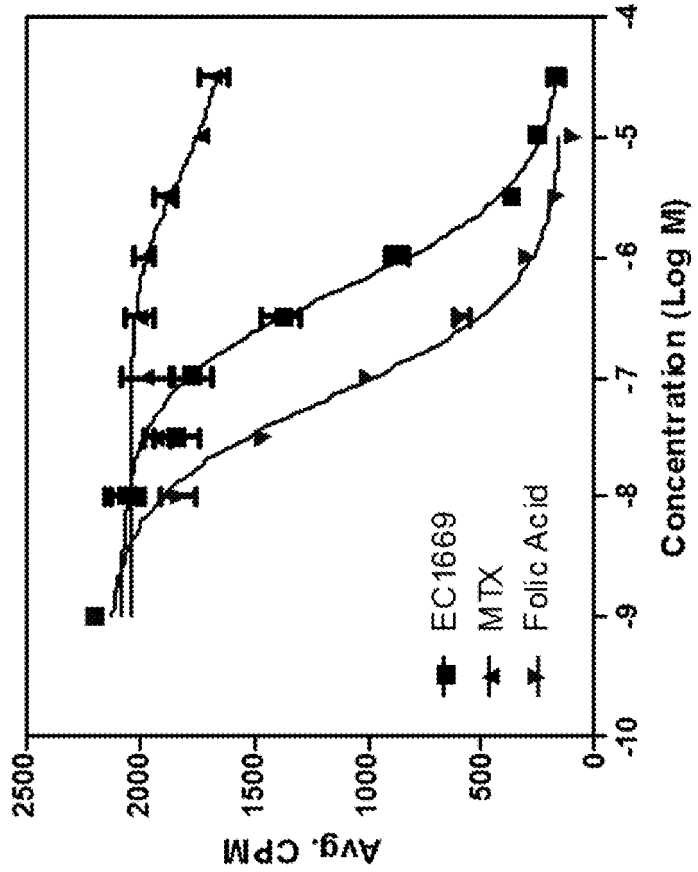
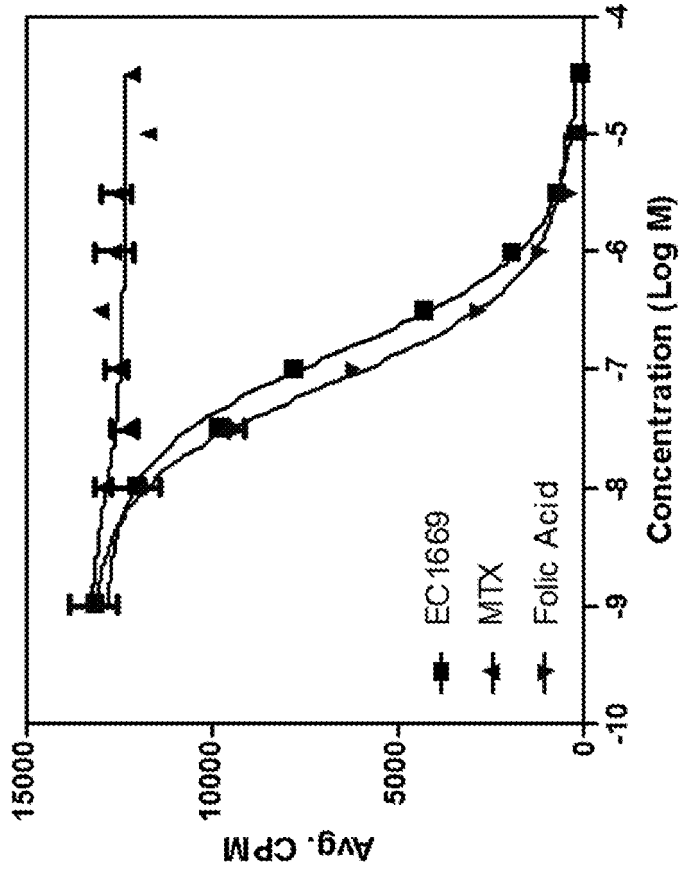

Avg. CPM
2500
2000
1500
1000
500
0
-4
-5
-6
-7
-8
-9
-10
Concentration (Log M)
EC1669
MTX
Folic Acid

B


Avg. CPM
15000
10000
5000
0
-4
-5
-6
-7
-8
-9
-10
Concentration (Log M)
EC1669
MTX
Folic Acid

A

FIG. 1

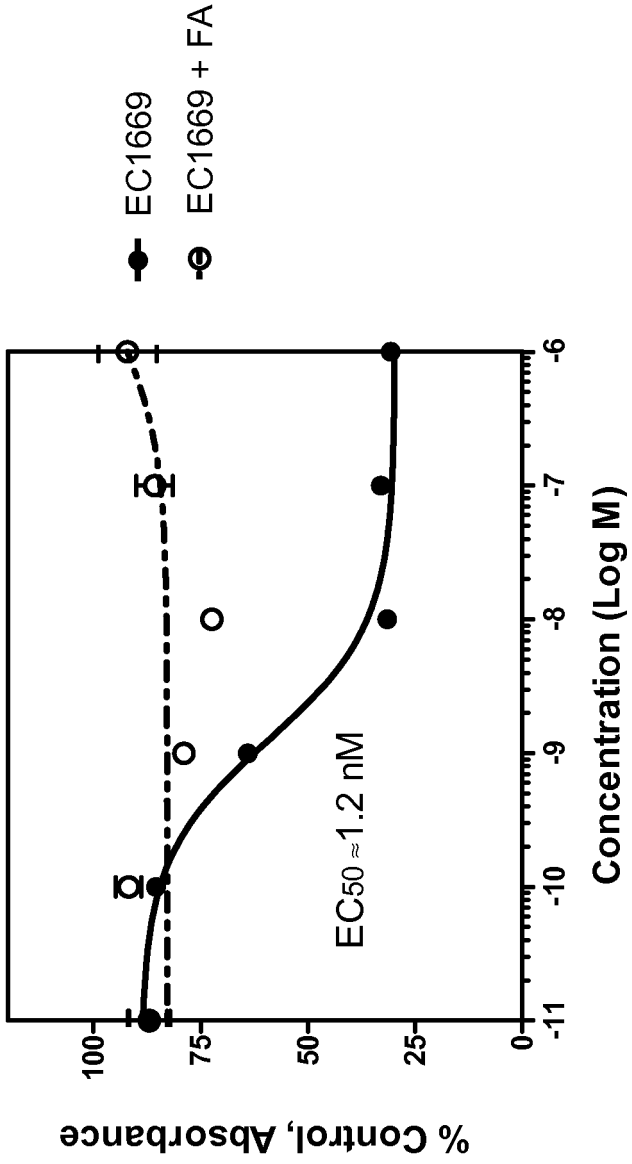
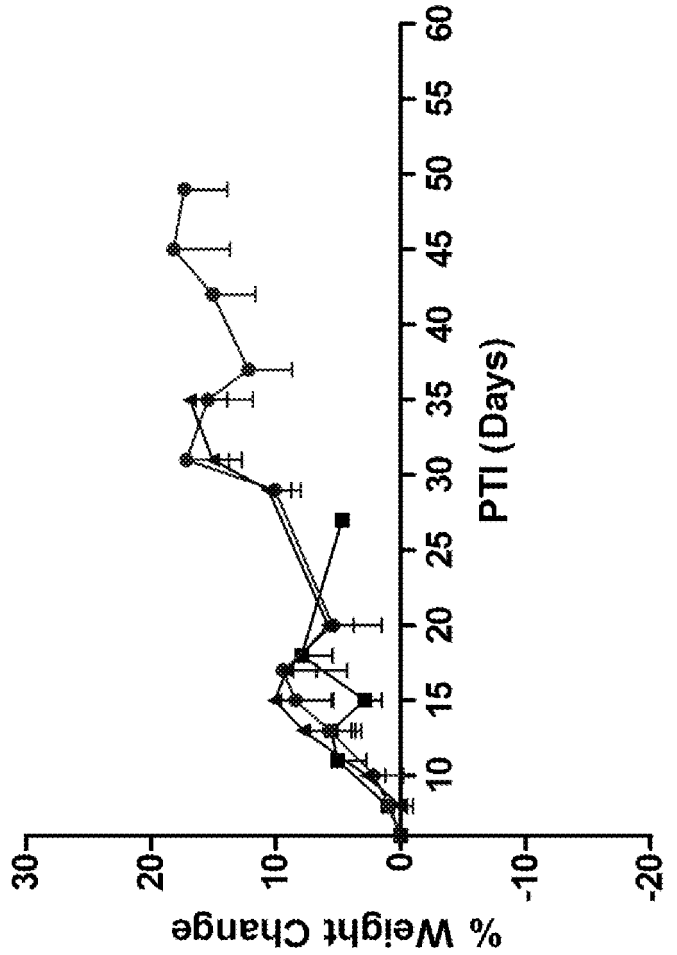
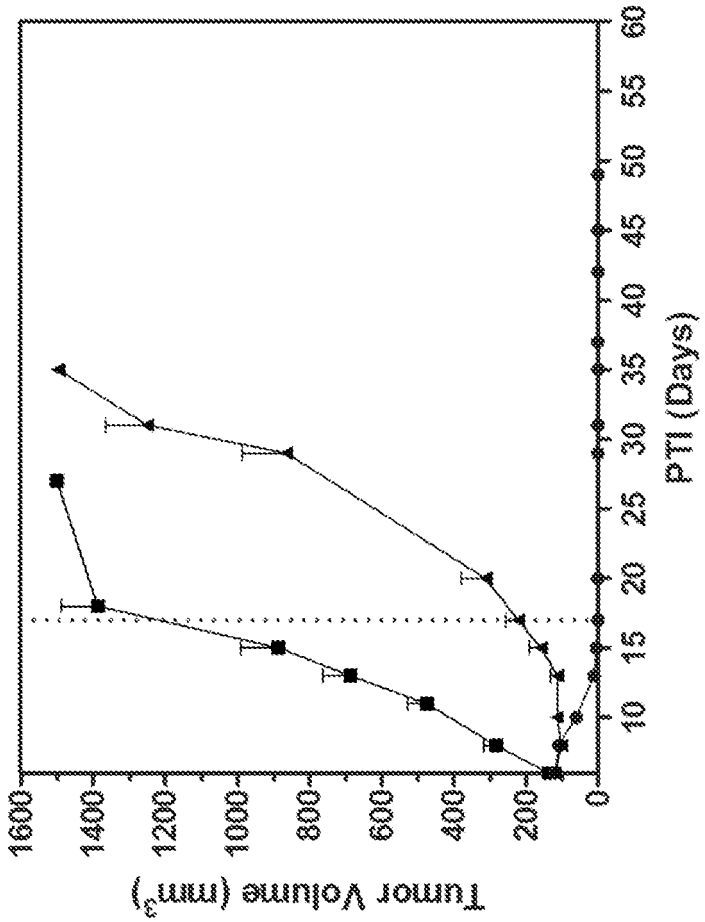

EC1669
EC1669 + FA
EC50 ≈1.2 nM
% Control, Absorbance
Concentration (Log M)
100
75
50
25
0
-6
-7
-8
-9
-10
-11

FIG. 2

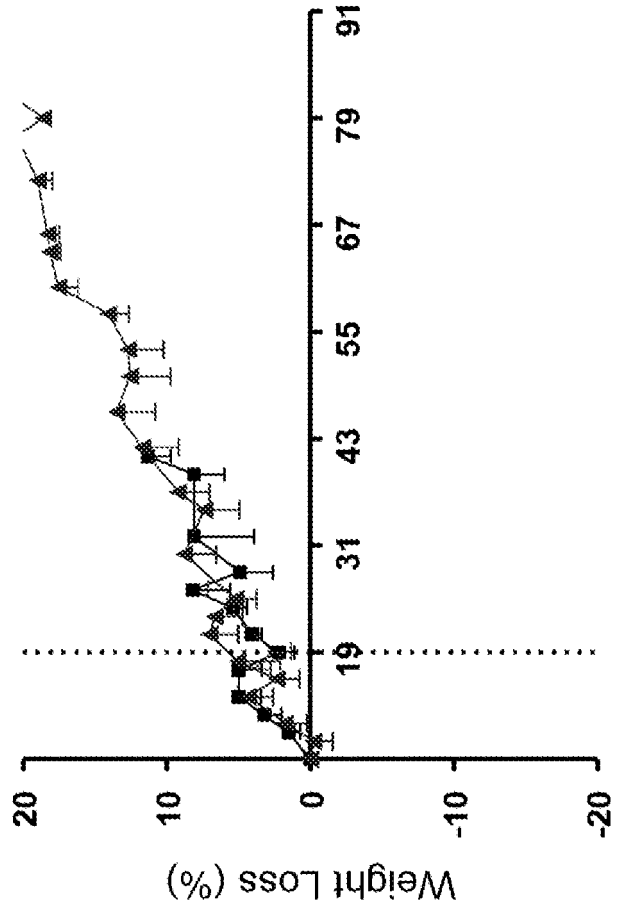

% Weight Change
30
20
10
0
-10
-20
10
15
20
25
30
35
40
45
50
55
60
PTI (Days)

B

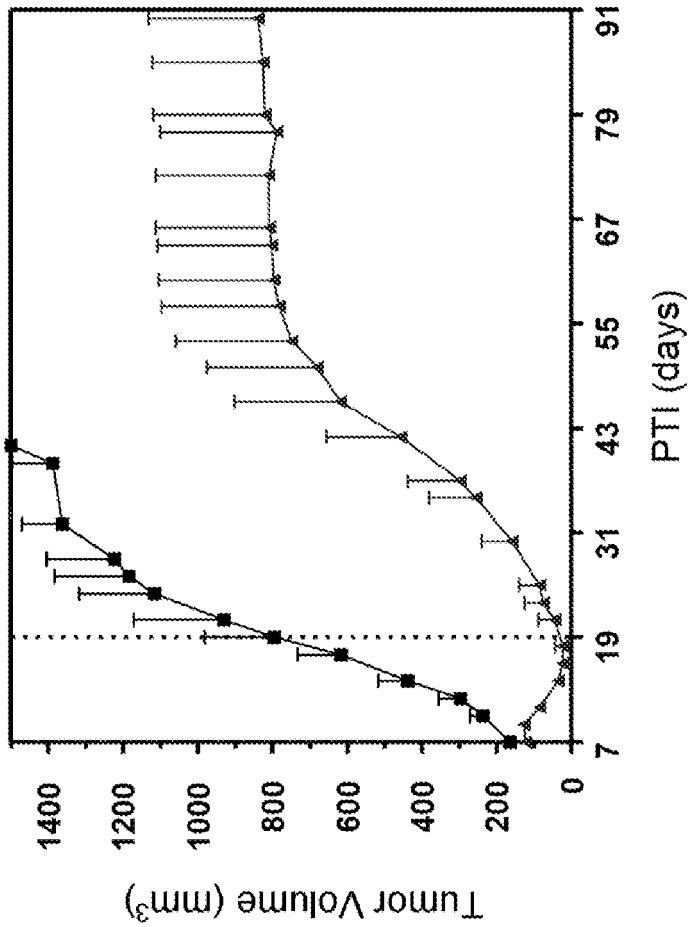

Tumor Volume (mm³)
1600
1400
1200
1000
800
600
400
200
0
10
15
20
25
30
35
40
45
50
55
60
PTI (Days)

A

FIG. 3


Weight Loss (%)
20
10
0
-10
-20
19
31
43
55
67
79
91
X

B


Tumor Volume (mm3)
1400
1200
1000
800
600
400
200
0
7
19
31
43
55
67
79
91
PTI (days)

A

FIG. 4

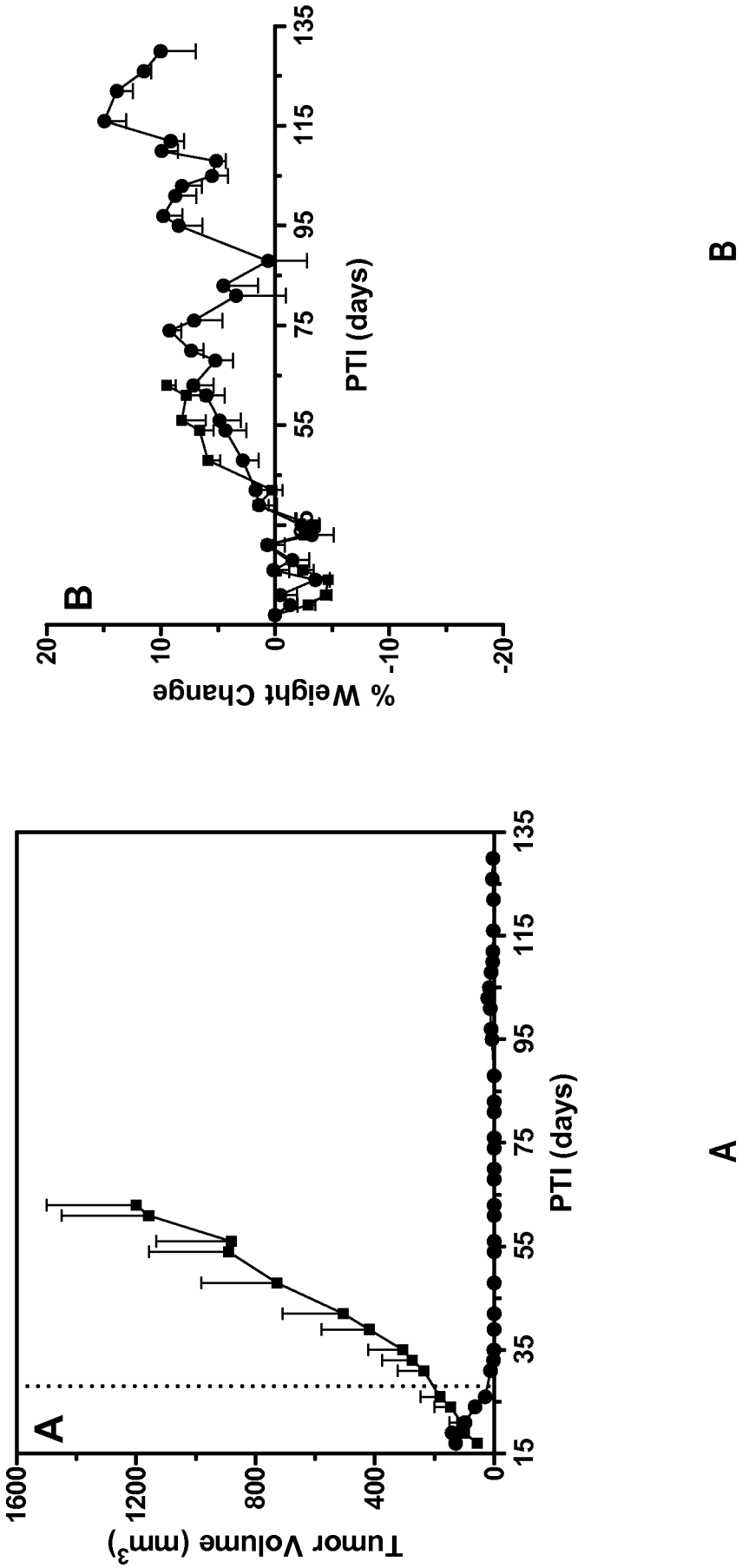

A
Tumor Volume (mm3)
1600
1200
800
400
0
15
35
55
75
95
115
135
PTI (days)
B
% Weight Change
20
10
0
-10
-20
15
35
55
75
95
115
135
PTI (days)

FIG. 5

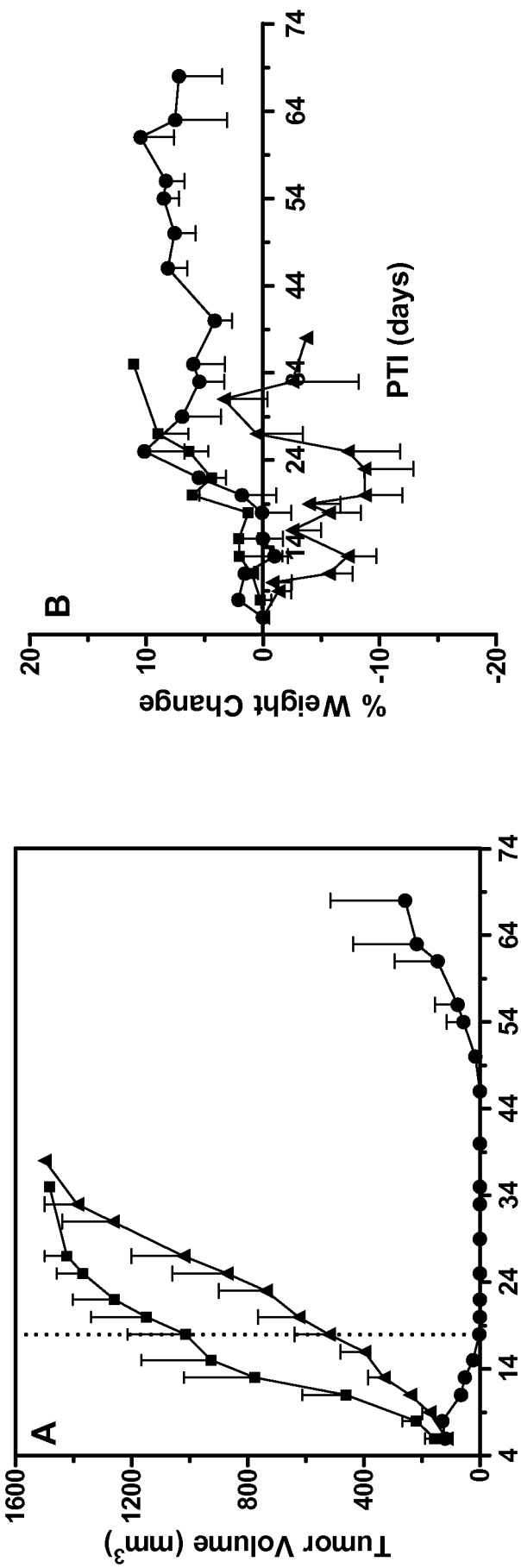

A
Tumor Volume (mm3)
1600
1200
800
400
0
4
14
24
34
44
54
64
74
PTI (days)
B
% Weight Change
20
10
0
-10
-20
4
14
24
34
44
54
64
74
PTI (days)

FIG. 6

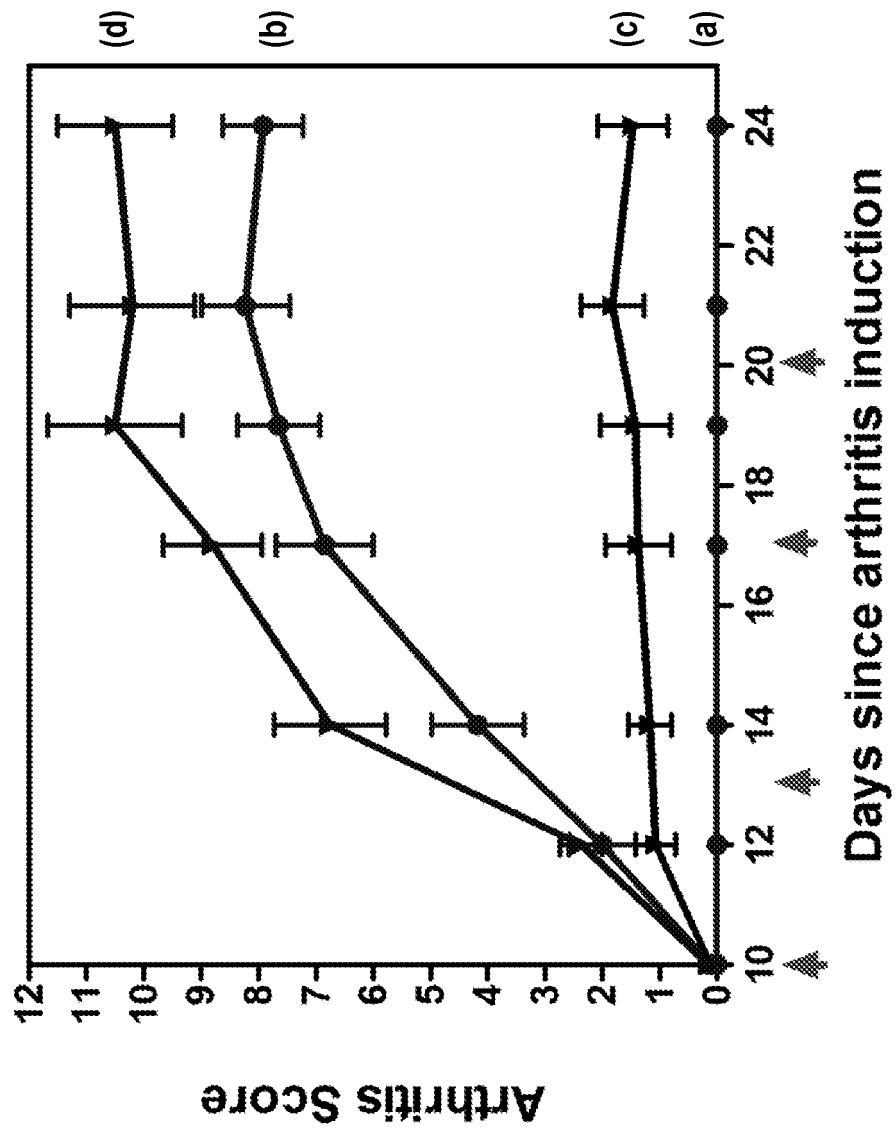
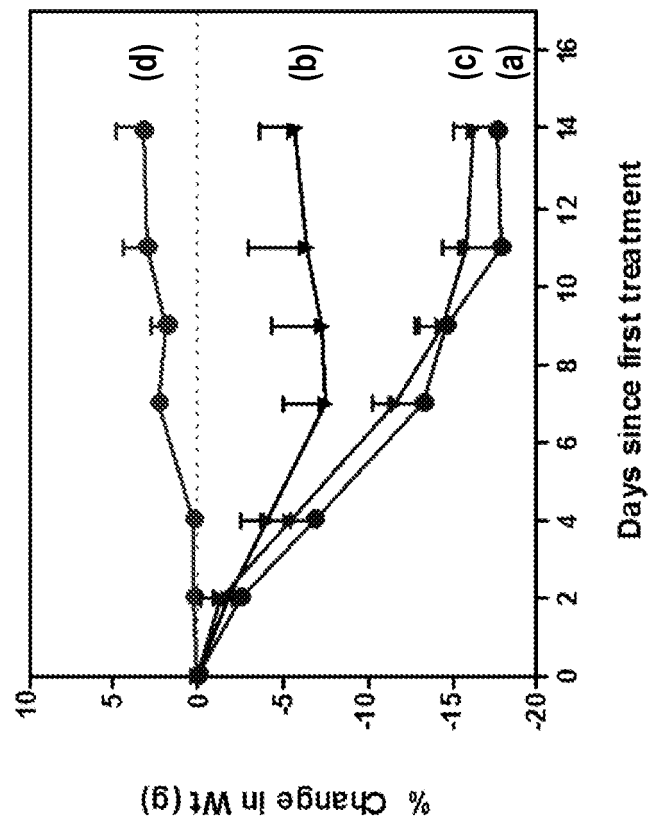
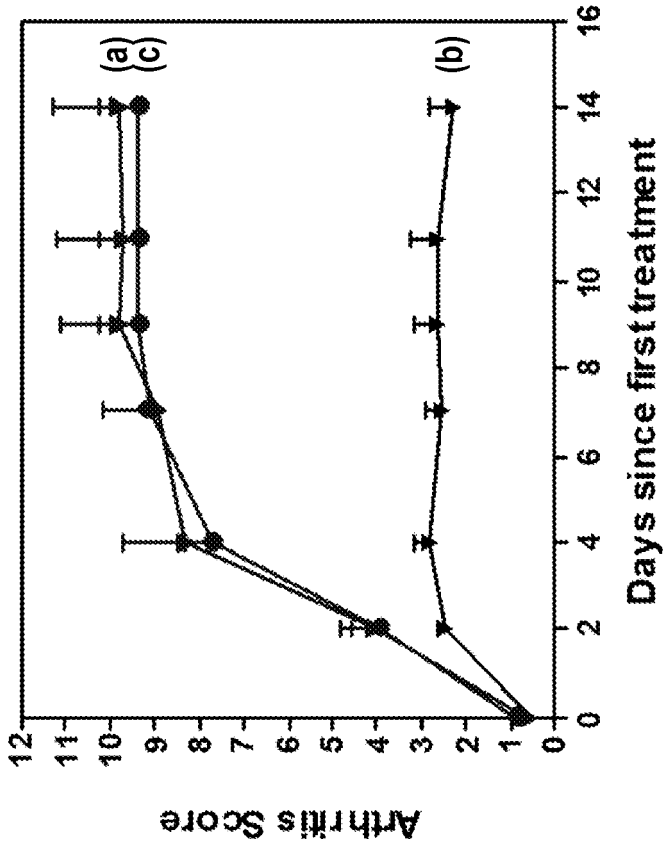

Arthritis Score
0
1
2
3
4
5
6
7
8
9
10
11
12
10
12
14
16
18
20
22
24
Days since arthritis induction
(a)
(c)
(b)
(d)

FIG. 7

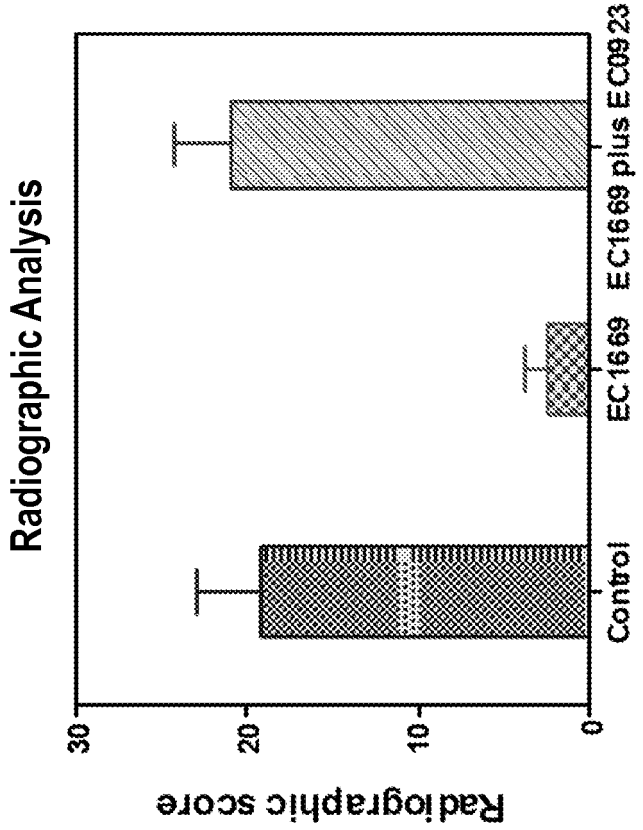

% Change in Wt (g)
10
5
0
-5
-10
-15
-20
0
2
4
6
8
10
12
14
16
Days since first treatment
(d)
(b)
(c)
(a)

B

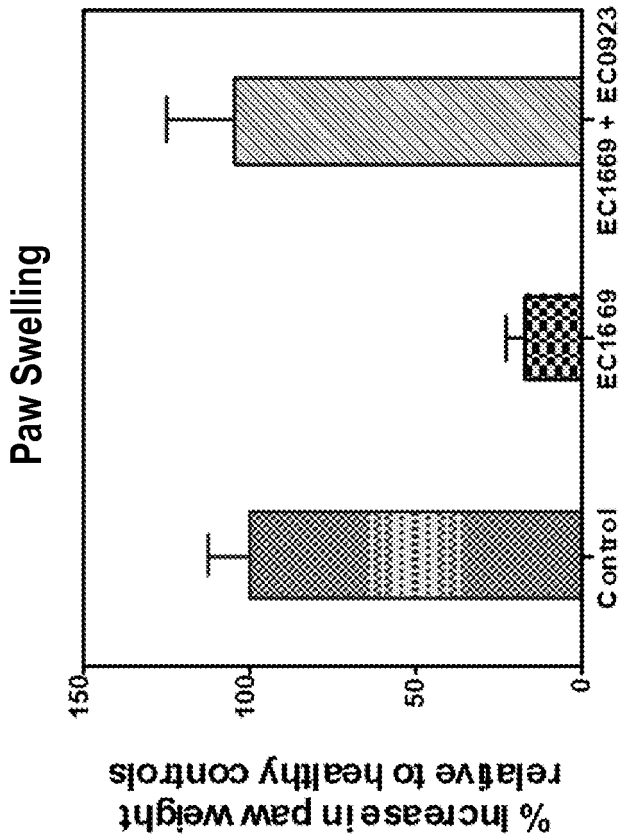

Arthritis Score
12
11
10
9
8
7
6
5
4
3
2
1
0
0
2
4
6
8
10
12
14
16
Days since first treatment
(a)
(c)
(b)

A

FIG. 8

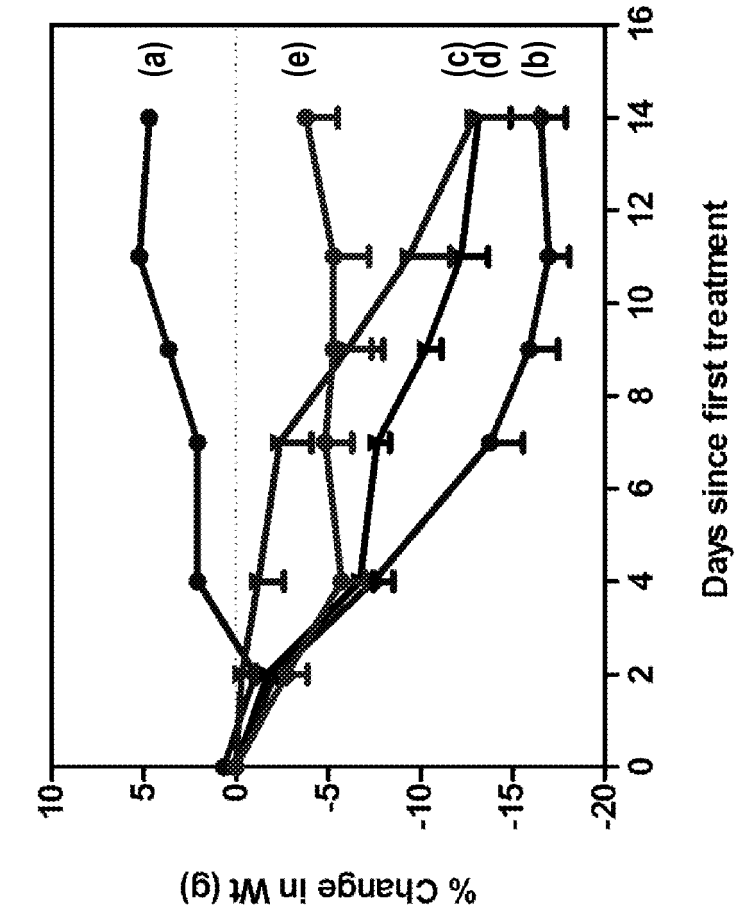

Radiographic Analysis
Radiographic score
30
20
10
0
Control
EC1669
EC1669 plus EC0923

B

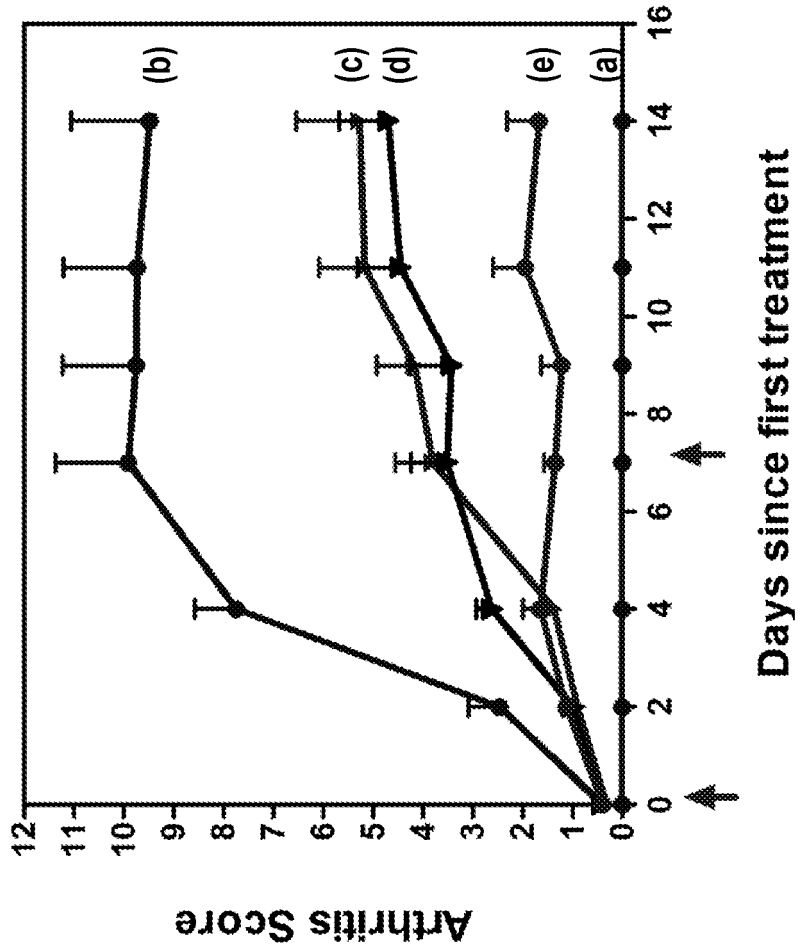

Paw Swelling
% Increase in paw weight relative to healthy controls
150
100
50
0
Control
EC1669
EC1669 + EC0923

A

FIG. 9


% Change in Wt (g)
10
5
0
-5
-10
-15
-20
0
2
4
6
8
10
12
14
16
Days since first treatment
(a)
(e)
(c)
(d)
(b)

B


Arthritis Score
12
11
10
9
8
7
6
5
4
3
2
1
0
0
2
4
6
8
10
12
14
16
Days since first treatment
(b)
(c)
(d)
(e)
(a)

A

FIG. 10

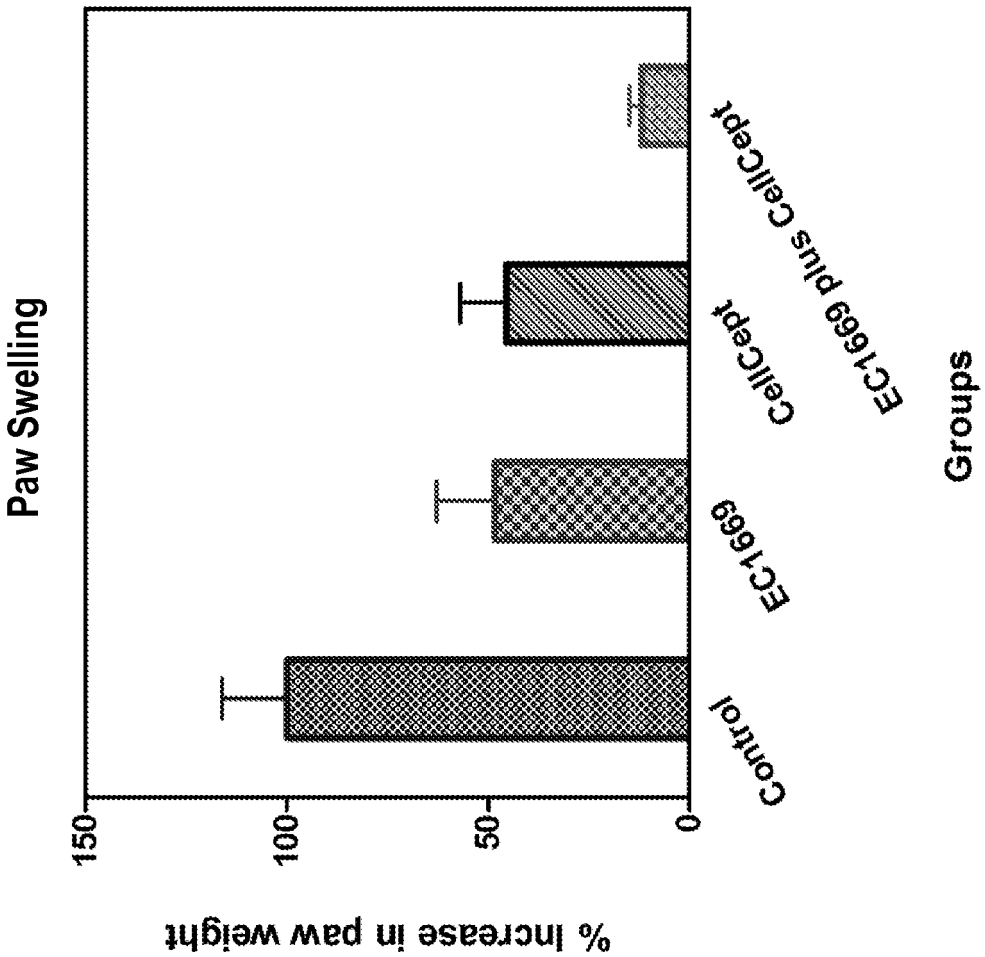
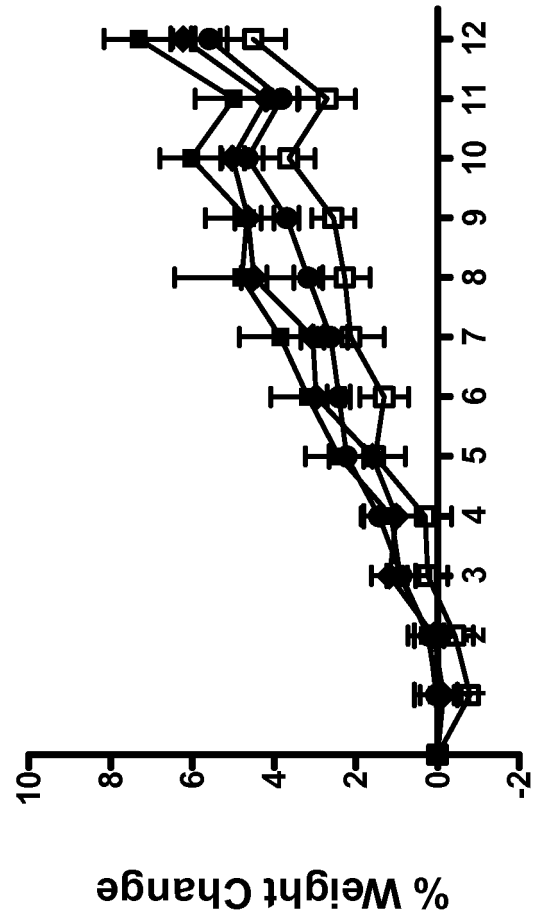

Paw Swelling
% Increase in paw weight
150
100
50
0
Control
EC1669
CelliCept
EC1669 plus CelliCept
Groups

FIG. 11


% Weight Change
10
8
6
4
2
0
-2
0
1
2
3
4
5
6
7
8
9
10
11
12
Days
B

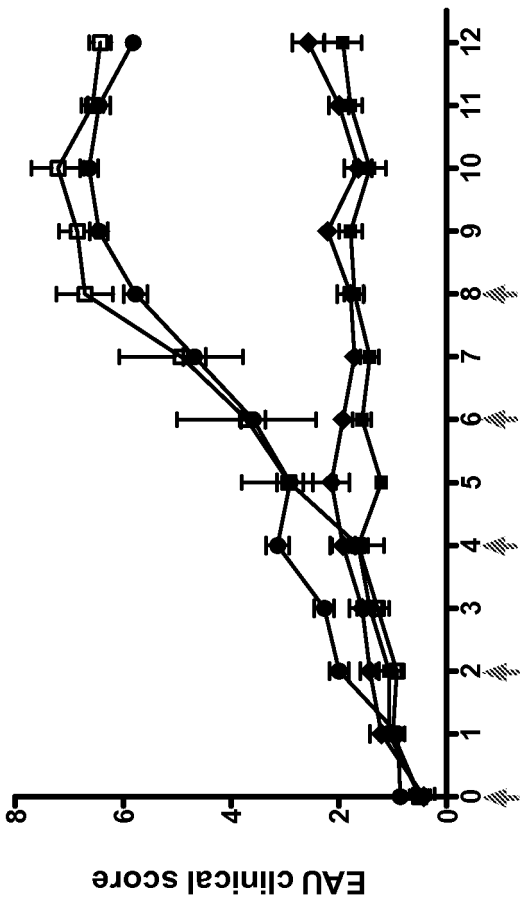
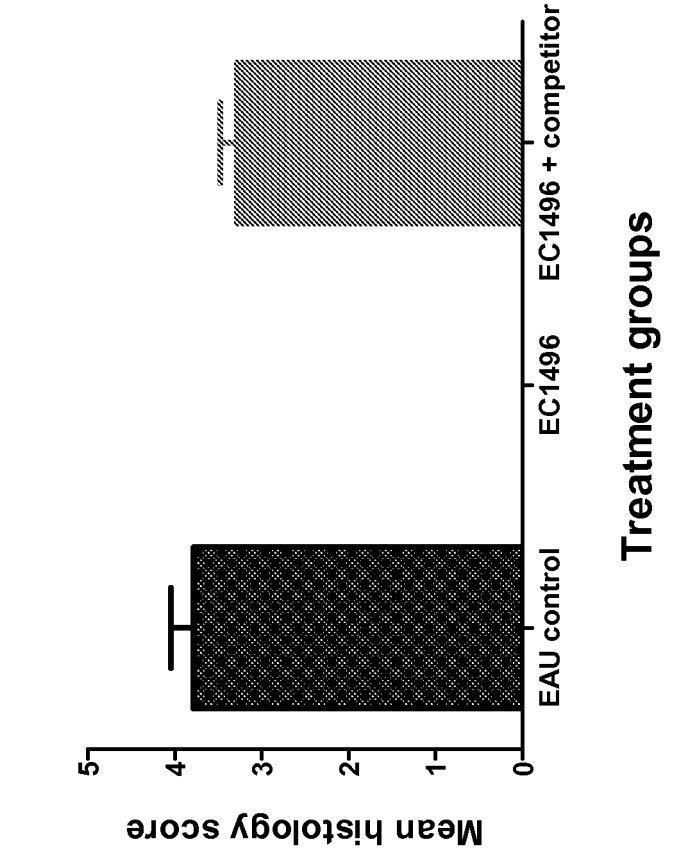
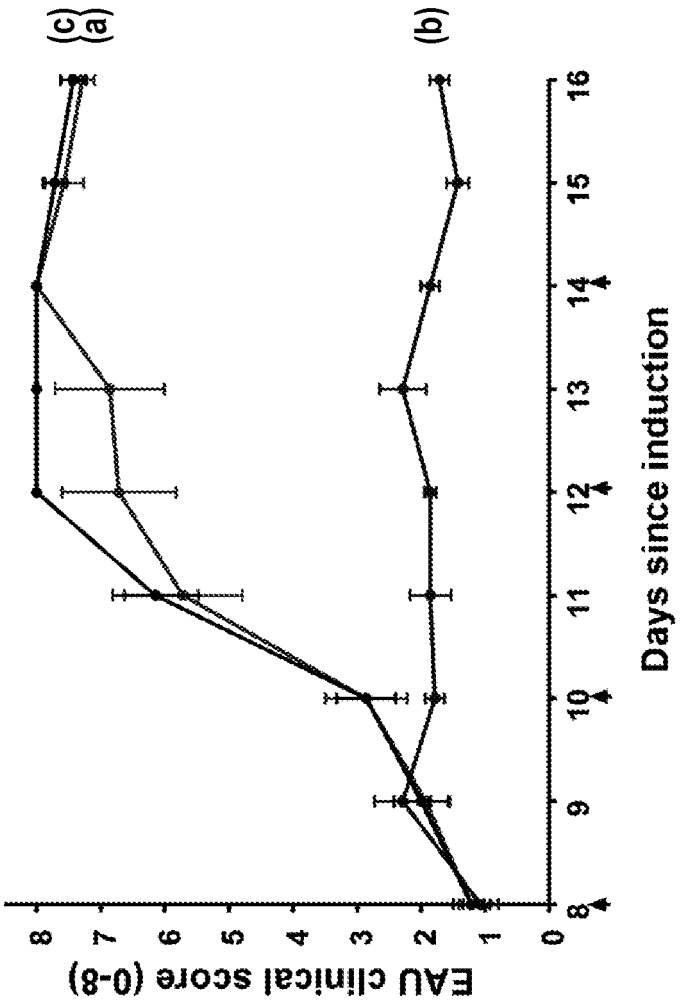

EAU clinical score
8
6
4
2
0
0
1
2
3
4
5
6
7
8
9
10
11
12
Days
A

FIG. 12

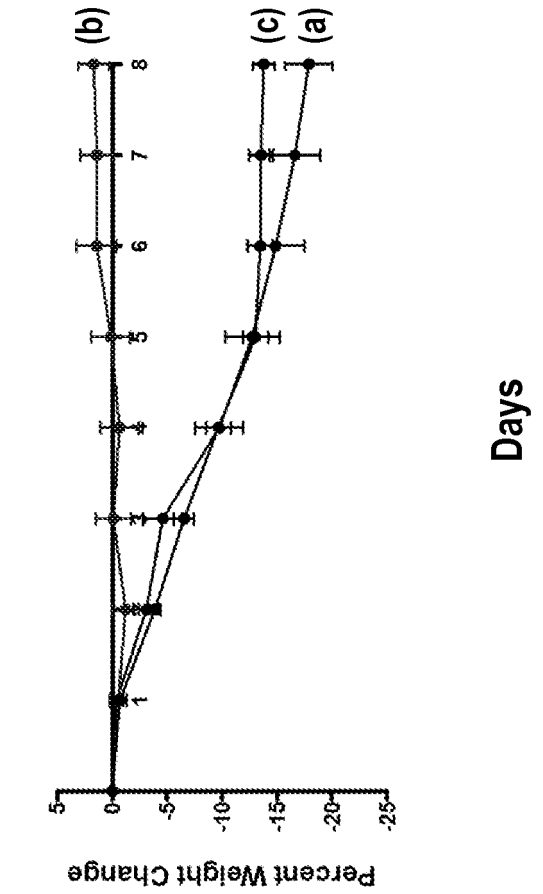

Mean histology score
0
1
2
3
4
5
EAU control
EC1496
EC1496 + competitor
Treatment groups

B


EAU clinical score (0-8)
0
1
2
3
4
5
6
7
8
(c)
(a)
(b)
8
9
10
11
12
13
14
15
16
Days since induction

A

FIG. 13


(b)
(c)
(a)
Percent Weight Change
Days
B

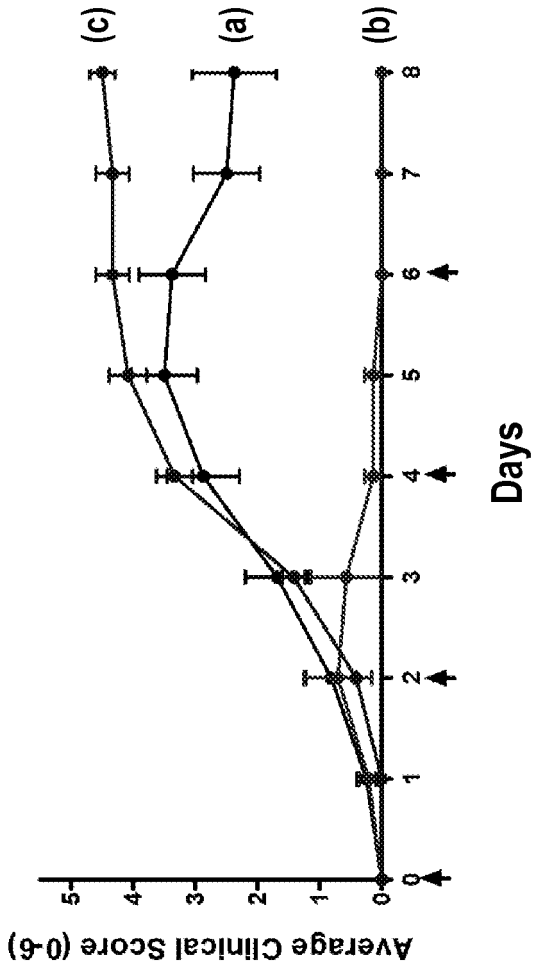

(c)
(a)
(b)
Average Clinical Score (0-6)
Days
A

FIG. 14

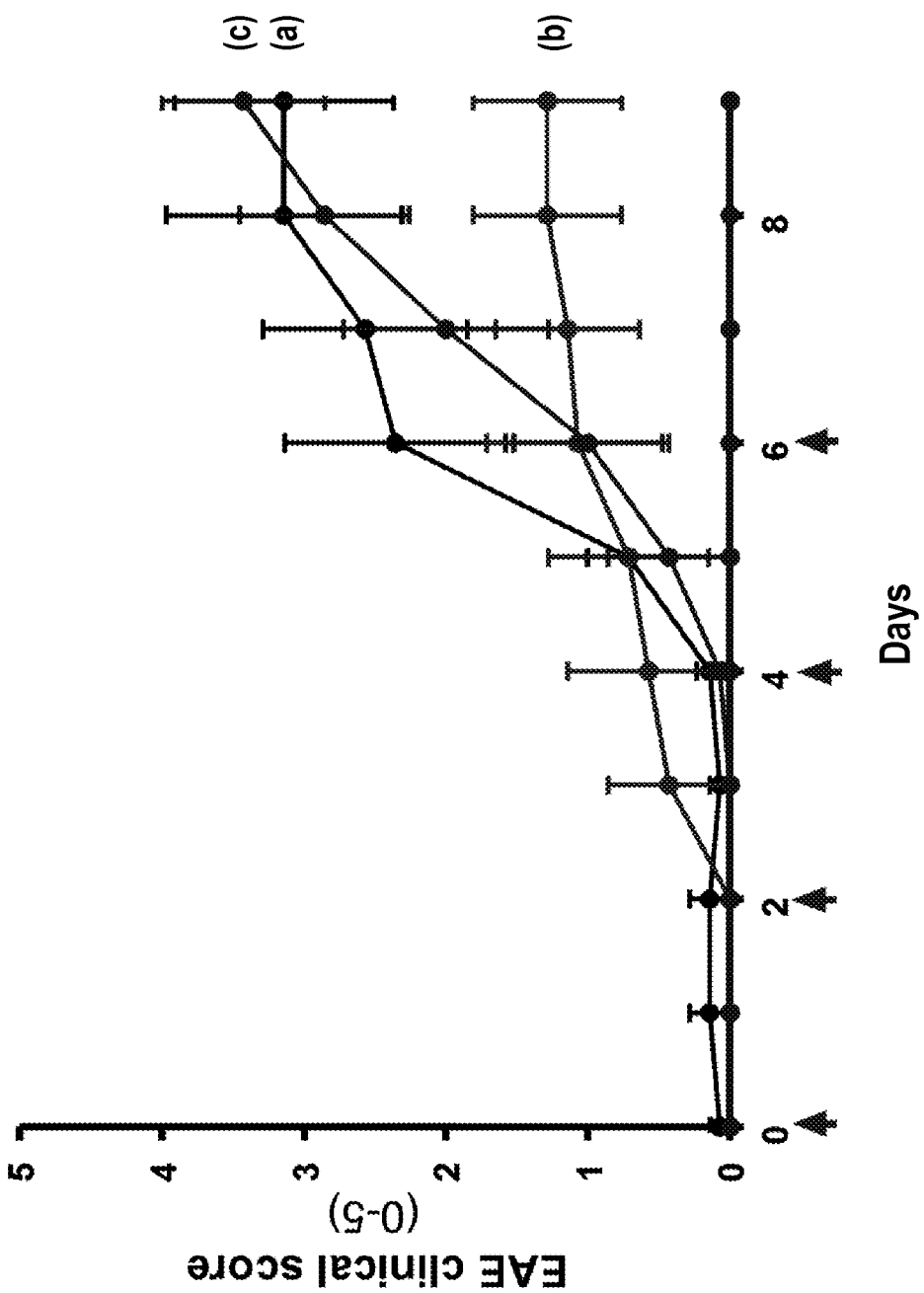
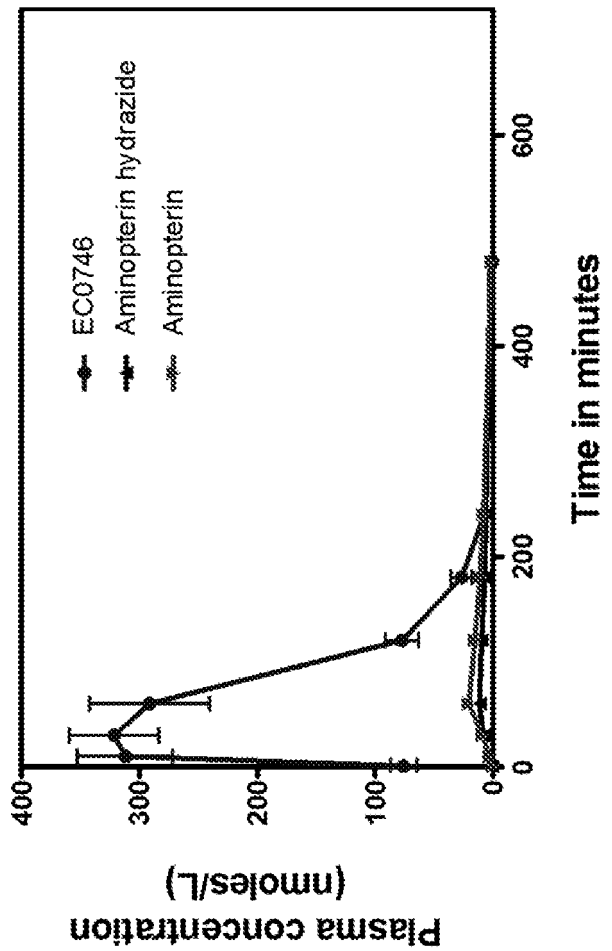
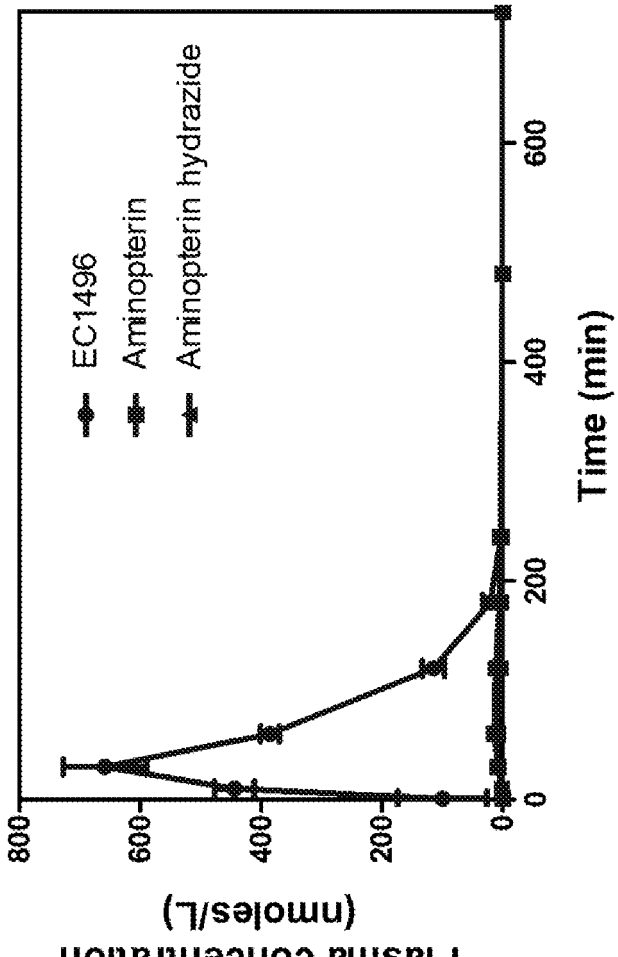


FIG. 15


EC0746
Aminopterin hydrazide
Aminopterin
Plasma concentration (nmoles/L)
0
100
200
300
400
0
200
400
600
Time in minutes

B


EC1496
Aminopterin
Aminopterin hydrazide
Plasma concentration (nmoles/L)
0
200
400
600
800
0
200
400
600
Time (min)

A

FIG. 16

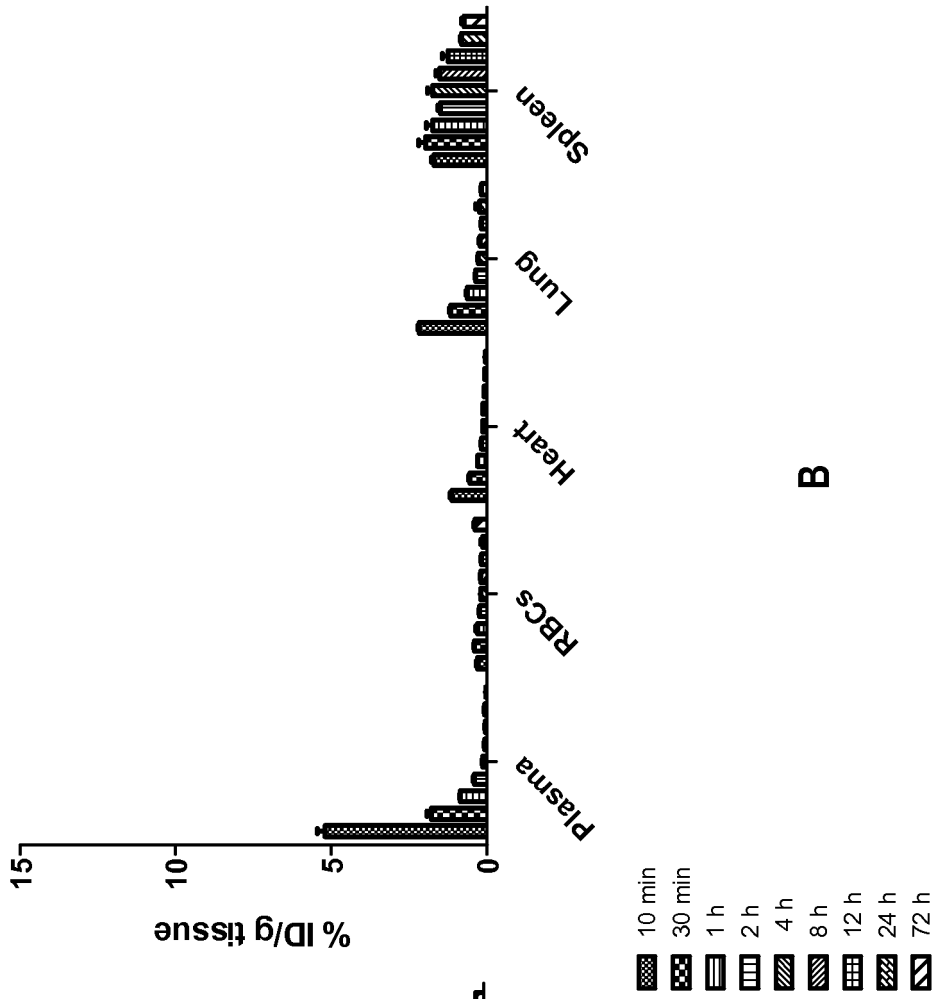
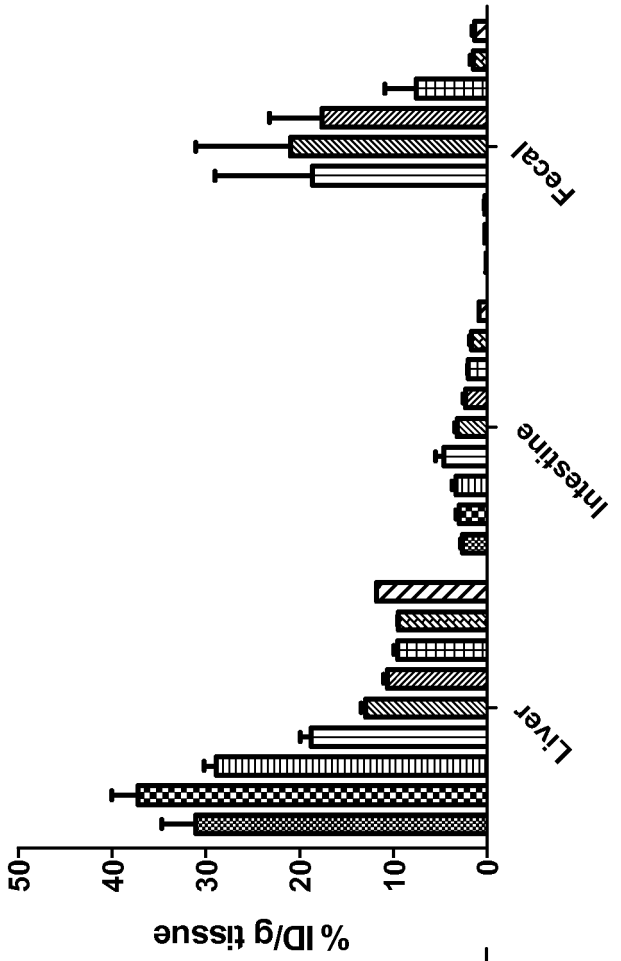
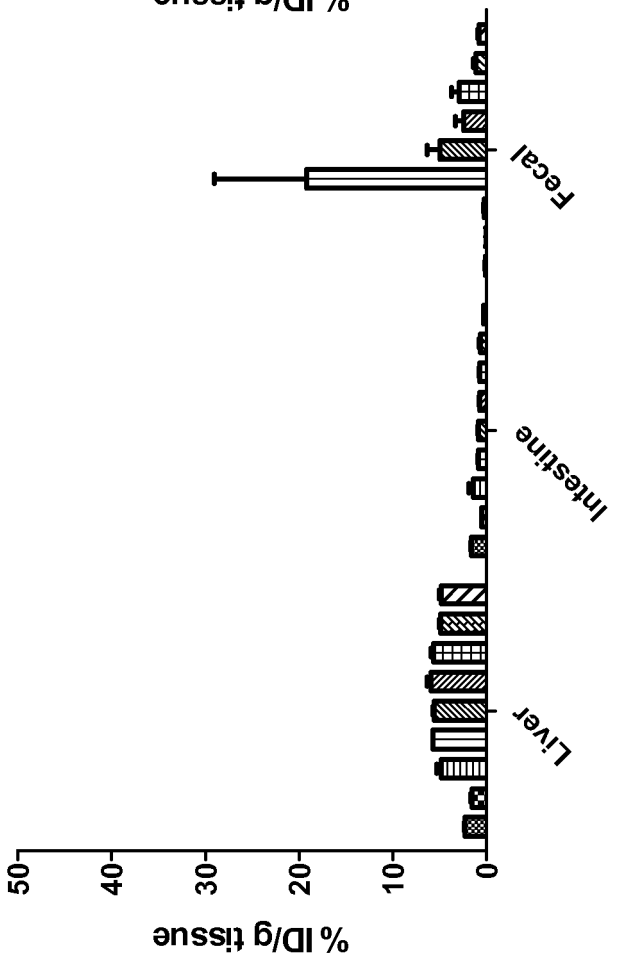

% ID/g tissue
15
10
5
0
Plasma
RBCs
Heart
Lung
Spleen
A
B
10 min
30 min
1 h
2 h
4 h
8 h
12 h
24 h
72 h

FIG. 17

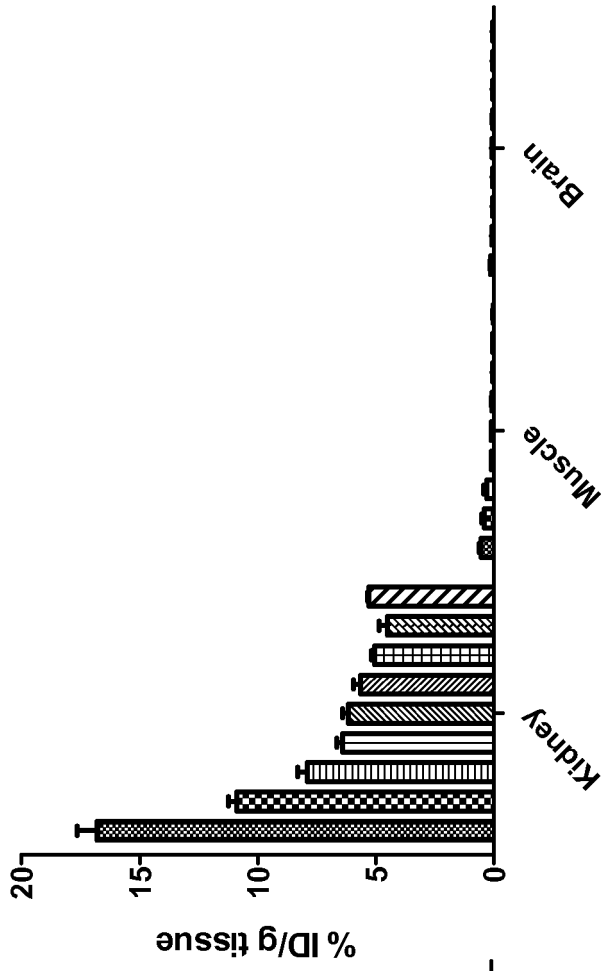


D

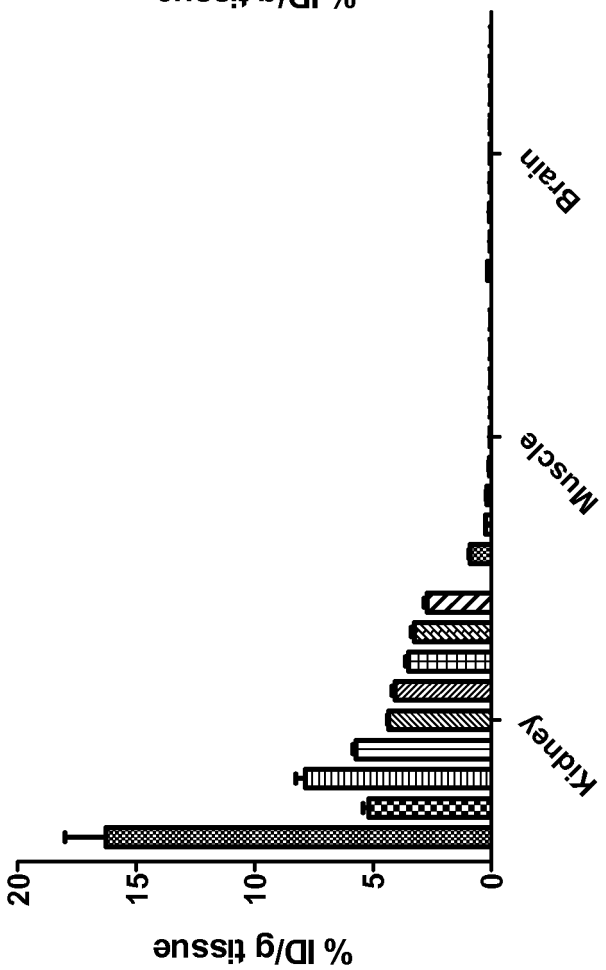


C

FIG. 17 (continued)



F



E

FIG. 17 (continued)

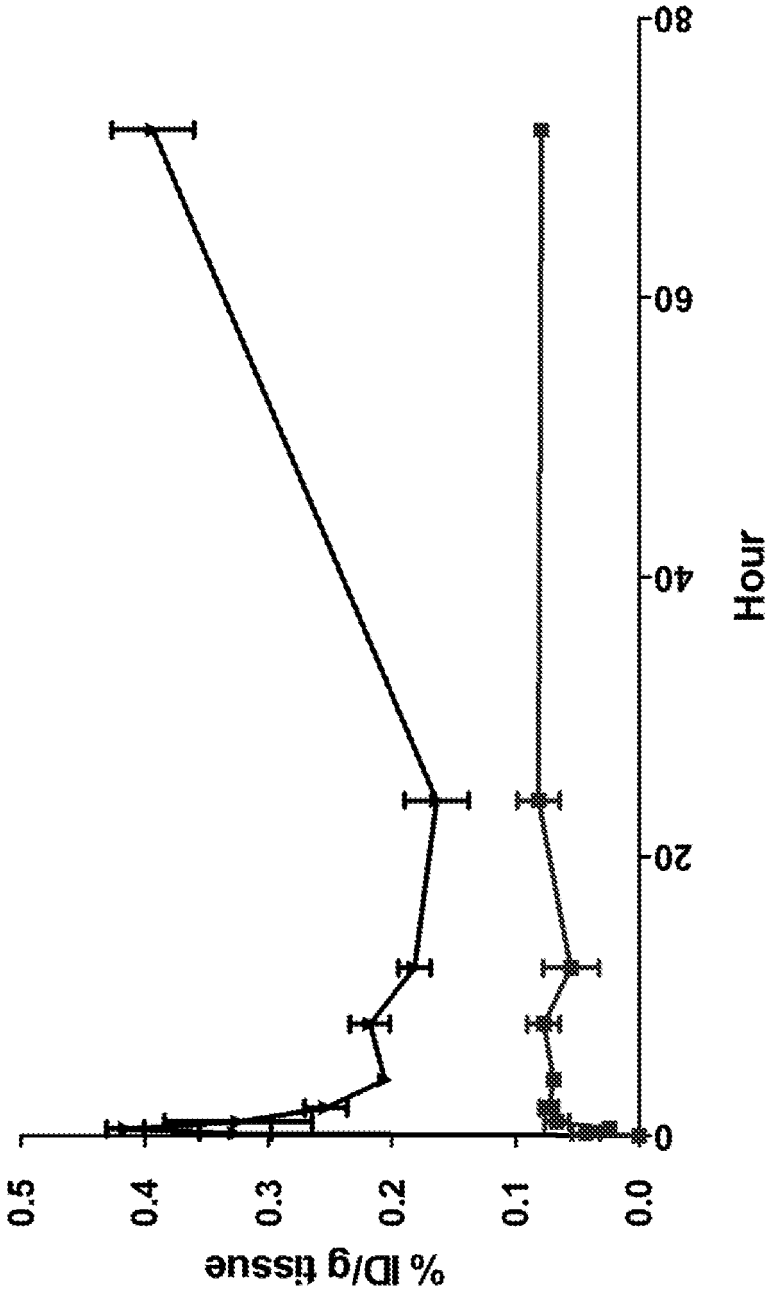


FIG. 18

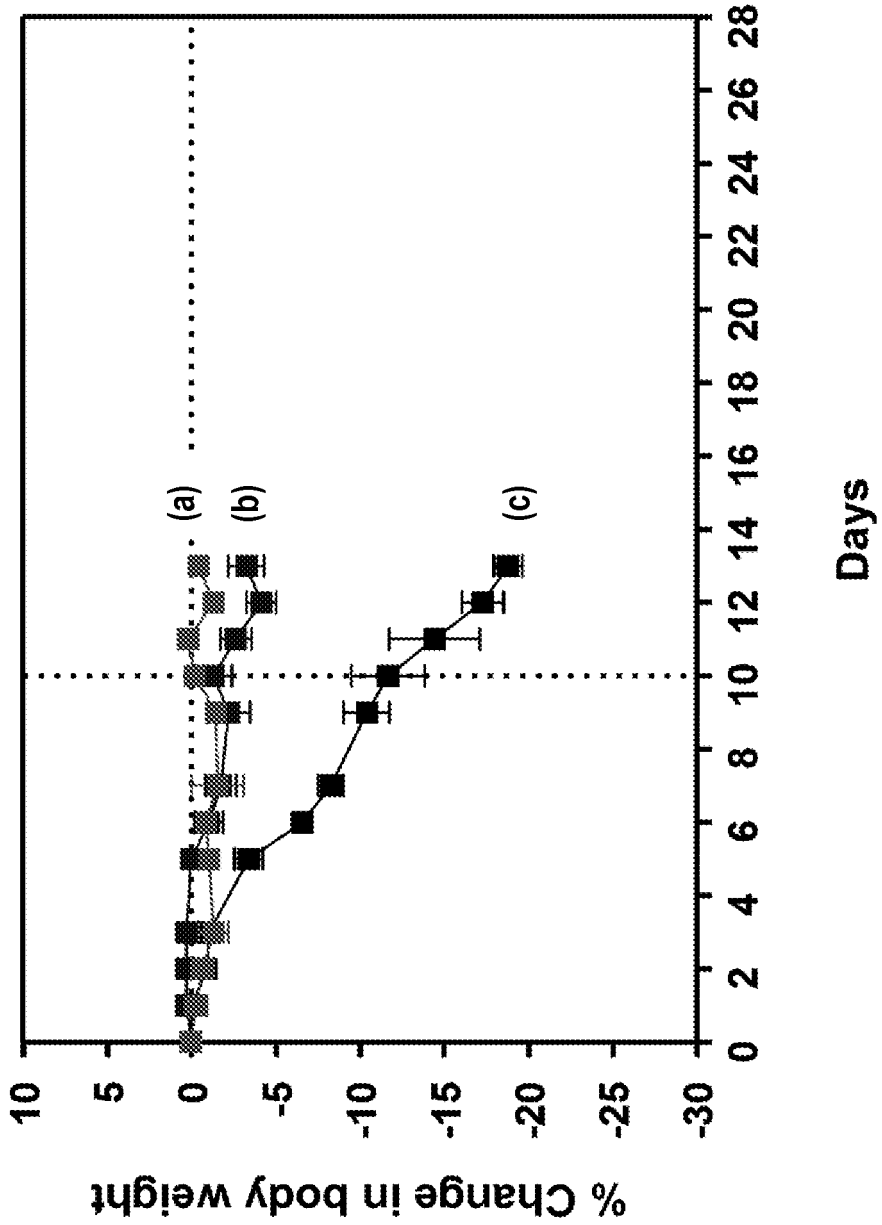

% Change in body weight
10
5
0
-5
-10
-15
-20
-25
-30
0
2
4
6
8
10
12
14
16
18
20
22
24
26
28
Days
(a)
(b)
(c)

FIG. 19

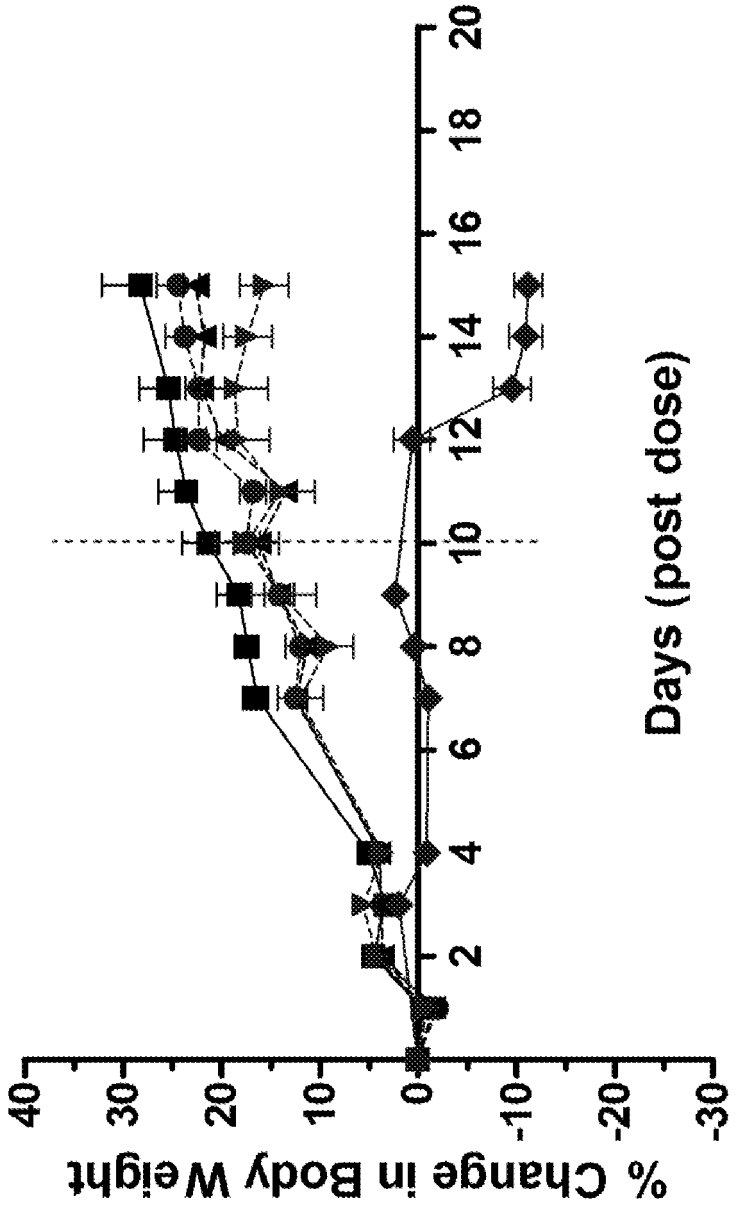

% Change in Body Weight
40
30
20
10
0
-10
-20
-30
2
4
6
8
10
12
14
16
18
20
Days (post dose)

FIG. 20