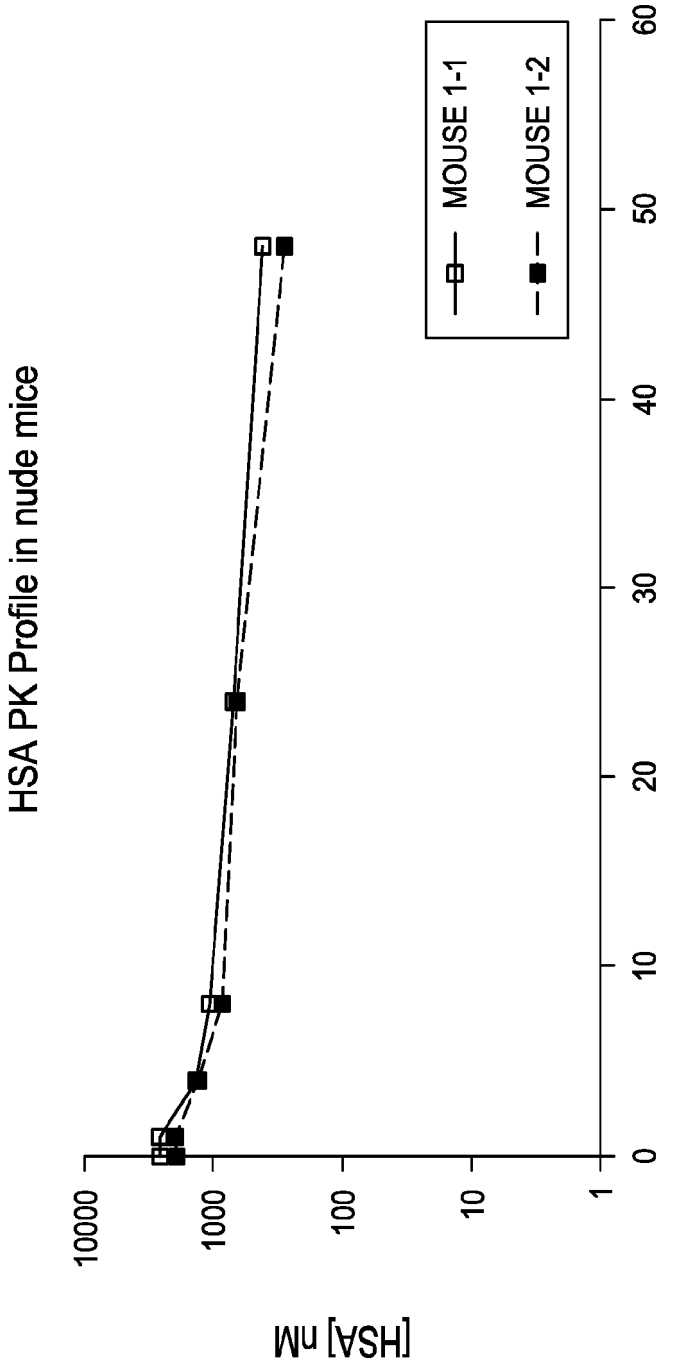

HSA PK Profile in nude mice
MOUSE 1-1
MOUSE 1-2
[HSA] nM
10000
1000
100
10
1
0
10
20
30
40
50
60
TIME (hrs)

FIGURE 1A

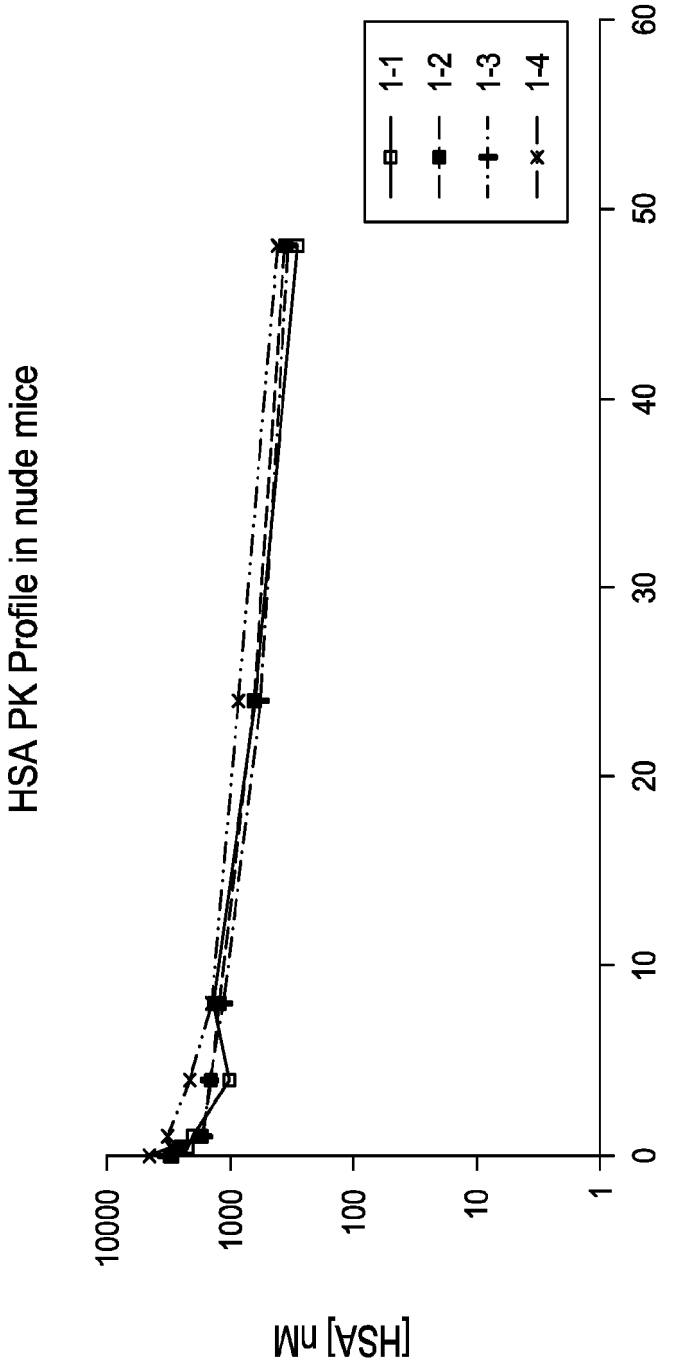

HSA PK Profile in nude mice
[HSA] nM
10000
1000
100
10
1
0
10
20
30
40
50
60
TIME (hrs)
1-1
1-2
1-3
1-4

FIGURE 1B

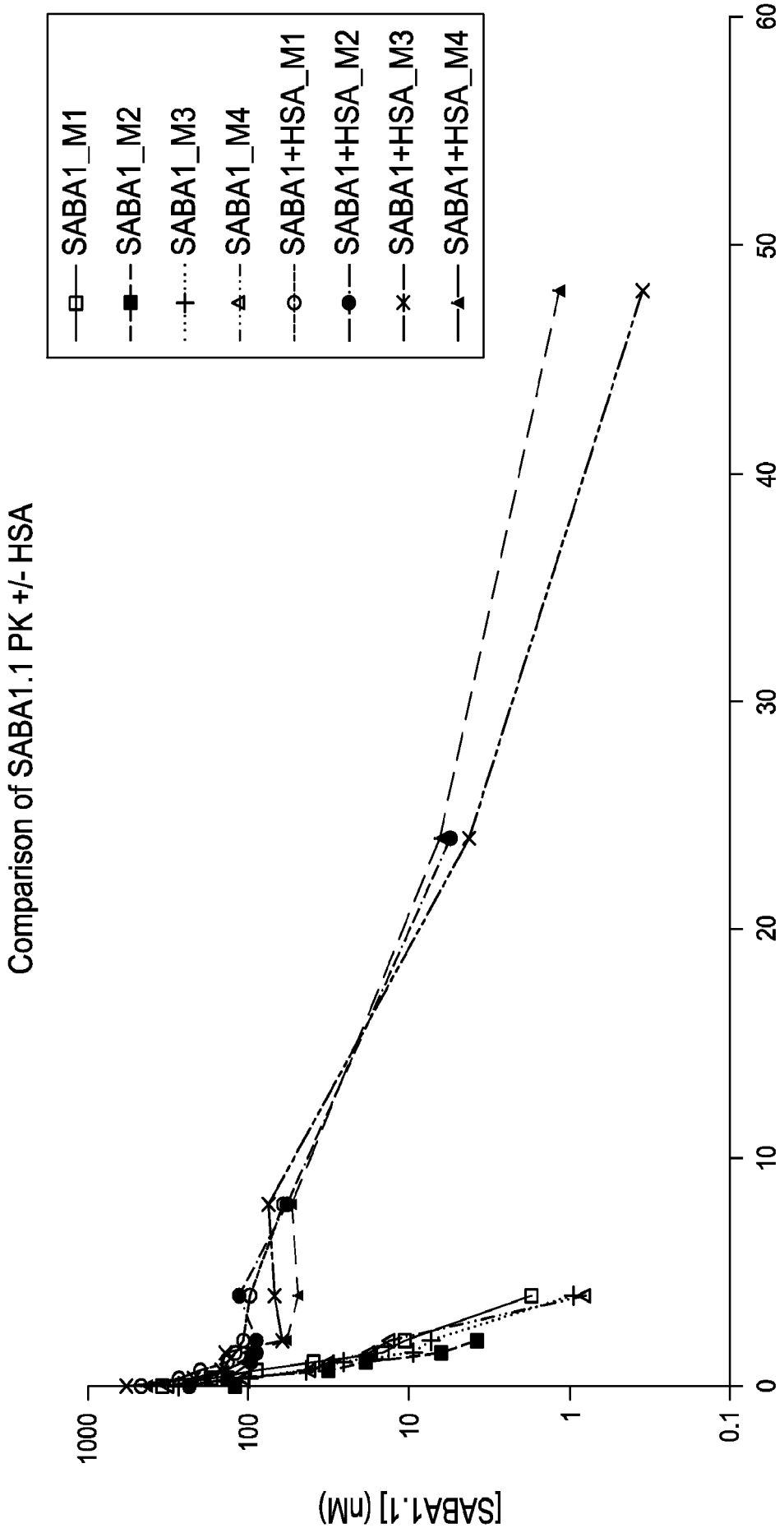

Comparison of SABA1.1 PK +/- HSA
SABA1_M1
SABA1_M2
SABA1_M3
SABA1_M4
SABA1+HSA_M1
SABA1+HSA_M2
SABA1+HSA_M3
SABA1+HSA_M4
[SABA1.1] (nM)
1000
100
10
1
0.1
0
10
20
30
40
50
60
TIME (hrs)

FIGURE 2A

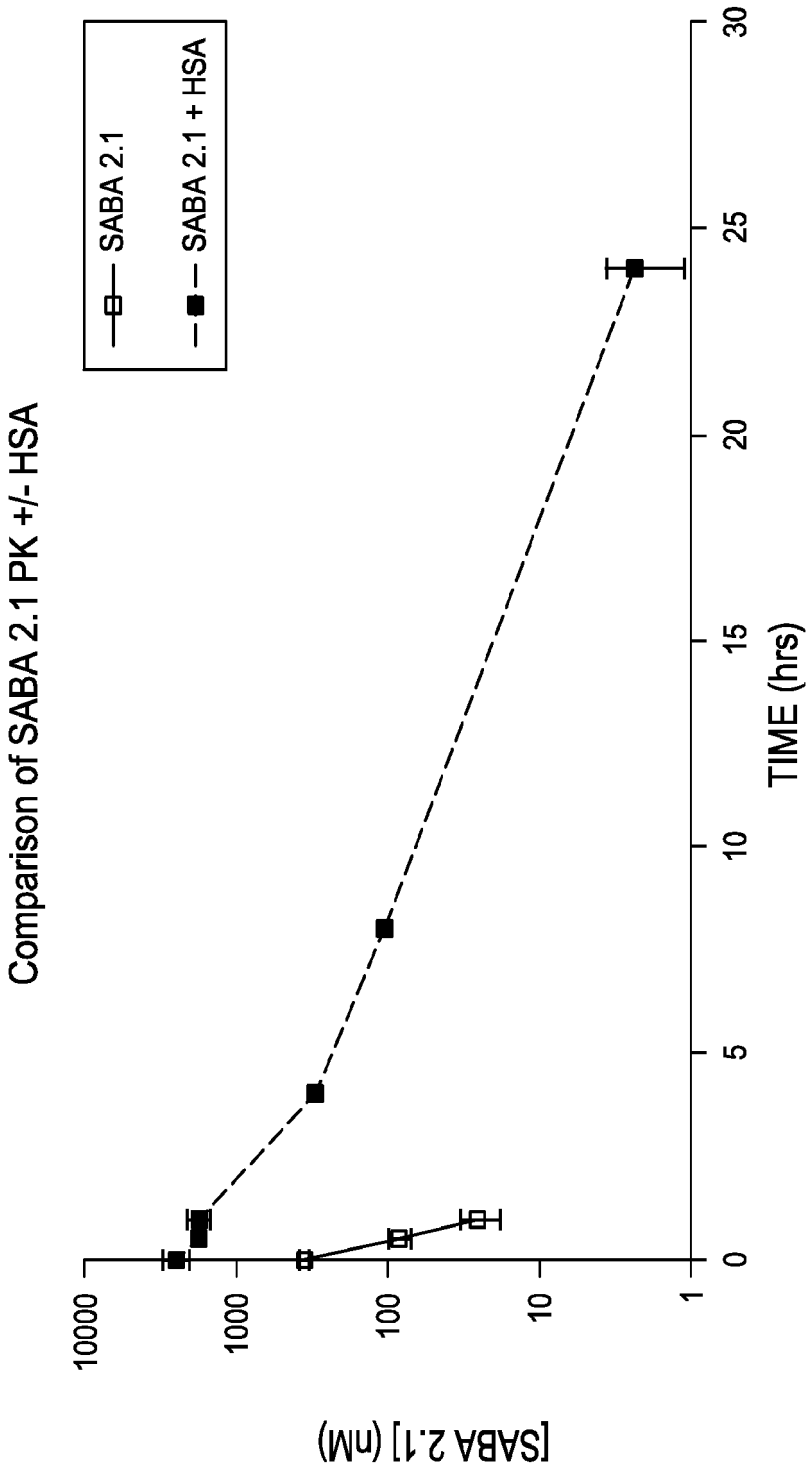

Comparison of SABA 2.1 PK +/- HSA
SABA 2.1
SABA 2.1 + HSA
[SABA 2.1] (nM)
10000
1000
100
10
1
0
5
10
15
20
25
30
TIME (hrs)

FIGURE 2B

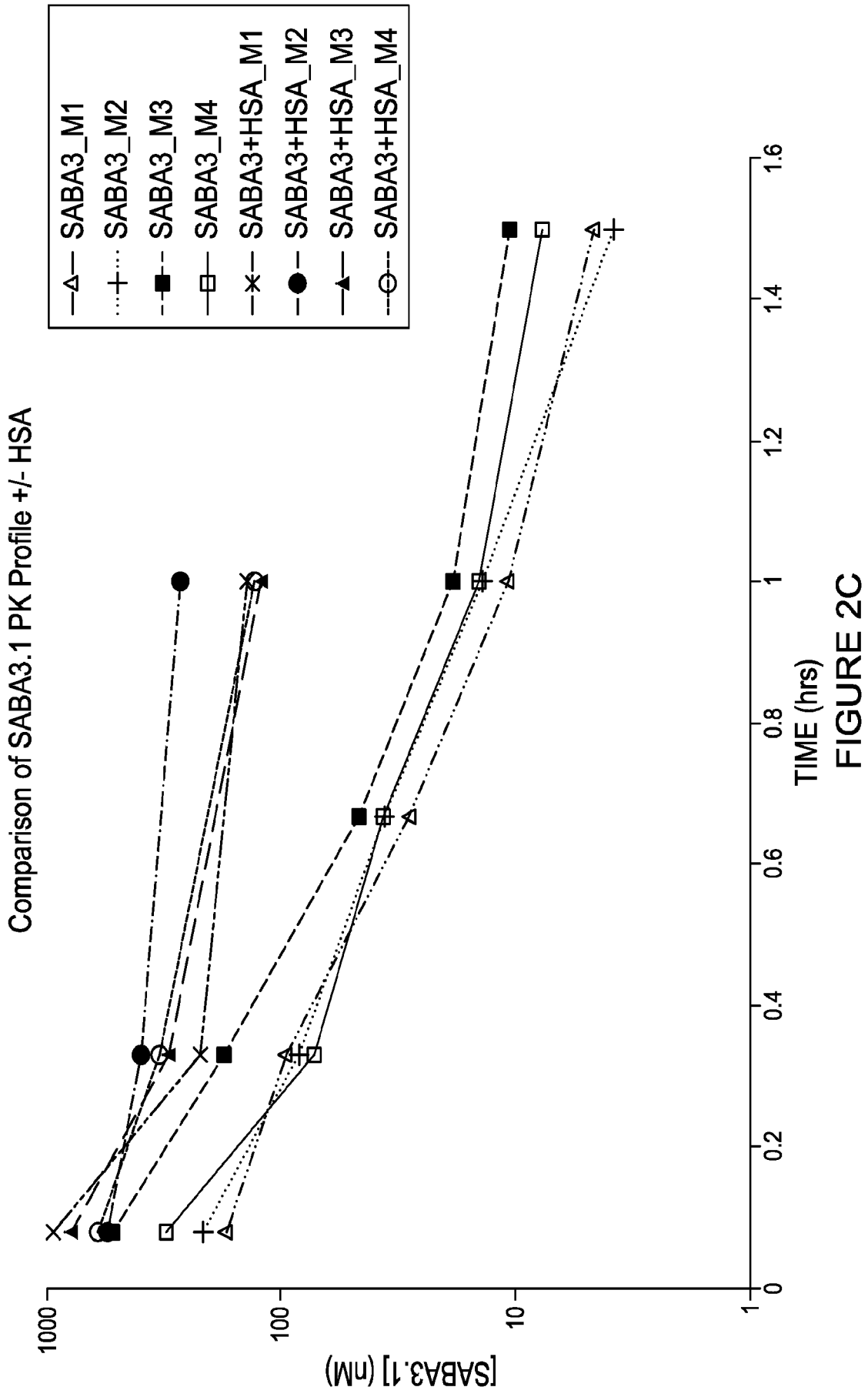

Comparison of SABA3.1 PK Profile +/- HSA
SABA3_M1
SABA3_M2
SABA3_M3
SABA3_M4
SABA3+HSA_M1
SABA3+HSA_M2
SABA3+HSA_M3
SABA3+HSA_M4
[SABA3.1] (nM)
1000
100
10
1
0
0.2
0.4
0.6
0.8
1
1.2
1.4
1.6
TIME (hrs)

FIGURE 2C

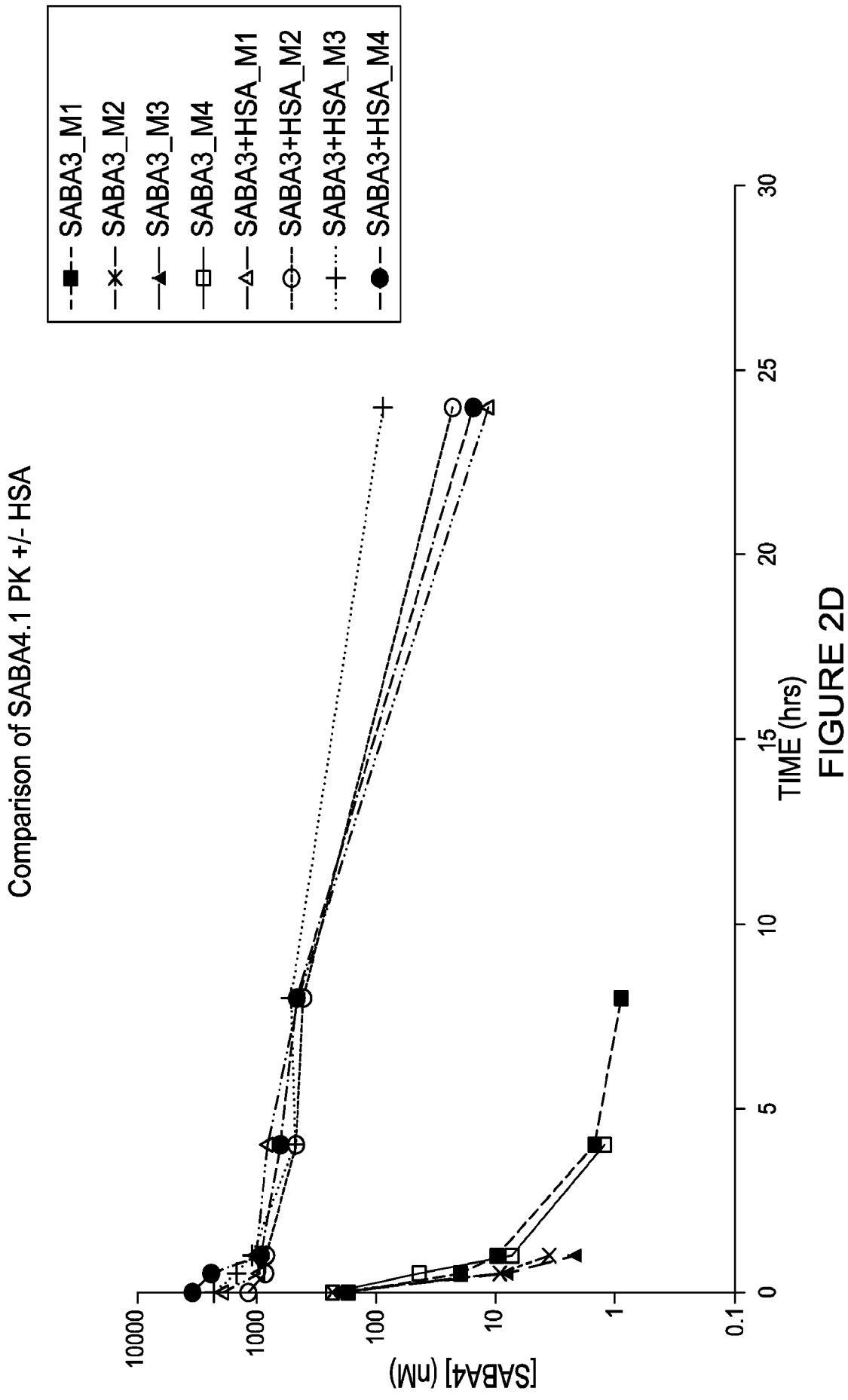

Comparison of SABA4.1 PK +/- HSA
SABA3_M1
SABA3_M2
SABA3_M3
SABA3_M4
SABA3+HSA_M1
SABA3+HSA_M2
SABA3+HSA_M3
SABA3+HSA_M4
[SABA4] (nM)
10000
1000
100
10
1
0.1
0
5
10
15
20
25
30
TIME (hrs)

FIGURE 2D

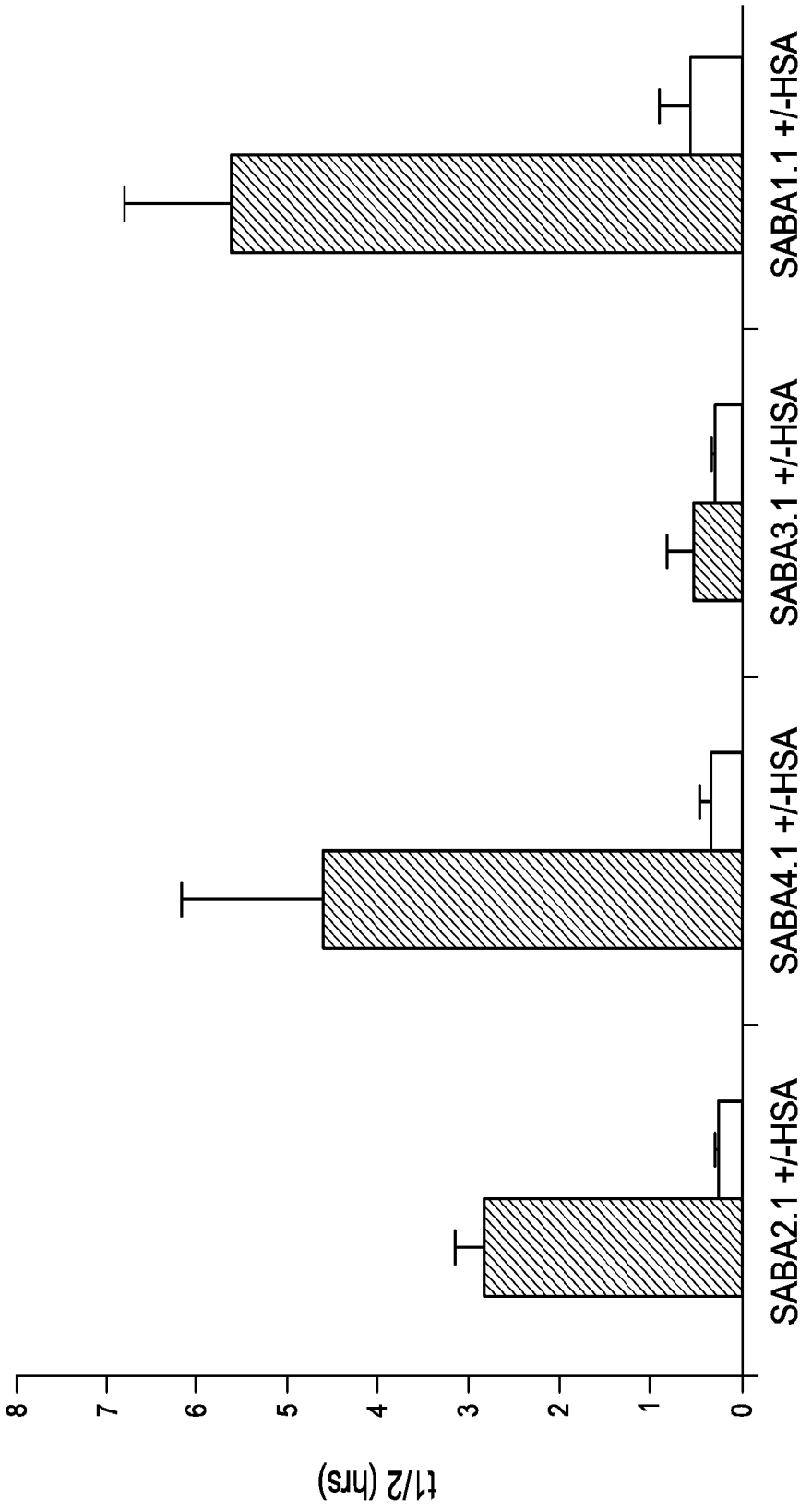

t1/2 (hrs)
0
1
2
3
4
5
6
7
8
SABA2.1 +/-HSA
SABA4.1 +/-HSA
SABA3.1 +/-HSA
SABA1.1 +/-HSA

FIGURE 3

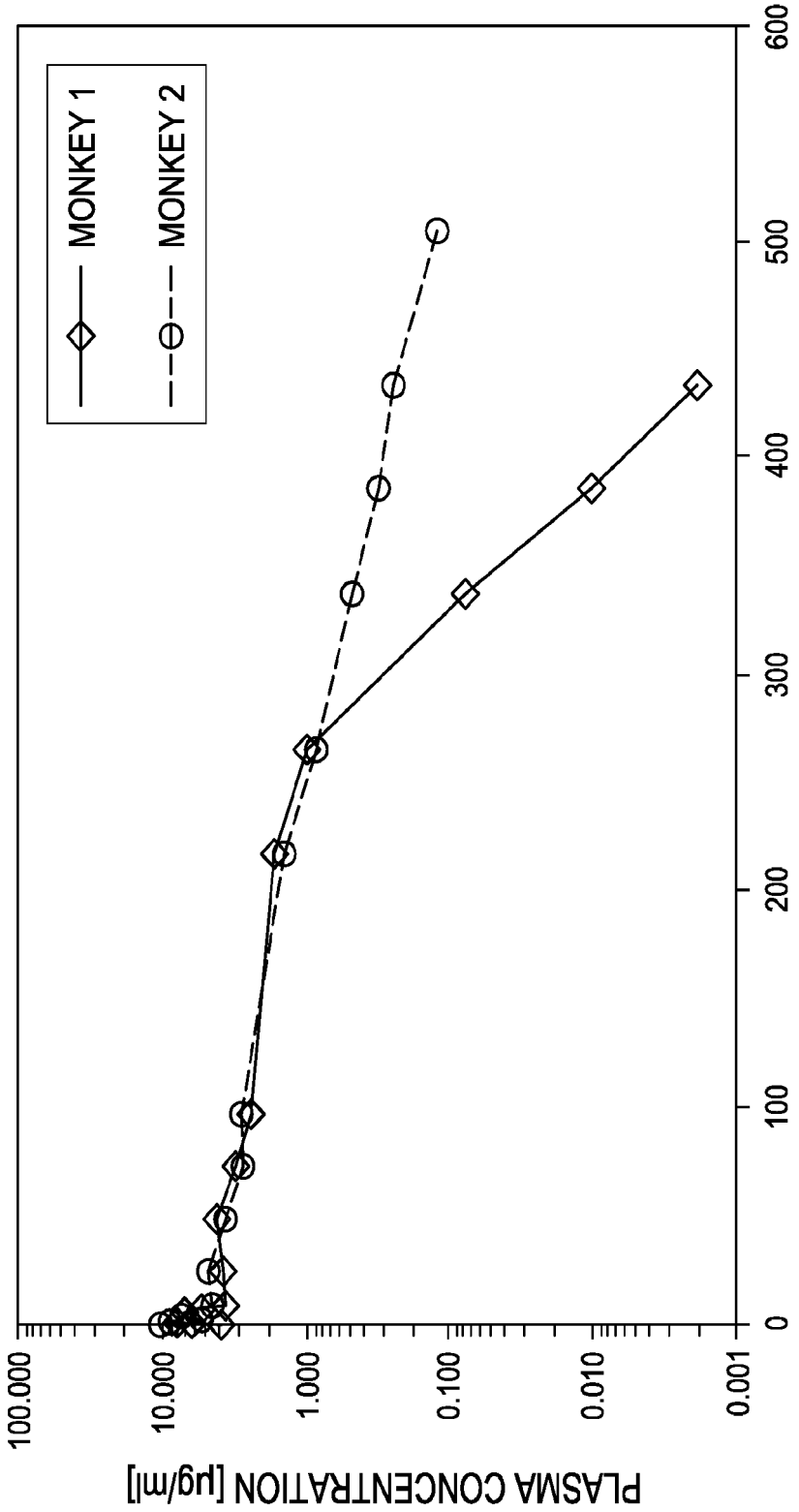

MONKEY 1
MONKEY 2
PLASMA CONCENTRATION [µg/ml]
100.000
10.000
1.000
0.100
0.010
0.001
0
100
200
300
400
500
600
TIME [hours]

FIGURE 4A

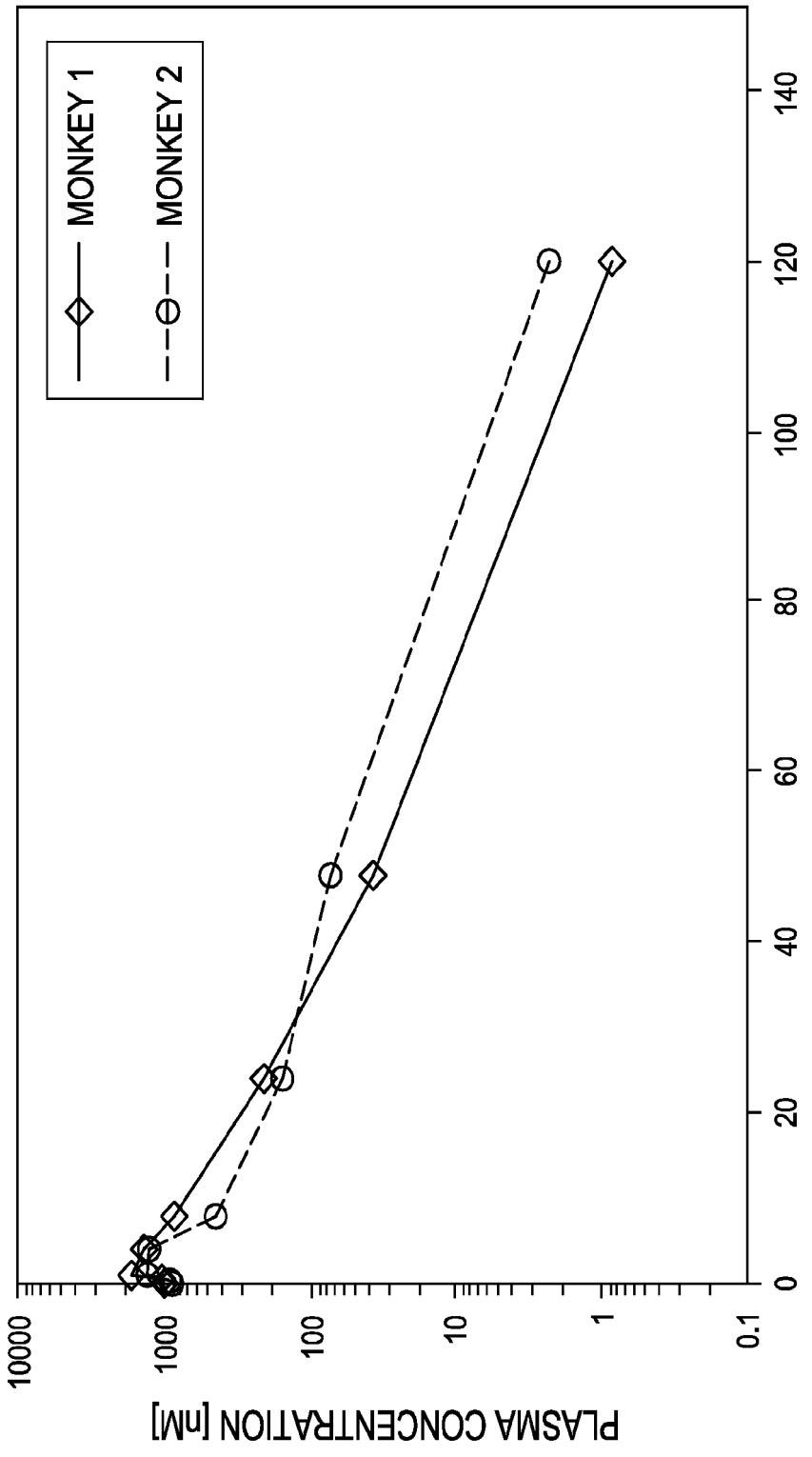

MONKEY 1
MONKEY 2
PLASMA CONCENTRATION [nM]
10000
1000
100
10
1
0.1
0
20
40
60
80
100
120
140
TIME [hours]

FIGURE 4B

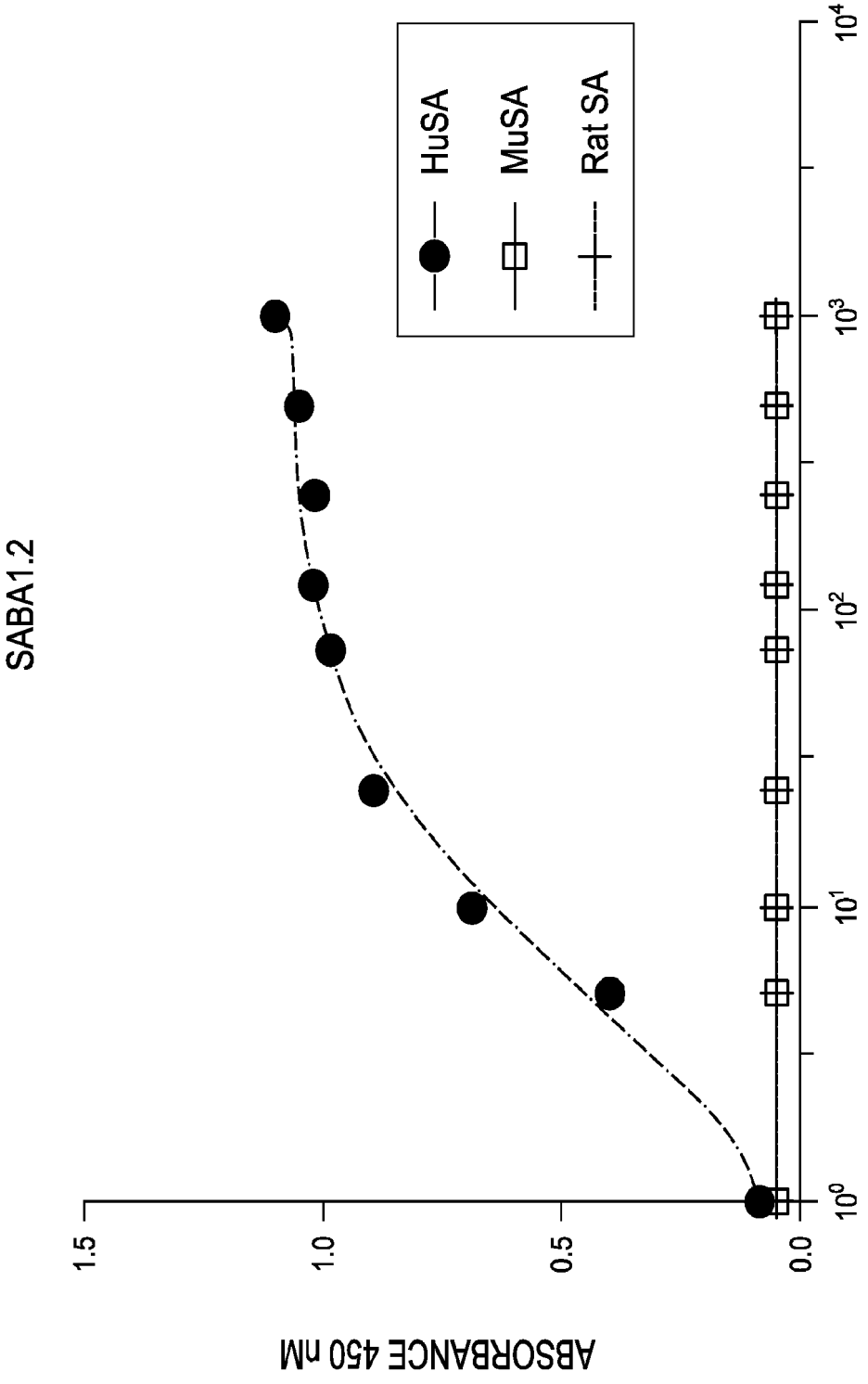

SABA1.2
HuSA
MuSA
Rat SA
ABSORBANCE 450 nM
0.0
0.5
1.0
1.5
10^0
10^1
10^2
10^3
10^4
Log (Conc. nM)

FIGURE 5

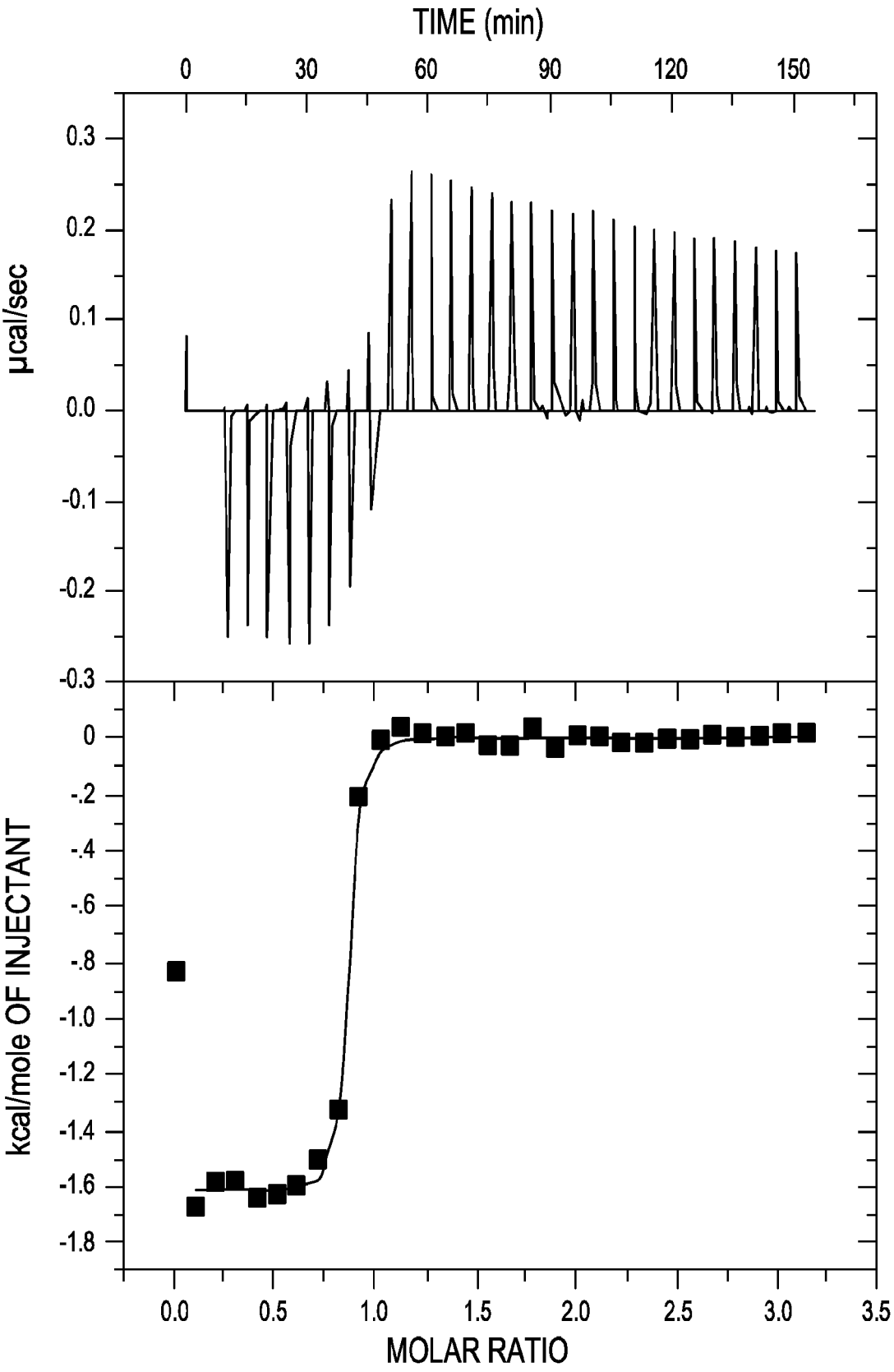

TIME (min)
0
30
60
90
120
150
0.3
0.2
0.1
0.0
-0.1
-0.2
-0.3
µcal/sec
0
-.2
-.4
-.6
-.8
-1.0
-1.2
-1.4
-1.6
-1.8
kcal/mole OF INJECTANT
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
MOLAR RATIO

FIGURE 6

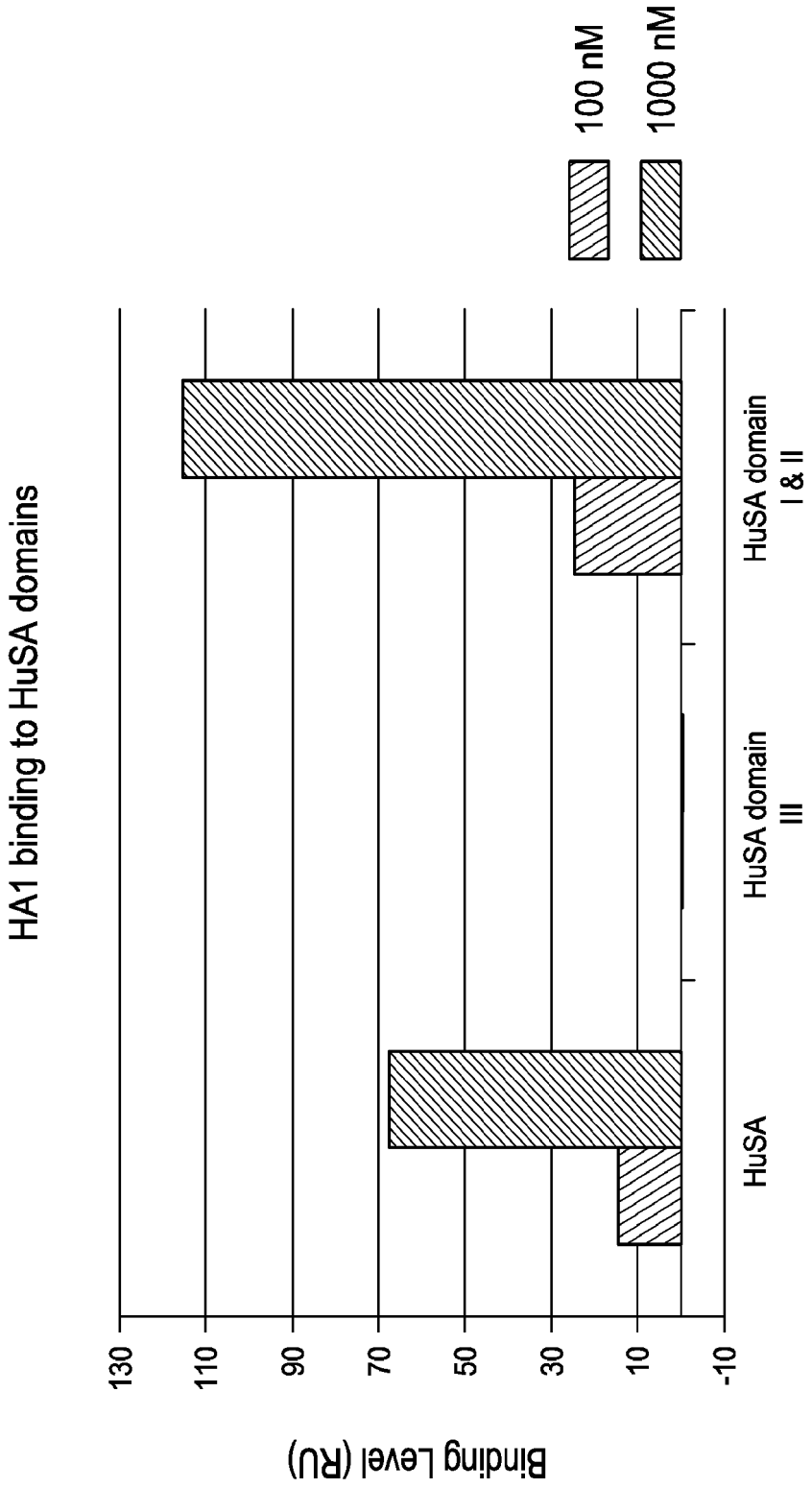

HA1 binding to HuSA domains
100 nM
1000 nM
Binding Level (RU)
130
110
90
70
50
30
10
-10
HuSA
HuSA domain III
HuSA domain I & II

FIGURE 7

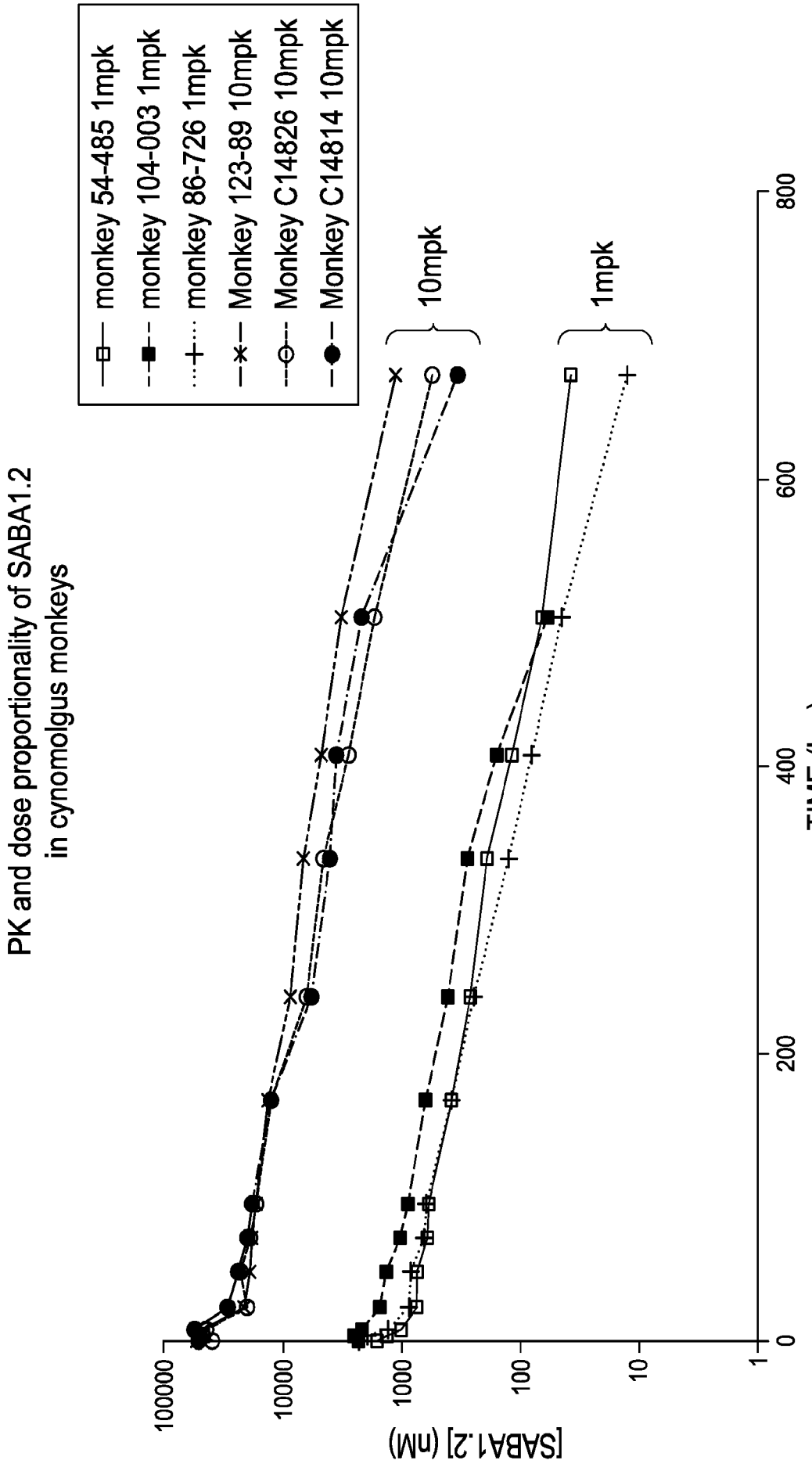

PK and dose proportionality of SABA1.2
in cynomolgus monkeys
monkey 54-485 1mpk
monkey 104-003 1mpk
monkey 86-726 1mpk
Monkey 123-89 10mpk
Monkey C14826 10mpk
Monkey C14814 10mpk
10mpk
1mpk
[SABA1.2] (nM)
100000
10000
1000
100
10
1
0
200
400
600
800
TIME (hrs)

FIGURE 8

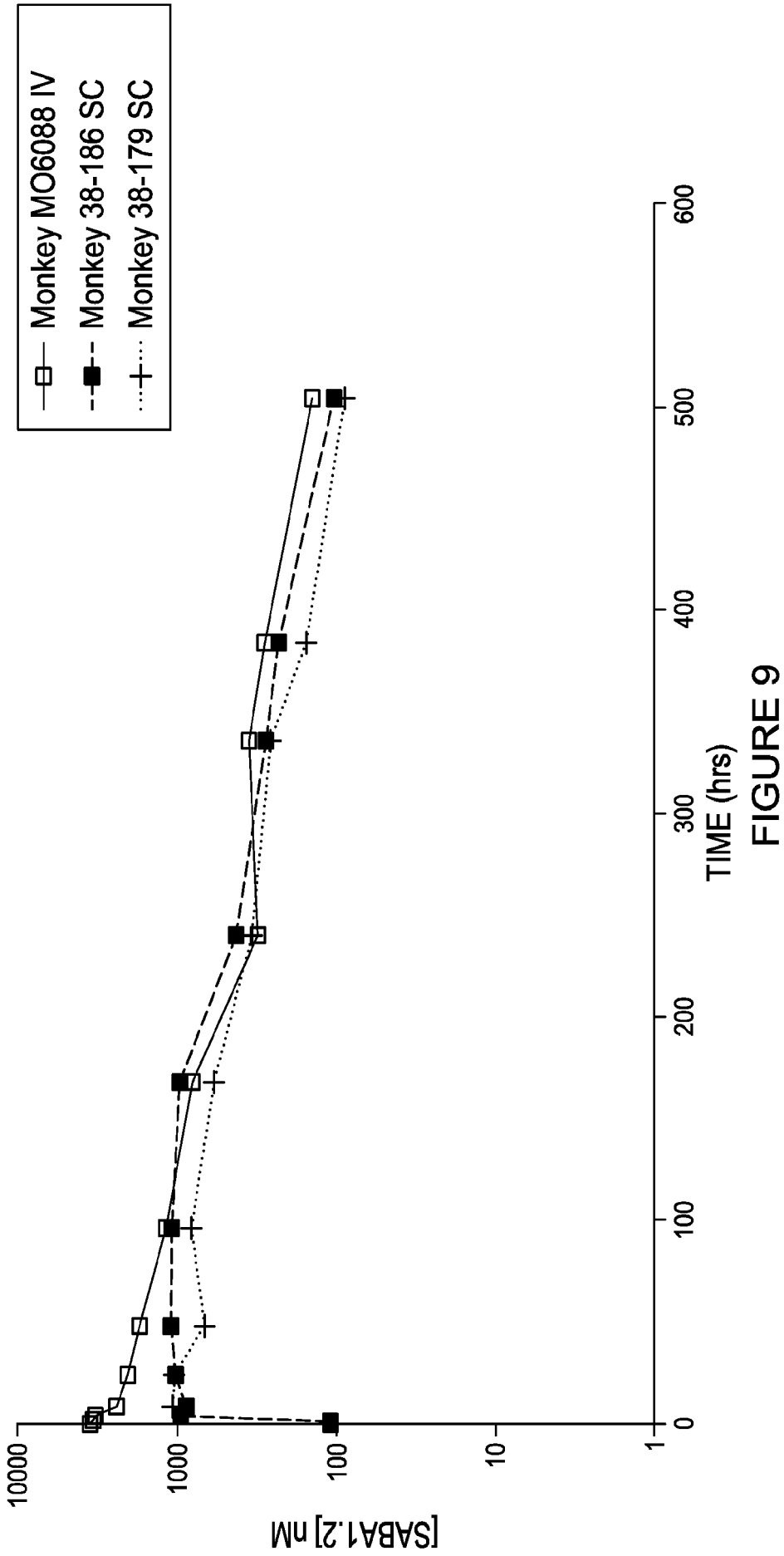

Monkey MO6088 IV
Monkey 38-186 SC
Monkey 38-179 SC
[SABA1.2] nM
10000
1000
100
10
1
0
100
200
300
400
500
600
TIME (hrs)

FIGURE 9

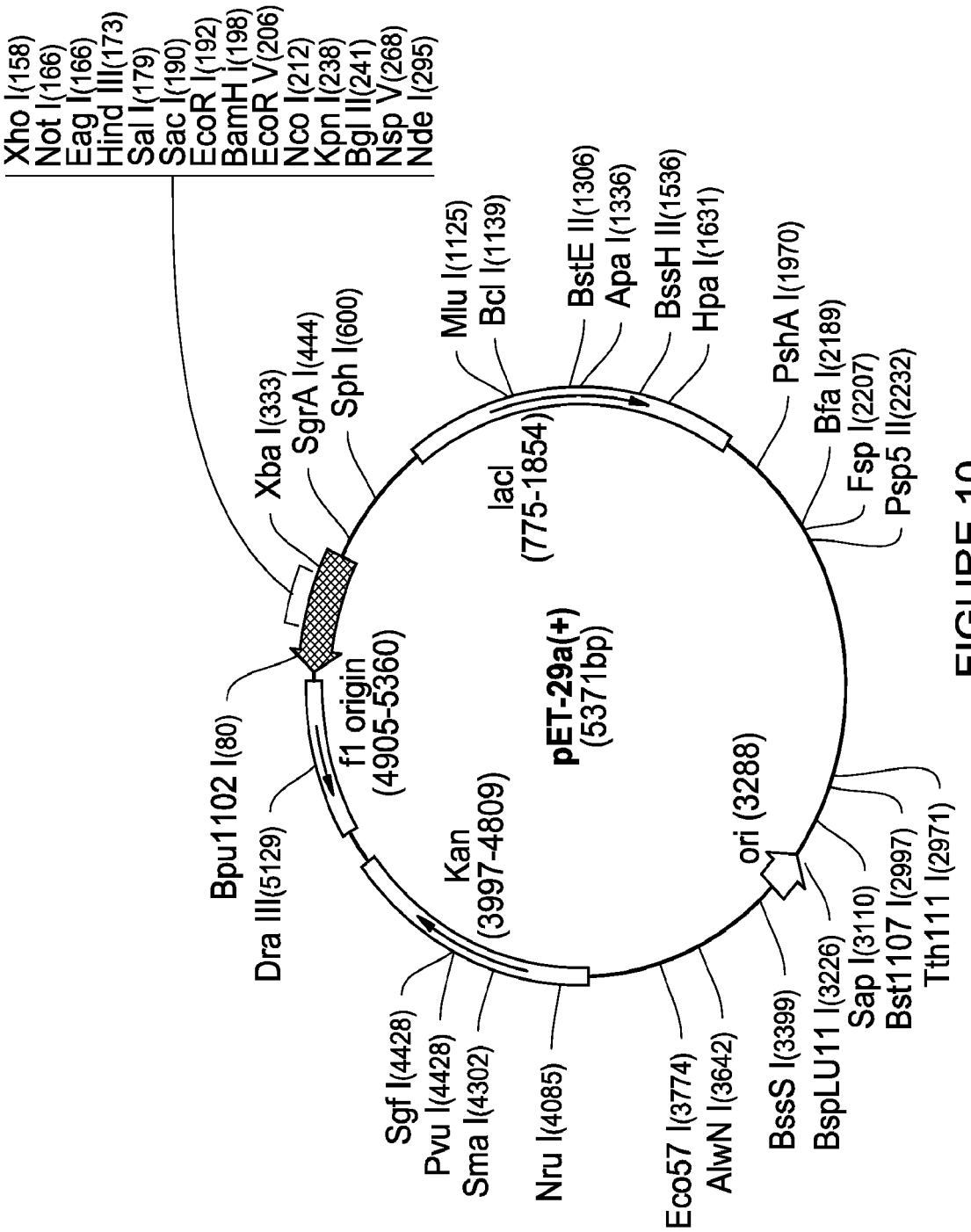

Xho I(158)
Not I(166)
Eag I(166)
Hind III(173)
Sal I(179)
Sac I(190)
EcoR I(192)
BamH I(198)
EcoR V(206)
Nco I(212)
Kpn I(238)
Bgl II(241)
Nsp V(268)
Nde I(295)
Xba I(333)
SgrA I(444)
Sph I(600)
Mlu I(1125)
Bcl I(1139)
BstE II(1306)
Apa I(1336)
BssH II(1536)
Hpa I(1631)
PshA I(1970)
Bfa I(2189)
Fsp I(2207)
Psp5 II(2232)
Tth111 I(2971)
Bst1107 I(2997)
Sap I(3110)
BspLU11 I(3226)
BssS I(3399)
AlwN I(3642)
Eco57 I(3774)
Nru I(4085)
Sma I(4302)
Pvu I(4428)
Sgf I(4428)
Dra III(5129)
Bpu1102 I(80)
f1 origin
(4905-5360)
Kan
(3997-4809)
pET-29a(+)
(5371bp)
lacI
(775-1854)
ori (3288)

FIGURE 10

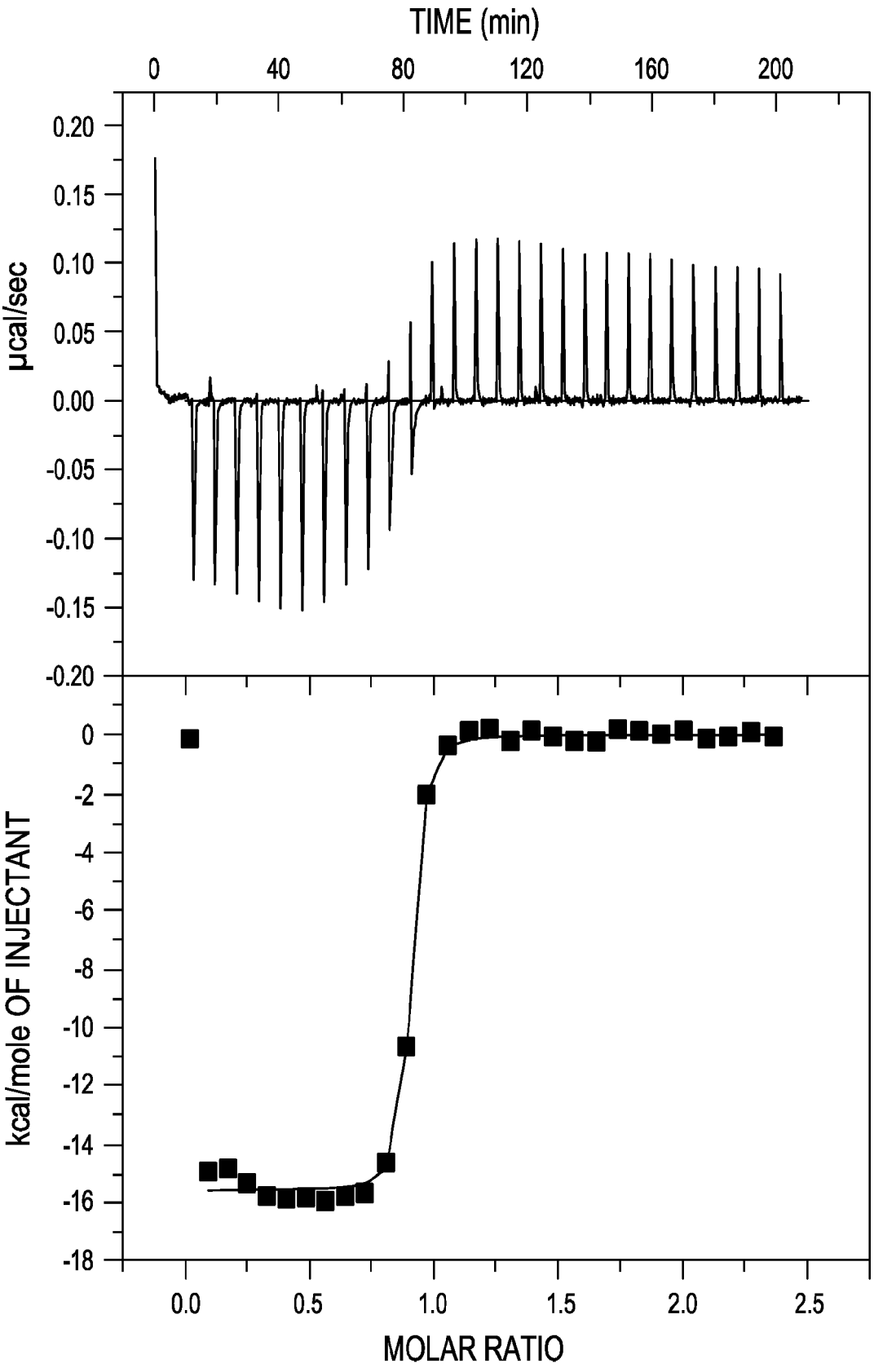

TIME (min)
0
40
80
120
160
200
µcal/sec
0.20
0.15
0.10
0.05
0.00
-0.05
-0.10
-0.15
-0.20
kcal/mole OF INJECTANT
0
-2
-4
-6
-8
-10
-12
-14
-16
-18
0.0
0.5
1.0
1.5
2.0
2.5
MOLAR RATIO

FIGURE 11

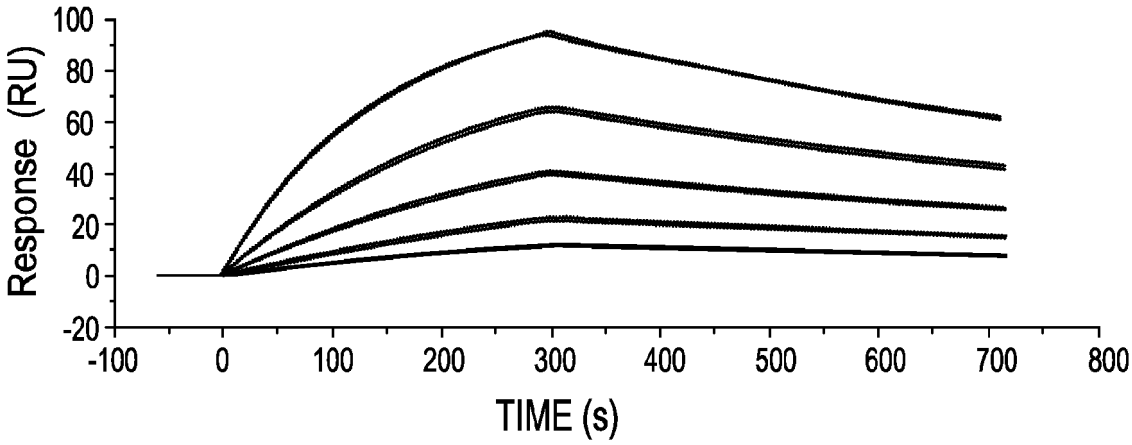


FIGURE 12A

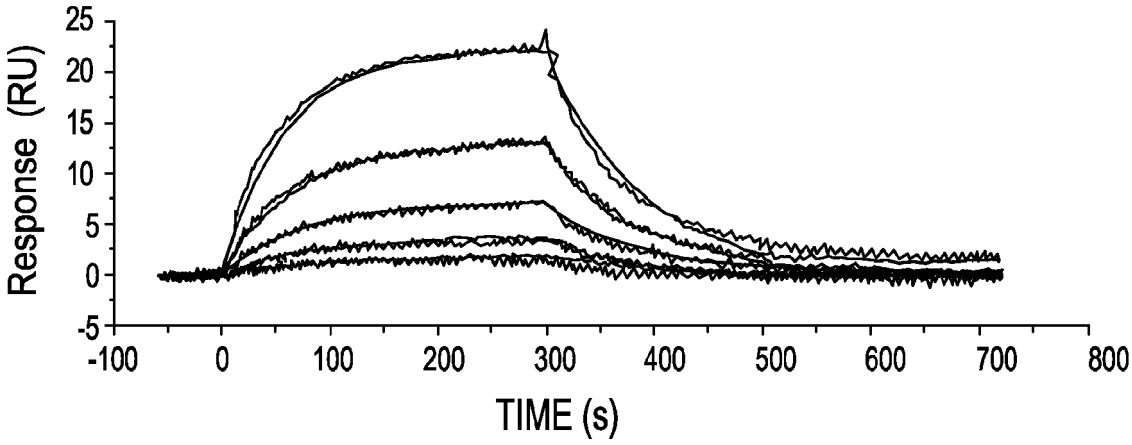


FIGURE 12B

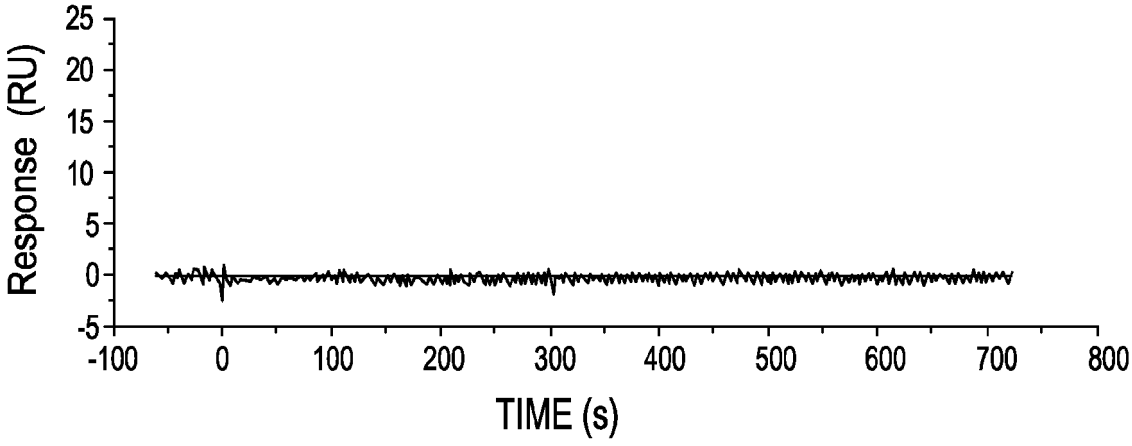


FIGURE 12C

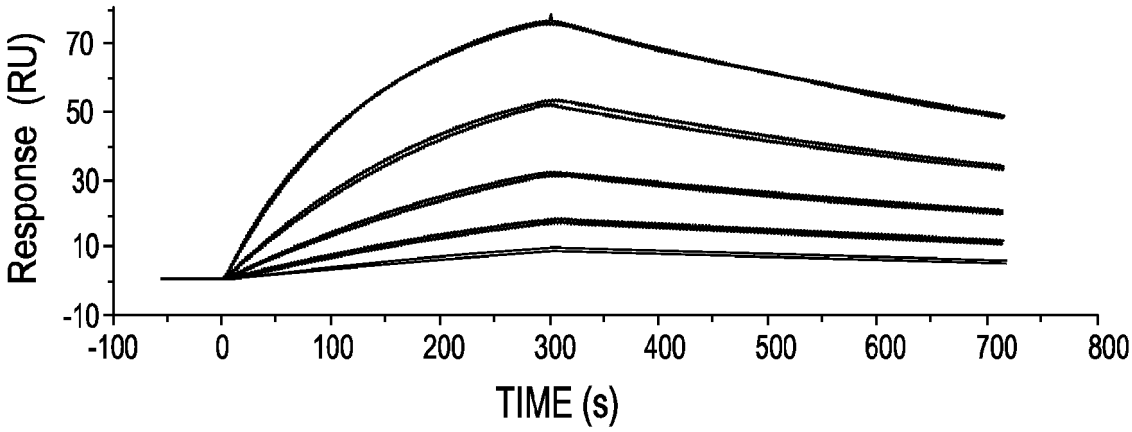


FIGURE 12D

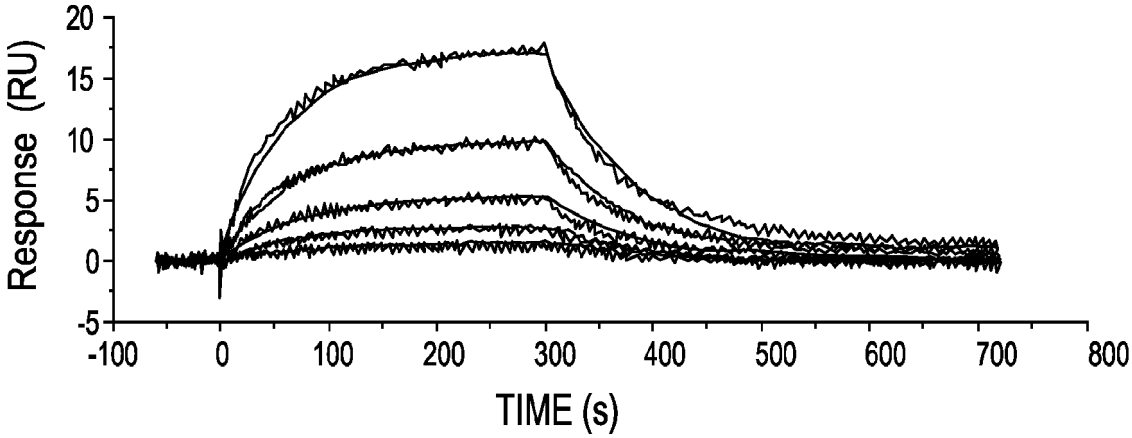


FIGURE 12E

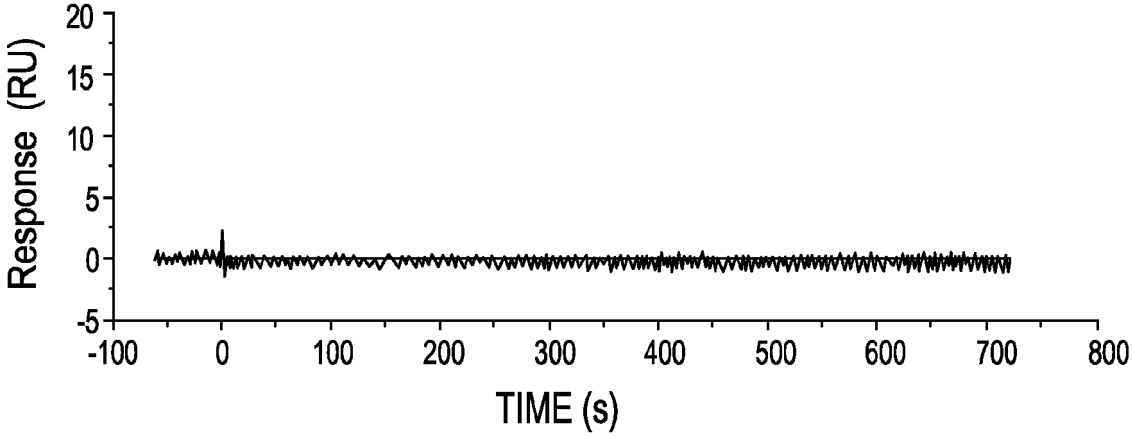


FIGURE 12F

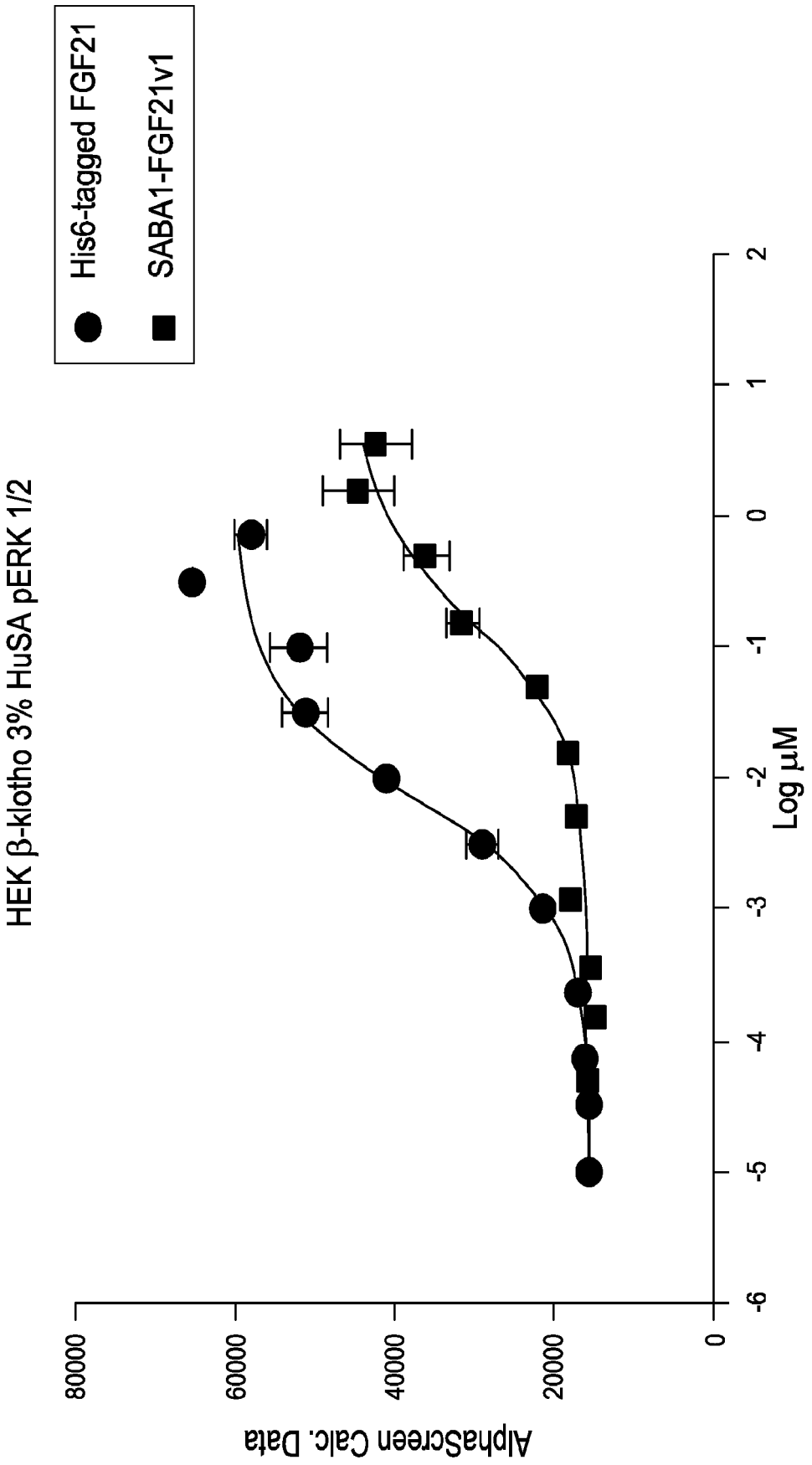

His6-tagged FGF21
SABA1-FGF21v1
HEK β-klotho 3% HuSA pERK 1/2
AlphaScreen Calc. Data
80000
60000
40000
20000
0
-6
-5
-4
-3
-2
-1
0
1
2
Log µM

FIGURE 13

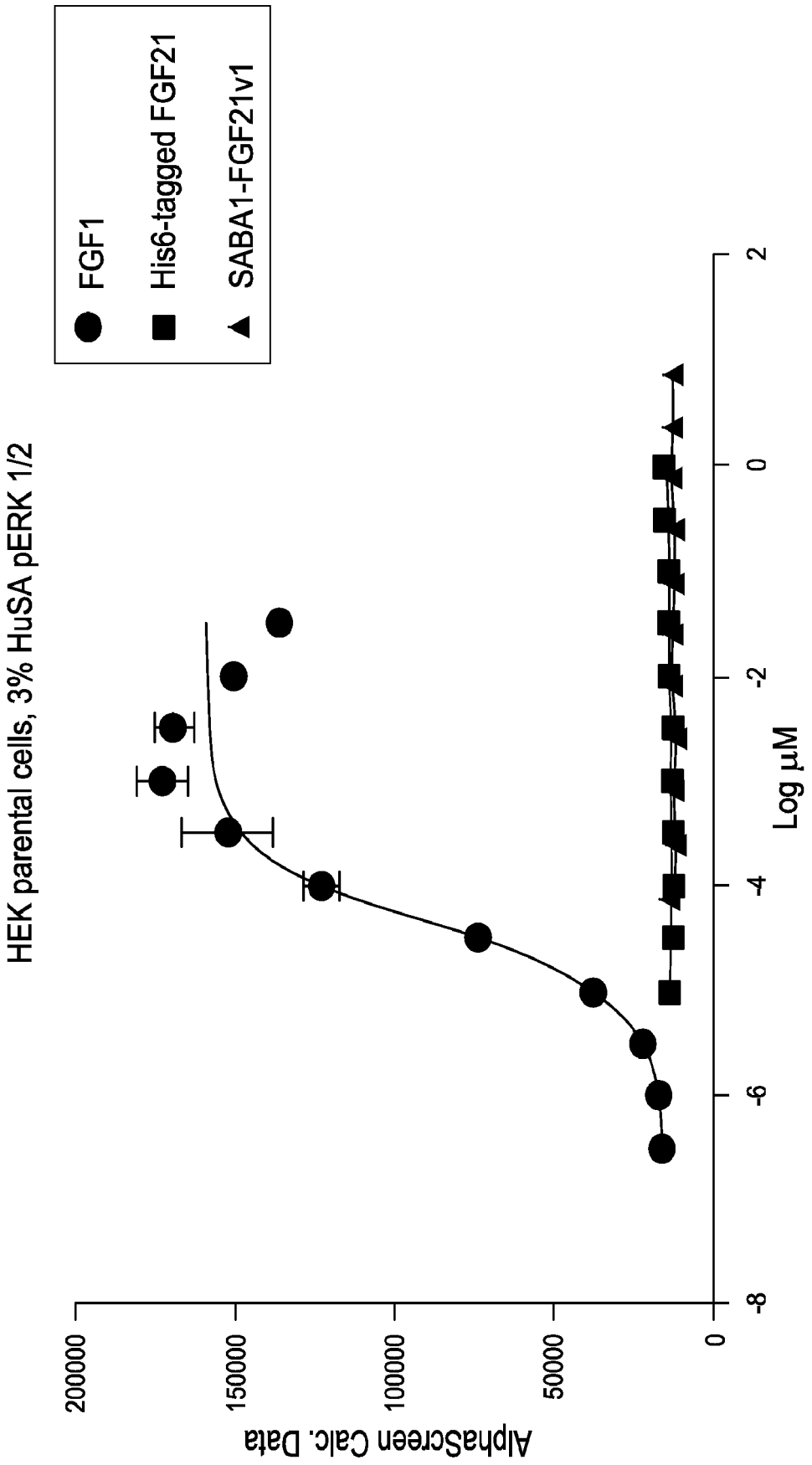

HEK parental cells, 3% HuSA pERK 1/2
FGF1
His6-tagged FGF21
SABA1-FGF21v1
AlphaScreen Calc. Data
200000
150000
100000
50000
0
-8
-6
-4
-2
0
2
Log µM

FIGURE 14A

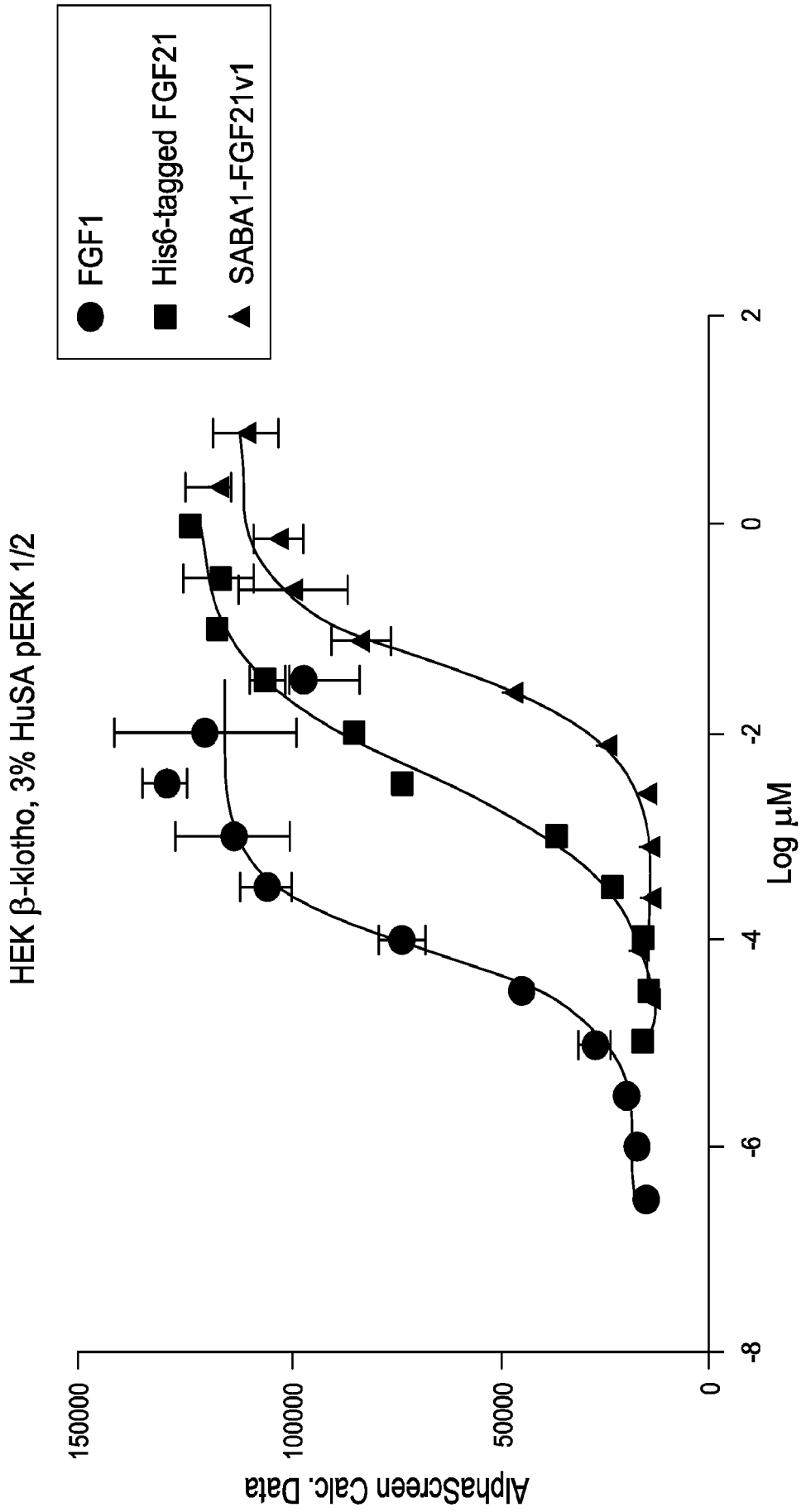

FGF1
His6-tagged FGF21
SABA1-FGF21v1
HEK β-klotho, 3% HuSA pERK 1/2
AlphaScreen Calc. Data
150000
100000
50000
0
-8
-6
-4
-2
0
2
Log µM

FIGURE 14B

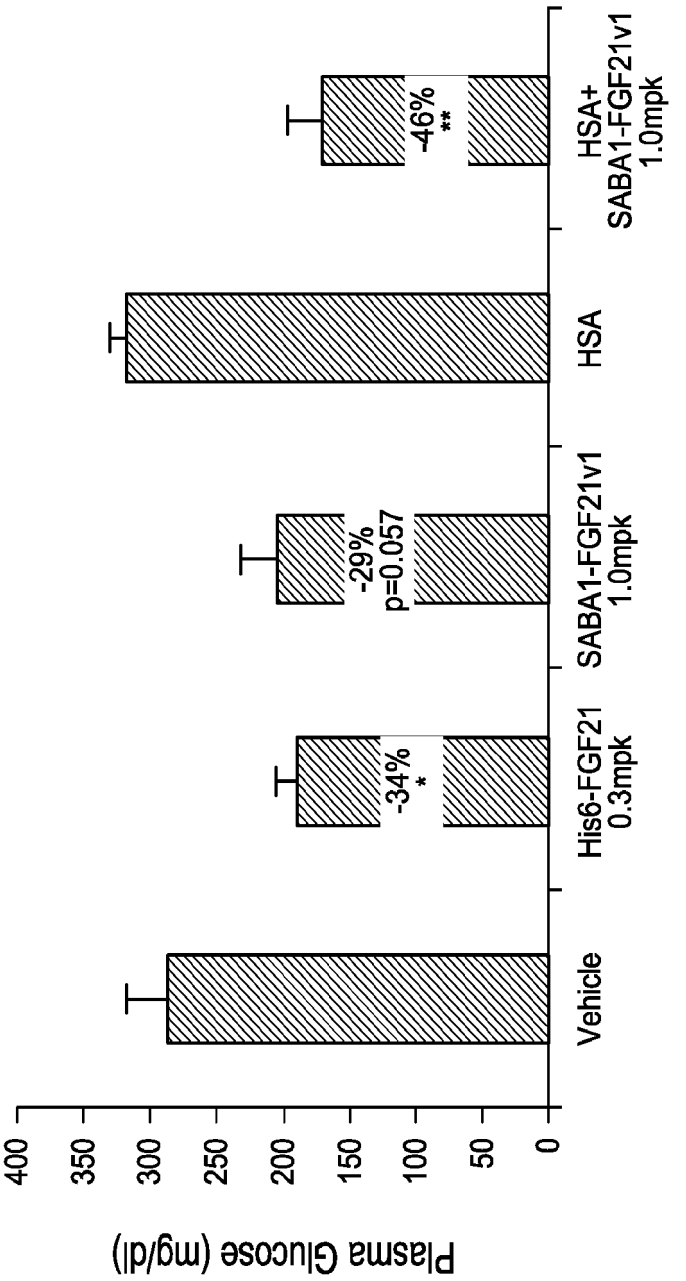

Plasma Glucose
3 hr post-dose Day 7 (postprandial)
Plasma Glucose (mg/dl)
400
350
300
250
200
150
100
50
0
Vehicle
His6-FGF21 0.3mpk
SABA1-FGF21v1 1.0mpk
HSA
HSA+ SABA1-FGF21v1 1.0mpk
-34% *
-29% p=0.057
-46% **
* P<0.05, ** P<0.01 vs. respective control

FIGURE 15A

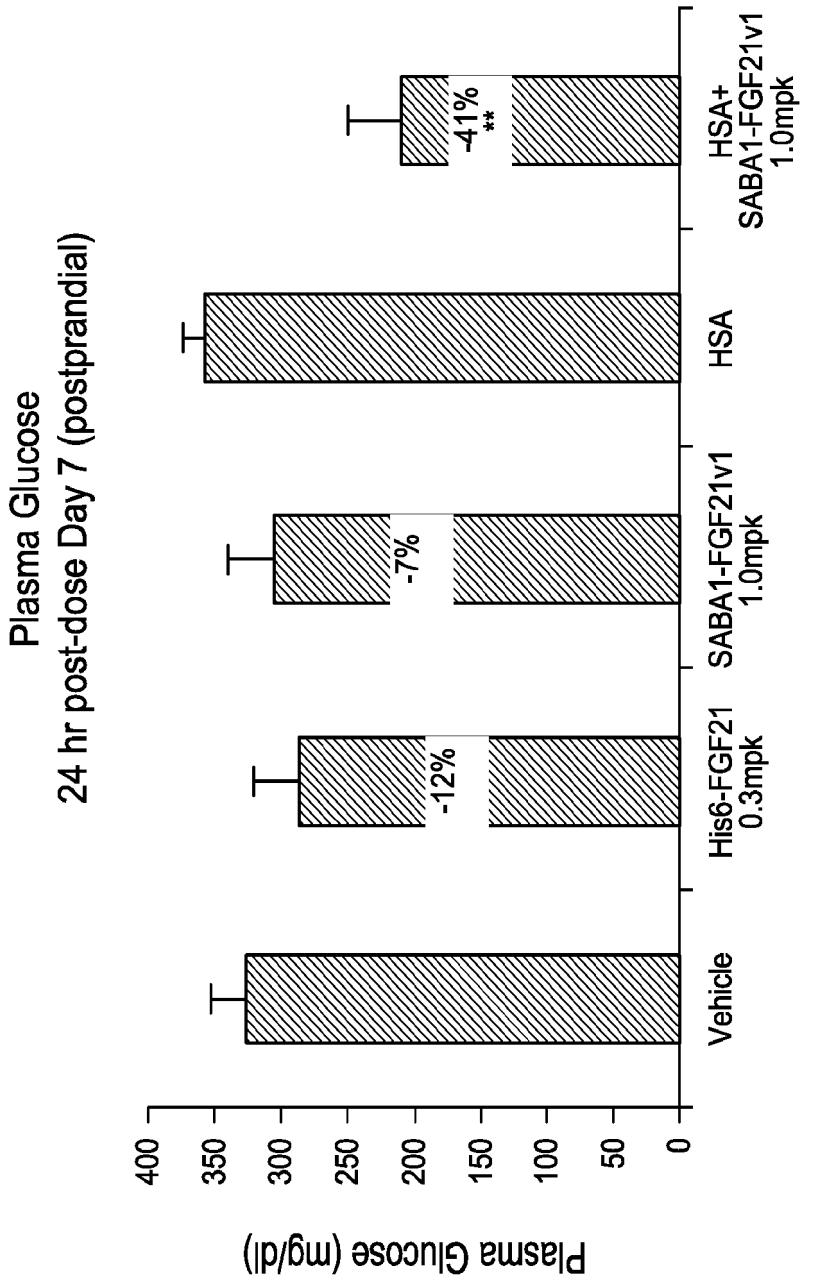

Plasma Glucose
24 hr post-dose Day 7 (postprandial)
Plasma Glucose (mg/dl)
400
350
300
250
200
150
100
50
0
-12%
-7%
-41%
**
Vehicle
His6-FGF21 0.3mpk
SABA1-FGF21v1 1.0mpk
HSA
HSA+ SABA1-FGF21v1 1.0mpk
** P<0.01 vs. HSA

FIGURE 15B

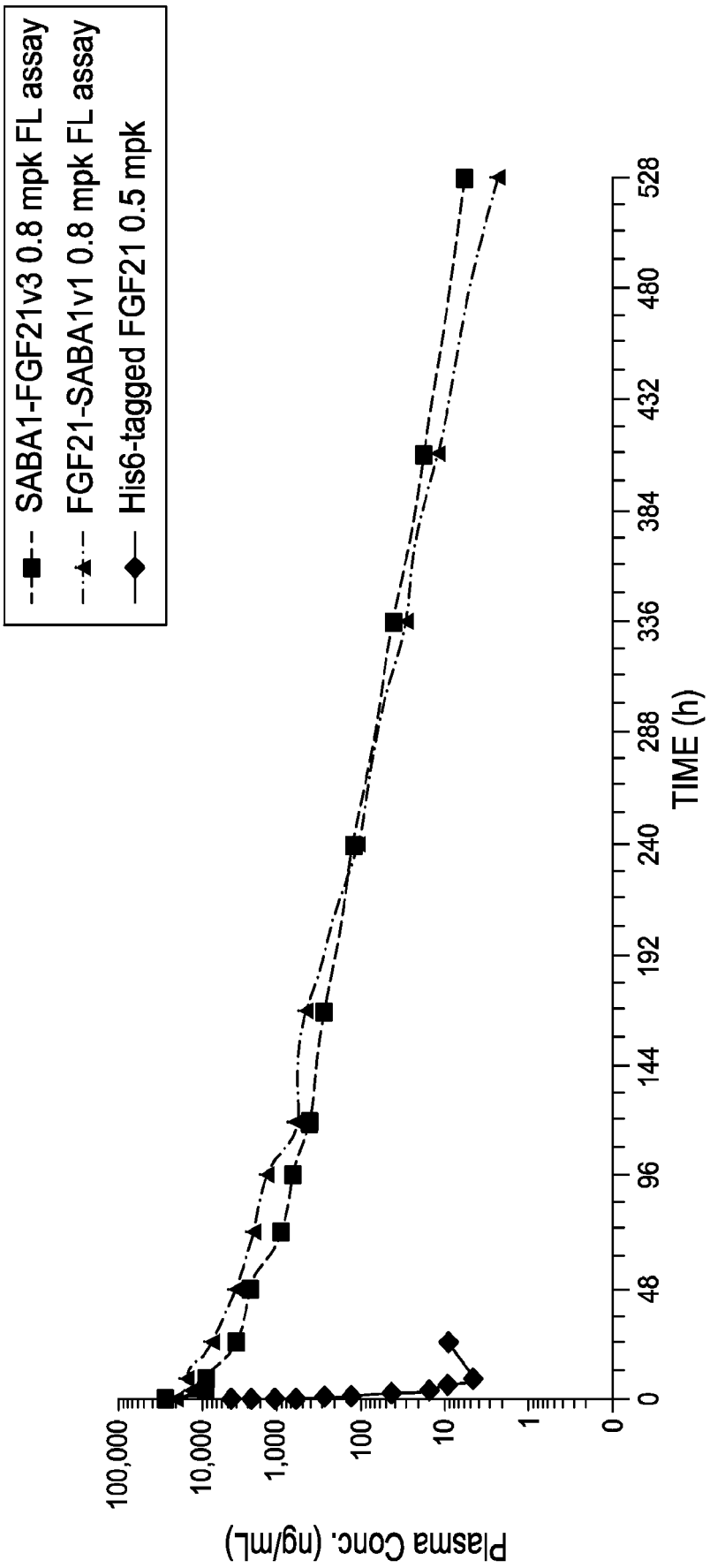

SABA1-FGF21v3 0.8 mpk FL assay
FGF21-SABA1v1 0.8 mpk FL assay
His6-tagged FGF21 0.5 mpk
Plasma Conc. (ng/mL)
100,000
10,000
1,000
100
10
1
0
TIME (h)
0
48
96
144
192
240
288
336
384
432
480
528

FIGURE 16

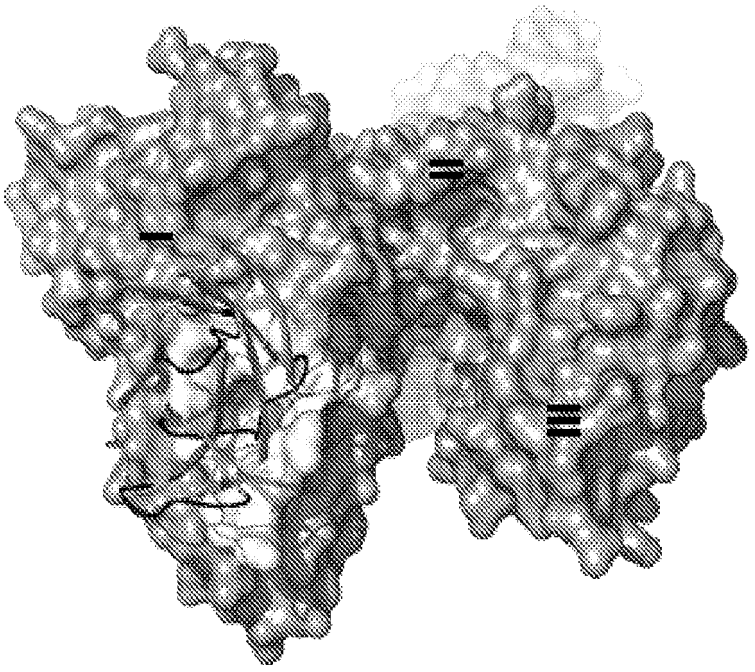


FIGURE 17B

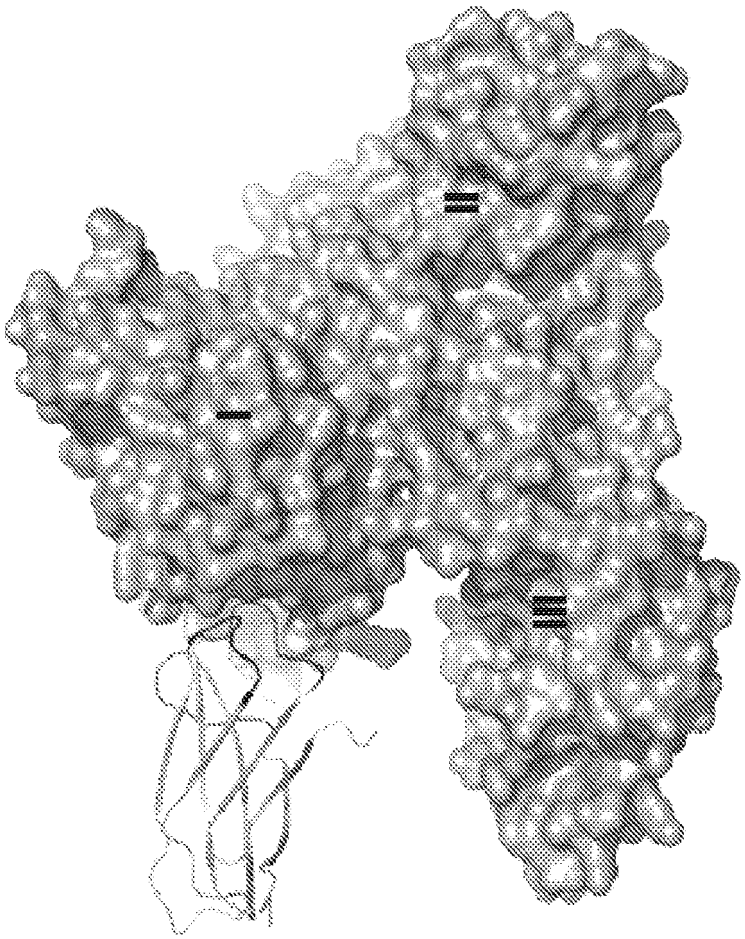


FIGURE 17A

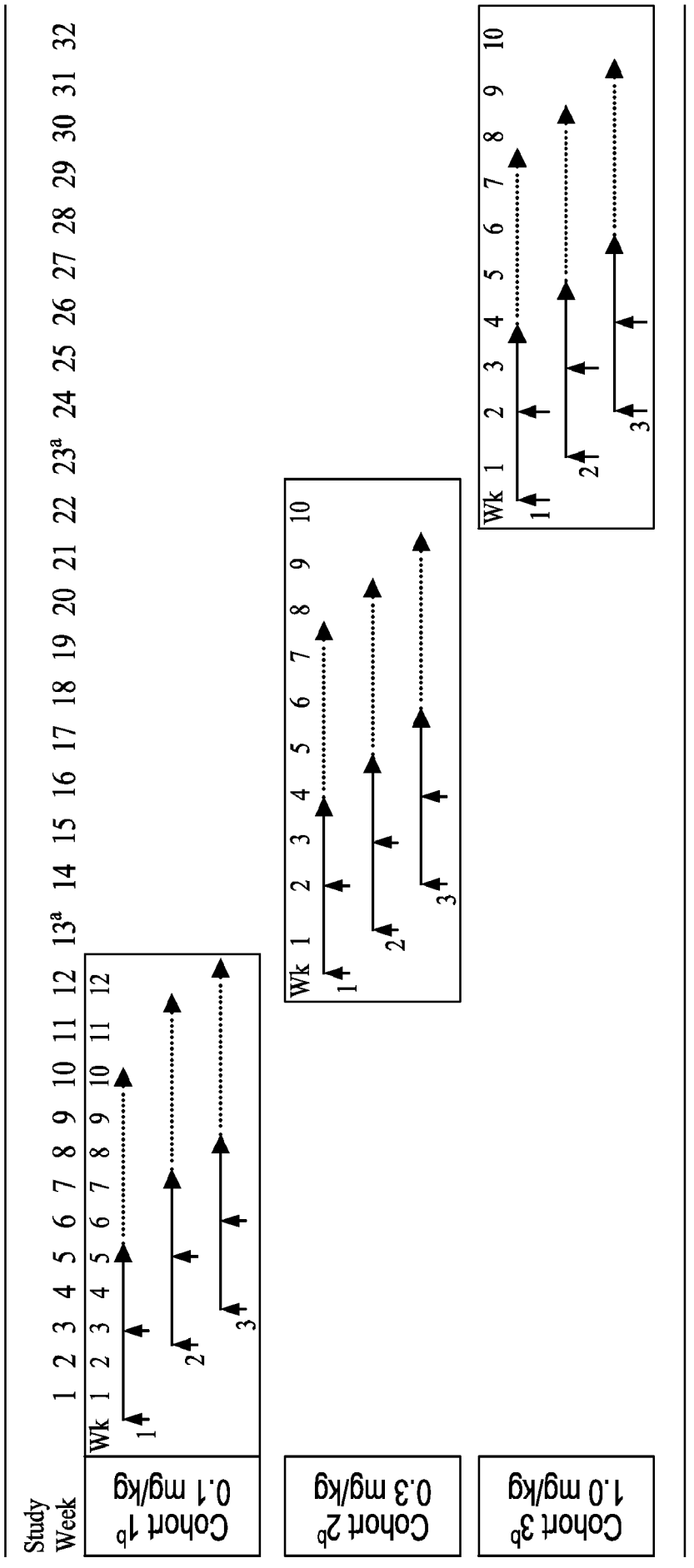

Study Week
1 2 3 4 5 6 7 8 9 10 11 12 13[a] 14 15 16 17 18 19 20 21 22 23[a] 24 25 26 27 28 29 30 31 32
Cohort 1[b] 0.1 mg/kg
Cohort 2[b] 0.3 mg/kg
Cohort 3[b] 1.0 mg/kg
Wk 1 2 3 4 5 6 7 8 9 10 11 12
Wk 1 2 3 4 5 6 7 8 9 10
Wk 1 2 3 4 5 6 7 8 9 10

FIGURE 18

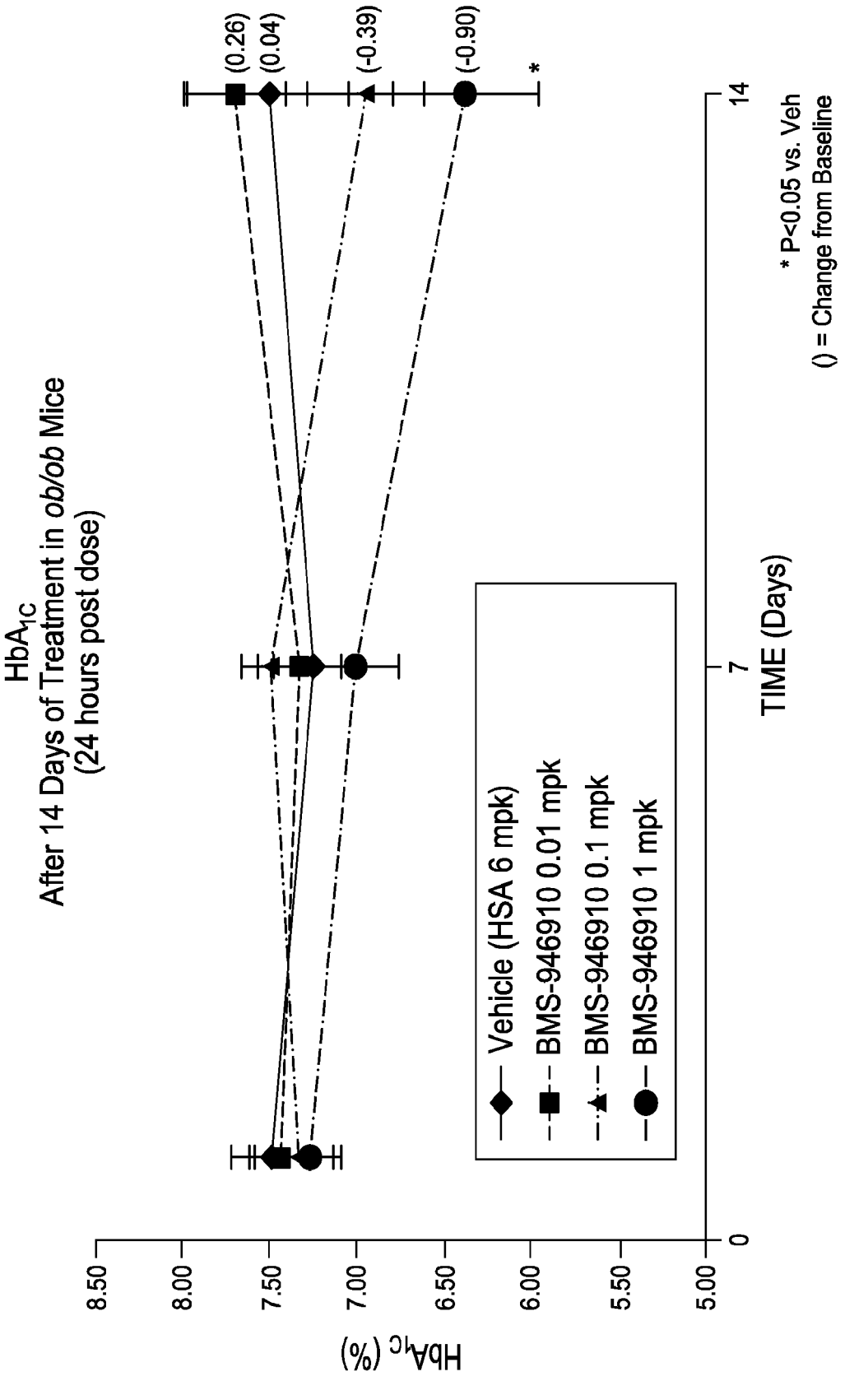

HbA1C
After 14 Days of Treatment in ob/ob Mice
(24 hours post dose)
HbA1C (%)
8.50
8.00
7.50
7.00
6.50
6.00
5.50
5.00
0
7
14
TIME (Days)
(0.26)
(0.04)
(-0.39)
(-0.90)
*
* P<0.05 vs. Veh
() = Change from Baseline
Vehicle (HSA 6 mpk)
BMS-946910 0.01 mpk
BMS-946910 0.1 mpk
BMS-946910 1 mpk

FIGURE 19

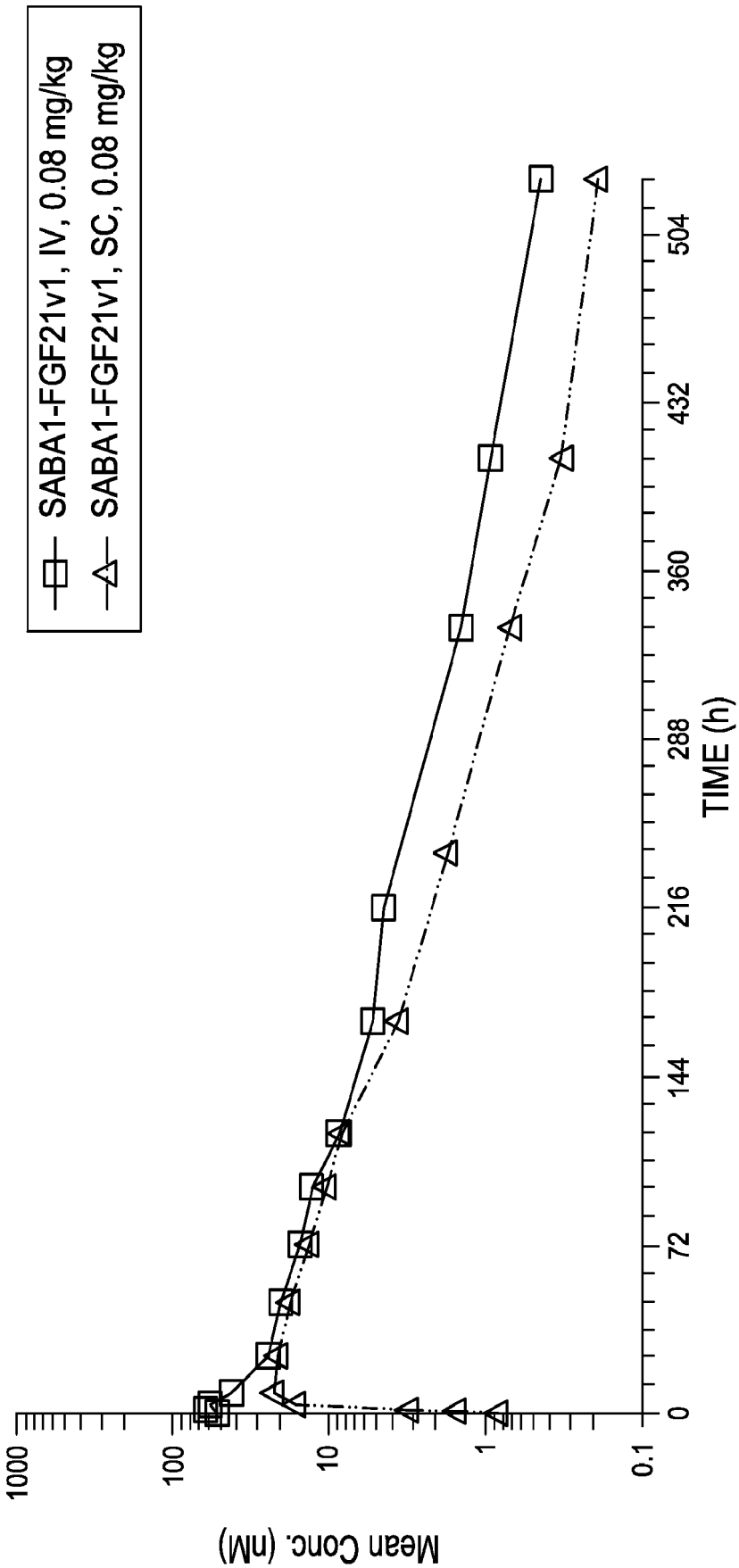

SABA1-FGF21v1, IV, 0.08 mg/kg
SABA1-FGF21v1, SC, 0.08 mg/kg
Mean Conc. (nM)
1000
100
10
1
0.1
0
72
144
216
288
360
432
504
TIME (h)

FIGURE 20

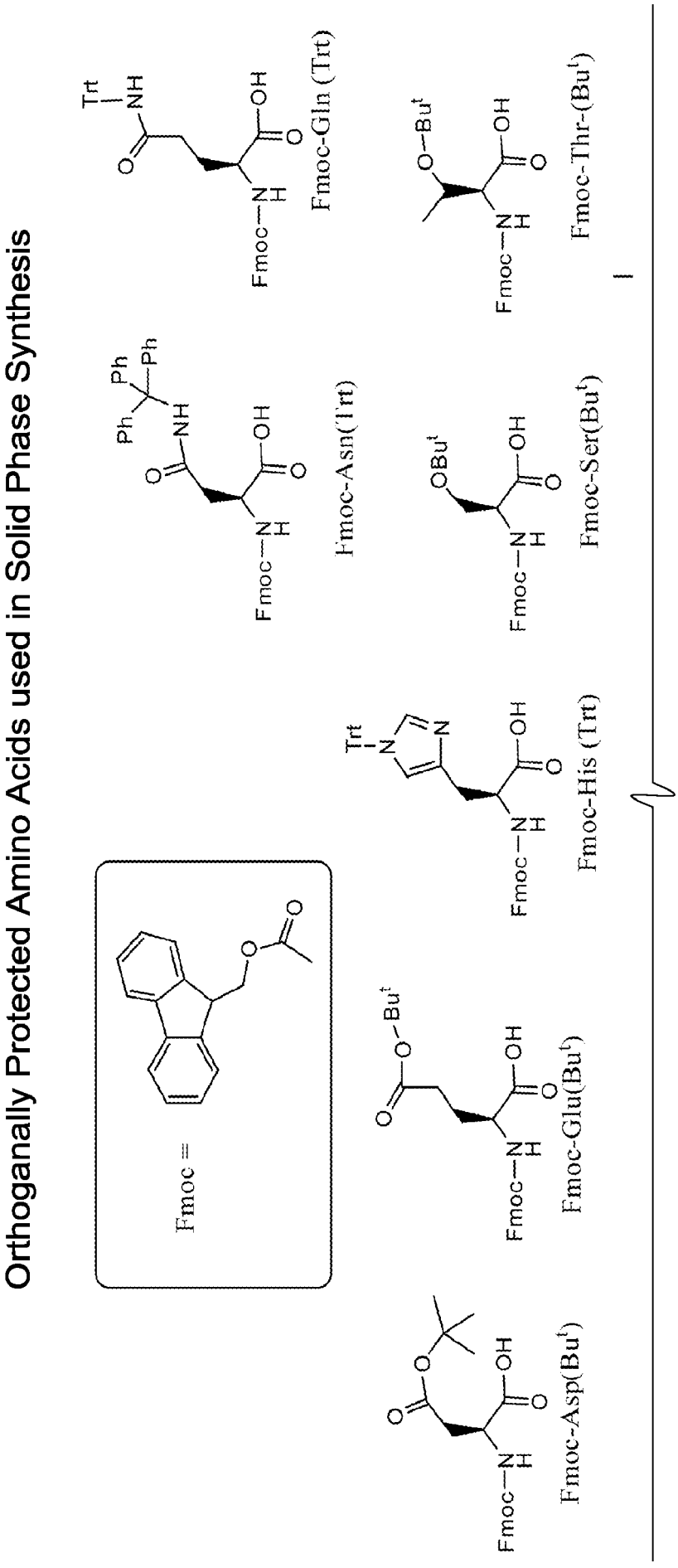


FIGURE 21 (part 1)

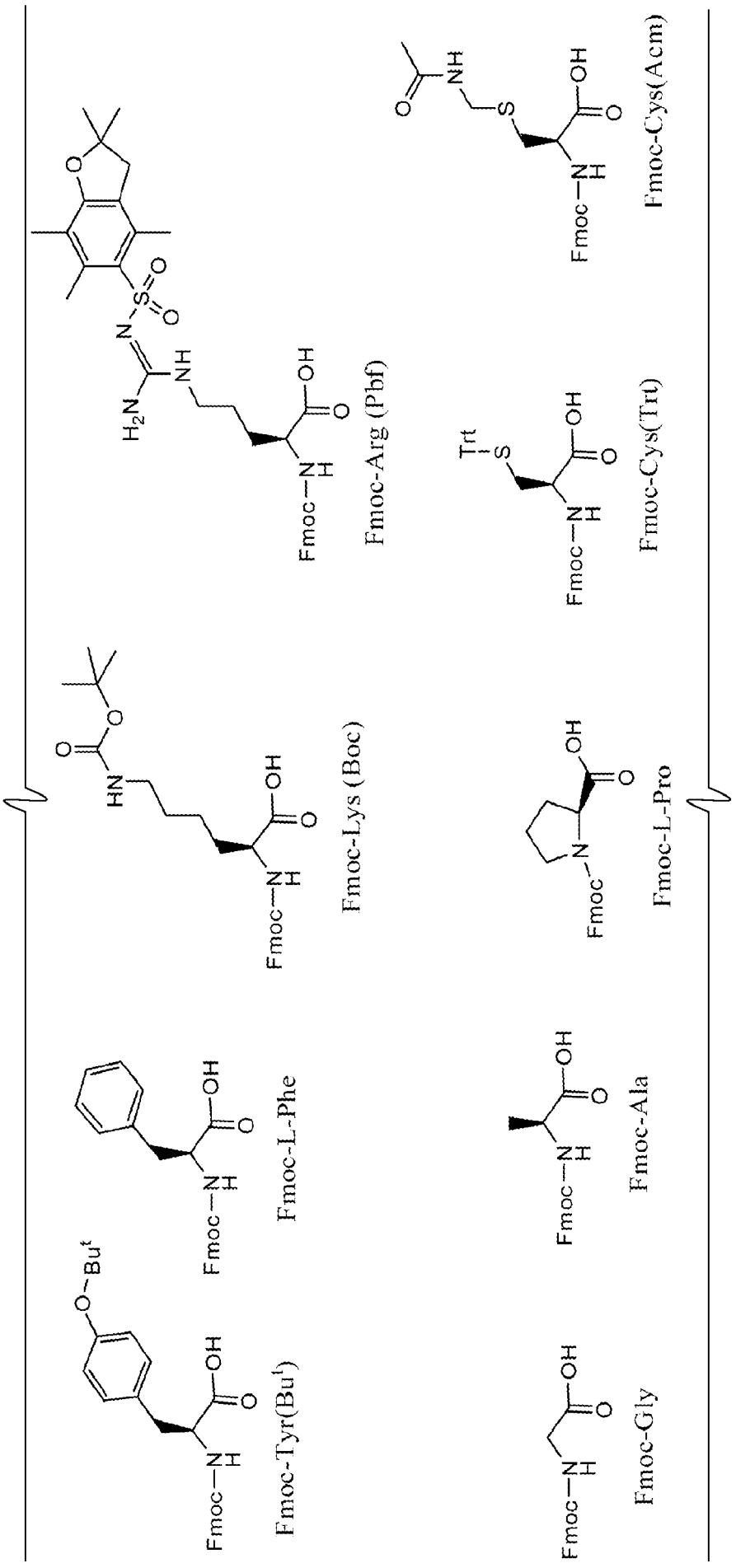
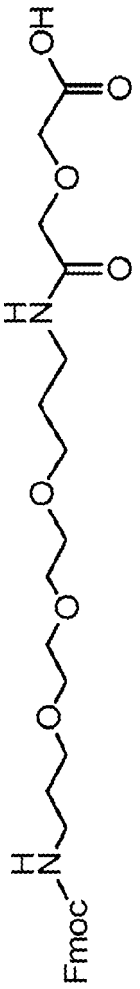
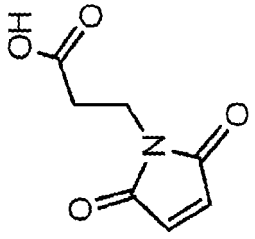


FIGURE 21 (part 2)

Other Building Blocks Used for Solid Phase Synthesis



O-(N-Fmoc-3-aminopropyl)-O'-(N-diglycolyl-3-aminopropyl)-diethyleneglycol (Fmoc-PEG$_{20}$) - 20 atom PEG spacer



3-Maleimidopropionic acid (Mal)



N-Fmoc-6-aminohexanoic acid (Fmoc-Ahx)

FIGURE 21 (part 3)