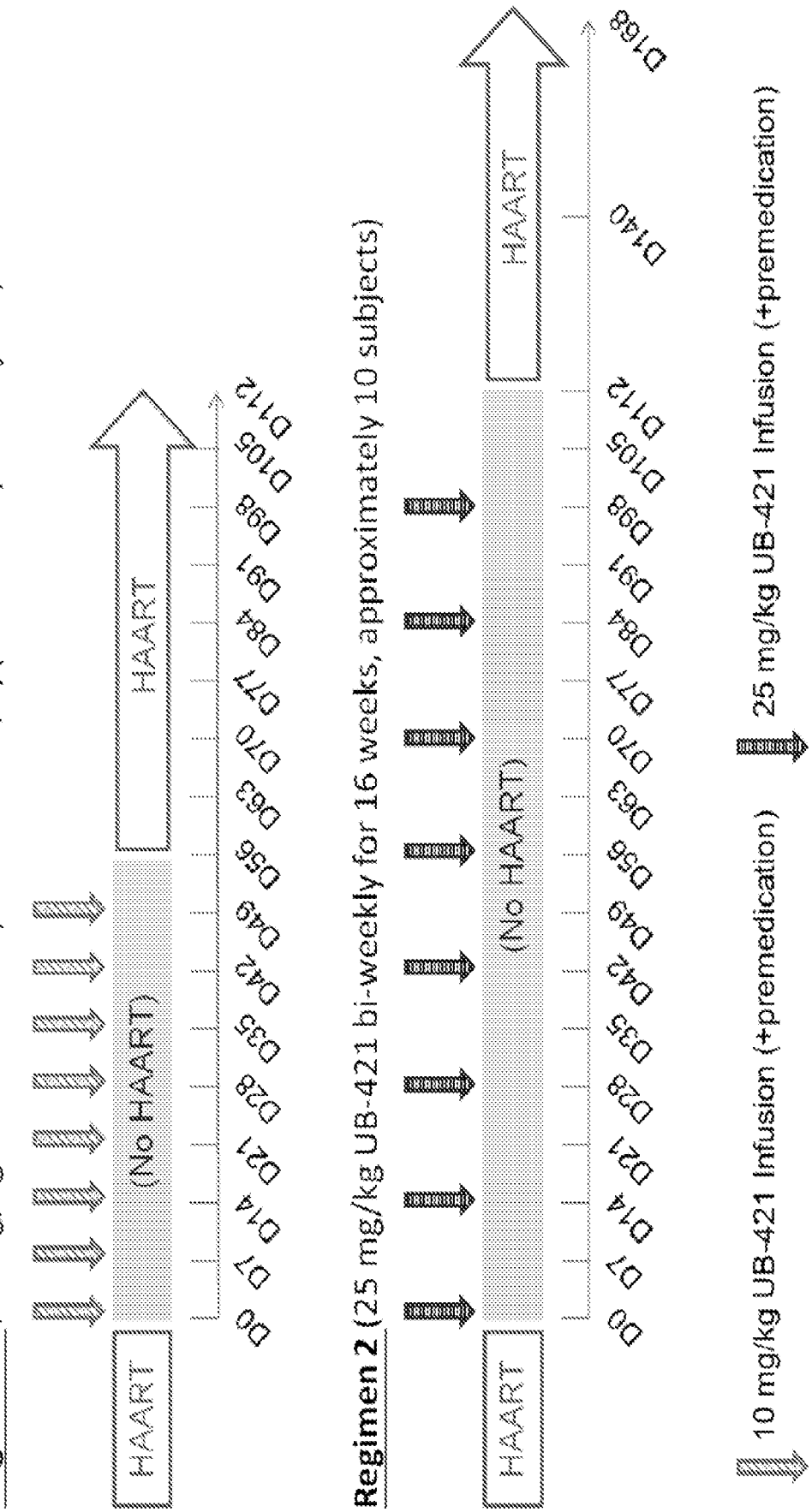


Figure 28. Combination of UB421 and HAART for Functional Cure of HIV Infection

