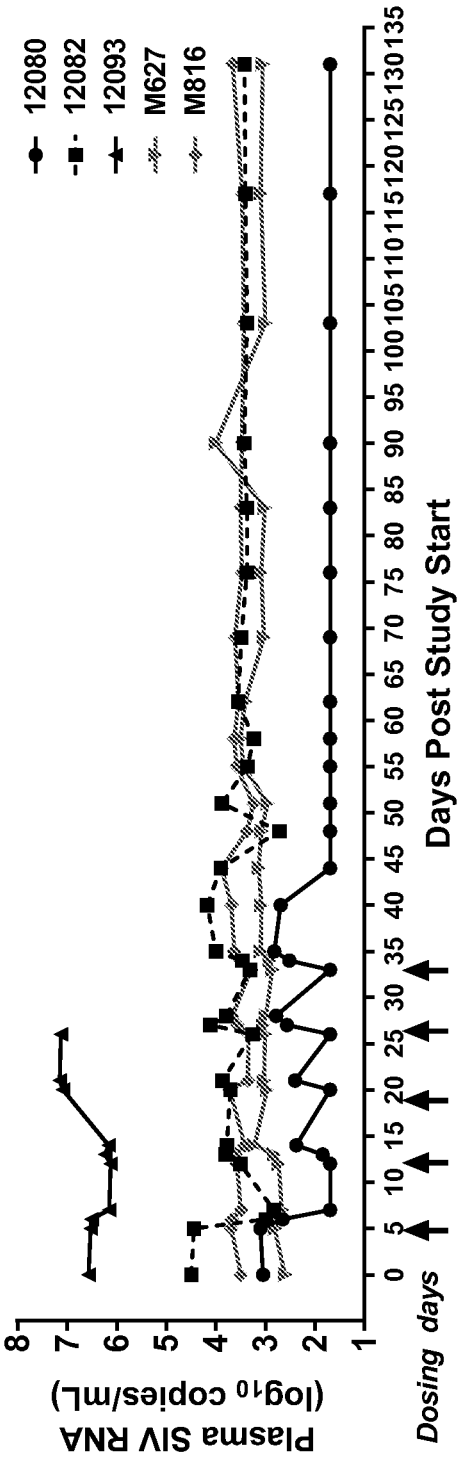

12080
12082
12093
M627
M816
Plasma SIV RNA
(log10 copies/mL)
8
7
6
5
4
3
2
1
Dosing days
0 5 10 15 20 25 30 35 40 45 50 55 60 65 70 75 80 85 90 95 100 105 110 115 120 125 130 135
Days Post Study Start

Fig. 1

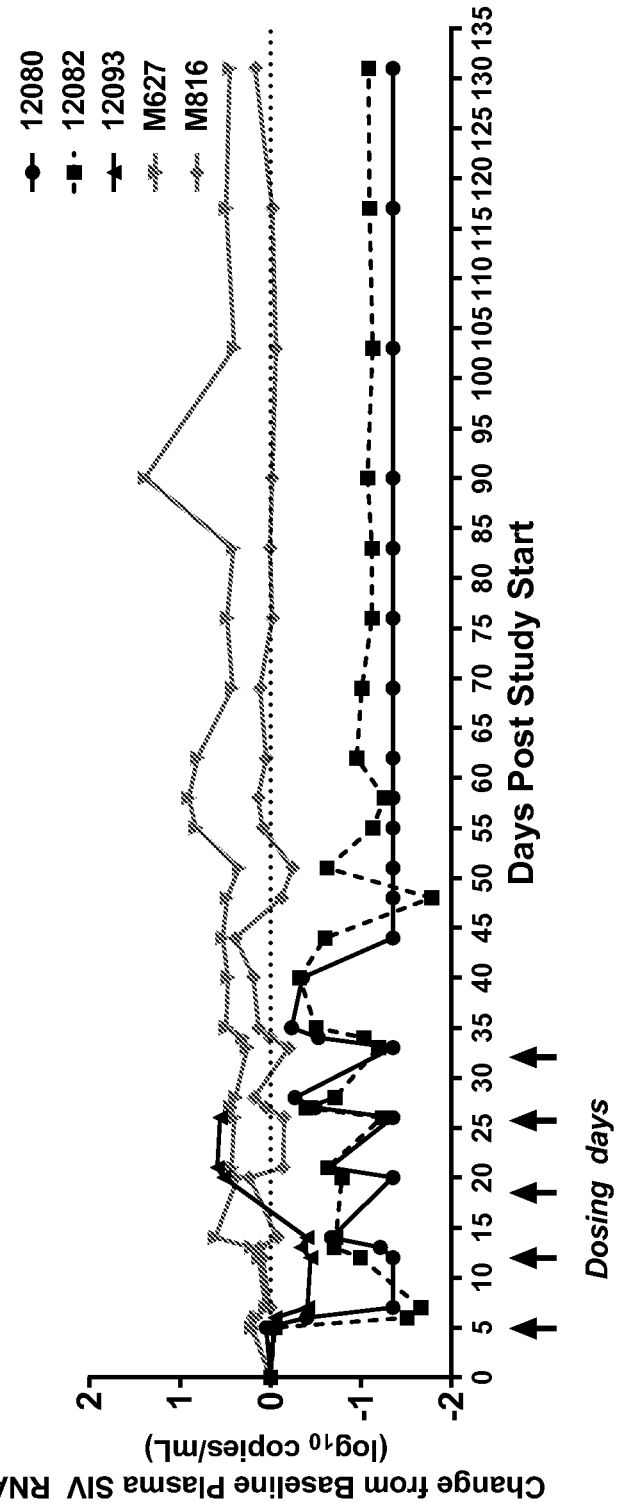

12080
12082
12093
M627
M816
Change from Baseline Plasma SIV RNA
(log10 copies/mL)
2
1
0
-1
-2
0 5 10 15 20 25 30 35 40 45 50 55 60 65 70 75 80 85 90 95 100 105 110 115 120 125 130 135
Days Post Study Start
Dosing days

Fig. 2

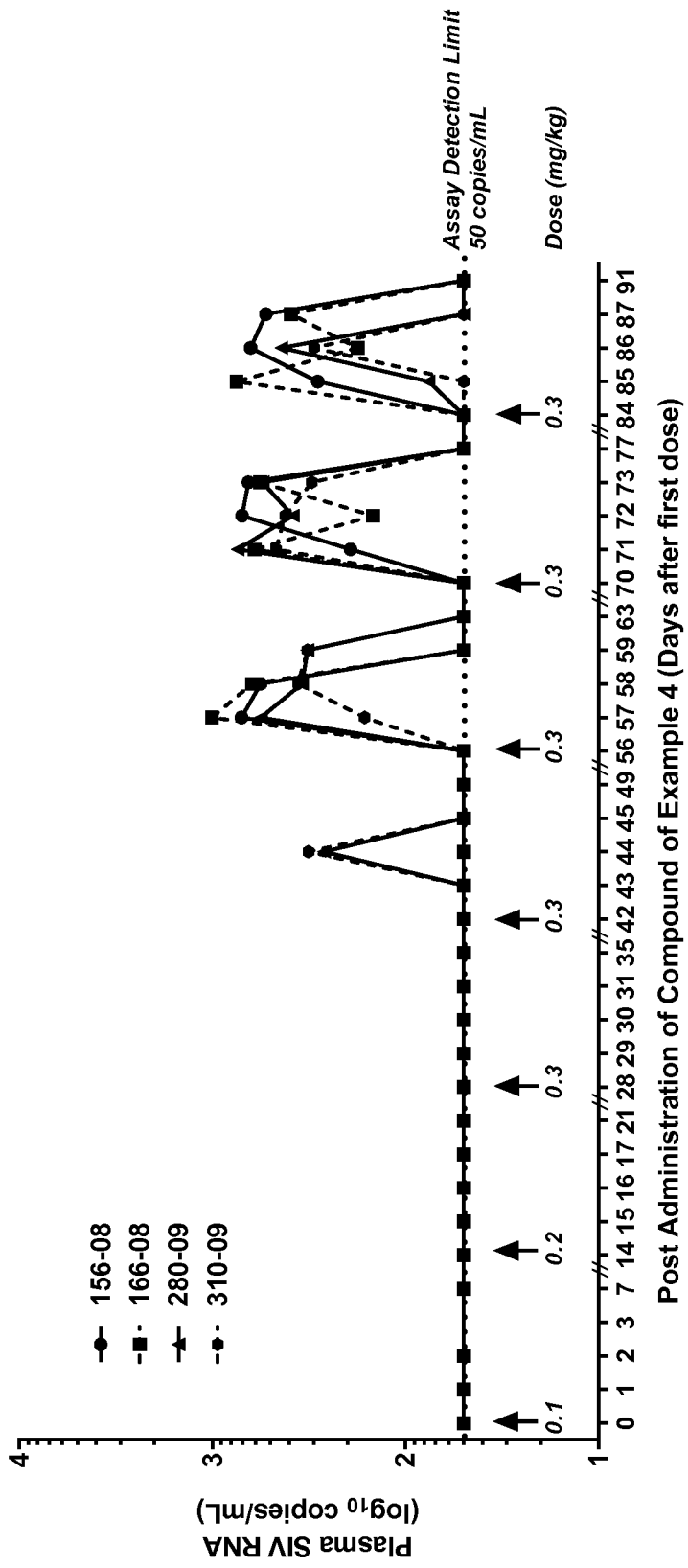

Plasma SIV RNA
(log10 copies/mL)
4
3
2
1
156-08
166-08
280-09
310-09
Assay Detection Limit
50 copies/mL
Dose (mg/kg)
0.1
0.2
0.3
0.3
0.3
0.3
0.3
0 1 2 3 7 14 15 16 17 21 28 29 30 31 35 42 43 44 45 49 56 57 58 59 63 70 71 72 73 77 84 85 86 87 91
Post Administration of Compound of Example 4 (Days after first dose)

Fig. 3

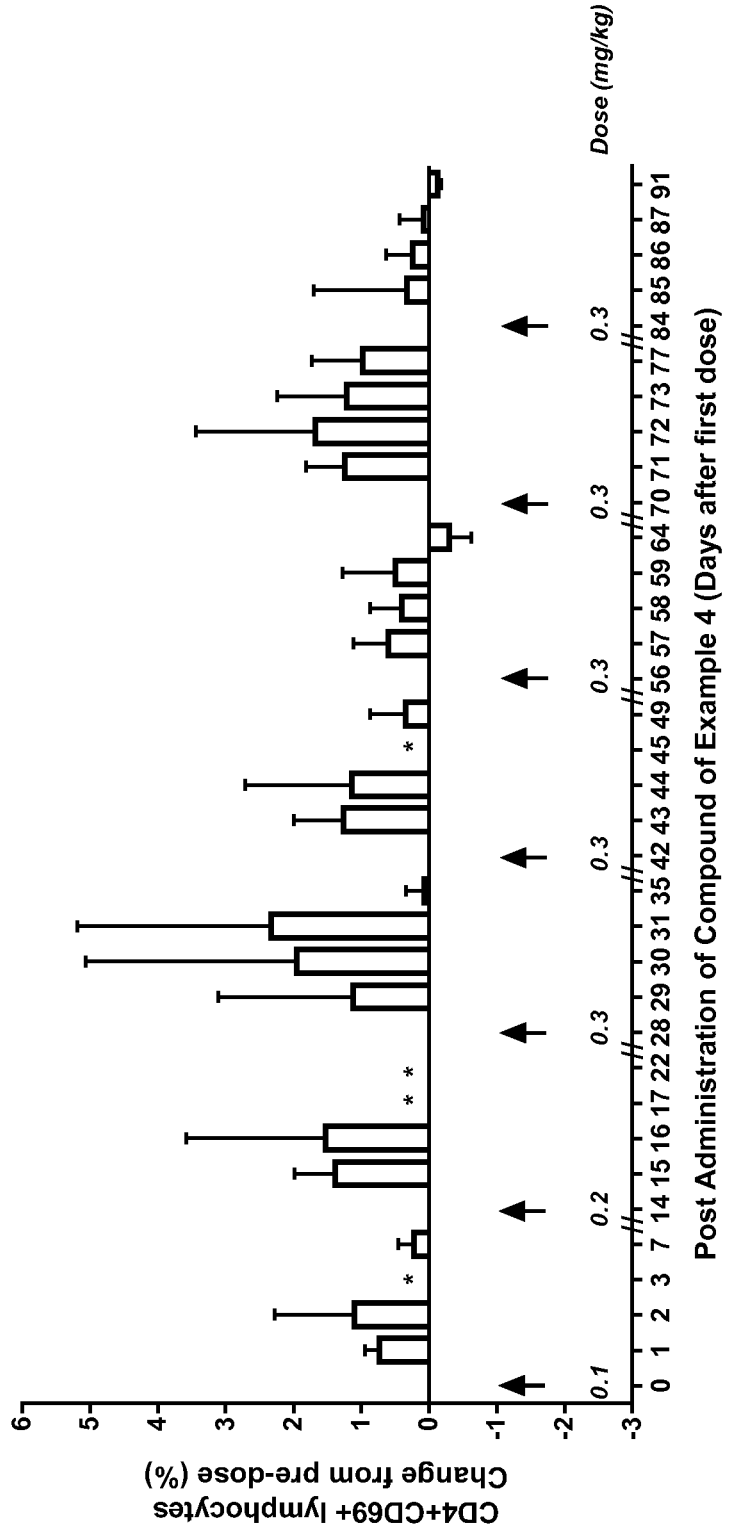

CD4+CD69+ lymphocytes
Change from pre-dose (%)
6
5
4
3
2
1
0
-1
-2
-3
0 1 2 3 7 14 15 16 17 22 28 29 30 31 35 42 43 44 45 49 56 57 58 59 64 70 71 72 73 77 84 85 86 87 91
Post Administration of Compound of Example 4 (Days after first dose)
Dose (mg/kg)
0.1
0.2
0.3
0.3
0.3
0.3
0.3
*
*
*
*

Fig. 4

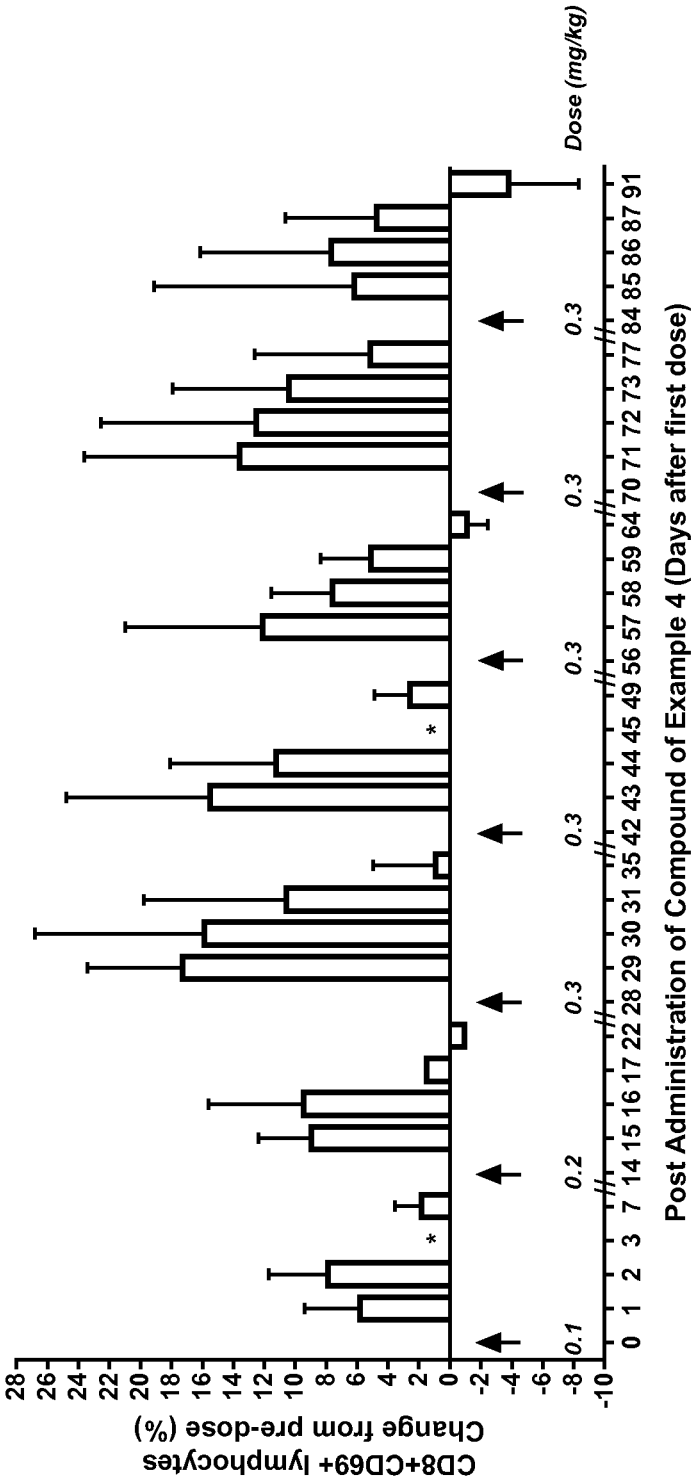

CD8+CD69+ lymphocytes
Change from pre-dose (%)
28 26 24 22 20 18 16 14 12 10 8 6 4 2 0 -2 -4 -6 -8 -10
0 1 2 3 7 14 15 16 17 22 28 29 30 31 35 42 43 44 45 49 56 57 58 59 64 70 71 72 73 77 84 85 86 87 91
Post Administration of Compound of Example 4 (Days after first dose)
Dose (mg/kg)
0.1
0.2
0.3
0.3
0.3
0.3
0.3
*
*

Fig. 5

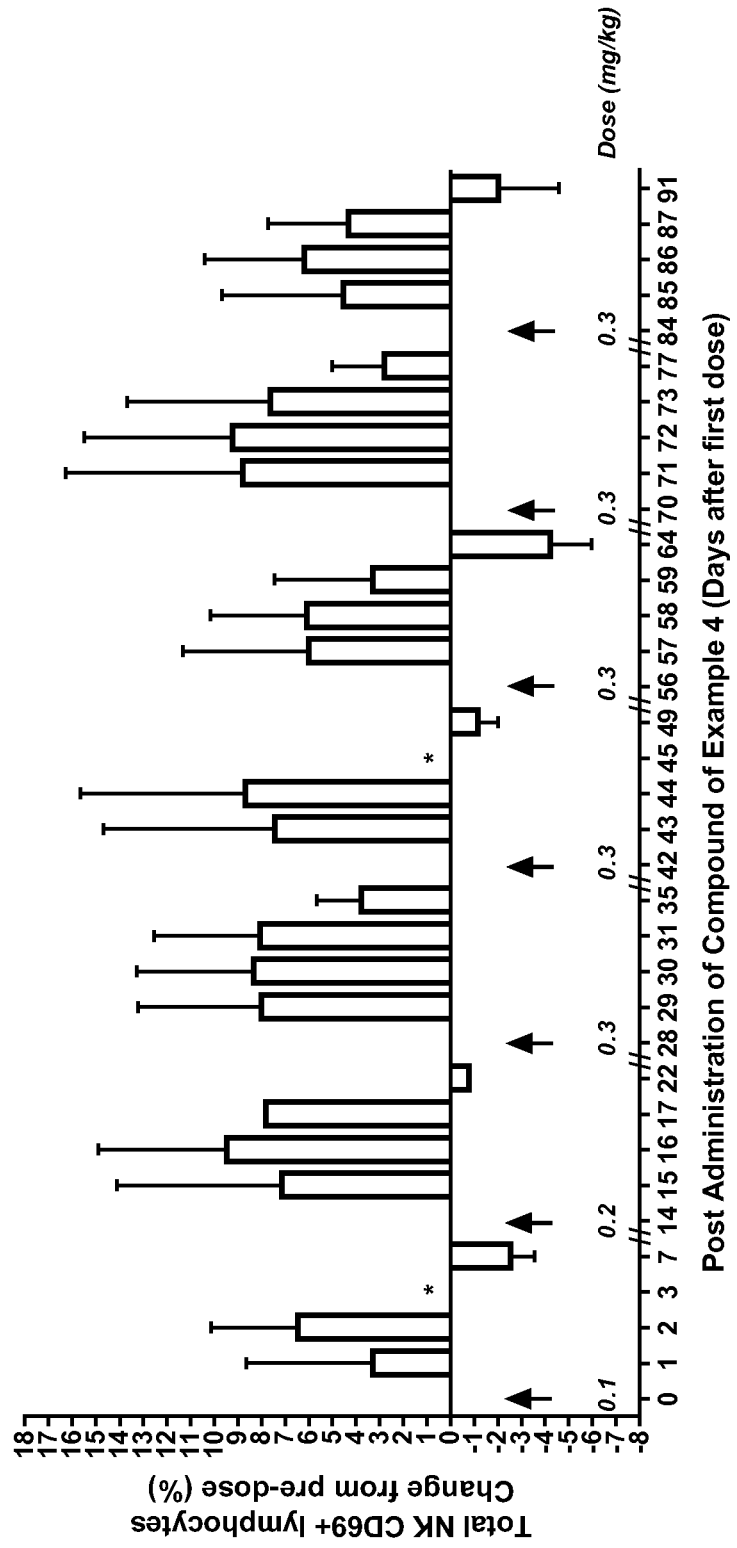

Total NK CD69+ lymphocytes
Change from pre-dose (%)
18 17 16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4 -5 -6 -7 -8
0 1 2 3 7 14 15 16 17 22 28 29 30 31 35 42 43 44 45 49 56 57 58 59 64 70 71 72 73 77 84 85 86 87 91
Post Administration of Compound of Example 4 (Days after first dose)
Dose (mg/kg)
0.1
0.2
0.3
0.3
0.3
0.3
*
*

Fig. 6

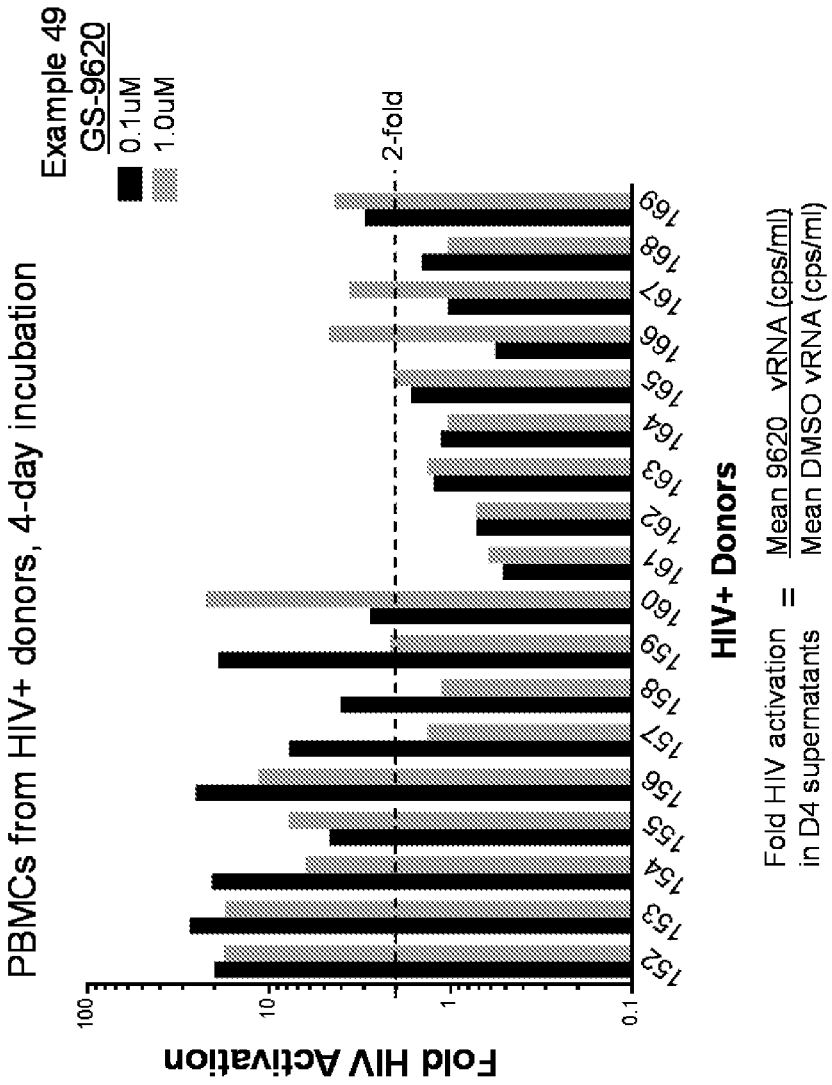

PBMCs from HIV+ donors, 4-day incubation
Example 49
GS-9620
0.1uM
1.0uM
2-fold
Fold HIV Activation
100
10
1
0.1
152
153
154
155
156
157
158
159
160
161
162
163
164
165
166
167
168
169
HIV+ Donors
Fold HIV activation in D4 supernatants = Mean 9620 vRNA (cps/ml) / Mean DMSO vRNA (cps/ml)

Fig. 7.


GS-9620
GS-9620 + IFNAR block
Donor 2
Fold HIV Activation
0
10
20
30
10
100
1000
10000
GS-9620 [nM]
Donor 1
Fold HIV Activation
0
5
10
15
20
10
100
1000
10000
GS-9620 [nM]

Fig. 8

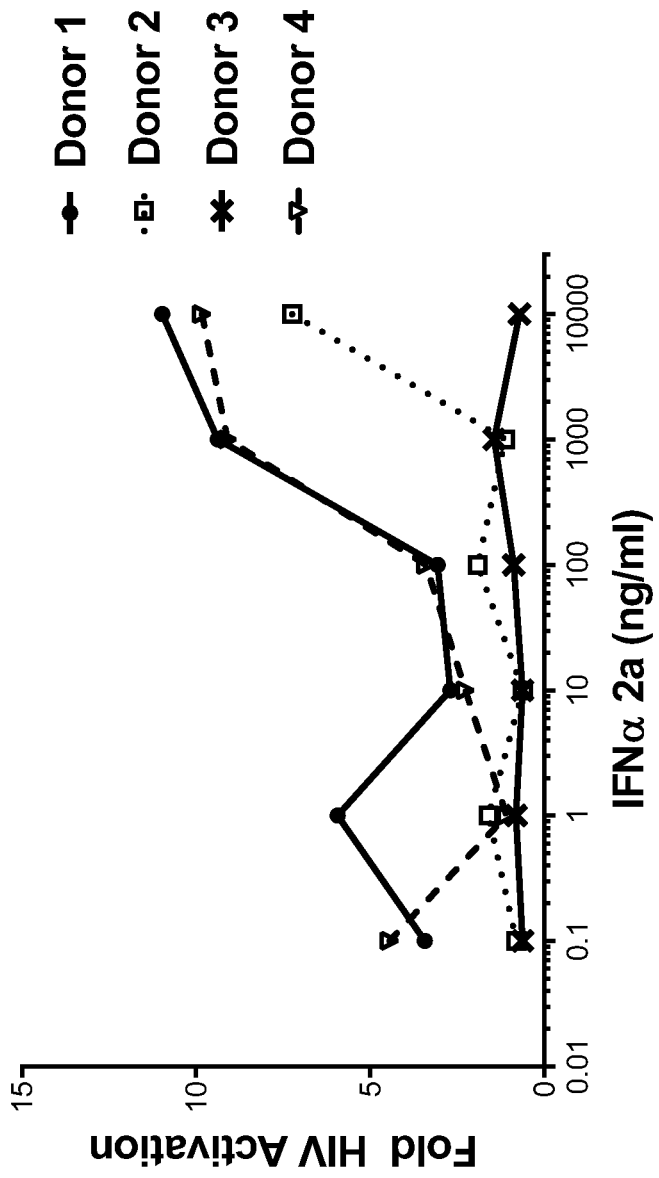
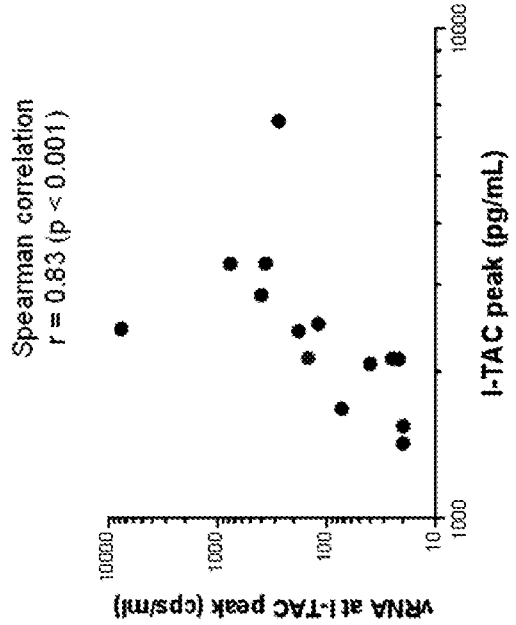

Donor 1
Donor 2
Donor 3
Donor 4
Fold HIV Activation
15
10
5
0
0.01
0.1
1
10
100
1000
10000
IFNα 2a (ng/ml)

Fig. 9


Spearman correlation
r = 0.83 (p < 0.001)
vRNA at I-TAC peak (cps/ml)
I-TAC peak (pg/mL)
10000
1000
100
10
1000
10000

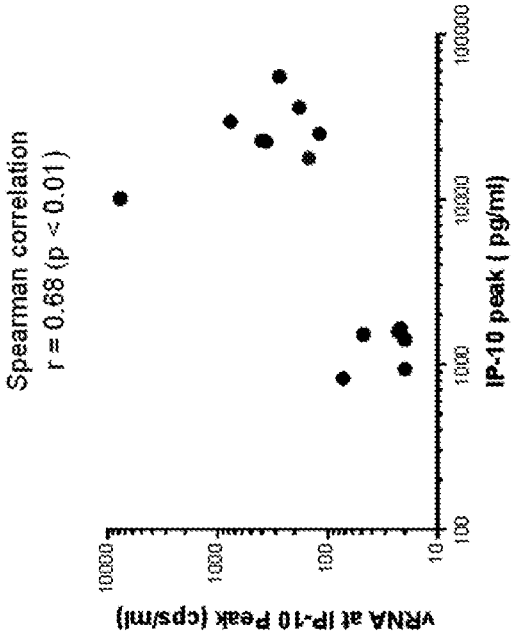
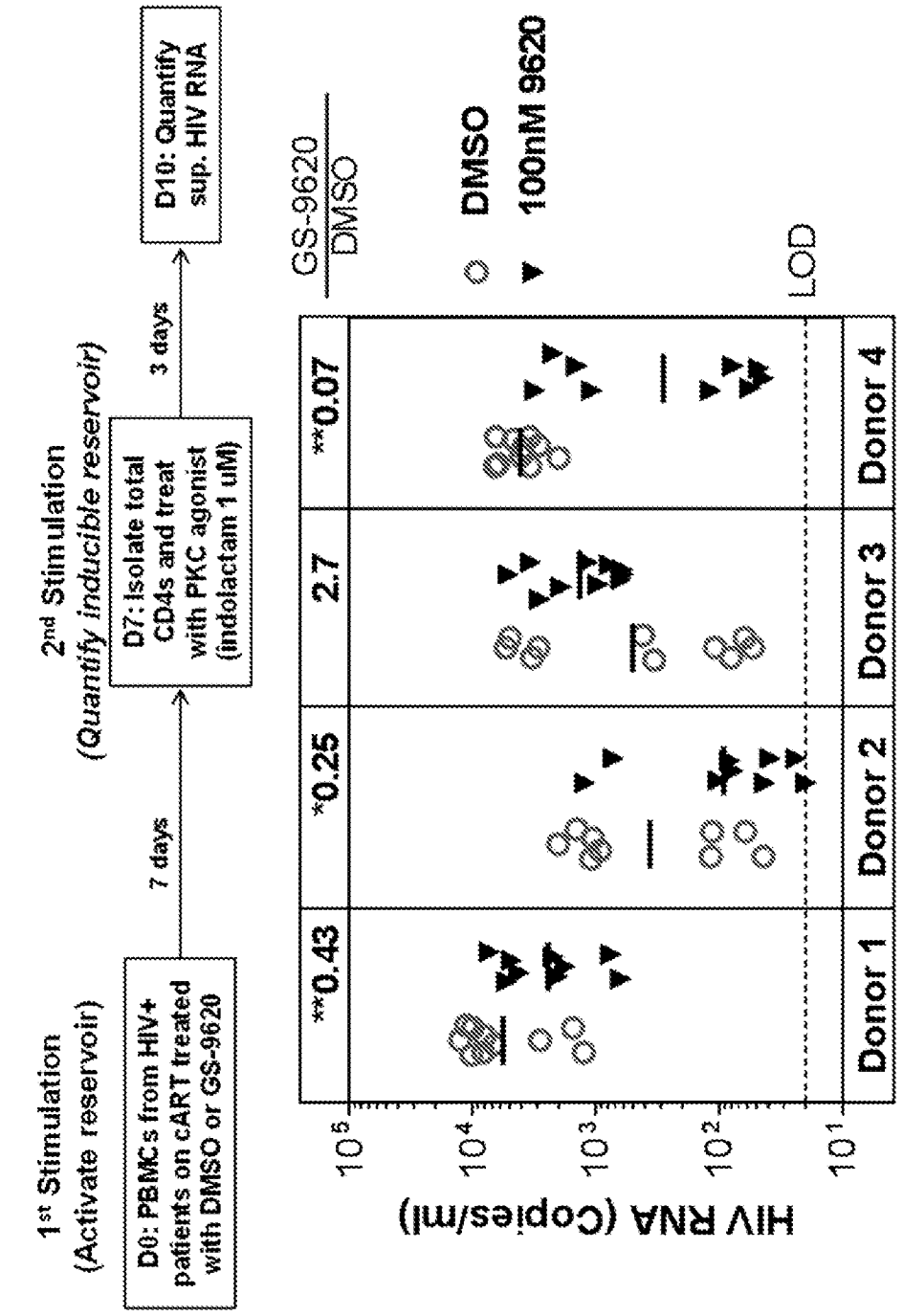

Spearman correlation
r = 0.68 (p < 0.01)
vRNA at IP-10 Peak (cps/ml)
IP-10 peak (pg/ml)
10000
1000
100
10
100
1000
10000
100000

Fig. 10

Fig. 11


1st Stimulation
(Activate reservoir)
D0: PBMCs from HIV+ patients on cART treated with DMSO or GS-9620
7 days
2nd Stimulation
(Quantify inducible reservoir)
D7: Isolate total CD4s and treat with PKC agonist (indolactam 1 uM)
3 days
D10: Quantify sup. HIV RNA
GS-9620 / DMSO
**0.43
*0.25
2.7
**0.07
DMSO
100nM 9620
LOD
HIV RNA (Copies/ml)
10^5
10^4
10^3
10^2
10^1
Donor 1
Donor 2
Donor 3
Donor 4

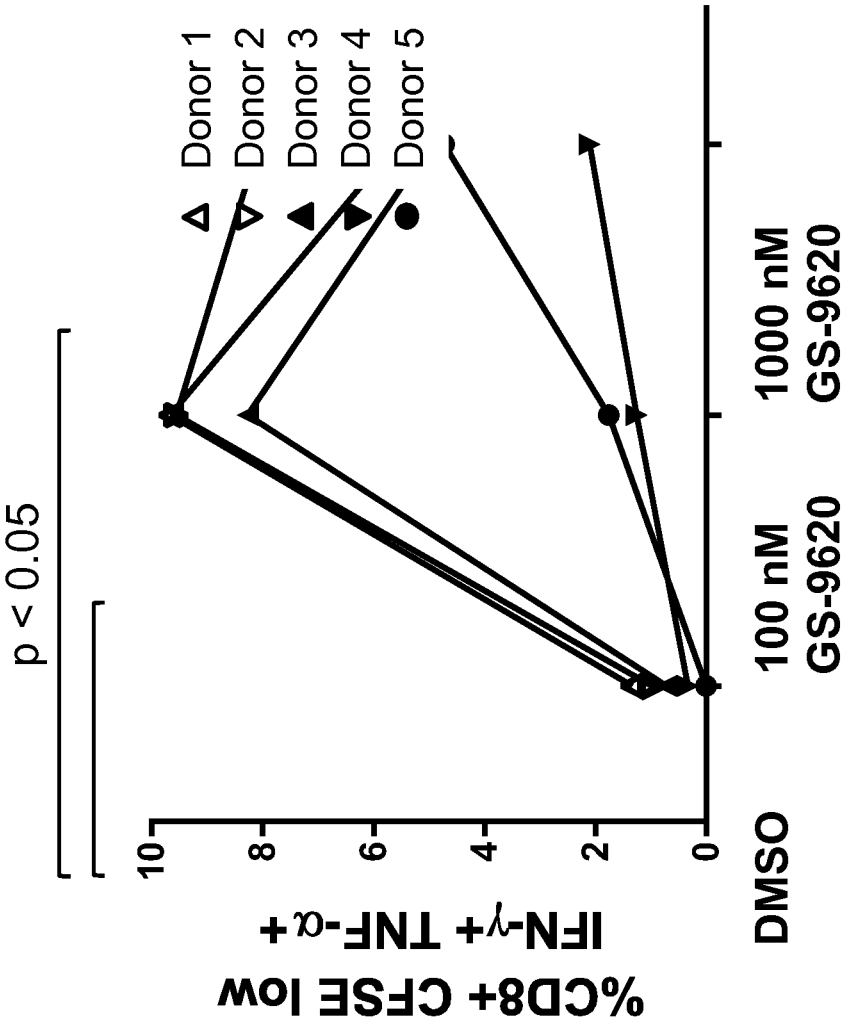

%CD8+ CFSE low
IFN-γ+ TNF-α+
10
8
6
4
2
0
p < 0.05
Donor 1
Donor 2
Donor 3
Donor 4
Donor 5
DMSO
100 nM GS-9620
1000 nM GS-9620

Fig. 12

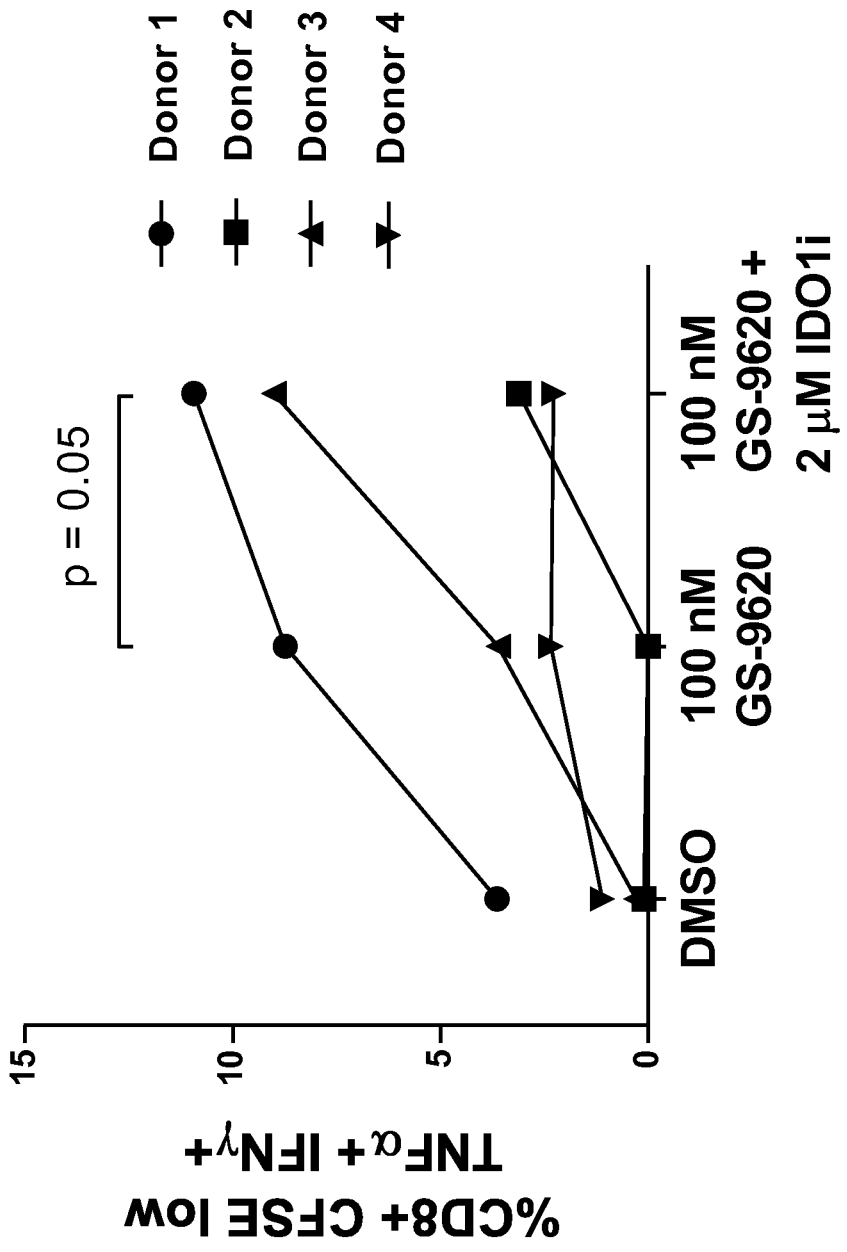

%CD8+ CFSE low
TNFα+ IFNγ+
15
10
5
0
p = 0.05
Donor 1
Donor 2
Donor 3
Donor 4
DMSO
100 nM GS-9620
100 nM GS-9620 + 2 μM IDO1i

Fig. 13

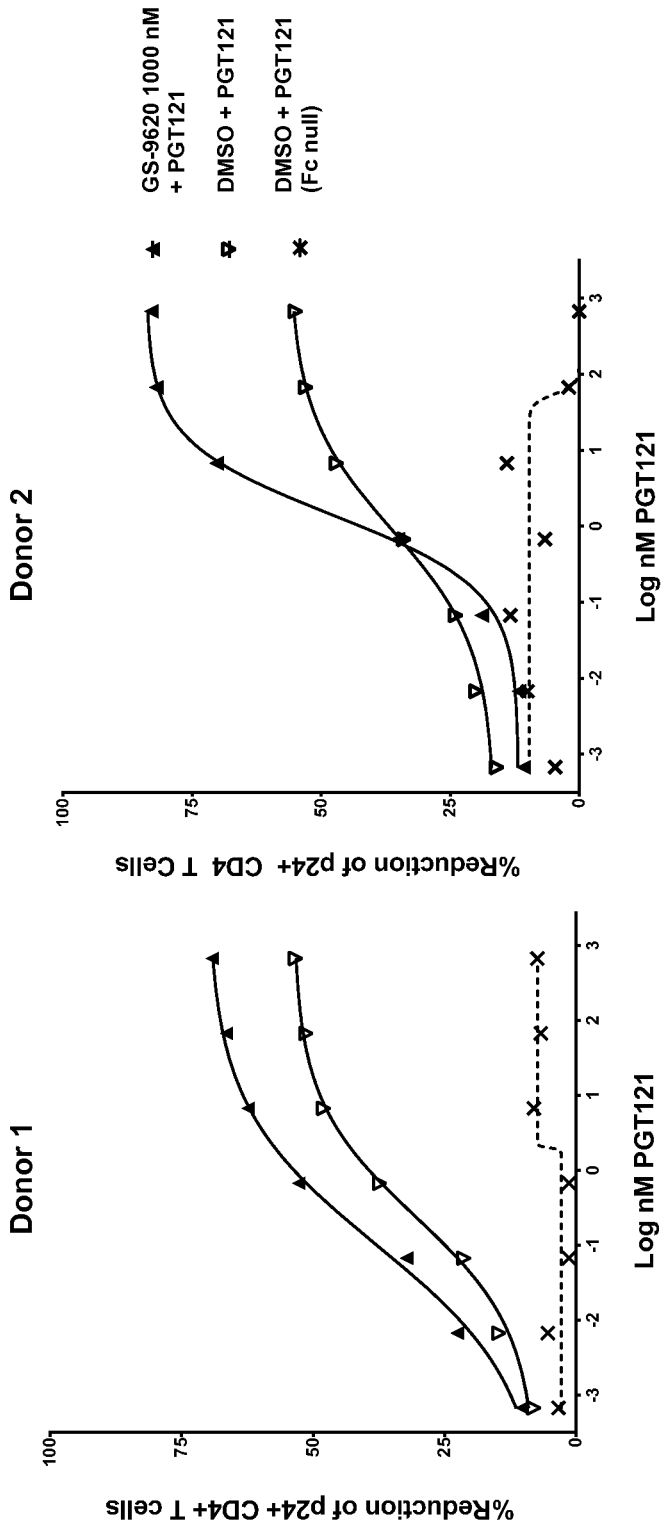

Donor 1
%Reduction of p24+ CD4+ T cells
Log nM PGT121
Donor 2
%Reduction of p24+ CD4+ T Cells
Log nM PGT121
GS-9620 1000 nM + PGT121
DMSO + PGT121
DMSO + PGT121 (Fc null)

Fig. 14