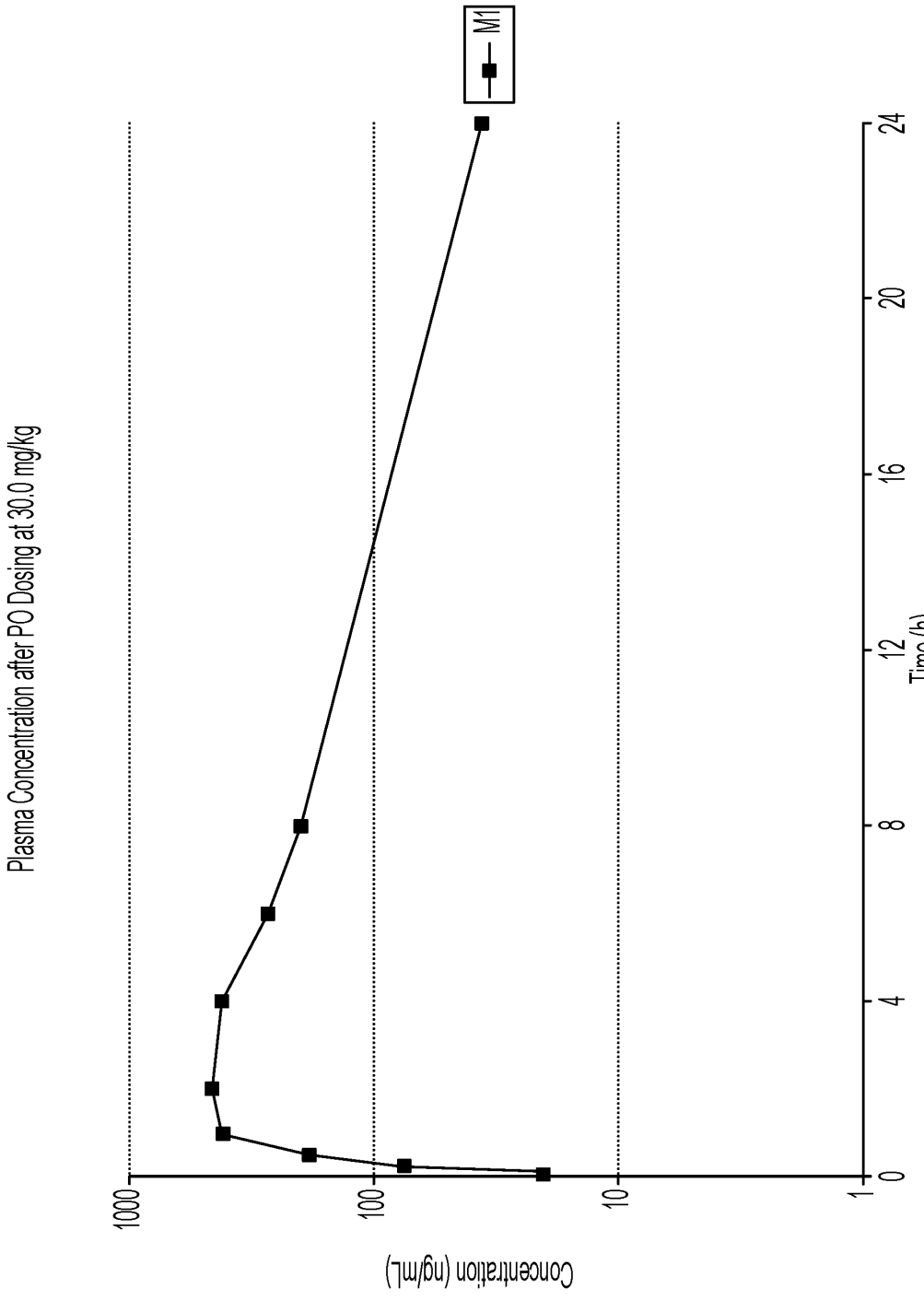
Plasma Concentration after PO Dosing at 30.0 mg/kg
M1
Concentration (ng/mL)
1000
100
10
1
0
4
8
12
16
20
24
Time (h)

FIG. 1

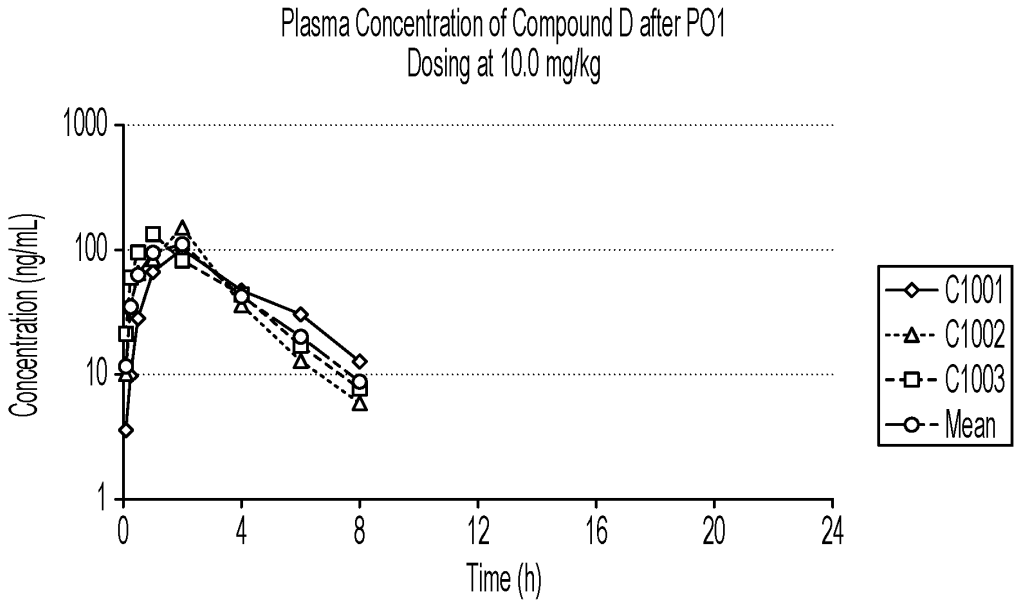
Plasma Concentration of Compound D after PO1
Dosing at 10.0 mg/kg
Concentration (ng/mL)
1000
100
10
1
0
4
8
12
16
20
24
Time (h)
C1001
C1002
C1003
Mean

FIG. 2A

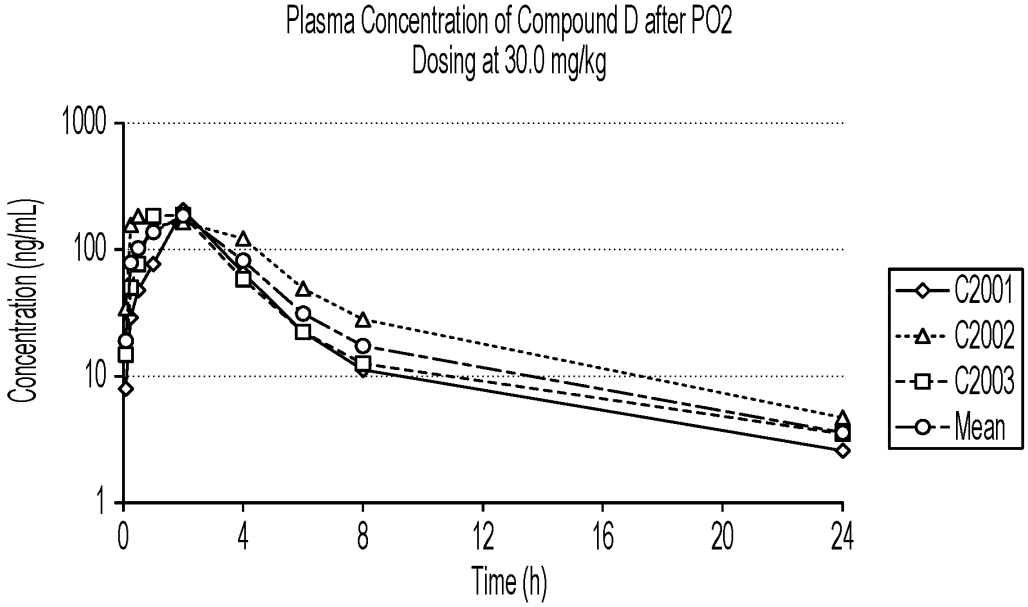
Plasma Concentration of Compound D after PO2
Dosing at 30.0 mg/kg
Concentration (ng/mL)
1000
100
10
1
0
4
8
12
16
20
24
Time (h)
C2001
C2002
C2003
Mean

FIG. 2B

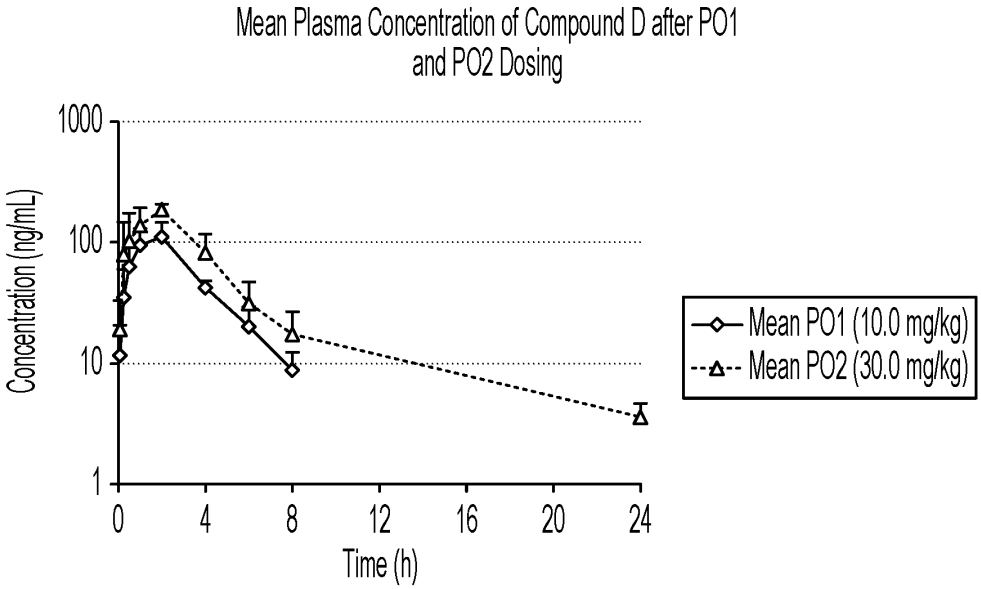
Mean Plasma Concentration of Compound D after PO1 and PO2 Dosing
Concentration (ng/mL)
1000
100
10
1
0
4
8
12
16
20
24
Time (h)
Mean PO1 (10.0 mg/kg)
Mean PO2 (30.0 mg/kg)

FIG. 2C

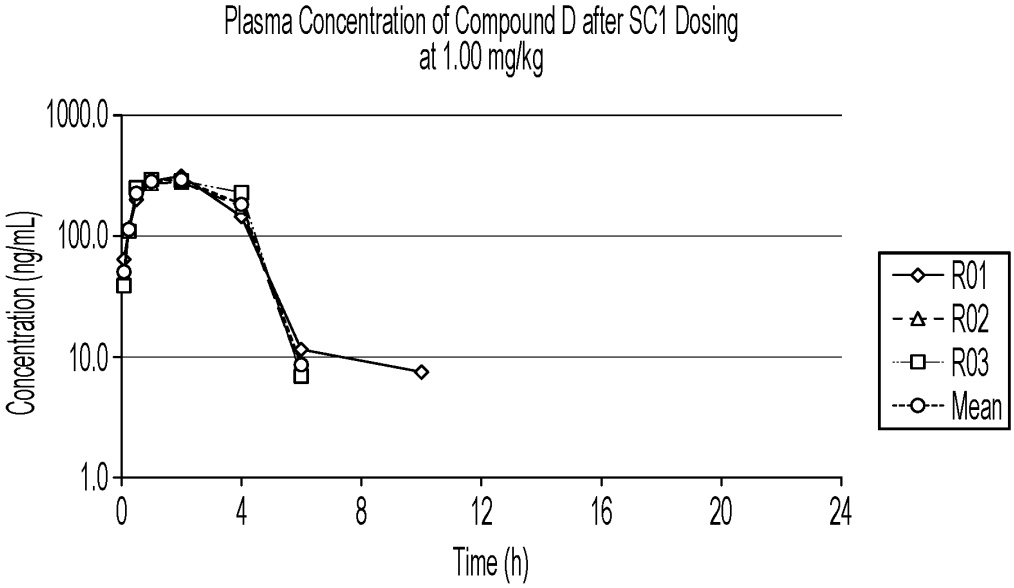
Plasma Concentration of Compound D after SC1 Dosing
at 1.00 mg/kg
1000.0
100.0
10.0
1.0
Concentration (ng/mL)
0
4
8
12
16
20
24
Time (h)
R01
R02
R03
Mean

FIG. 3A

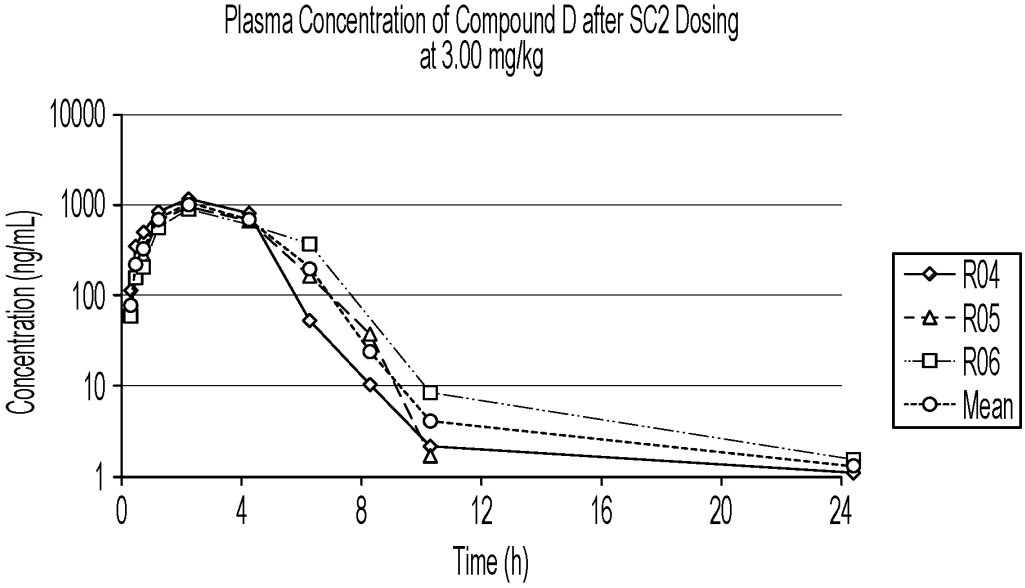
Plasma Concentration of Compound D after SC2 Dosing
at 3.00 mg/kg
10000
1000
100
10
1
Concentration (ng/mL)
0
4
8
12
16
20
24
Time (h)
R04
R05
R06
Mean

FIG. 3B

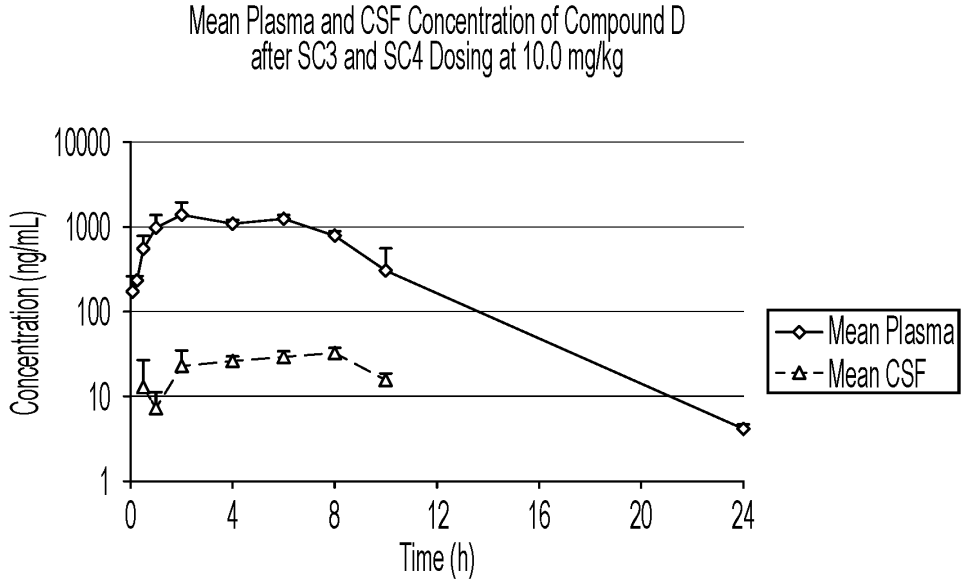
Mean Plasma and CSF Concentration of Compound D after SC3 and SC4 Dosing at 10.0 mg/kg
Concentration (ng/mL)
10000
1000
100
10
1
0
4
8
12
16
20
24
Time (h)
Mean Plasma
Mean CSF

FIG. 3C

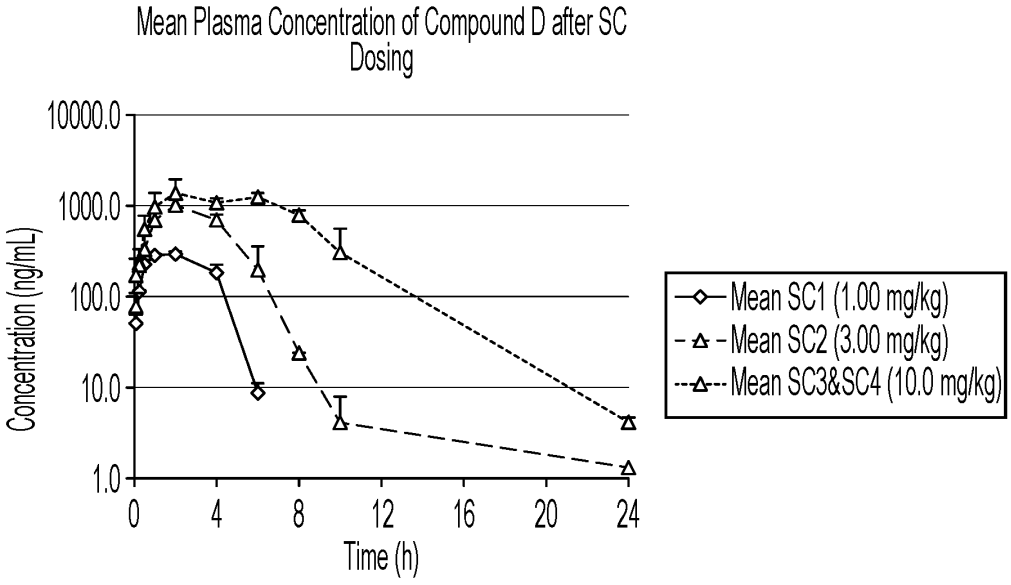
Mean Plasma Concentration of Compound D after SC Dosing
Concentration (ng/mL)
10000.0
1000.0
100.0
10.0
1.0
0
4
8
12
16
20
24
Time (h)
Mean SC1 (1.00 mg/kg)
Mean SC2 (3.00 mg/kg)
Mean SC3&SC4 (10.0 mg/kg)

FIG. 3D

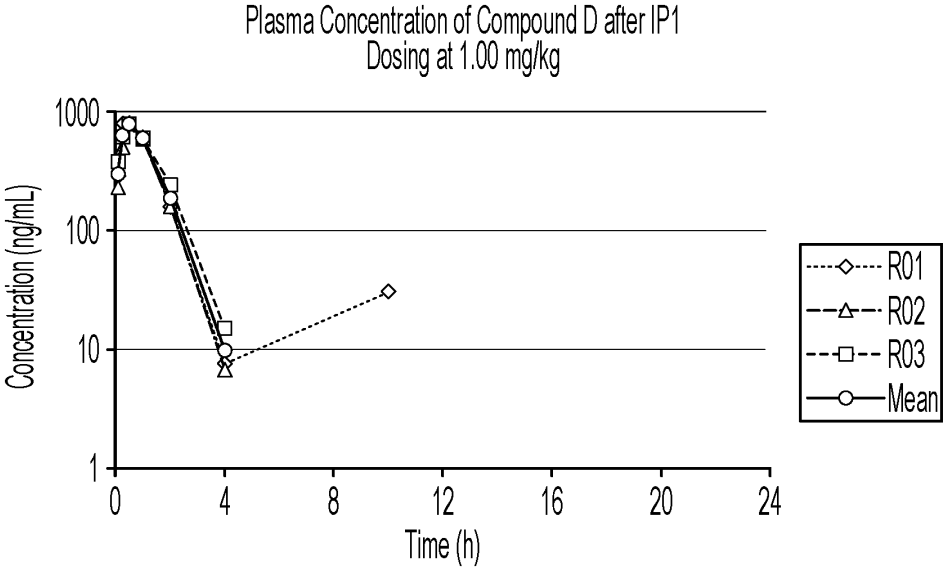
Plasma Concentration of Compound D after IP1
Dosing at 1.00 mg/kg
Concentration (ng/mL)
1000
100
10
1
0
4
8
12
16
20
24
Time (h)
R01
R02
R03
Mean

FIG. 4A

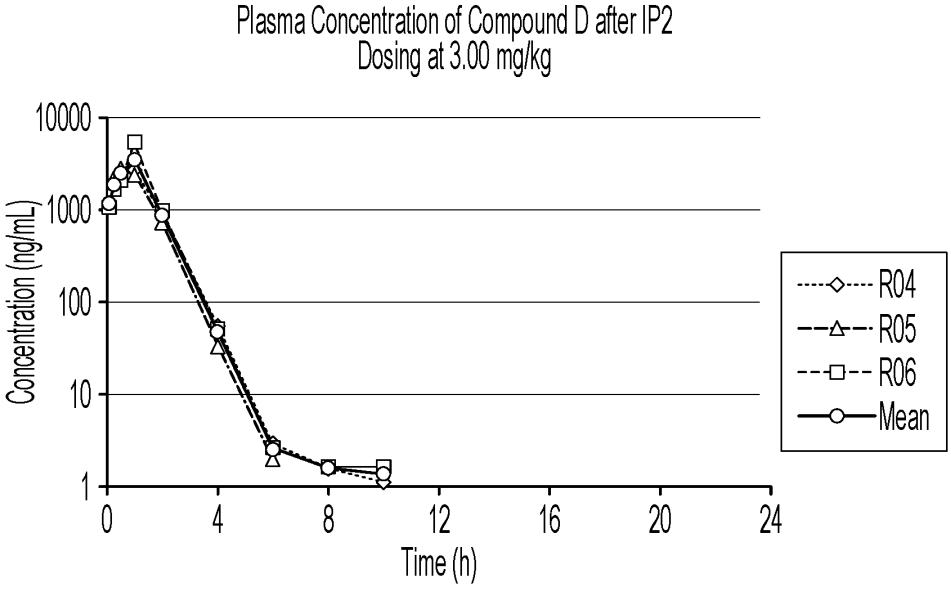
Plasma Concentration of Compound D after IP2
Dosing at 3.00 mg/kg
Concentration (ng/mL)
10000
1000
100
10
1
0
4
8
12
16
20
24
Time (h)
R04
R05
R06
Mean

FIG. 4B

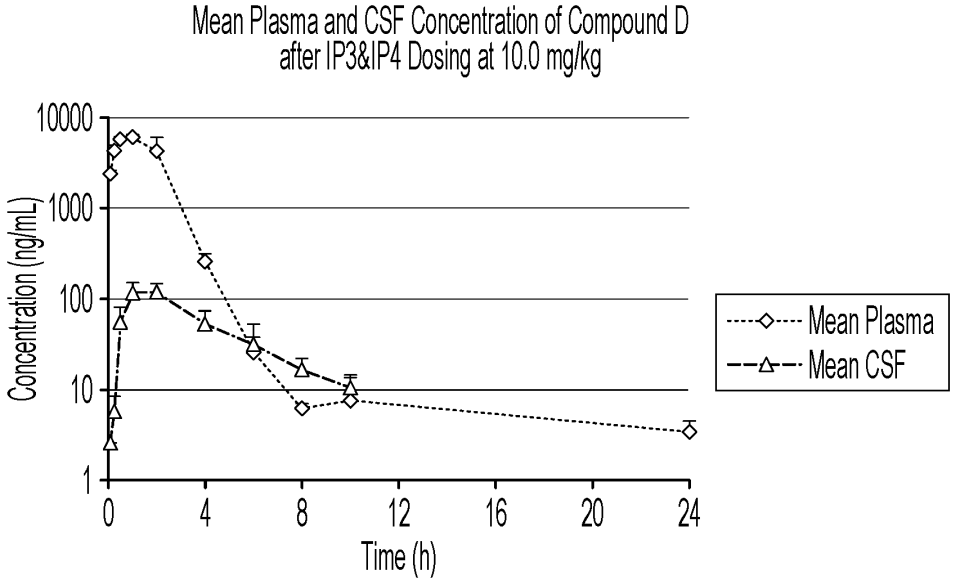
Mean Plasma and CSF Concentration of Compound D
after IP3&IP4 Dosing at 10.0 mg/kg
Concentration (ng/mL)
10000
1000
100
10
1
0
4
8
12
16
20
24
Time (h)
Mean Plasma
Mean CSF

FIG. 4C

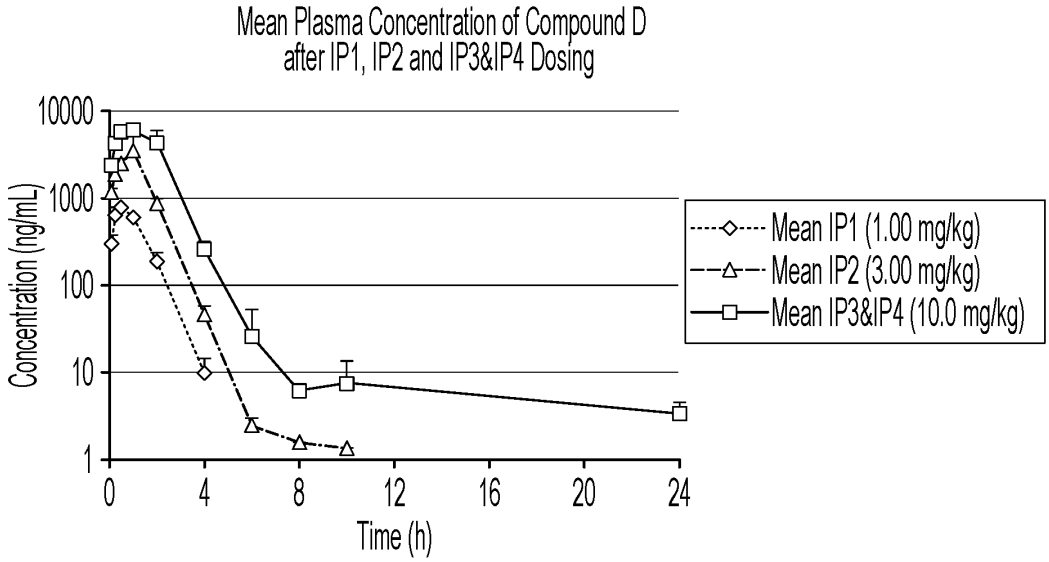
Mean Plasma Concentration of Compound D
after IP1, IP2 and IP3&IP4 Dosing
Concentration (ng/mL)
10000
1000
100
10
1
0
4
8
12
16
20
24
Time (h)
Mean IP1 (1.00 mg/kg)
Mean IP2 (3.00 mg/kg)
Mean IP3&IP4 (10.0 mg/kg)

FIG. 4D

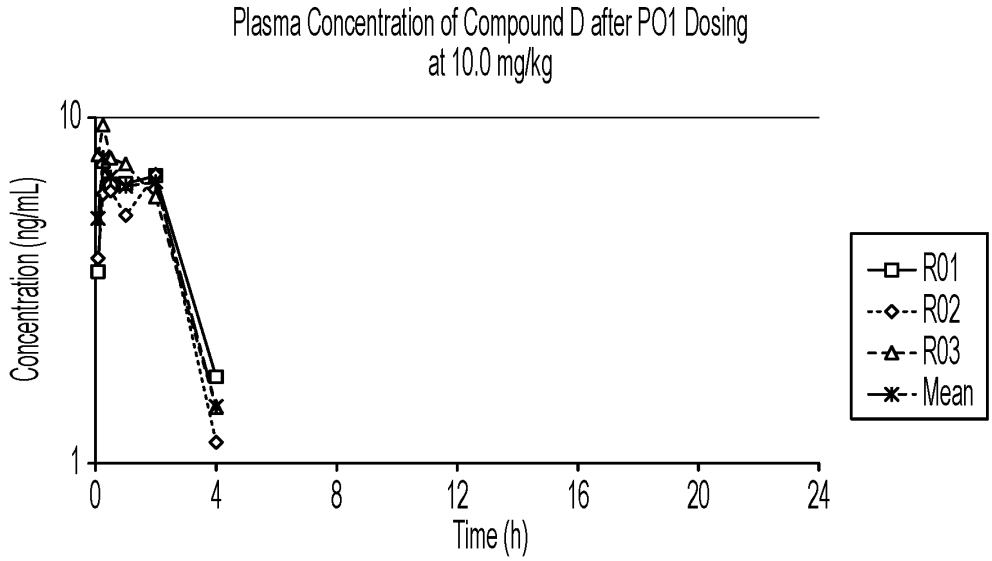
Plasma Concentration of Compound D after PO1 Dosing
at 10.0 mg/kg
Concentration (ng/mL)
10
1
0
4
8
12
16
20
24
Time (h)
R01
R02
R03
Mean

FIG. 5A

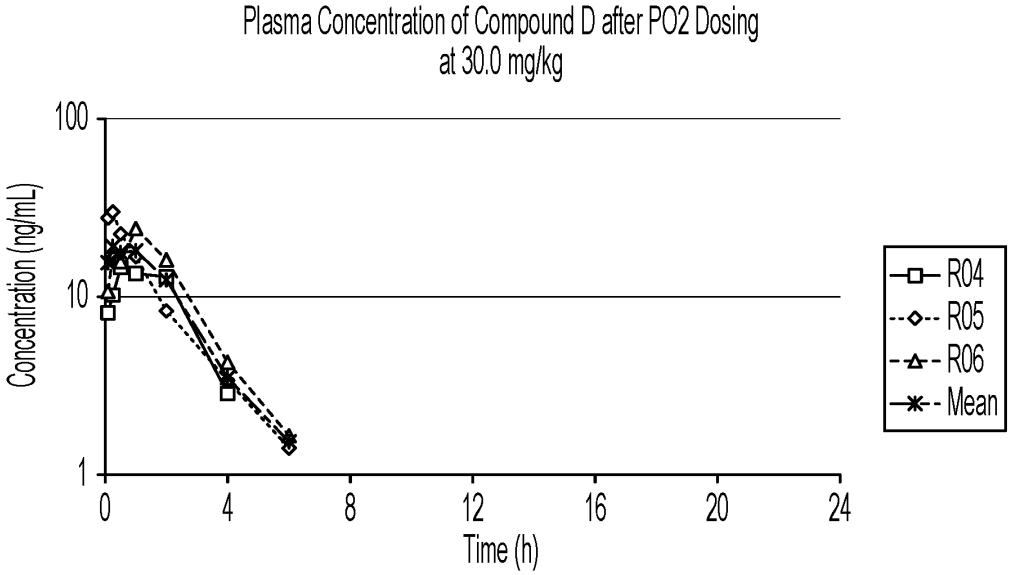
Plasma Concentration of Compound D after PO2 Dosing
at 30.0 mg/kg
Concentration (ng/mL)
100
10
1
0
4
8
12
16
20
24
Time (h)
R04
R05
R06
Mean

FIG. 5B

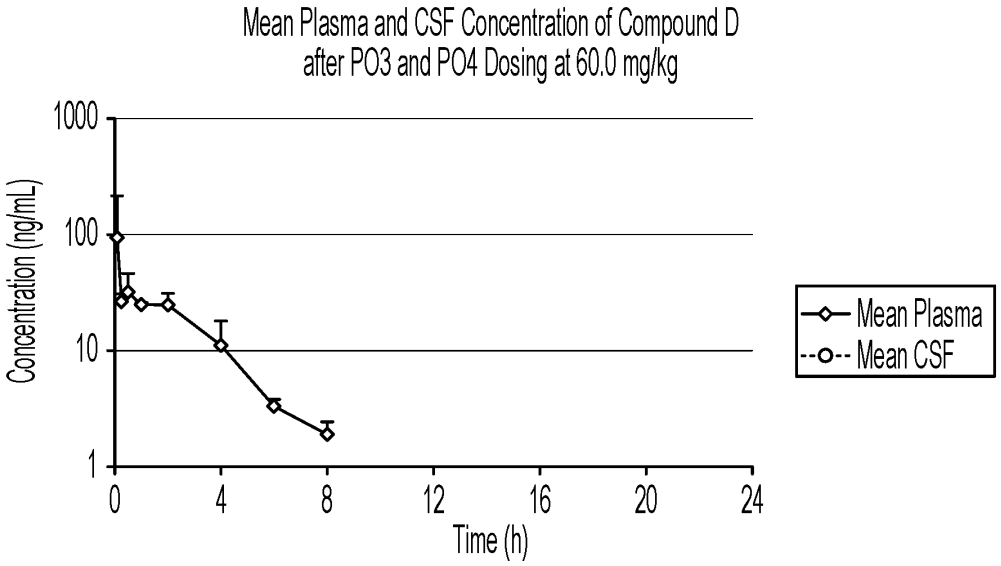
Mean Plasma and CSF Concentration of Compound D
after PO3 and PO4 Dosing at 60.0 mg/kg
Concentration (ng/mL)
1000
100
10
1
0
4
8
12
16
20
24
Time (h)
Mean Plasma
Mean CSF

FIG. 5C

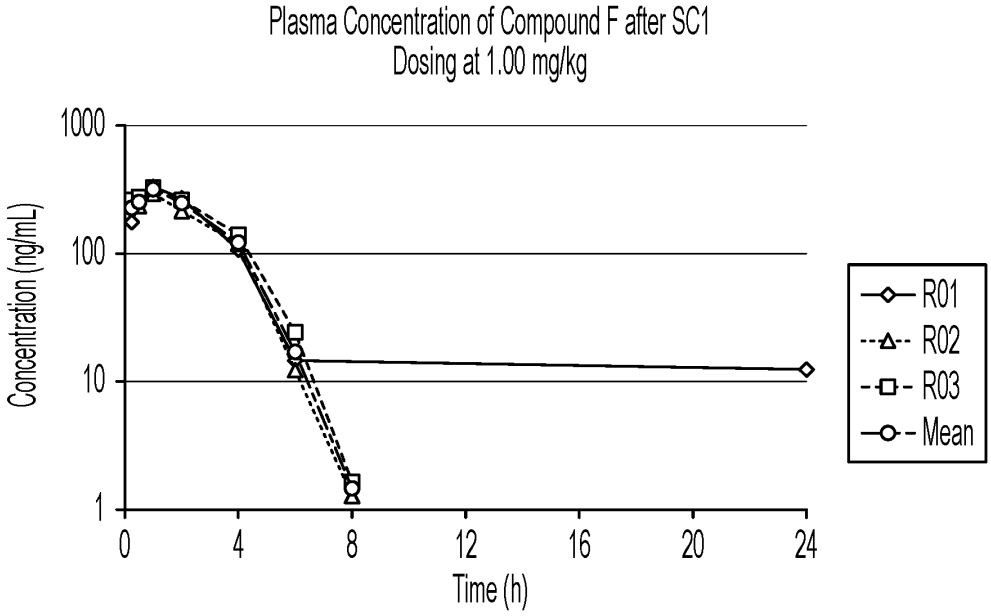
Plasma Concentration of Compound F after SC1
Dosing at 1.00 mg/kg
Concentration (ng/mL)
1000
100
10
1
0
4
8
12
16
20
24
Time (h)
R01
R02
R03
Mean

FIG. 6A

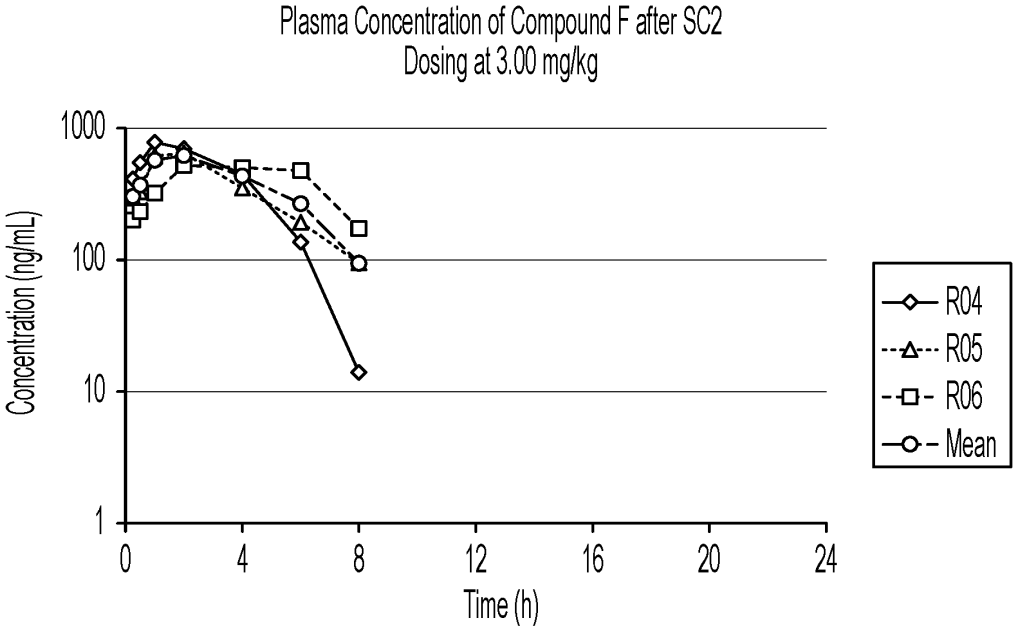
Plasma Concentration of Compound F after SC2
Dosing at 3.00 mg/kg
Concentration (ng/mL)
1000
100
10
1
0
4
8
12
16
20
24
Time (h)
R04
R05
R06
Mean

FIG. 6B

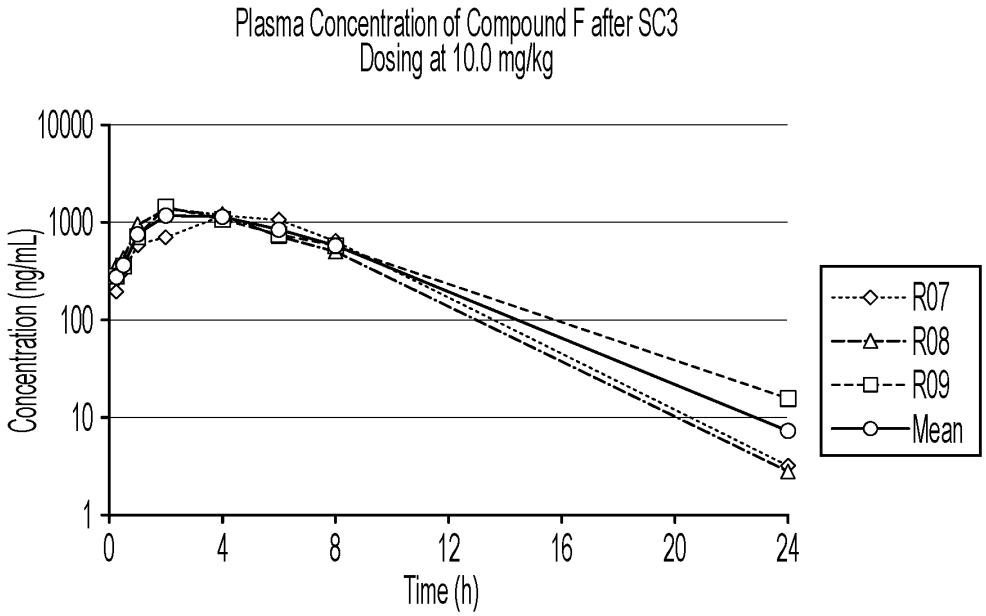
Plasma Concentration of Compound F after SC3 Dosing at 10.0 mg/kg
Concentration (ng/mL)
10000
1000
100
10
1
0
4
8
12
16
20
24
Time (h)
R07
R08
R09
Mean

FIG. 6C

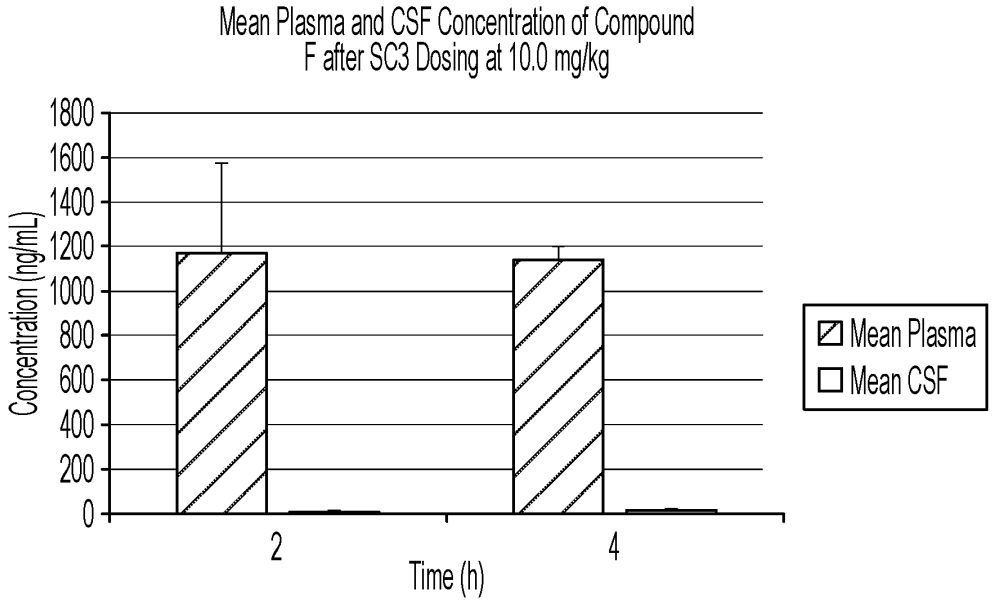
Mean Plasma and CSF Concentration of Compound F after SC3 Dosing at 10.0 mg/kg
Concentration (ng/mL)
1800
1600
1400
1200
1000
800
600
400
200
0
2
4
Time (h)
Mean Plasma
Mean CSF

FIG. 6D

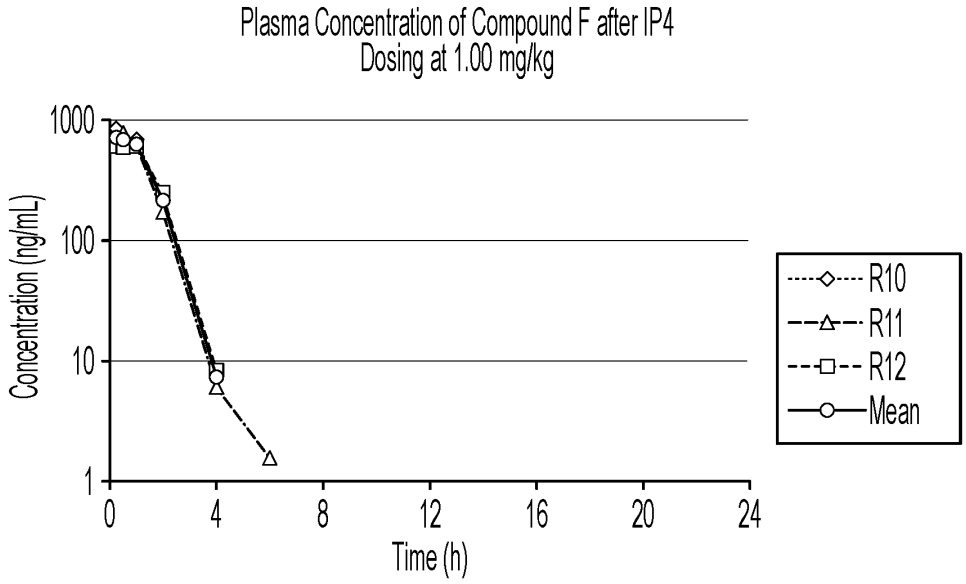
Plasma Concentration of Compound F after IP4
Dosing at 1.00 mg/kg
Concentration (ng/mL)
1000
100
10
1
0
4
8
12
16
20
24
Time (h)
R10
R11
R12
Mean

FIG. 7A

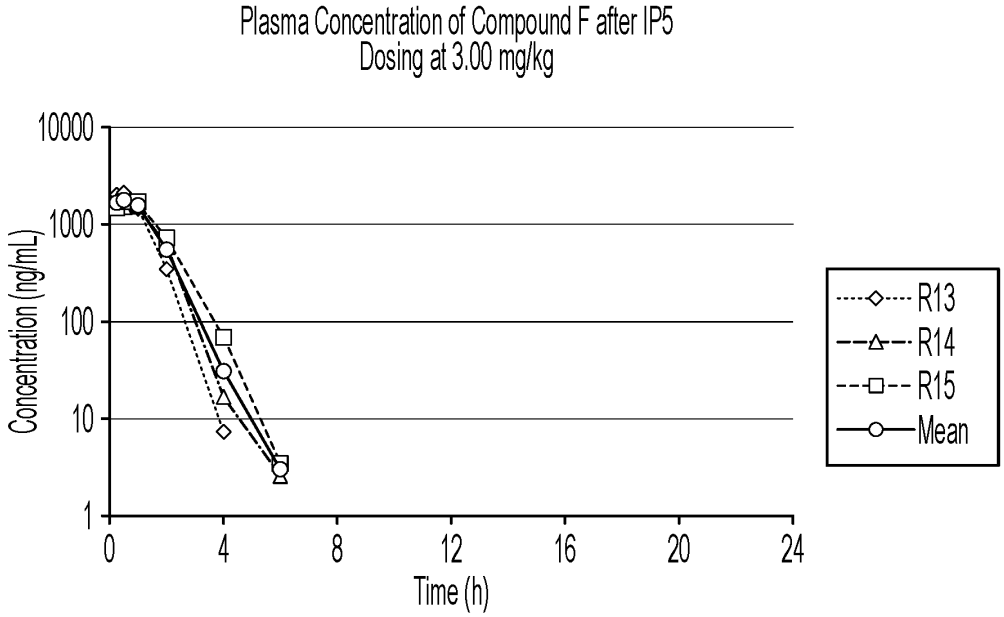
Plasma Concentration of Compound F after IP5
Dosing at 3.00 mg/kg
Concentration (ng/mL)
10000
1000
100
10
1
0
4
8
12
16
20
24
Time (h)
R13
R14
R15
Mean

FIG. 7B

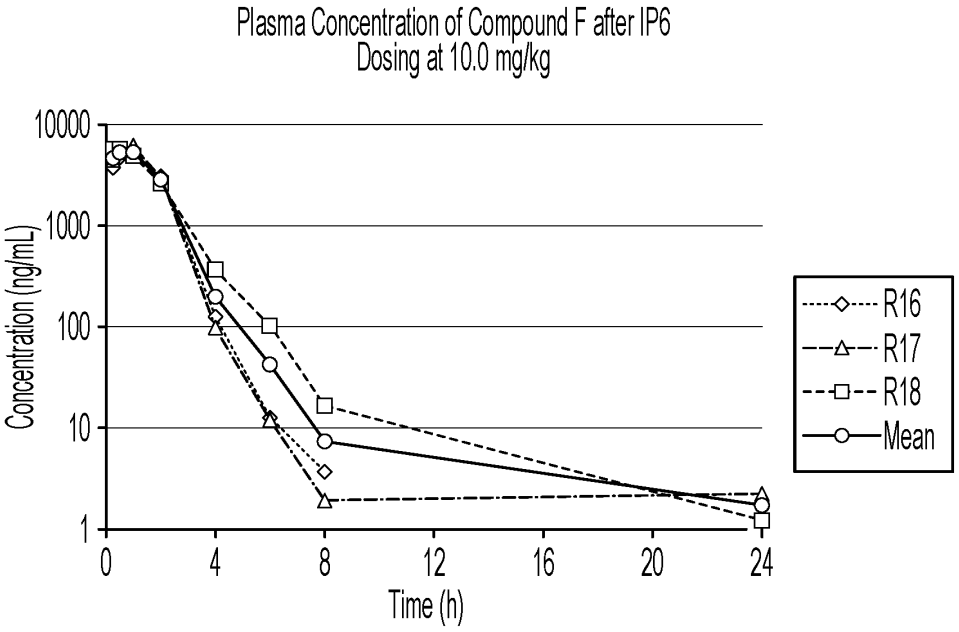
Plasma Concentration of Compound F after IP6
Dosing at 10.0 mg/kg
Concentration (ng/mL)
10000
1000
100
10
1
0
4
8
12
16
20
24
Time (h)
R16
R17
R18
Mean

FIG. 7C

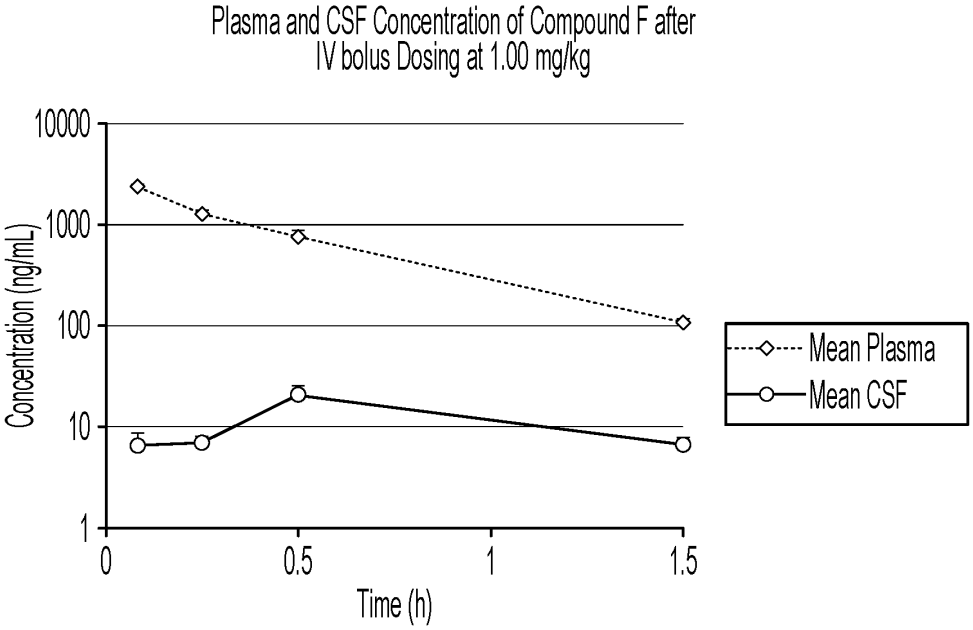
Plasma and CSF Concentration of Compound F after
IV bolus Dosing at 1.00 mg/kg
Concentration (ng/mL)
10000
1000
100
10
1
0
0.5
1
1.5
Time (h)
Mean Plasma
Mean CSF

FIG. 8

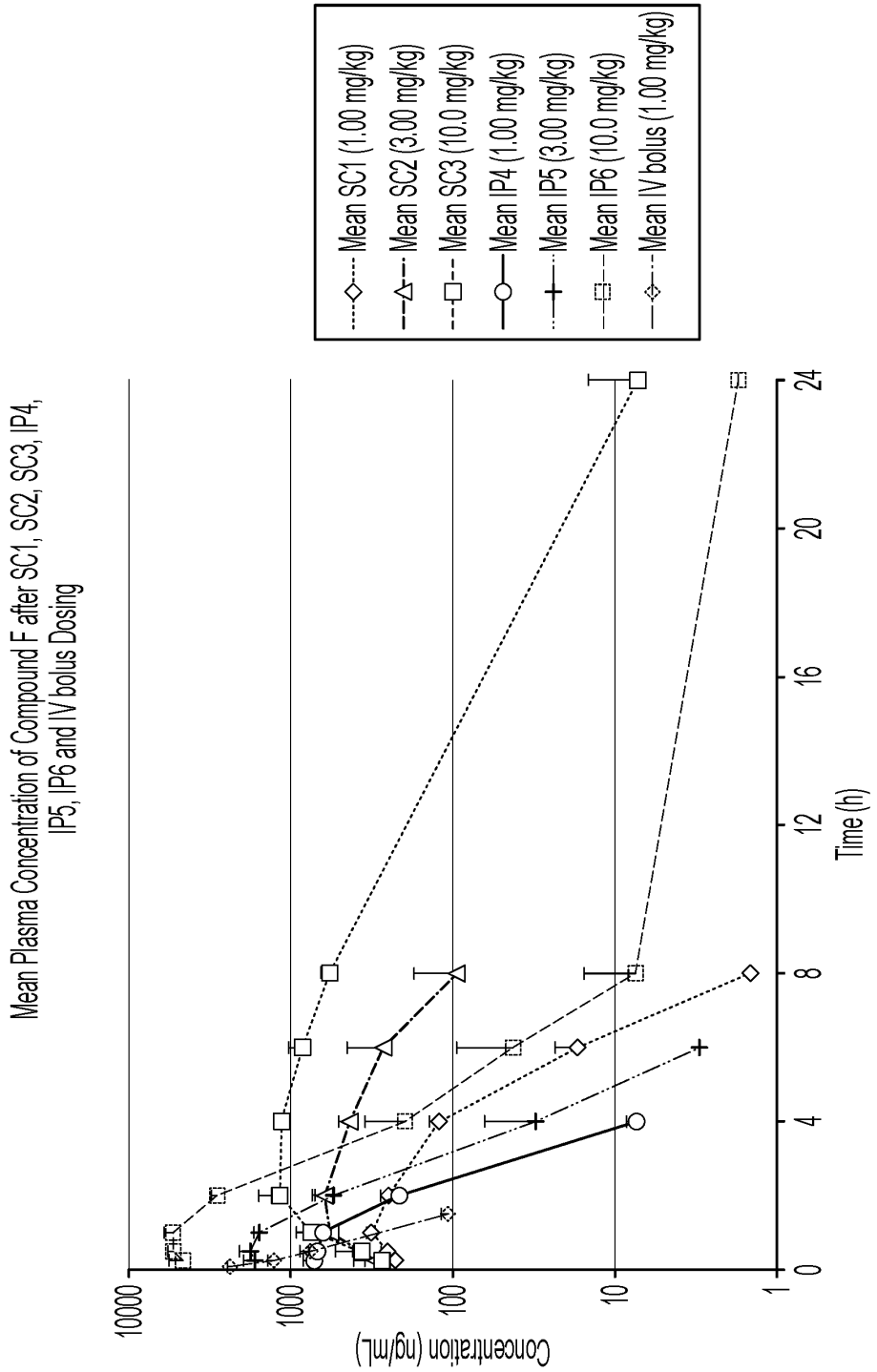
Mean Plasma Concentration of Compound F after SC1, SC2, SC3, IP4, IP5, IP6 and IV bolus Dosing
Concentration (ng/mL)
10000
1000
100
10
1
0
4
8
12
16
20
24
Time (h)
Mean SC1 (1.00 mg/kg)
Mean SC2 (3.00 mg/kg)
Mean SC3 (10.0 mg/kg)
Mean IP4 (1.00 mg/kg)
Mean IP5 (3.00 mg/kg)
Mean IP6 (10.0 mg/kg)
Mean IV bolus (1.00 mg/kg)

FIG. 9

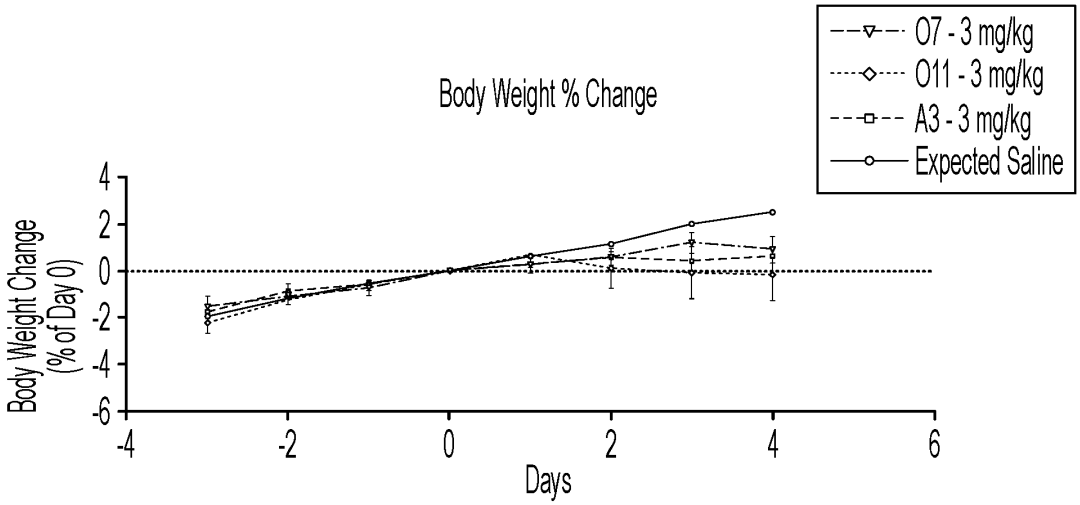

FIG. 10A

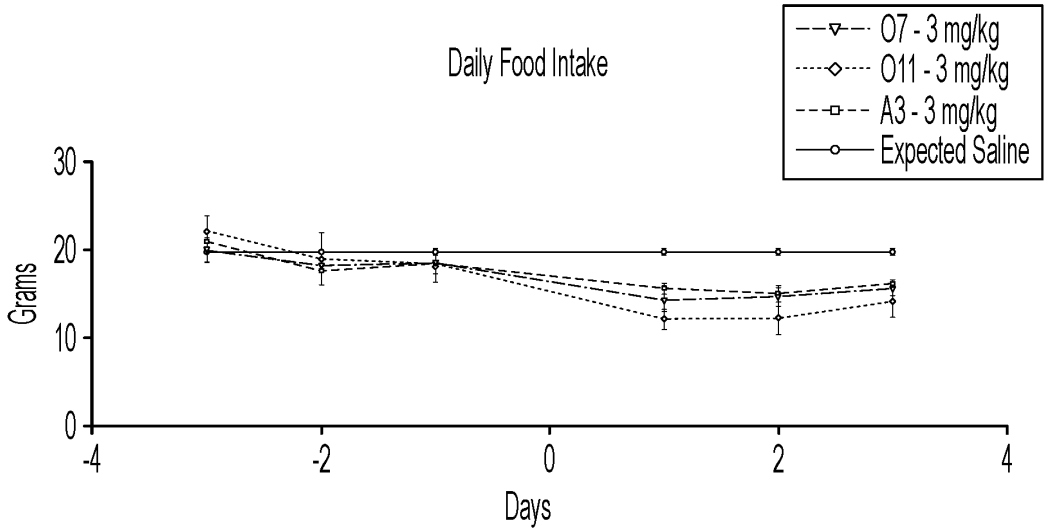

FIG. 10B

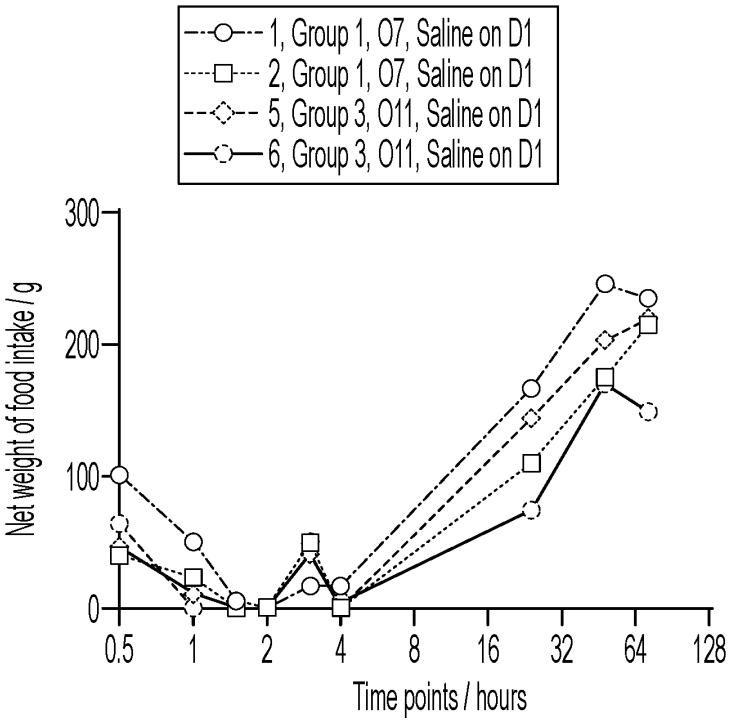

FIG. 11A

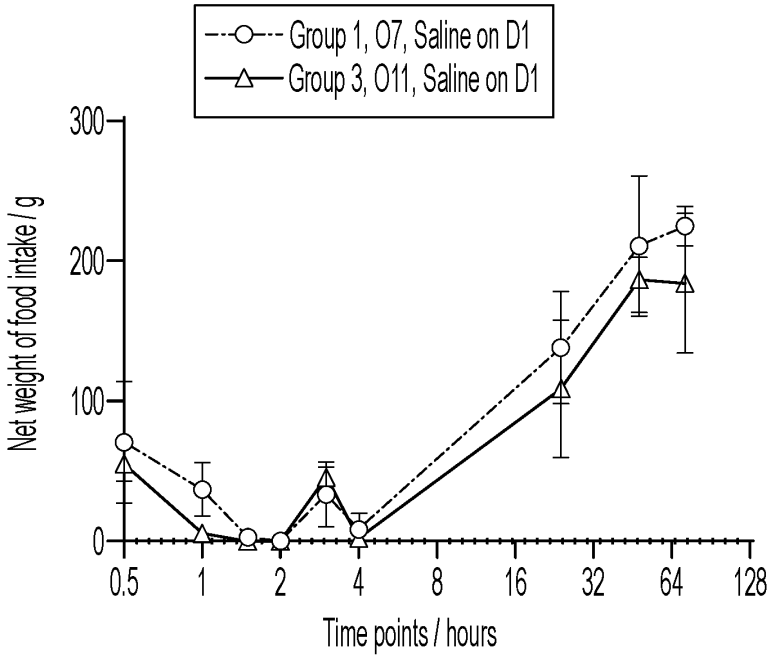

FIG. 11B

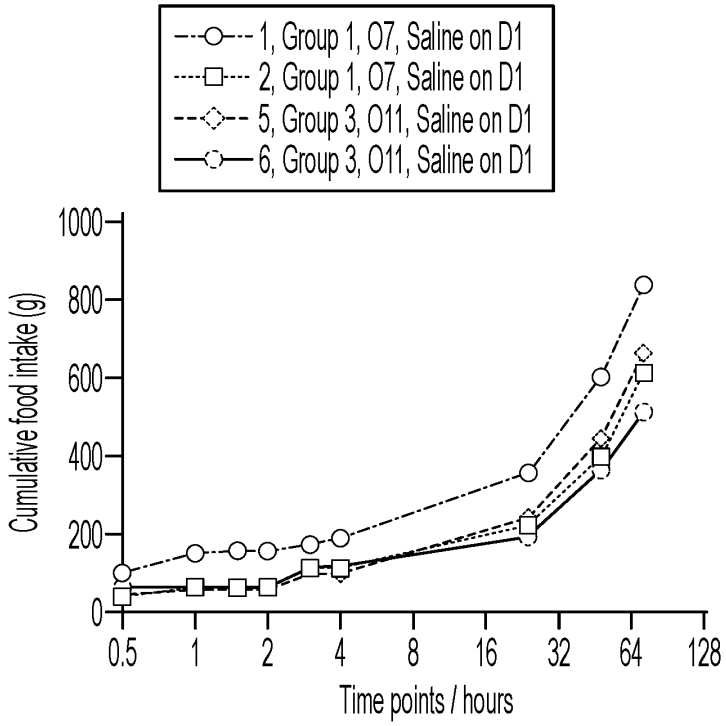

FIG. 11C

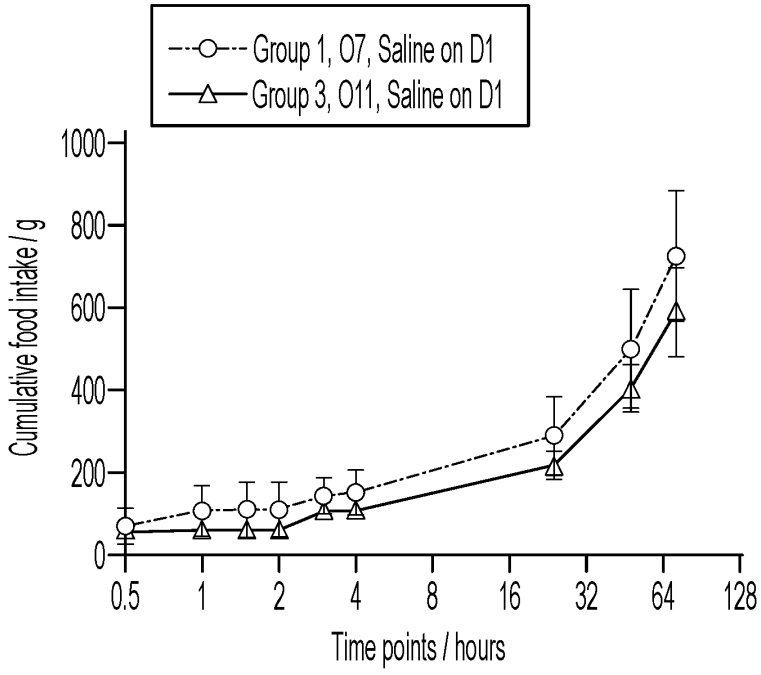

FIG. 11D

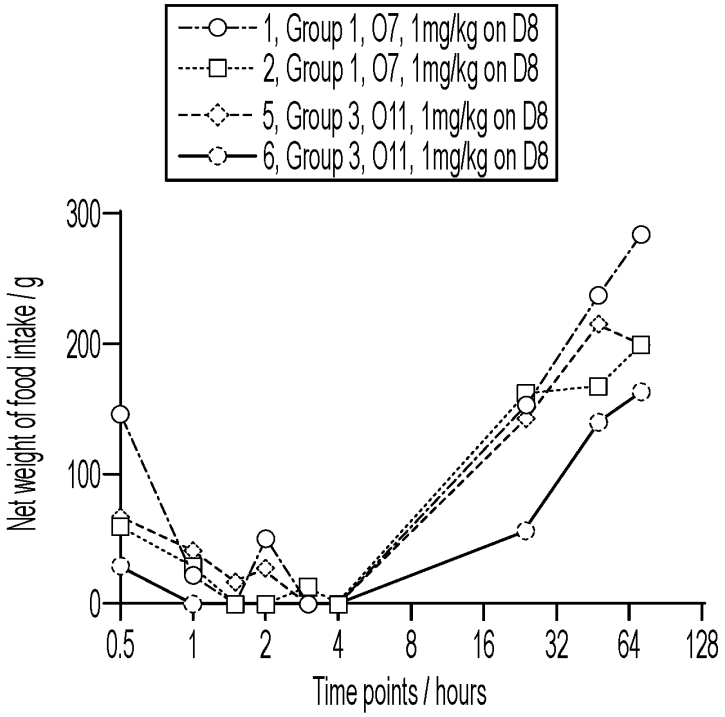

FIG. 12A

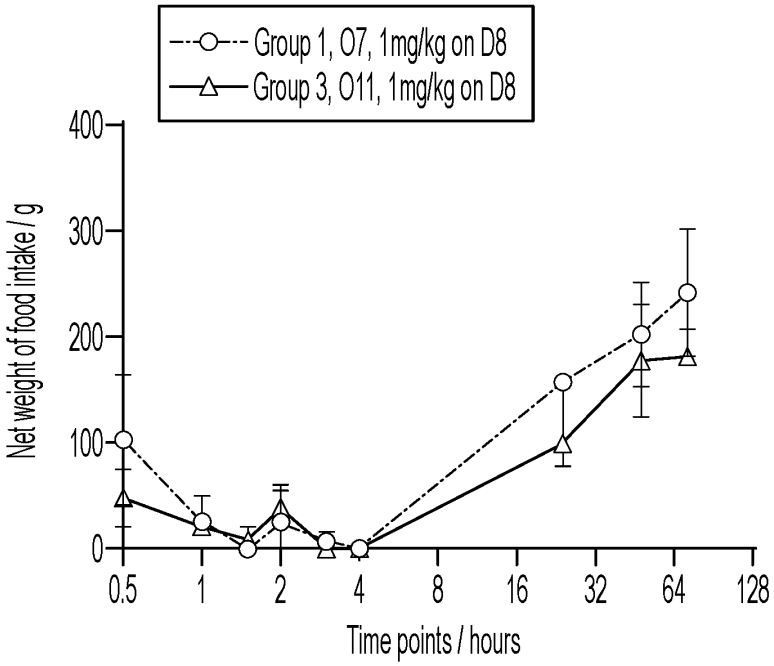

FIG. 12B

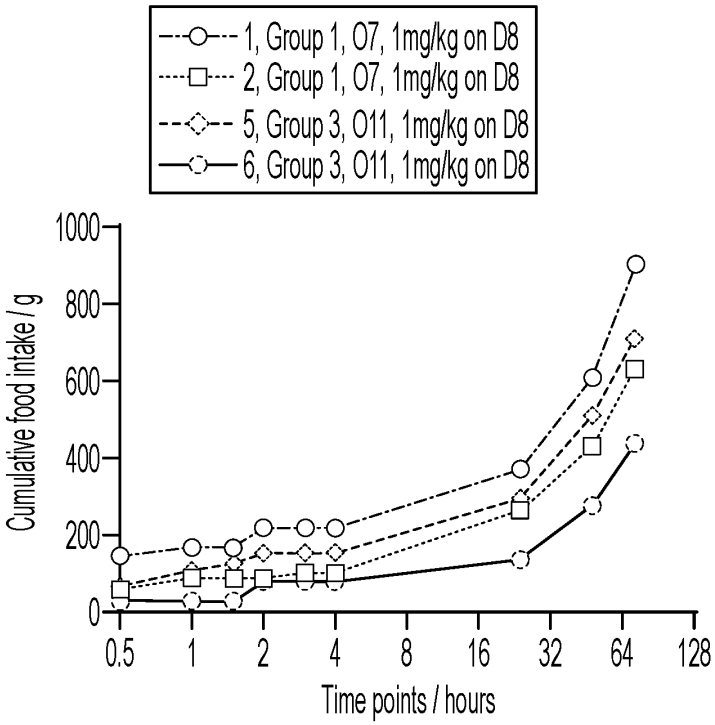

FIG. 12C

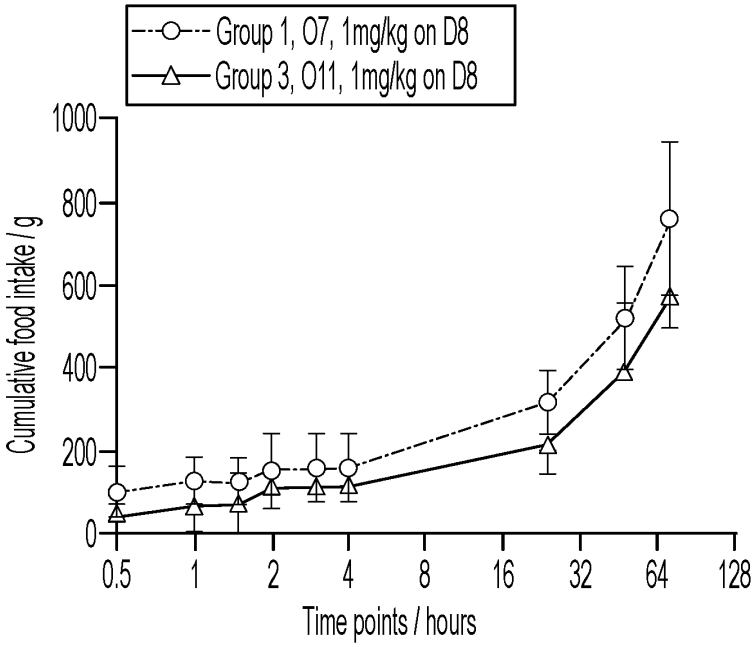

FIG. 12D

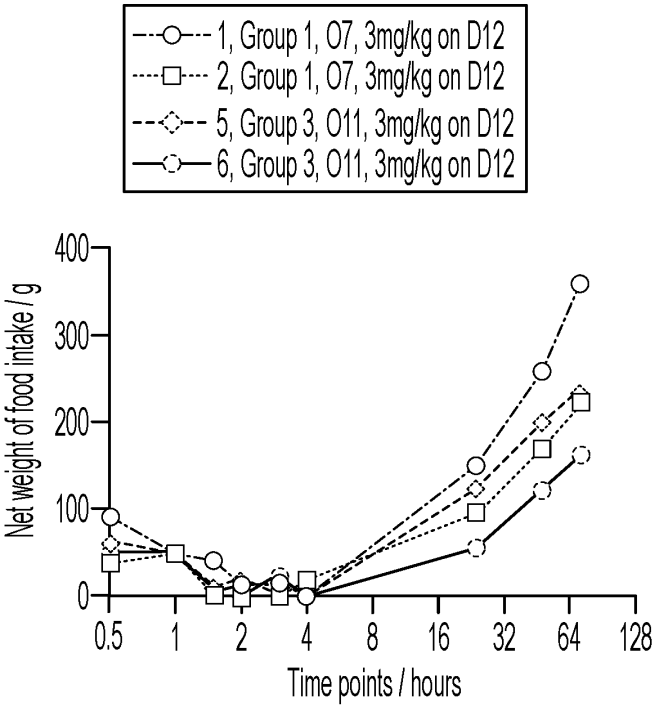

FIG. 12E

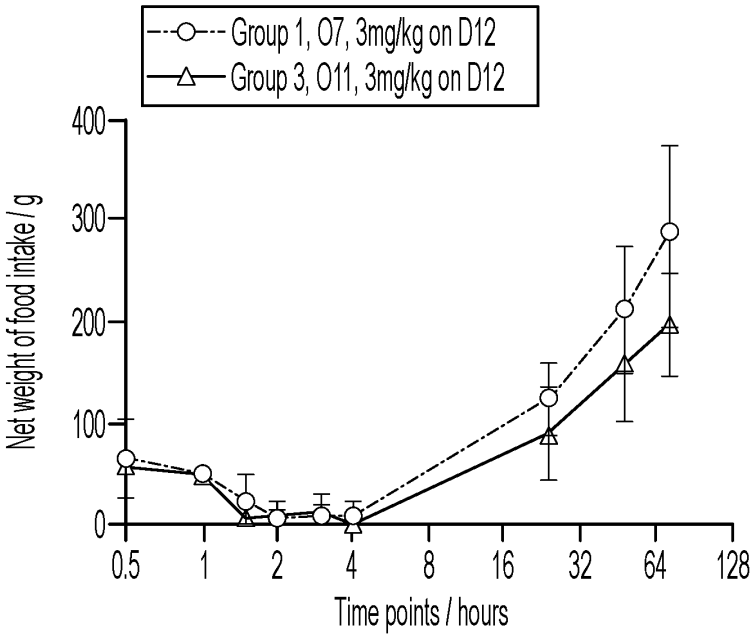

FIG. 12F

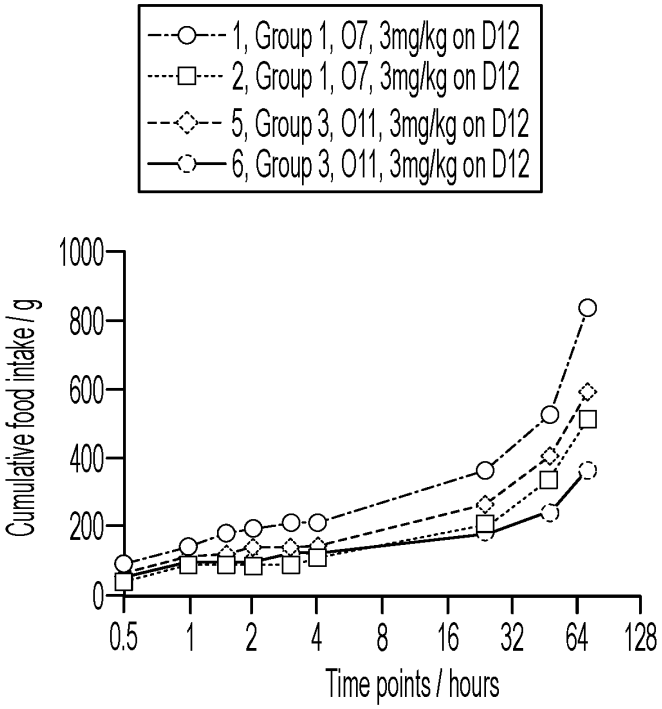

FIG. 12G

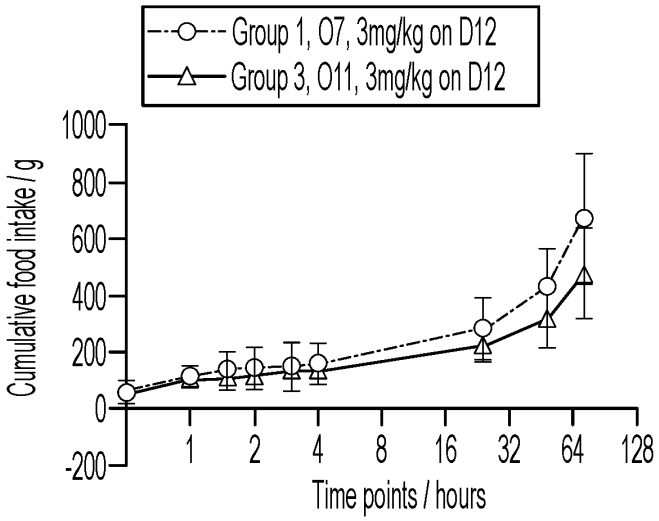

FIG. 12H

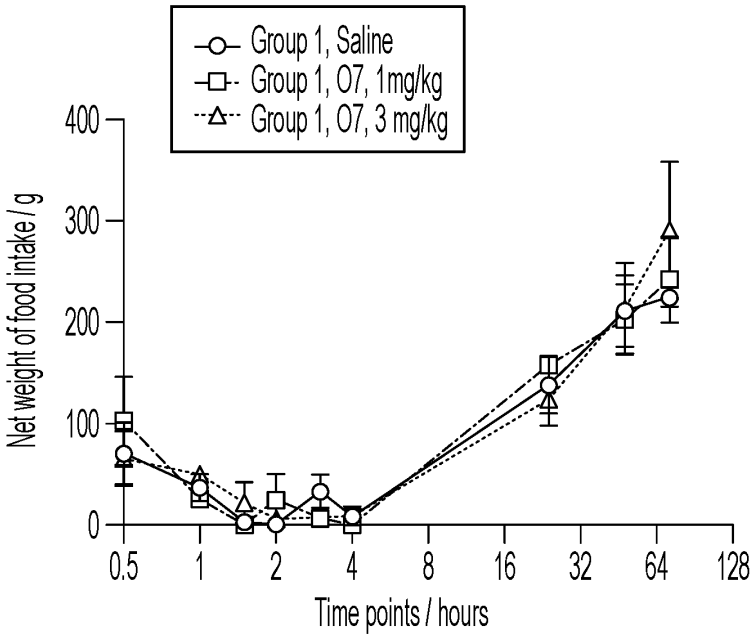

FIG. 13A

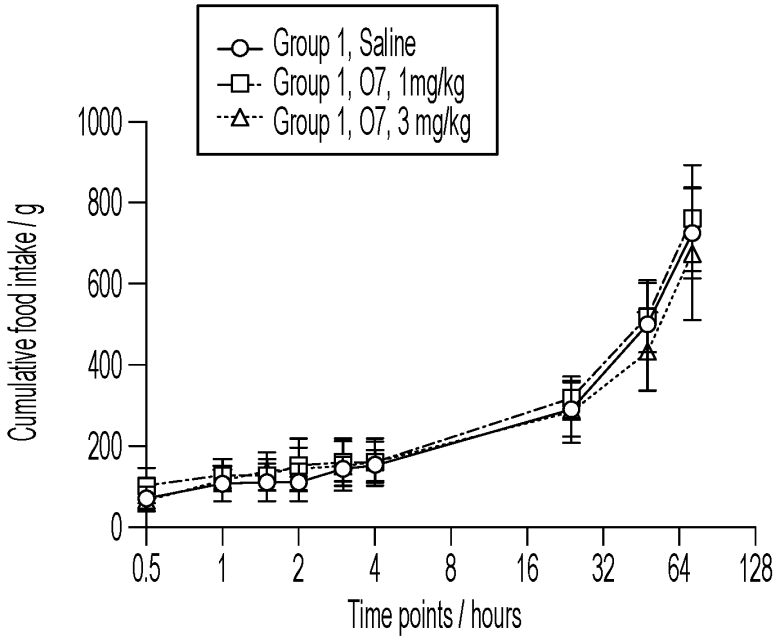

FIG. 13B

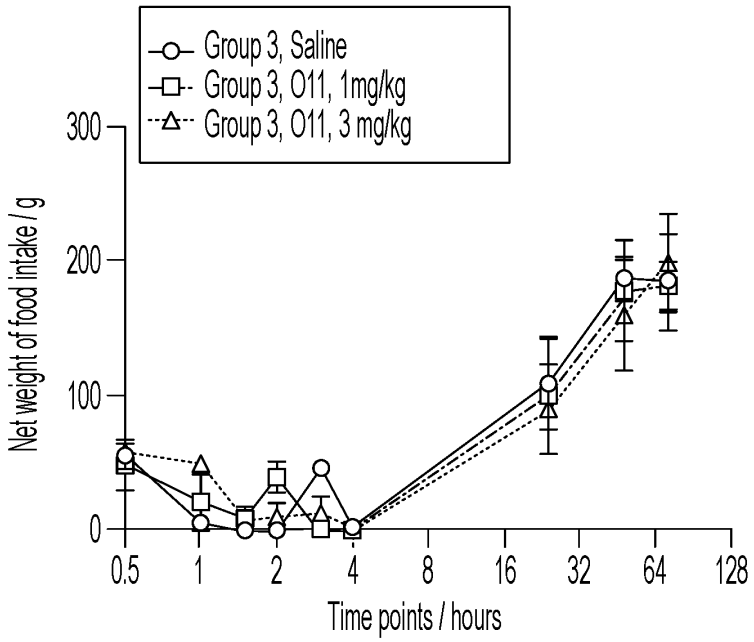

FIG. 13C

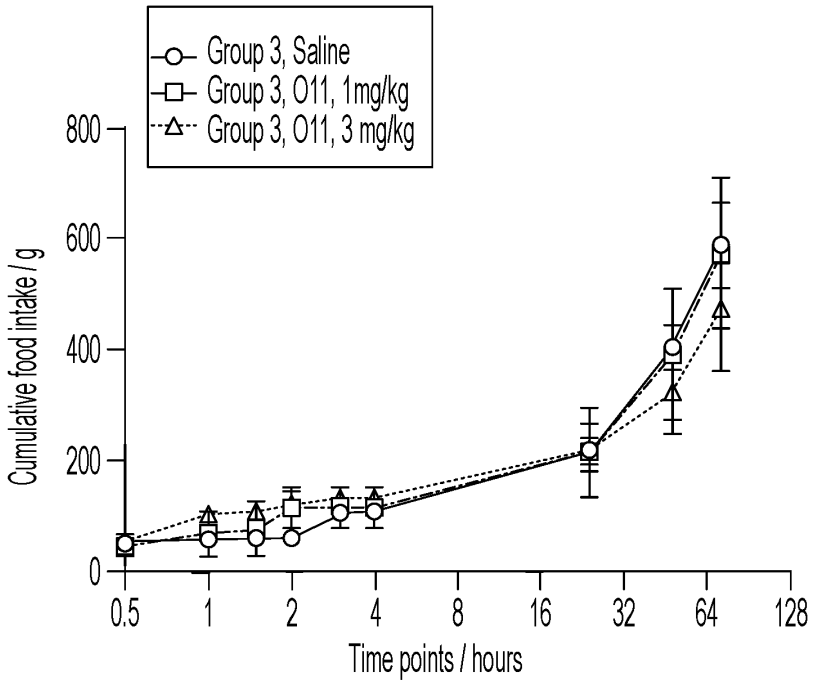

FIG. 13D

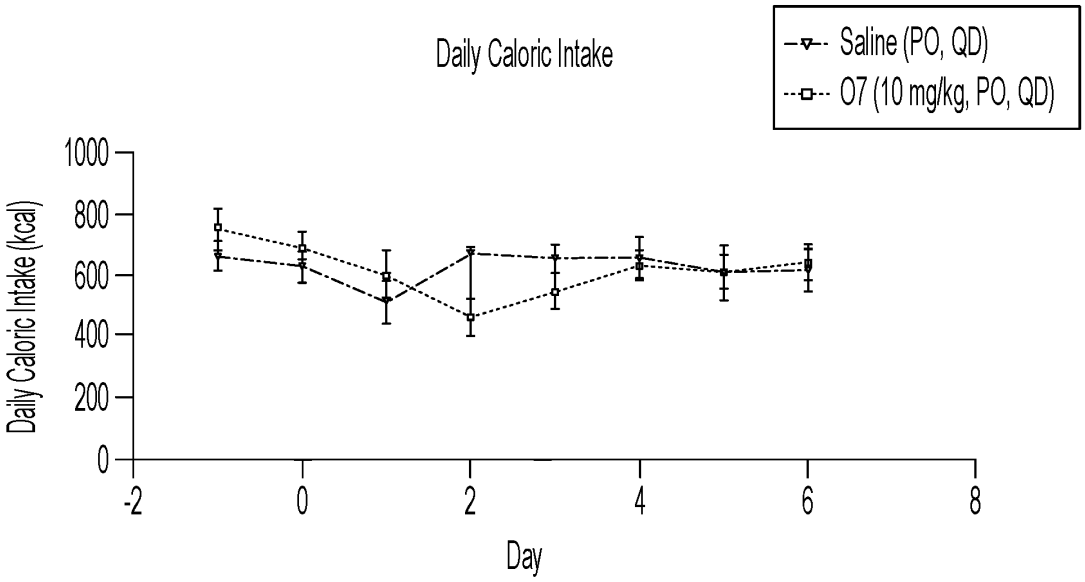

FIG. 14A

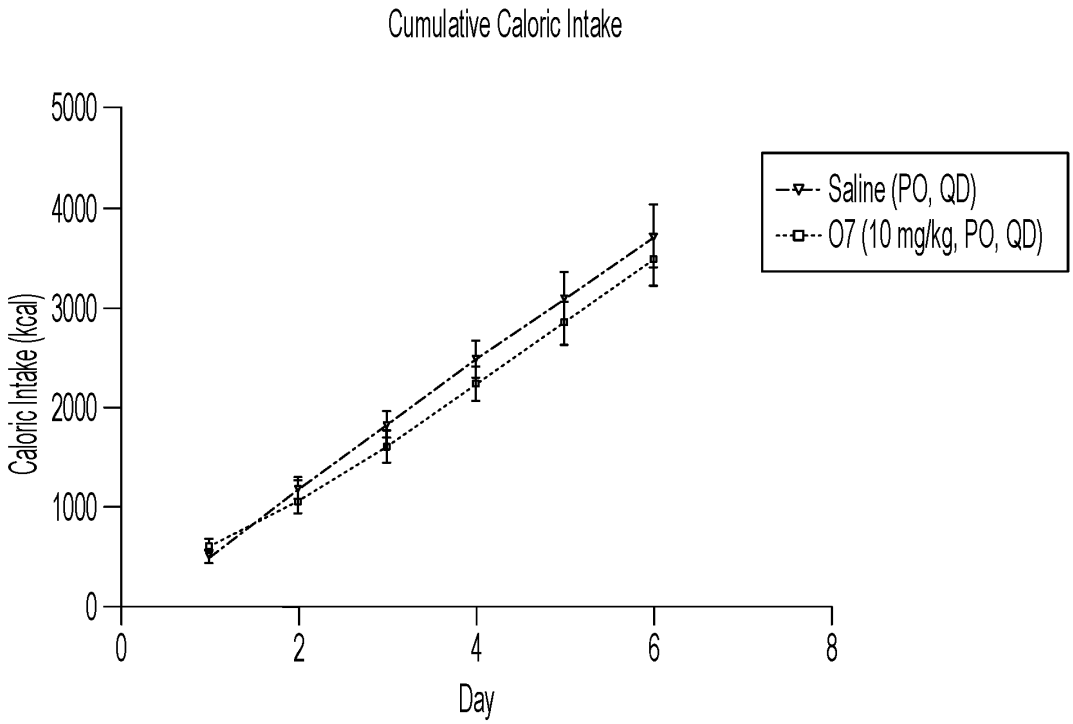

FIG. 14B

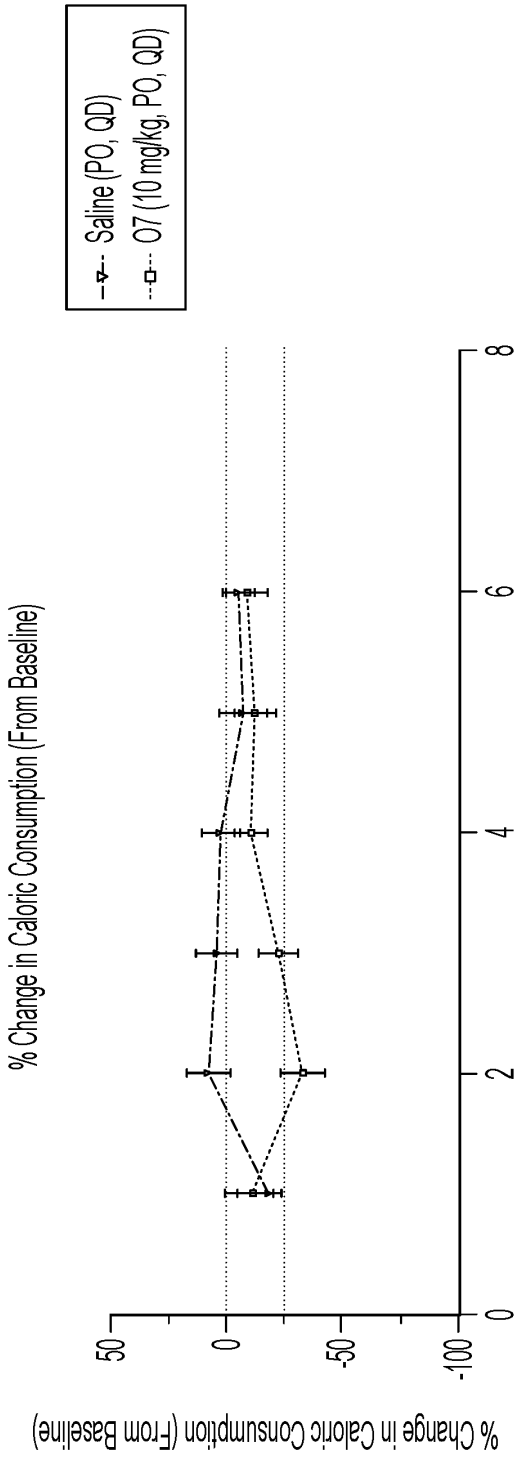
Saline (PO, QD)
O7 (10 mg/kg, PO, QD)
% Change in Caloric Consumption (From Baseline)
50
0
-50
-100
0
2
4
6
8
Day
% Change in Caloric Consumption (From Baseline)

FIG. 14C

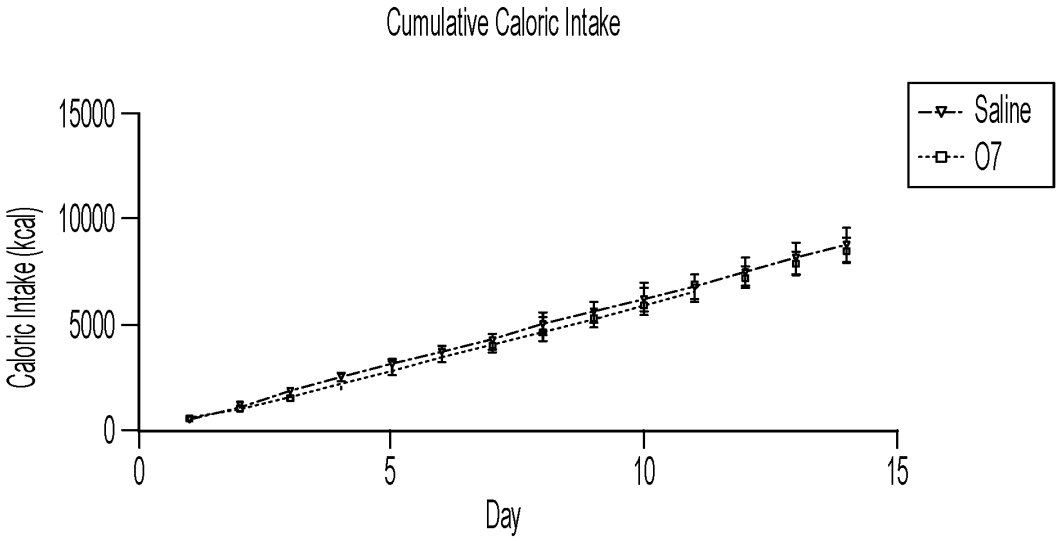

FIG. 15A

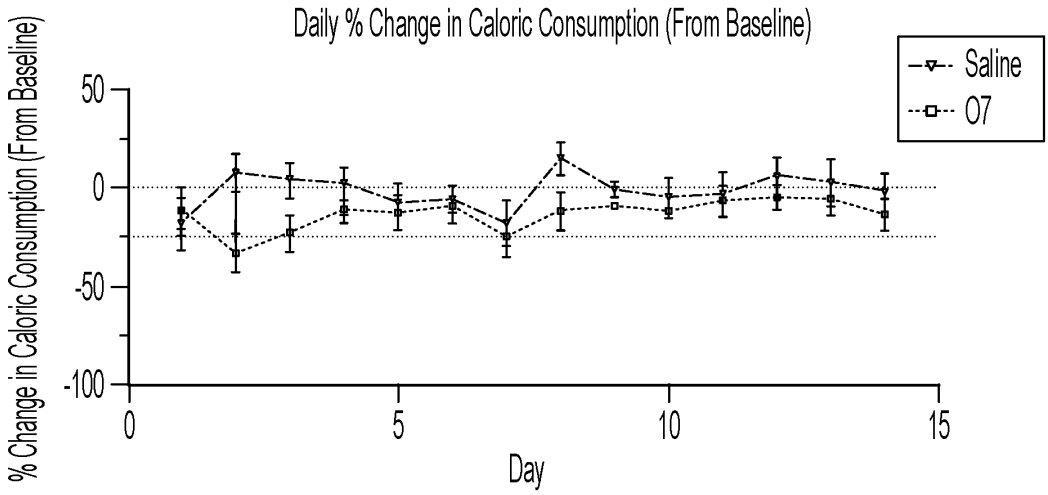

FIG. 15B

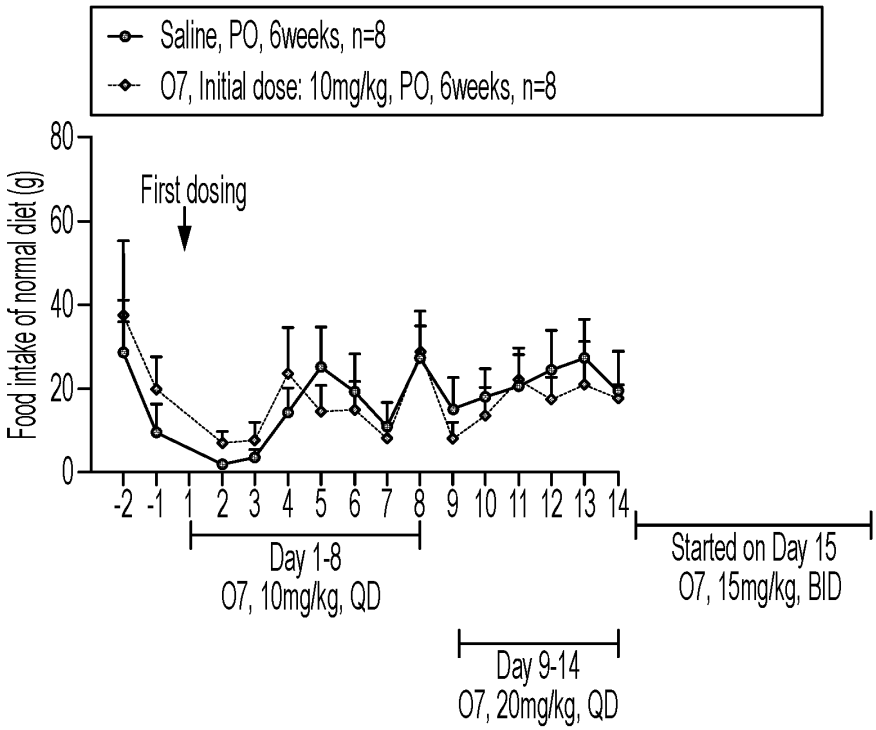
Saline, PO, 6weeks, n=8
O7, Initial dose: 10mg/kg, PO, 6weeks, n=8
Food intake of normal diet (g)
80
60
40
20
0
First dosing
-2 -1 1 2 3 4 5 6 7 8 9 10 11 12 13 14
Day 1-8
O7, 10mg/kg, QD
Day 9-14
O7, 20mg/kg, QD
Started on Day 15
O7, 15mg/kg, BID

FIG. 15C

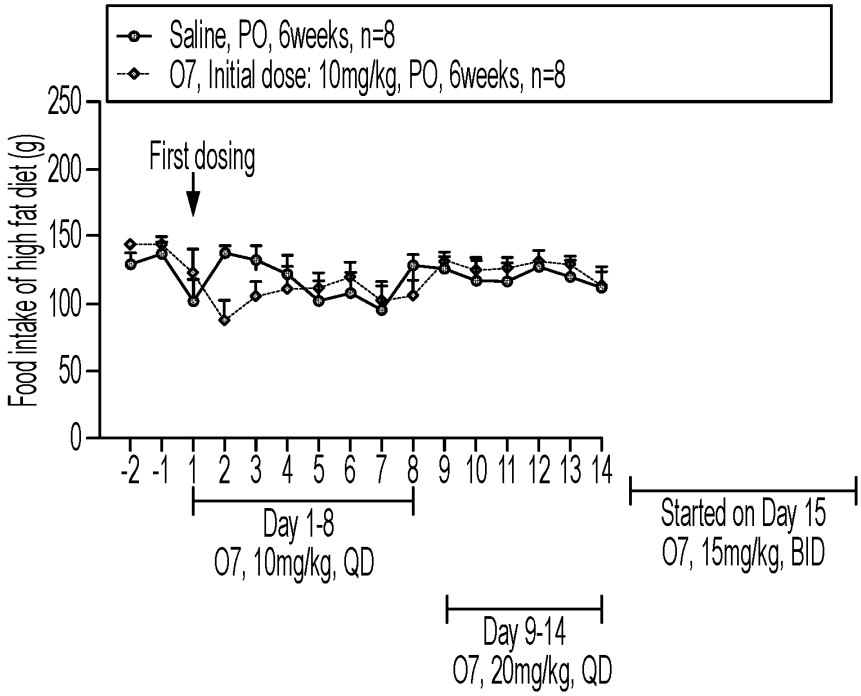
Saline, PO, 6weeks, n=8
O7, Initial dose: 10mg/kg, PO, 6weeks, n=8
Food intake of high fat diet (g)
250
200
150
100
50
0
First dosing
-2 -1 1 2 3 4 5 6 7 8 9 10 11 12 13 14
Day 1-8
O7, 10mg/kg, QD
Day 9-14
O7, 20mg/kg, QD
Started on Day 15
O7, 15mg/kg, BID

FIG. 15D

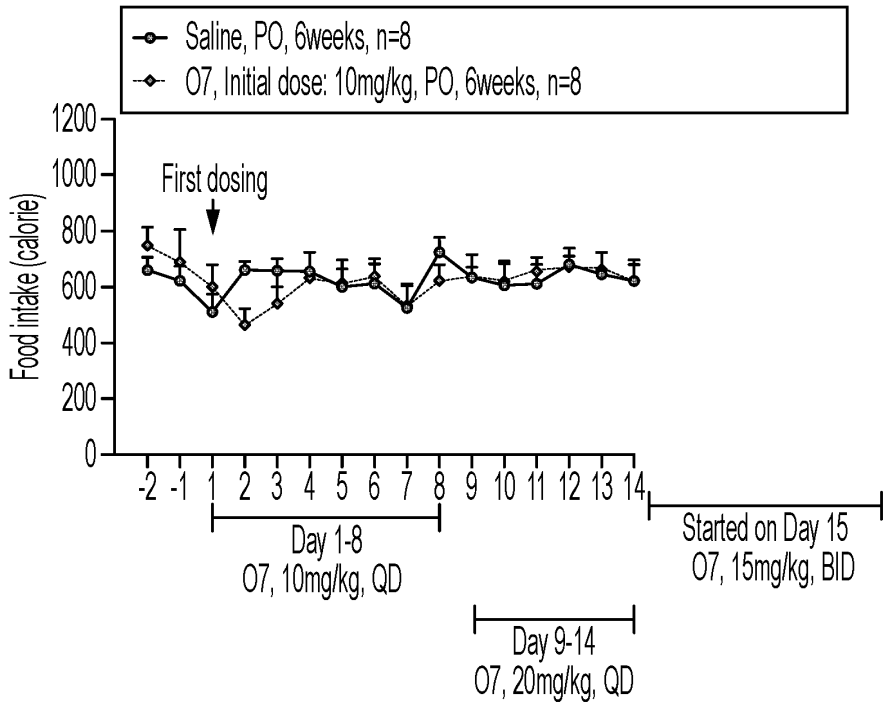
Saline, PO, 6weeks, n=8
O7, Initial dose: 10mg/kg, PO, 6weeks, n=8
Food intake (calorie)
1200
1000
800
600
400
200
0
First dosing
-2 -1 1 2 3 4 5 6 7 8 9 10 11 12 13 14
Day 1-8
O7, 10mg/kg, QD
Day 9-14
O7, 20mg/kg, QD
Started on Day 15
O7, 15mg/kg, BID

FIG. 15E

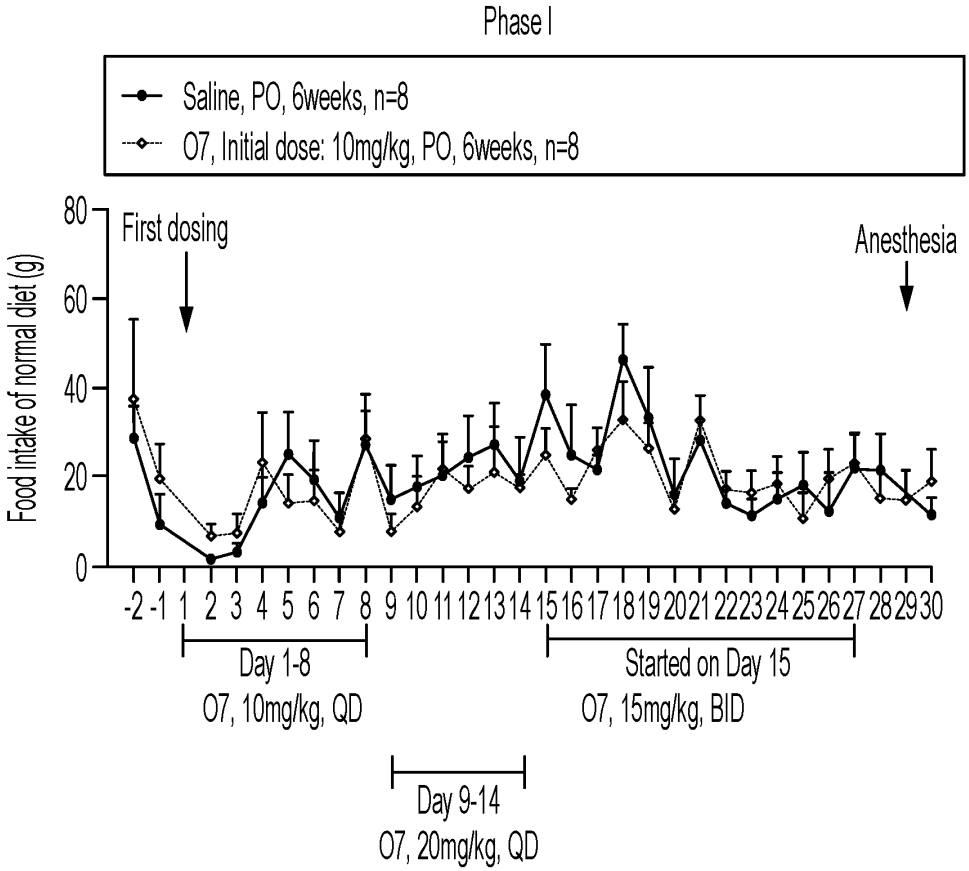
Phase I
Saline, PO, 6weeks, n=8
O7, Initial dose: 10mg/kg, PO, 6weeks, n=8
Food intake of normal diet (g)
0
20
40
60
80
First dosing
Anesthesia
-2 -1 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30
Day 1-8
O7, 10mg/kg, QD
Started on Day 15
O7, 15mg/kg, BID
Day 9-14
O7, 20mg/kg, QD

FIG. 15F

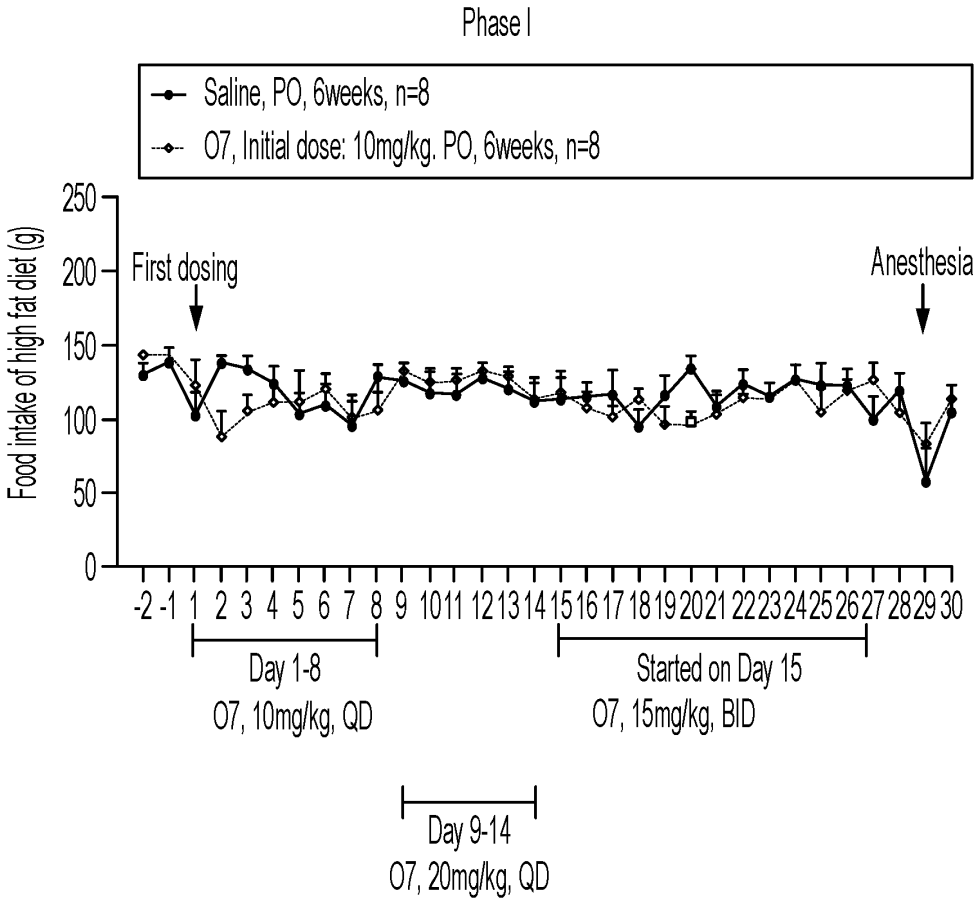
Phase I
Saline, PO, 6weeks, n=8
O7, Initial dose: 10mg/kg. PO, 6weeks, n=8
Food intake of high fat diet (g)
250
200
150
100
50
0
First dosing
Anesthesia
-2 -1 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30
Day 1-8
O7, 10mg/kg, QD
Started on Day 15
O7, 15mg/kg, BID
Day 9-14
O7, 20mg/kg, QD

FIG. 15G

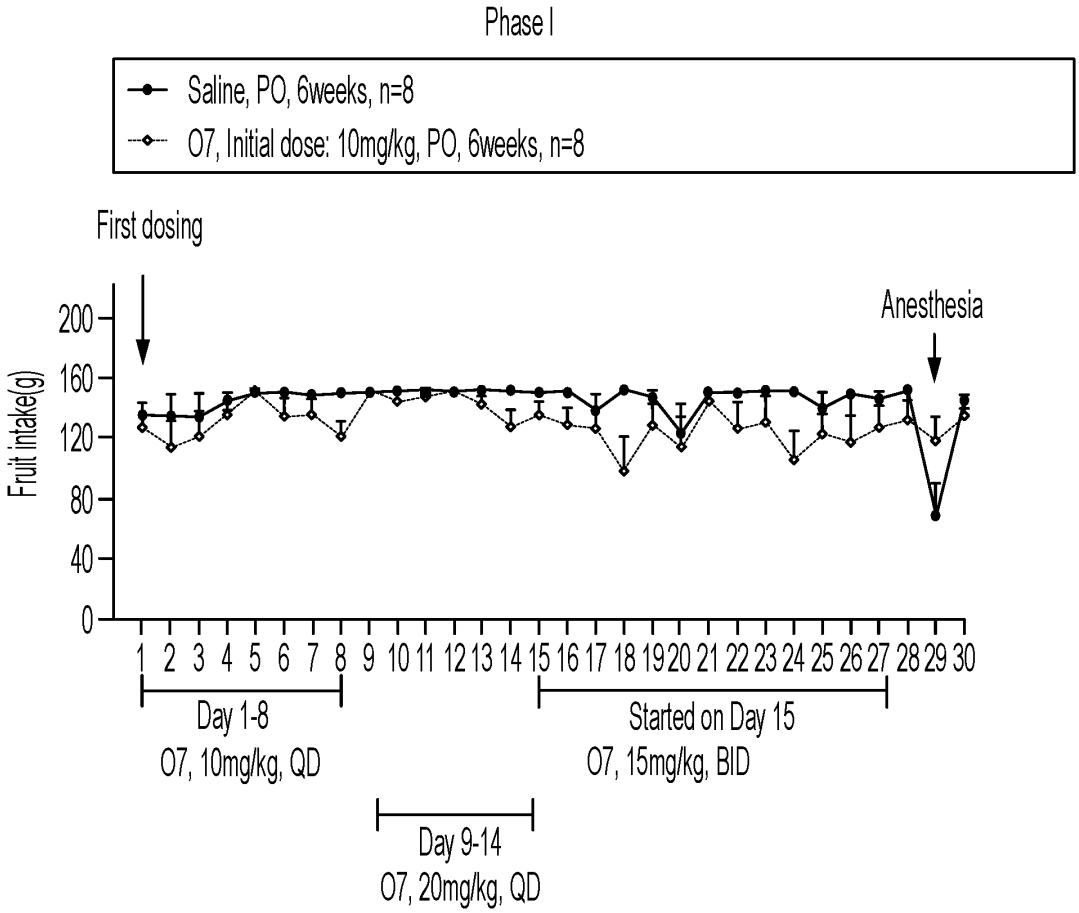
Phase I
Saline, PO, 6weeks, n=8
O7, Initial dose: 10mg/kg, PO, 6weeks, n=8
First dosing
Anesthesia
Fruit intake(g)
200
160
120
80
40
0
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30
Day 1-8
O7, 10mg/kg, QD
Started on Day 15
O7, 15mg/kg, BID
Day 9-14
O7, 20mg/kg, QD

FIG. 15H

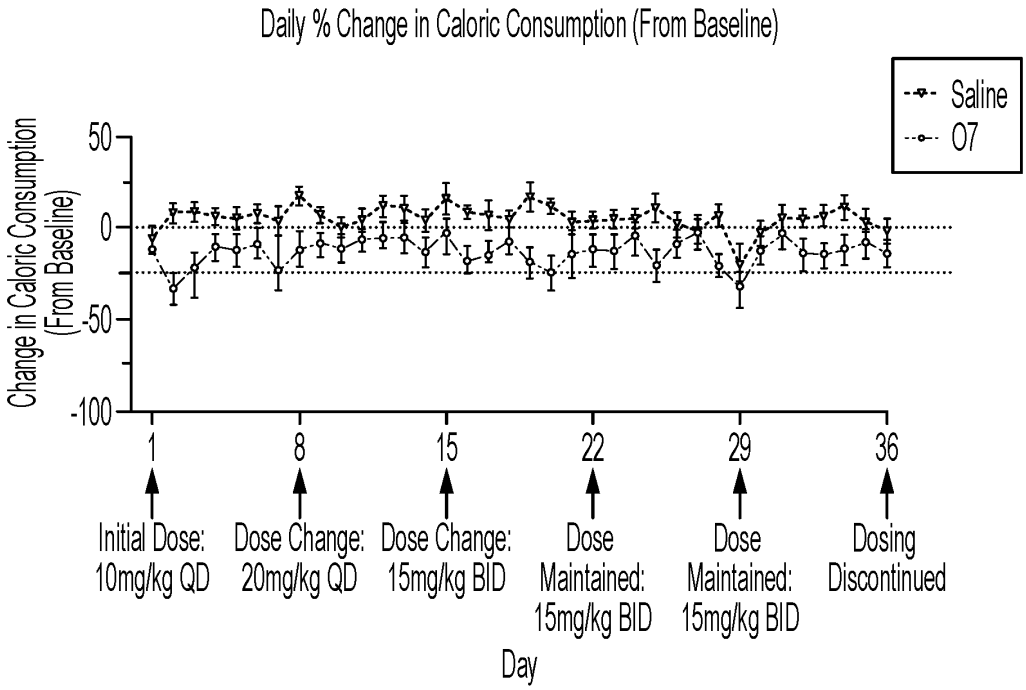
Daily % Change in Caloric Consumption (From Baseline)
Saline
O7
Change in Caloric Consumption (From Baseline)
50
0
-50
-100
1
8
15
22
29
36
Initial Dose: 10mg/kg QD
Dose Change: 20mg/kg QD
Dose Change: 15mg/kg BID
Dose Maintained: 15mg/kg BID
Dose Maintained: 15mg/kg BID
Dosing Discontinued
Day

FIG. 15I

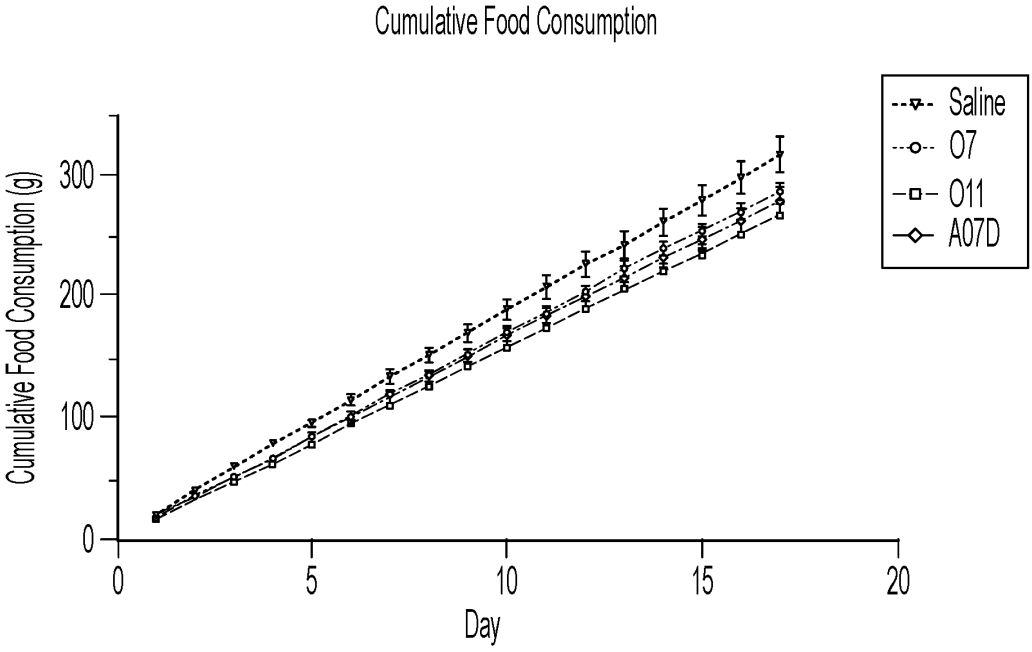
Cumulative Food Consumption
Cumulative Food Consumption (g)
300
200
100
0
0
5
10
15
20
Day
Saline
O7
O11
A07D

FIG. 15J

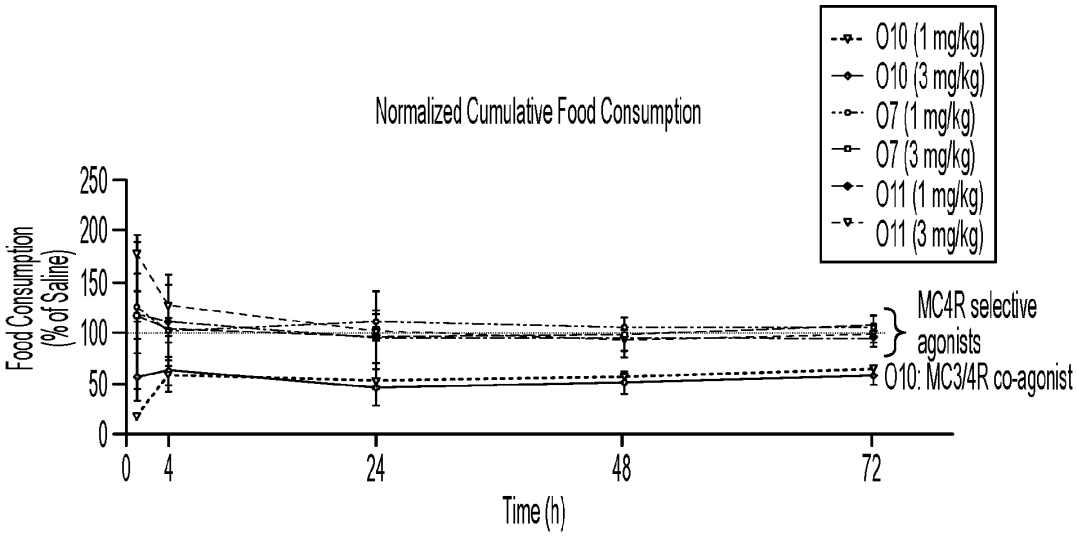
Normalized Cumulative Food Consumption
O10 (1 mg/kg)
O10 (3 mg/kg)
O7 (1 mg/kg)
O7 (3 mg/kg)
O11 (1 mg/kg)
O11 (3 mg/kg)
Food Consumption (% of Saline)
250
200
150
100
50
0
0
4
24
48
72
Time (h)
MC4R selective agonists
O10: MC3/4R co-agonist

FIG. 15K

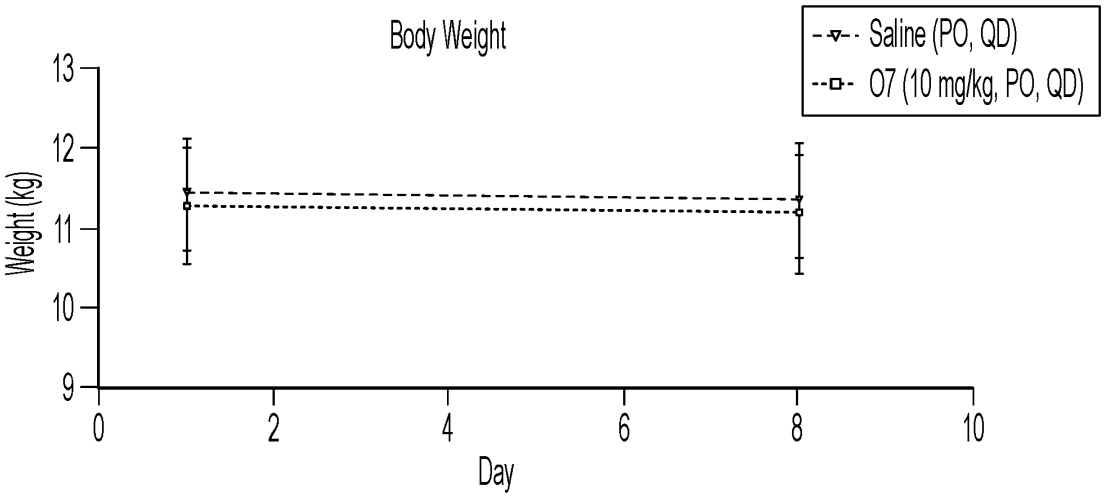

FIG. 16A

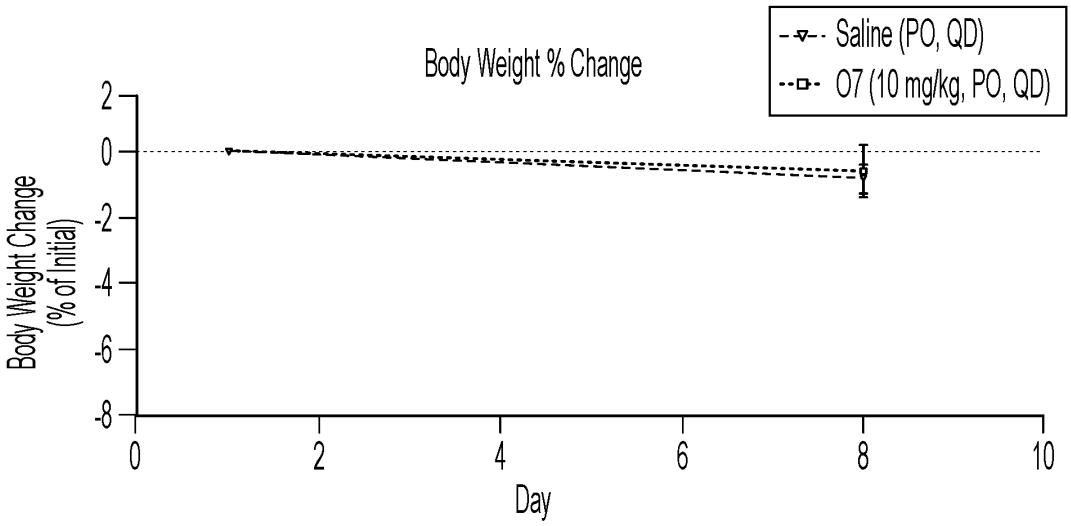

FIG. 16B

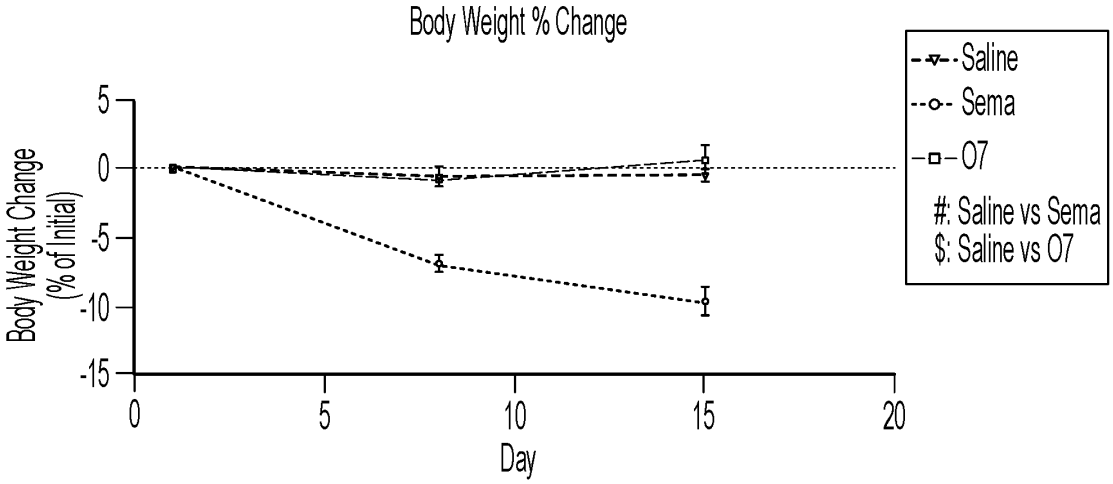

FIG. 16C

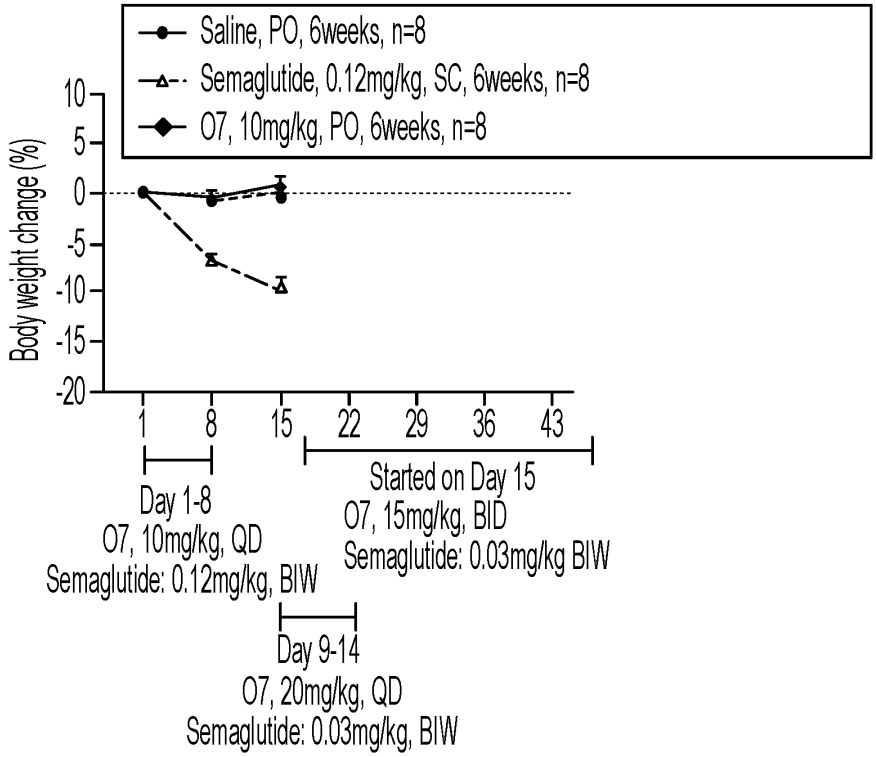

FIG. 16D

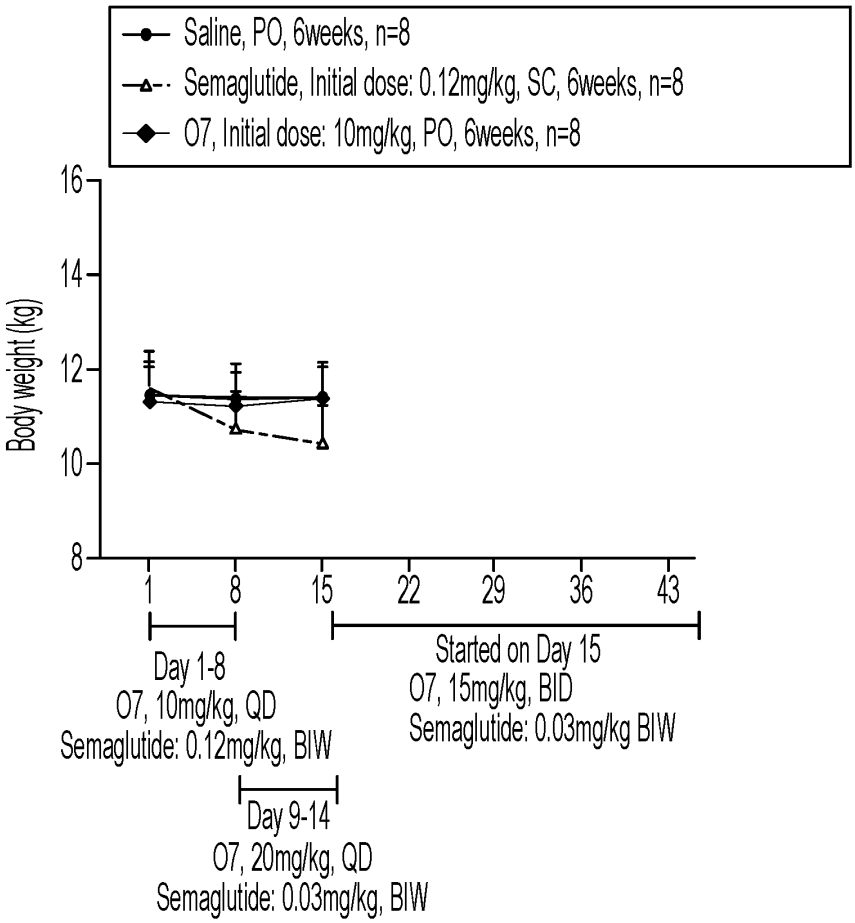
Saline, PO, 6weeks, n=8
Semaglutide, Initial dose: 0.12mg/kg, SC, 6weeks, n=8
O7, Initial dose: 10mg/kg, PO, 6weeks, n=8
Body weight (kg)
16
14
12
10
8
1
8
15
22
29
36
43
Day 1-8
O7, 10mg/kg, QD
Semaglutide: 0.12mg/kg, BIW
Day 9-14
O7, 20mg/kg, QD
Semaglutide: 0.03mg/kg, BIW
Started on Day 15
O7, 15mg/kg, BID
Semaglutide: 0.03mg/kg BIW

FIG. 16E

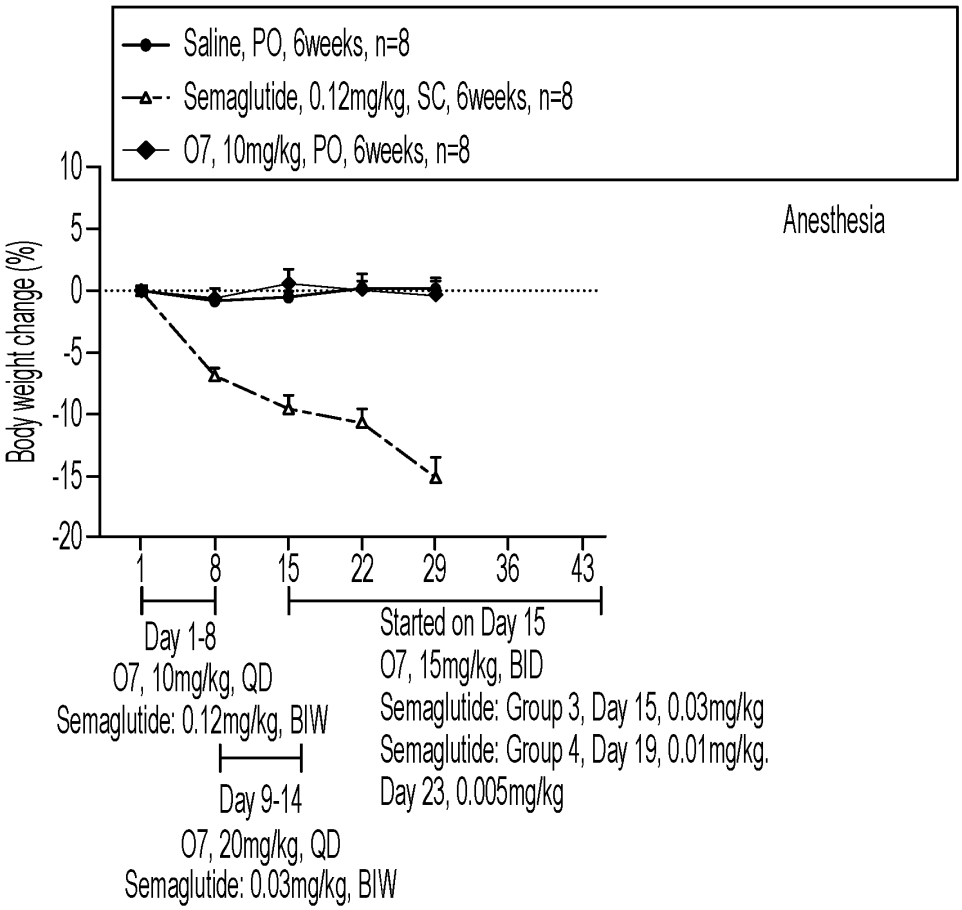
Saline, PO, 6weeks, n=8
Semaglutide, 0.12mg/kg, SC, 6weeks, n=8
O7, 10mg/kg, PO, 6weeks, n=8
Anesthesia
Body weight change (%)
10
5
0
-5
-10
-15
-20
1
8
15
22
29
36
43
Day 1-8
O7, 10mg/kg, QD
Semaglutide: 0.12mg/kg, BIW
Day 9-14
O7, 20mg/kg, QD
Semaglutide: 0.03mg/kg, BIW
Started on Day 15
O7, 15mg/kg, BID
Semaglutide: Group 3, Day 15, 0.03mg/kg
Semaglutide: Group 4, Day 19, 0.01mg/kg.
Day 23, 0.005mg/kg

FIG. 16F

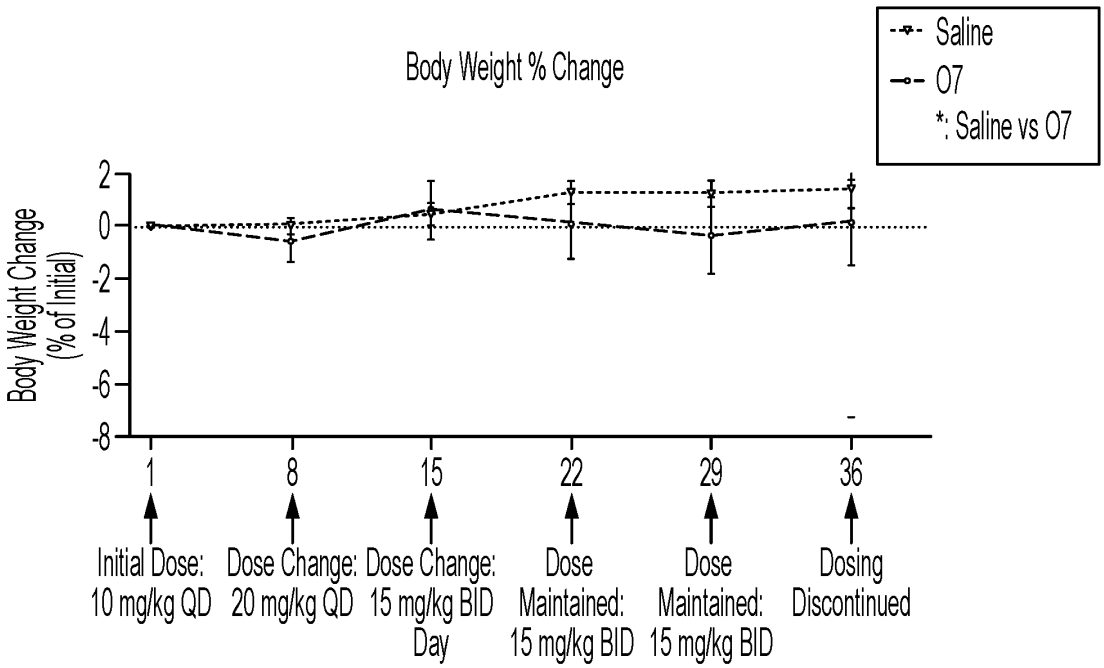
Body Weight % Change
Saline
O7
*: Saline vs O7
Body Weight Change (% of Initial)
2
0
-2
-4
-6
-8
1
8
15
22
29
36
Initial Dose: 10 mg/kg QD
Dose Change: 20 mg/kg QD
Dose Change: 15 mg/kg BID
Day
Dose Maintained: 15 mg/kg BID
Dose Maintained: 15 mg/kg BID
Dosing Discontinued

FIG. 16G

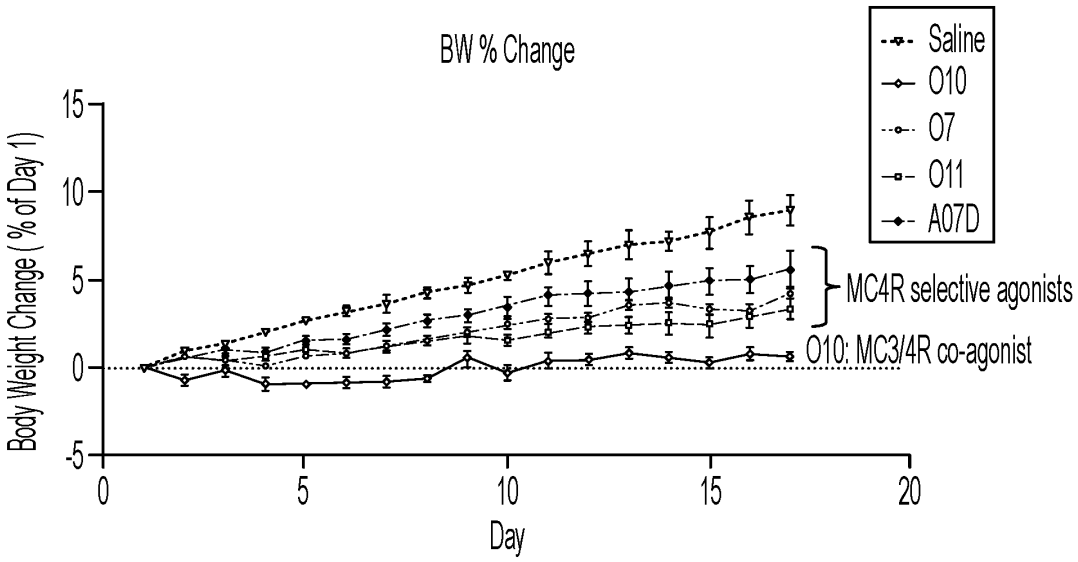
BW % Change
Body Weight Change (% of Day 1)
15
10
5
0
-5
0
5
10
15
20
Day
Saline
O10
O7
O11
A07D
MC4R selective agonists
O10: MC3/4R co-agonist

FIG. 16H

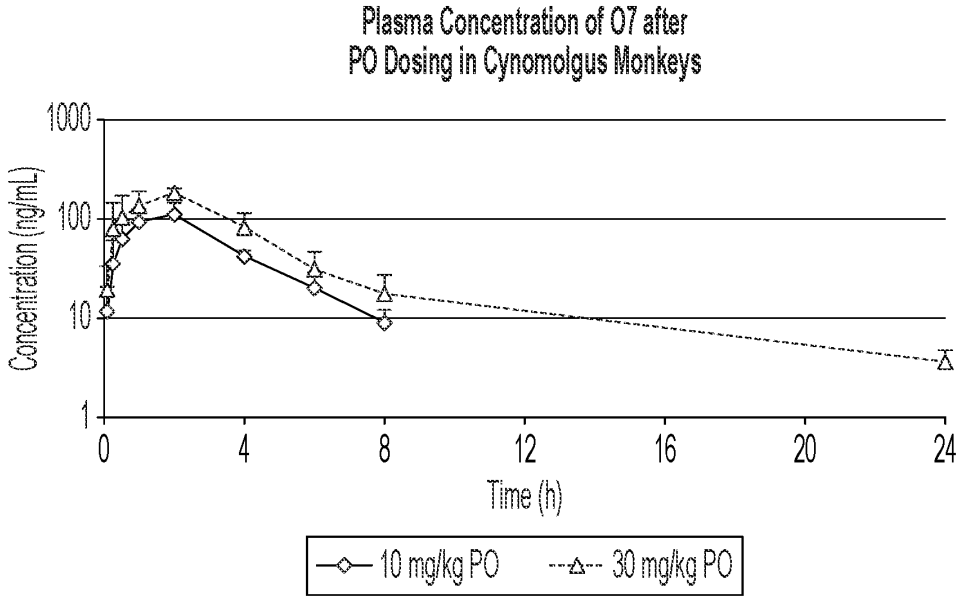
Plasma Concentration of O7 after
PO Dosing in Cynomolgus Monkeys
Concentration (ng/mL)
1000
100
10
1
0
4
8
12
16
20
24
Time (h)
10 mg/kg PO
30 mg/kg PO

FIG. 17

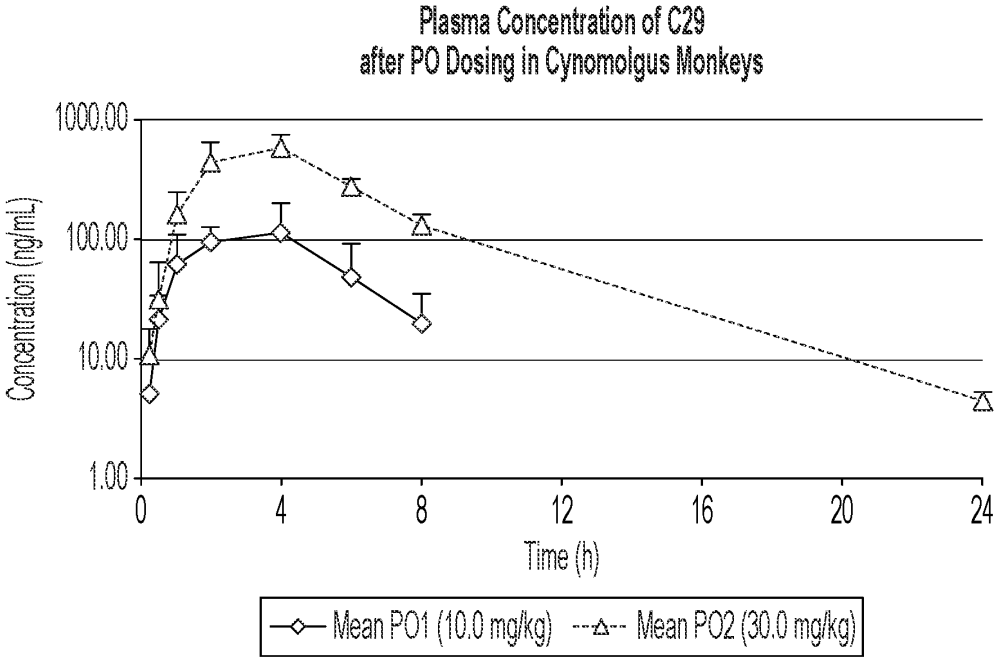
Plasma Concentration of C29
after PO Dosing in Cynomolgus Monkeys
1000.00
100.00
10.00
1.00
Concentration (ng/mL)
0
4
8
12
16
20
24
Time (h)
Mean PO1 (10.0 mg/kg)
Mean PO2 (30.0 mg/kg)

FIG. 18

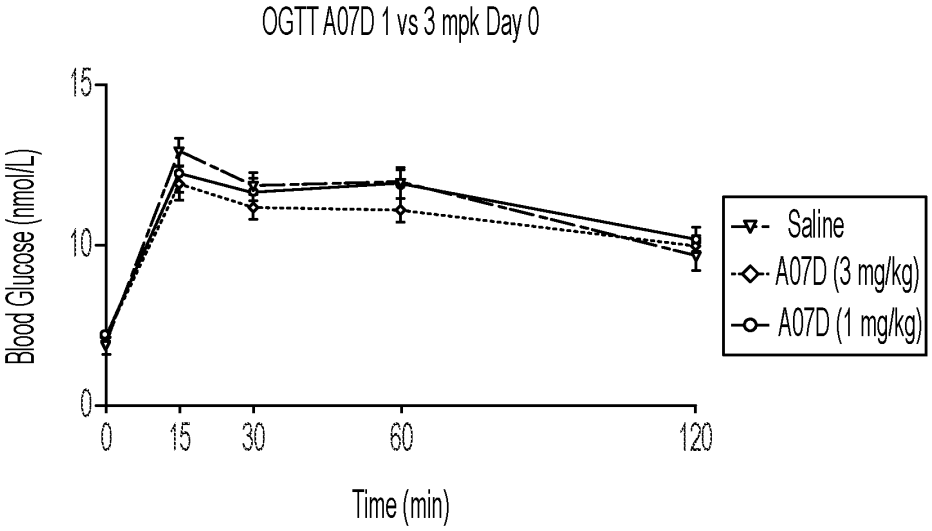

FIG. 19A

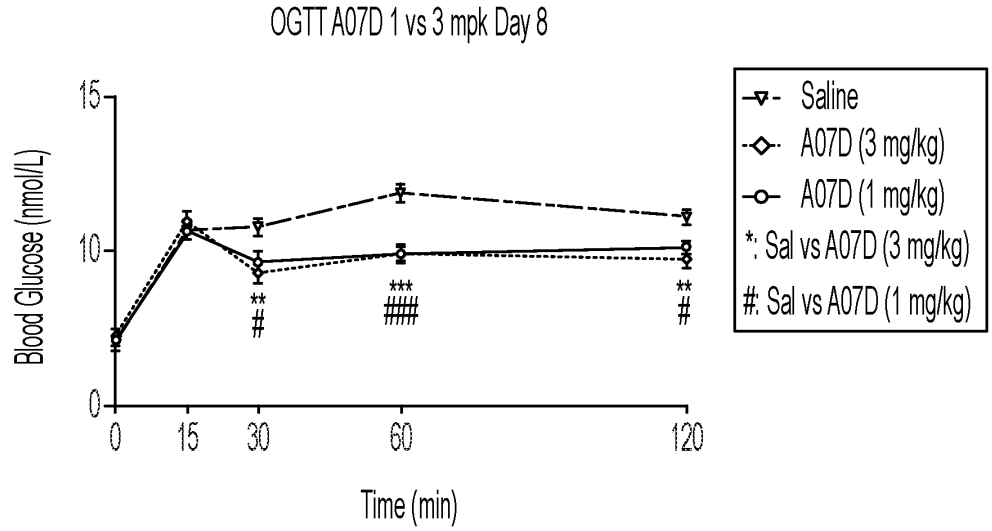

FIG. 19B

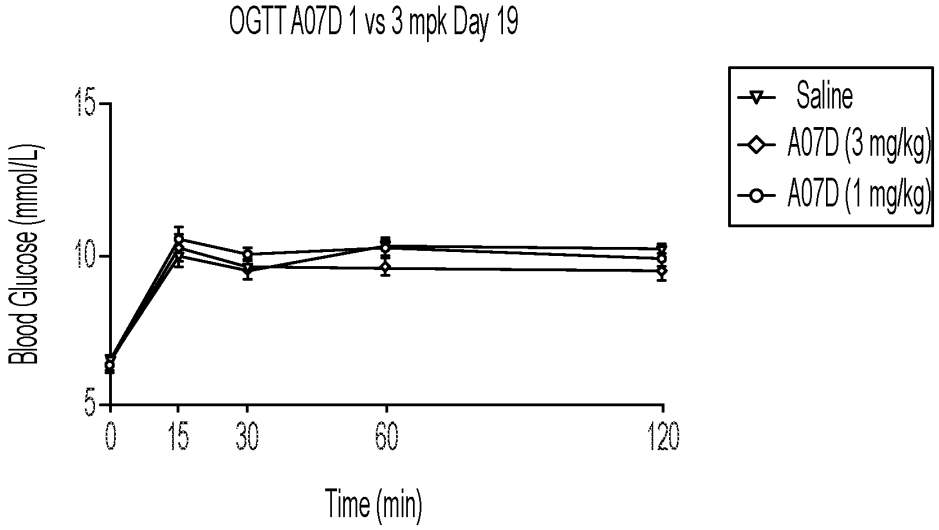

FIG. 19C

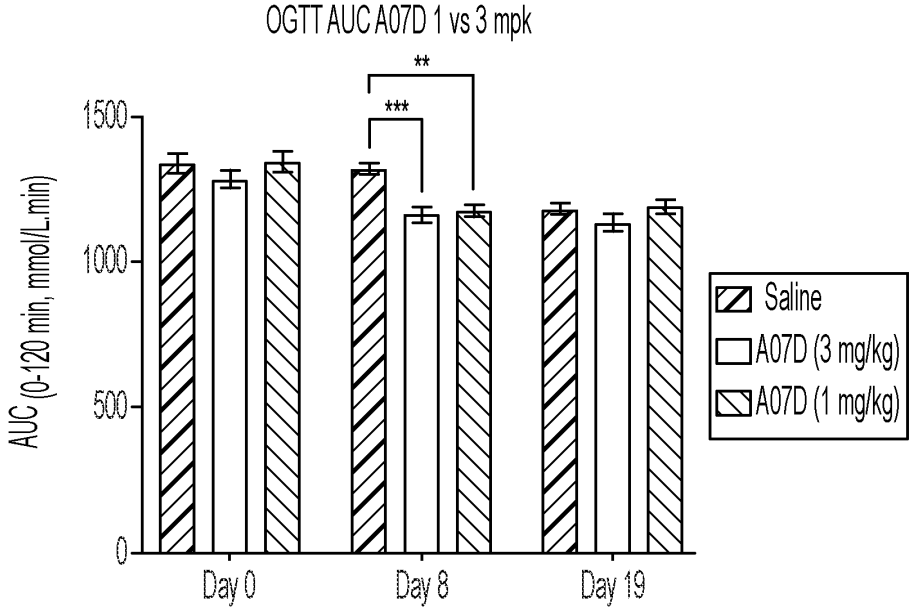

FIG. 19D

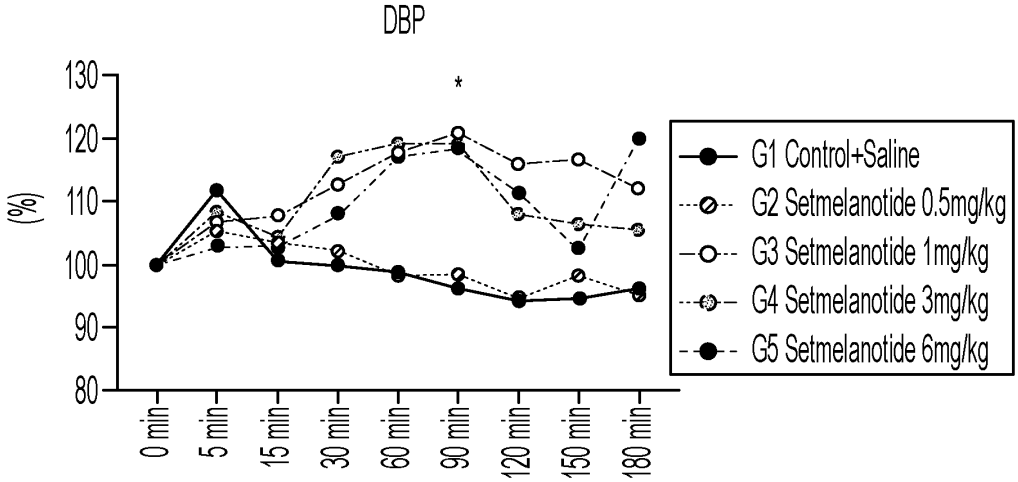

FIG. 20A

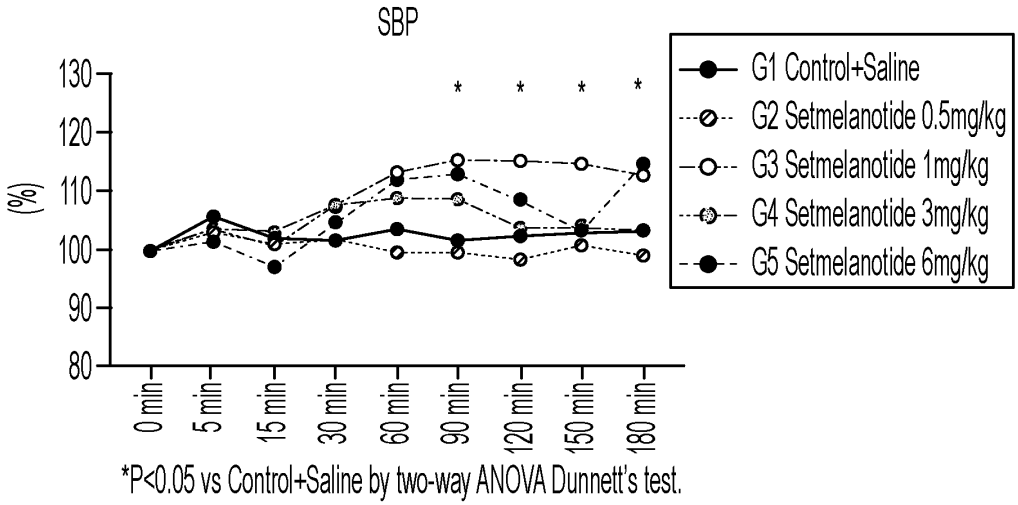

FIG. 20B

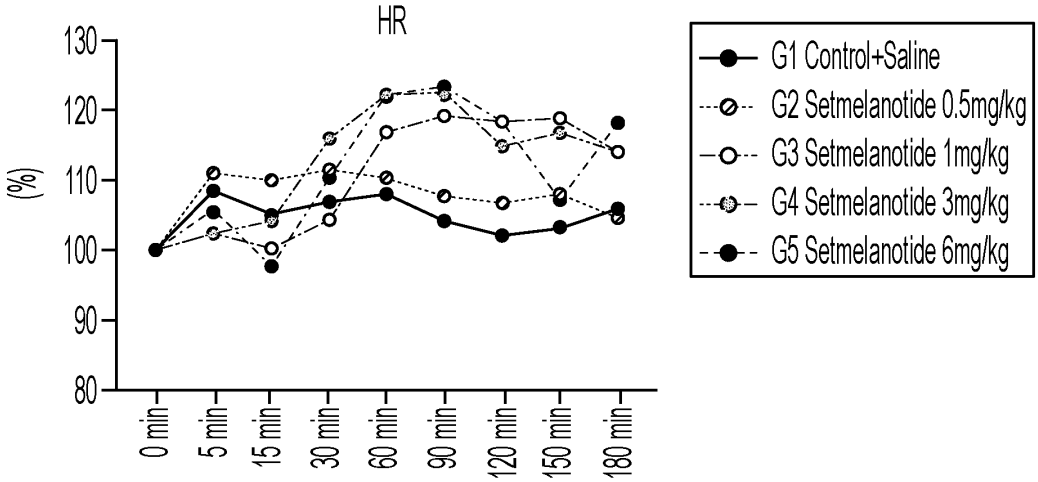

FIG. 20C

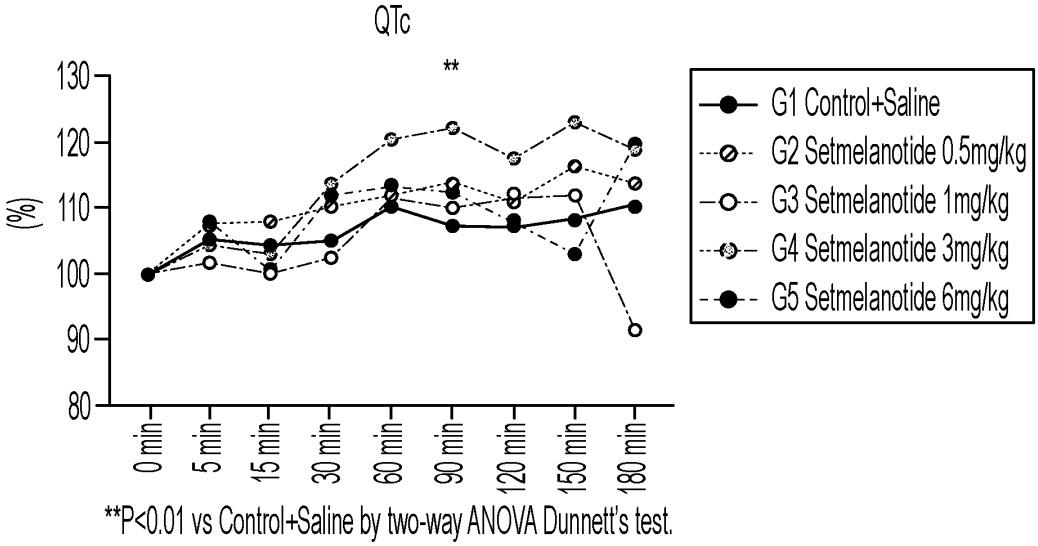

FIG. 20D

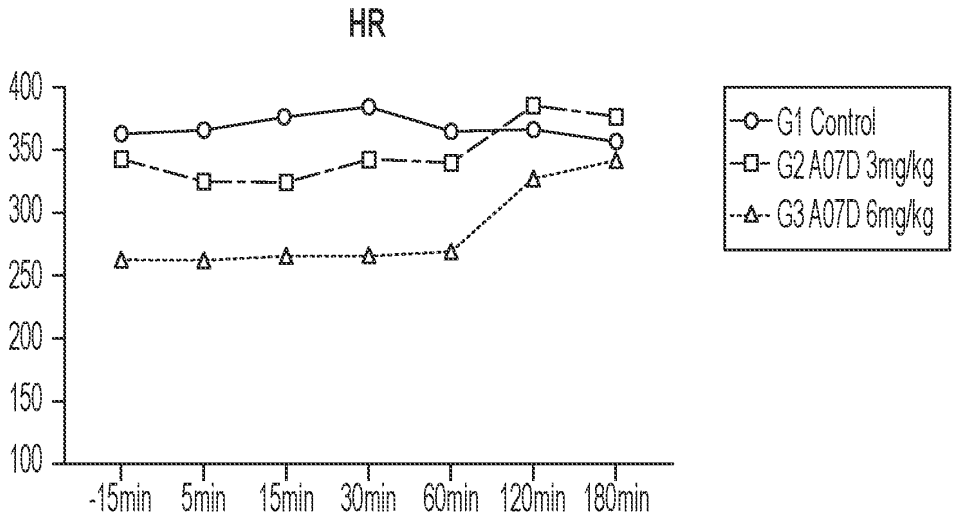

FIG. 20E

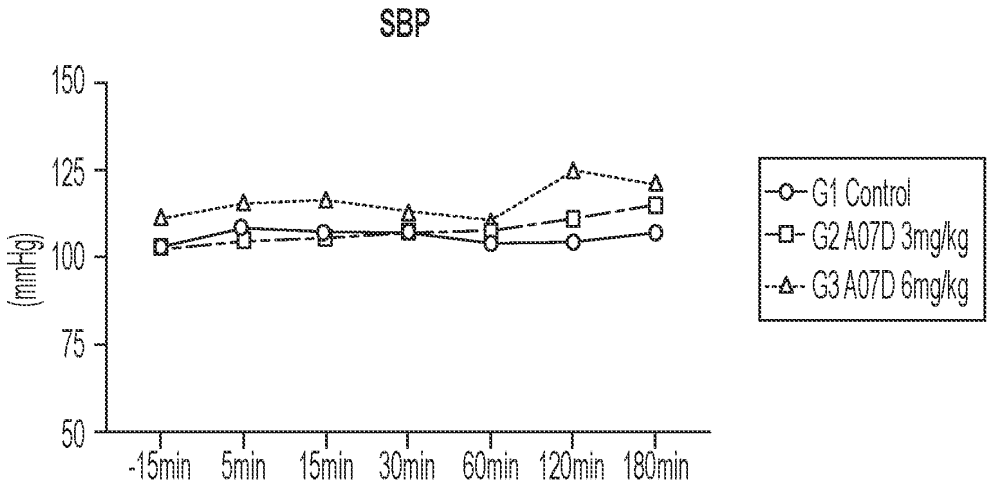

FIG. 20F

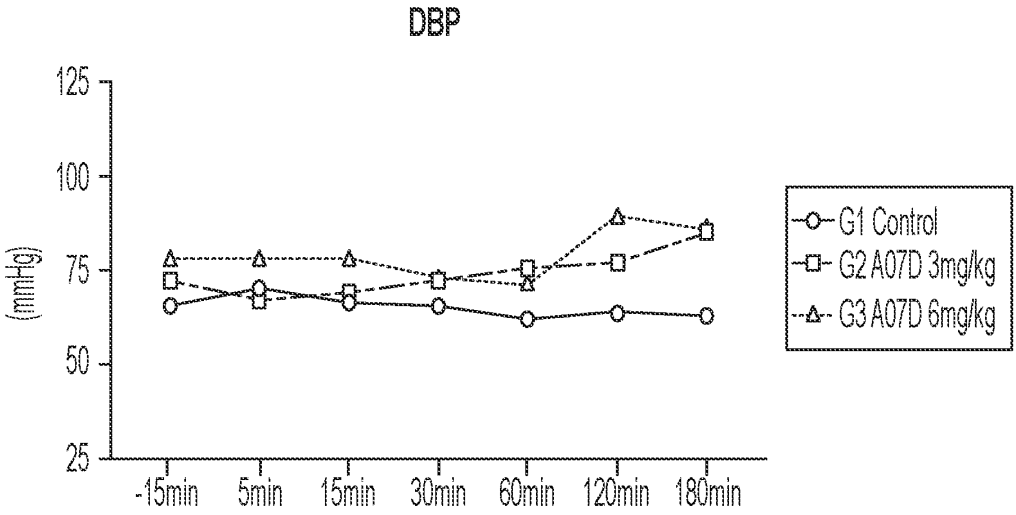
DBP
125
100
75
50
25
(mmHg)
-15min
5min
15min
30min
60min
120min
180min
G1 Control
G2 A07D 3mg/kg
G3 A07D 6mg/kg

FIG. 20G

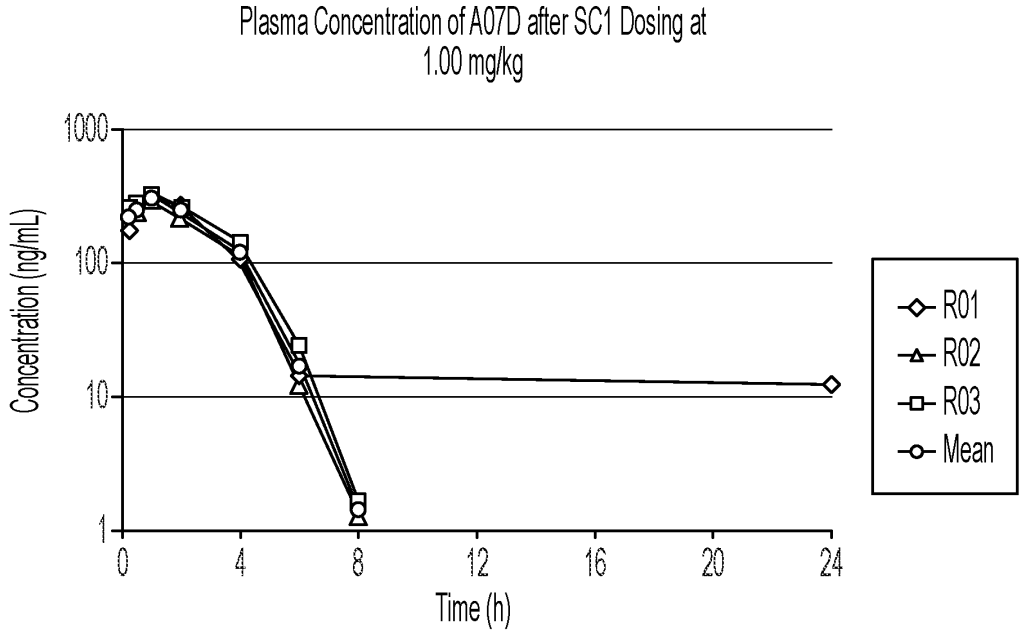

FIG. 21A

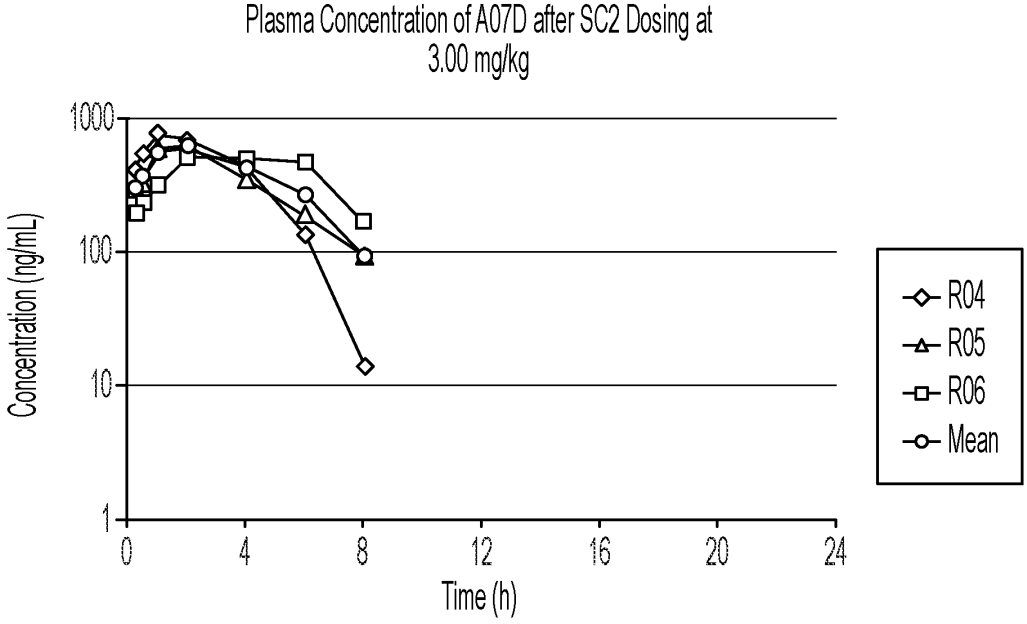

FIG. 21B

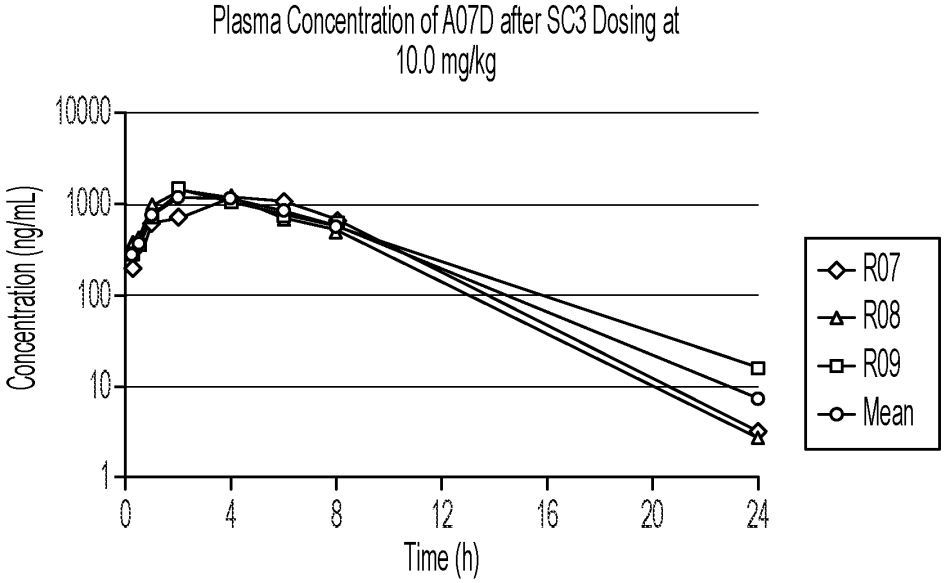

FIG. 21C

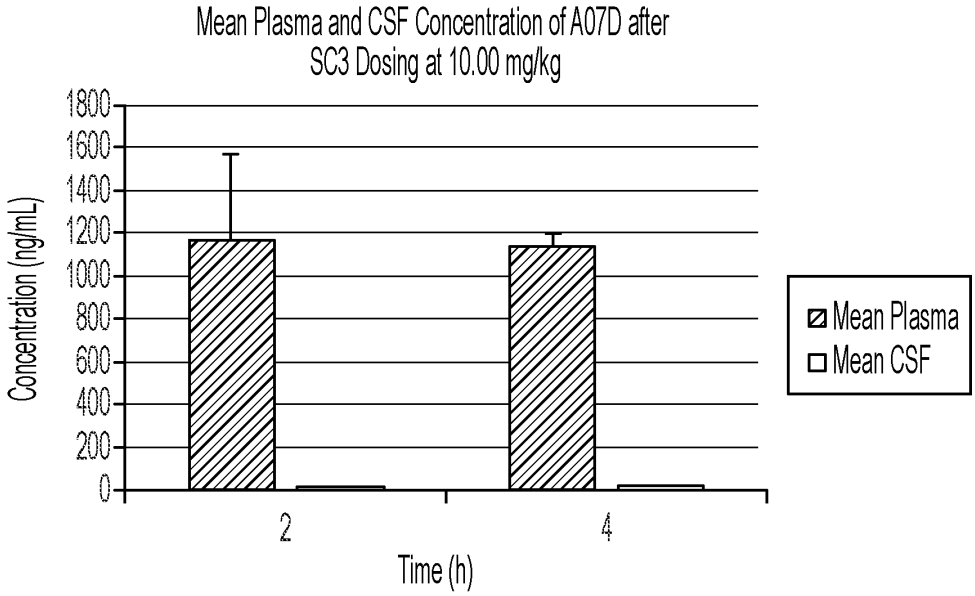

FIG. 21D

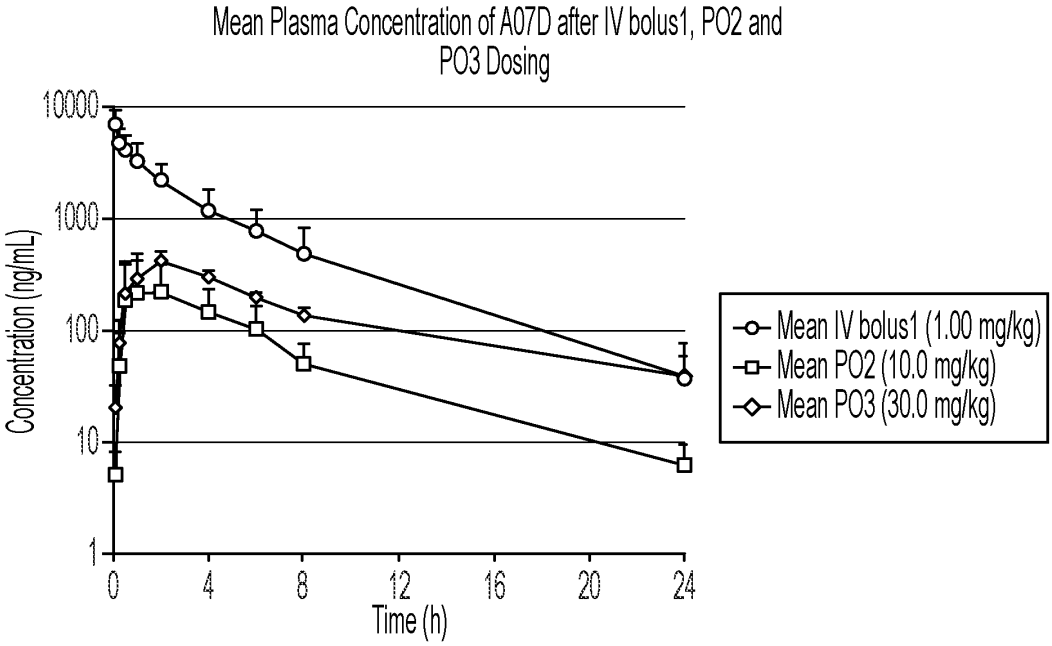
Mean Plasma Concentration of A07D after IV bolus1, PO2 and PO3 Dosing
Concentration (ng/mL)
10000
1000
100
10
1
0
4
8
12
16
20
24
Time (h)
Mean IV bolus1 (1.00 mg/kg)
Mean PO2 (10.0 mg/kg)
Mean PO3 (30.0 mg/kg)

FIG. 22



FIG. 23A

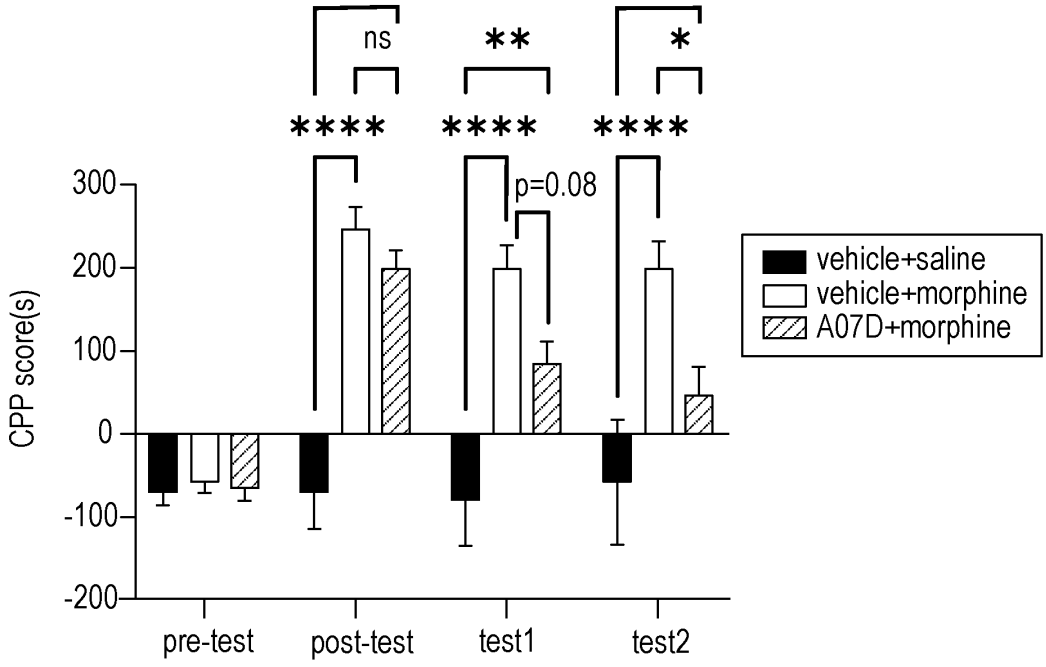

FIG. 23B