FIG. 1

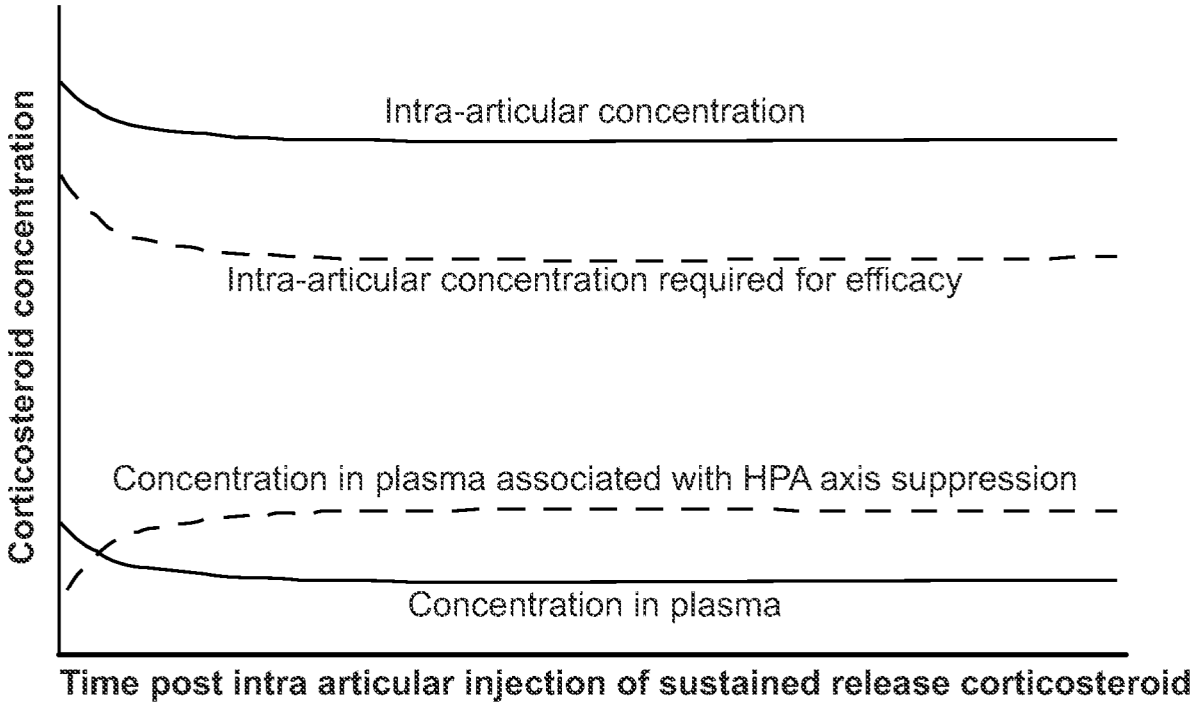

Corticosteroid concentration
Intra-articular concentration
Intra-articular concentration required for efficacy
Concentration in plasma associated with HPA axis suppression
Concentration in plasma
Time post intra articular injection of sustained release corticosteroid

FIG. 2

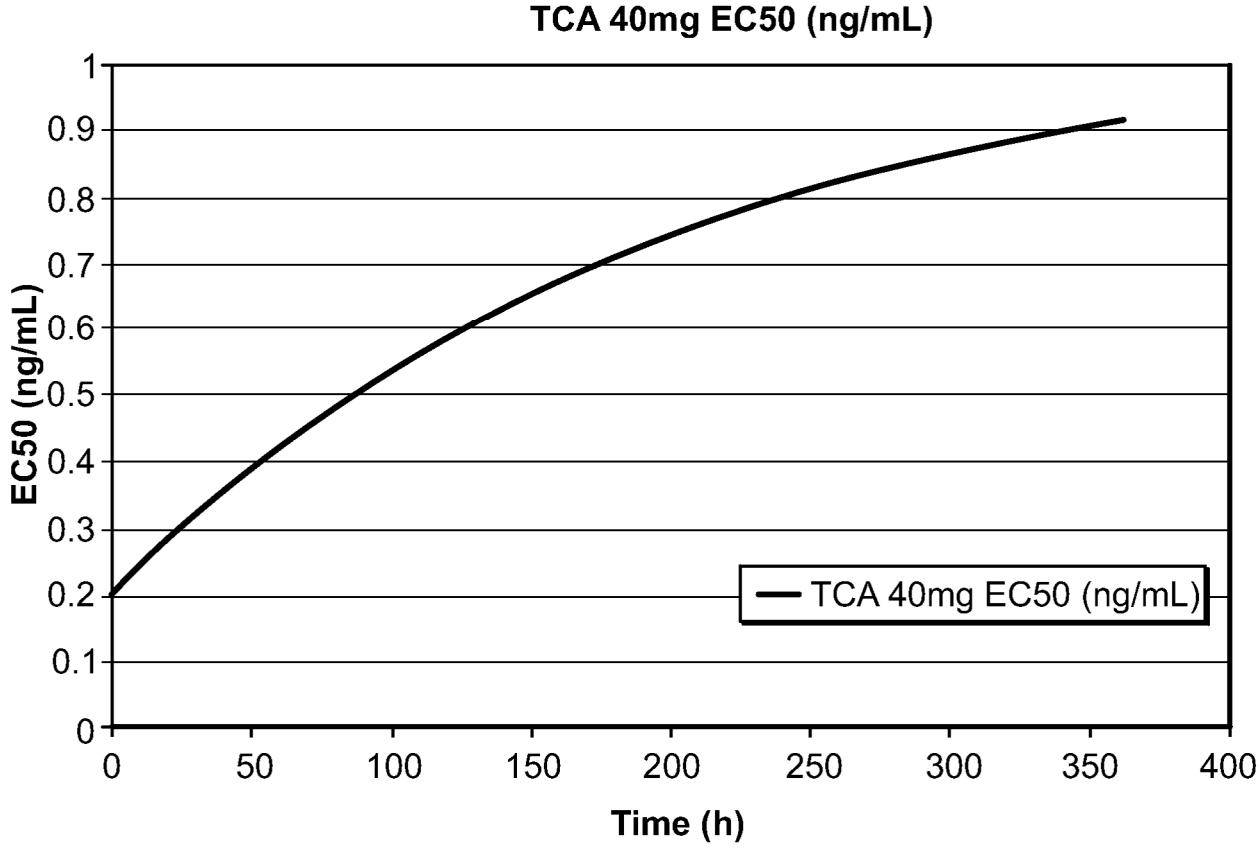

TCA 40mg EC50 (ng/mL)
EC50 (ng/mL)
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
50
100
150
200
250
300
350
400
Time (h)
TCA 40mg EC50 (ng/mL)

FIG. 3

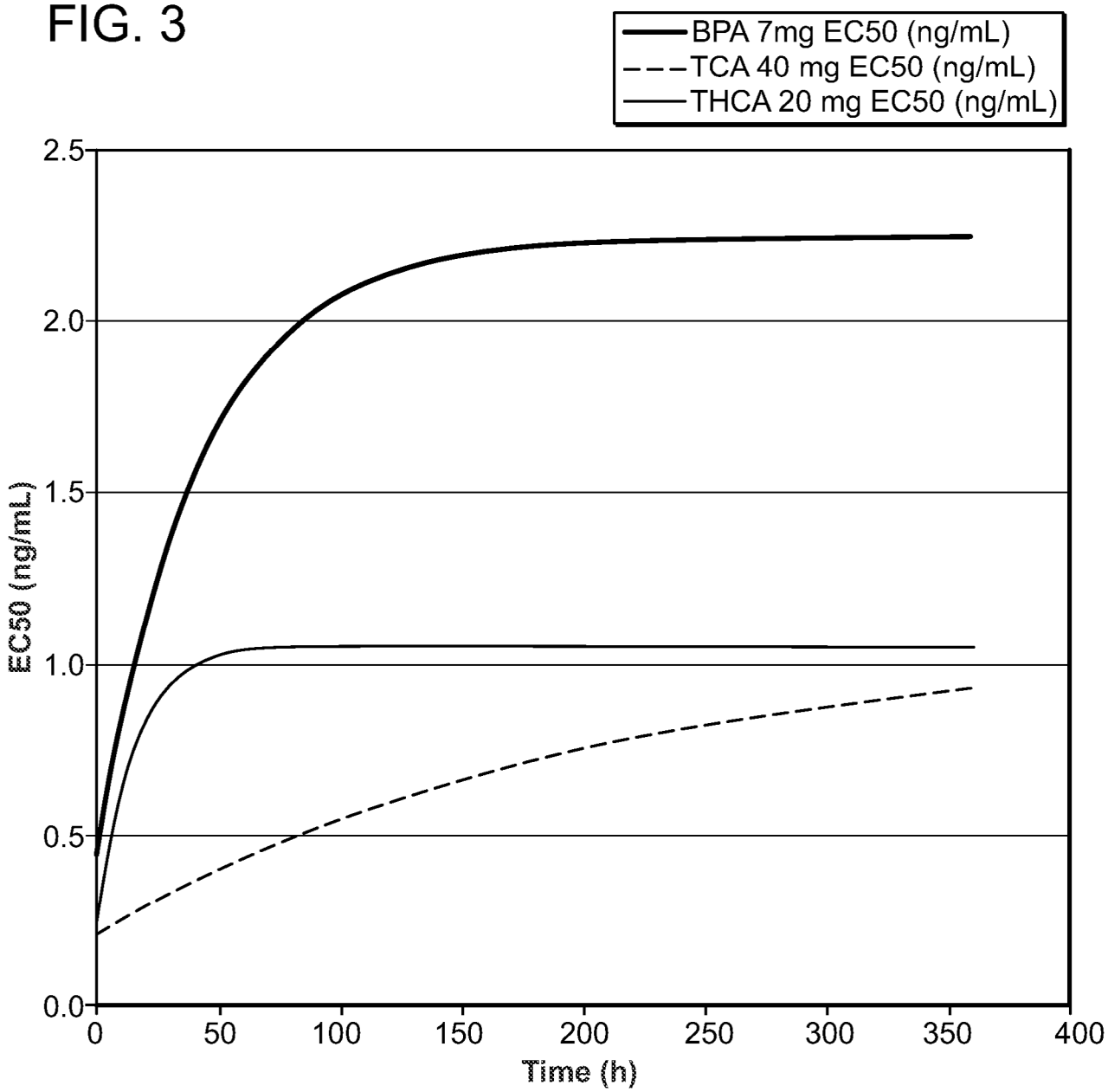

BPA 7mg EC50 (ng/mL)
TCA 40 mg EC50 (ng/mL)
THCA 20 mg EC50 (ng/mL)
EC50 (ng/mL)
2.5
2.0
1.5
1.0
0.5
0.0
0
50
100
150
200
250
300
350
400
Time (h)

FIG. 4A

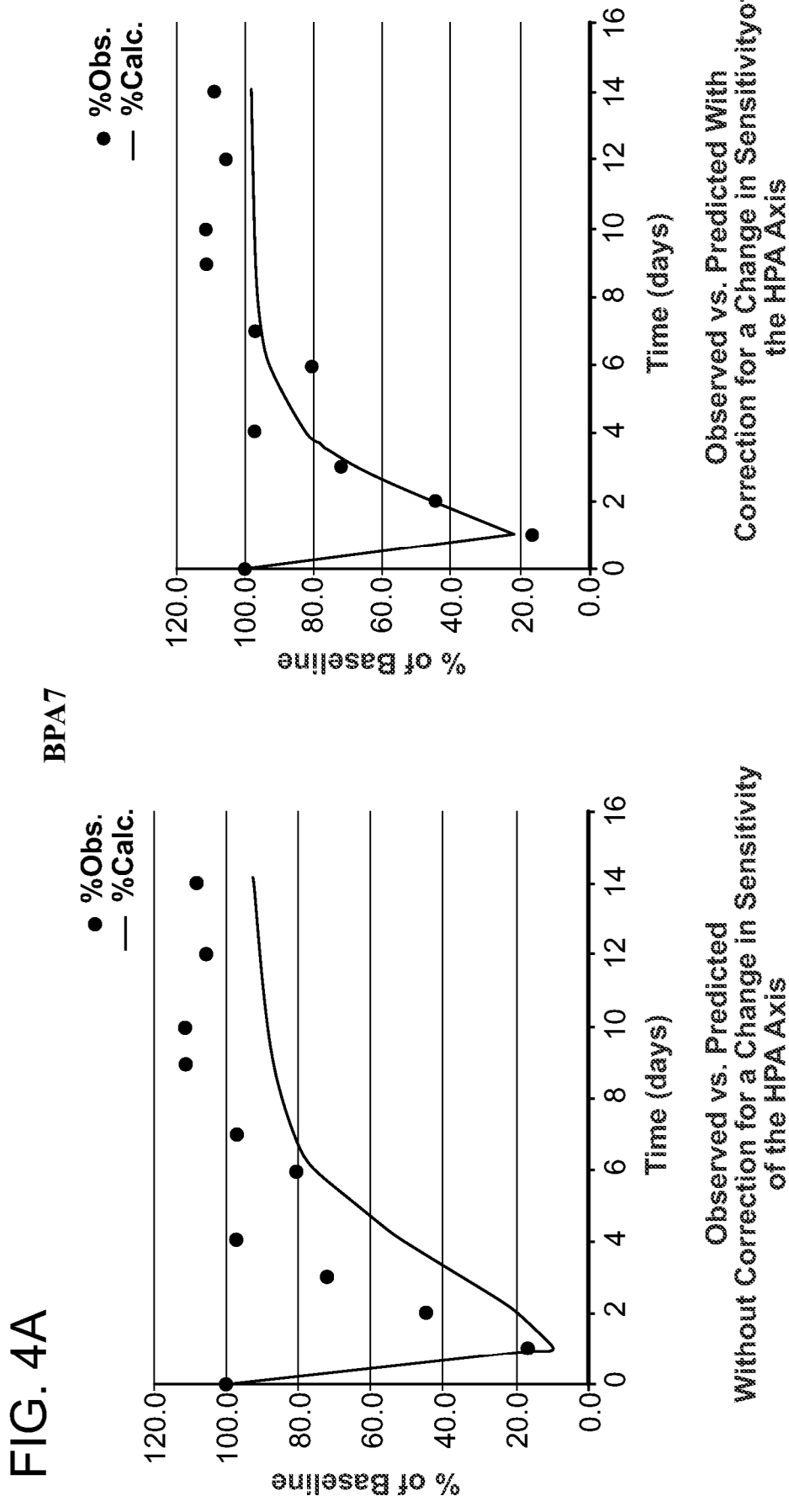

BPA7
● %Obs.
— %Calc.
% of Baseline
120.0
100.0
80.0
60.0
40.0
20.0
0.0
0
2
4
6
8
10
12
14
16
Time (days)
Observed vs. Predicted
Without Correction for a Change in Sensitivity
of the HPA Axis
● %Obs.
— %Calc.
% of Baseline
120.0
100.0
80.0
60.0
40.0
20.0
0.0
0
2
4
6
8
10
12
14
16
Time (days)
Observed vs. Predicted With
Correction for a Change in Sensitivityof
the HPA Axis

FIG. 4B

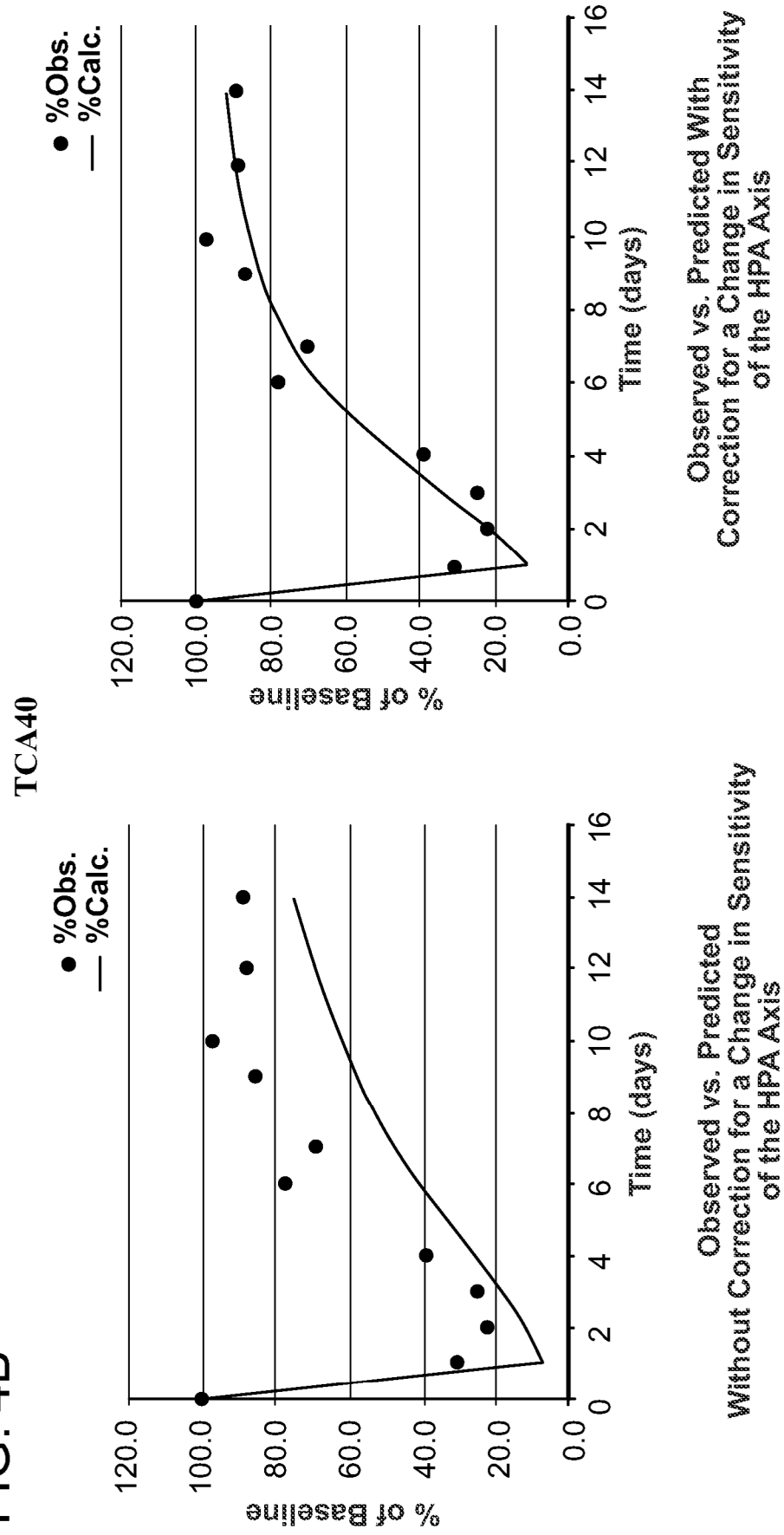

TCA40
● %Obs.
— %Calc.
% of Baseline
120.0
100.0
80.0
60.0
40.0
20.0
0.0
0
2
4
6
8
10
12
14
16
Time (days)
Observed vs. Predicted
Without Correction for a Change in Sensitivity
of the HPA Axis
● %Obs.
— %Calc.
% of Baseline
120.0
100.0
80.0
60.0
40.0
20.0
0.0
0
2
4
6
8
10
12
14
16
Time (days)
Observed vs. Predicted With
Correction for a Change in Sensitivity
of the HPA Axis

FIG. 4C

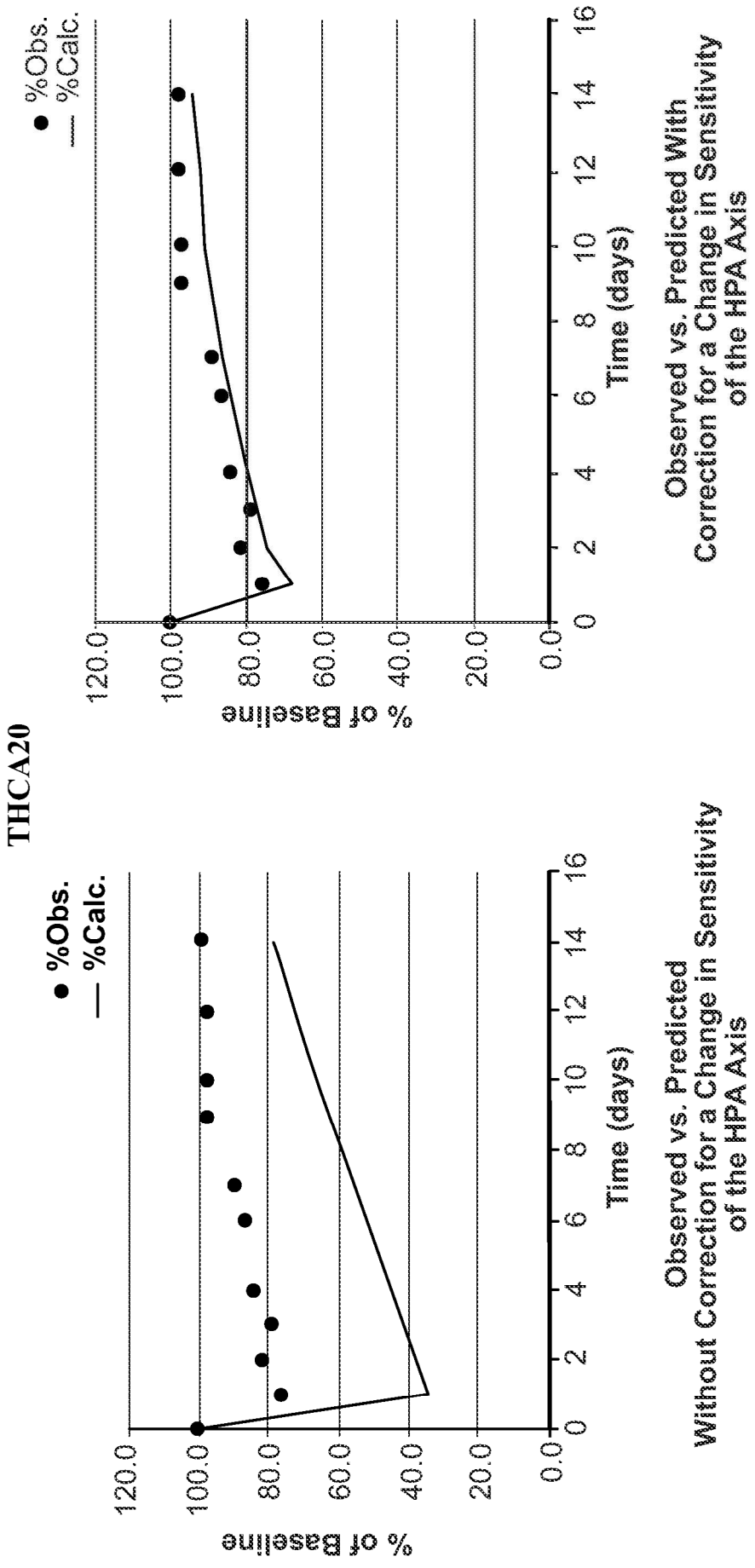

THCA20
● %Obs.
— %Calc.
% of Baseline
120.0
100.0
80.0
60.0
40.0
20.0
0.0
0
2
4
6
8
10
12
14
16
Time (days)
Observed vs. Predicted
Without Correction for a Change in Sensitivity
of the HPA Axis
● %Obs.
— %Calc.
% of Baseline
Time (days)
Observed vs. Predicted With
Correction for a Change in Sensitivity
of the HPA Axis

FIG. 5

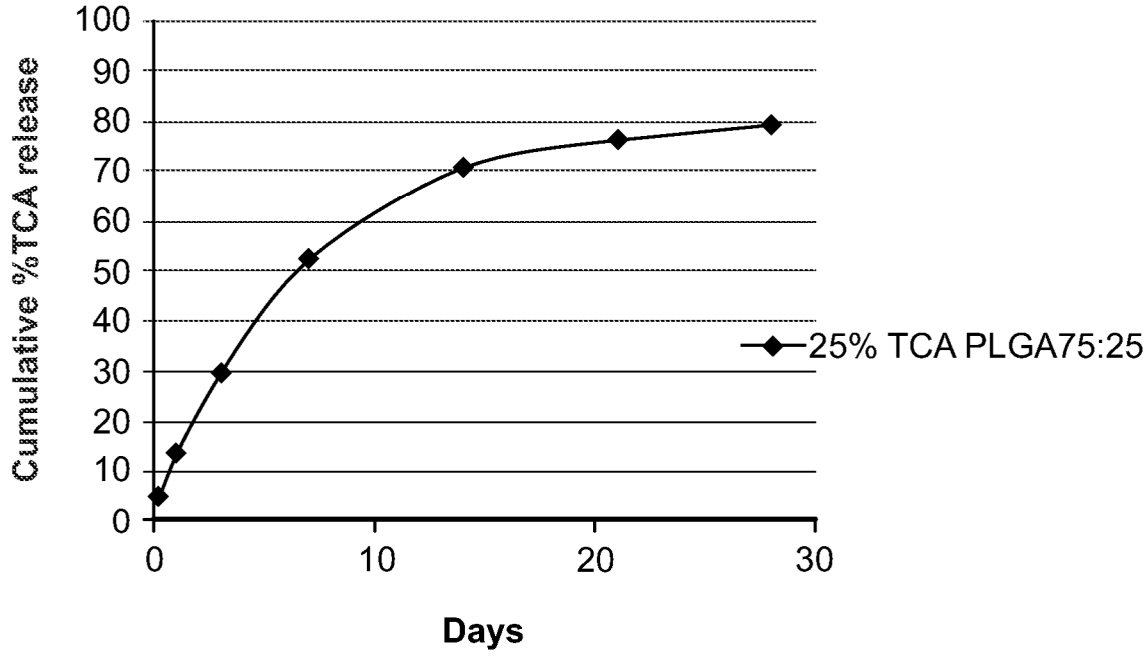

Cumulative %TCA release
100
90
80
70
60
50
40
30
20
10
0
0
10
20
30
Days
25% TCA PLGA75:25

FIG. 6

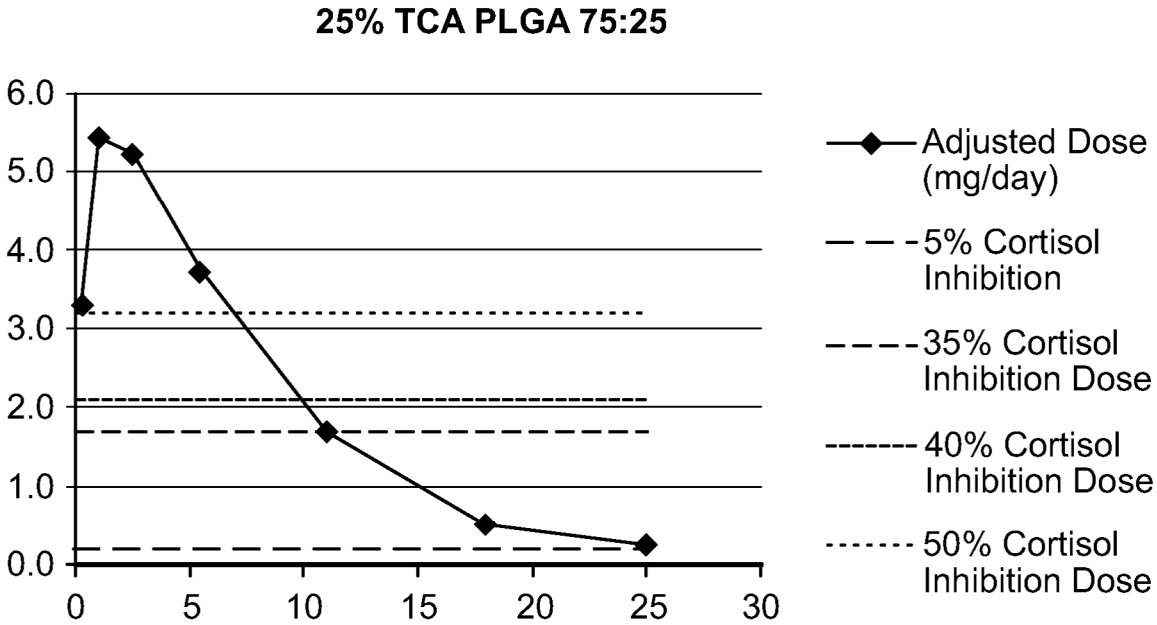

25% TCA PLGA 75:25
6.0
5.0
4.0
3.0
2.0
1.0
0.0
0
5
10
15
20
25
30
Adjusted Dose (mg/day)
5% Cortisol Inhibition
35% Cortisol Inhibition Dose
40% Cortisol Inhibition Dose
50% Cortisol Inhibition Dose

FIG. 7

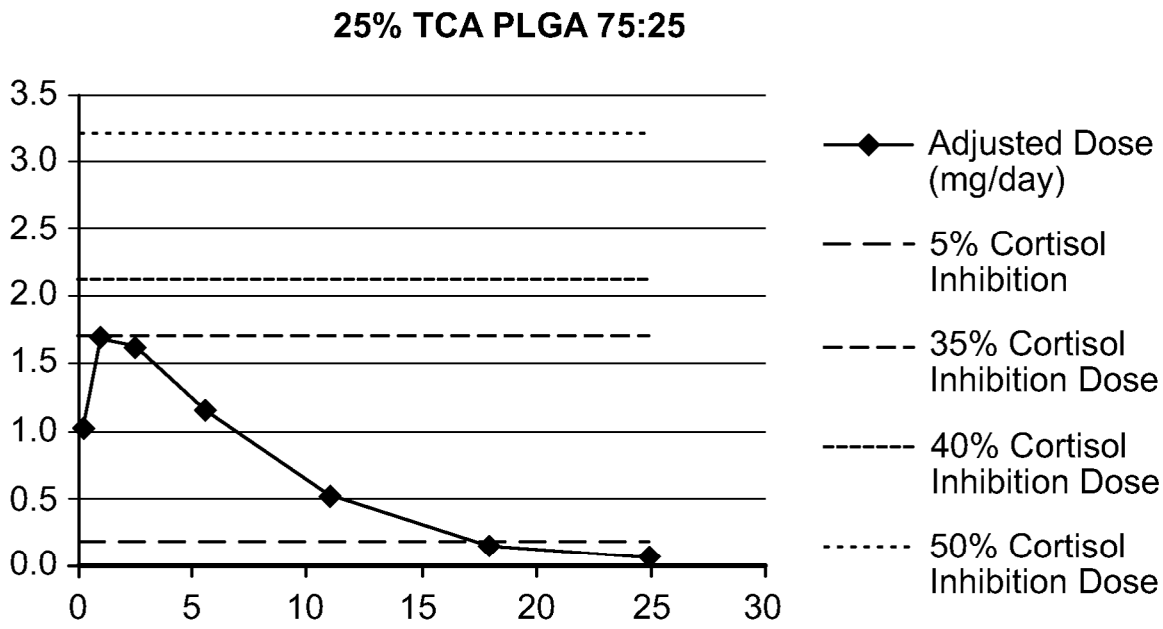

25% TCA PLGA 75:25
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0
5
10
15
20
25
30
Adjusted Dose (mg/day)
5% Cortisol Inhibition
35% Cortisol Inhibition Dose
40% Cortisol Inhibition Dose
50% Cortisol Inhibition Dose

FIG. 8

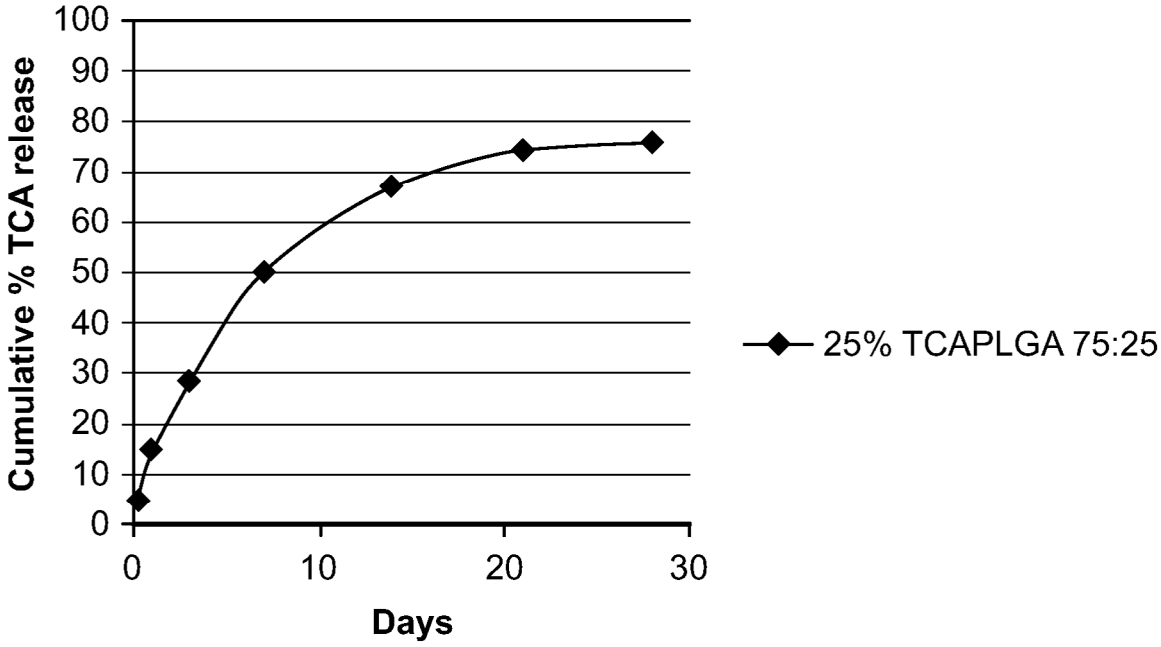

Cumulative % TCA release
100
90
80
70
60
50
40
30
20
10
0
0
10
20
30
Days
25% TCAPLGA 75:25

FIG. 9

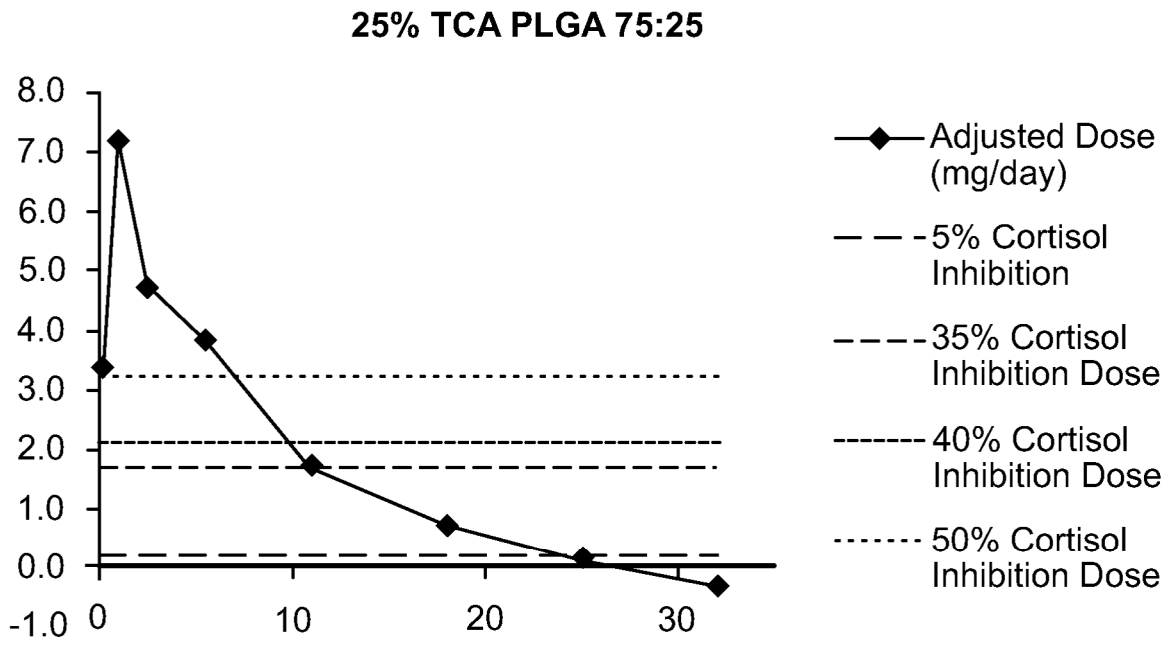

25% TCA PLGA 75:25
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
0
10
20
30
Adjusted Dose (mg/day)
5% Cortisol Inhibition
35% Cortisol Inhibition Dose
40% Cortisol Inhibition Dose
50% Cortisol Inhibition Dose

FIG. 10

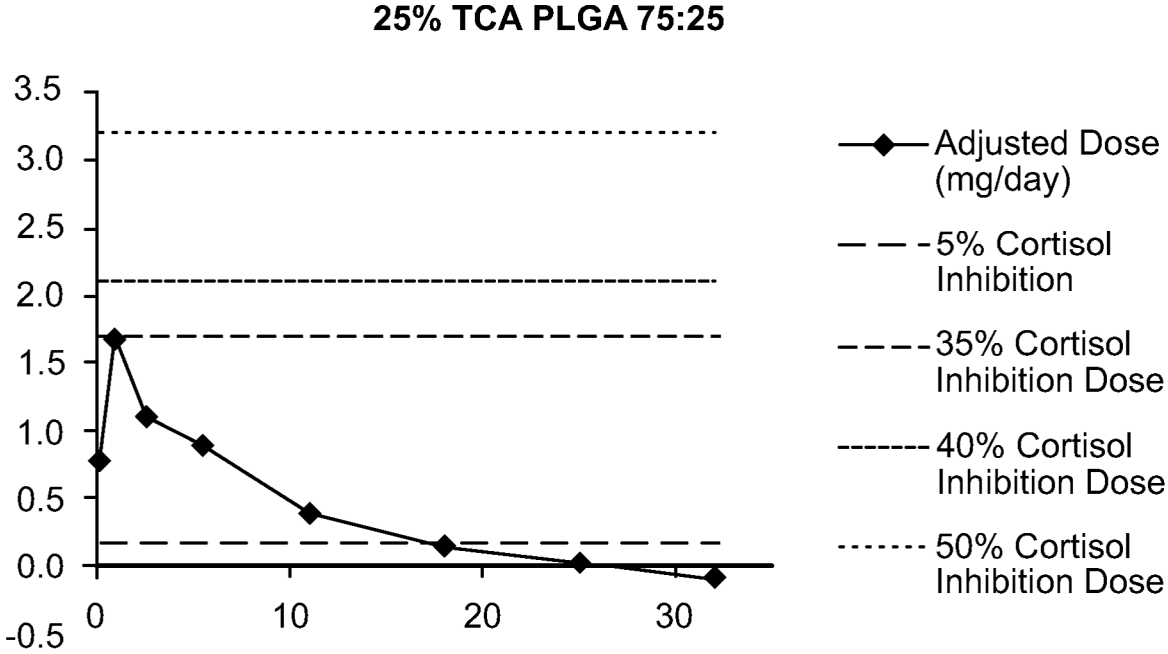

25% TCA PLGA 75:25
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
0
10
20
30
Adjusted Dose (mg/day)
5% Cortisol Inhibition
35% Cortisol Inhibition Dose
40% Cortisol Inhibition Dose
50% Cortisol Inhibition Dose

FIG. 11

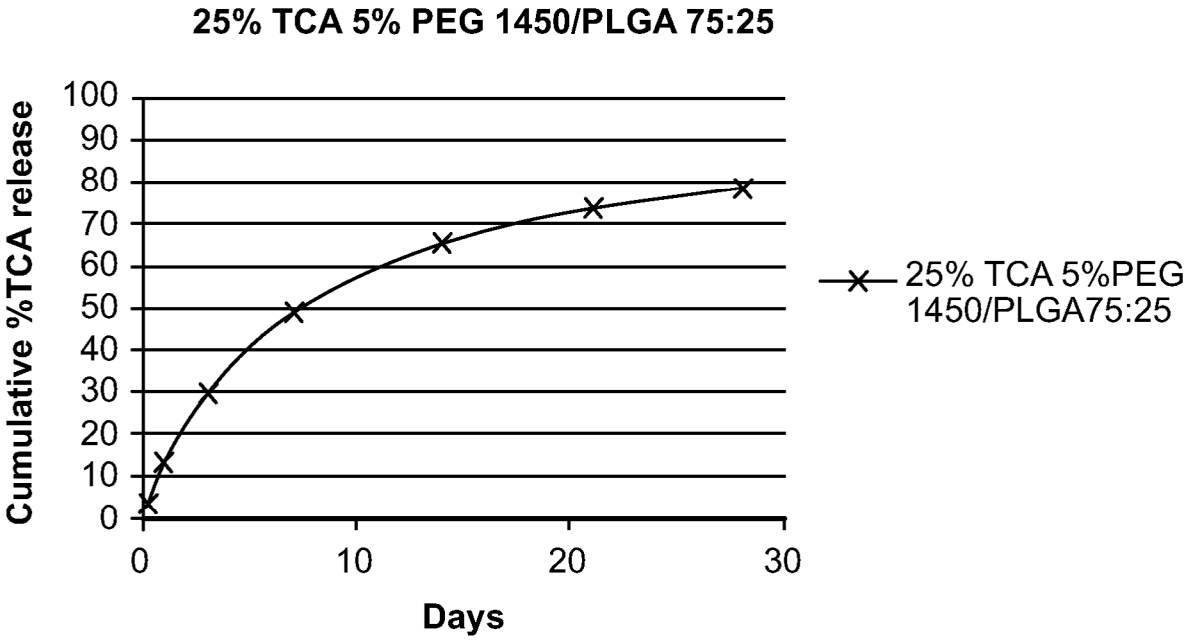

25% TCA 5% PEG 1450/PLGA 75:25
Cumulative %TCA release
100
90
80
70
60
50
40
30
20
10
0
0
10
20
30
Days
25% TCA 5%PEG 1450/PLGA75:25

FIG. 12

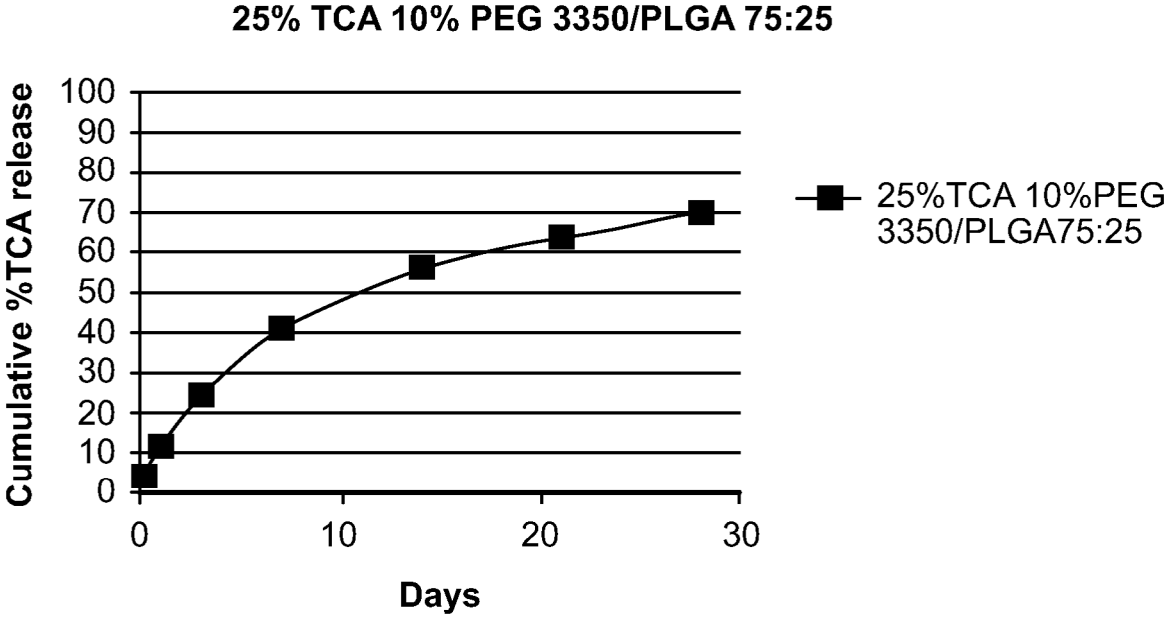

25% TCA 10% PEG 3350/PLGA 75:25
Cumulative %TCA release
100
90
80
70
60
50
40
30
20
10
0
0
10
20
30
Days
25%TCA 10%PEG 3350/PLGA75:25

FIG. 13

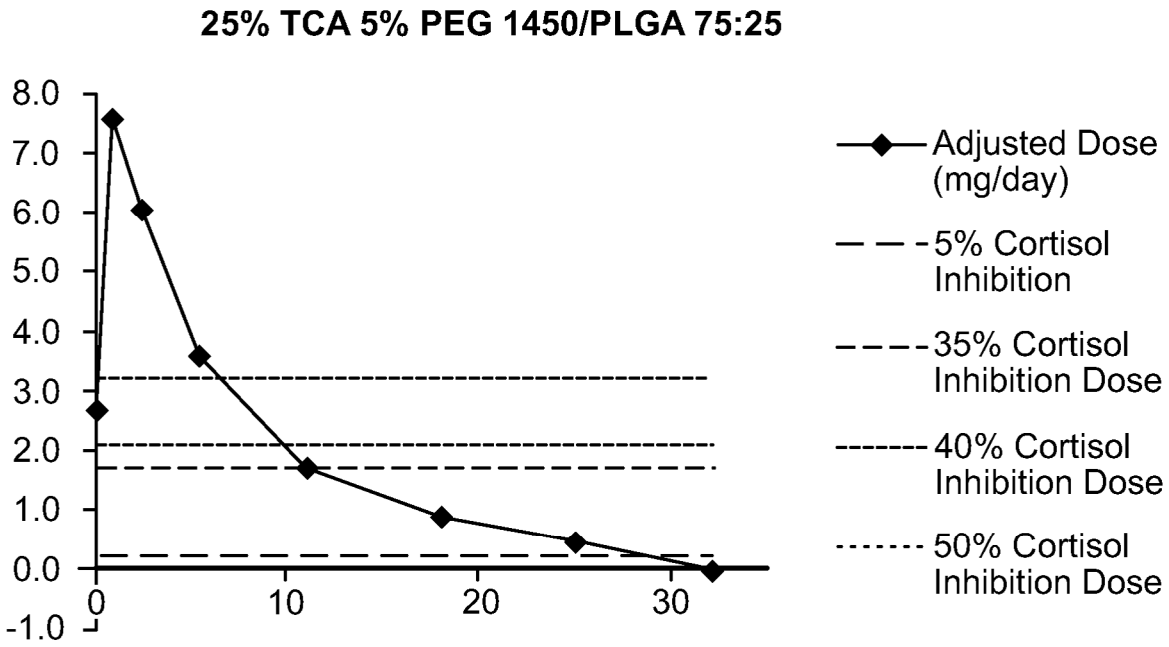

25% TCA 5% PEG 1450/PLGA 75:25
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
0
10
20
30
Adjusted Dose (mg/day)
5% Cortisol Inhibition
35% Cortisol Inhibition Dose
40% Cortisol Inhibition Dose
50% Cortisol Inhibition Dose

FIG. 14

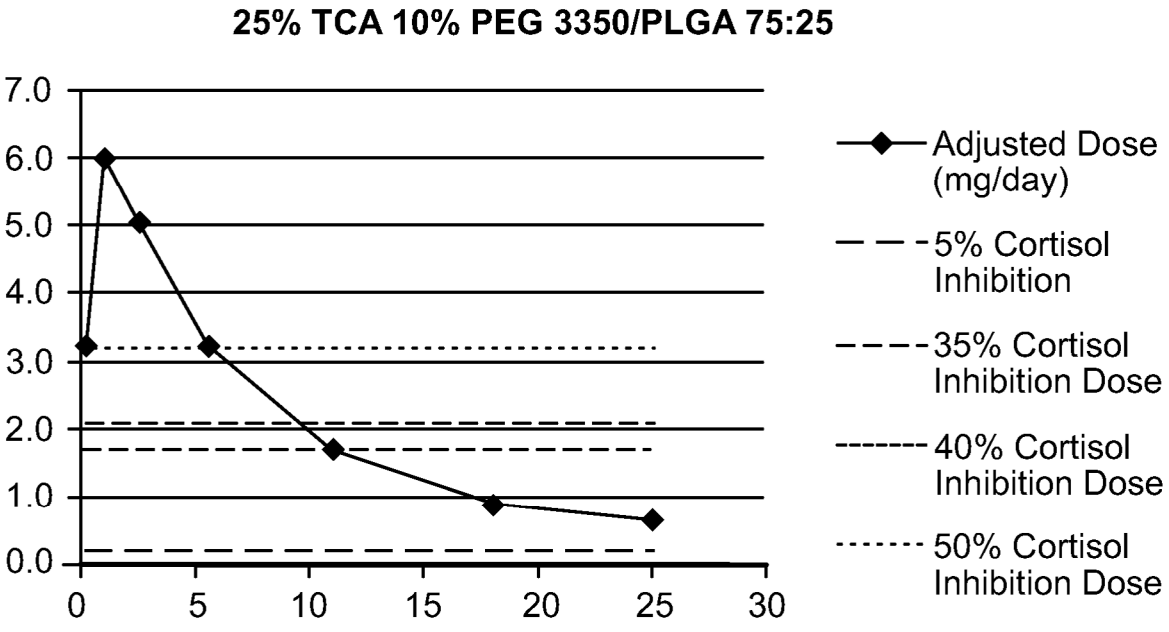

25% TCA 10% PEG 3350/PLGA 75:25
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
0
5
10
15
20
25
30
Adjusted Dose (mg/day)
5% Cortisol Inhibition
35% Cortisol Inhibition Dose
40% Cortisol Inhibition Dose
50% Cortisol Inhibition Dose

FIG. 15

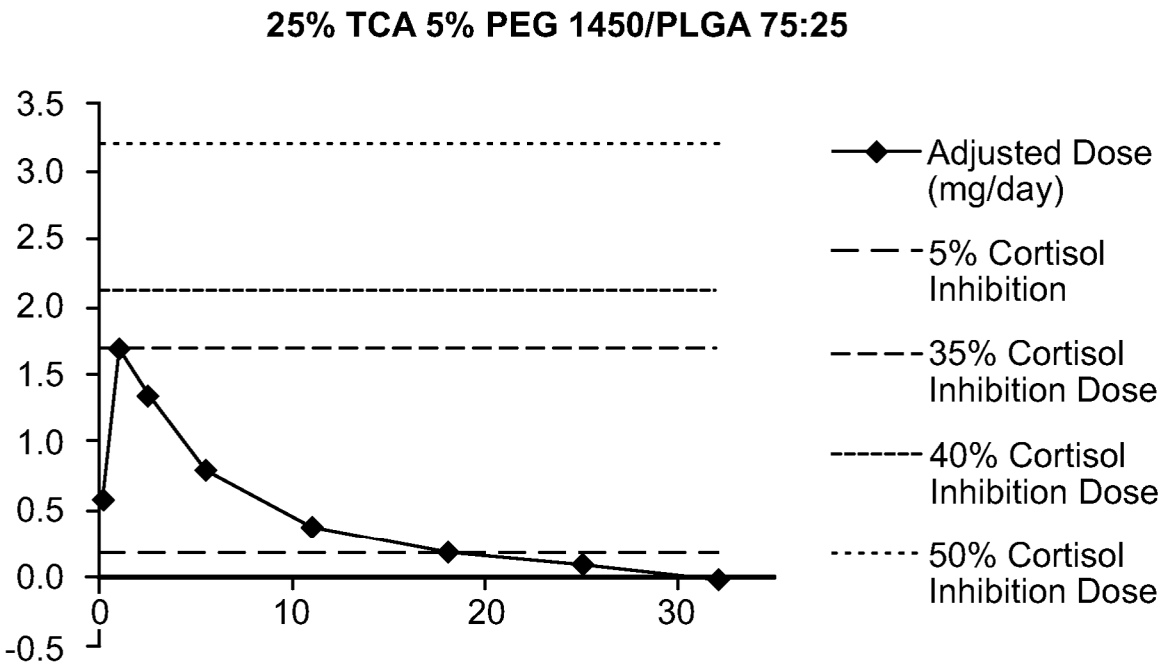

25% TCA 5% PEG 1450/PLGA 75:25
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
0
10
20
30
Adjusted Dose (mg/day)
5% Cortisol Inhibition
35% Cortisol Inhibition Dose
40% Cortisol Inhibition Dose
50% Cortisol Inhibition Dose

FIG. 16

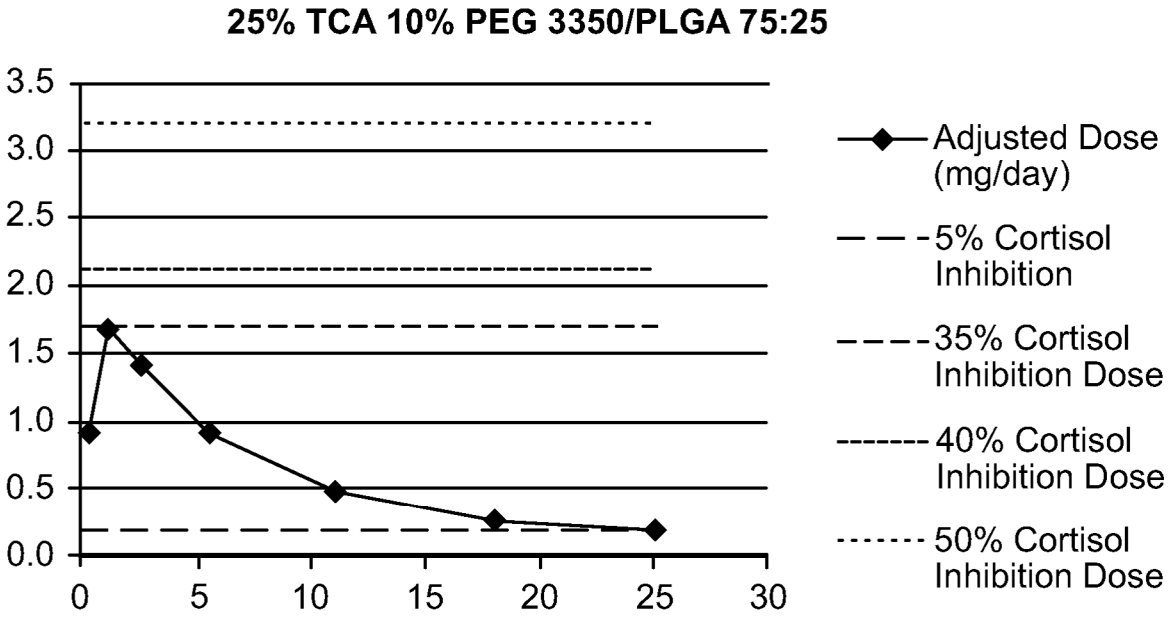

25% TCA 10% PEG 3350/PLGA 75:25
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0
5
10
15
20
25
30
Adjusted Dose (mg/day)
5% Cortisol Inhibition
35% Cortisol Inhibition Dose
40% Cortisol Inhibition Dose
50% Cortisol Inhibition Dose

FIG. 17

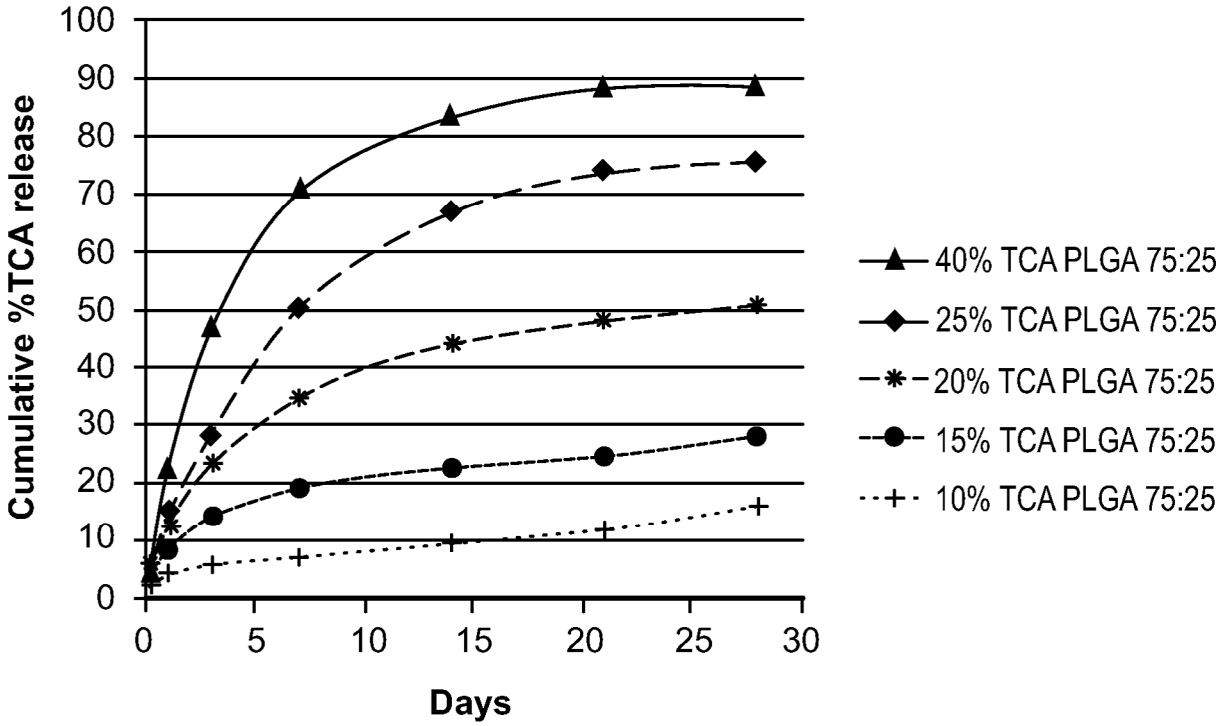

Cumulative %TCA release
100
90
80
70
60
50
40
30
20
10
0
0
5
10
15
20
25
30
Days
40% TCA PLGA 75:25
25% TCA PLGA 75:25
20% TCA PLGA 75:25
15% TCA PLGA 75:25
10% TCA PLGA 75:25

FIG. 18

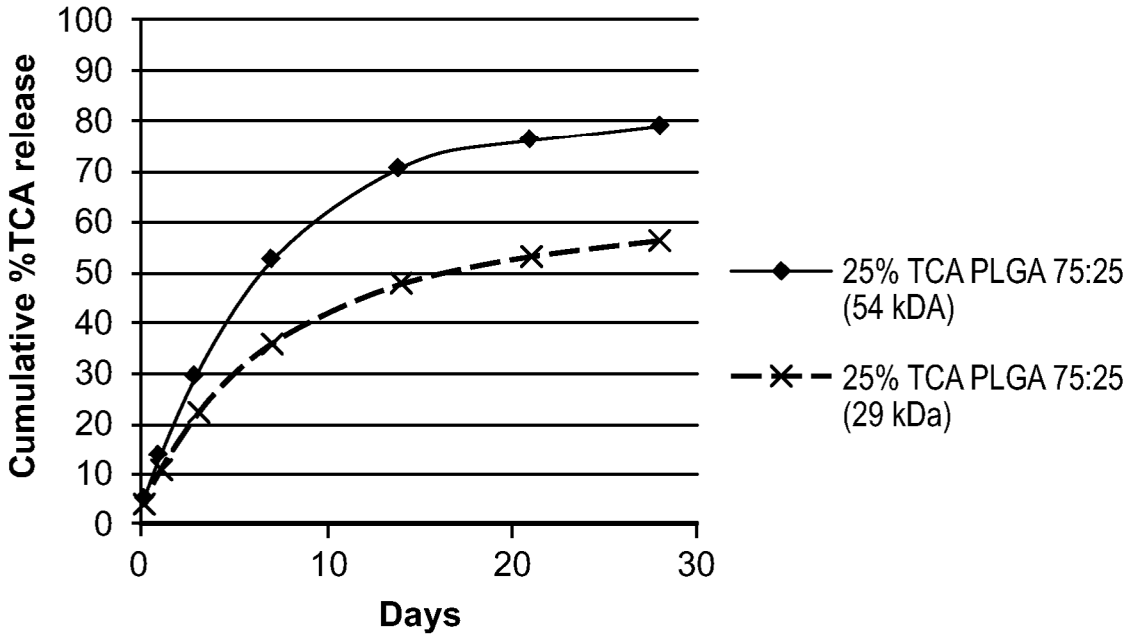

Cumulative %TCA release
100
90
80
70
60
50
40
30
20
10
0
0
10
20
30
Days
25% TCA PLGA 75:25 (54 kDA)
25% TCA PLGA 75:25 (29 kDa)

FIG. 19

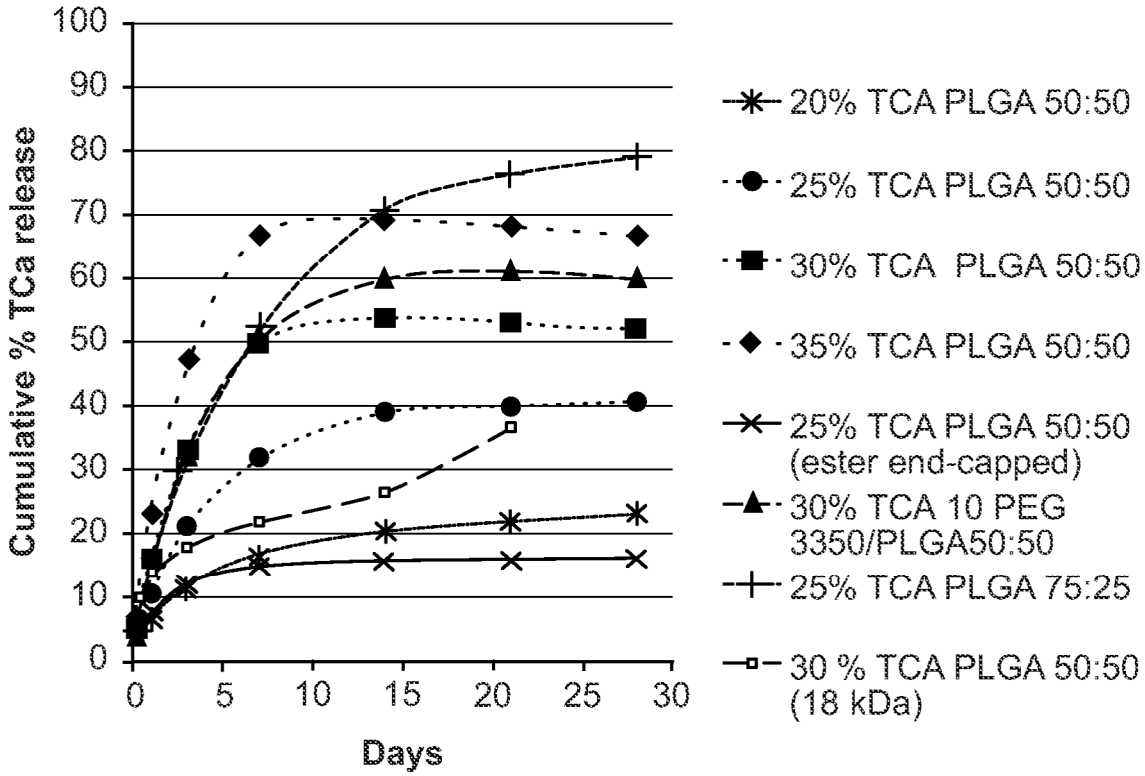

Cumulative % TCa release
100
90
80
70
60
50
40
30
20
10
0
0
5
10
15
20
25
30
Days
20% TCA PLGA 50:50
25% TCA PLGA 50:50
30% TCA PLGA 50:50
35% TCA PLGA 50:50
25% TCA PLGA 50:50 (ester end-capped)
30% TCA 10 PEG 3350/PLGA50:50
25% TCA PLGA 75:25
30 % TCA PLGA 50:50 (18 kDa)

FIG. 20

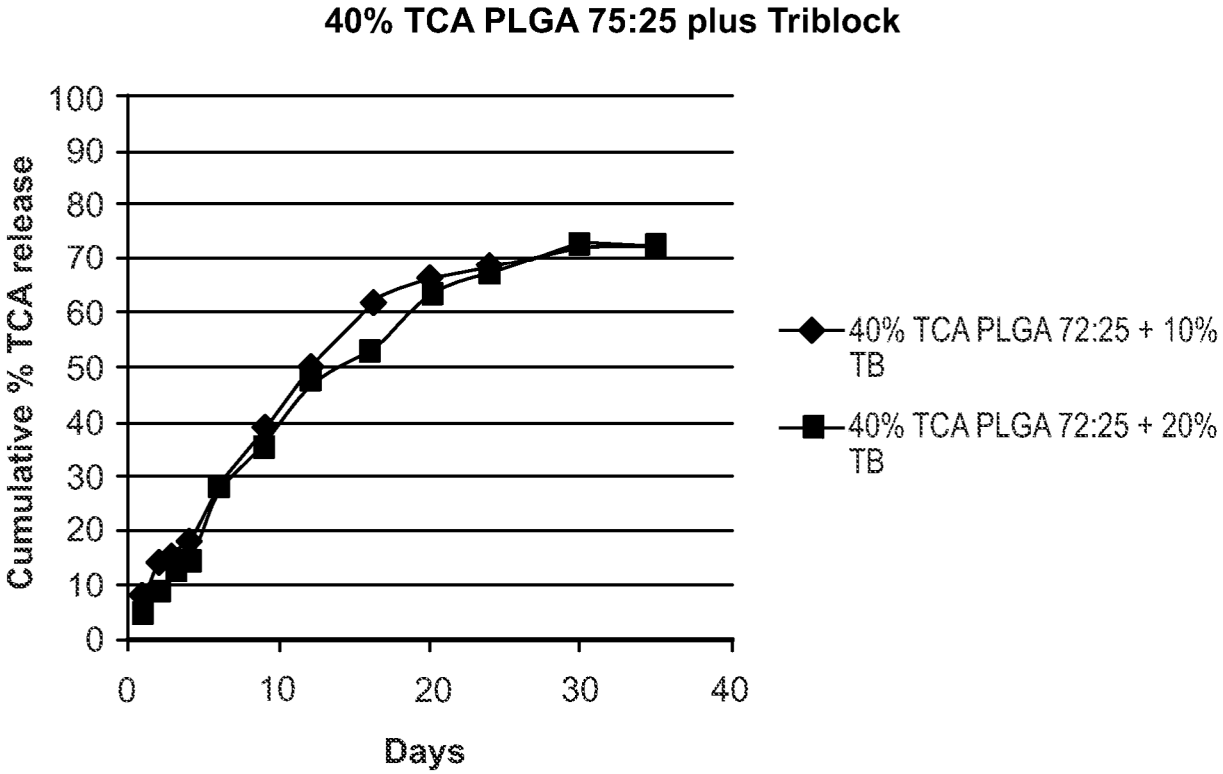

40% TCA PLGA 75:25 plus Triblock
Cumulative % TCA release
100
90
80
70
60
50
40
30
20
10
0
0
10
20
30
40
Days
40% TCA PLGA 72:25 + 10% TB
40% TCA PLGA 72:25 + 20% TB

FIG. 21

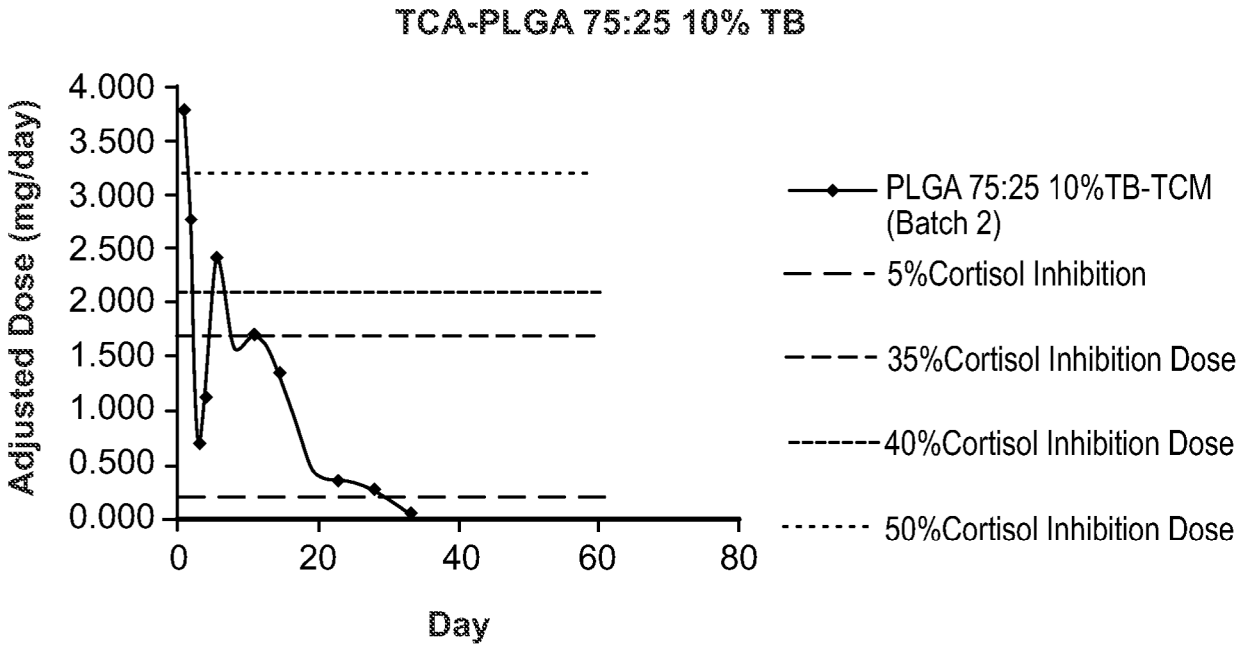

TCA-PLGA 75:25 10% TB
Adjusted Dose (mg/day)
4.000
3.500
3.000
2.500
2.000
1.500
1.000
0.500
0.000
0
20
40
60
80
Day
PLGA 75:25 10%TB-TCM (Batch 2)
5%Cortisol Inhibition
35%Cortisol Inhibition Dose
40%Cortisol Inhibition Dose
50%Cortisol Inhibition Dose

FIG. 22

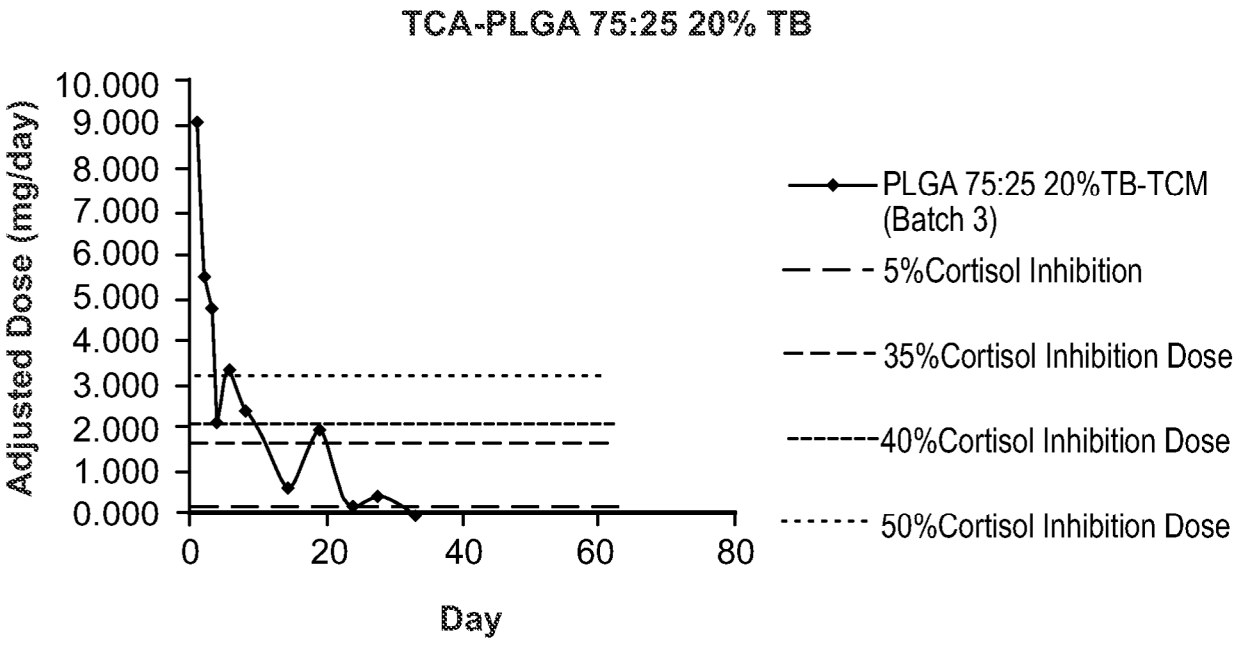

TCA-PLGA 75:25 20% TB
Adjusted Dose (mg/day)
10.000
9.000
8.000
7.000
6.000
5.000
4.000
3.000
2.000
1.000
0.000
0
20
40
60
80
Day
PLGA 75:25 20%TB-TCM (Batch 3)
5%Cortisol Inhibition
35%Cortisol Inhibition Dose
40%Cortisol Inhibition Dose
50%Cortisol Inhibition Dose

FIG. 23

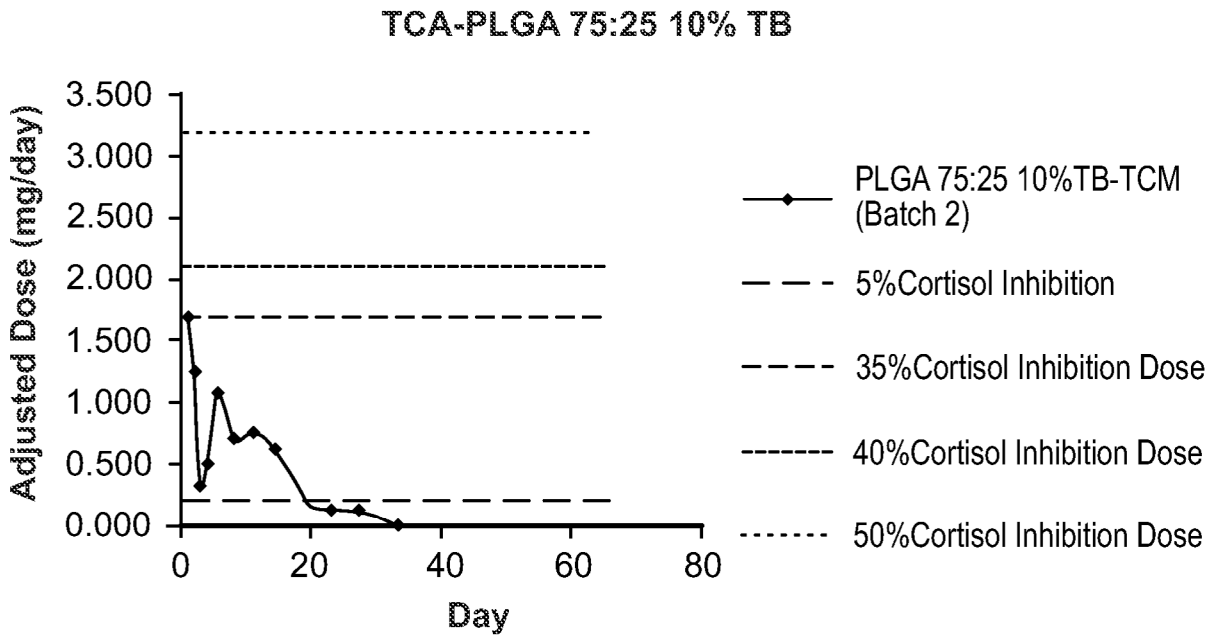

TCA-PLGA 75:25 10% TB
Adjusted Dose (mg/day)
3.500
3.000
2.500
2.000
1.500
1.000
0.500
0.000
0
20
40
60
80
Day
PLGA 75:25 10%TB-TCM (Batch 2)
5%Cortisol Inhibition
35%Cortisol Inhibition Dose
40%Cortisol Inhibition Dose
50%Cortisol Inhibition Dose

FIG. 24

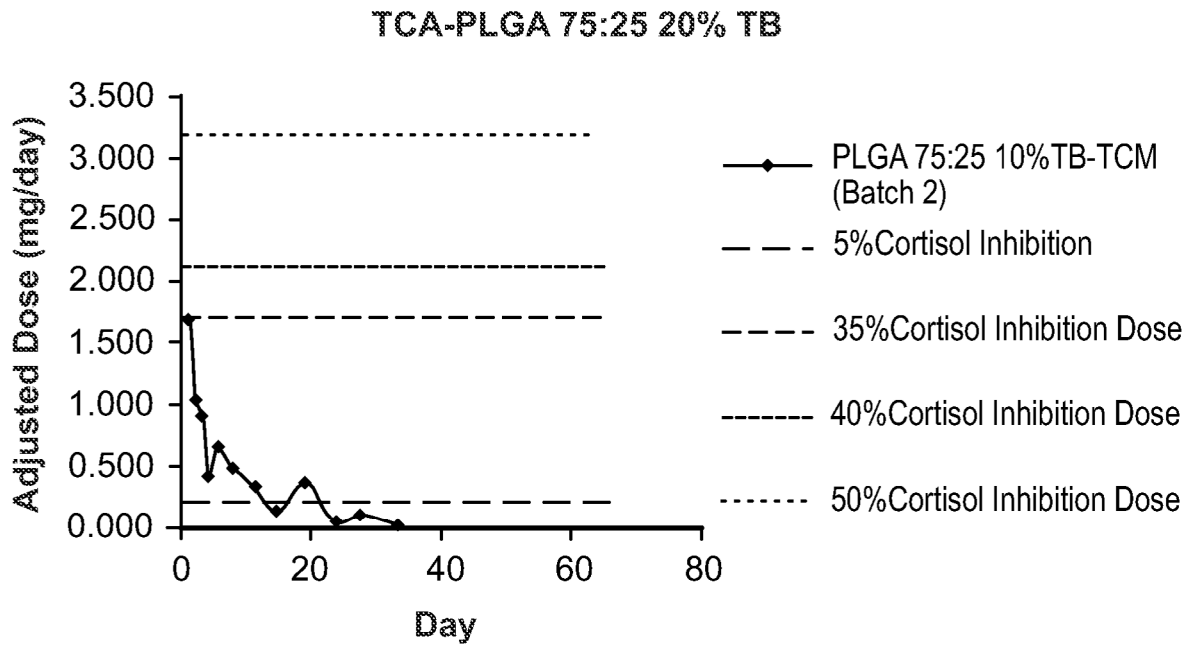

TCA-PLGA 75:25 20% TB
Adjusted Dose (mg/day)
3.500
3.000
2.500
2.000
1.500
1.000
0.500
0.000
0
20
40
60
80
Day
PLGA 75:25 10%TB-TCM (Batch 2)
5%Cortisol Inhibition
35%Cortisol Inhibition Dose
40%Cortisol Inhibition Dose
50%Cortisol Inhibition Dose

FIG. 25

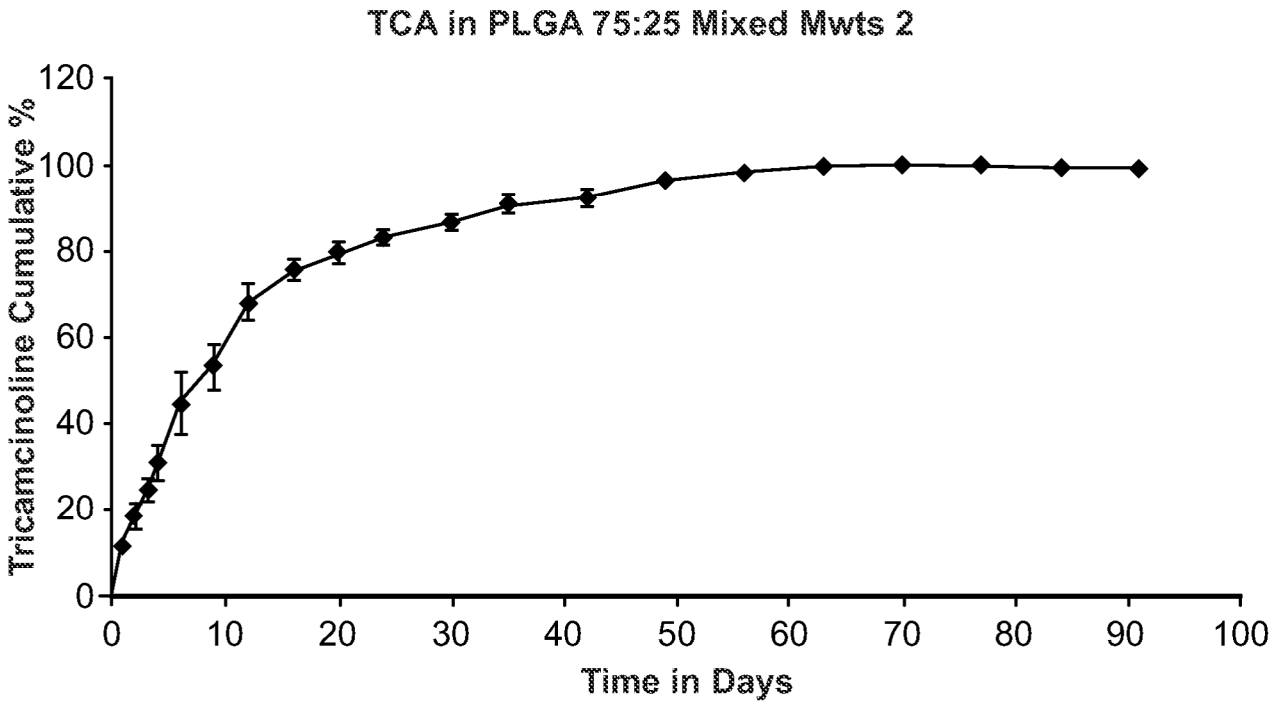

TCA in PLGA 75:25 Mixed Mwts 2
Tricamcinoline Cumulative %
120
100
80
60
40
20
0
0
10
20
30
40
50
60
70
80
90
100
Time in Days

FIG. 26

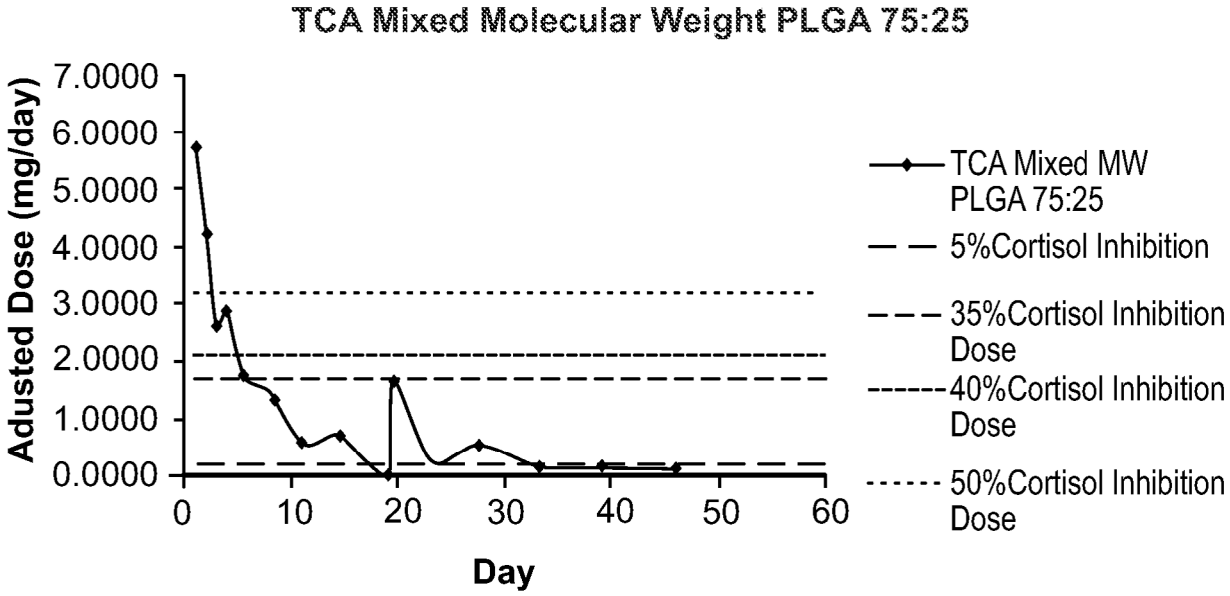

TCA Mixed Molecular Weight PLGA 75:25
Adusted Dose (mg/day)
7.0000
6.0000
5.0000
4.0000
3.0000
2.0000
1.0000
0.0000
0
10
20
30
40
50
60
Day
TCA Mixed MW PLGA 75:25
5%Cortisol Inhibition
35%Cortisol Inhibition Dose
40%Cortisol Inhibition Dose
50%Cortisol Inhibition Dose

FIG. 27

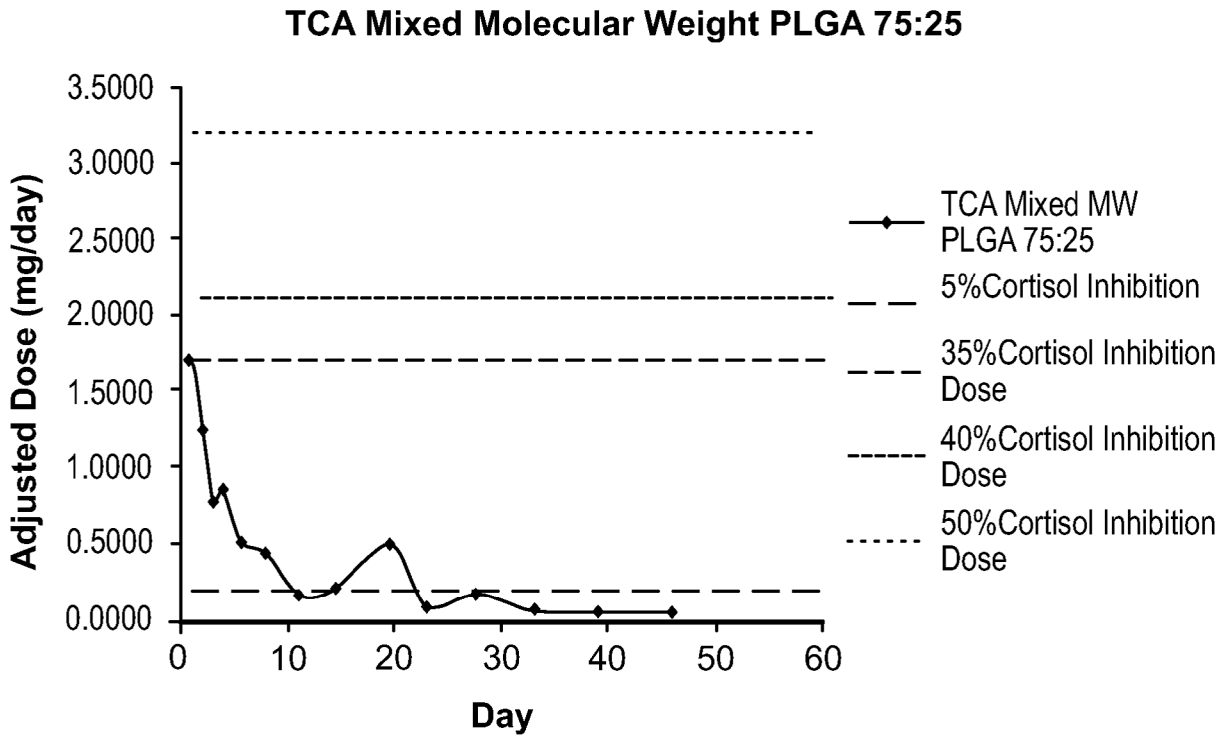

TCA Mixed Molecular Weight PLGA 75:25
Adjusted Dose (mg/day)
3.5000
3.0000
2.5000
2.0000
1.5000
1.0000
0.5000
0.0000
0
10
20
30
40
50
60
Day
TCA Mixed MW PLGA 75:25
5%Cortisol Inhibition
35%Cortisol Inhibition Dose
40%Cortisol Inhibition Dose
50%Cortisol Inhibition Dose

FIG. 28

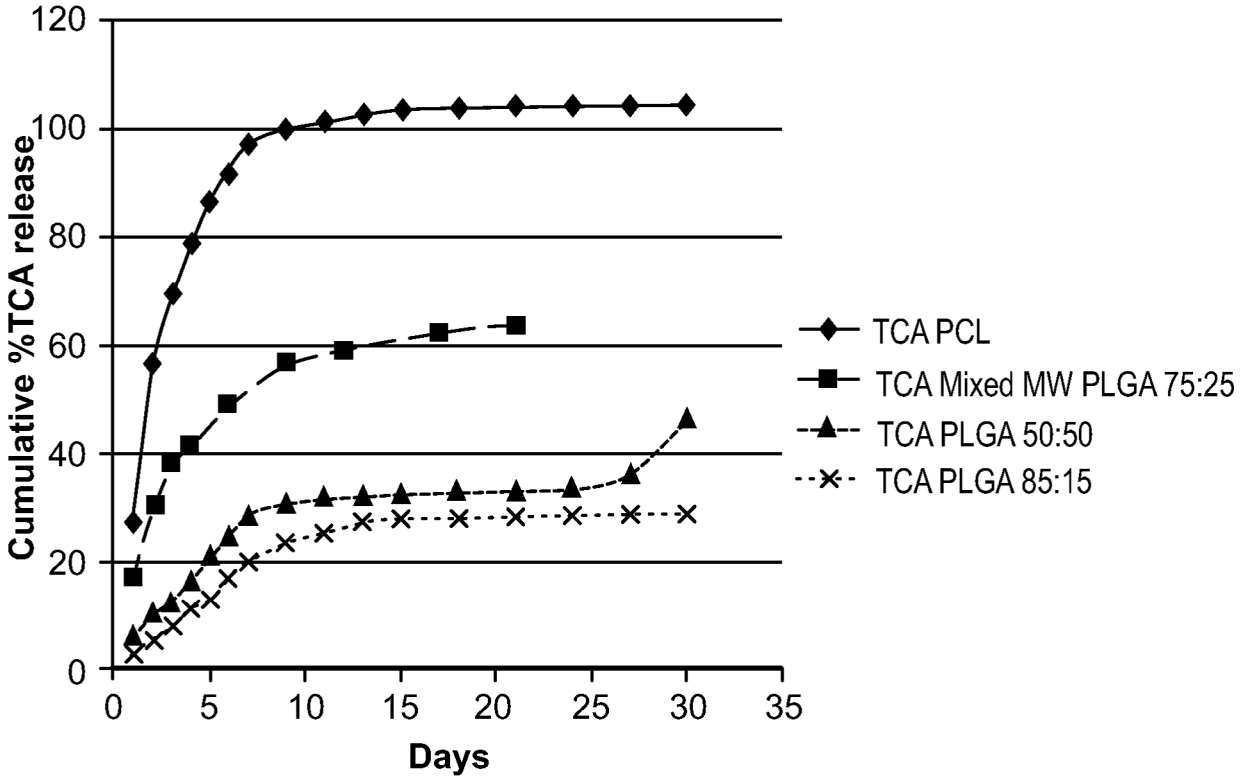

Cumulative %TCA release
120
100
80
60
40
20
0
0
5
10
15
20
25
30
35
Days
TCA PCL
TCA Mixed MW PLGA 75:25
TCA PLGA 50:50
TCA PLGA 85:15

FIG. 29

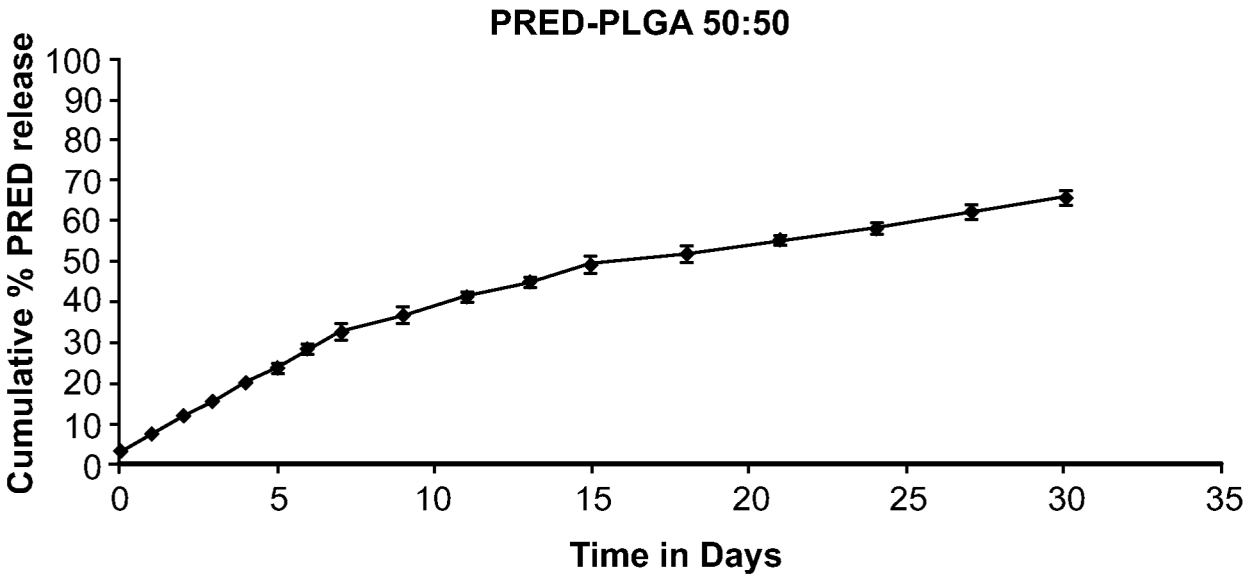

PRED-PLGA 50:50
Cumulative % PRED release
100
90
80
70
60
50
40
30
20
10
0
0
5
10
15
20
25
30
35
Time in Days

FIG. 30

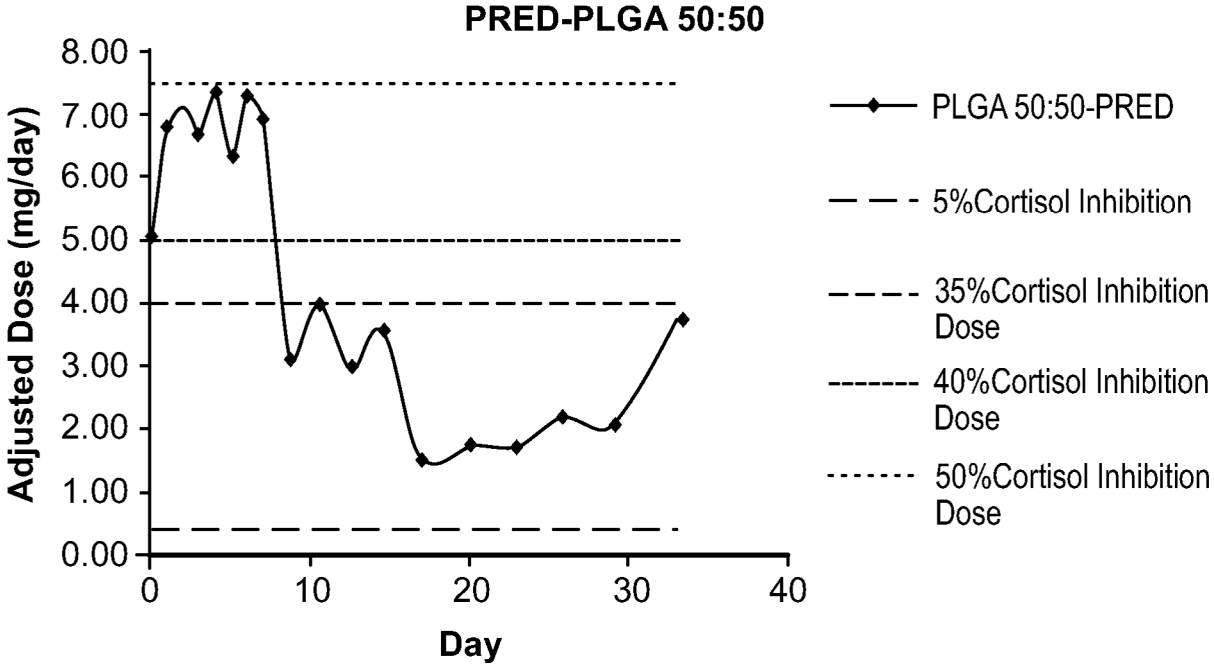

PRED-PLGA 50:50
Adjusted Dose (mg/day)
8.00
7.00
6.00
5.00
4.00
3.00
2.00
1.00
0.00
0
10
20
30
40
Day
PLGA 50:50-PRED
5%Cortisol Inhibition
35%Cortisol Inhibition Dose
40%Cortisol Inhibition Dose
50%Cortisol Inhibition Dose

FIG. 31

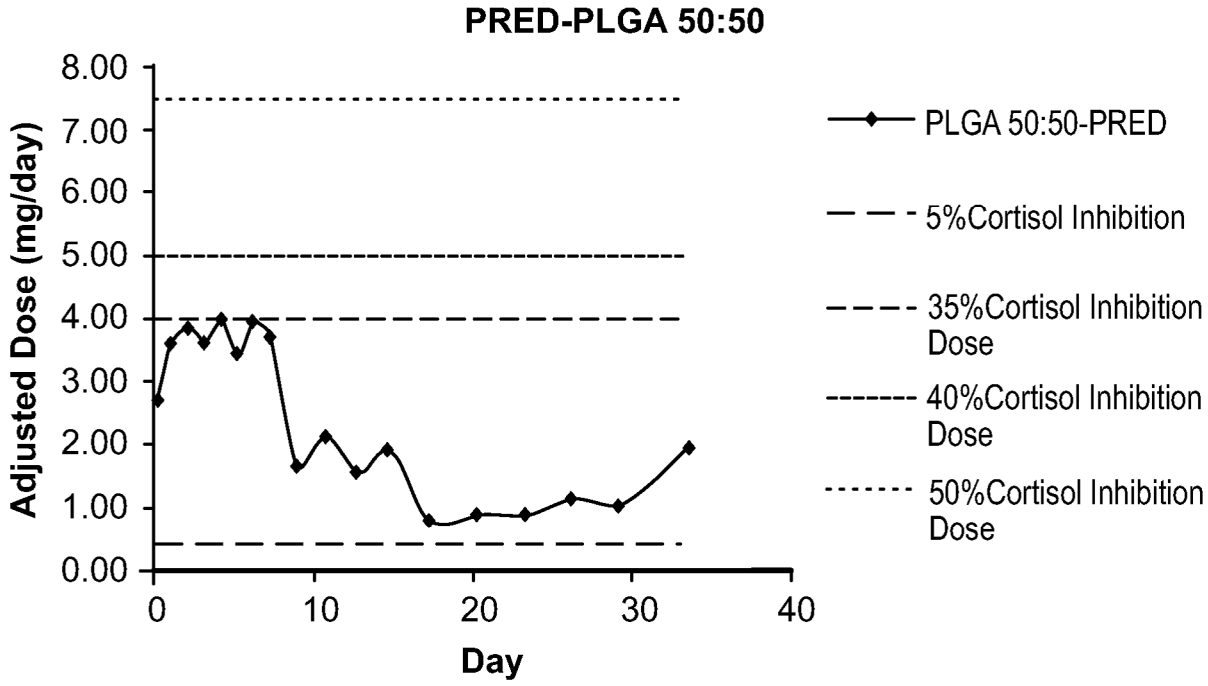

PRED-PLGA 50:50
Adjusted Dose (mg/day)
8.00
7.00
6.00
5.00
4.00
3.00
2.00
1.00
0.00
0
10
20
30
40
Day
PLGA 50:50-PRED
5%Cortisol Inhibition
35%Cortisol Inhibition Dose
40%Cortisol Inhibition Dose
50%Cortisol Inhibition Dose

FIG. 32

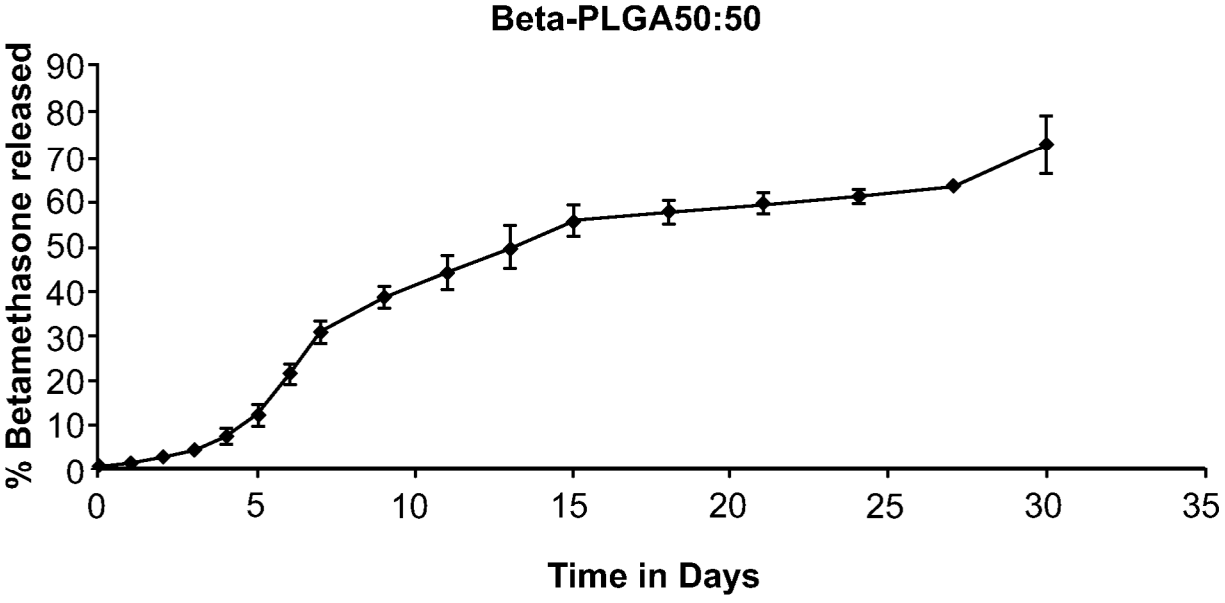

Beta-PLGA50:50
% Betamethasone released
90
80
70
60
50
40
30
20
10
0
0
5
10
15
20
25
30
35
Time in Days

FIG. 33

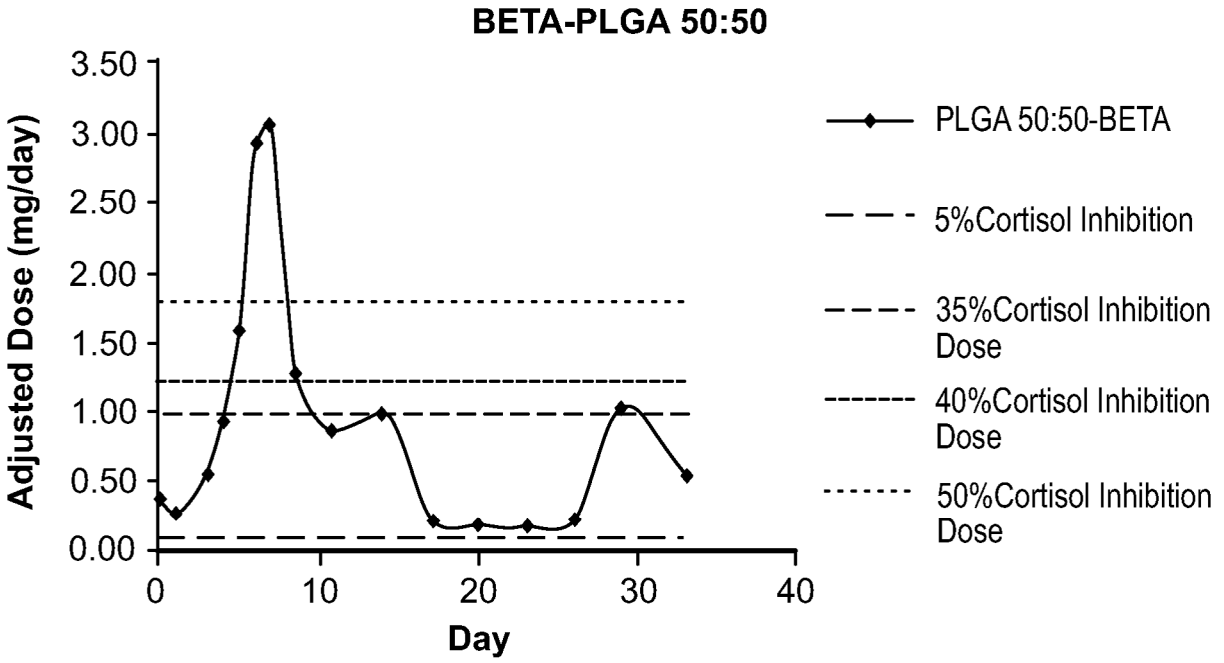

BETA-PLGA 50:50
Adjusted Dose (mg/day)
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
0
10
20
30
40
Day
PLGA 50:50-BETA
5%Cortisol Inhibition
35%Cortisol Inhibition Dose
40%Cortisol Inhibition Dose
50%Cortisol Inhibition Dose

FIG. 34

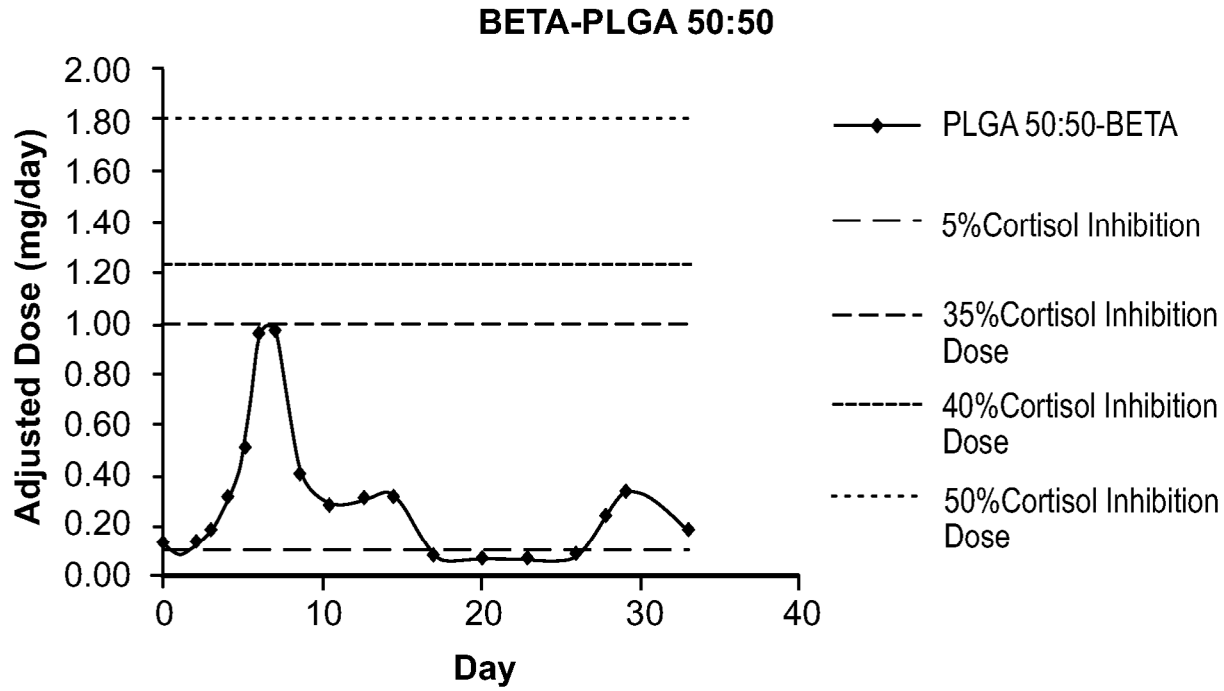

BETA-PLGA 50:50
Adjusted Dose (mg/day)
2.00
1.80
1.60
1.40
1.20
1.00
0.80
0.60
0.40
0.20
0.00
0
10
20
30
40
Day
PLGA 50:50-BETA
5%Cortisol Inhibition
35%Cortisol Inhibition Dose
40%Cortisol Inhibition Dose
50%Cortisol Inhibition Dose

FIG. 35

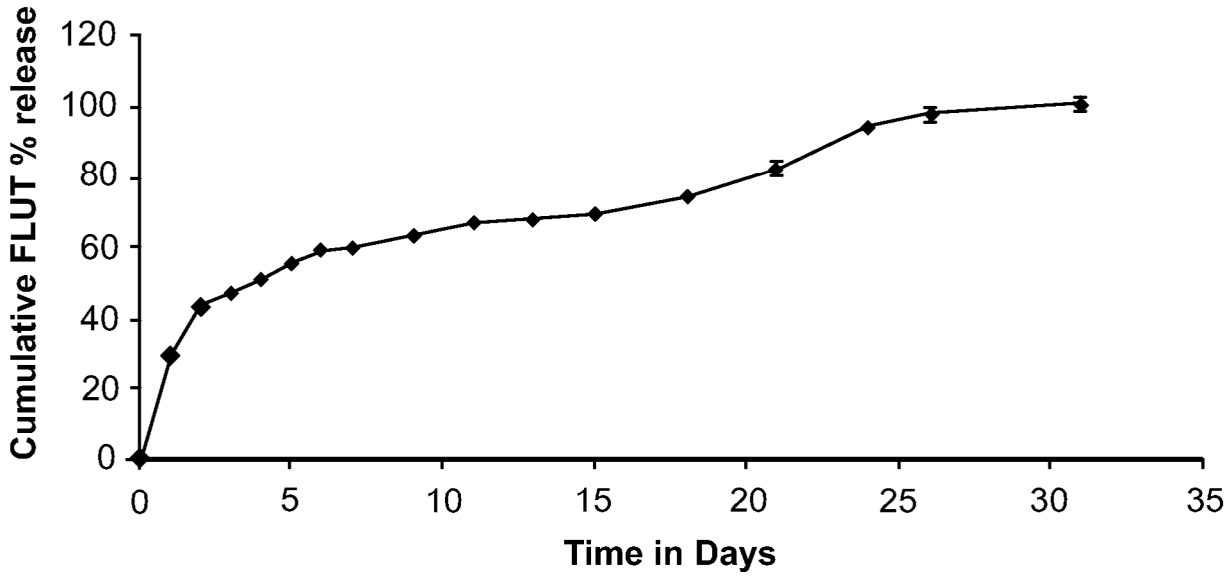

Cumulative FLUT % release
120
100
80
60
40
20
0
0
5
10
15
20
25
30
35
Time in Days

FIG. 36

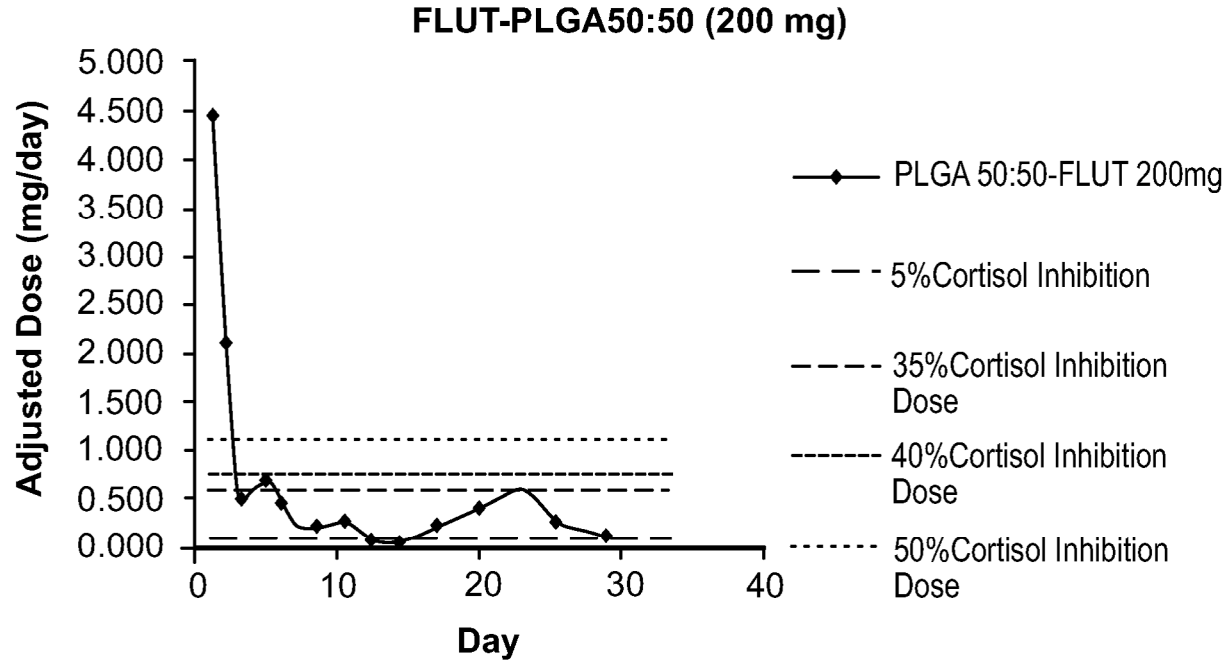

FLUT-PLGA50:50 (200 mg)
Adjusted Dose (mg/day)
5.000
4.500
4.000
3.500
3.000
2.500
2.000
1.500
1.000
0.500
0.000
0
10
20
30
40
Day
PLGA 50:50-FLUT 200mg
5%Cortisol Inhibition
35%Cortisol Inhibition Dose
40%Cortisol Inhibition Dose
50%Cortisol Inhibition Dose

FIG. 37

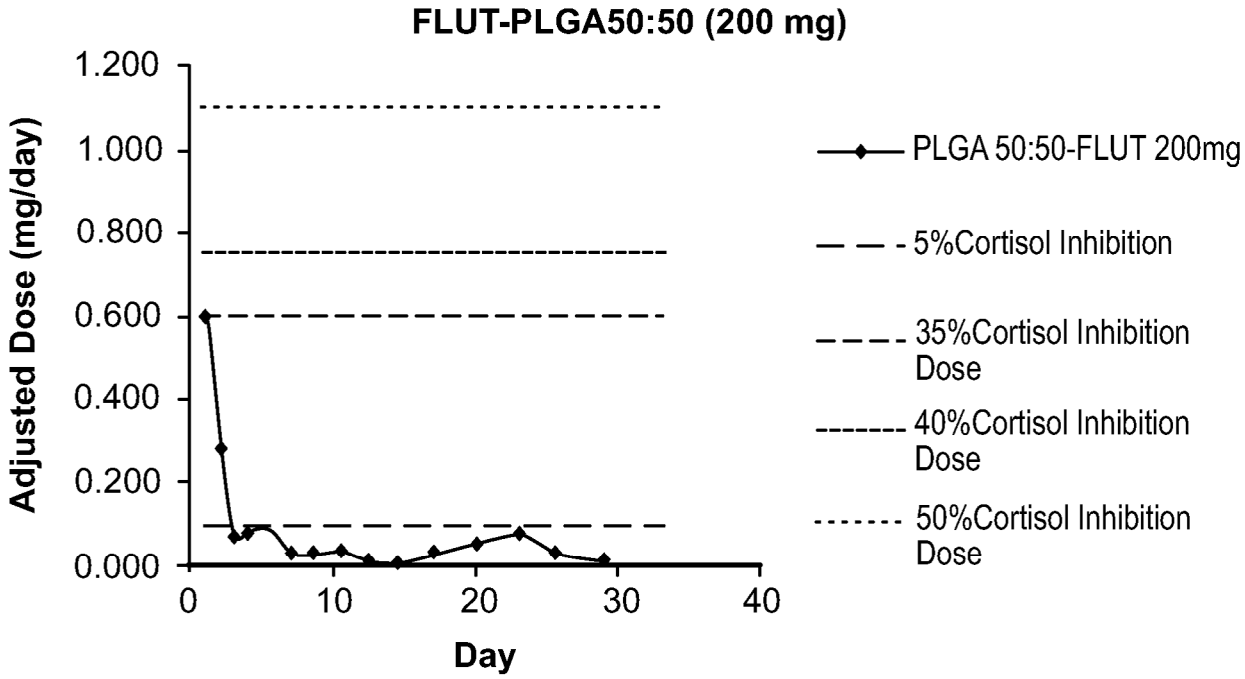

FLUT-PLGA50:50 (200 mg)
Adjusted Dose (mg/day)
1.200
1.000
0.800
0.600
0.400
0.200
0.000
0
10
20
30
40
Day
PLGA 50:50-FLUT 200mg
5%Cortisol Inhibition
35%Cortisol Inhibition Dose
40%Cortisol Inhibition Dose
50%Cortisol Inhibition Dose

FIG. 38

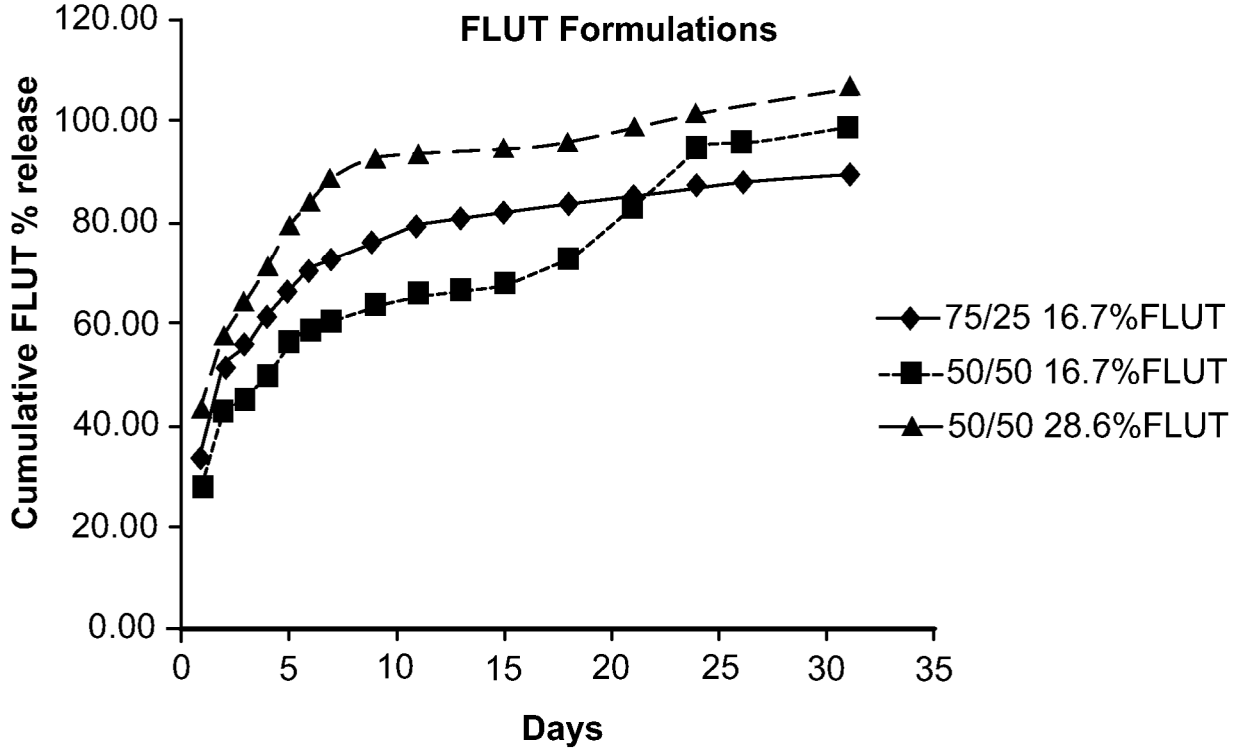

FLUT Formulations
Cumulative FLUT % release
120.00
100.00
80.00
60.00
40.00
20.00
0.00
0
5
10
15
20
25
30
35
Days
75/25 16.7%FLUT
50/50 16.7%FLUT
50/50 28.6%FLUT

FIG. 39

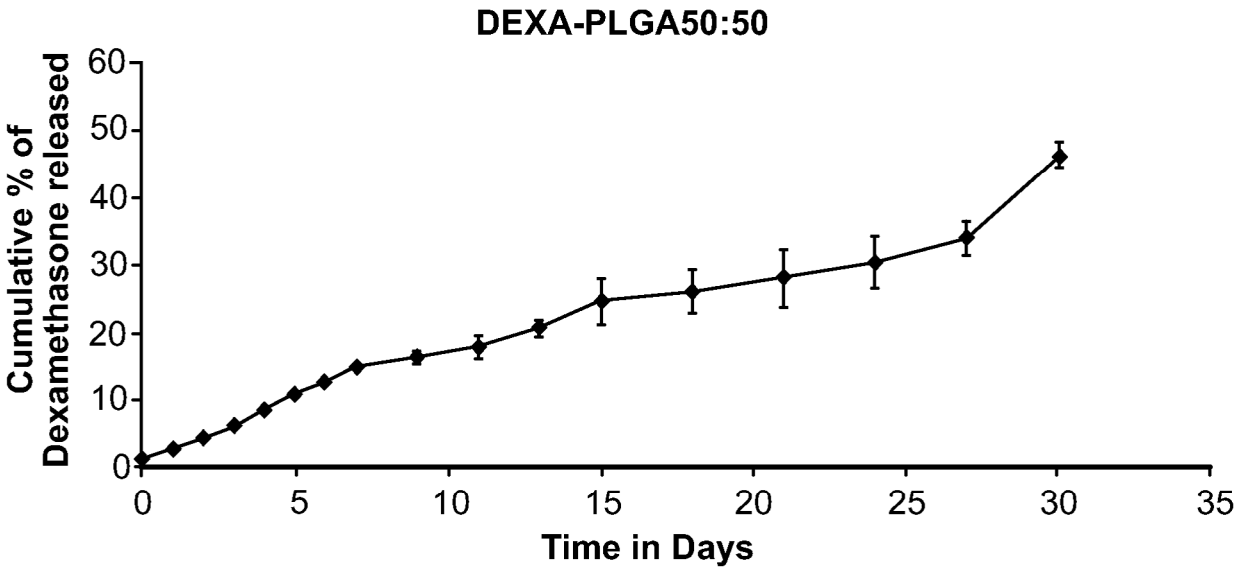

DEXA-PLGA50:50
Cumulative % of Dexamethasone released
60
50
40
30
20
10
0
0
5
10
15
20
25
30
35
Time in Days

FIG. 40

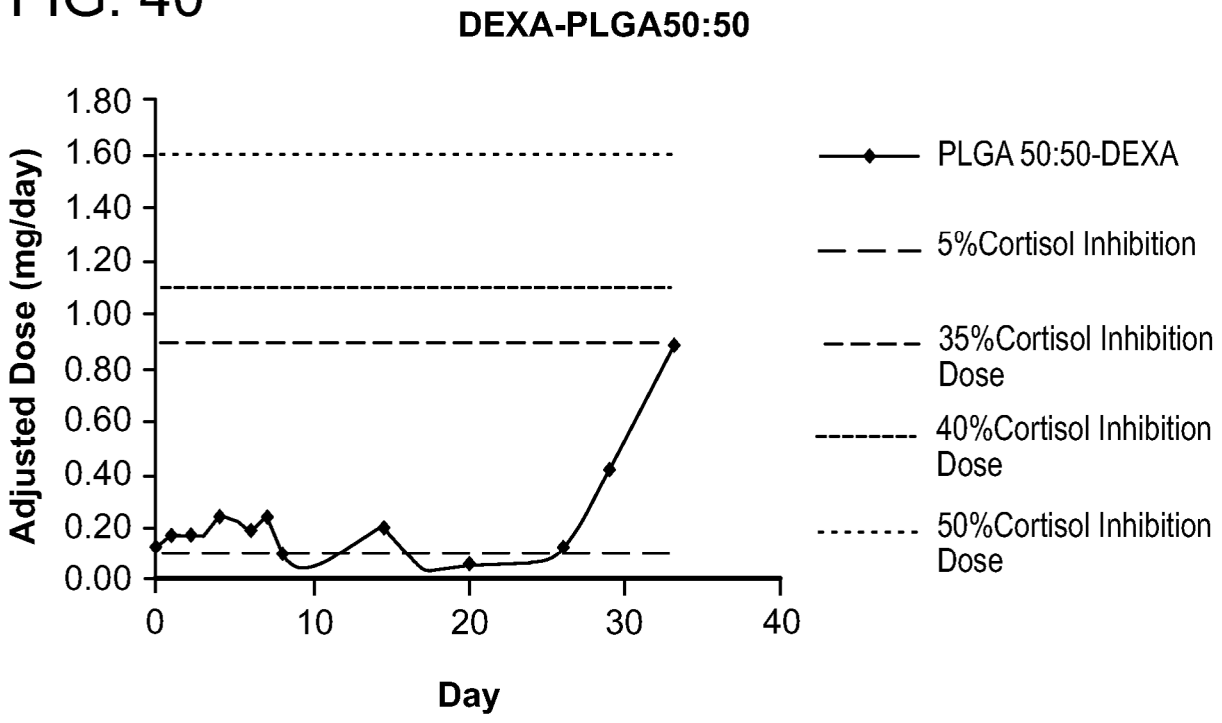

DEXA-PLGA50:50
Adjusted Dose (mg/day)
1.80
1.60
1.40
1.20
1.00
0.80
0.60
0.40
0.20
0.00
0
10
20
30
40
Day
PLGA 50:50-DEXA
5%Cortisol Inhibition
35%Cortisol Inhibition Dose
40%Cortisol Inhibition Dose
50%Cortisol Inhibition Dose

FIG. 41A

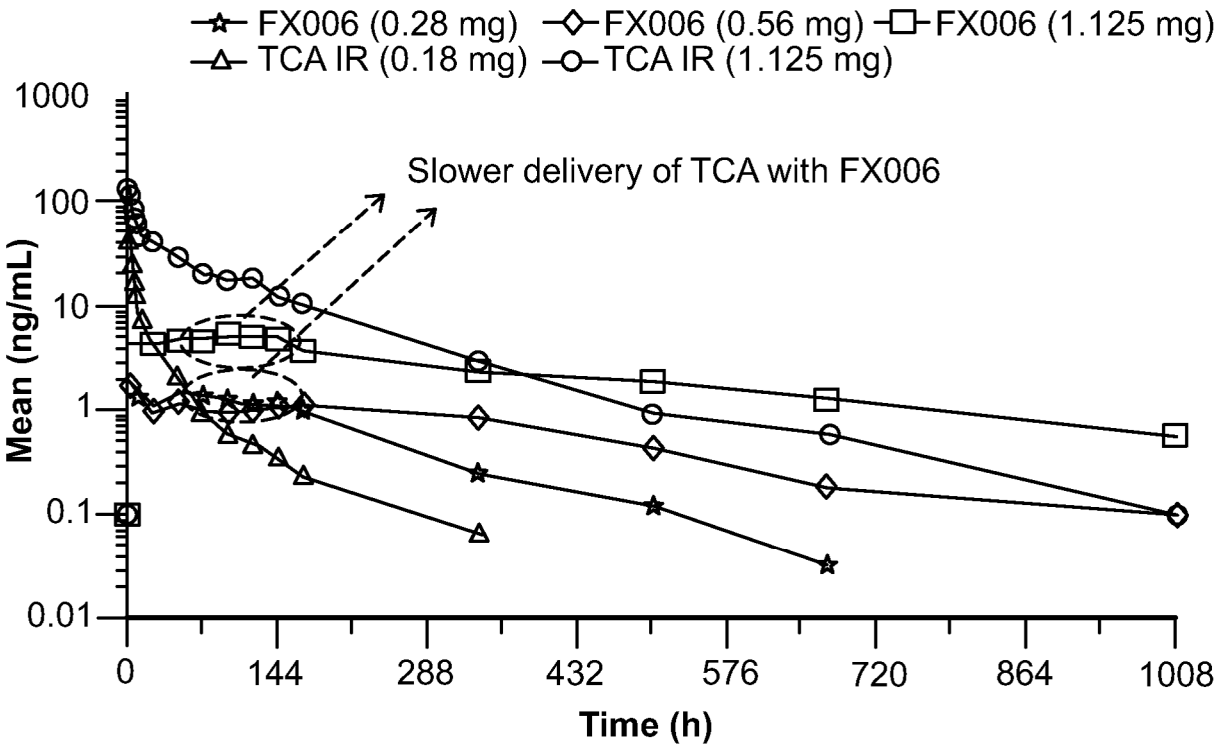


FIG. 41B

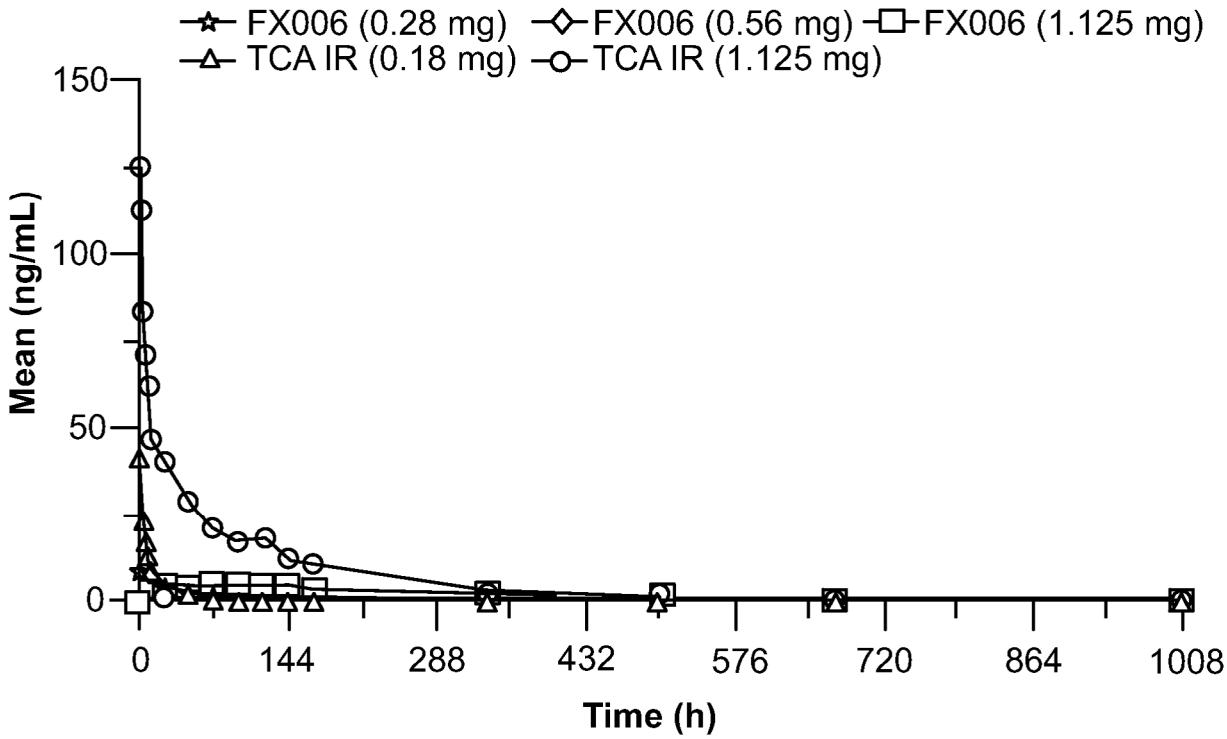


FIG. 41C

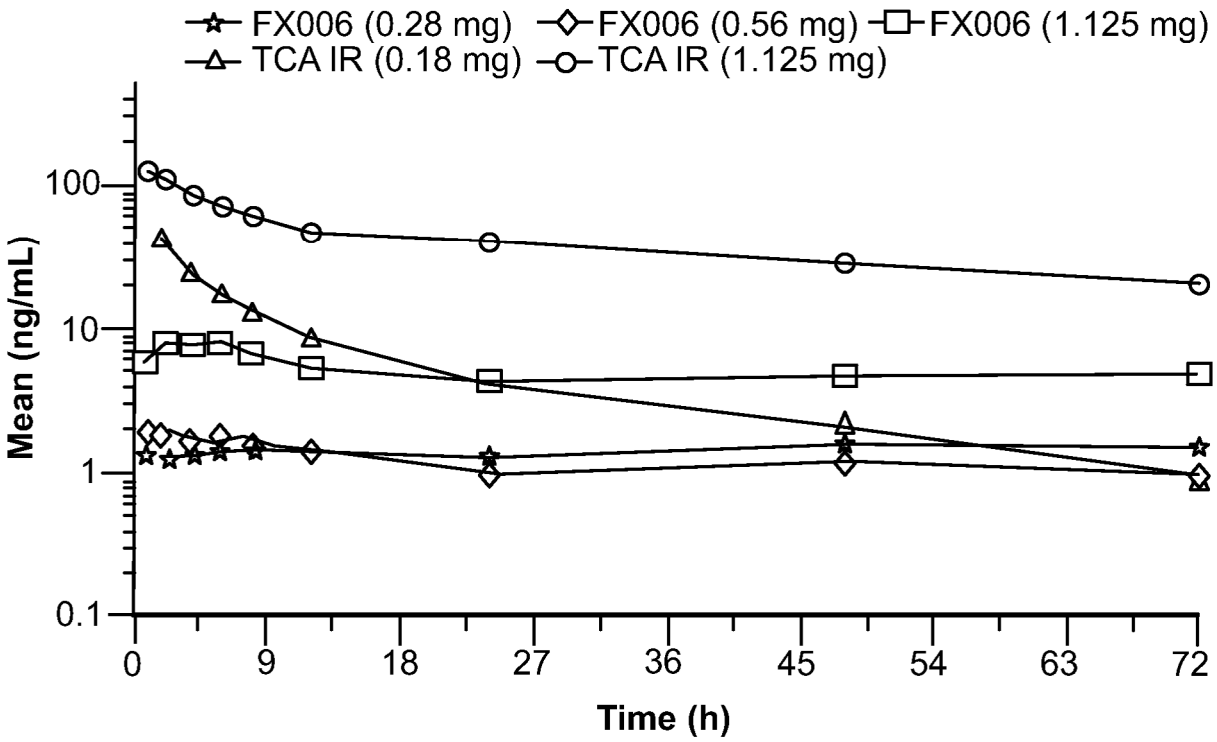


FIG. 41D

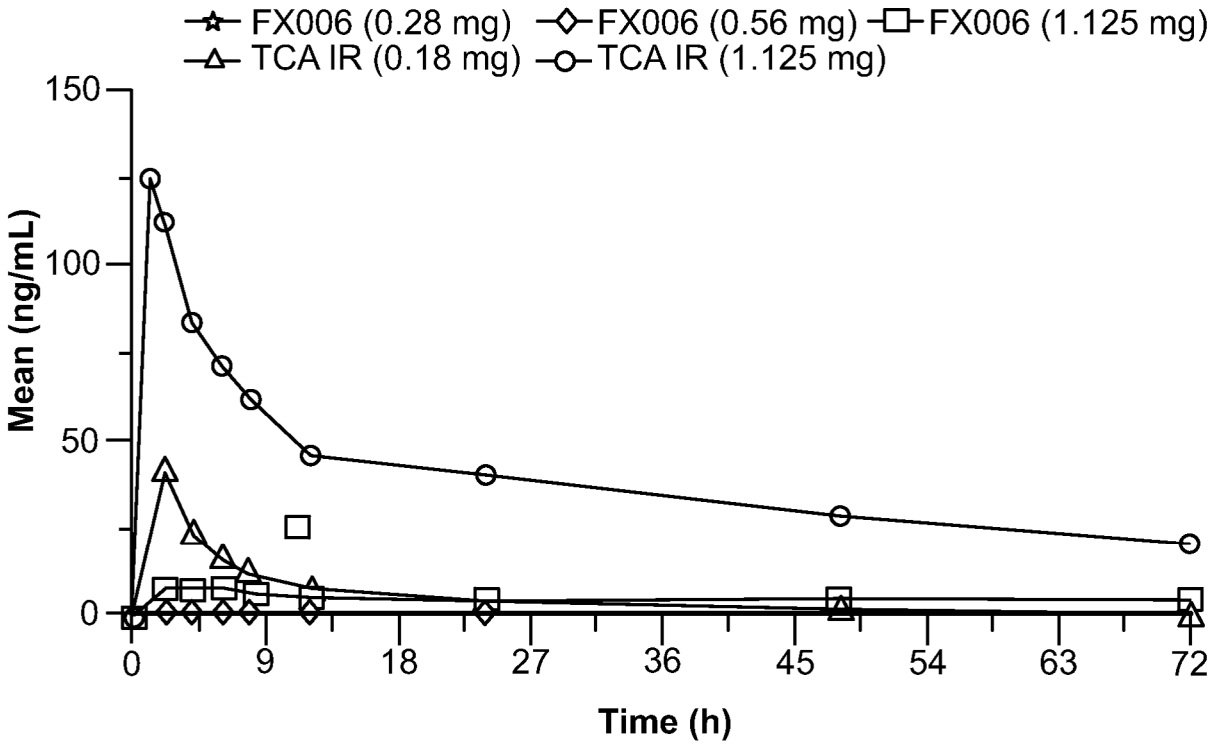


FIG. 42

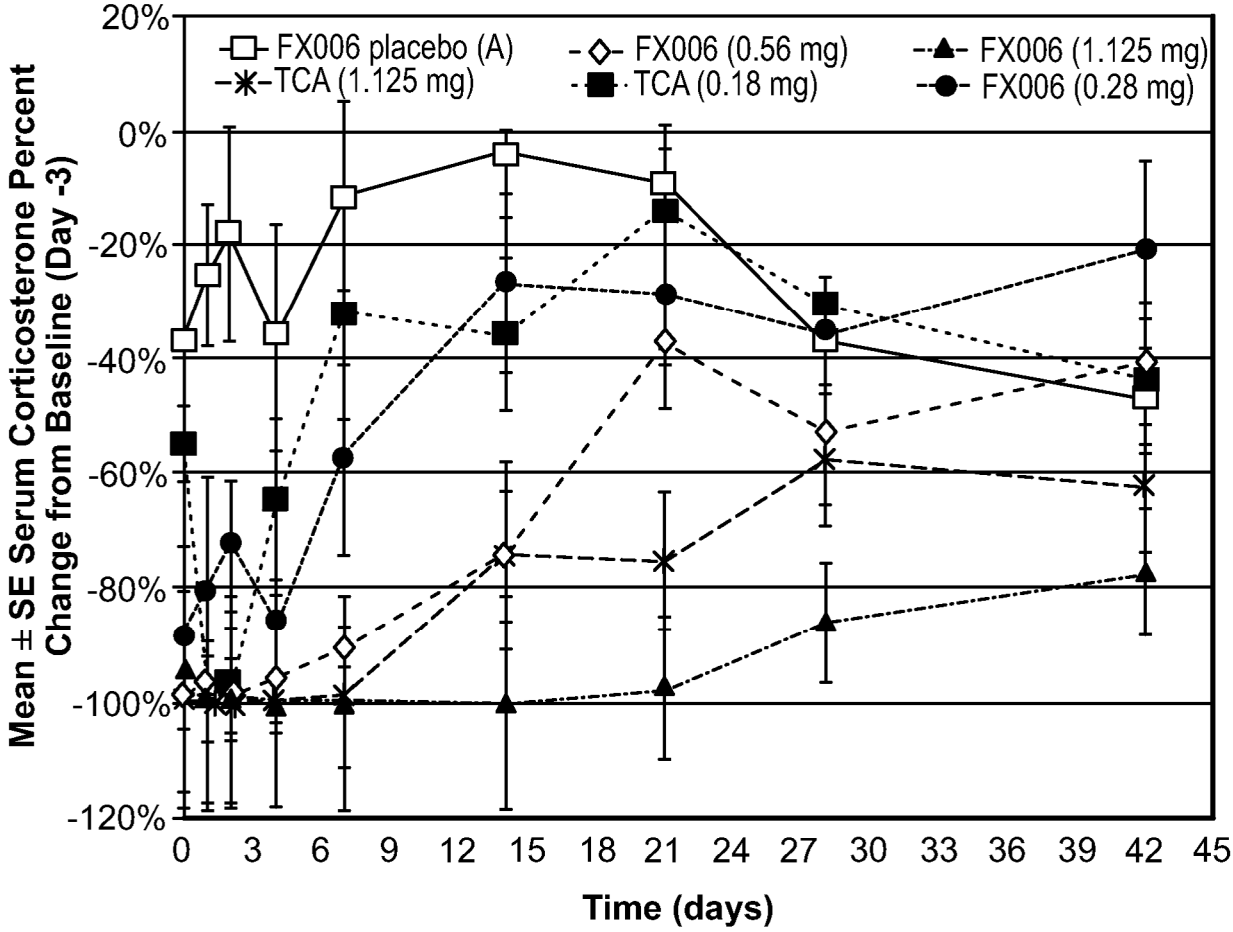

FX006 placebo (A)
FX006 (0.56 mg)
FX006 (1.125 mg)
TCA (1.125 mg)
TCA (0.18 mg)
FX006 (0.28 mg)
Mean ± SE Serum Corticosterone Percent Change from Baseline (Day -3)
20%
0%
-20%
-40%
-60%
-80%
-100%
-120%
0 3 6 9 12 15 18 21 24 27 30 33 36 39 42 45
Time (days)

FIG. 43

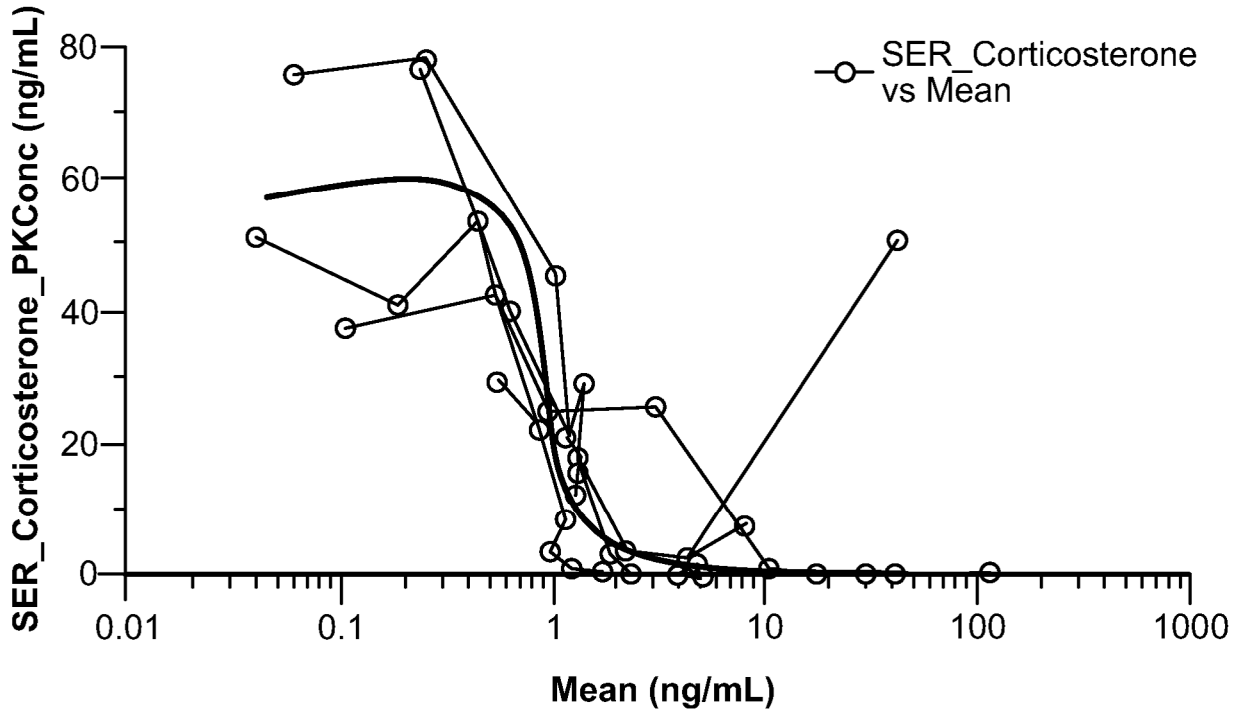

SER_Corticosterone vs Mean
SER_Corticosterone_PKConc (ng/mL)
80
60
40
20
0
0.01 0.1 1 10 100 1000
Mean (ng/mL)

FIG. 44A

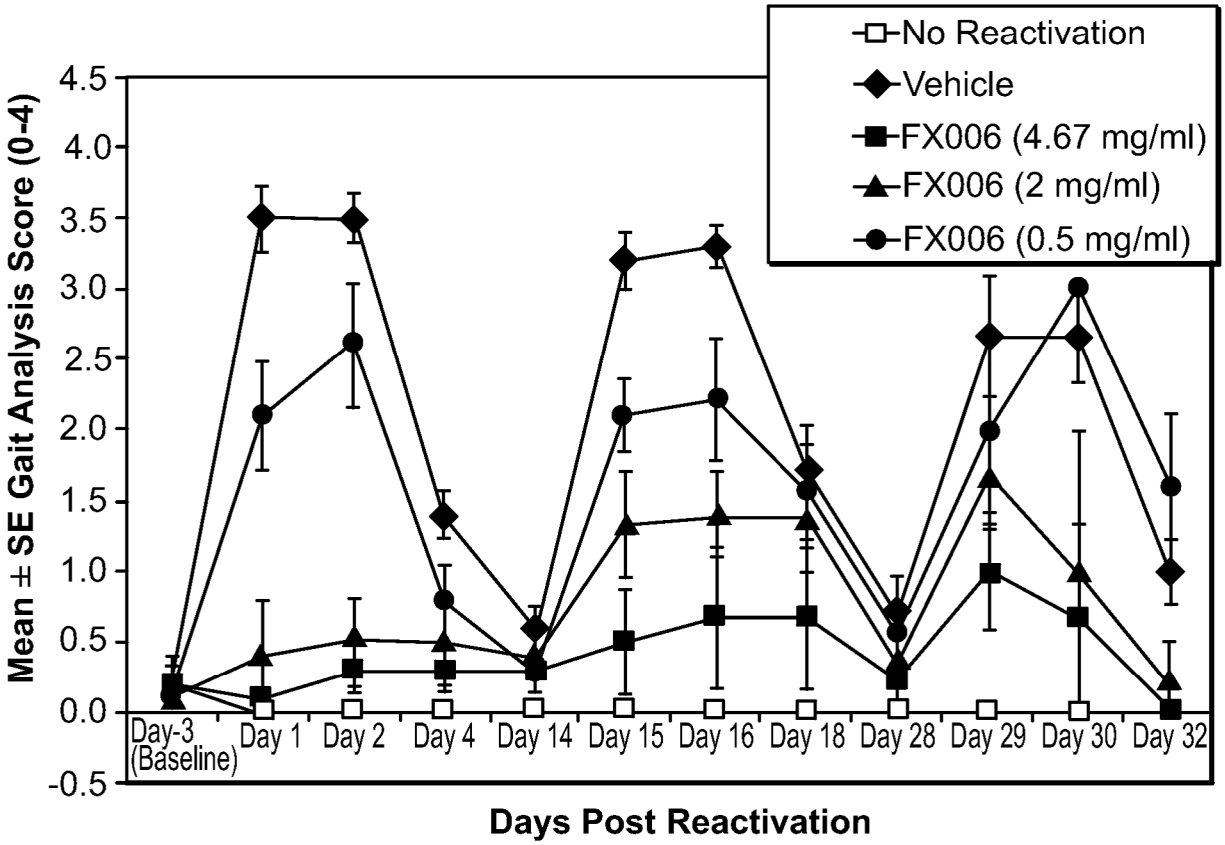


FIG. 44B

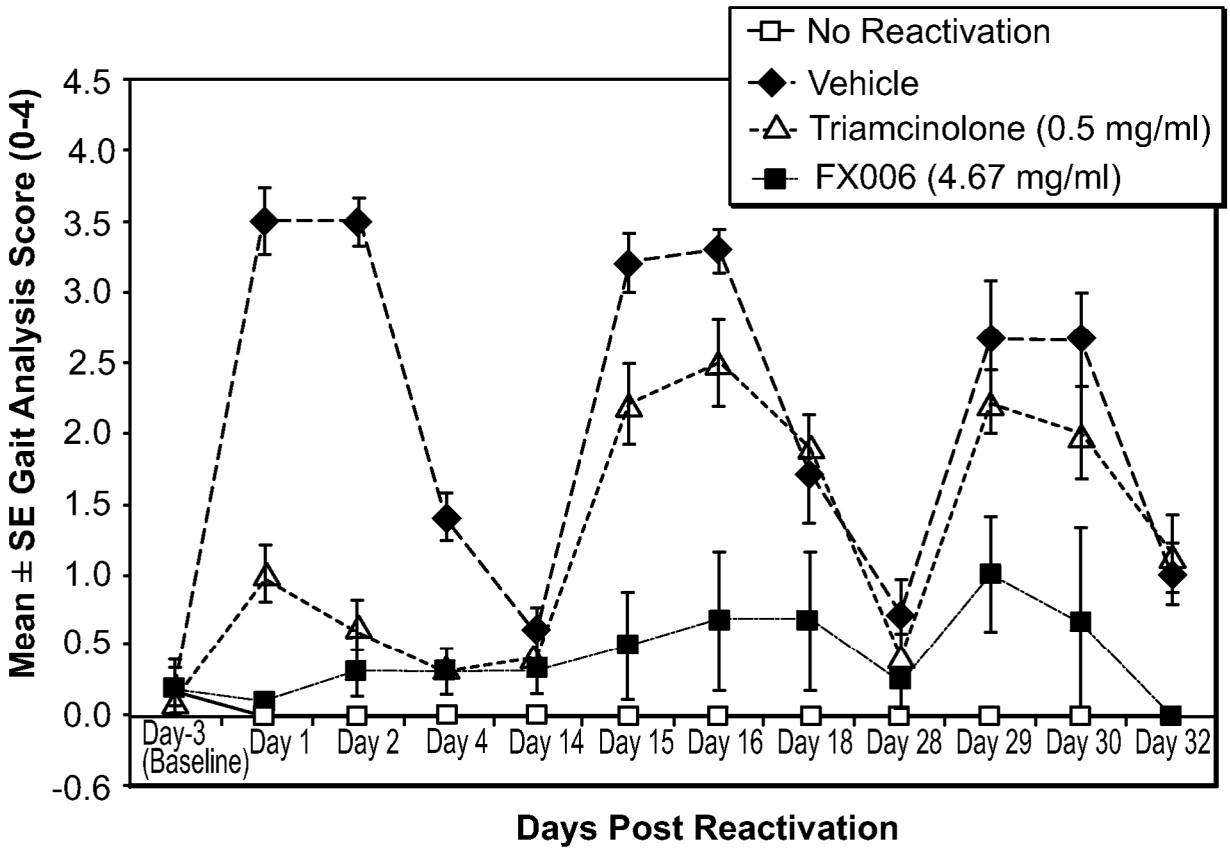


FIG. 44C

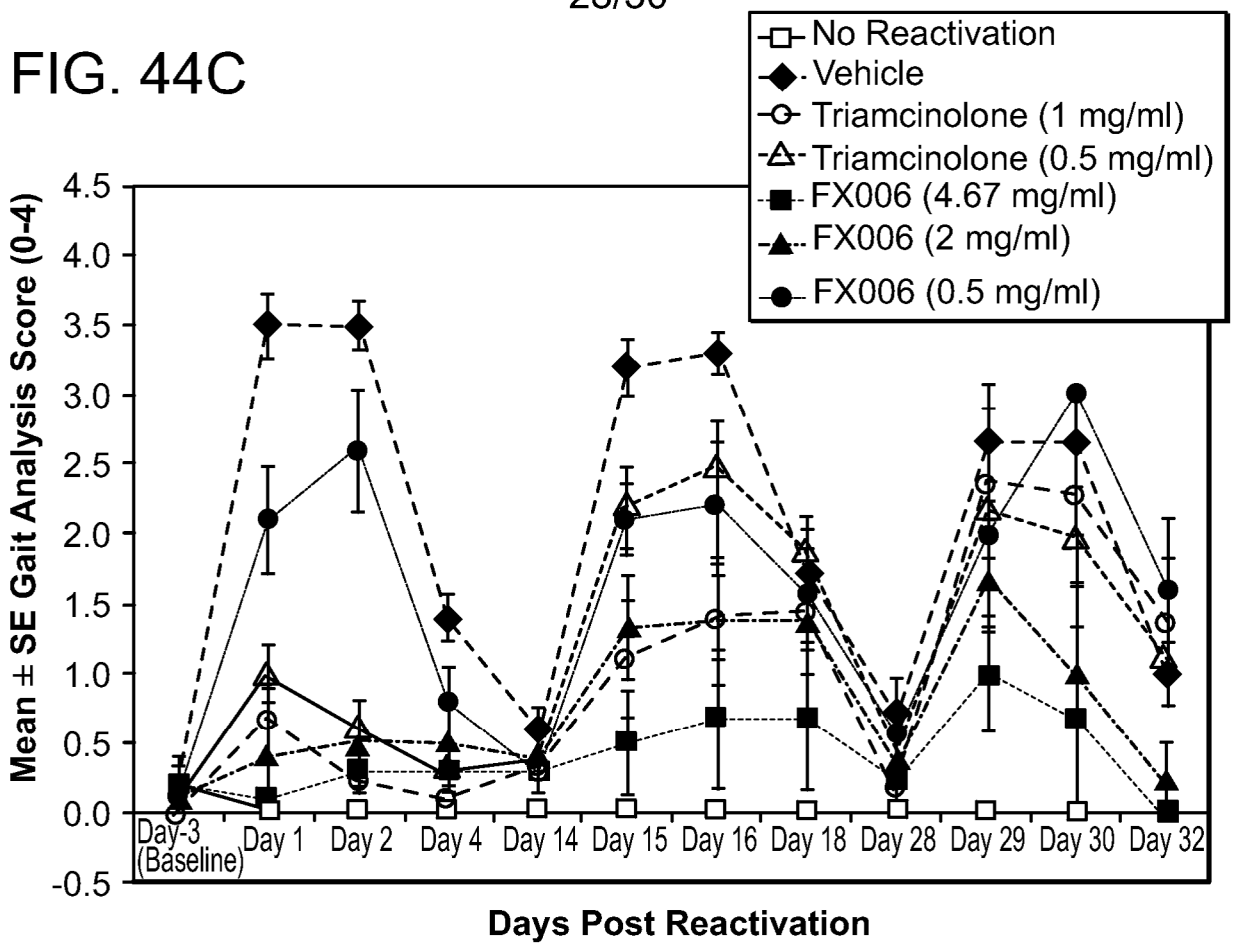
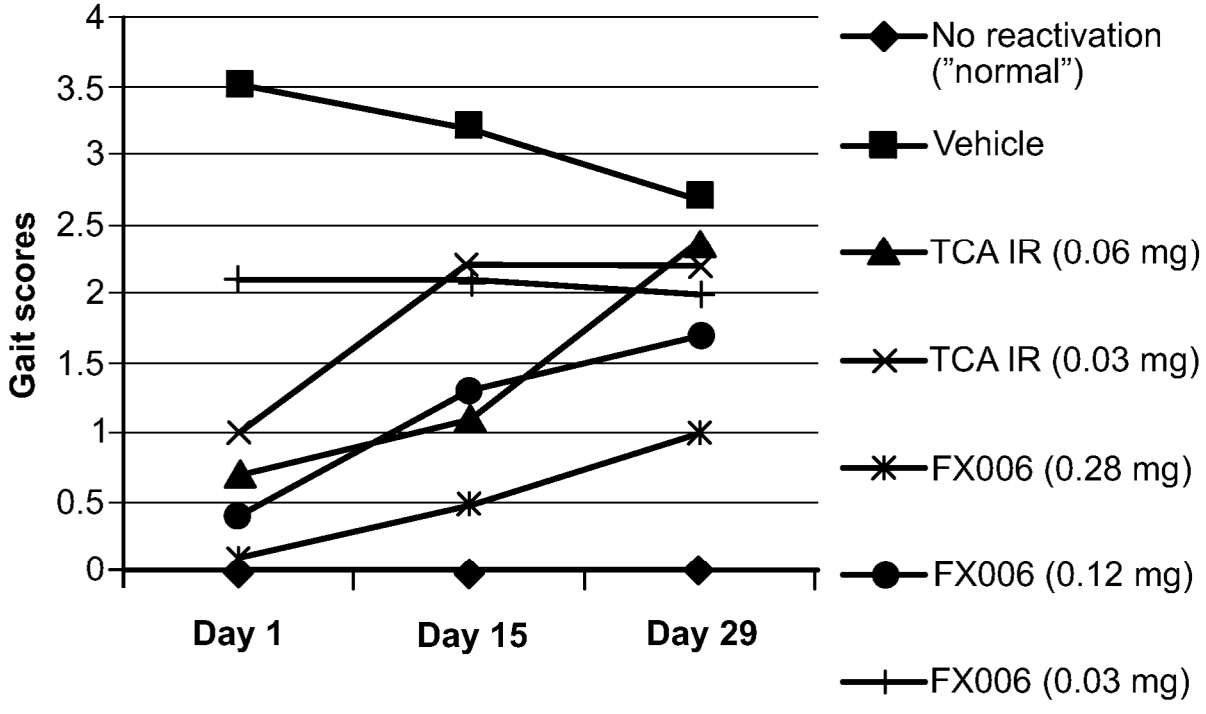


FIG. 45



Peak pain response upon reactivation of knee arthritis

FIG. 46

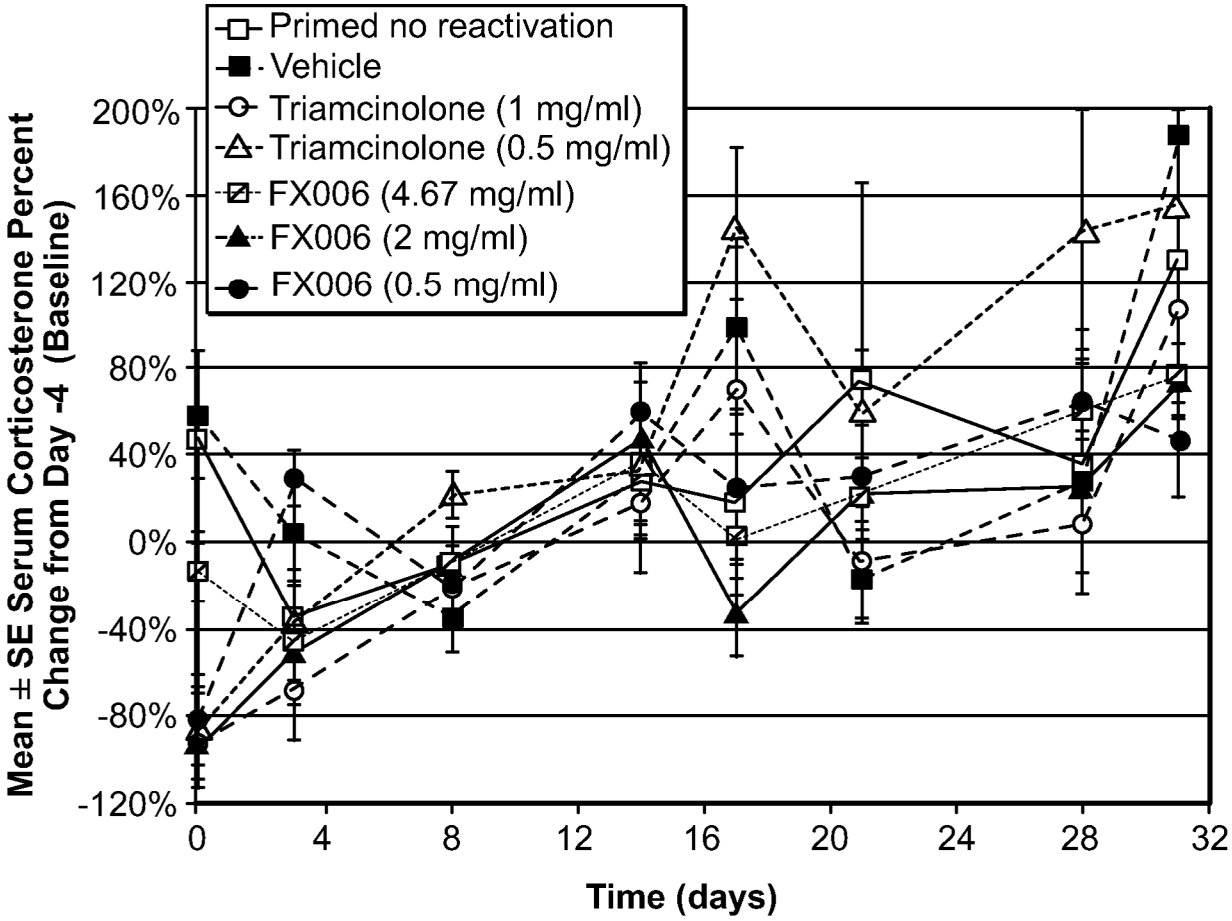


FIG. 47A

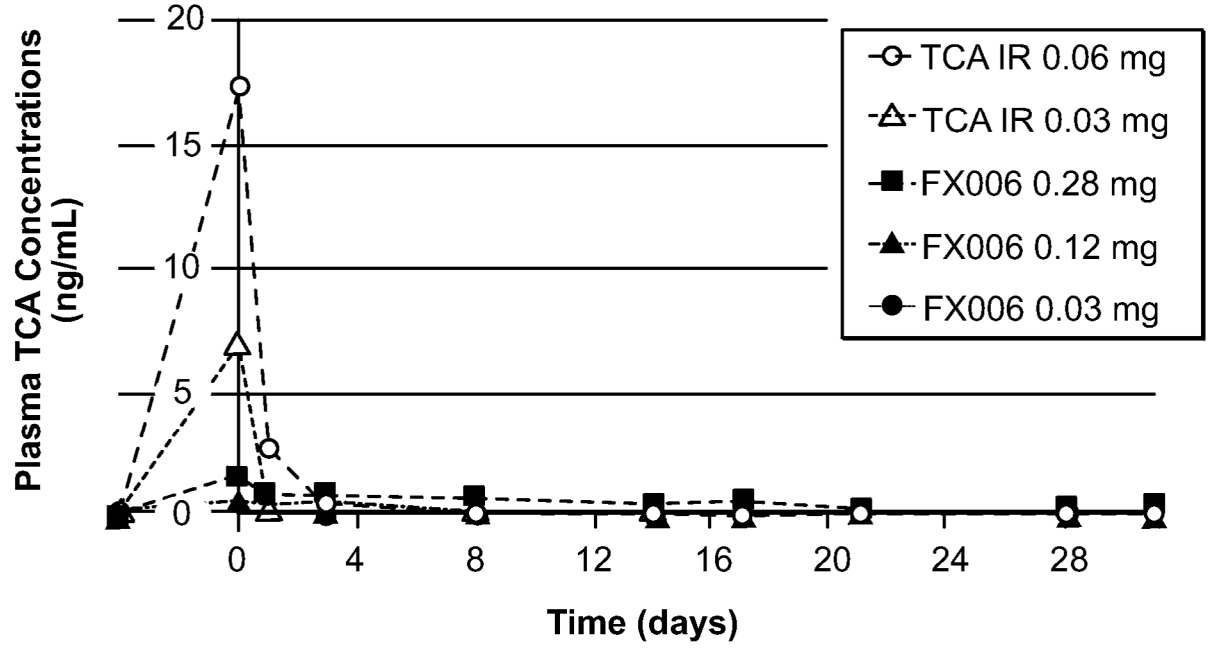


FIG. 47B

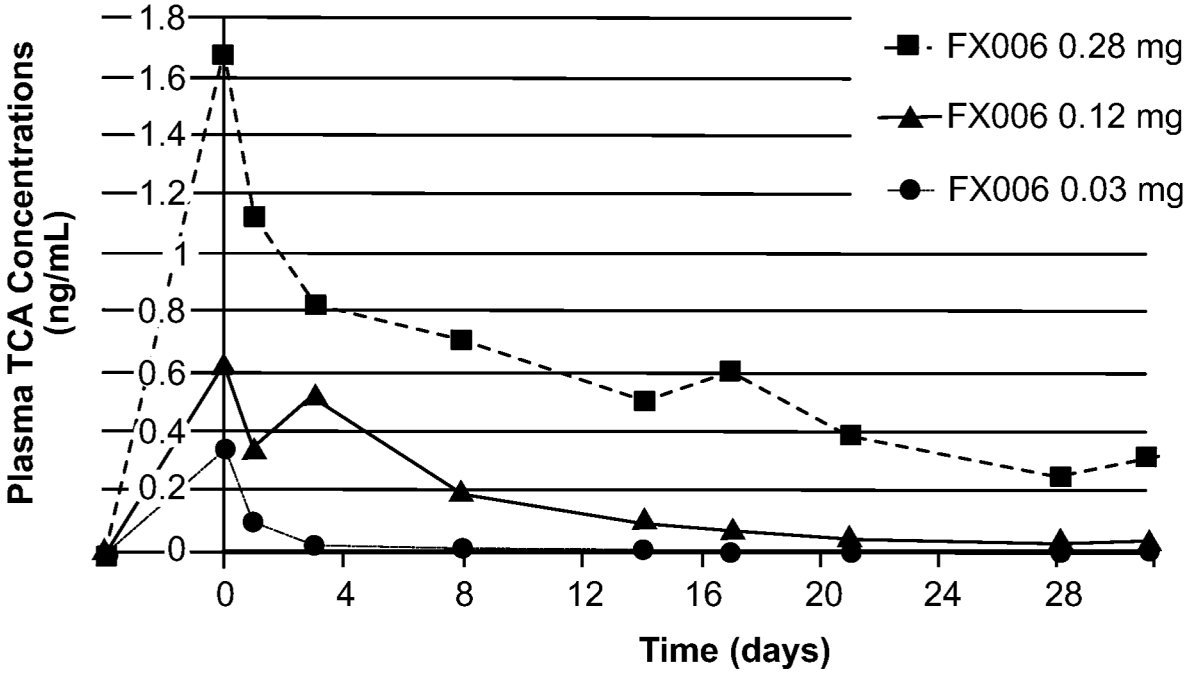


FIG. 48

