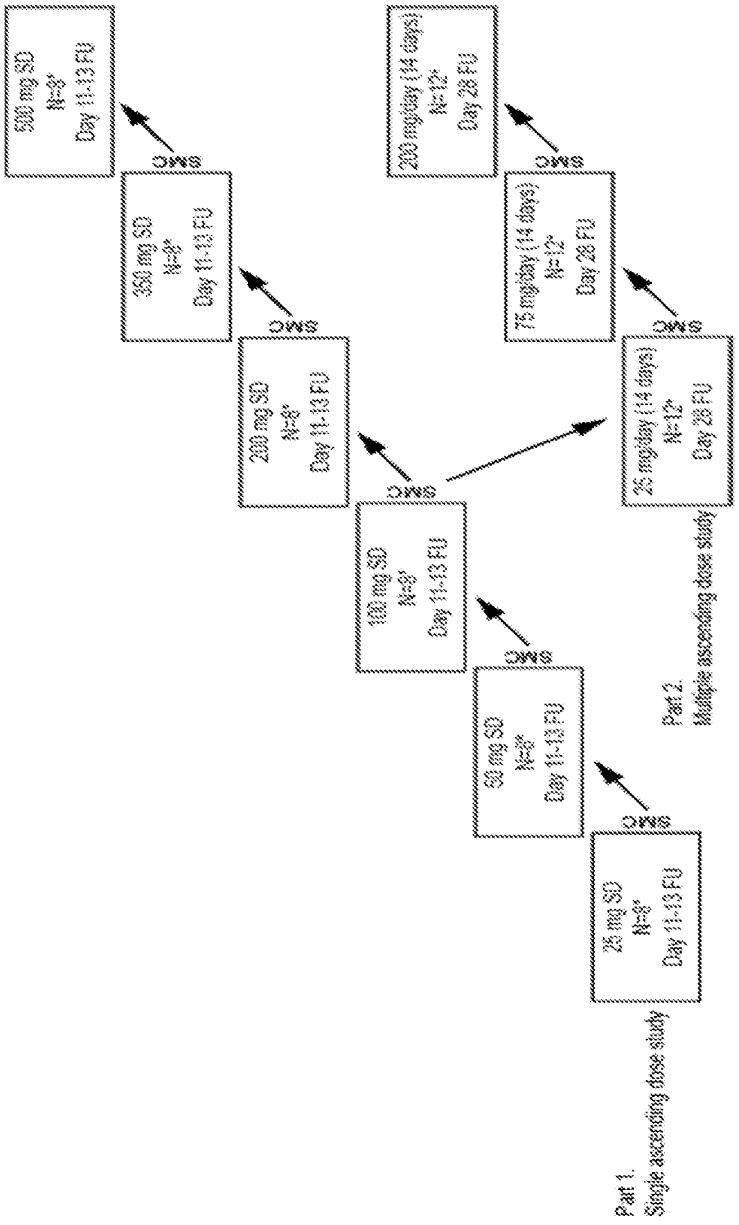

Part 1.
Single ascending dose study
Part 2.
Multiple ascending dose study
SMC
SMC
SMC
SMC
SMC
SMC
SMC
SMC
SMC
25 mg SD
N=8*
Day 11-13 FU
50 mg SD
N=8*
Day 11-13 FU
100 mg SD
N=8*
Day 11-13 FU
200 mg SD
N=8*
Day 11-13 FU
350 mg SD
N=8*
Day 11-13 FU
500 mg SD
N=8*
Day 11-13 FU
25 mg/day (14 days)
N=12*
Day 28 FU
75 mg/day (14 days)
N=12*
Day 28 FU
200 mg/day (14 days)
N=12*
Day 28 FU

FIG. 1

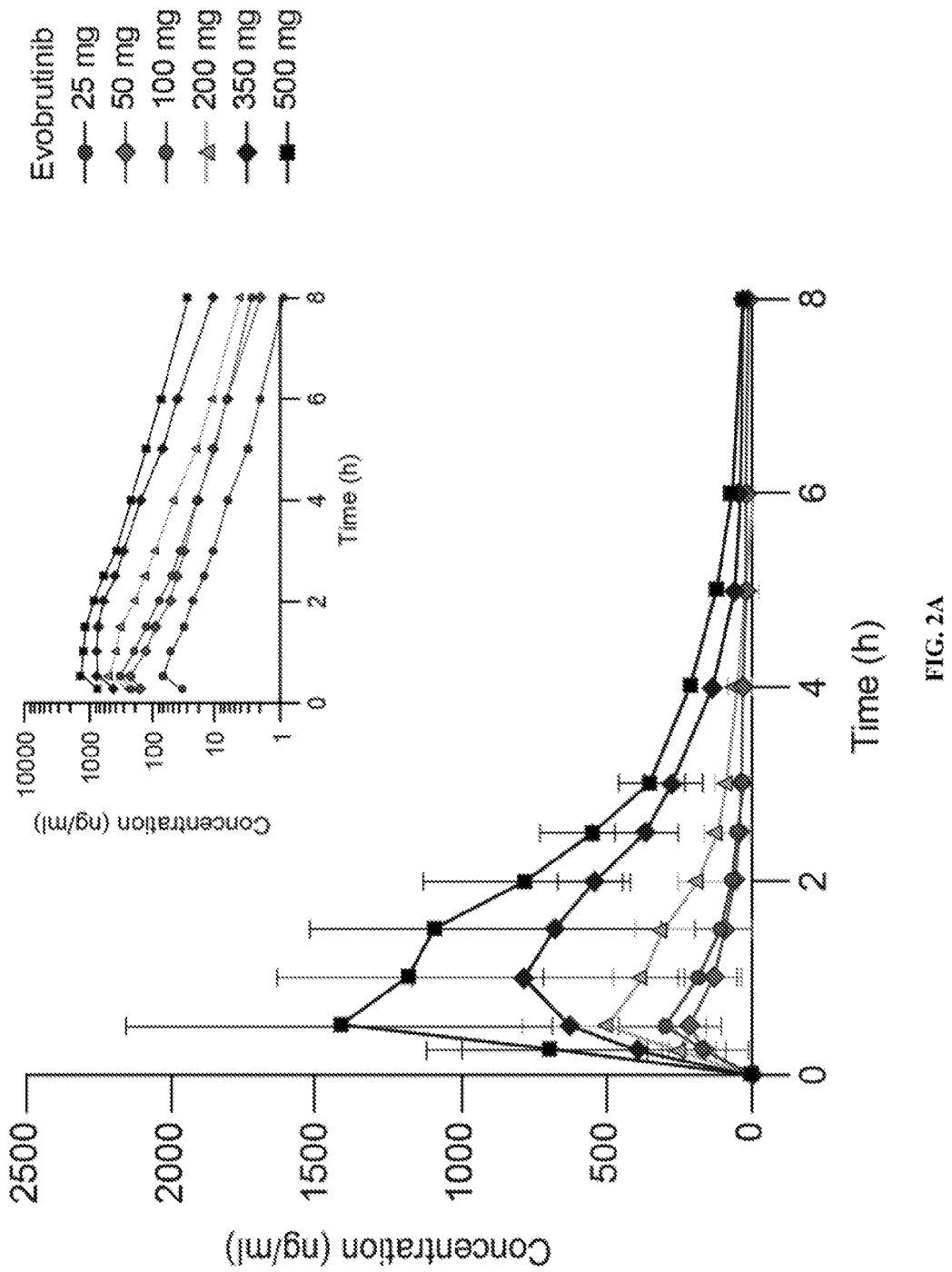

Evobrutinib
25 mg
50 mg
100 mg
200 mg
350 mg
500 mg
Concentration (ng/ml)
Time (h)
Concentration (ng/ml)
Time (h)

FIG. 2A

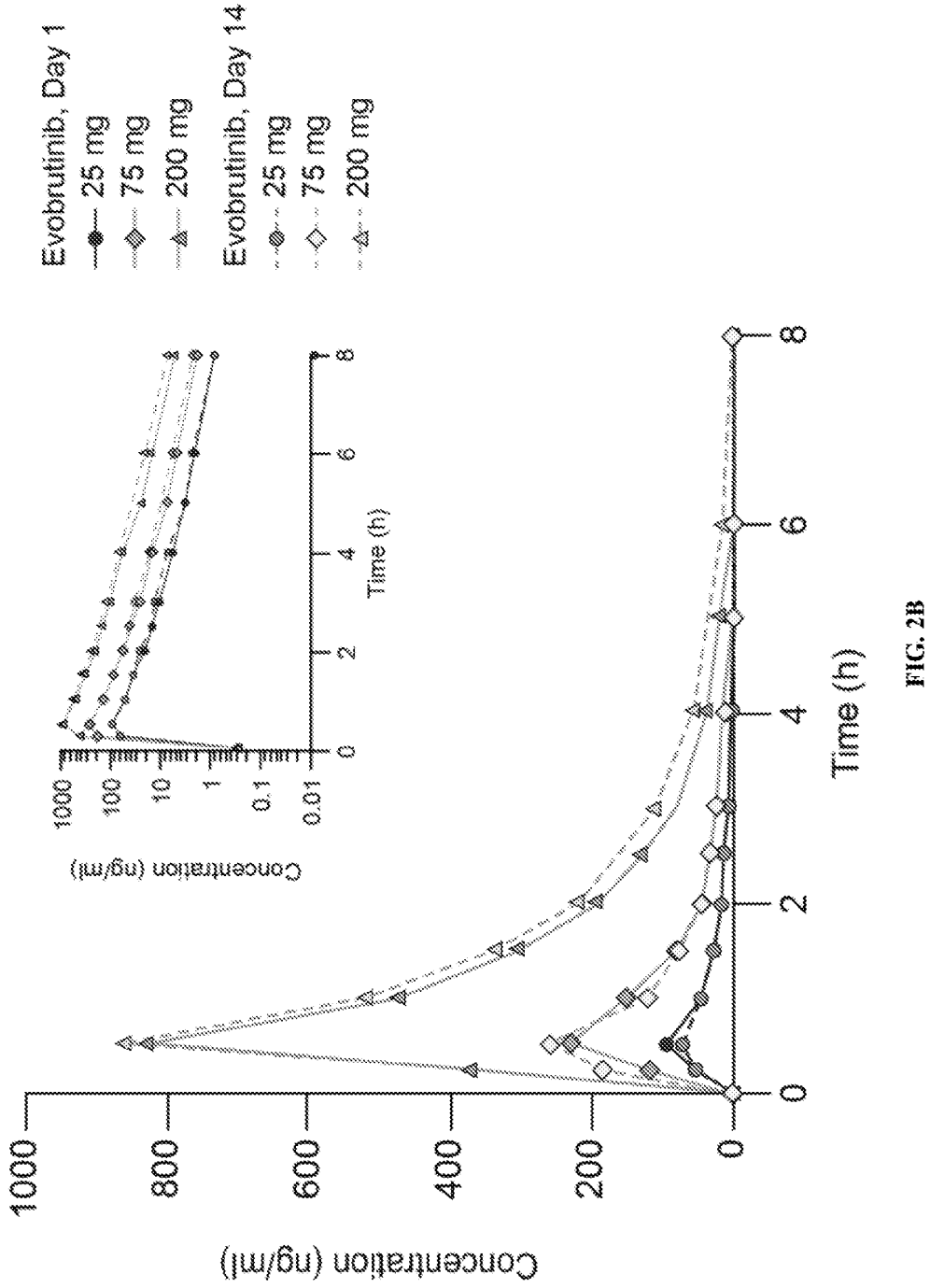

Evobrutinib, Day 1
25 mg
75 mg
200 mg
Evobrutinib, Day 14
25 mg
75 mg
200 mg
Concentration (ng/ml)
1000
800
600
400
200
0
0
2
4
6
8
Time (h)
Concentration (ng/ml)
1000
100
10
1
0.1
0.01
0
2
4
6
8
Time (h)

FIG. 2B

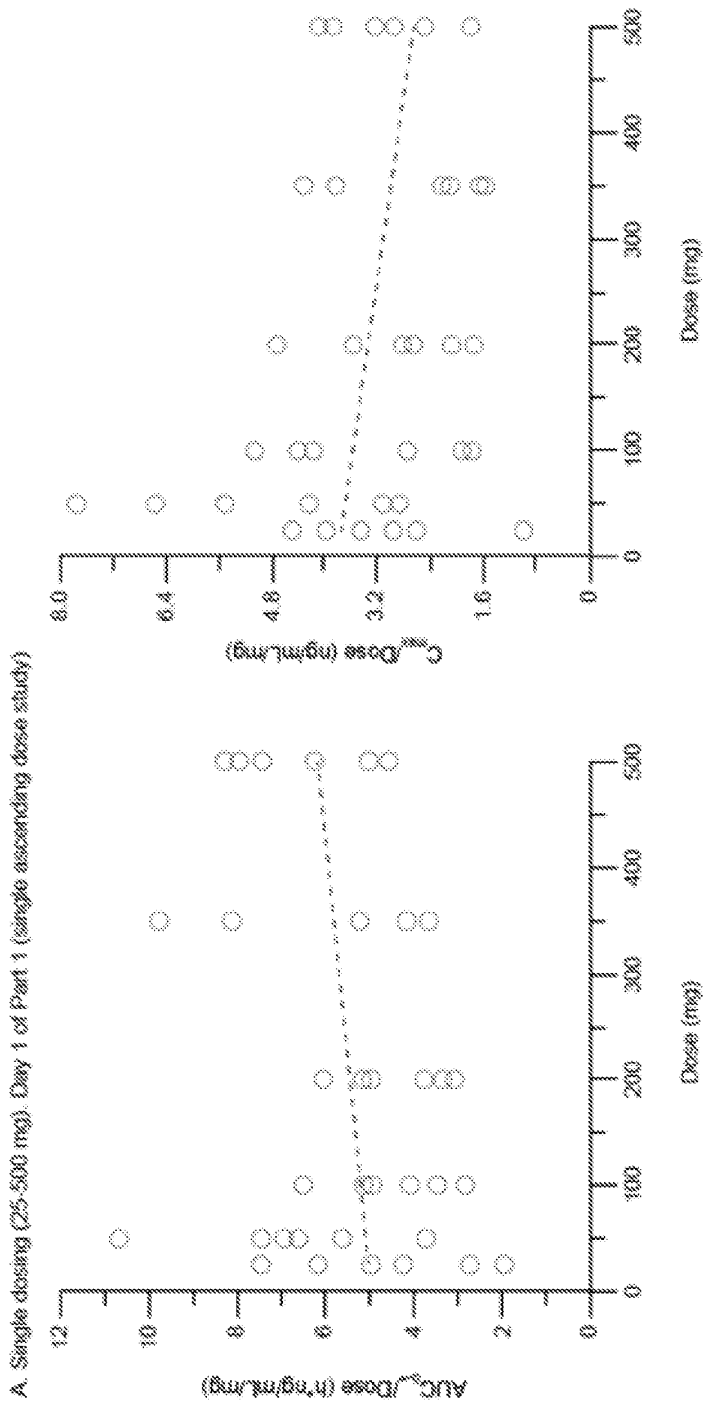

A. Single dosing (25-500 mg): Day 1 of Part 1 (single ascending dose study)
AUC∞/Dose (h*ng/mL/mg)
0
2
4
6
8
10
12
0
100
200
300
400
500
Dose (mg)
C∞/Dose (ng/mL/mg)
0.0
1.6
3.2
4.8
6.4
8.0
0
100
200
300
400
500
Dose (mg)

FIG. 3A

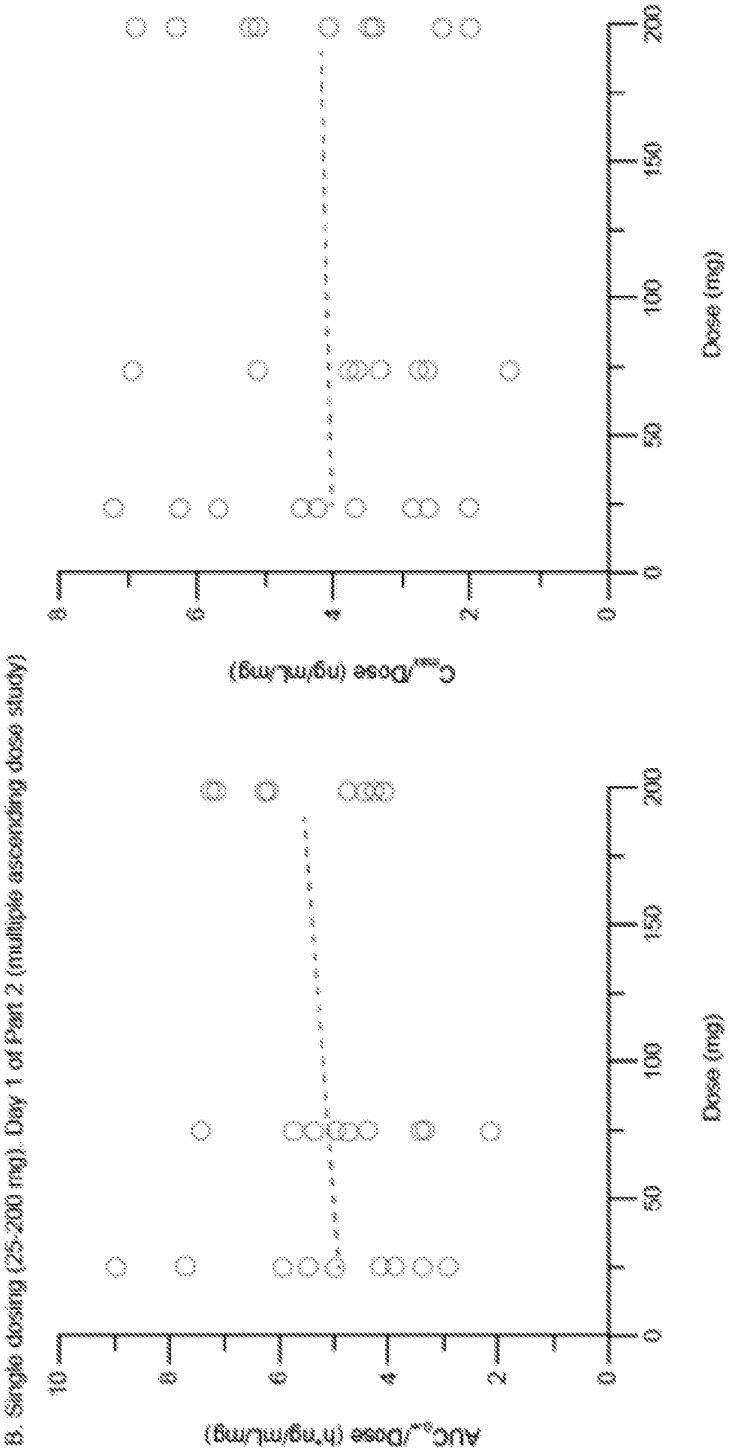

B. Single dosing (25-200 mg). Day 1 of Part 2 (multiple ascending dose study)
AUC∞/Dose (h*ng/mL/mg)
0
2
4
6
8
10
0
50
100
150
200
Dose (mg)
Cmax/Dose (ng/mL/mg)
0
2
4
6
8
0
50
100
150
200
Dose (mg)

FIG. 3B

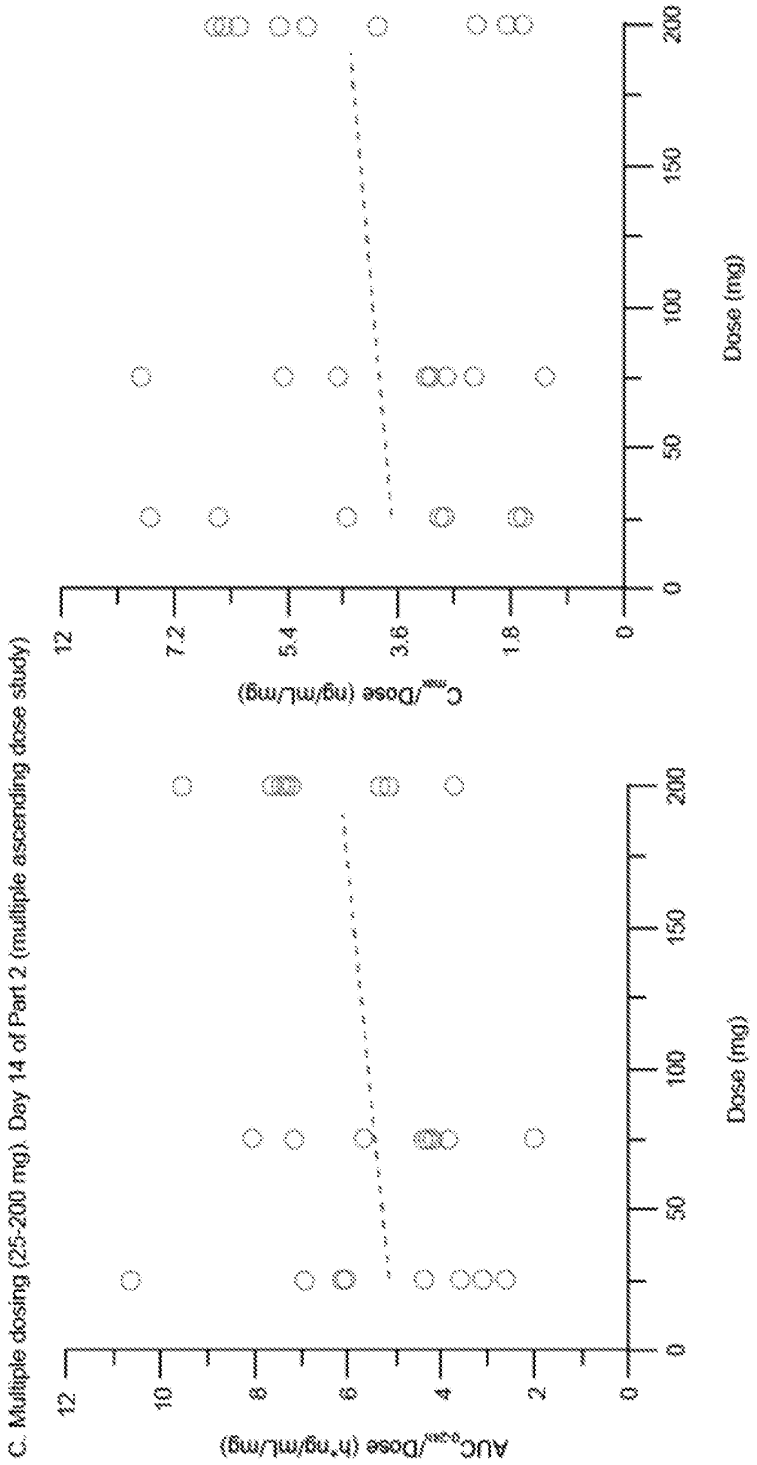

C. Multiple dosing (25-200 mg). Day 14 of Part 2 (multiple ascending dose study)
AUC$_{0-\infty}$/Dose (h*ng/mL/mg)
0
2
4
6
8
10
12
Dose (mg)
0
50
100
150
200
C$_{max}$/Dose (ng/mL/mg)
0
1.8
3.6
5.4
7.2
12
Dose (mg)
0
50
100
150
200

FIG. 3C

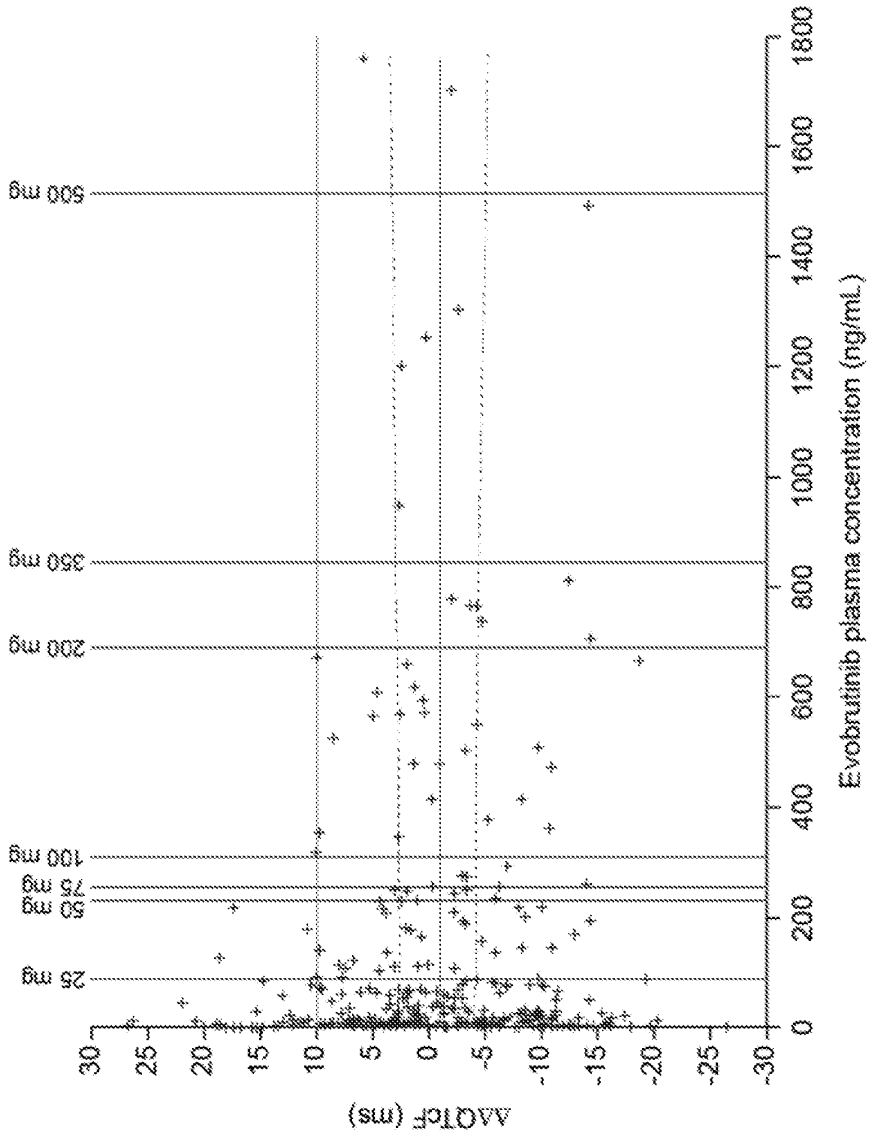

ΔΔQTcF (ms)
30
25
20
15
10
5
0
-5
-10
-15
-20
-25
-30
25 mg
50 mg
75 mg
100 mg
200 mg
350 mg
500 mg
0
200
400
600
800
1000
1200
1400
1600
1800
Evobrutinib plasma concentration (ng/mL)

FIG. 4

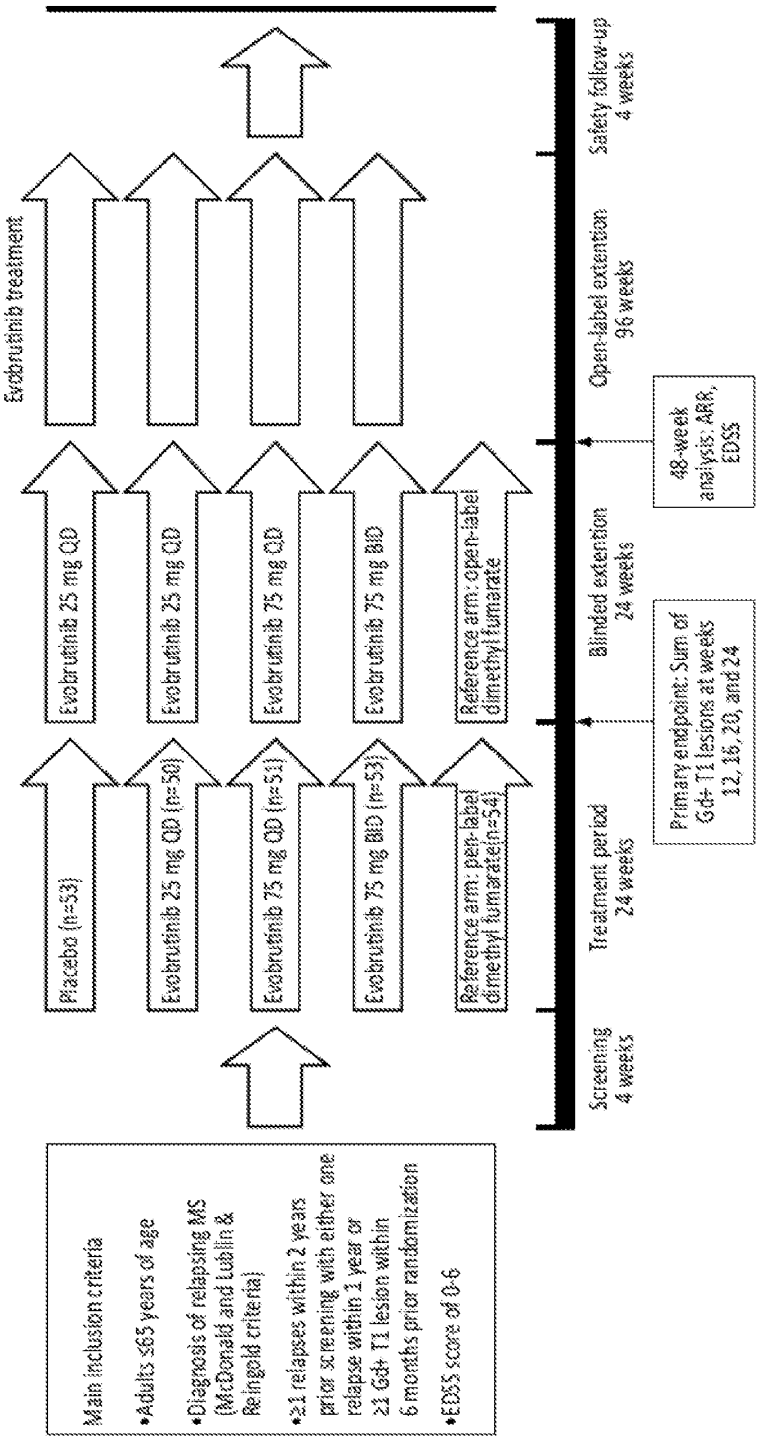

Main inclusion criteria
•Adults ≤65 years of age
•Diagnosis of relapsing MS (McDonald and Lublin & Reingold criteria)
•≥1 relapses within 2 years prior screening with either one relapse within 1 year or ≥1 Gd+ T1 lesion within 6 months prior randomization
•EDSS score of 0-6
Screening 4 weeks
Treatment period 24 weeks
Blinded extention 24 weeks
Open-label extention 96 weeks
Safety follow-up 4 weeks
Primary endpoint: Sum of Gd+ T1 lesions at weeks 12, 16, 20, and 24
48-week analysis: ARR, EDSS
Placebo (n=53)
Evobrutinib 25 mg QD (n=50)
Evobrutinib 75 mg QD (n=51)
Evobrutinib 75 mg BID (n=53)
Reference arm: peg-label dimethyl fumarate(n=54)
Evobrutinib 25 mg QD
Evobrutinib 25 mg QD
Evobrutinib 75 mg QD
Evobrutinib 75 mg BID
Reference arm: open-label dimethyl fumarate
Evobrutinib treatment

FIG. 5

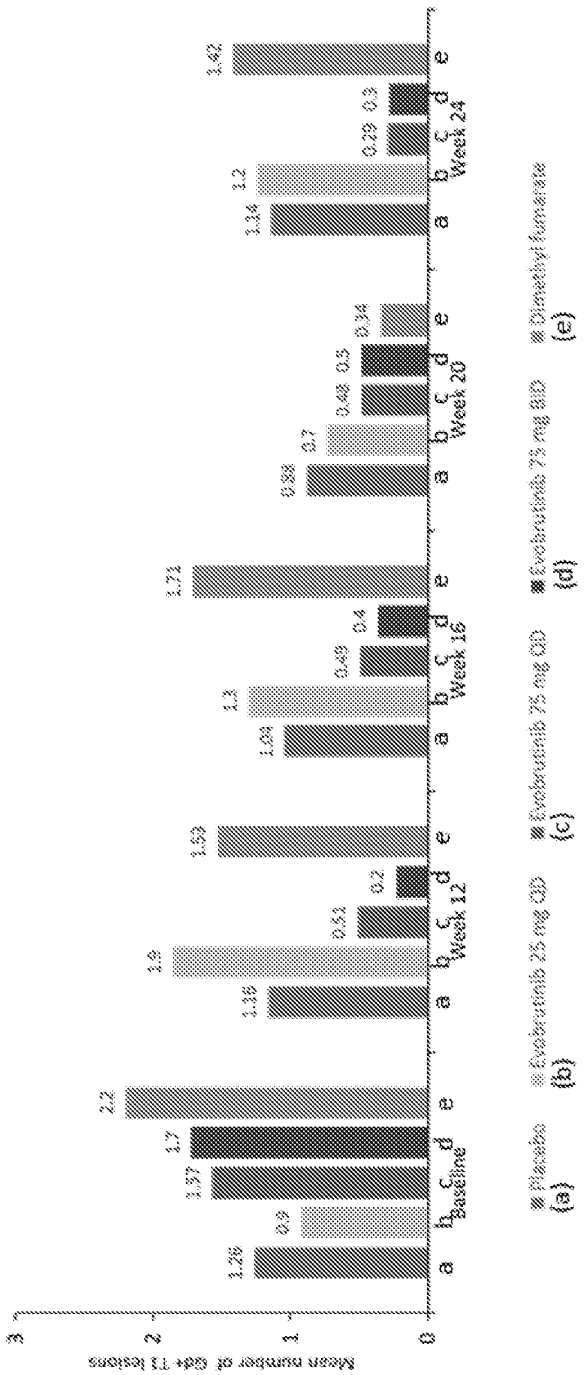

Mean number of Gd+ T1 lesions
0
1
2
3
Baseline
Week 12
Week 16
Week 20
Week 24
a
b
c
d
e
1.26
0.9
1.97
1.7
2.2
1.16
1.9
0.51
0.2
1.53
1.03
1.3
0.49
0.4
1.71
0.88
0.7
0.48
0.3
0.34
1.14
1.2
0.29
0.3
1.42
Placebo (a)
Evobrutinib 25 mg OD (b)
Evobrutinib 75 mg OD (c)
Evobrutinib 75 mg BID (d)
Dimethyl fumarate (e)

FIG. 6

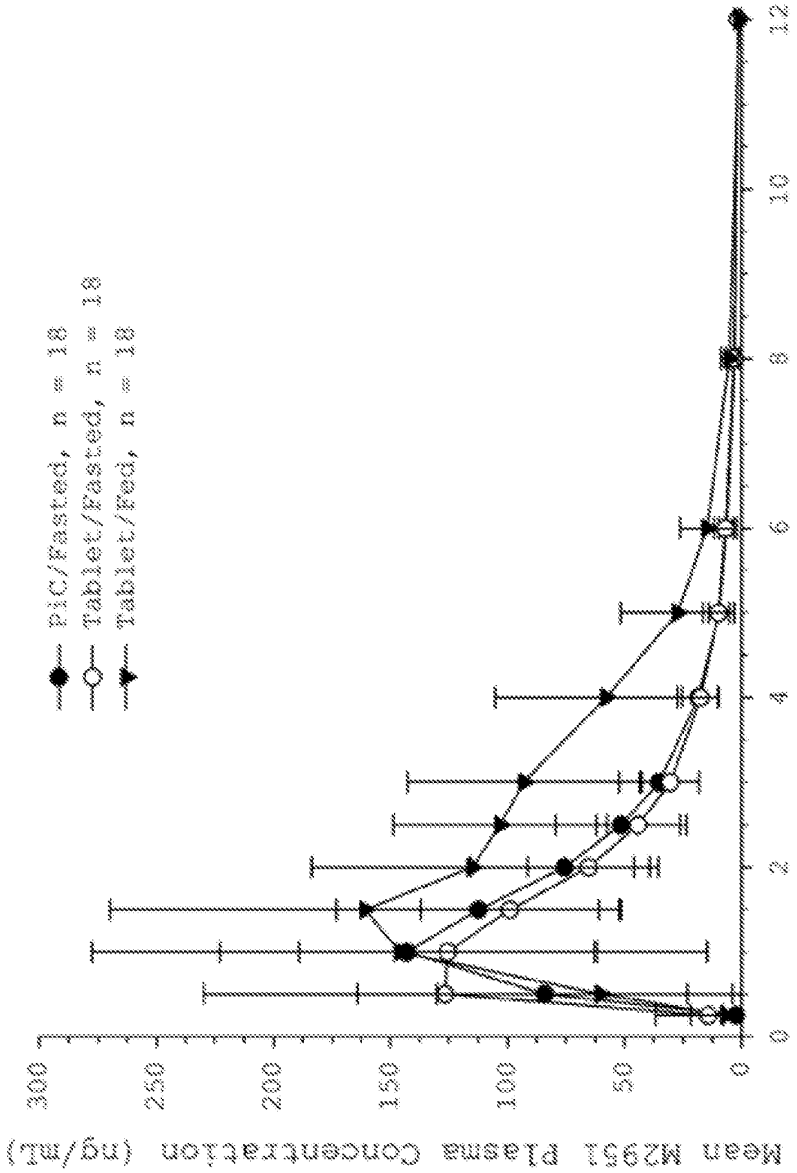

PIC/Fasted, n = 18
Tablet/Fasted, n = 18
Tablet/Fed, n = 18
Mean M2951 Plasma Concentration (ng/mL)
Time (hour)
0
50
100
150
200
250
300
0
2
4
6
8
10
12

FIG. 7

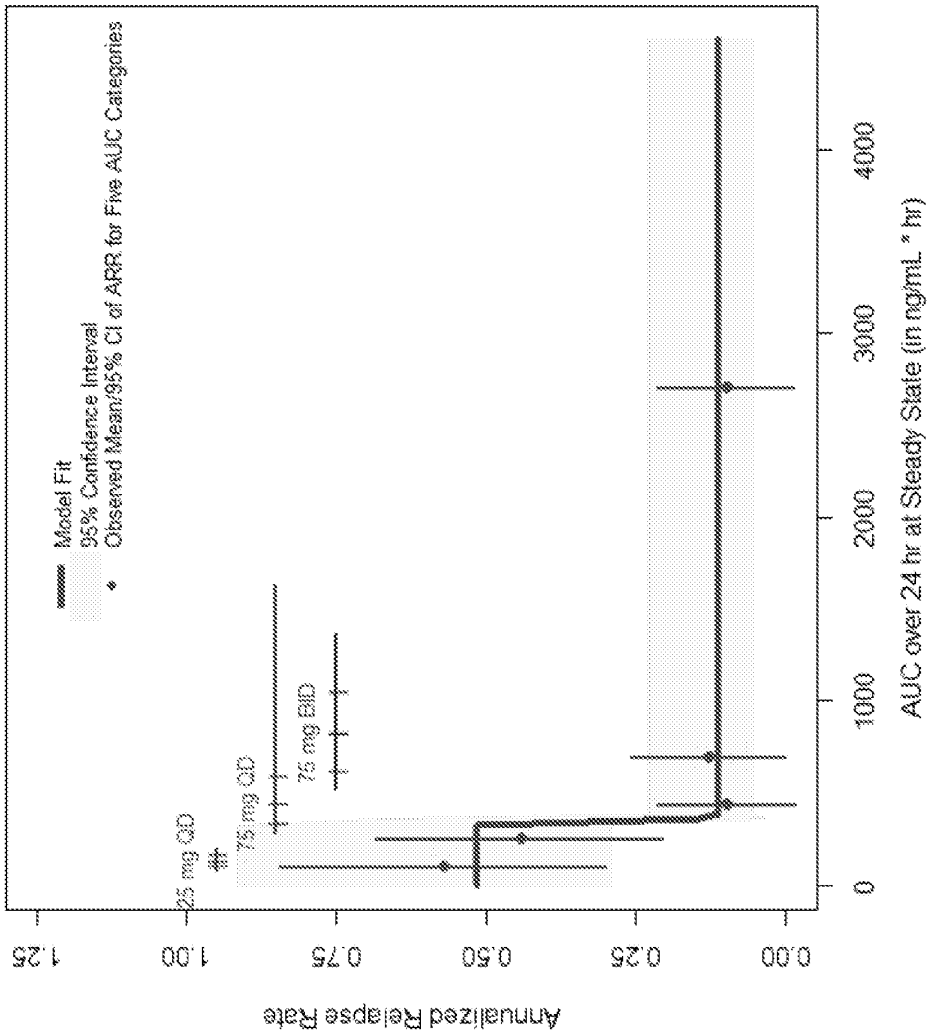

Annualized Relapse Rate
0.00
0.25
0.50
0.75
1.00
1.25
0
1000
2000
3000
4000
AUC over 24 hr at Steady State (in ng/mL * hr)
Model Fit
95% Confidence Interval
Observed Mean/95% CI of ARR for Five AUC Categories
25 mg QD
75 mg QD
75 mg BID

FIG. 8

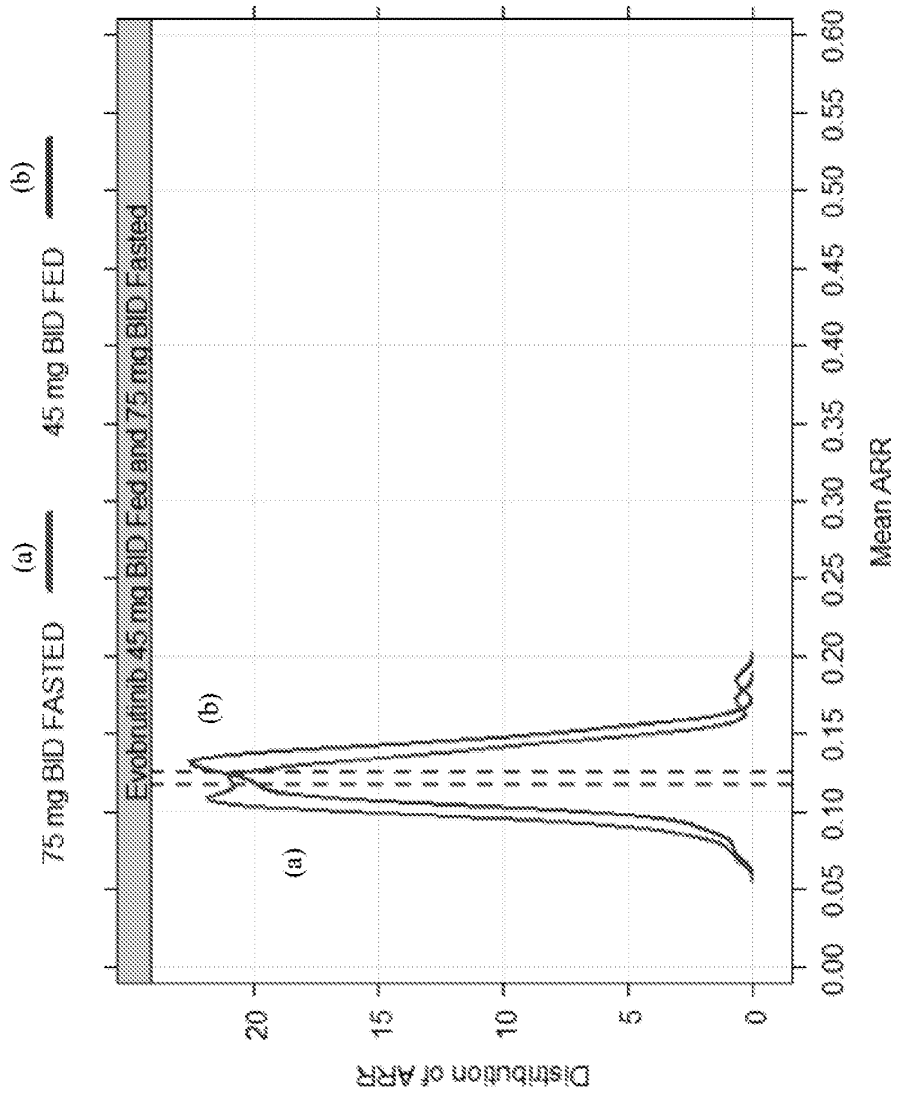

(a)
75 mg BID FASTED
(b)
45 mg BID FED
Evobrutinib 45 mg BID Fed and 75 mg BID Fasted
(a)
(b)
Distribution of ARR
0
5
10
15
20
0.00
0.05
0.10
0.15
0.20
0.25
0.30
0.35
0.40
0.45
0.50
0.55
0.60
Mean ARR

FIG. 9

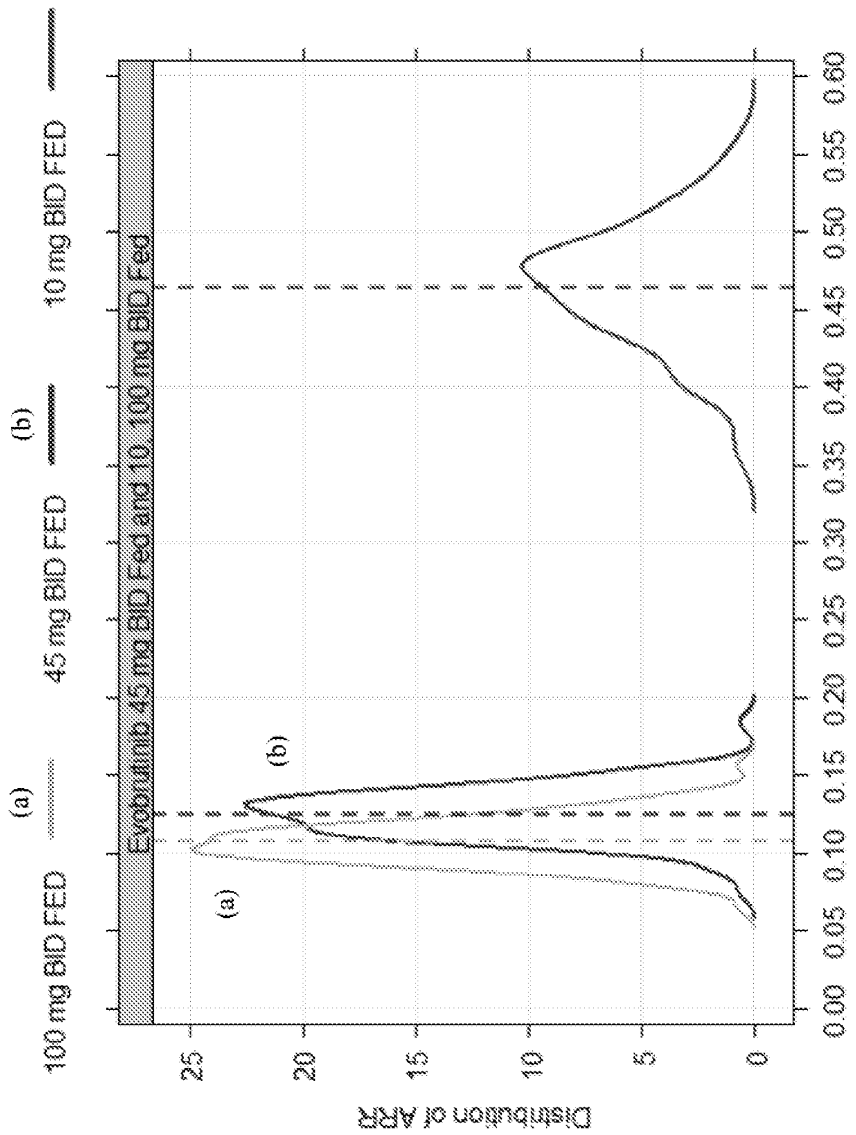

(a)
100 mg BID FED
(b)
45 mg BID FED
10 mg BID FED
Evon.dlmb 45 mg BID Fed and 10, 100 mg BID Fed
(a)
(b)
Distribution of ARR
Mean ARR
0
5
10
15
20
25
0.00
0.05
0.10
0.15
0.20
0.25
0.30
0.35
0.40
0.45
0.50
0.55
0.60

FIG. 10

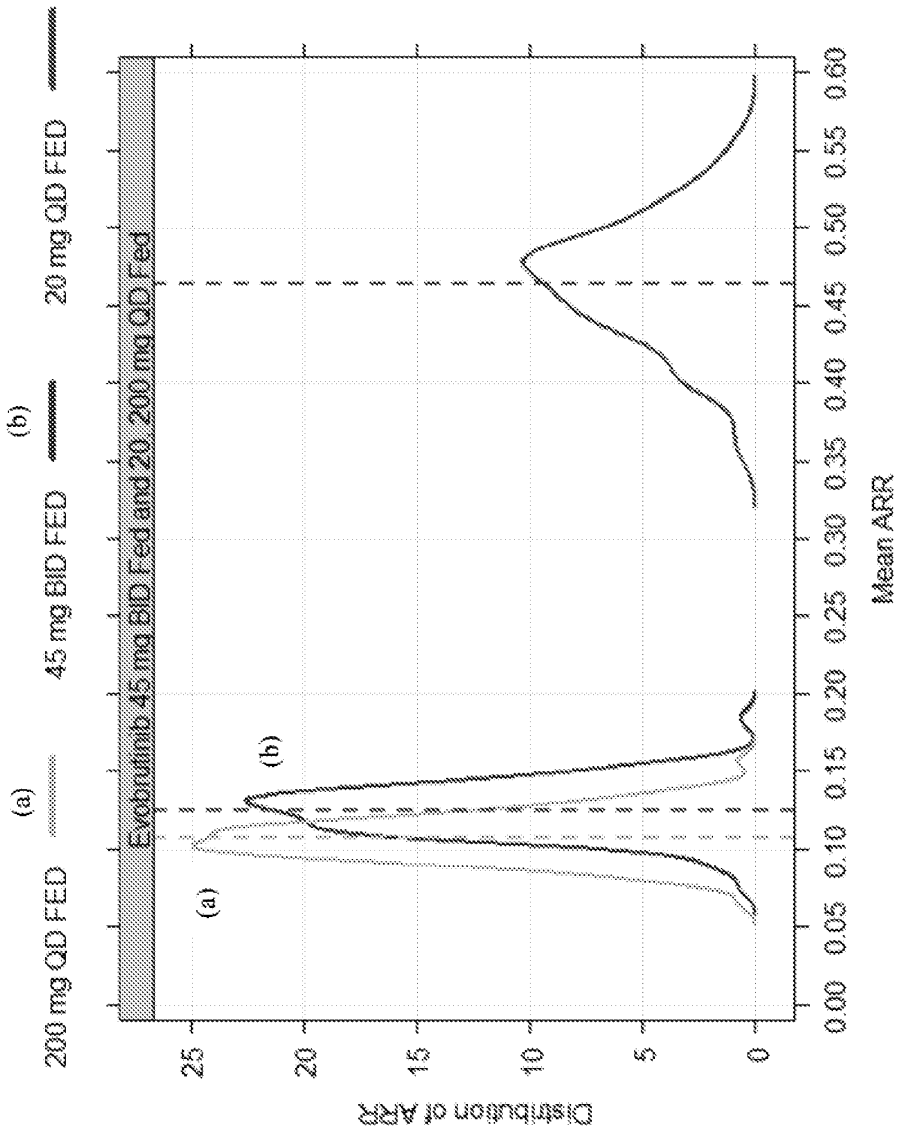

(a)
200 mg QD FED
(b)
45 mg BID FED
20 mg QD FED
Evobrutinib 45 mg BID Fed and 20, 200 mg QD Fed
(a)
(b)
Distribution of ARR
Mean ARR
0
5
10
15
20
25
0.00
0.05
0.10
0.15
0.20
0.25
0.30
0.35
0.40
0.45
0.50
0.55
0.60

FIG. 11

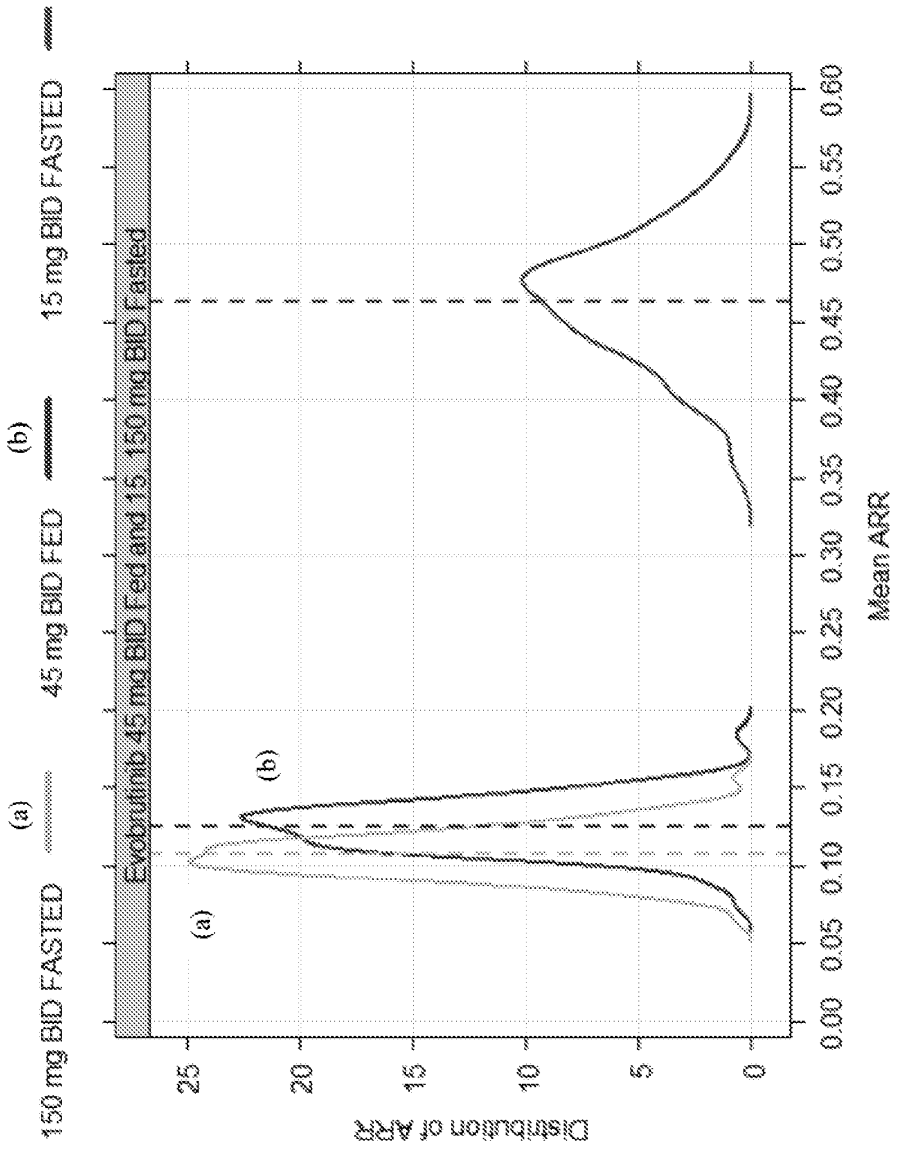

(a)
150 mg BID FASTED
(b)
45 mg BID FED
15 mg BID FASTED
Evobrutinib 45 mg BID Fed and 15, 150 mg BID Fasted
(a)
(b)
Distribution of ARR
Mean ARR
0
5
10
15
20
25
0.00
0.05
0.10
0.15
0.20
0.25
0.30
0.35
0.40
0.45
0.50
0.55
0.60

FIG. 12

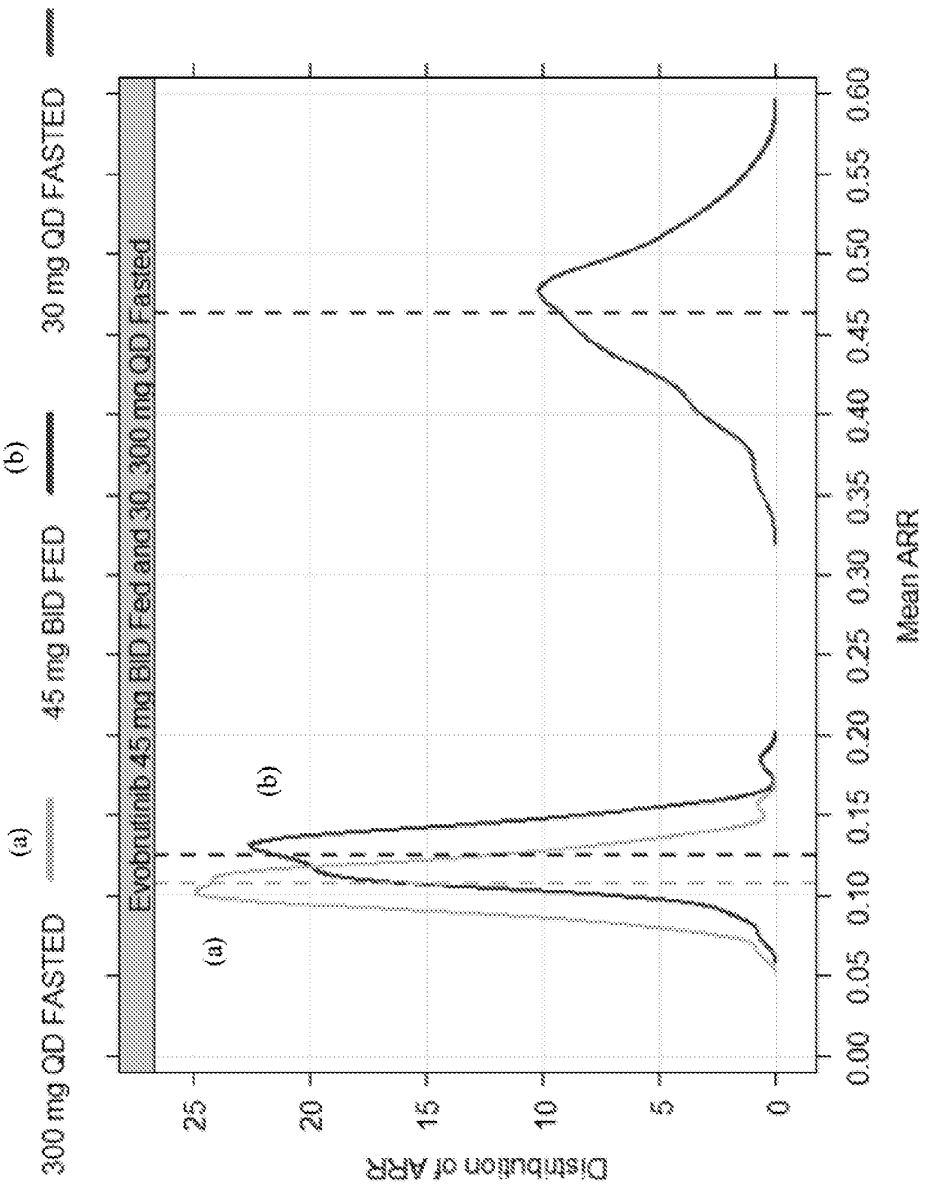

(a) 300 mg QD FASTED
(b) 45 mg BID FED
30 mg QD FASTED
Evobrutinib 45 mg BID Fed and 30, 300 mg QD Fasted
(a)
(b)
Distribution of ARR
Mean ARR
0.00 0.05 0.10 0.15 0.20 0.25 0.30 0.35 0.40 0.45 0.50 0.55 0.60
0 5 10 15 20 25

FIG. 13