FIG. 1

```
1459D05          MGVSDVPRDLEVVAATPTSLLISWPPPSHGYGYYRITYGETGGNSPVQEFTVPPGKGTAT
1784F03          MGVSDVPRDLEVVAATPTSLLISWRPPIHAYGYYRITYGETGGNSPVQEFTVPIVEGTAT
1784F03-m1       MGVSDVPRDLEVVAATPTSLLISWDAPIHAYGYYRITYGETGGNSPVQEFTVPGSEGTAT
1784F03-m2       MGVSDVPRDLEVVAATPTSLLISWDAPAHAYGYYRITYGETGGNSPVQEFTVPGSKGTAT
1784F03-m3       MGVSDVPRDLEVVAATPTSLLISWDAPAVTYGYYRITYGETGGNSPVQEFTVPGSKSTAT
1813E02          MGVSDVPRDLEVVAATPTSLLISWSPPANGYGYYRITYGETGGNSPVQEFTVPVGRGTAT
1923B02          MGVSDVPRDLEVVAATPTSLLISWTPPPKGYGYYRITYGETGGNSPVQEFTVPVGEGTAT
1923B02_N82I_    MGVSDVPRDLEVVAATPTSLLISWTPPPKGYGYYRITYGETGGNSPVQEFTVPVGEGTAT
1923B02_N82E_    MGVSDVPRDLEVVAATPTSLLISWTPPPKGYGYYRITYGETGGNSPVQEFTVPVGEGTAT
1923B02_T80A_    MGVSDVPRDLEVVAATPTSLLISWTPPPKGYGYYRITYGETGGNSPVQEFTVPVGEGTAT
1922G04          MGVSDVPRDLEVVAATPTSLLISWRPPSHAYGYYRITYGETGGNSPVQEFTVPIGKGTAT
1922G04_R25D_    MGVSDVPRDLEVVAATPTSLLISWDPPSHAYGYYRITYGETGGNSPVQEFTVPIGKGTAT
1922G04_R25E_    MGVSDVPRDLEVVAATPTSLLISWEPPSHAYGYYRITYGETGGNSPVQEFTVPIGKGTAT
1922G04_R25S_    MGVSDVPRDLEVVAATPTSLLISWSPPSHAYGYYRITYGETGGNSPVQEFTVPIGKGTAT
2012A04          MGVSDVPRDLEVVAATPTSLLISWRPPSNGHGYYRITYGETGGNSPVQEFTVPVNEGTAT
2013E01          MGVSDVPRDLEVVAATPTSLLISWVPPSDDYGYYRITYGETGGNSPVQEFTVPIGKGTAT
2011H05          MGVSDVPRDLEVVAATPTSLLISWVPSSHAYGYYRITYGETGGNSPVQEFTVPVGVGTAT
2011H05_V23D_    MGVSDVPRDLEVVAATPTSLLISWDPSSHAYGYYRITYGETGGNSPVQEFTVPVGVGTAT
2011H05_V23E_    MGVSDVPRDLEVVAATPTSLLISWEPSSHAYGYYRITYGETGGNSPVQEFTVPVGVGTAT

1459D05          ISGLKPGVDYTITVYAVEYPYKHSGYYHRPISINYRTEIDKPSQHHHHHH(SEQ ID NO:39)
1784F03          ISGLKPGVDYTITVYAVEYTFKHSGYYHRPISINYRTEIDKPSQHHHHHH(SEQ ID NO:41)
1784F03-m1       ISGLKPGVDYTITVYAVEYTFKHSGYYHRPISINYRTEIDKPSQHHHHHH(SEQ ID NO:43)
1784F03-m2       ISGLKPGVDYTITVYAVEYTFKHSGYYHRPISINYRTEIDKPSQHHHHHH(SEQ ID NO:45)
1784F03-m3       ISGLKPGVDYTITVYAVEYTFKHSGYYHRPISINYRTEIDKPSQHHHHHH(SEQ ID NO:47)
1813E02          ISGLKPGVDYTITVYAVEYTYKGSGYYHRPISINYRTEIDKPSQHHHHHH(SEQ ID NO:49)
1923B02          ISGLKPGVDYTITVYAVEYTYNGAGYYHRPISINYRTEIDKPSQHHHHHH(SEQ ID NO:51)
1923B02_N82I_    ISGLKPGVDYTITVYAVEYTYIGAGYYHRPISINYRTG---SGSHHHHHH(SEQ ID NO:53)
1923B02_N82E_    ISGLKPGVDYTITVYAVEYTYEGAGYYHRPISINYRTG---SGSHHHHHH(SEQ ID NO:55)
1923B02_T80A_    ISGLKPGVDYTITVYAVEYAYNGAGYYHRPISINYRTG---SGSHHHHHH(SEQ ID NO:57)
1922G04          ISGLKPGVDYTITVYAVEYPWKGSGYYHRPISINYRTEIDKPSQHHHHHH(SEQ ID NO:59)
1922G04_R25D_    ISGLKPGVDYTITVYAVEYPWKGSGYYHRPISINYRTG---SGSHHHHHH(SEQ ID NO:61)
1922G04_R25E_    ISGLKPGVDYTITVYAVEYPWKGSGYYHRPISINYRTG---SGSHHHHHH(SEQ ID NO:63)
1922G04_R25S_    ISGLKPGVDYTITVYAVEYPWKGSGYYHRPISINYRTG---SGSHHHHHH(SEQ ID NO:65)
2012A04          ISGLKPGVDYTITVYAVEFPFKWSGYYHRPISINYRTEIDKPSQHHHHHH(SEQ ID NO:67)
2013E01          ISGLKPGVDYTITVYAVEFPWPHAGYYHRPISINYRTEIDKPSQHHHHHH(SEQ ID NO:69)
2011H05          ISGLKPGVDYTITVYAVEYAFEGAGYYHRPISINYRTEIDKPSQHHHHHH(SEQ ID NO:71)
2011H05_V23D_    ISGLKPGVDYTITVYAVEYAFEGAGYYHRPISINYRTEIDKPSQHHHHHH(SEQ ID NO:73)
2011H05_V23E_    ISGLKPGVDYTITVYAVEYAFEGAGYYHRPISINYRTEIDKPSQHHHHHH(SEQ ID NO:75)
```

FIG. 2

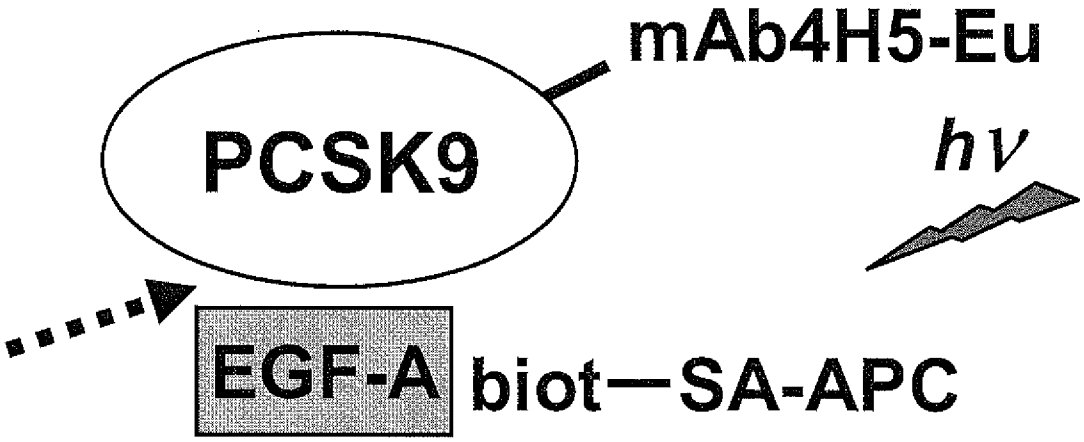


FIG. 3

A.

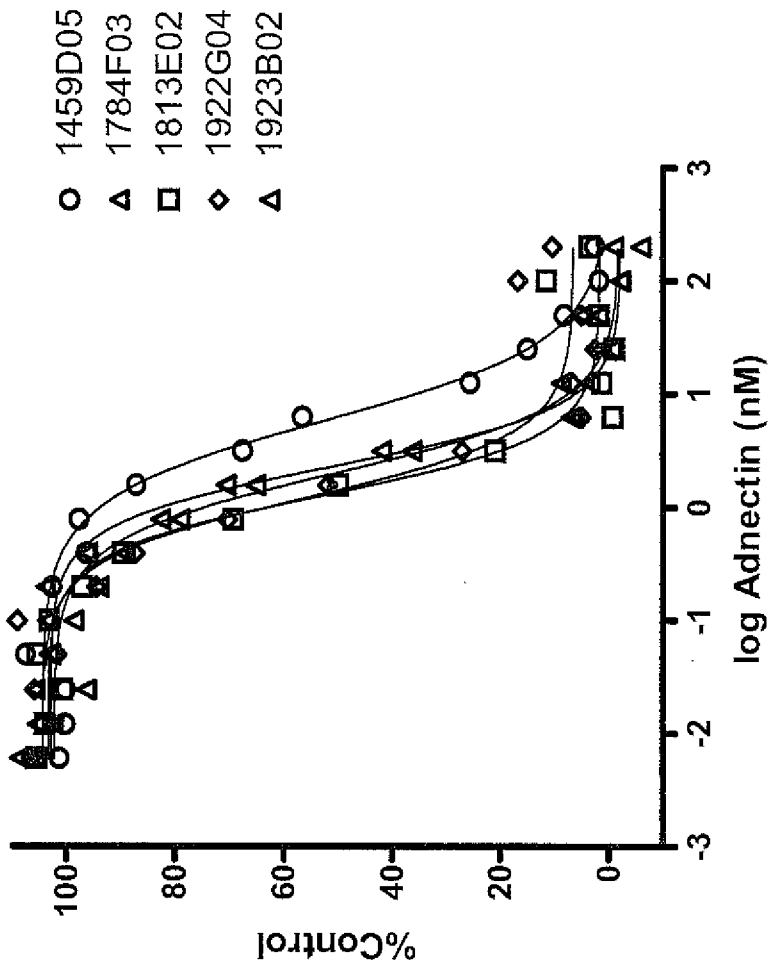

1459D05
1784F03
1813E02
1922G04
1923B02
%Control
100
80
60
40
20
0
-3
-2
-1
0
1
2
3
log Adnectin (nM)

FIG. 3 (continued)

B.

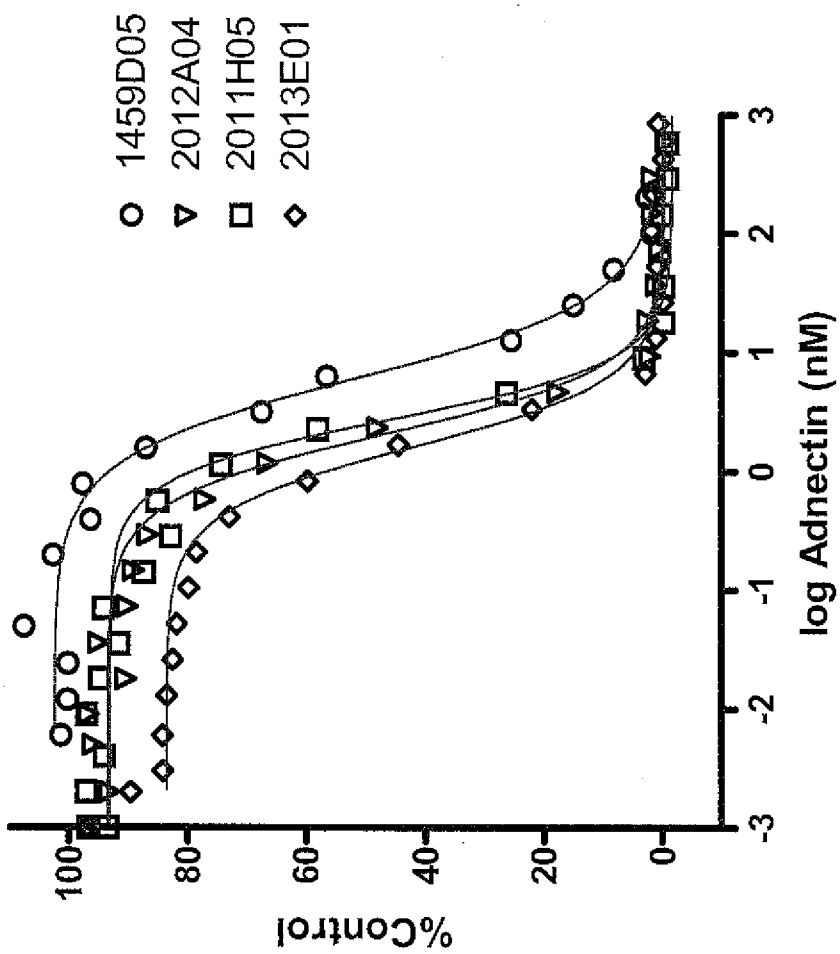


FIG. 4

A.

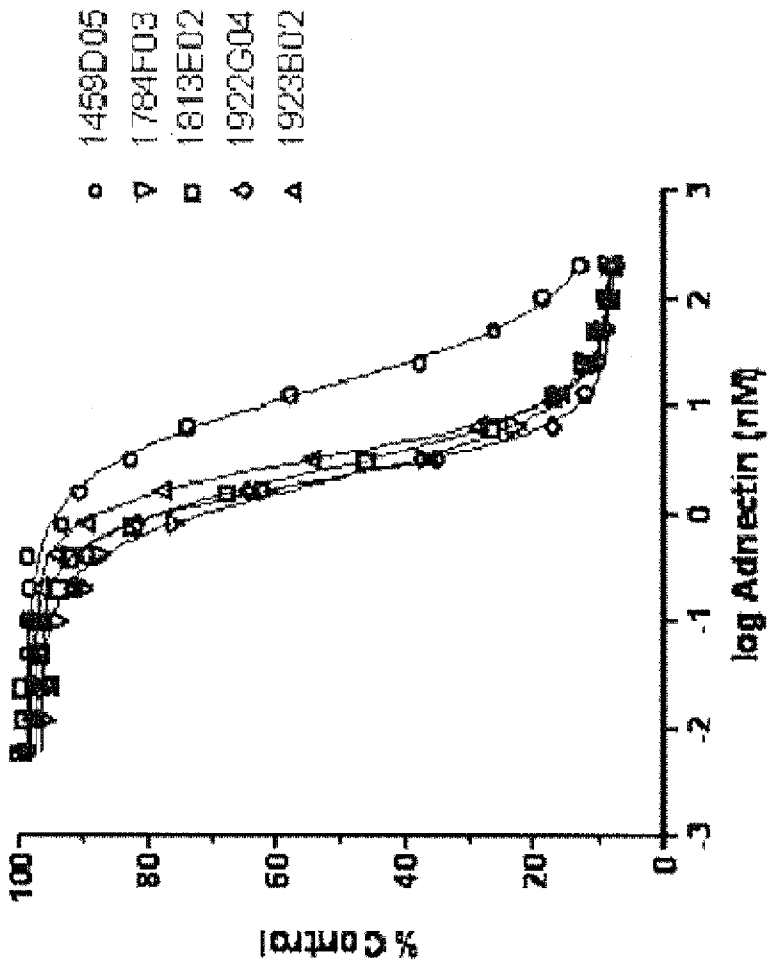

1459D05
1784F03
1813E02
1922G04
1923B02
% Control
log Adnectin (nM)
100
80
60
40
20
0
-3
-2
-1
0
1
2
3

FIG. 4 (continued)

B.

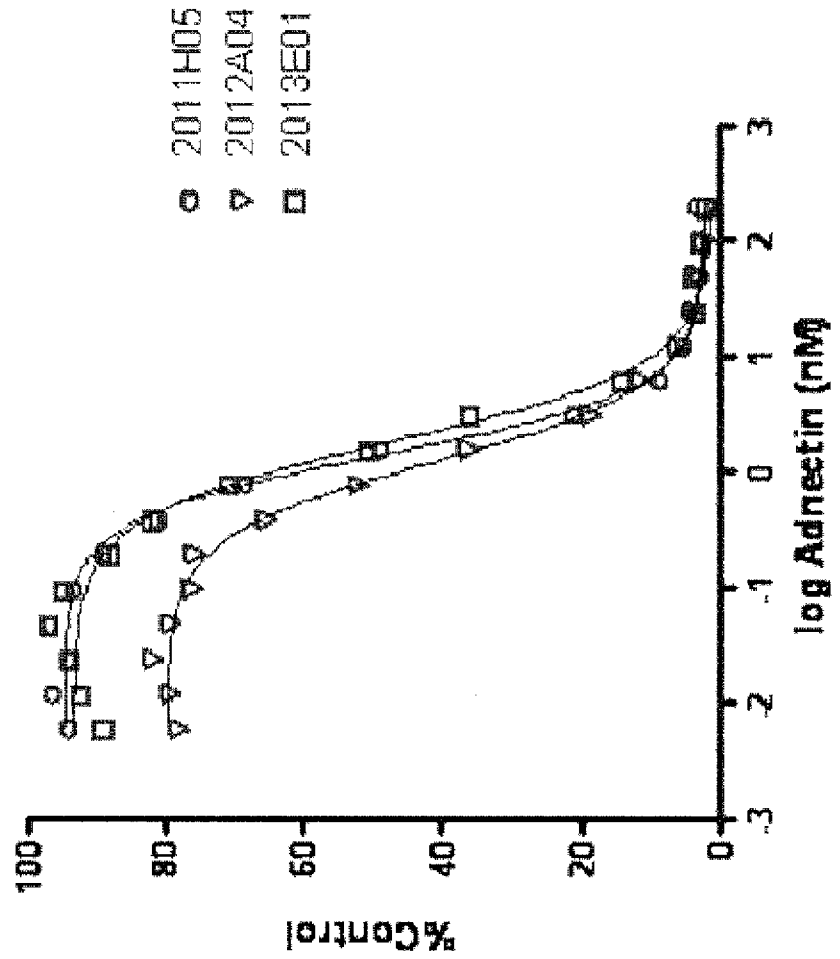


FIG. 5

A.

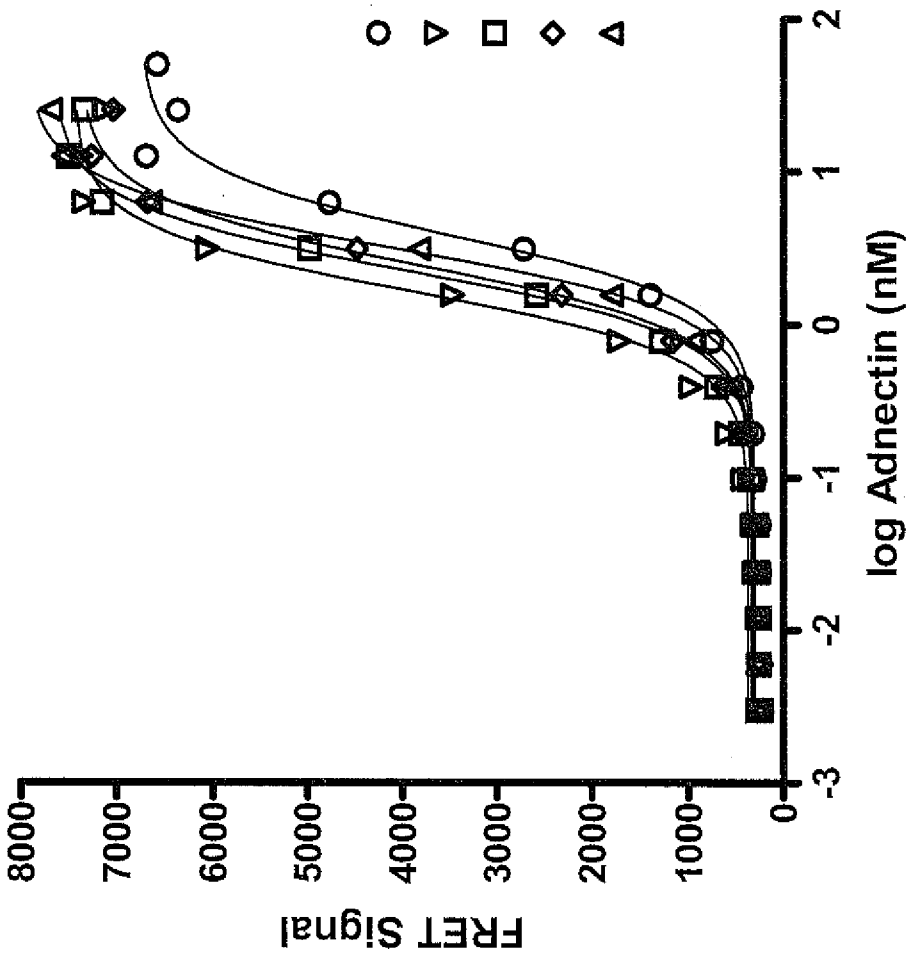

1459D05
1784F03
1813E02
1922G04
1923B02
FRET Signal
8000
7000
6000
5000
4000
3000
2000
1000
0
-3
-2
-1
0
1
2
log Adnectin (nM)

FIG. 5 (continued)

B.

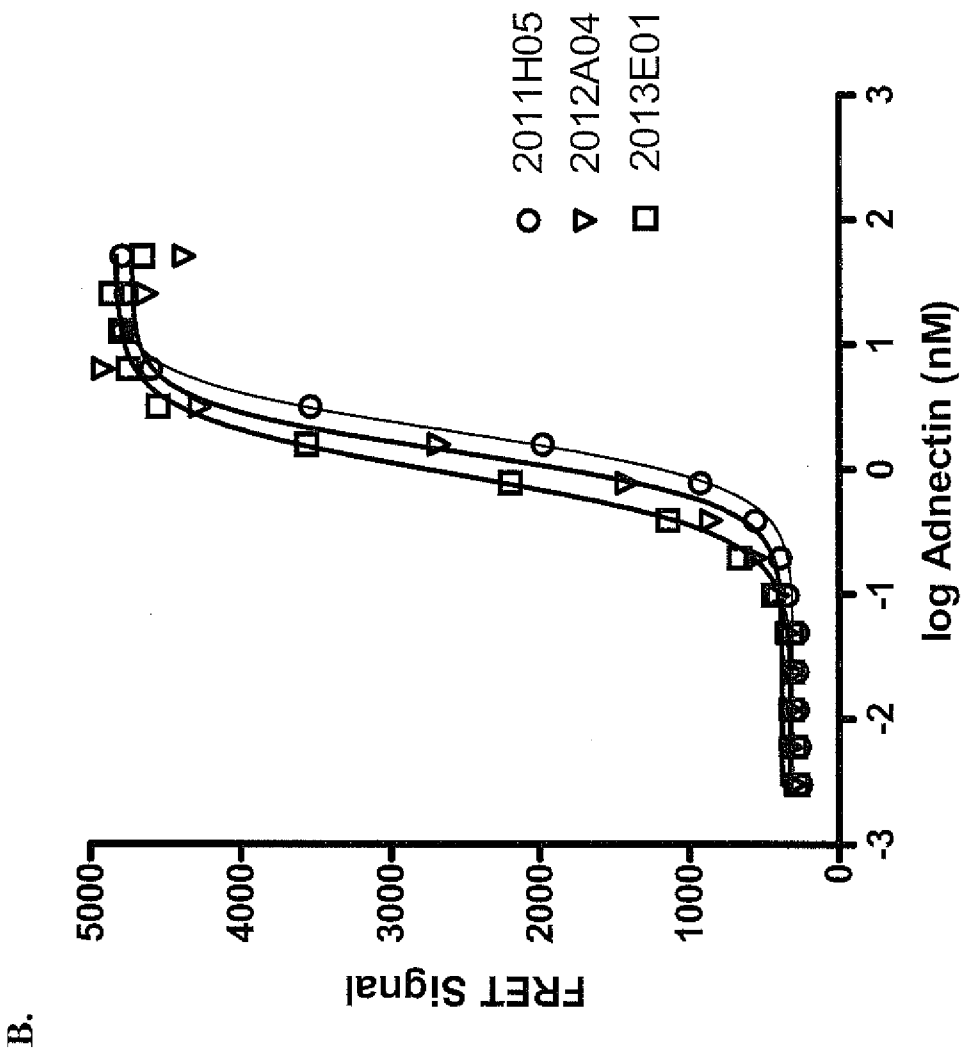


FIG. 6

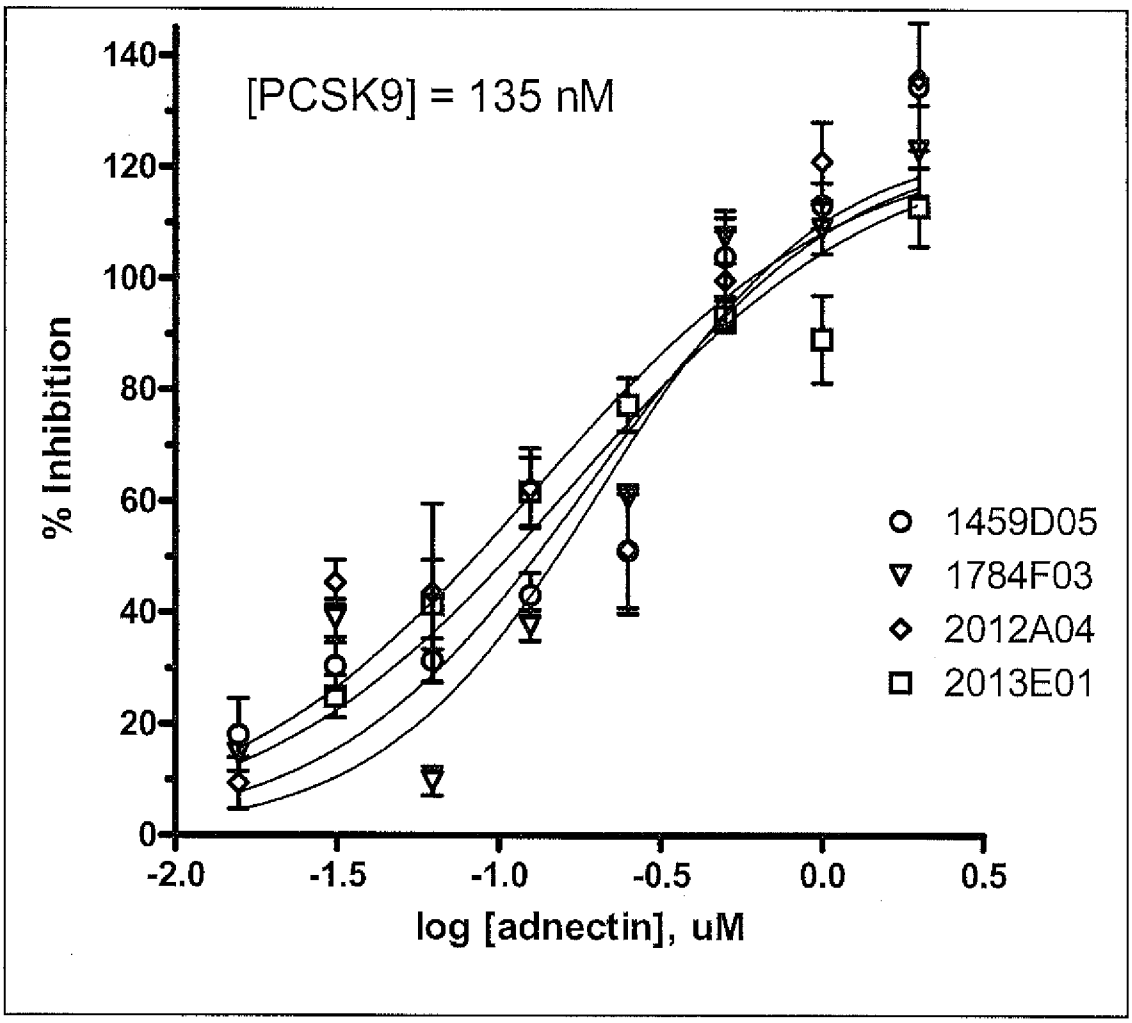

[PCSK9] = 135 nM
% Inhibition
140
120
100
80
60
40
20
0
-2.0
-1.5
-1.0
-0.5
0.0
0.5
log [adnectin], uM
1459D05
1784F03
2012A04
2013E01

FIG. 7

A.

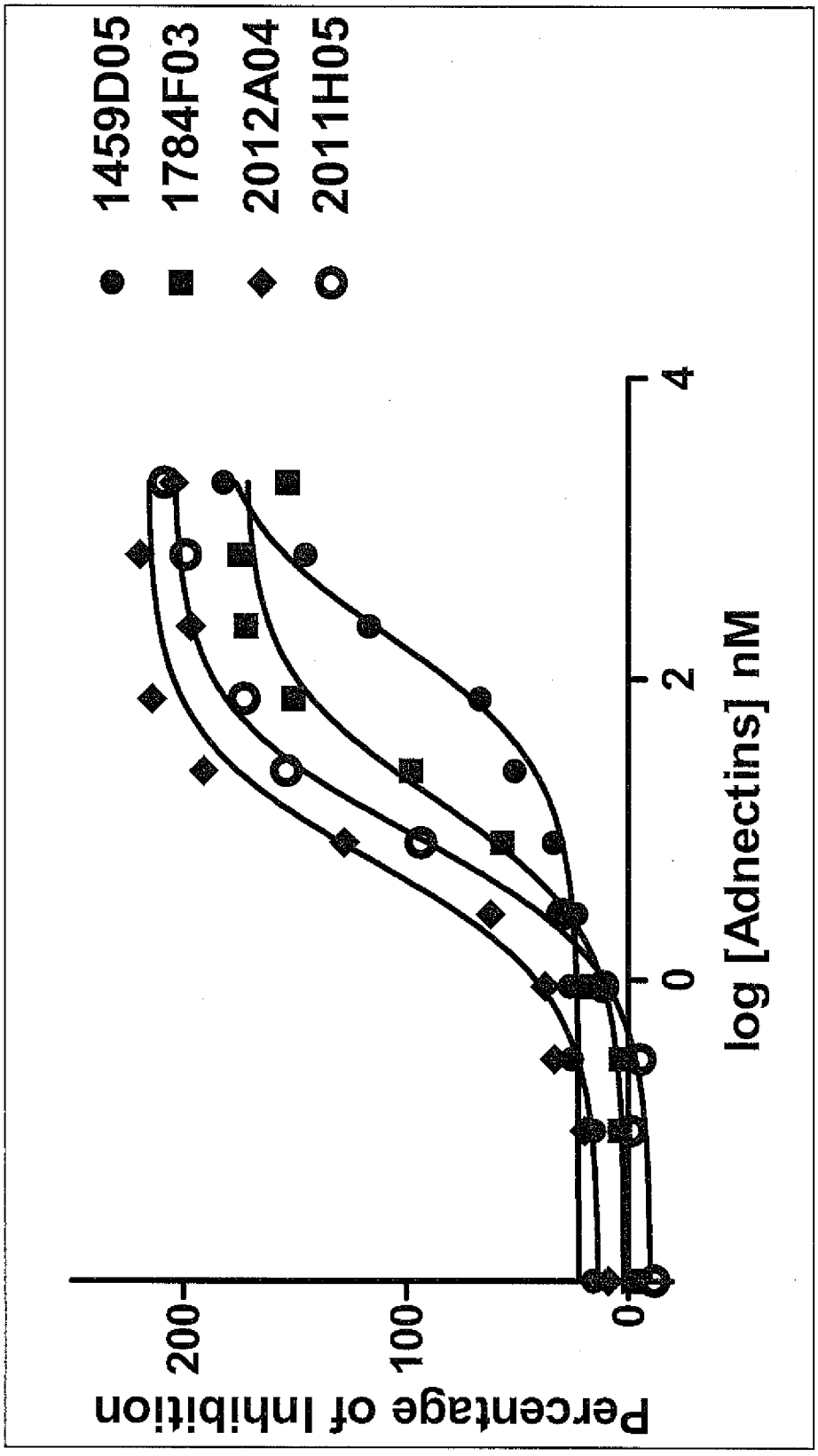

1459D05
1784F03
2012A04
2011H05
Percentage of Inhibition
200
100
0
log [Adnectins] nM
-4
-2
0
2
4

FIG. 7 (continued)

B.

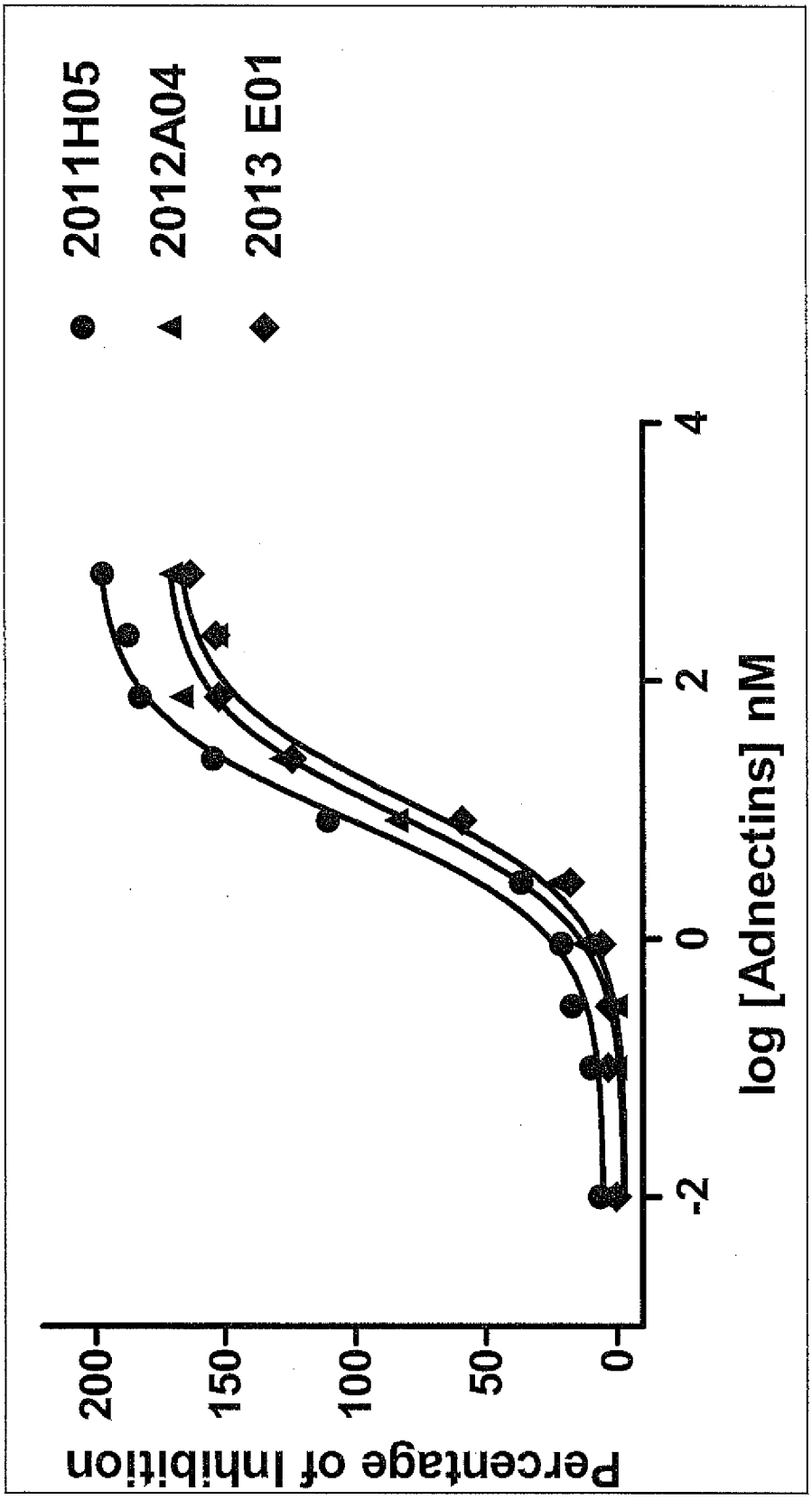


FIG. 8

A.

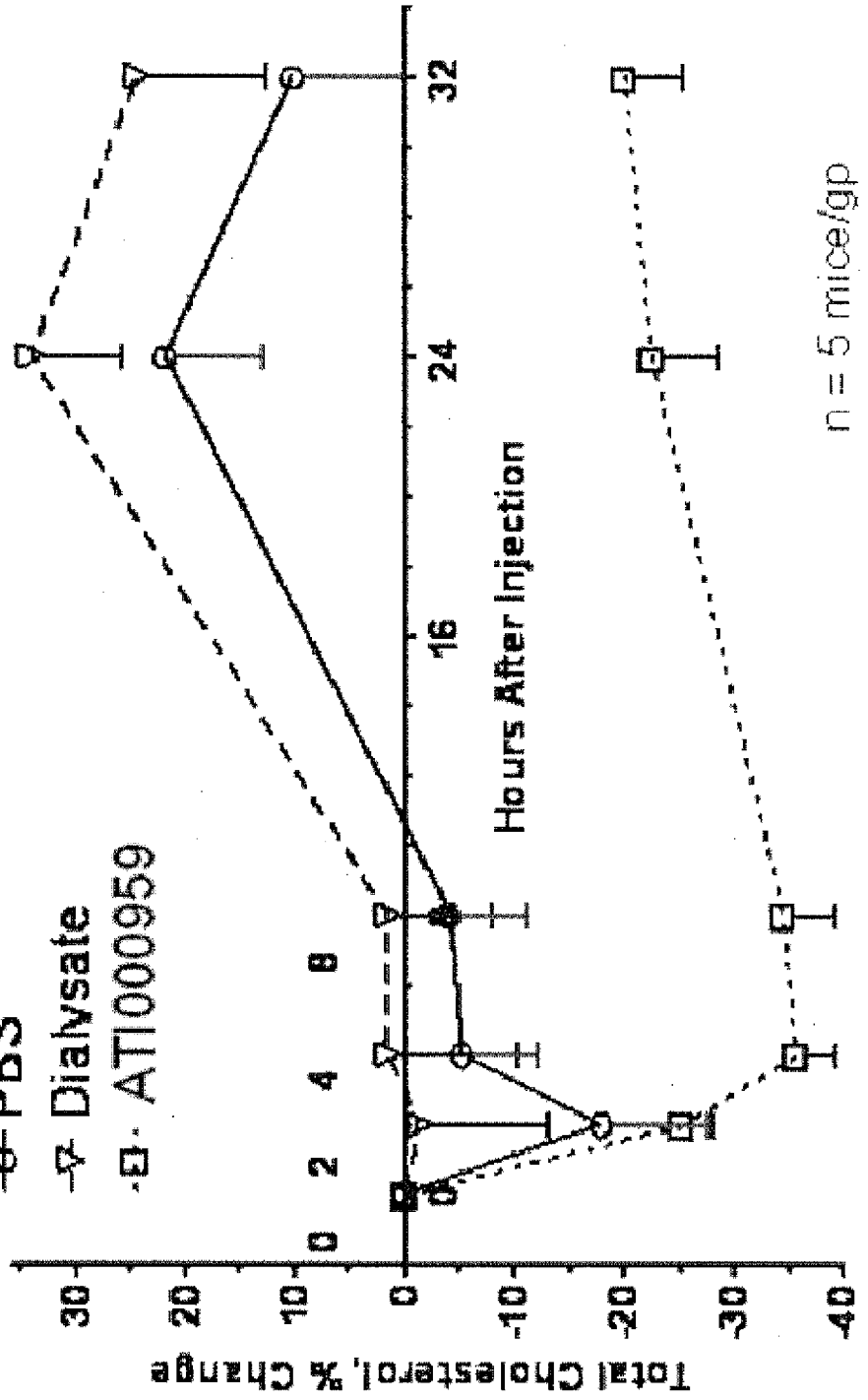

PBS
Dialysate
ATI000959
Hours After Injection
Total Cholesterol, % Change
n = 5 mice/gp
0
2
4
8
16
24
32
30
20
10
0
-10
-20
-30
-40

FIG. 8 (continued)

B.

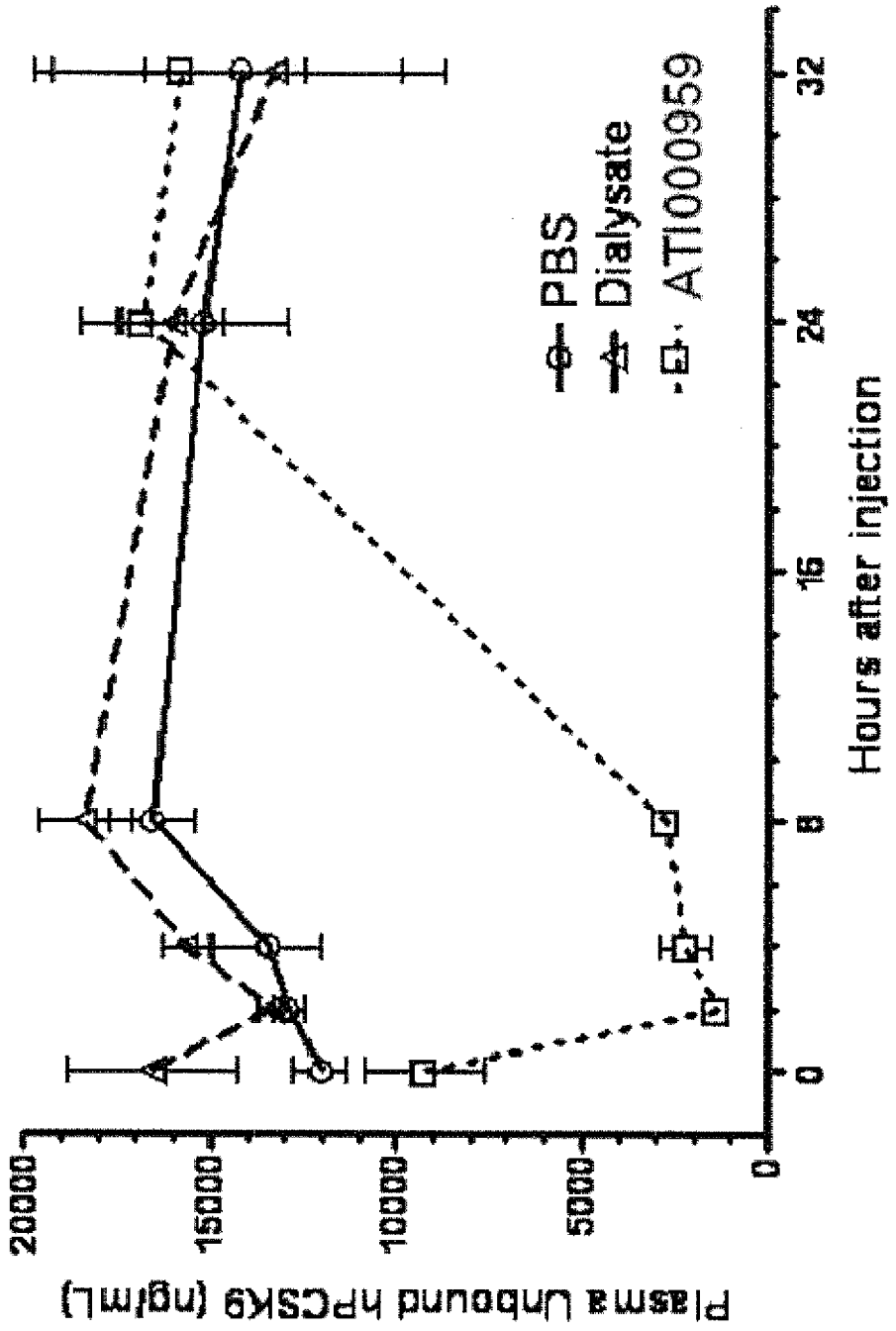


FIG. 9

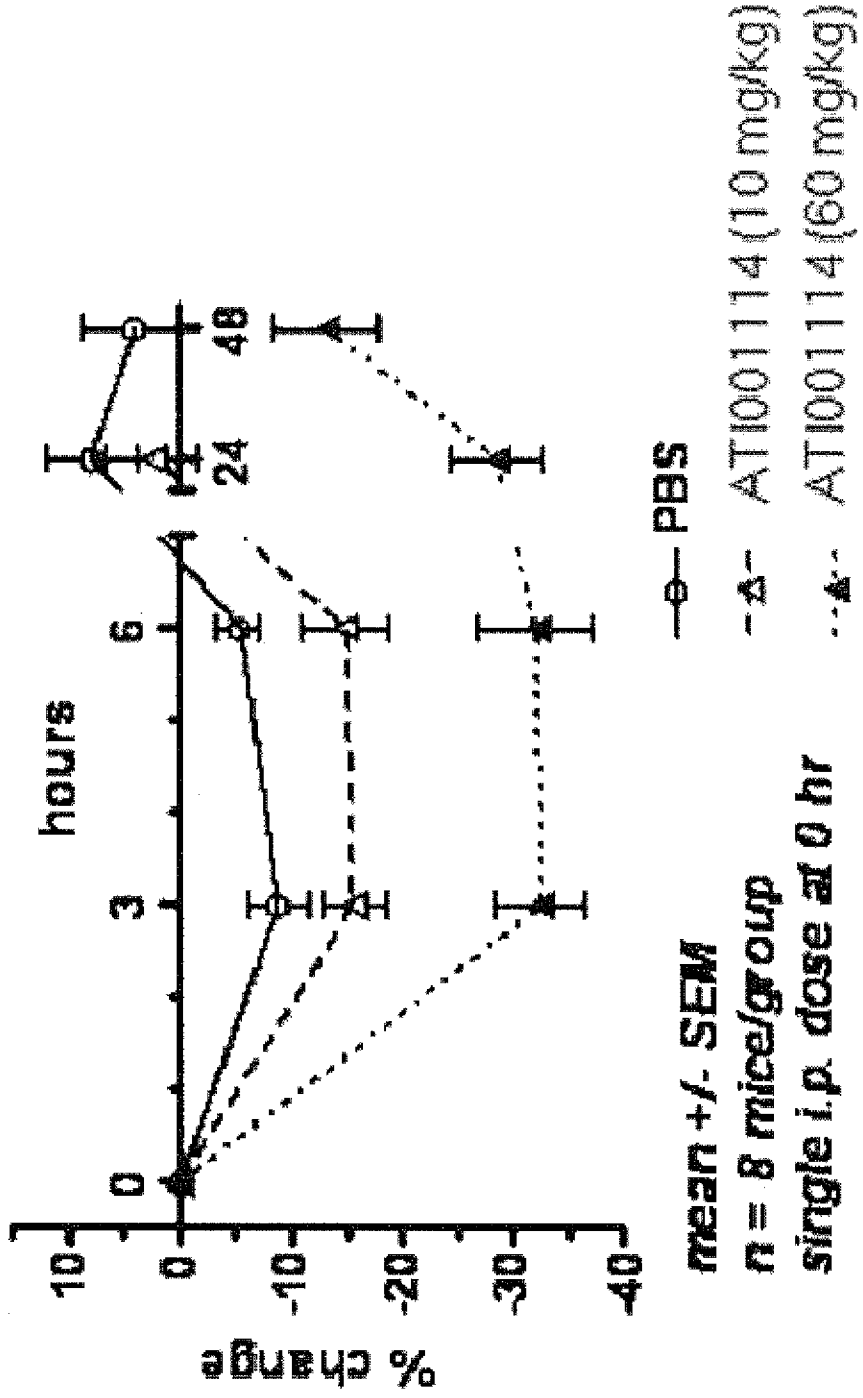
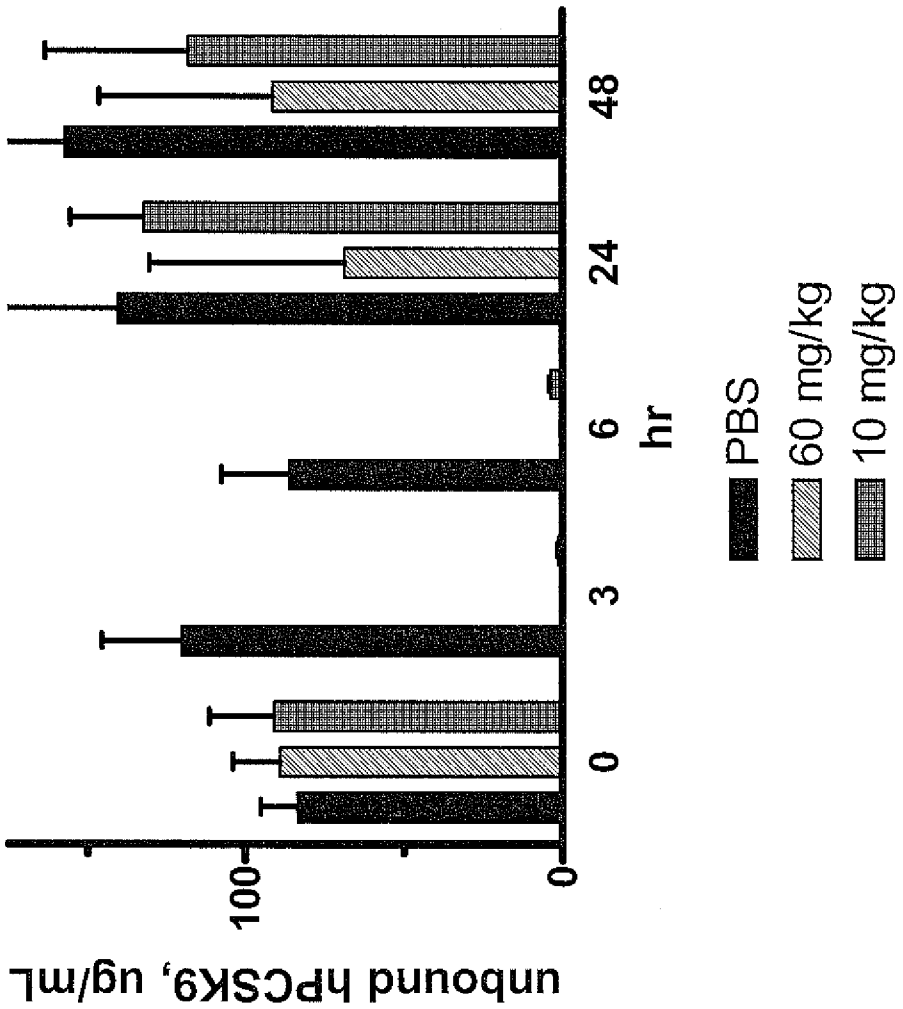

A.
% change
10
0
-10
-20
-30
-40
hours
0
3
6
24
48
PBS
AT1001114 (10 mg/kg)
AT1001114 (60 mg/kg)
mean +/- SEM
n = 8 mice/group
single i.p. dose at 0 hr

FIG. 9 (continued)



B.

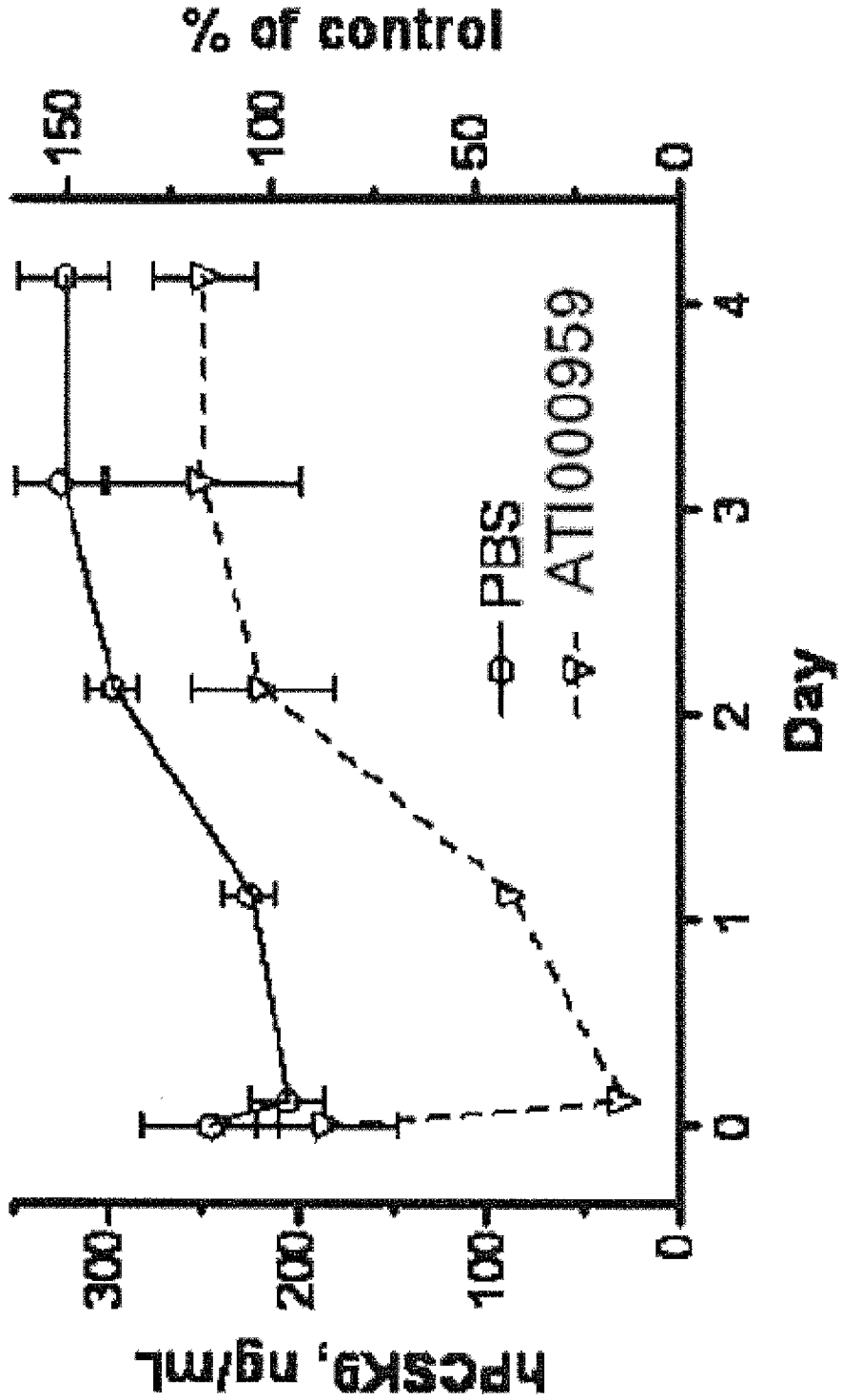

% of control
150
100
50
0
hPCSK9, ng/mL
300
200
100
0
0
1
2
3
4
Day
PBS
ATI000959

FIG. 10

A.

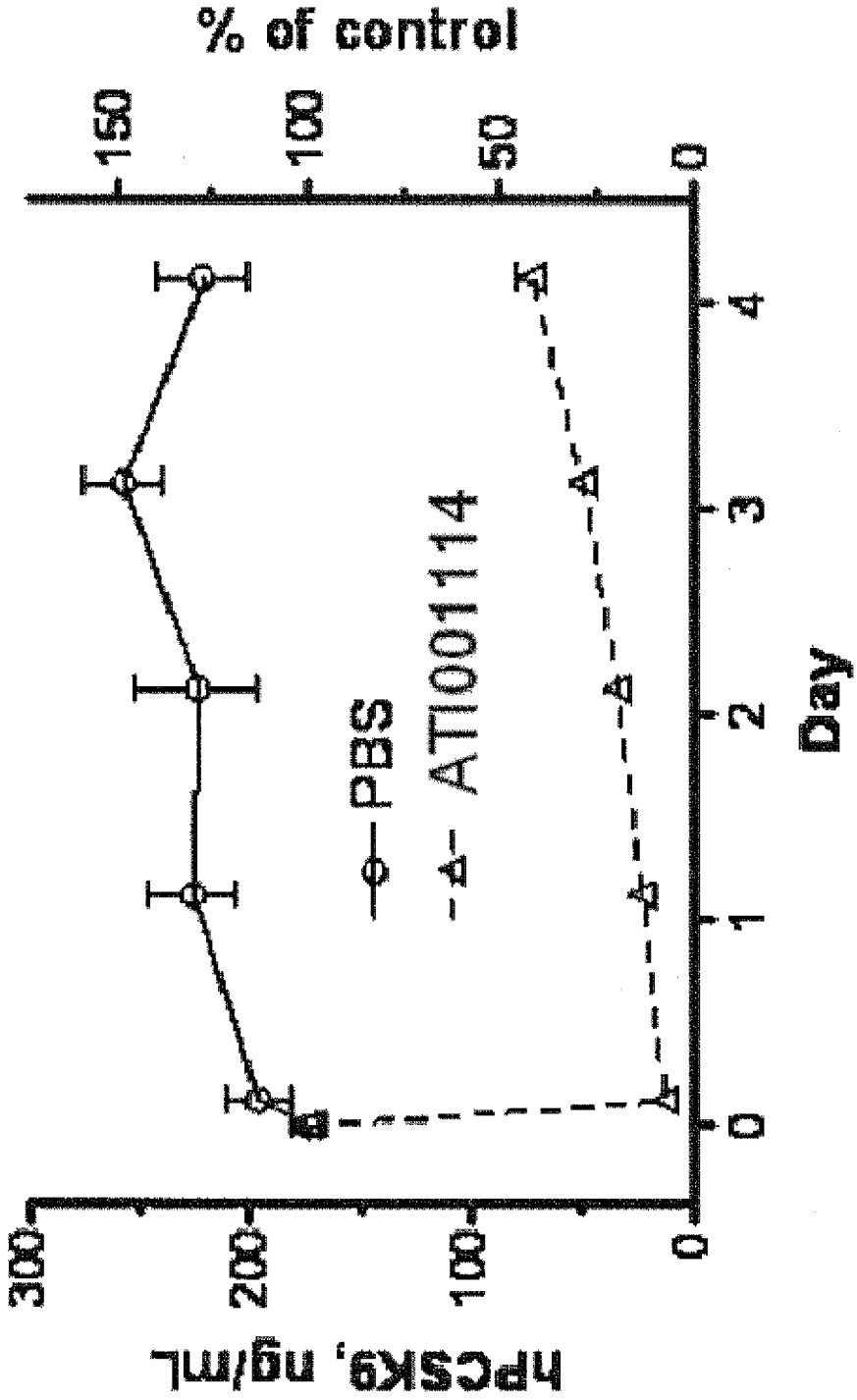
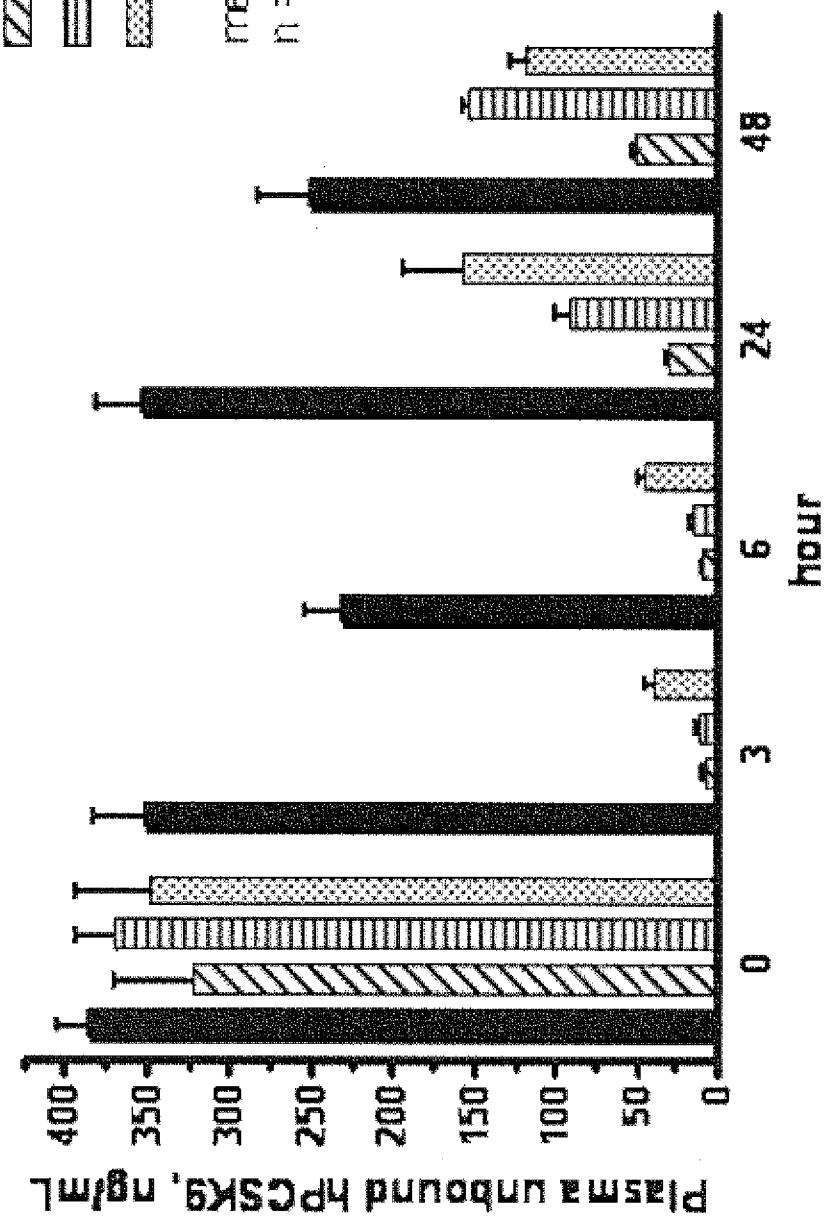


FIG. 10 (continued)

B.

FIG. 11


Control
1 mg/kg AT1001114
0.3 mg/kg AT1001114
0.1 mg/kg AT1001114
mean +/- SD
n = 5 or 6 /gp
Plasma unbound hPCSK9, ng/mL
400
350
300
250
200
150
100
50
0
0
3
6
24
48
hour

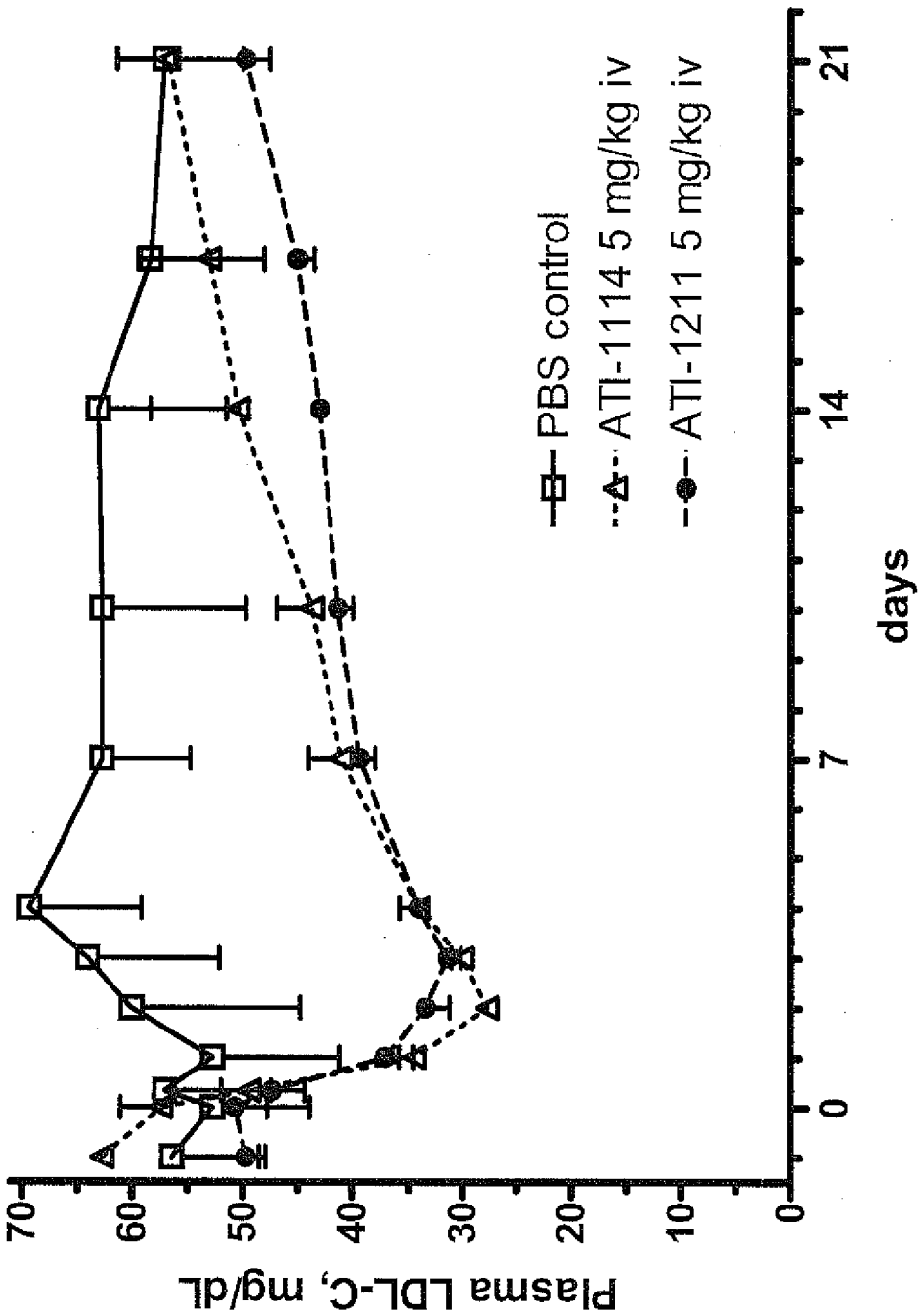

Plasma LDL-C, mg/dL
70
60
50
40
30
20
10
0
0
7
14
21
days
PBS control
ATI-1114 5 mg/kg iv
ATI-1211 5 mg/kg iv

FIG. 12

FIG. 13

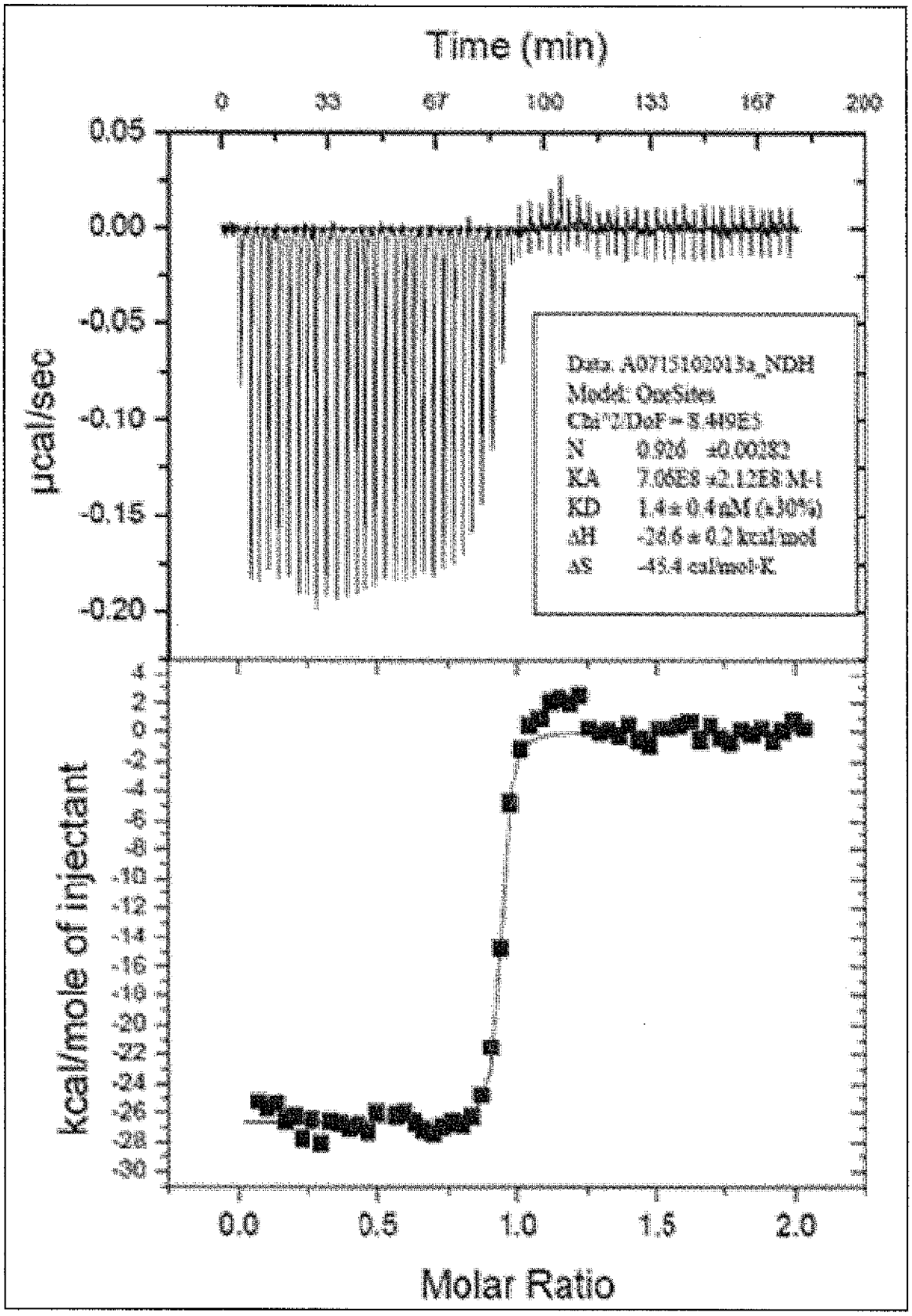
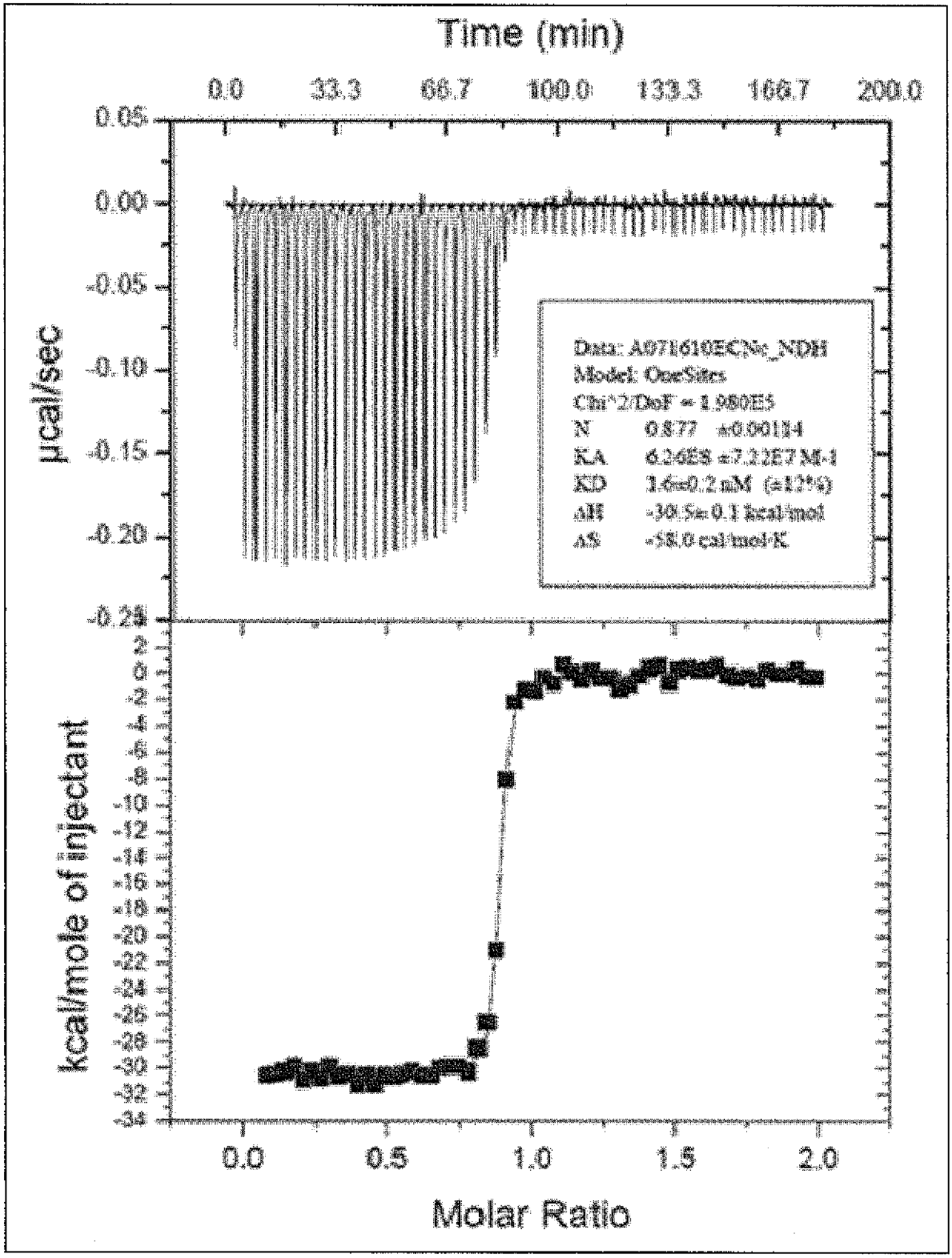

Time (min)
0
33
67
100
133
167
200
0.05
0.00
-0.05
-0.10
-0.15
-0.20
µcal/sec
Data: A071510201 3a_NDH
Model: OneSites
N 0.926 ±0.00282
KA 7.06E8 ±2.12E8 M-1
KD 1.4 ± 0.4 nM (±30%)
ΔH -26.6 ± 0.2 kcal/mol
ΔS -45.4 cal/mol·K
kcal/mole of injectant
0.0
0.5
1.0
1.5
2.0
Molar Ratio

FIG. 13 (continued)



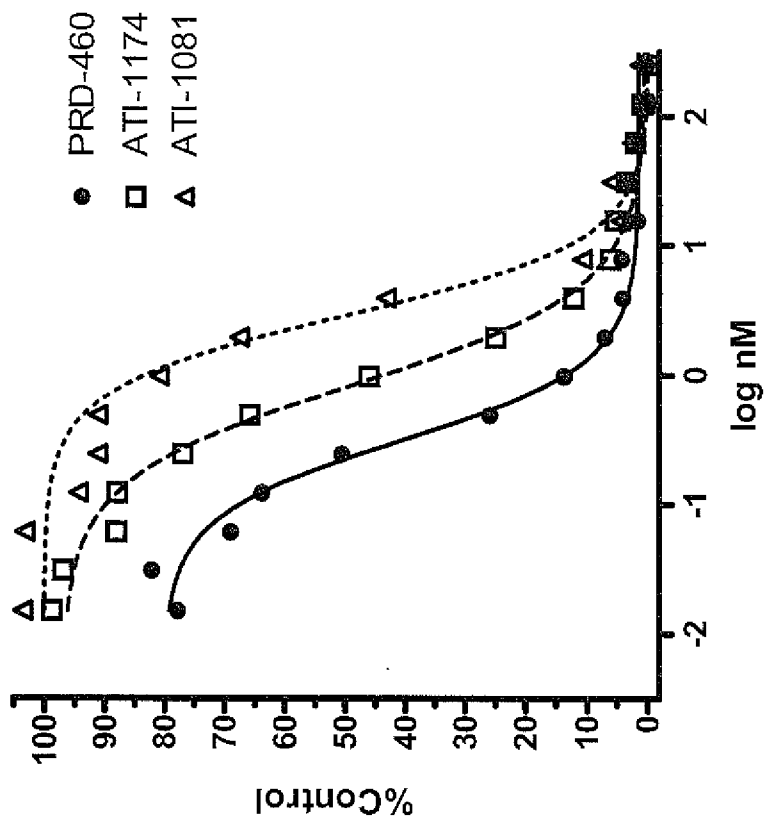

PRD-460
ATI-1174
ATI-1081
%Control
log nM

FIG. 14

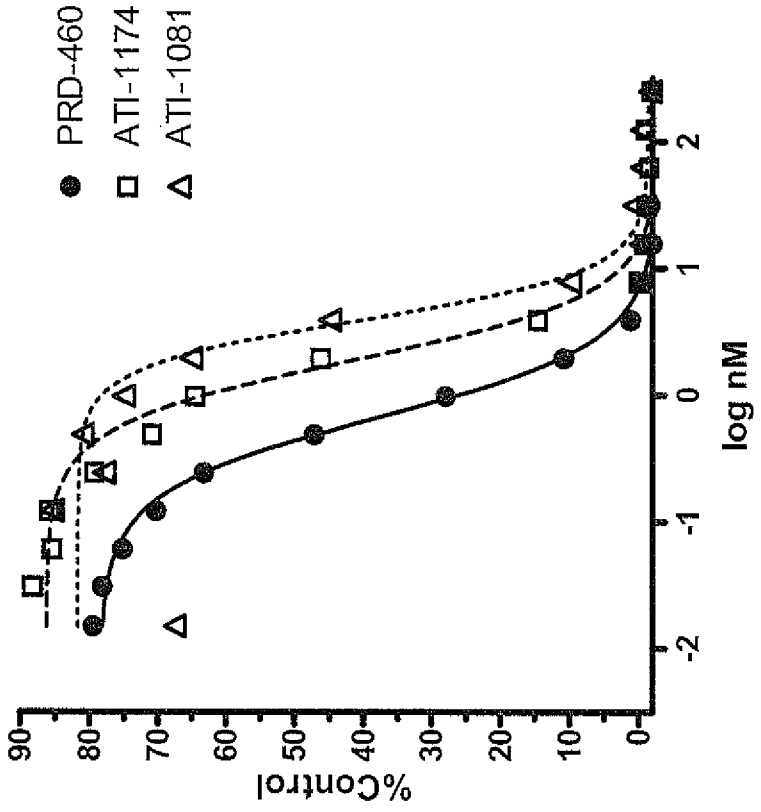
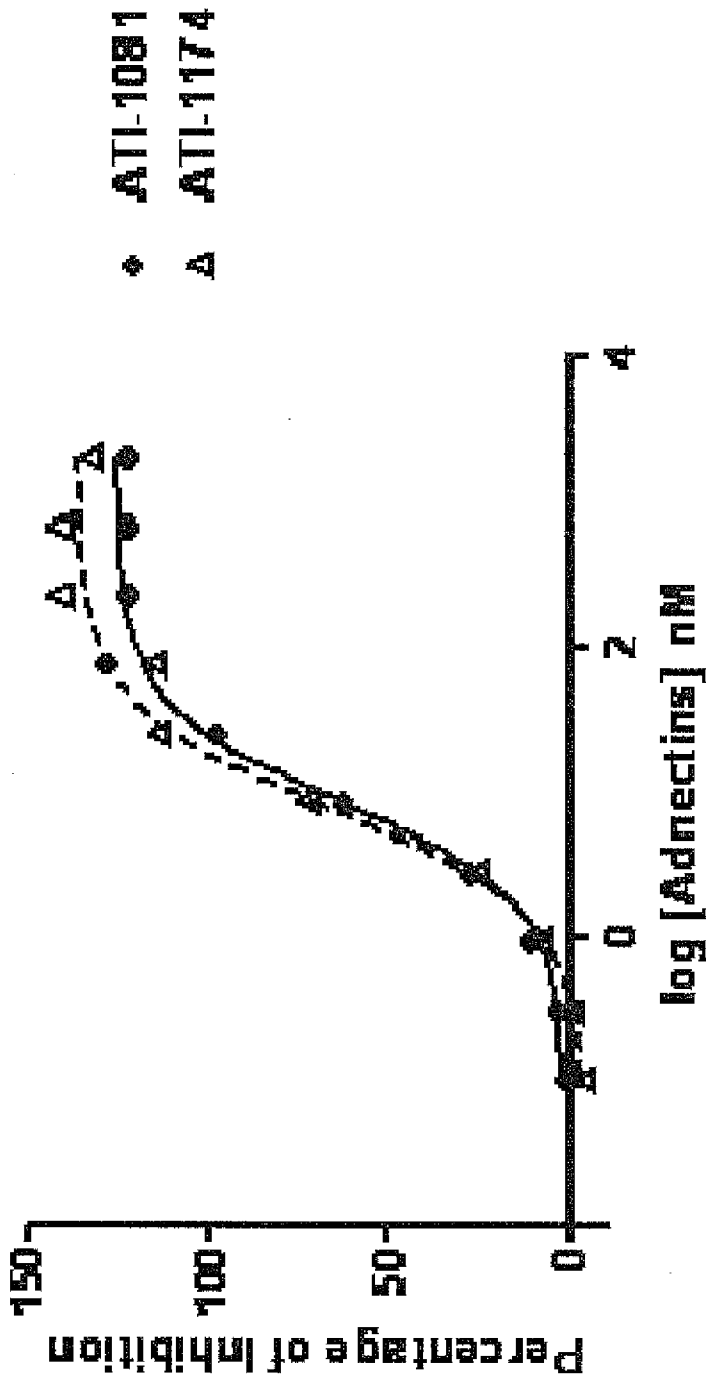

PRD-460
ATI-1174
ATI-1081
%Control
log nM

FIG. 15


ATI-1081
ATI-1174
Percentage of Inhibition
150
100
50
0
0
2
4
log [Adnectins] nM

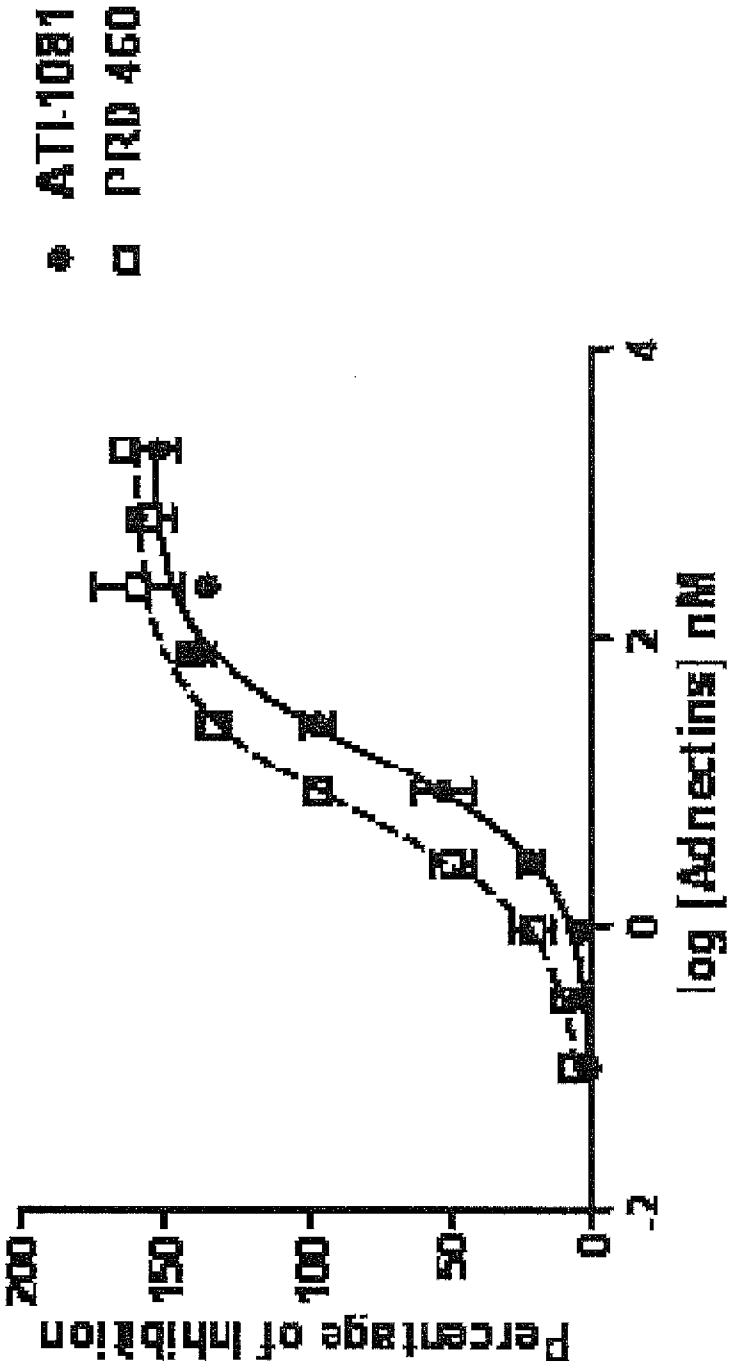
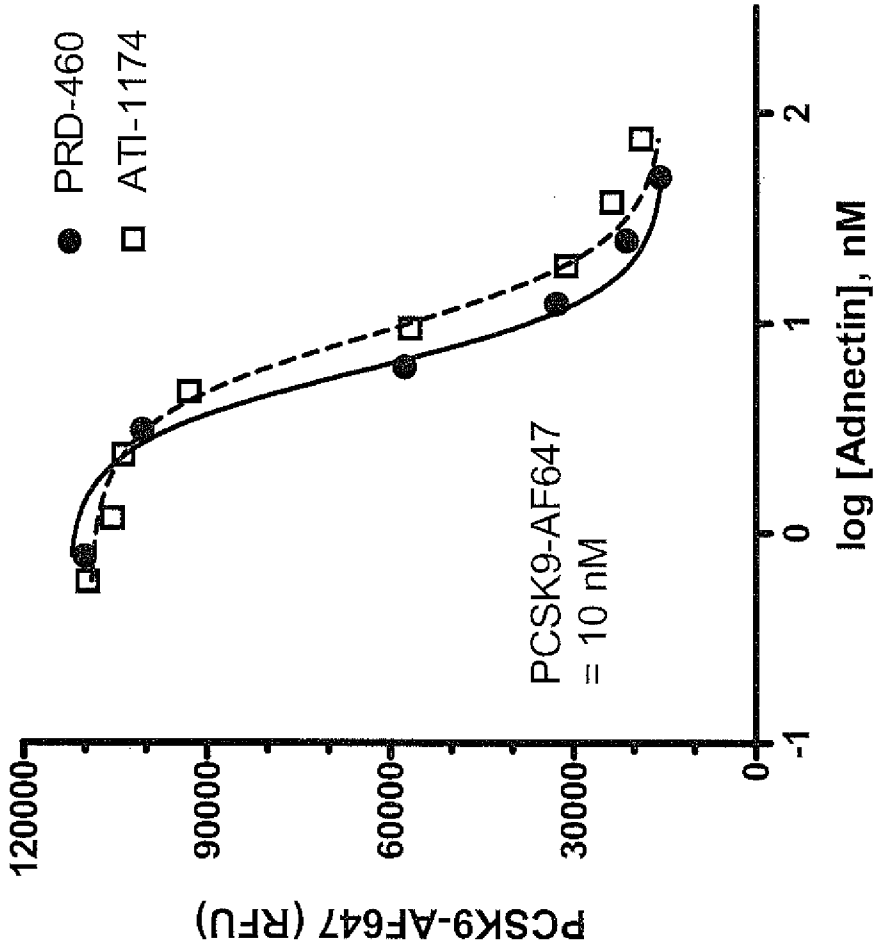


FIG. 15 (continued)

FIG. 16


PRD-460
ATI-1174
PCSK9-AF647
= 10 nM
PCSK9-AF647 (RFU)
120000
90000
60000
30000
0
-1
0
1
2
log [Adnectin], nM

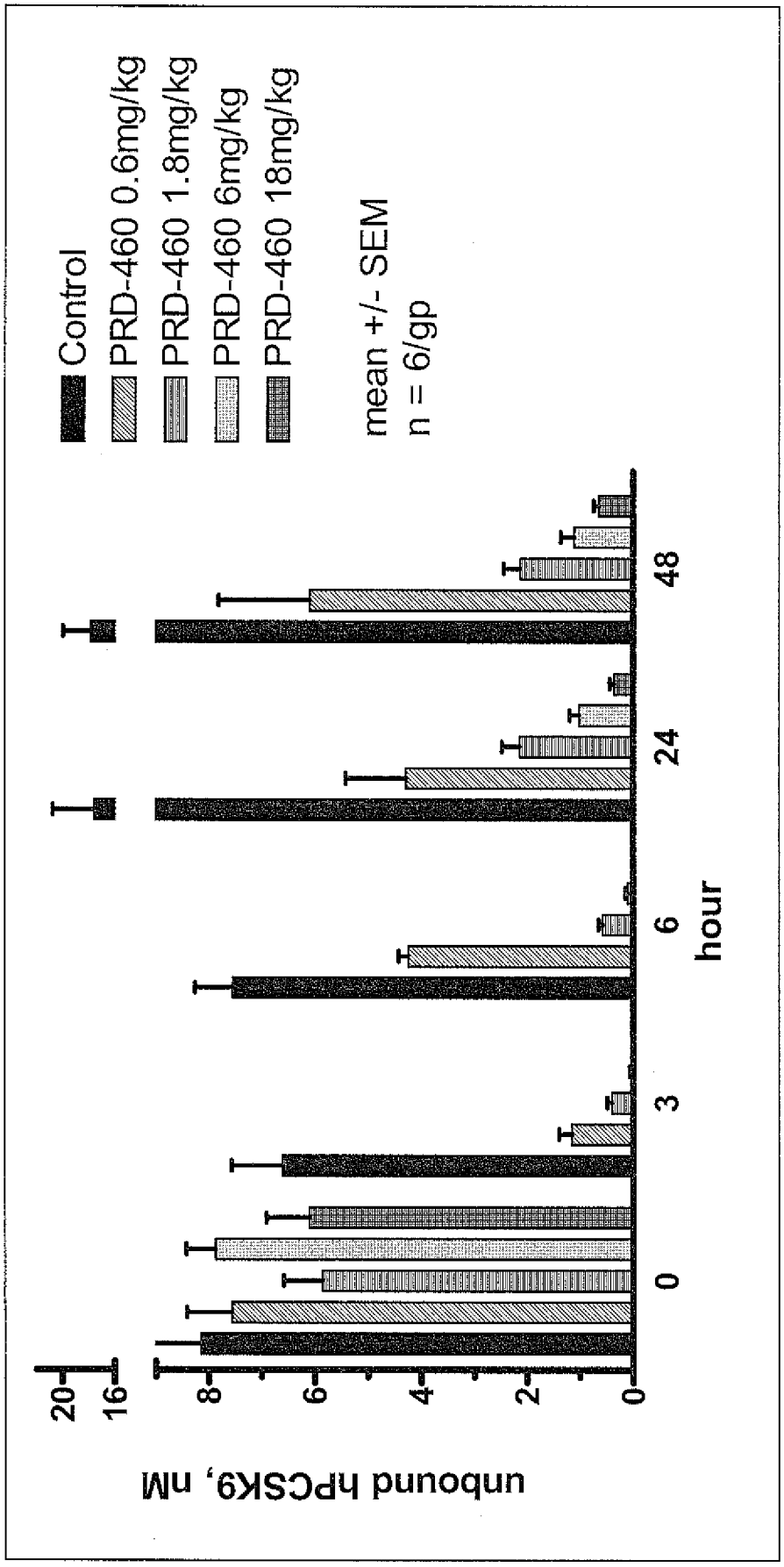
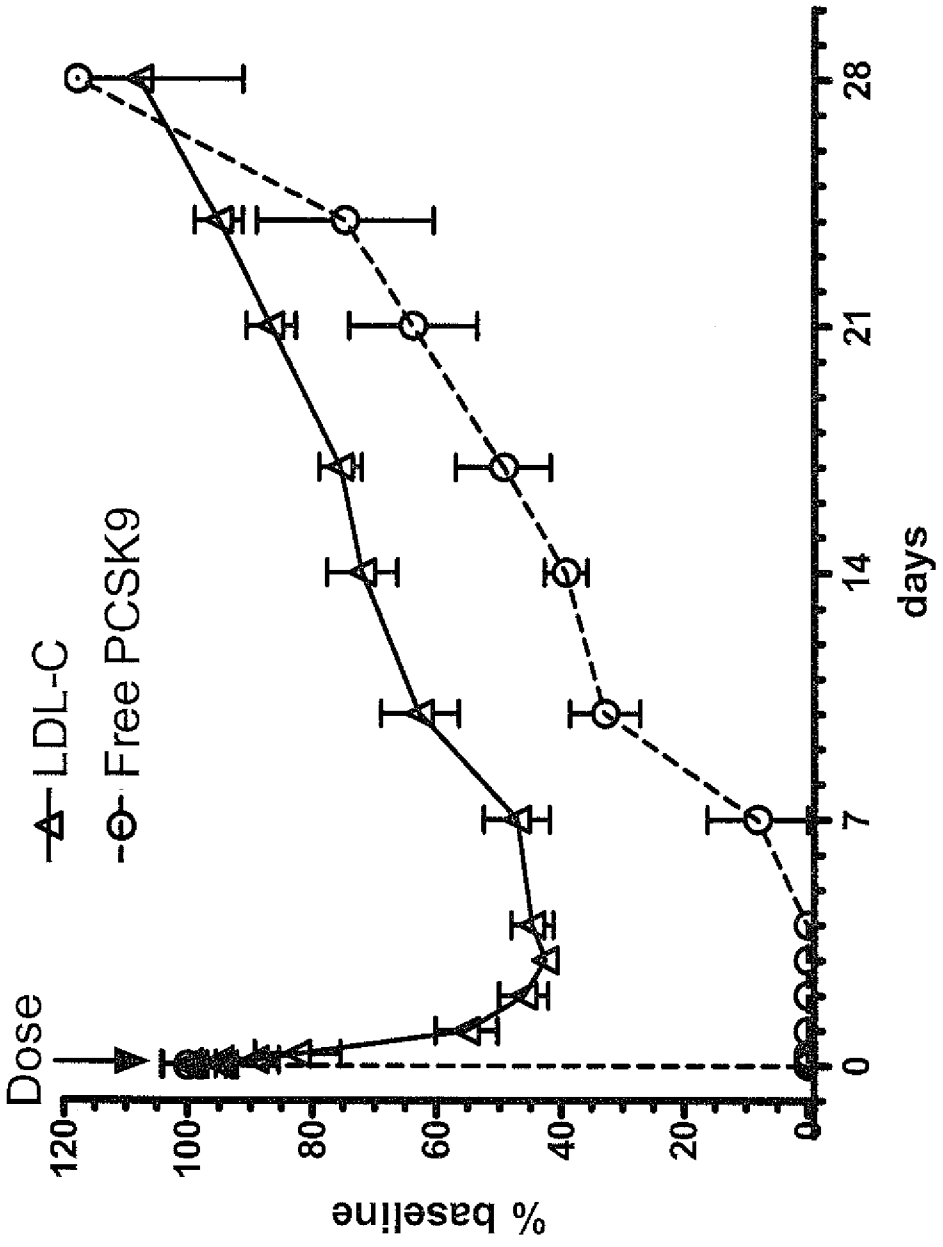

Control
PRD-460 0.6mg/kg
PRD-460 1.8mg/kg
PRD-460 6mg/kg
PRD-460 18mg/kg
mean +/- SEM
n = 6/gp
unbound hPCSK9, nM
20
16
8
6
4
2
0
0
3
6
24
48
hour

FIG. 17

FIG. 18


Dose
LDL-C
Free PCSK9
% baseline
0
20
40
60
80
100
120
0
7
14
21
28
days

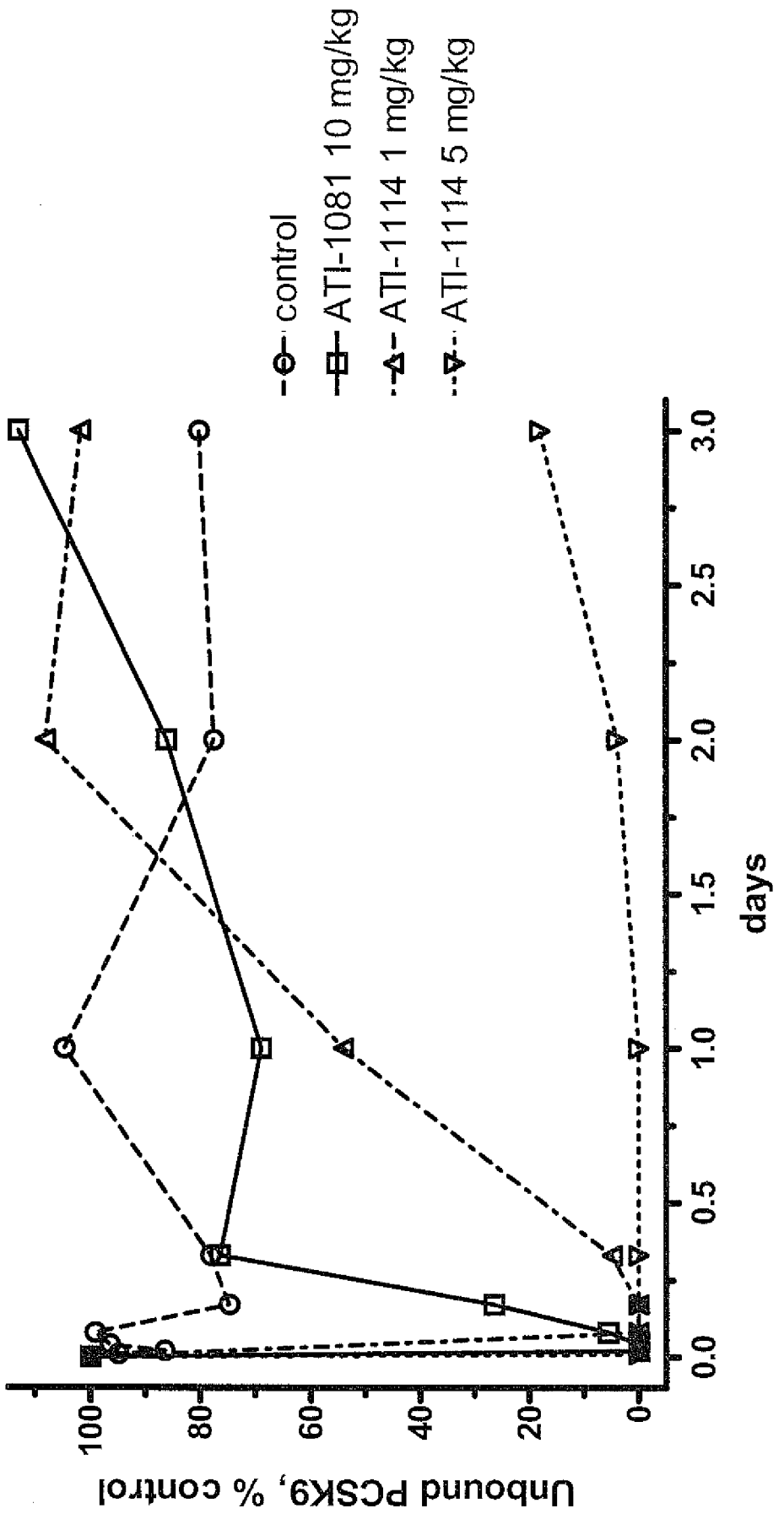

control
ATI-1081 10 mg/kg
ATI-1114 1 mg/kg
ATI-1114 5 mg/kg
Unbound PCSK9, % control
0
20
40
60
80
100
0.0
0.5
1.0
1.5
2.0
2.5
3.0
days

FIG. 19

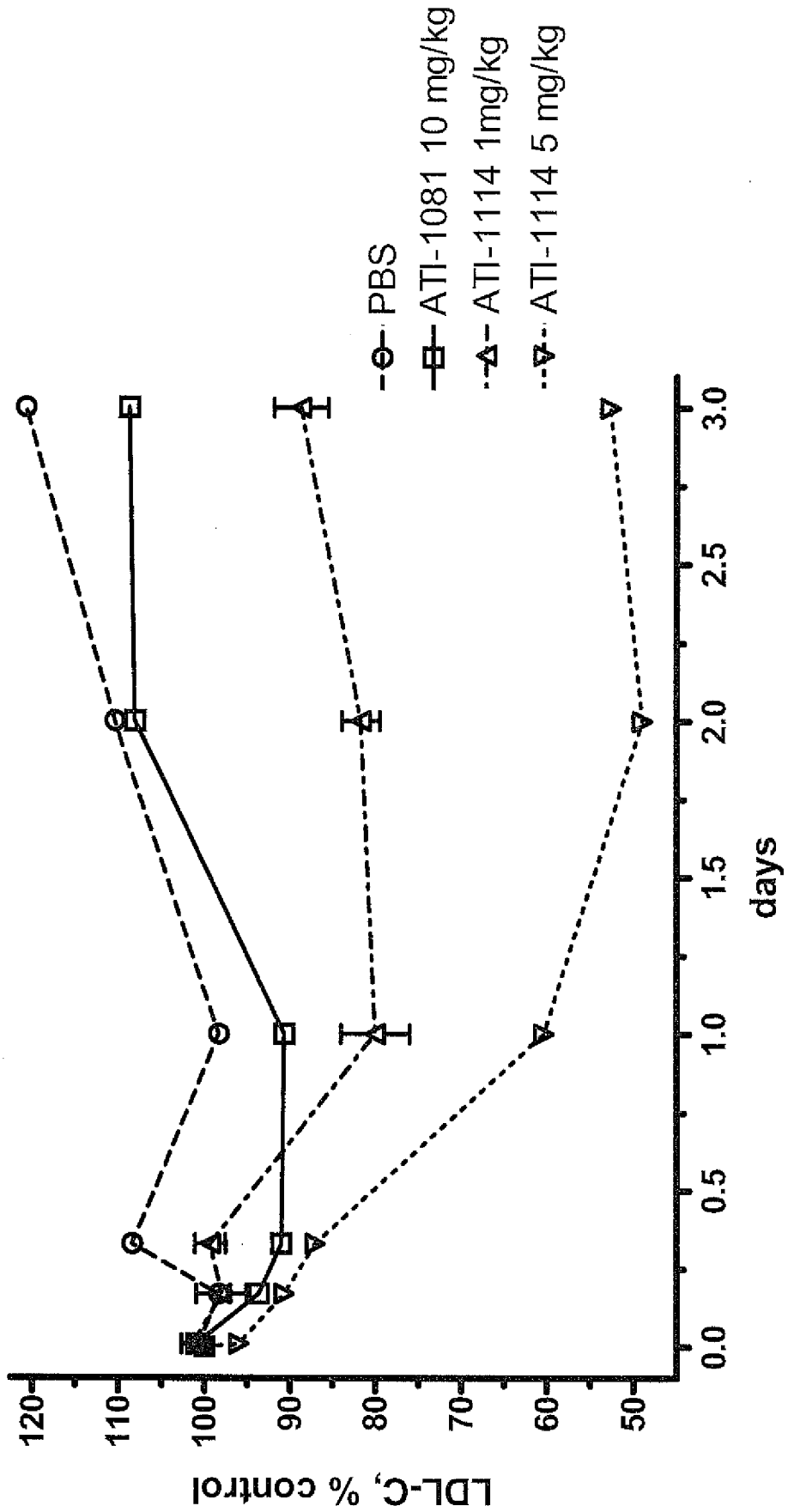

LDL-C, % control
120
110
100
90
80
70
60
50
0.0
0.5
1.0
1.5
2.0
2.5
3.0
days
PBS
ATI-1081 10 mg/kg
ATI-1114 1mg/kg
ATI-1114 5 mg/kg

FIG. 20

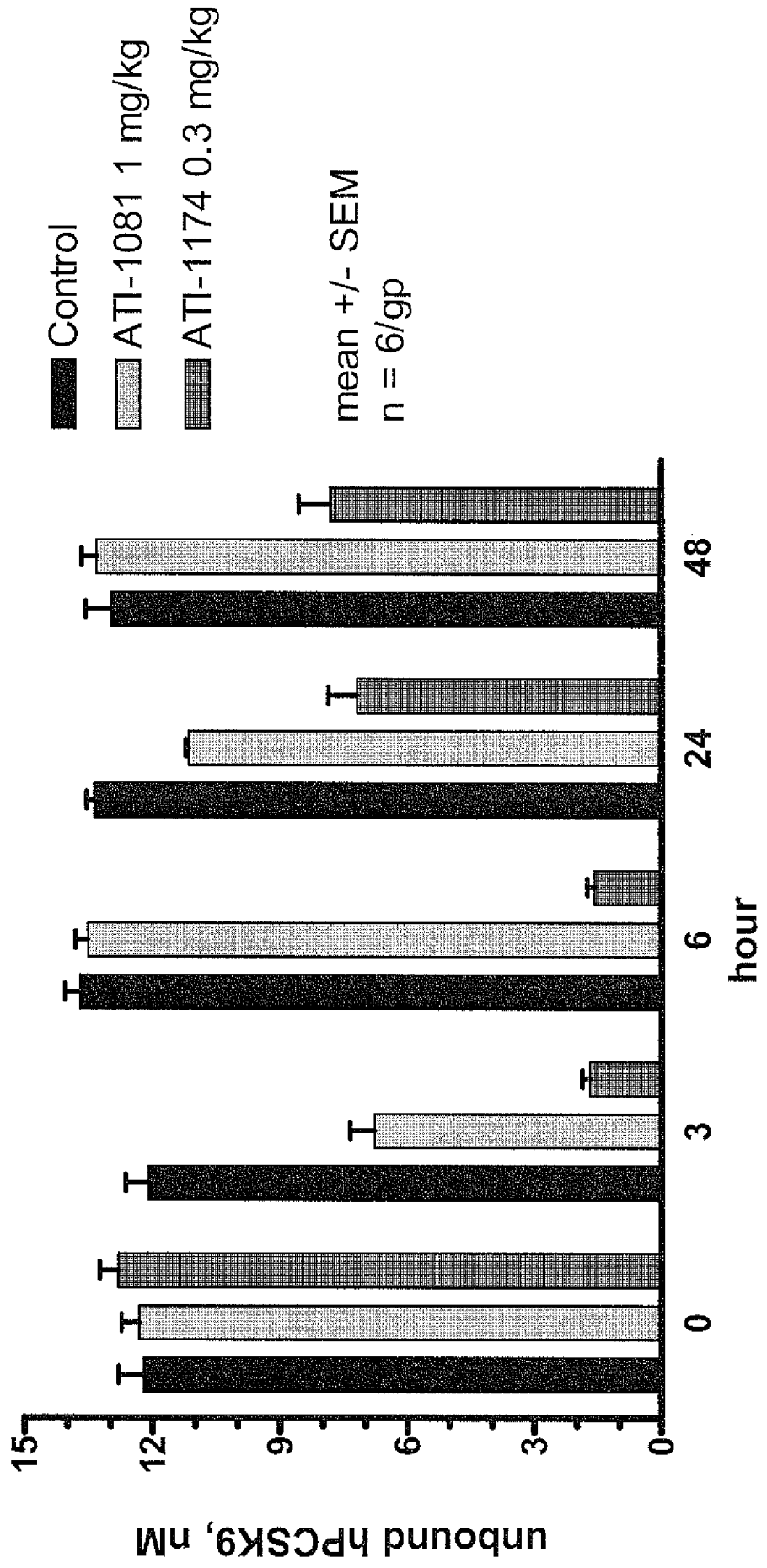

Control
ATI-1081 1 mg/kg
ATI-1174 0.3 mg/kg
mean +/- SEM
n = 6/gp
unbound hPCSK9, nM
15
12
9
6
3
0
0
3
6
24
48
hour

FIG. 21

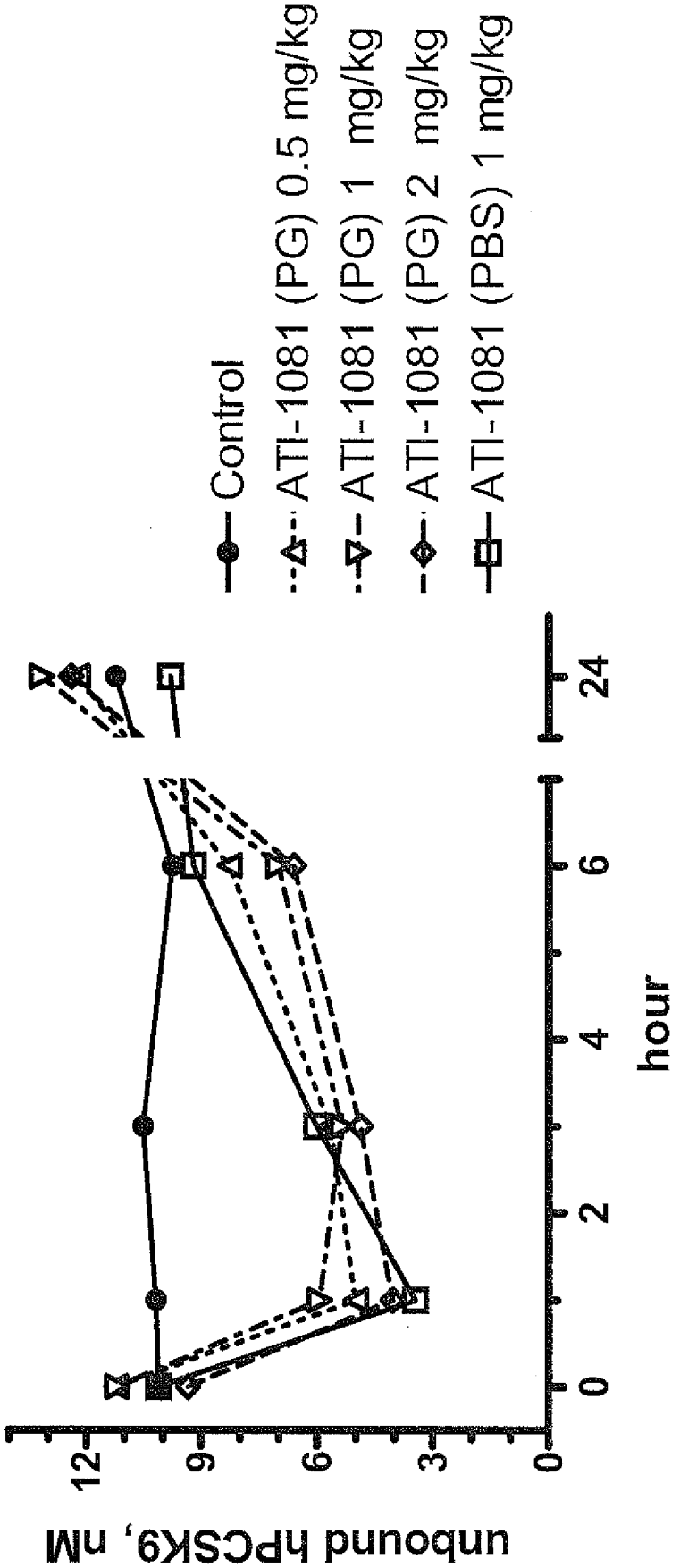

Control
ATI-1081 (PG) 0.5 mg/kg
ATI-1081 (PG) 1 mg/kg
ATI-1081 (PG) 2 mg/kg
ATI-1081 (PBS) 1 mg/kg
unbound hPCSK9, nM
0
3
6
9
12
0
2
4
6
24
hour

FIG. 22

FIG. 23

A.

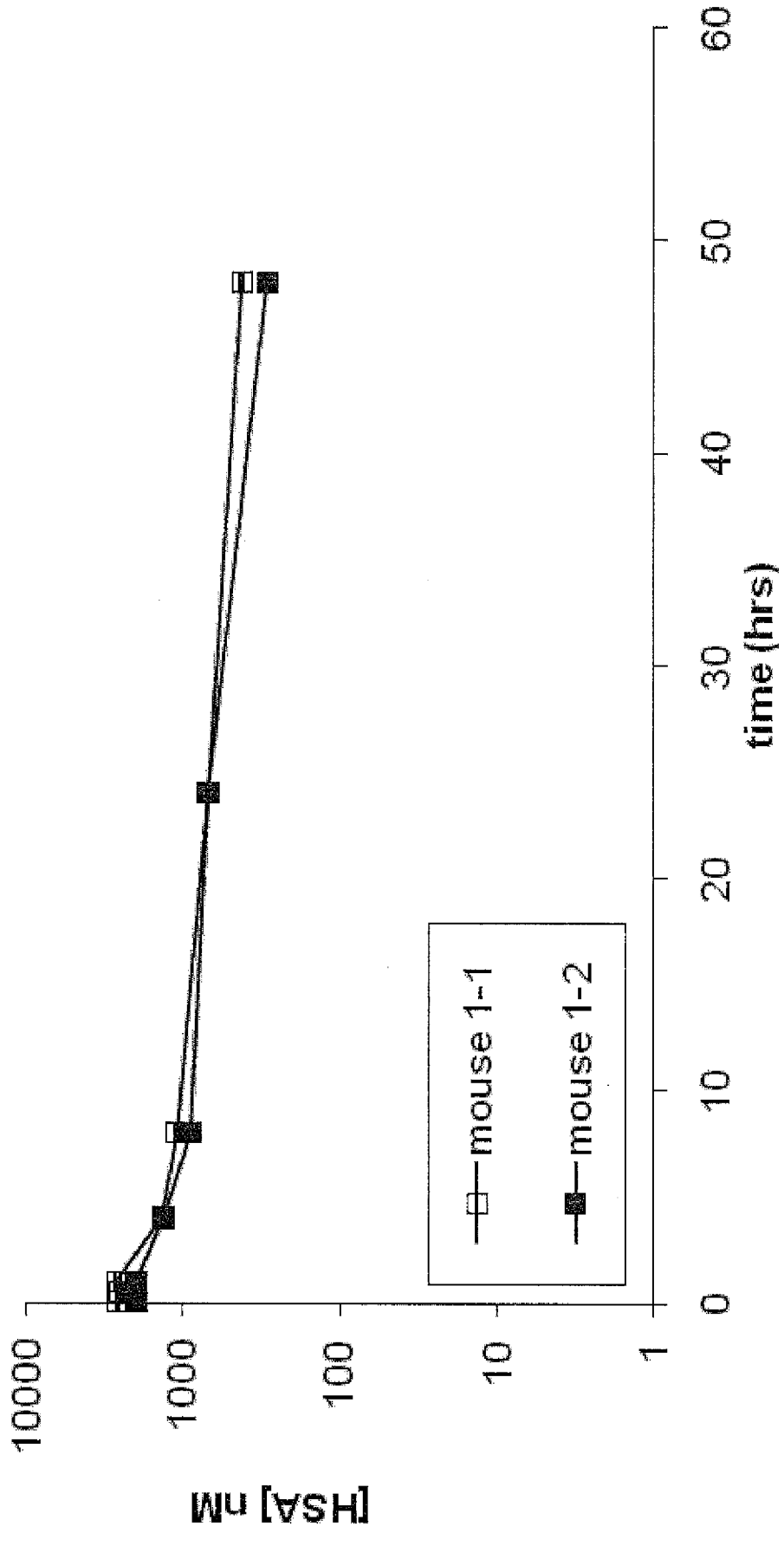

[HSA] nM
10000
1000
100
10
1
0
10
20
30
40
50
60
time (hrs)
mouse 1-1
mouse 1-2

FIG. 23 (continued)

B.

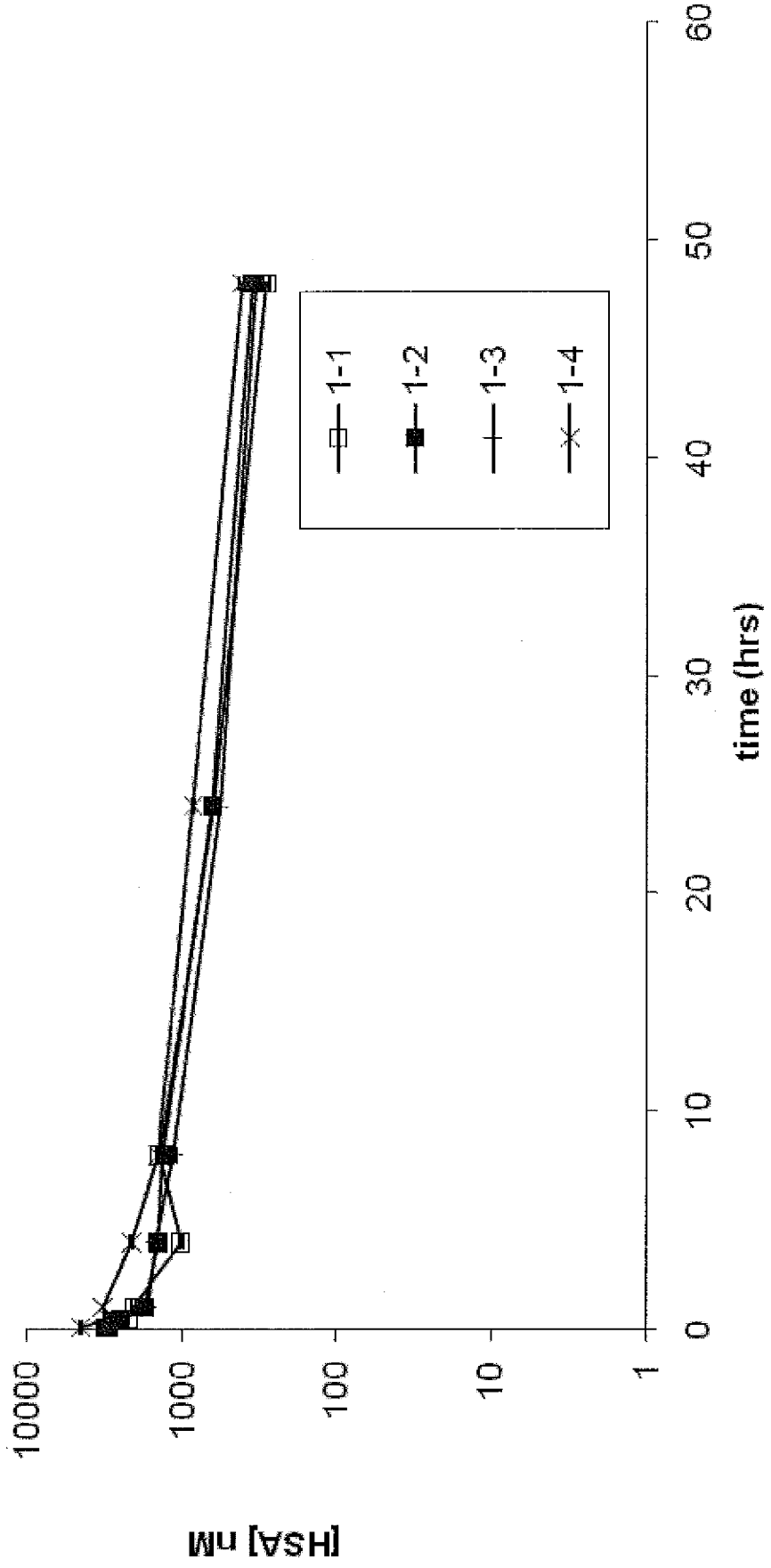


FIG. 24

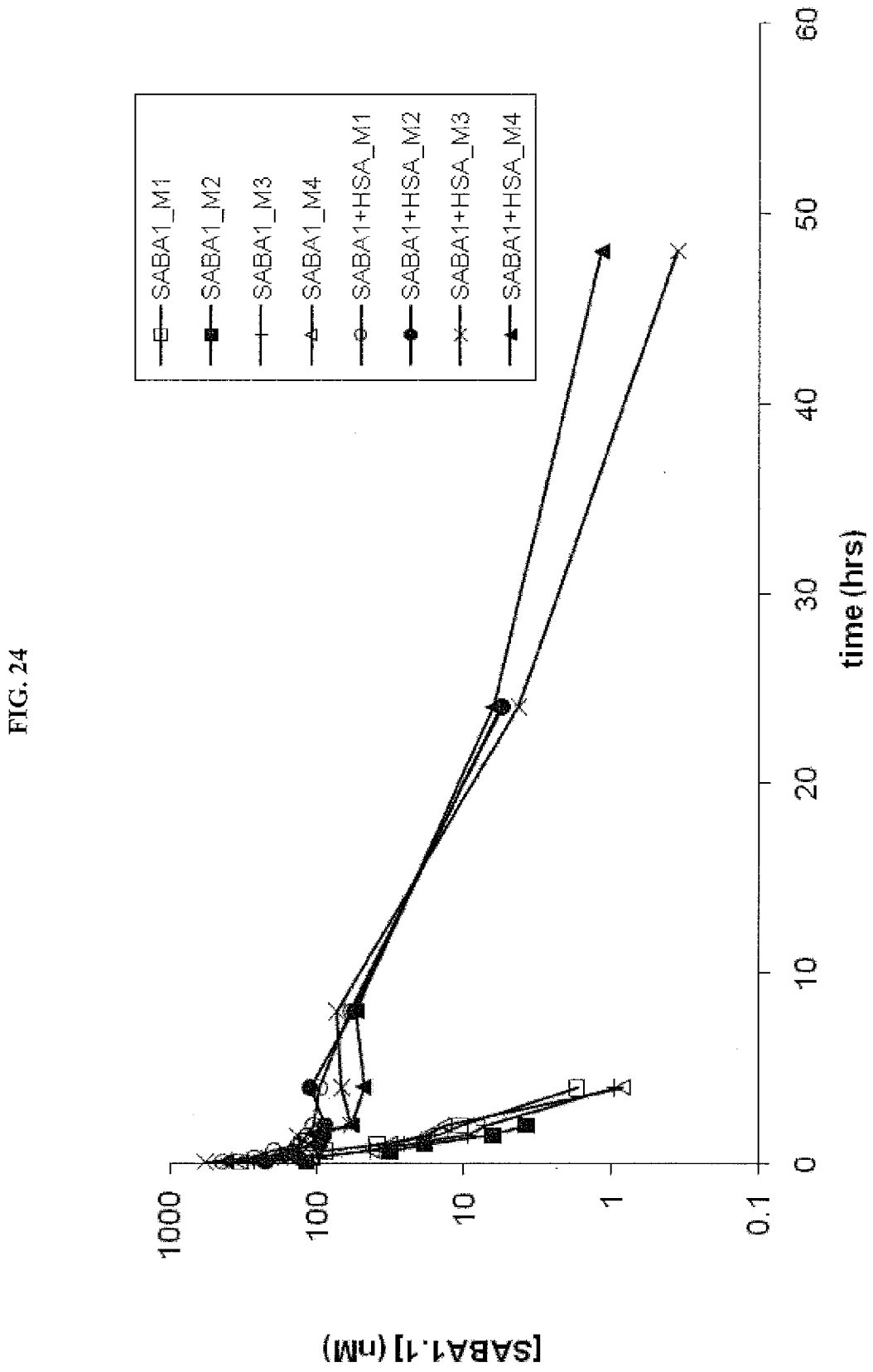
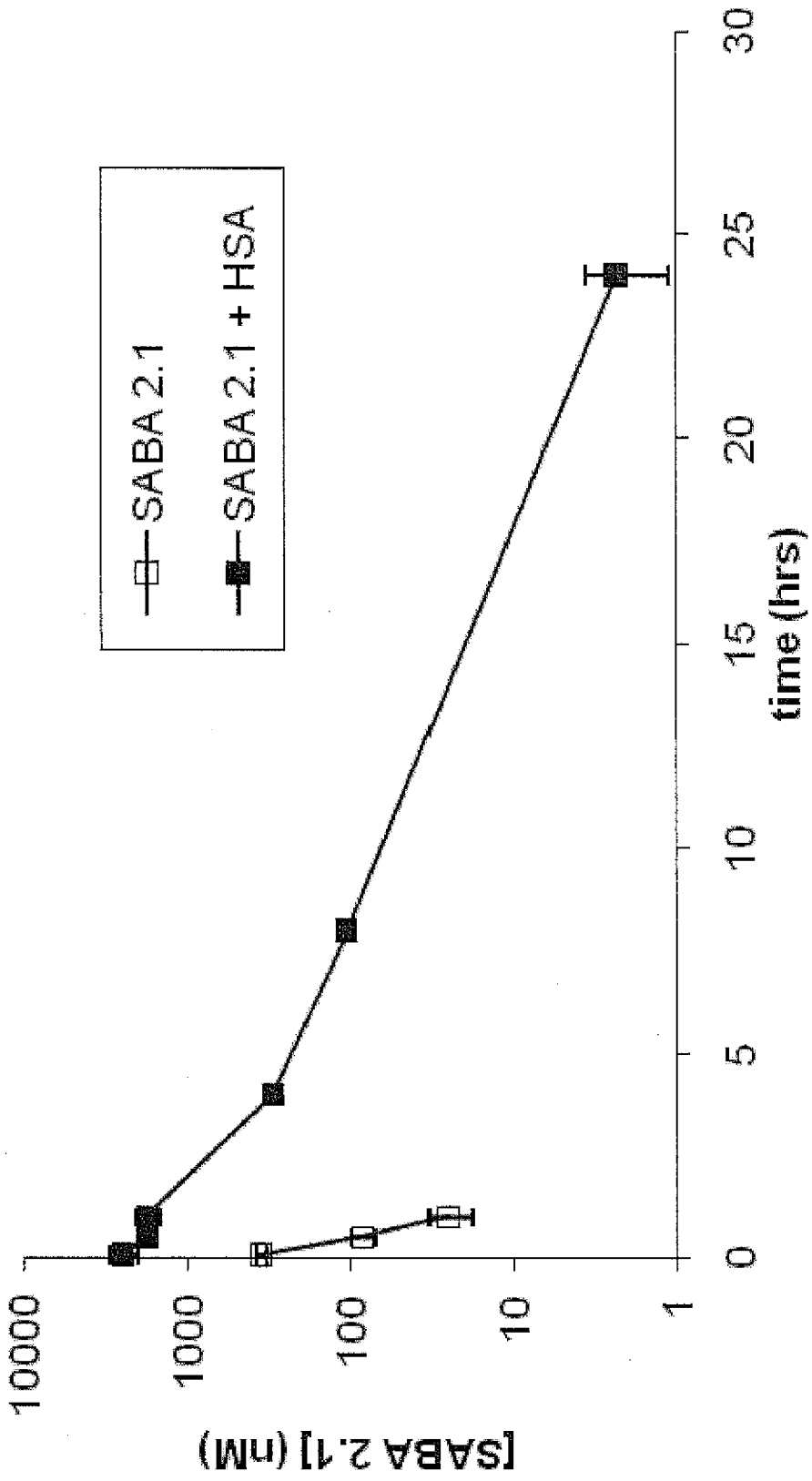

A.
[SABA1.1] (nM)
1000
100
10
1
0.1
0
10
20
30
40
50
60
time (hrs)
SABA1_M1
SABA1_M2
SABA1_M3
SABA1_M4
SABA1+HSA_M1
SABA1+HSA_M2
SABA1+HSA_M3
SABA1+HSA_M4

FIG. 24 (continued)

B.



C.

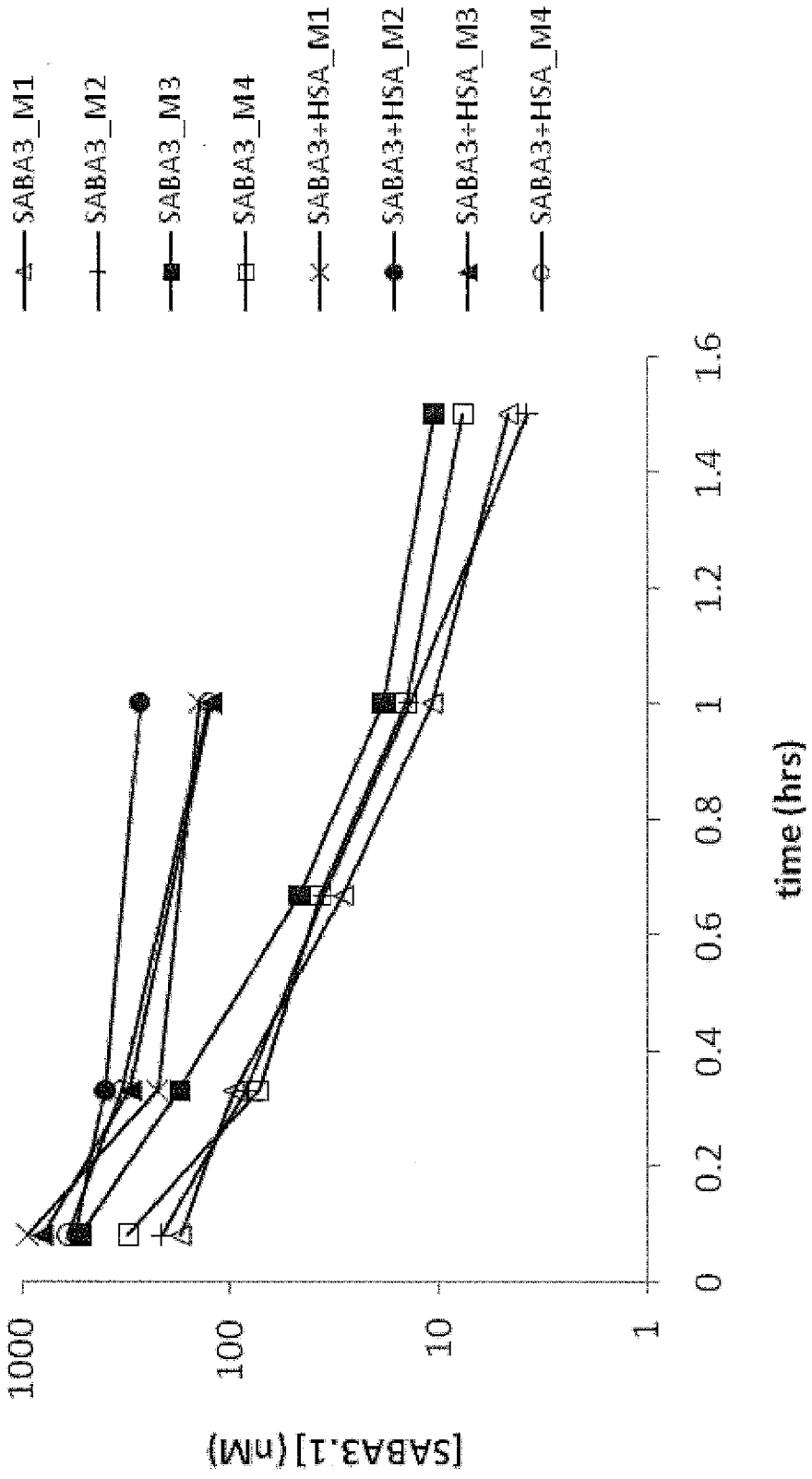


FIG. 24 (continued)

FIG. 24 (continued)

D.

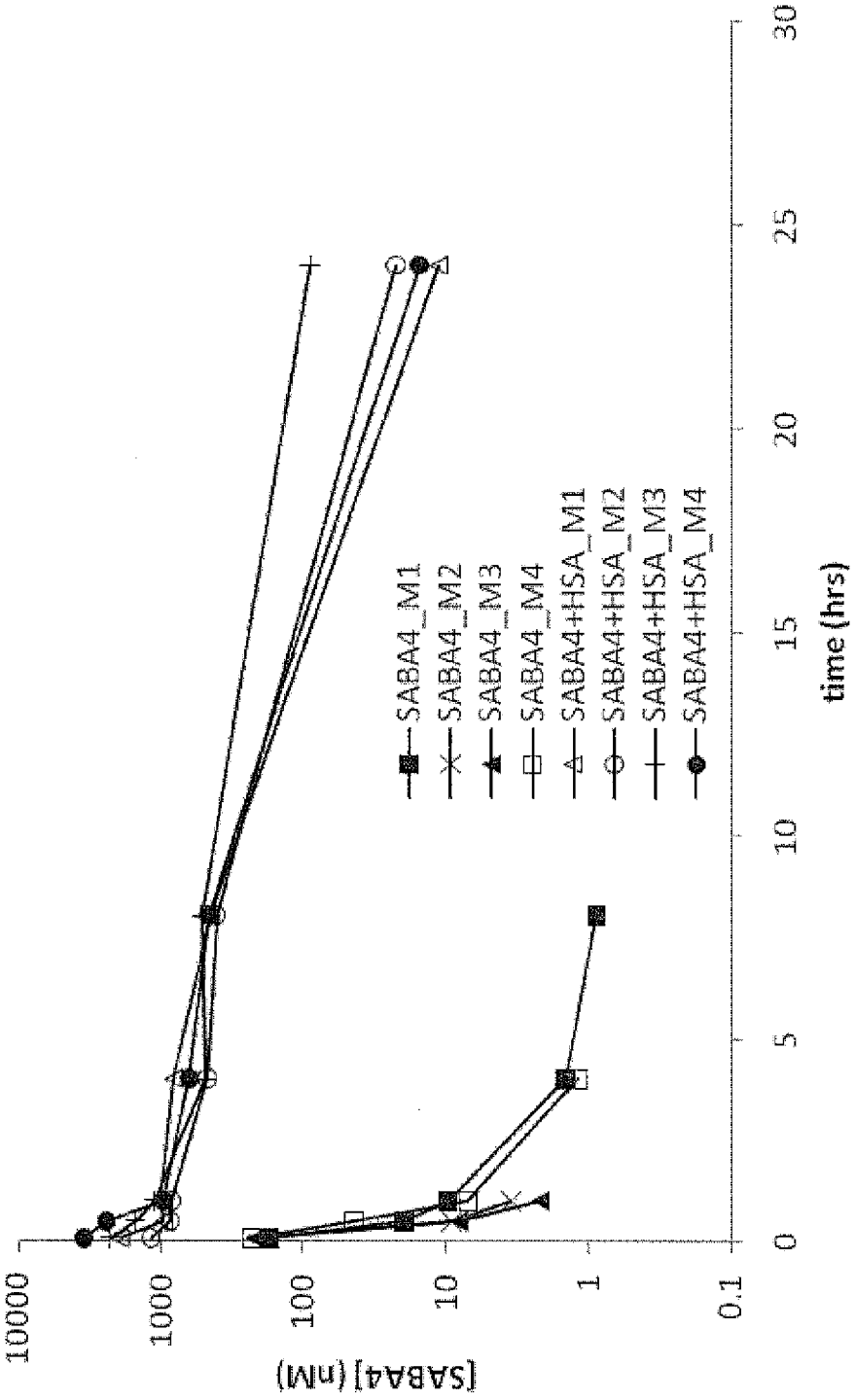


FIG. 25

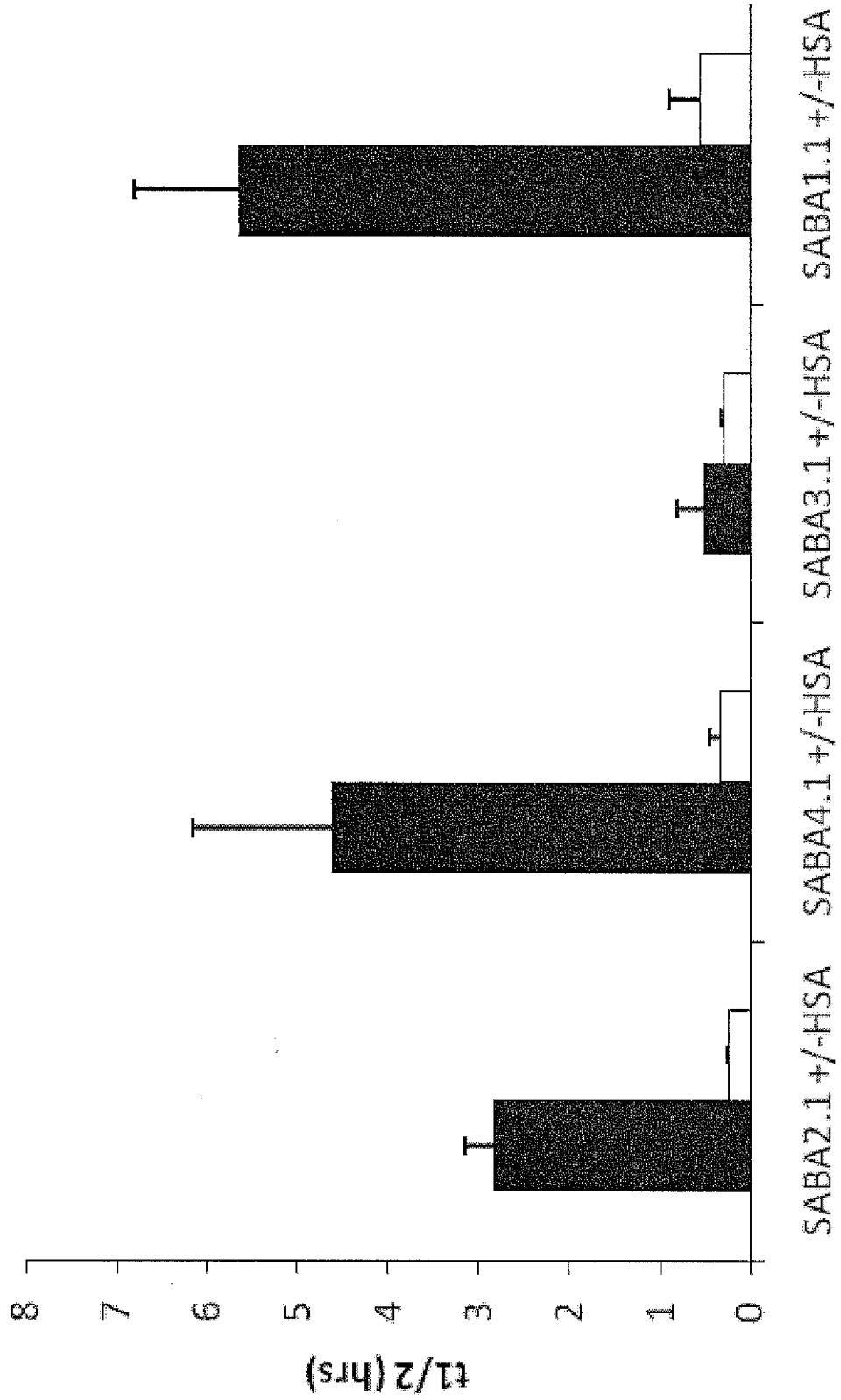
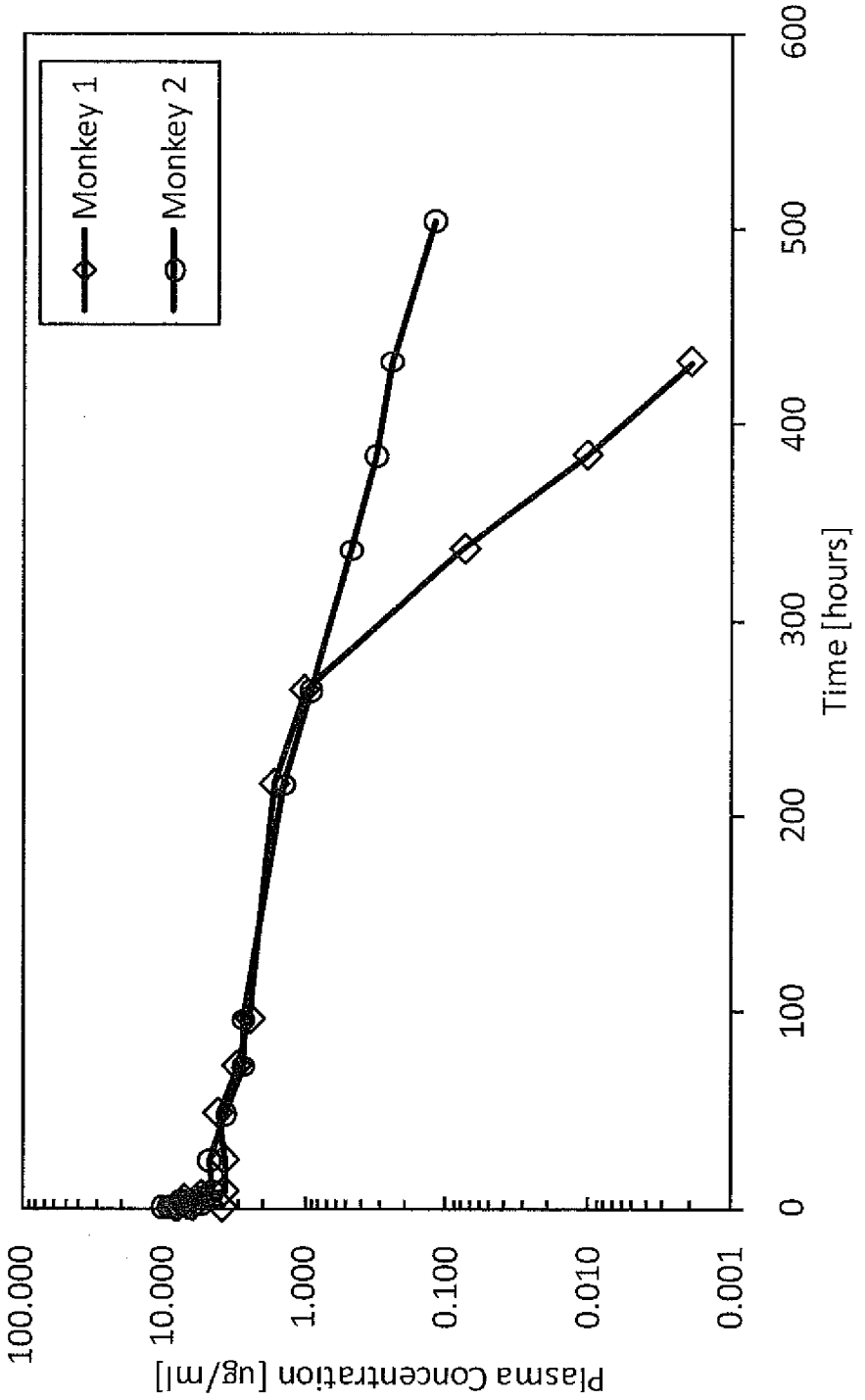

t1/2 (hrs)
0
1
2
3
4
5
6
7
8
SABA2.1 +/-HSA
SABA4.1 +/-HSA
SABA3.1 +/-HSA
SABA1.1 +/-HSA

FIG. 26


Monkey 1
Monkey 2
Plasma Concentration [ug/ml]
100.000
10.000
1.000
0.100
0.010
0.001
0
100
200
300
400
500
600
Time [hours]

A.

FIG. 26 (continued)

B.

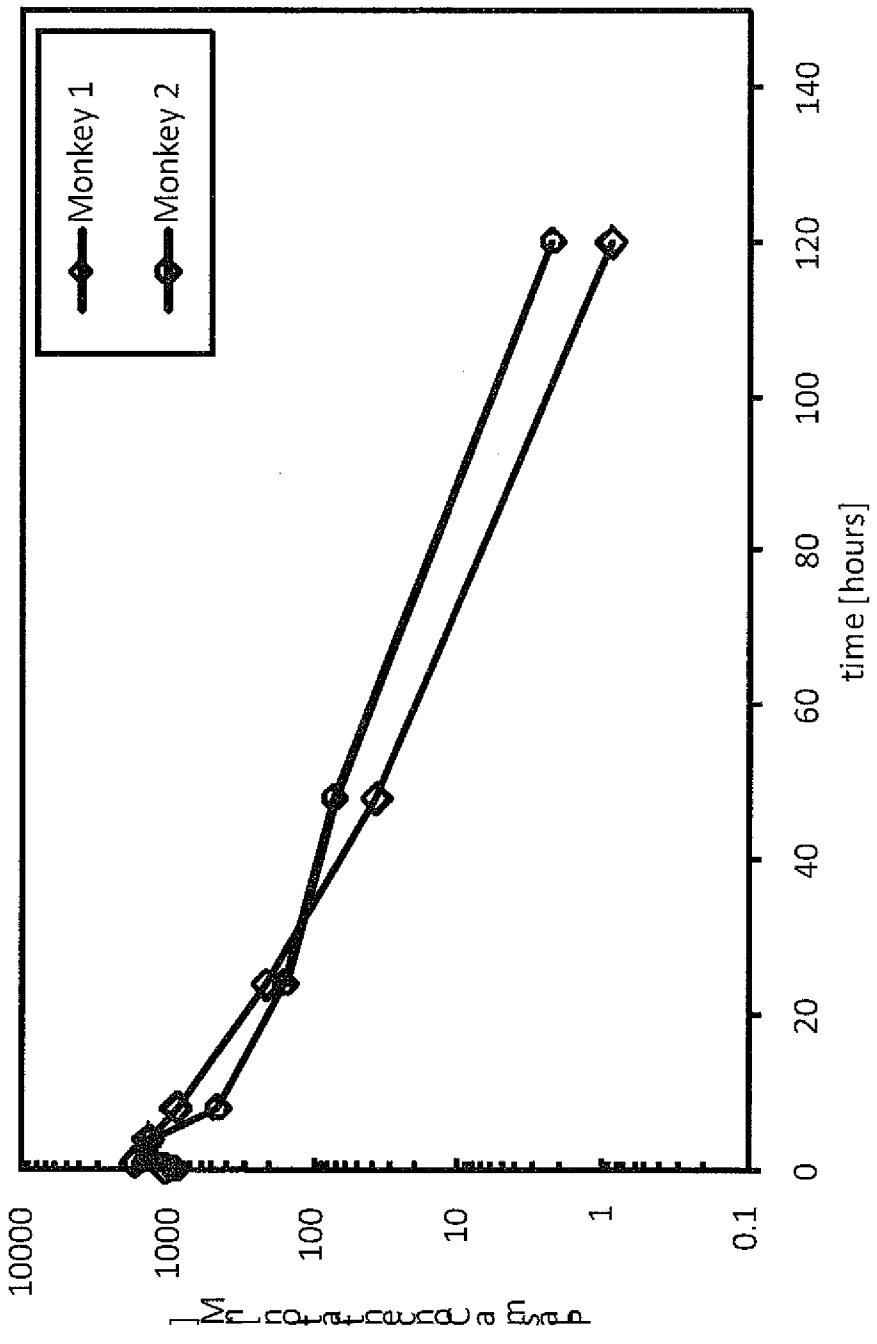


FIG. 27

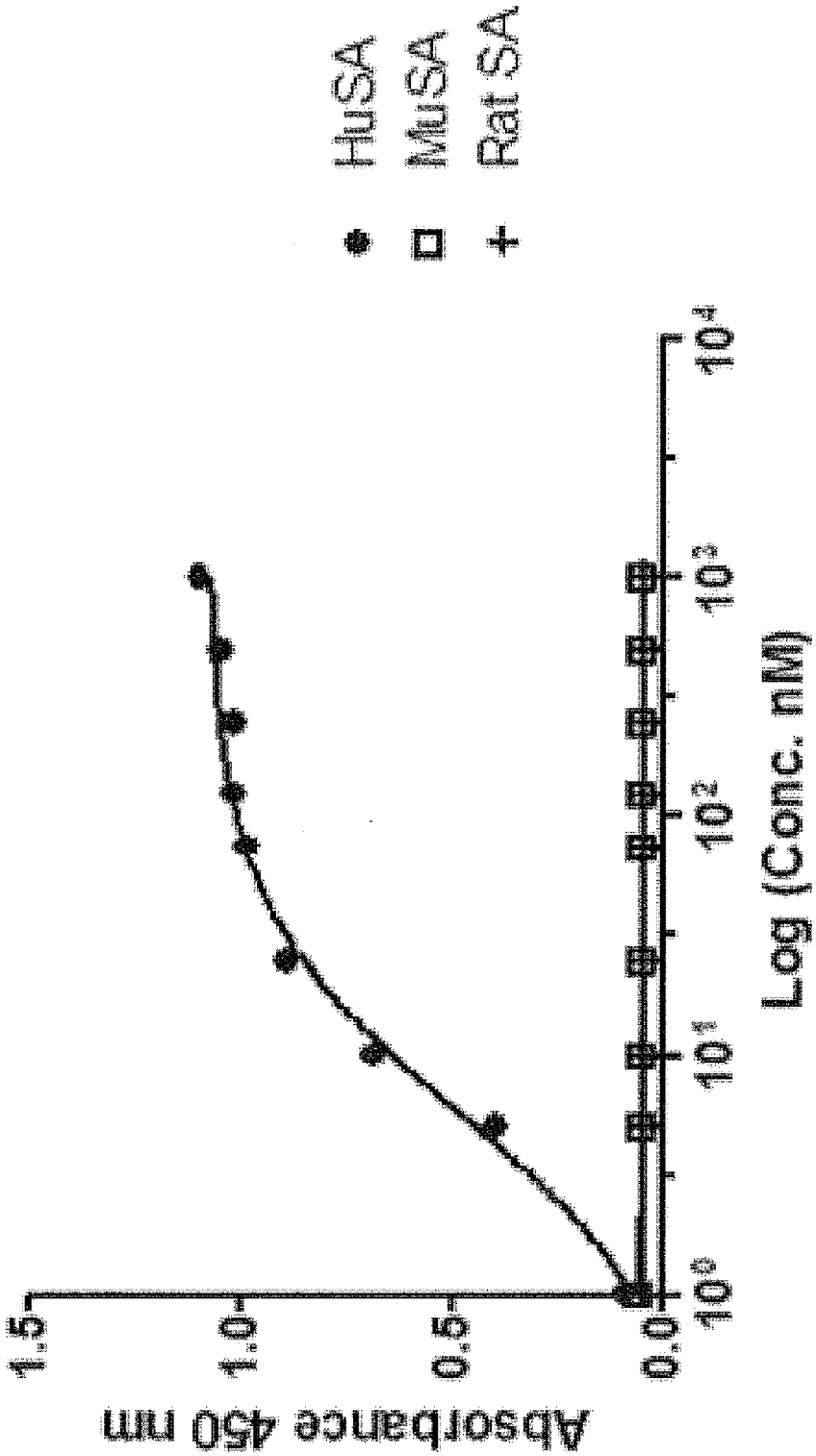
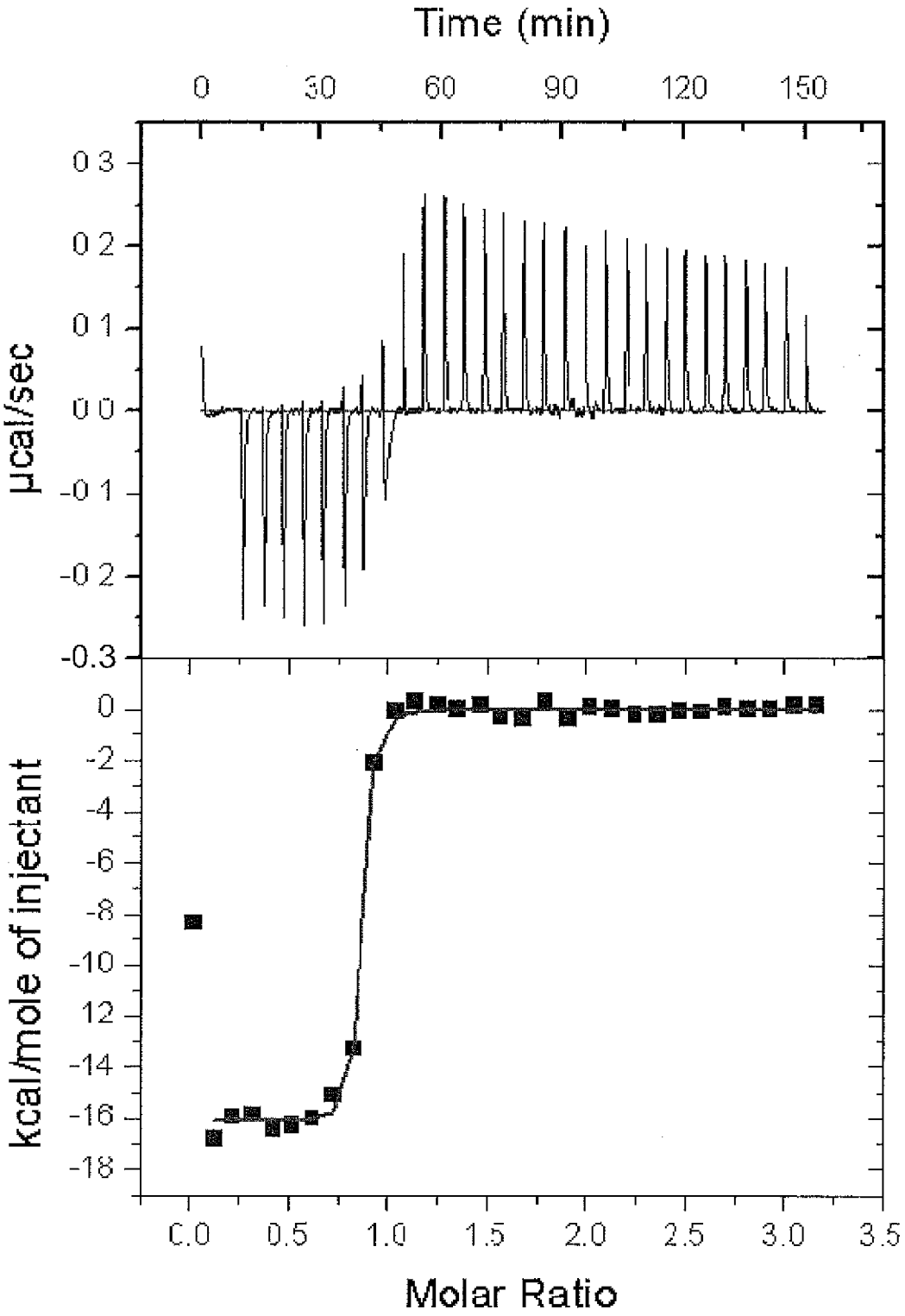

HuSA
MuSA
Rat SA
Absorbance 450 nm
1.5
1.0
0.5
0.0
10^0
10^1
10^2
10^3
10^4
Log (Conc. nM)

FIG. 28


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
-10
12
-14
-16
-18
kcal/mole of injectant
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
Molar Ratio

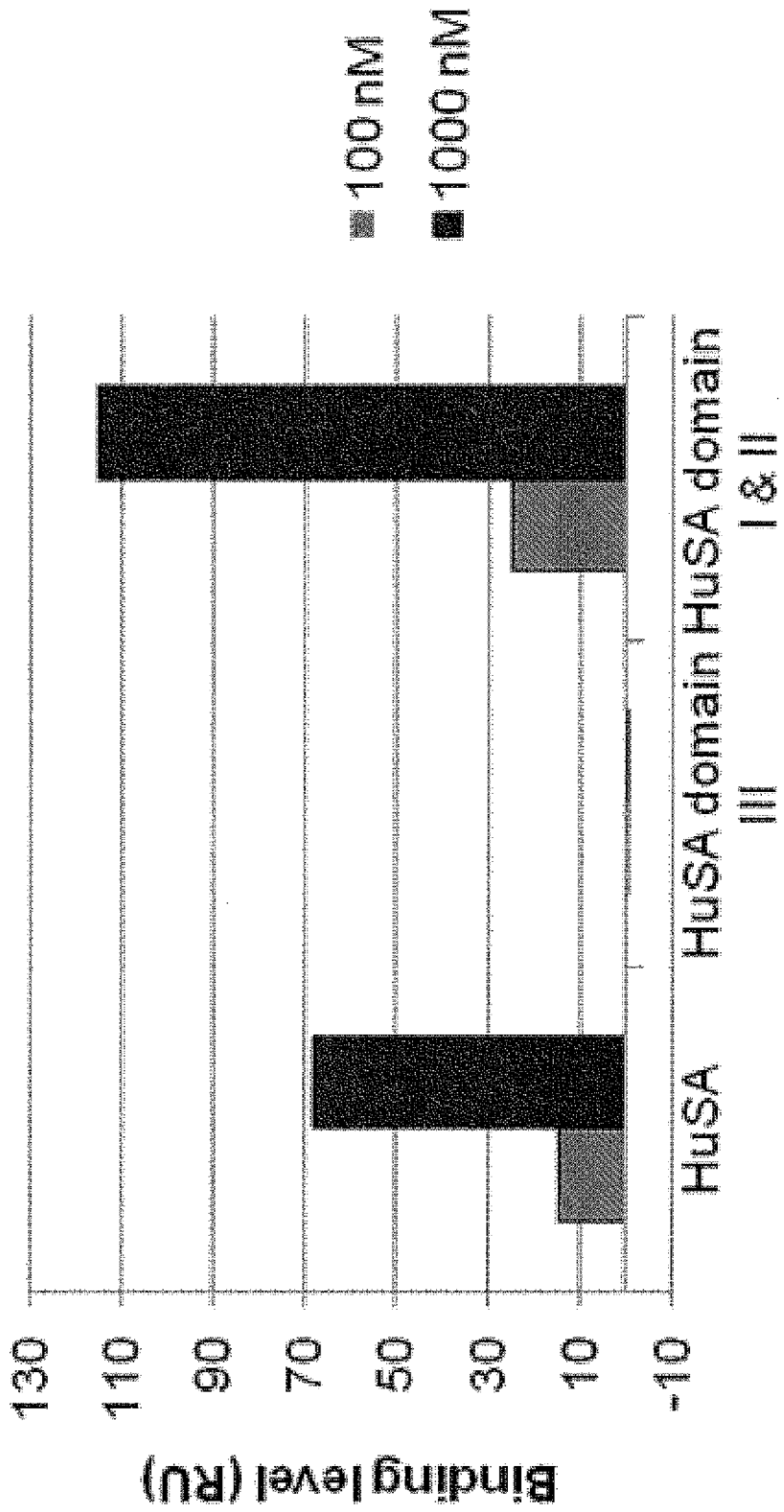

100 nM
1000 nM
Binding level (RU)
130
110
90
70
50
30
10
-10
HuSA
HuSA domain III
HuSA domain I & II

FIG. 29

FIG. 30

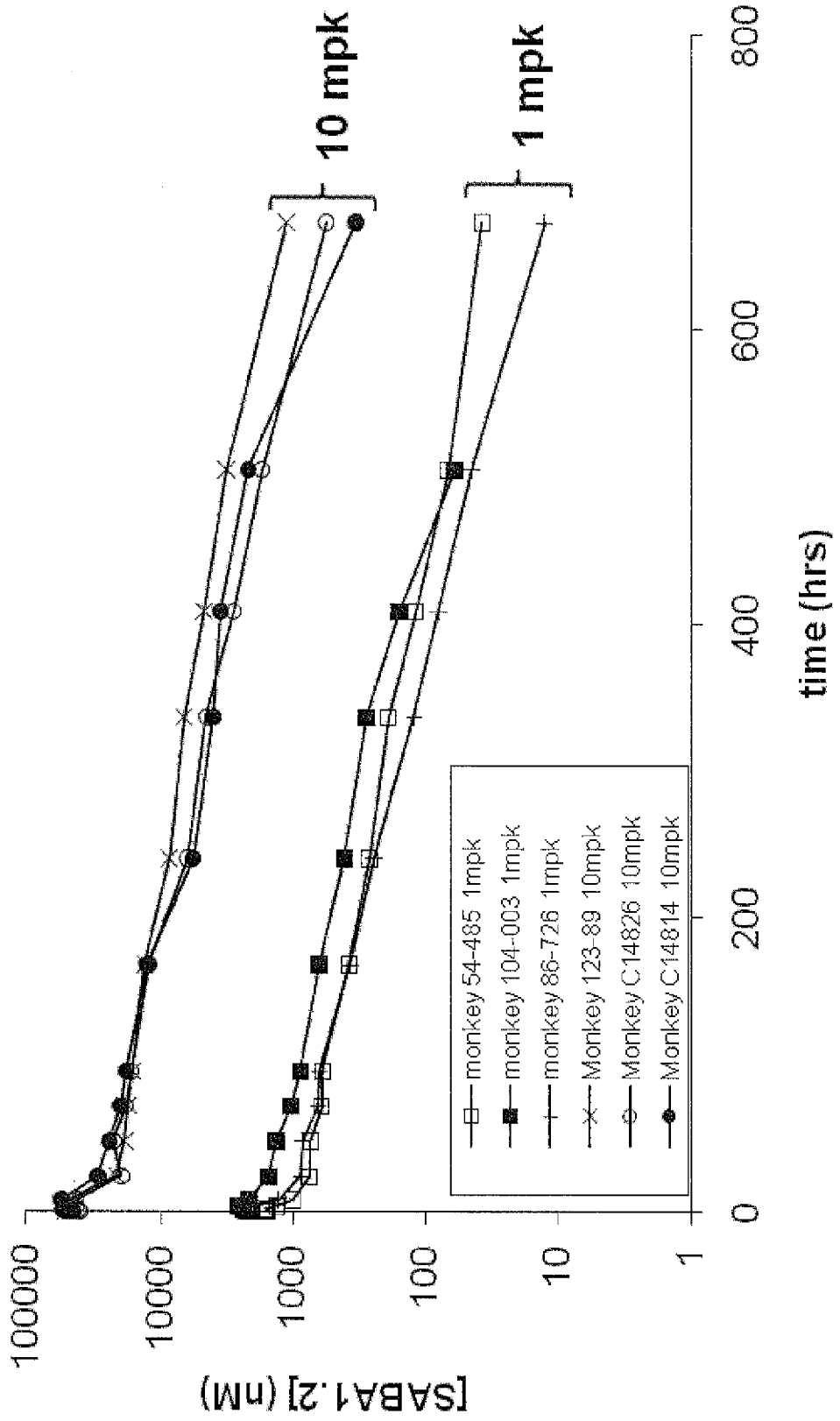
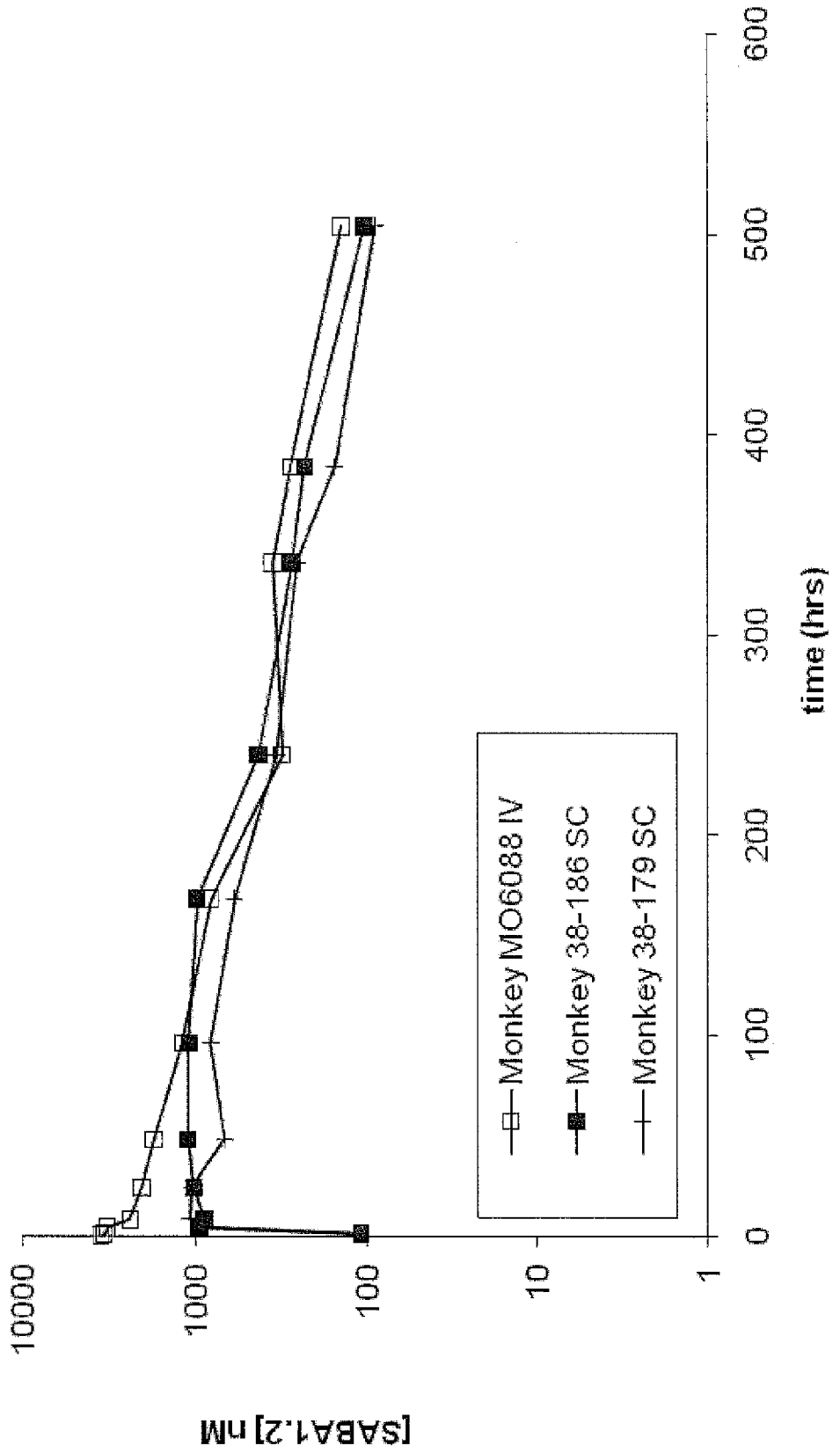

10 mpk
1 mpk
monkey 54-485 1mpk
monkey 104-003 1mpk
monkey 86-726 1mpk
Monkey 123-89 10mpk
Monkey C14826 10mpk
Monkey C14814 10mpk
[SABA1.2] (nM)
time (hrs)
100000
10000
1000
100
10
1
0
200
400
600
800

FIG. 31


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