FIG. 1

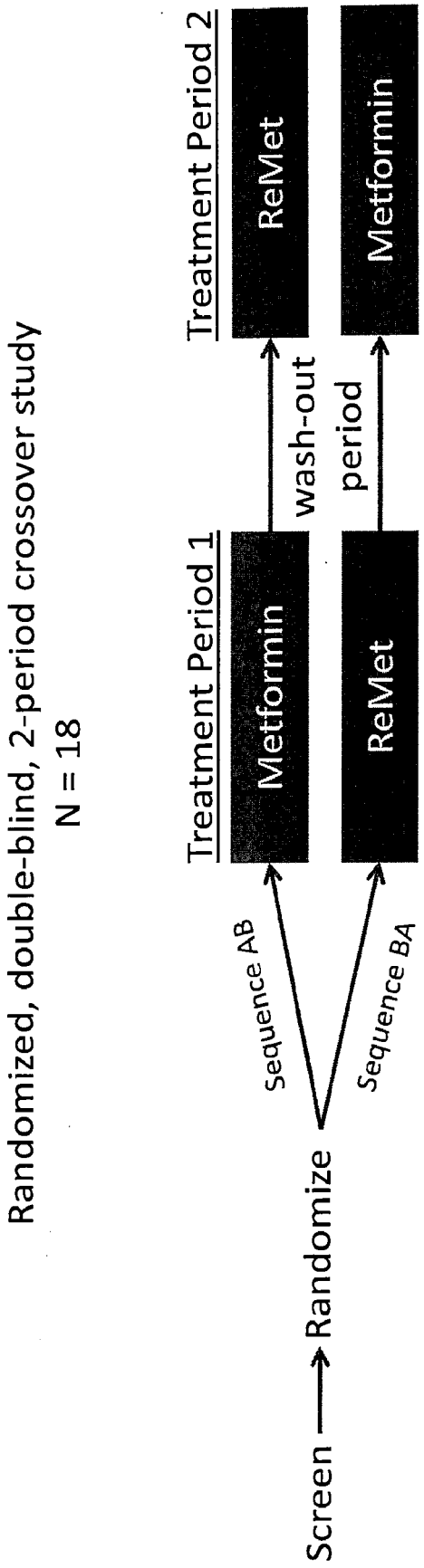

Randomized, double-blind, 2-period crossover study
N = 18
Screen
Randomize
Sequence AB
Sequence BA
Treatment Period 1
Metformin
ReMet
wash-out period
Treatment Period 2
ReMet
Metformin

FIG. 2

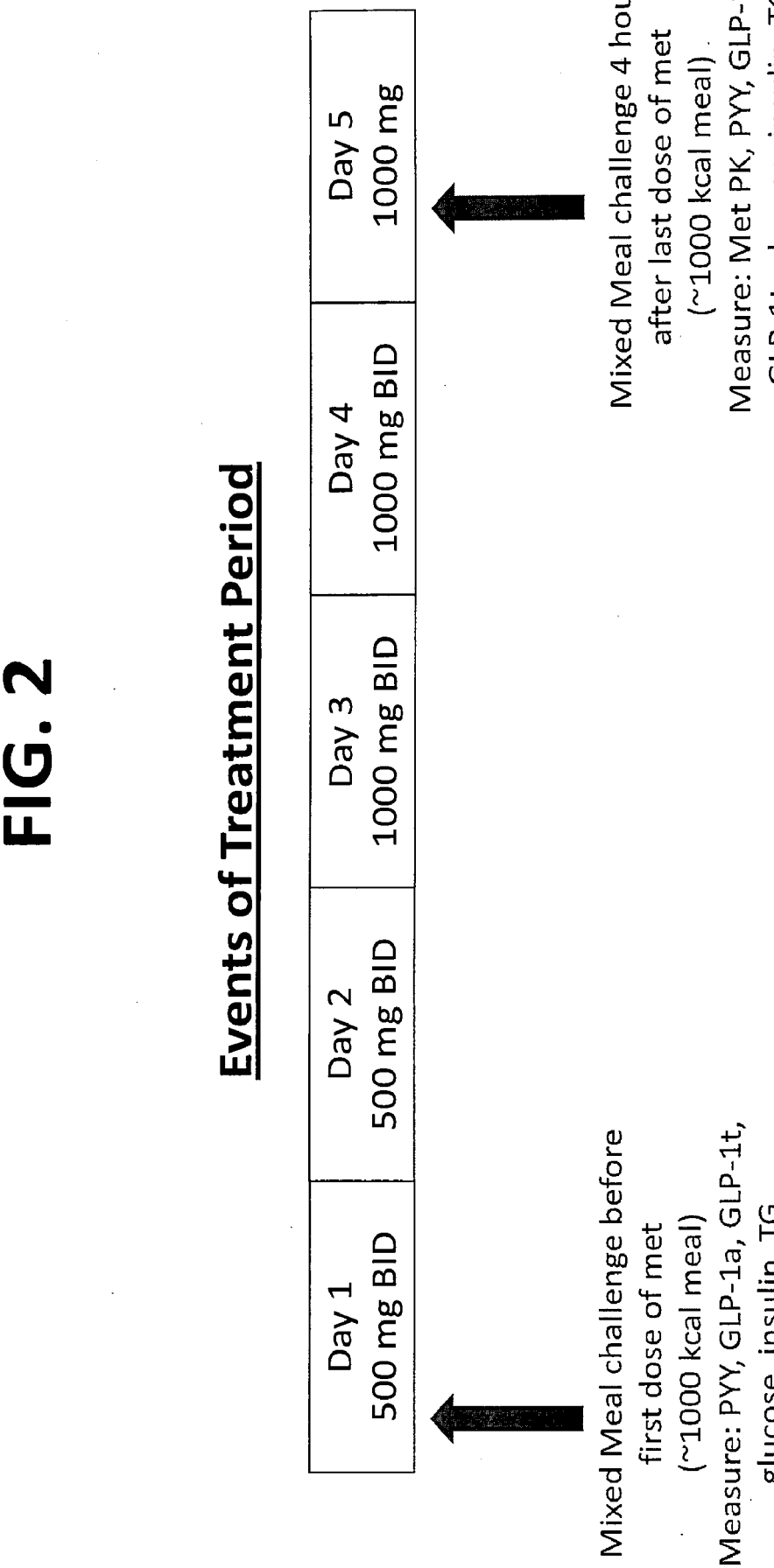

Events of Treatment Period
Day 1
500 mg BID
Day 2
500 mg BID
Day 3
1000 mg BID
Day 4
1000 mg BID
Day 5
1000 mg
Mixed Meal challenge before first dose of met (~1000 kcal meal)
Measure: PYY, GLP-1a, GLP-1t, glucose, insulin, TG
Mixed Meal challenge 4 hours after last dose of met (~1000 kcal meal)
Measure: Met PK, PYY, GLP-1a, GLP-1t, glucose, insulin, TG

FIG. 3

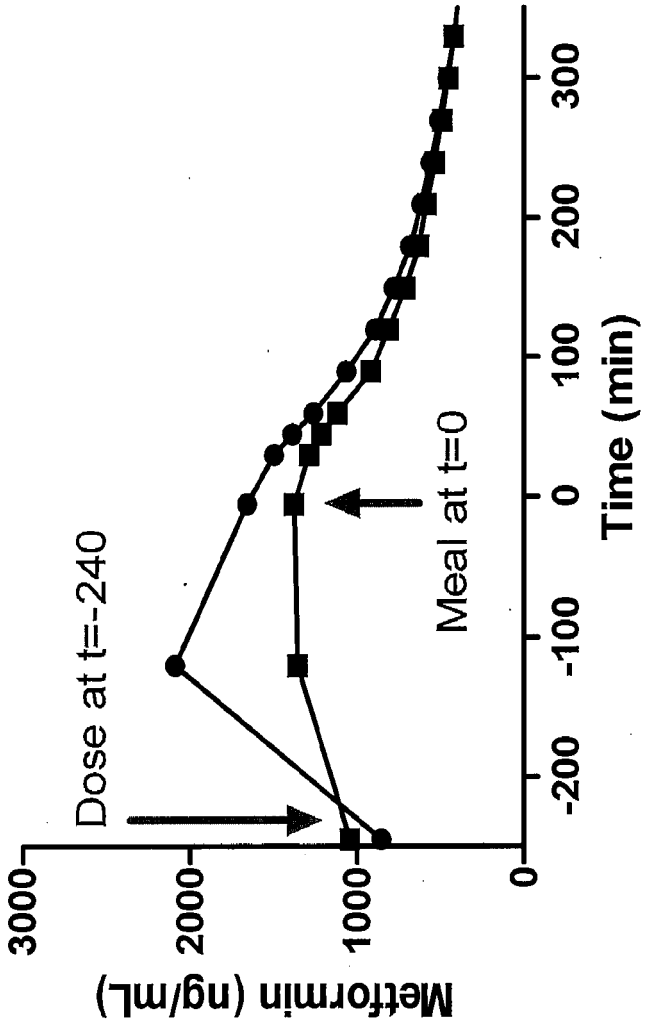

Metformin (ng/mL)
3000
2000
1000
0
-200
-100
0
100
200
300
Time (min)
Dose at t=-240
Meal at t=0

FIG. 4A

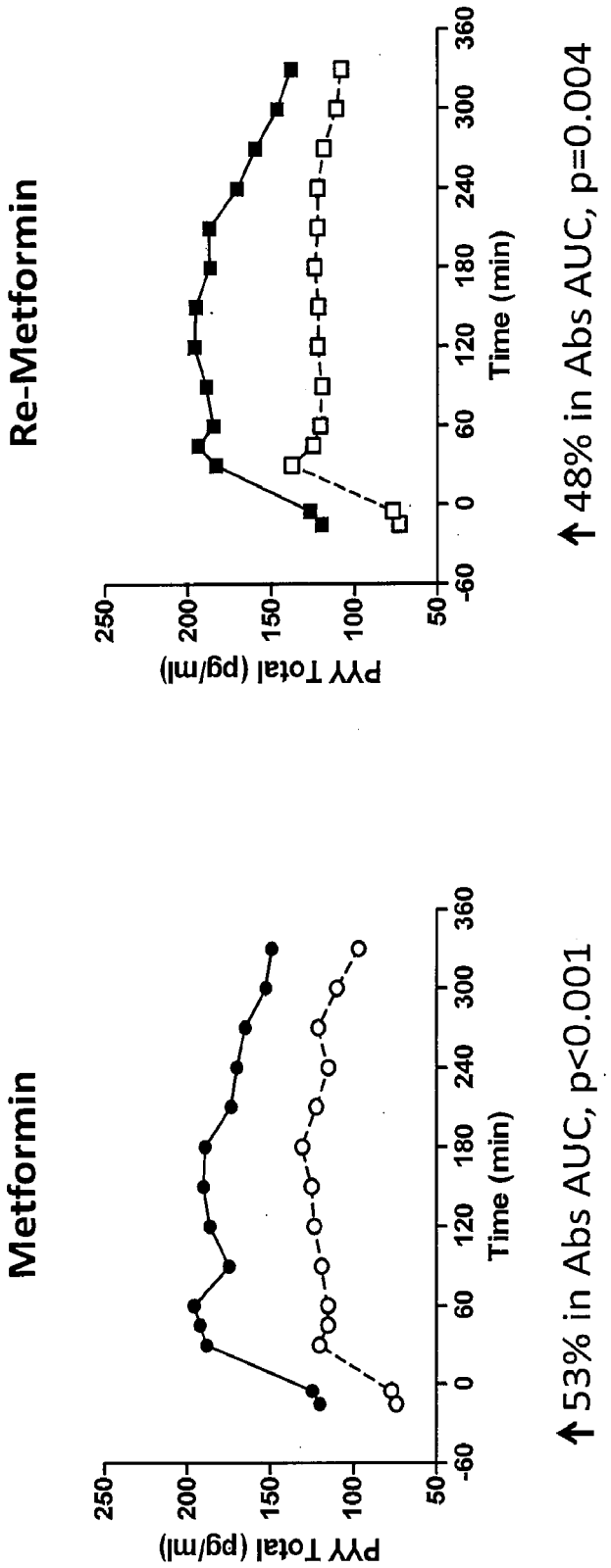

Re-Metformin
PYY Total (pg/ml)
250
200
150
100
50
-60
0
60
120
180
240
300
360
Time (min)
↑48% in Abs AUC, p=0.004
Metformin
PYY Total (pg/ml)
250
200
150
100
50
-60
0
60
120
180
240
300
360
Time (min)
↑53% in Abs AUC, p<0.001

FIG. 4B

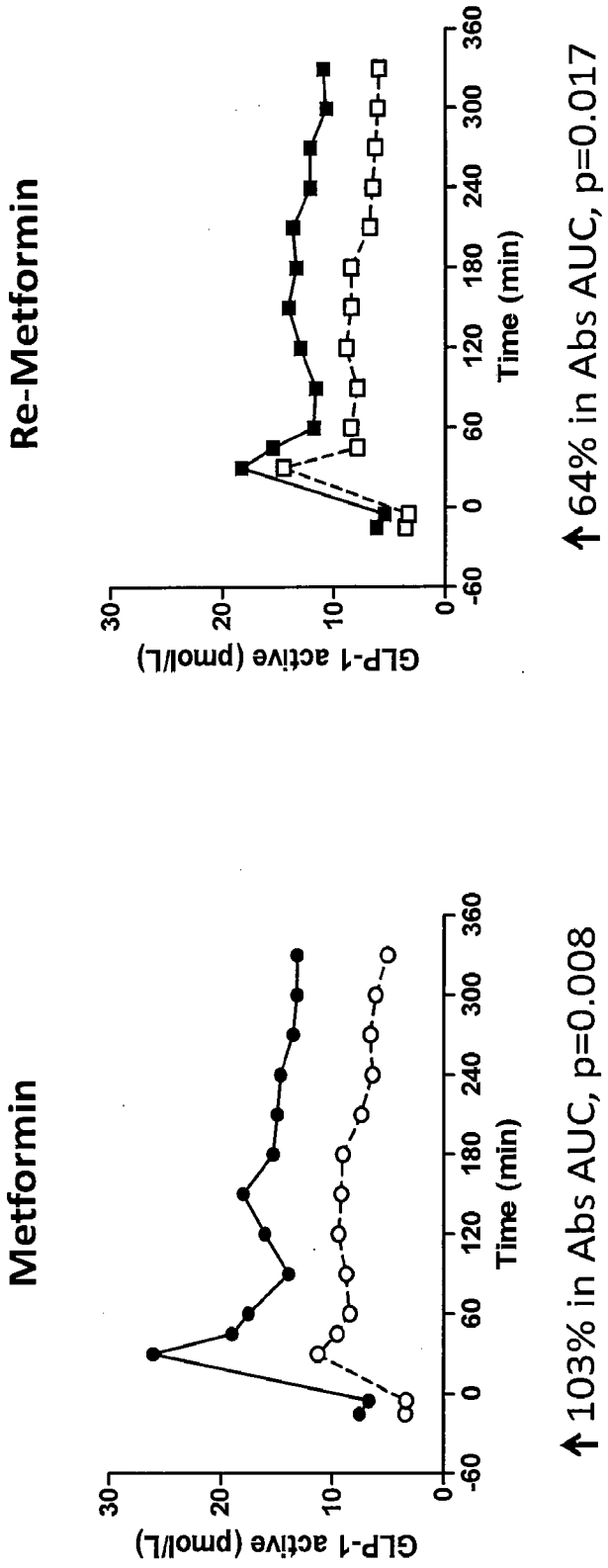

Re-Metformin
GLP-1 active (pmol/L)
30
20
10
0
-60
0
60
120
180
240
300
360
Time (min)
↑64% in Abs AUC, p=0.017
Metformin
GLP-1 active (pmol/L)
30
20
10
0
-60
0
60
120
180
240
300
360
Time (min)
↑103% in Abs AUC, p=0.008

FIG. 4C

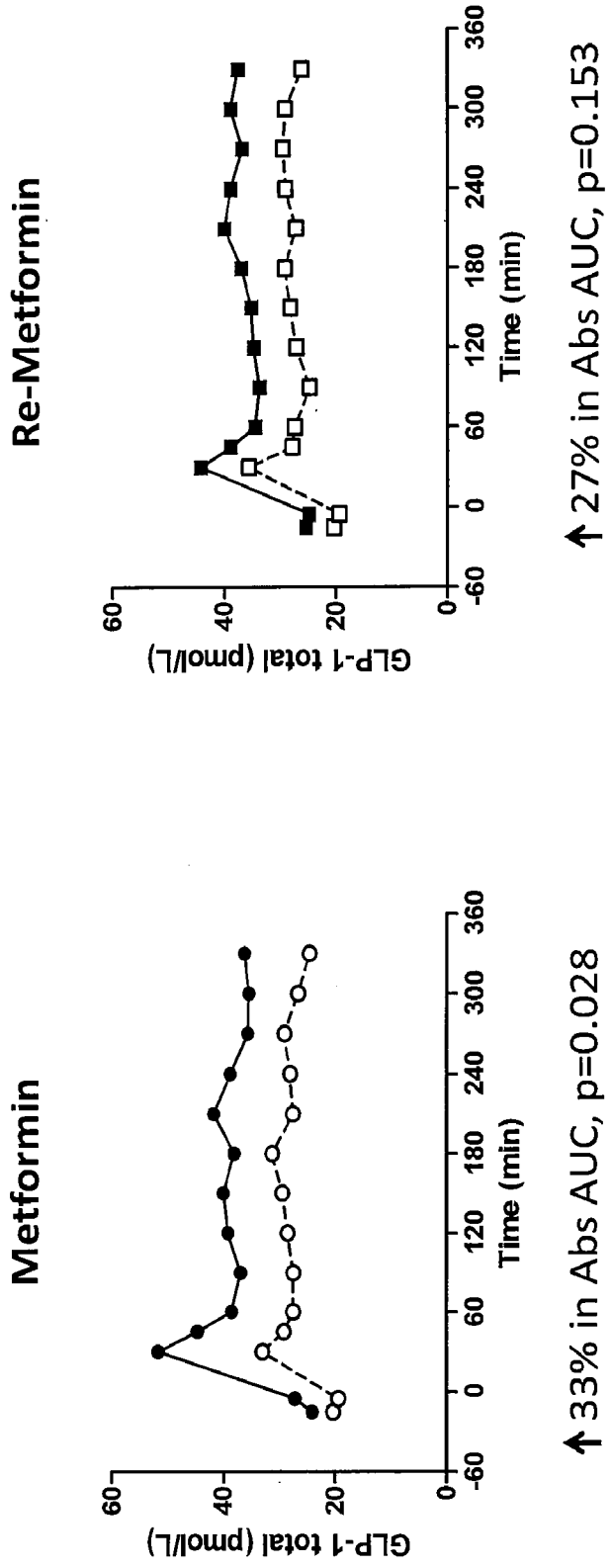

Re-Metformin
GLP-1 total (pmol/L)
60
40
20
0
-60
0
60
120
180
240
300
360
Time (min)
↑27% in Abs AUC, p=0.153
Metformin
GLP-1 total (pmol/L)
60
40
20
0
-60
0
60
120
180
240
300
360
Time (min)
↑33% in Abs AUC, p=0.028

FIG. 5A

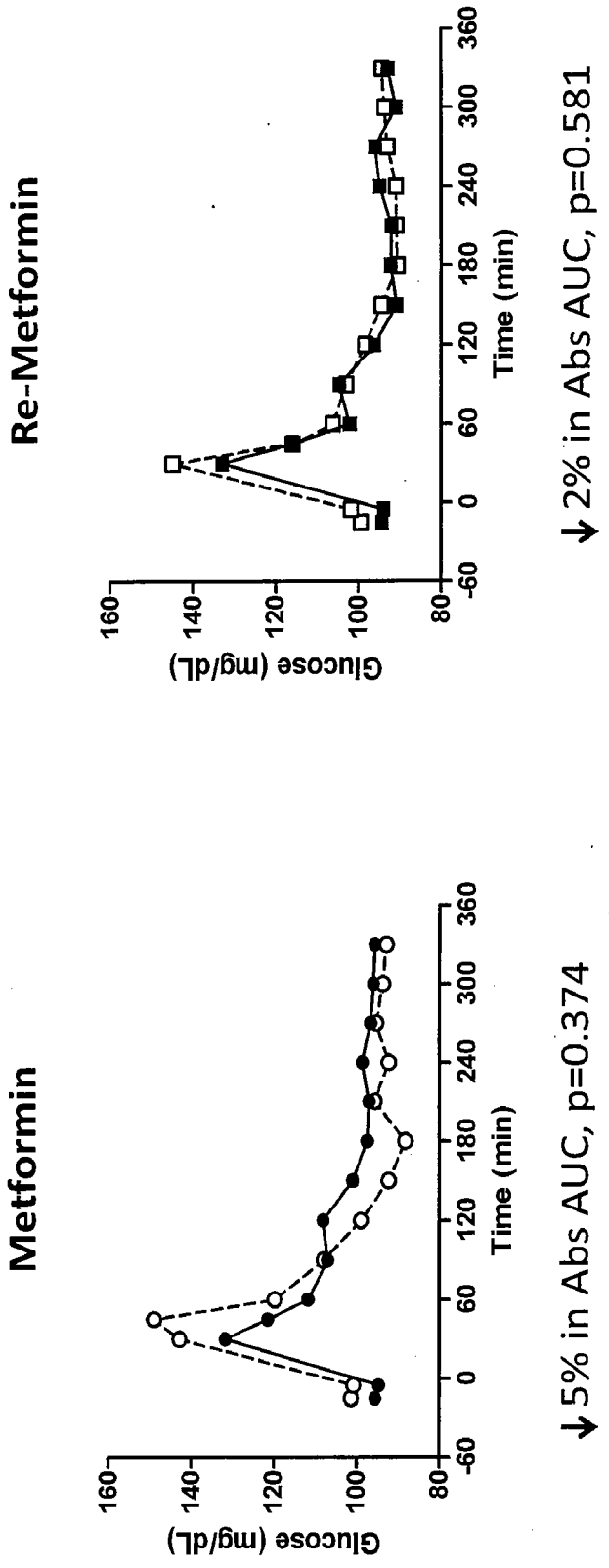

Re-Metformin
Glucose (mg/dL)
160
140
120
100
80
-60
0
60
120
180
240
300
360
Time (min)
↓2% in Abs AUC, p=0.581
Metformin
Glucose (mg/dL)
160
140
120
100
80
-60
0
60
120
180
240
300
360
Time (min)
↓5% in Abs AUC, p=0.374

FIG. 5B

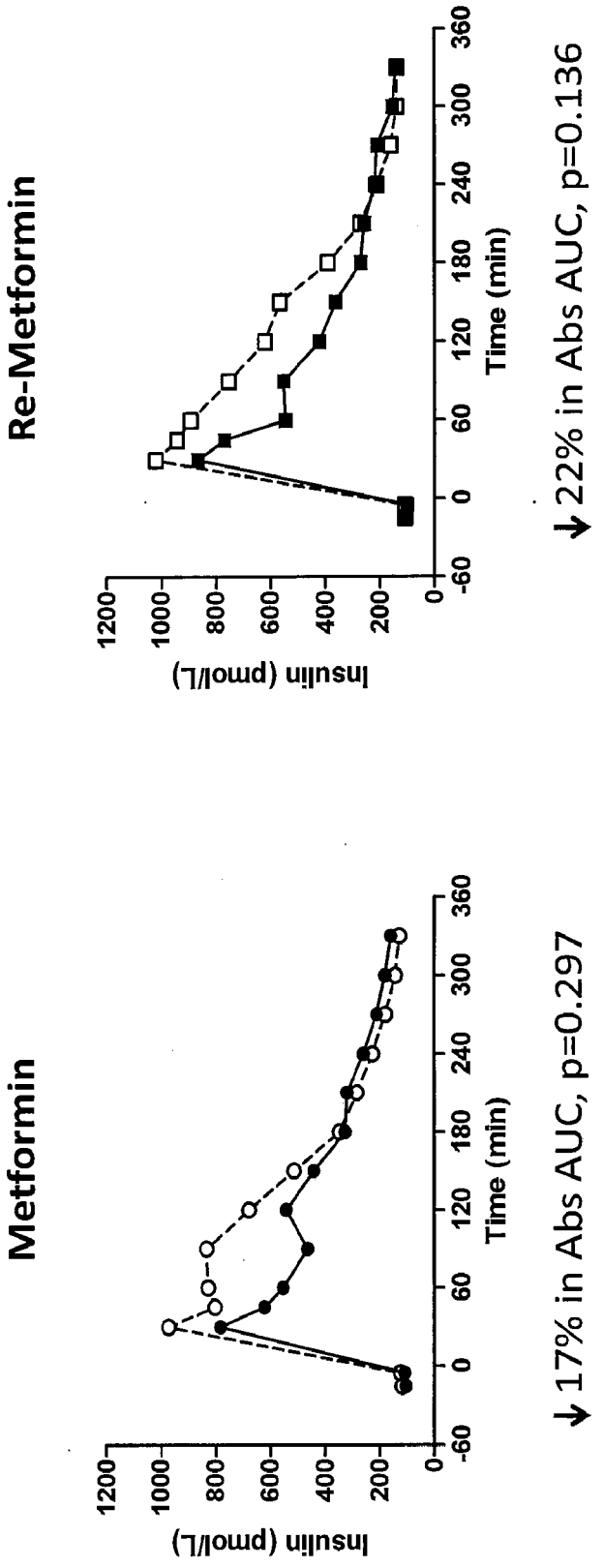

Re-Metformin
Insulin (pmol/L)
1200
1000
800
600
400
200
0
-60
0
60
120
180
240
300
360
Time (min)
↓ 22% in Abs AUC, p=0.136
Metformin
Insulin (pmol/L)
1200
1000
800
600
400
200
0
-60
0
60
120
180
240
300
360
Time (min)
↓ 17% in Abs AUC, p=0.297

FIG. 6

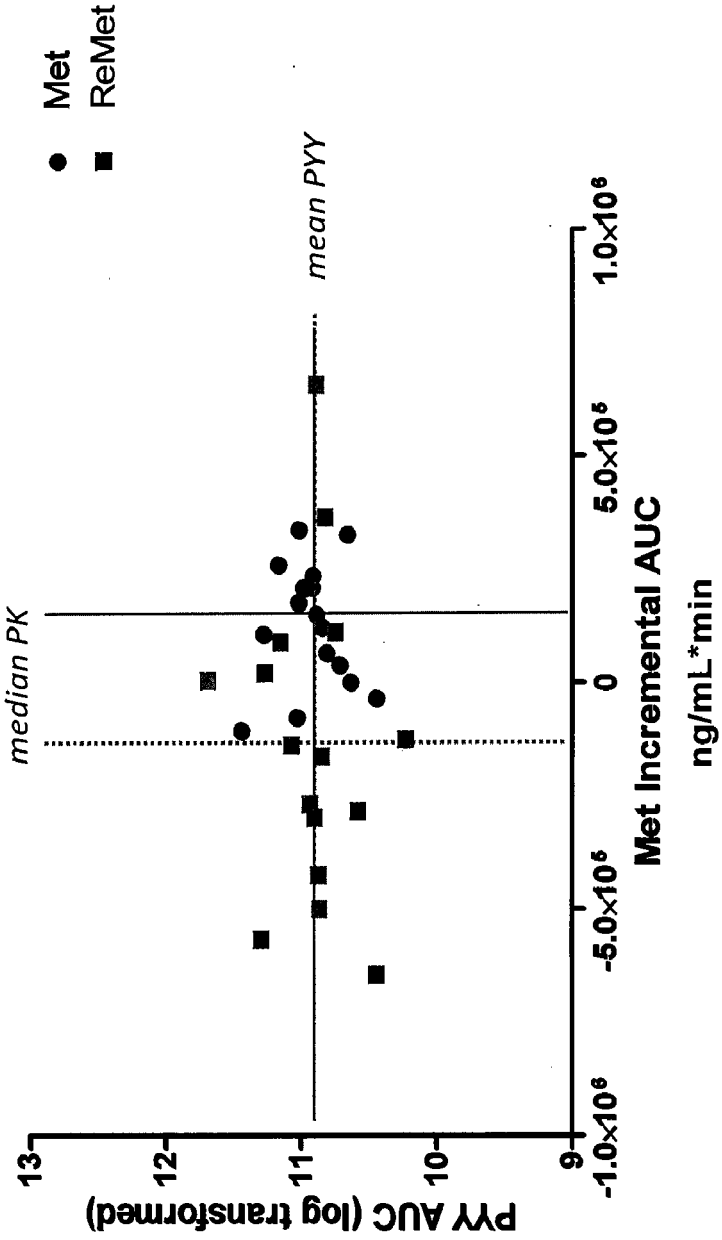

Met
ReMet
median PK
mean PYY
PYY AUC (log transformed)
13
12
11
10
9
-1.0x10⁶
-5.0x10⁵
0
5.0x10⁵
1.0x10⁶
Met Incremental AUC
ng/mL*min

FIG. 7A

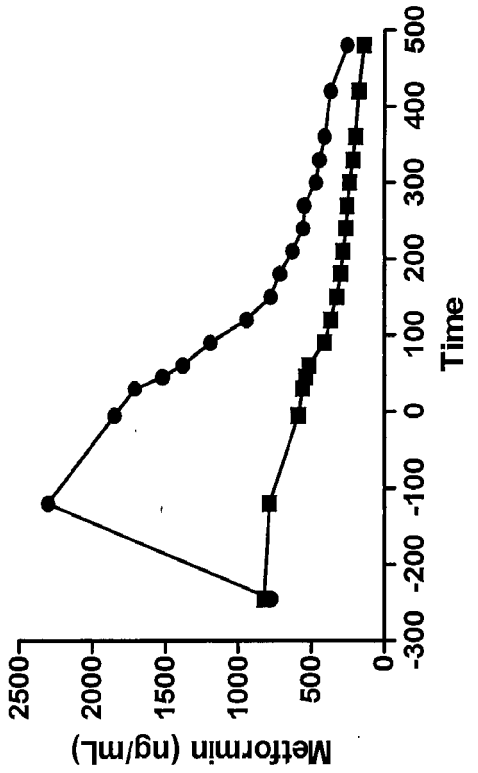

Metformin (ng/mL)
2500
2000
1500
1000
500
0
-300 -200 -100 0 100 200 300 400 500
Time
Baseline1
Baseline2
Metformin
Re-Metformin

FIG. 7B

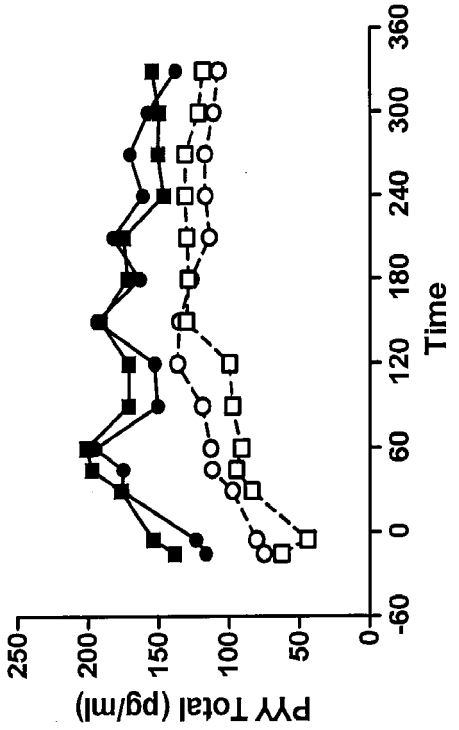
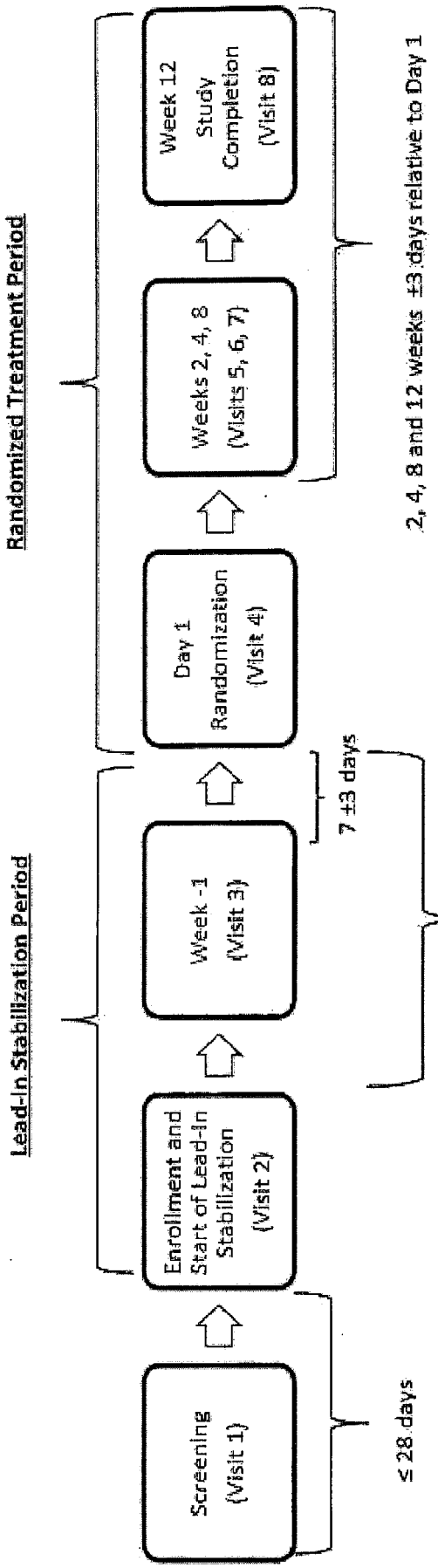

PYY Total (pg/ml)
250
200
150
100
50
0
-60 0 60 120 180 240 300 360
Time

FIG. 8


Lead-In Stabilization Period
Randomized Treatment Period
Screening (Visit 1)
Enrollment and Start of Lead-In Stabilization (Visit 2)
Week -1 (Visit 3)
Day 1 Randomization (Visit 4)
Weeks 2, 4, 8 (Visits 5, 6, 7)
Week 12 Study Completion (Visit 8)
≤ 28 days
7 ±3 days
6 weeks ±3 days
2, 4, 8 and 12 weeks ±3 days relative to Day 1