[Fig. 1]

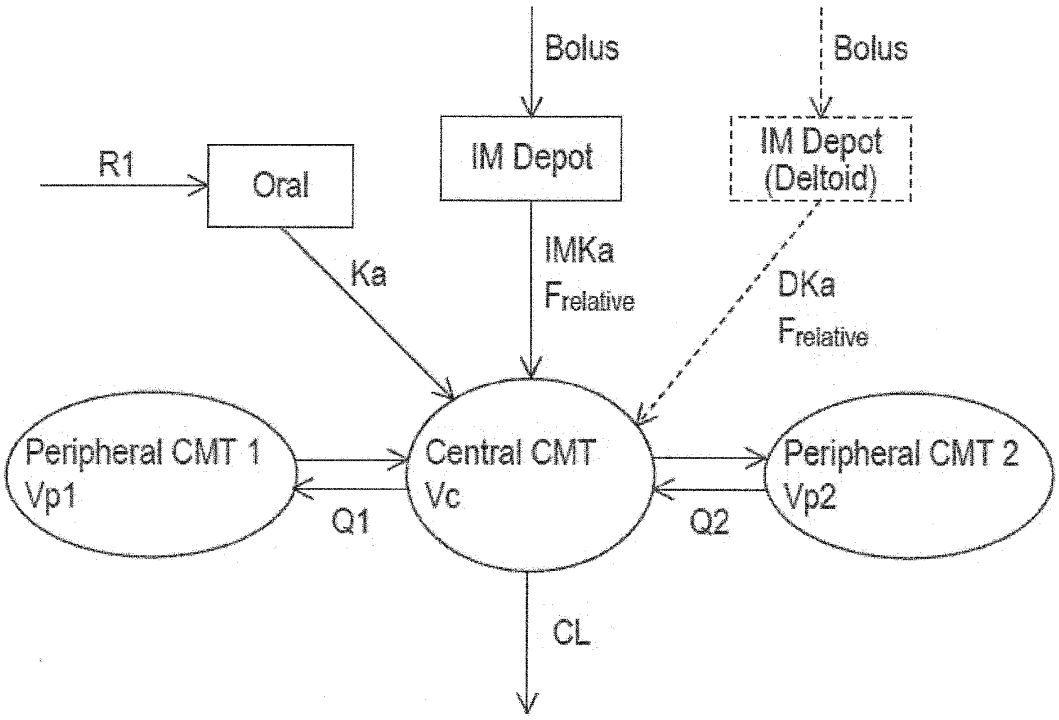
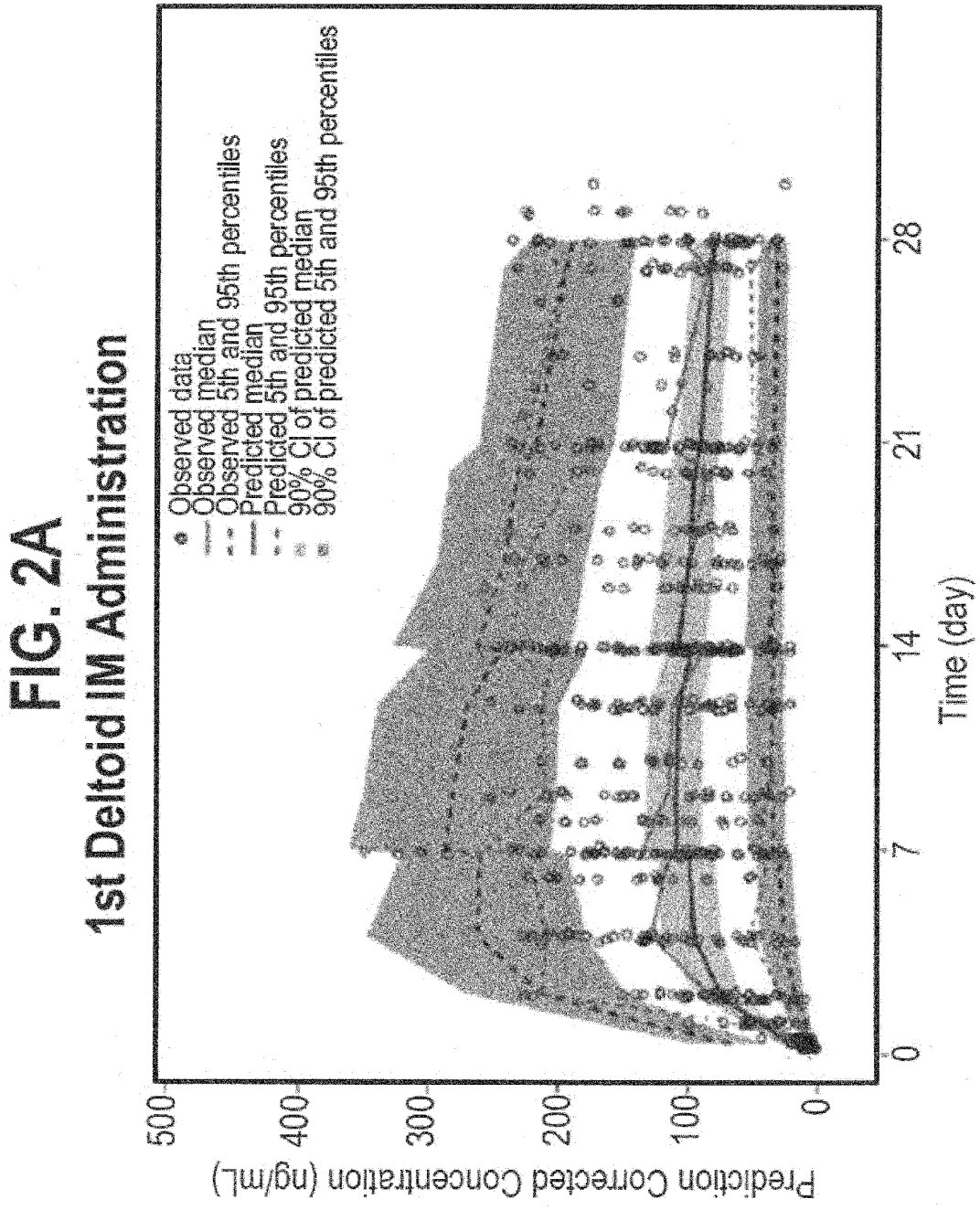
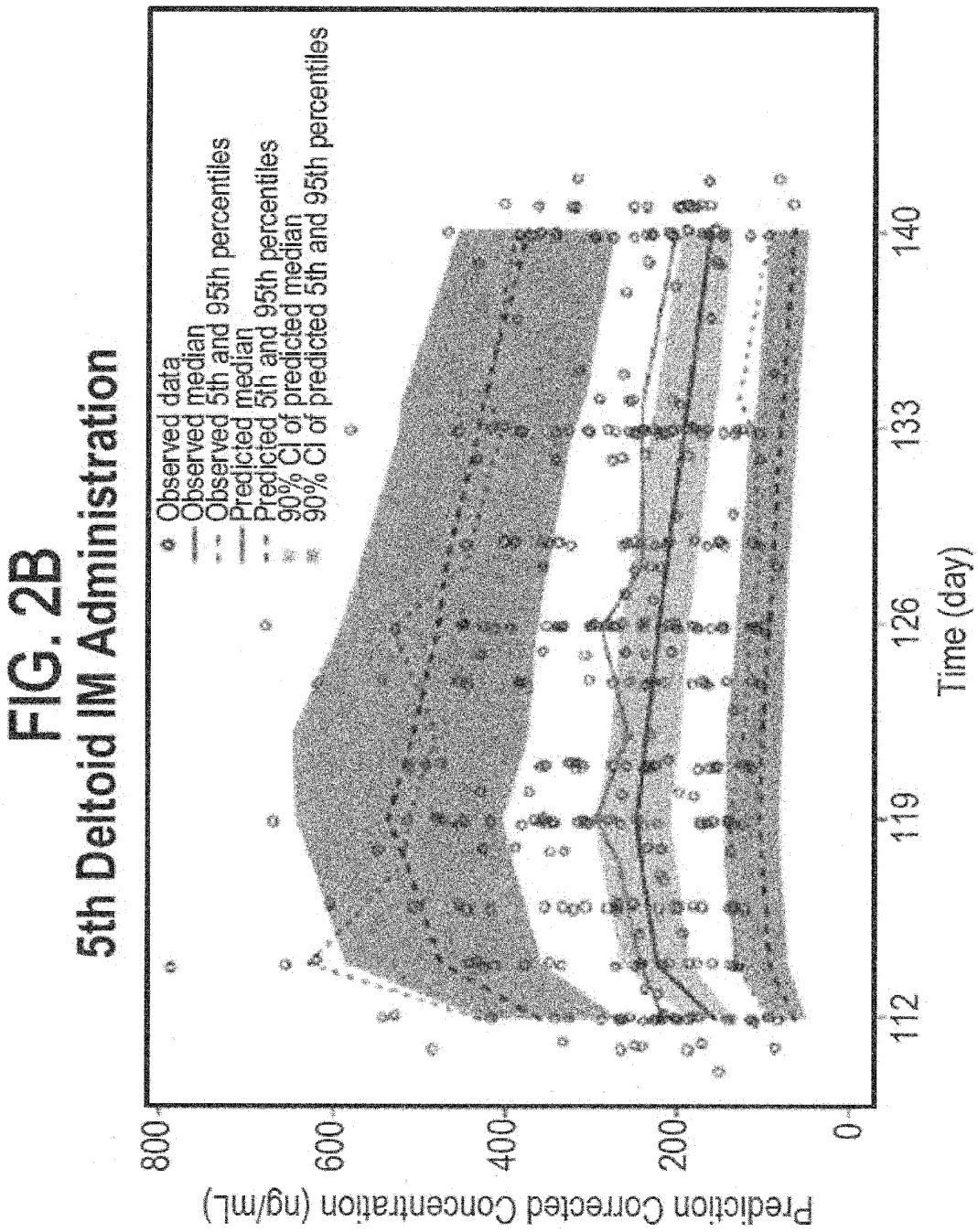

Bolus
Bolus
R1
Oral
IM Depot
IM Depot
(Deltoid)
Ka
IMKa
Frelative
DKa
Frelative
Peripheral CMT 1
Vp1
Central CMT
Vc
Peripheral CMT 2
Vp2
Q1
Q2
CL

FIG. 1

[Fig. 2A]


FIG. 2A
1st Deltoid IM Administration
Observed data
Observed median
Observed 5th and 95th percentiles
Predicted median
Predicted 5th and 95th percentiles
90% CI of predicted median
90% CI of predicted 5th and 95th percentiles
Prediction Corrected Concentration (ng/mL)
500
400
300
200
100
0
0
7
14
21
28
Time (day)

[Fig. 2B]


FIG. 2B
5th Deltoid IM Administration
Observed data
Observed median
Observed 5th and 95th percentiles
Predicted median
Predicted 5th and 95th percentiles
90% CI of predicted median
90% CI of predicted 5th and 95th percentiles
Prediction Corrected Concentration (ng/mL)
800
600
400
200
0
112
119
126
133
140
Time (day)

[Fig. 2C]

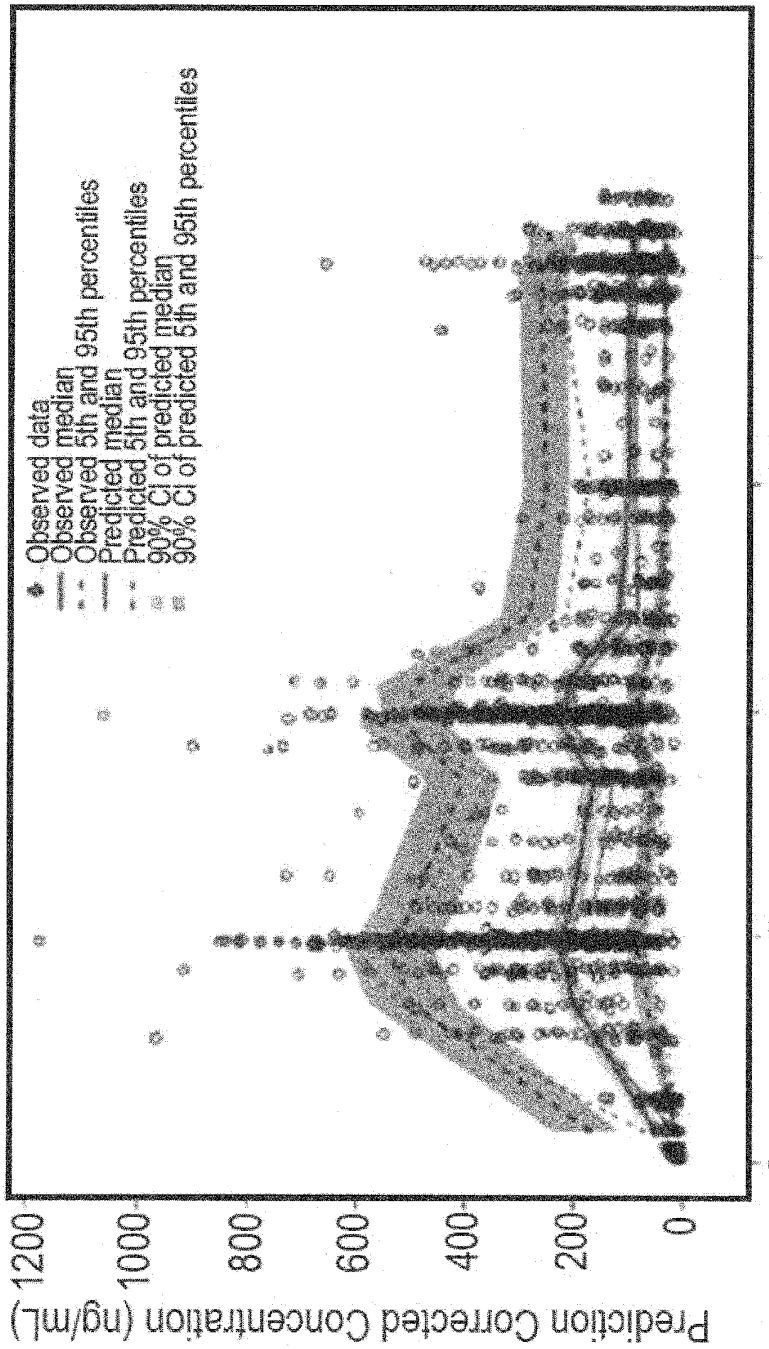

1st Gluteal IM Administration
Observed data
Observed median
Observed 5th and 95th percentiles
Predicted median
Predicted 5th and 95th percentiles
90% CI of predicted median
90% CI of predicted 5th and 95th percentiles
Prediction Corrected Concentration (ng/mL)
1200
1000
800
600
400
200
0
0
7
14
21
28
Time (day)

FIG. 2C

[Fig. 2D]

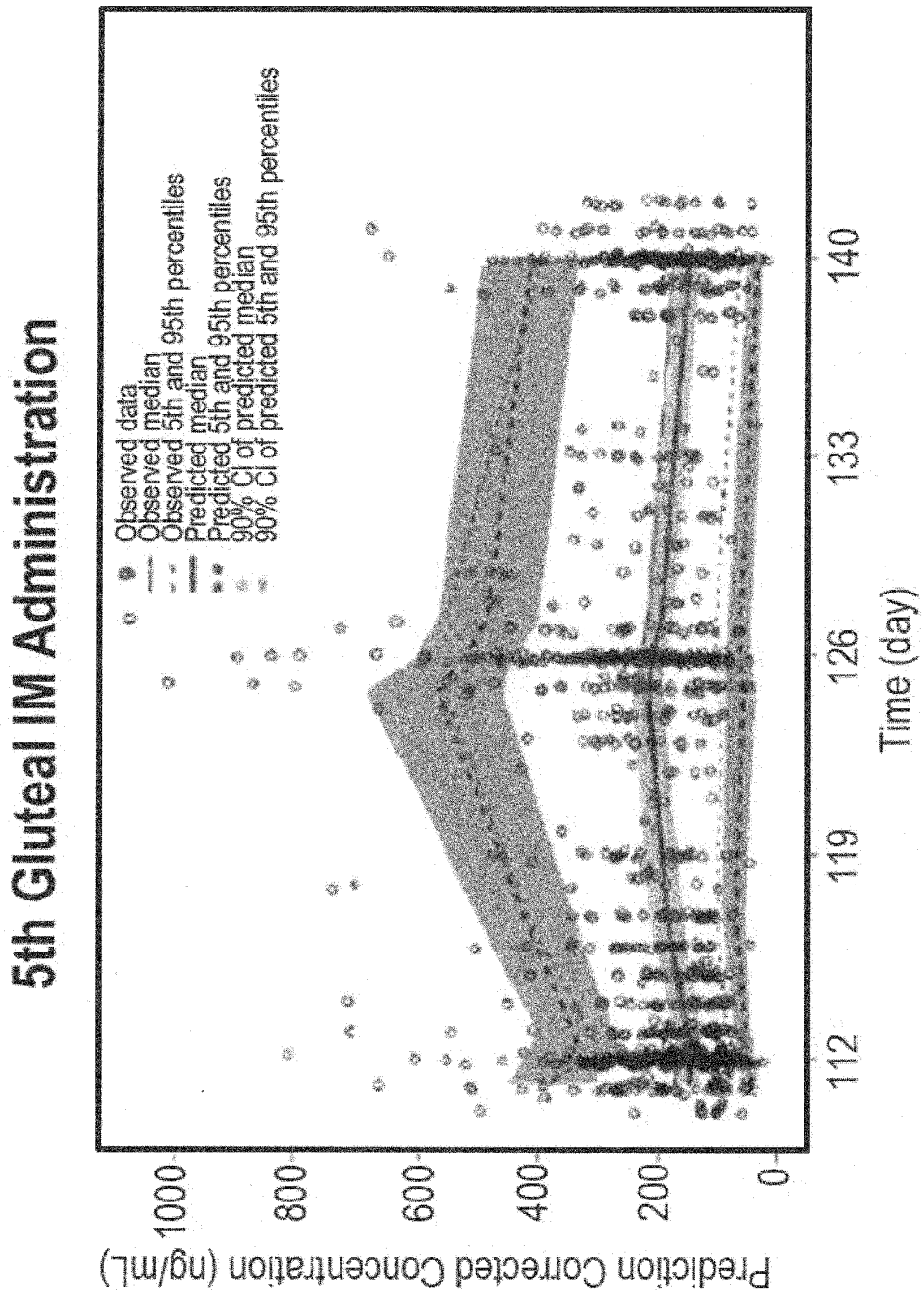

5th Gluteal IM Administration
Observed data
Observed median
Observed 5th and 95th percentiles
Predicted median
Predicted 5th and 95th percentiles
90% CI of predicted median
90% CI of predicted 5th and 95th percentiles
Prediction Corrected Concentration (ng/mL)
0
200
400
600
800
1000
112
119
126
133
140
Time (day)

FIG. 2D

[Fig. 3A]

Table 2.7.2.5.1-1 Purpose and Description of Simulations

Simulation Purpose	Number	Simulation Scenario
To compare the existing initiation regimens (g1 & g2 or d1 & d2) with other initiation regimens where 20 mg Oral + 2x300, 300+400, or 2x400 mg IM Depot were administered	g1	10 mg Oral (14 days) + 400 mg Gluteal (Day 1)
	g2	20 mg Oral (14 days) + 400 mg Gluteal (Day 1)
	g5	20 mg Oral (Day 1) + 2x400 mg Gluteal (Day 1)
	d1	10 mg Oral (14 days) + 400 mg Deltoid (Day 1)
	d2	20 mg Oral (14 days) + 400 mg Deltoid (Day 1)
	d5	20 mg Oral (Day 1) + 2x400 mg Deltoid (Day 1)
	g1	10 mg Oral (14 days) + 400 mg Gluteal (Day 1)
	g2	20 mg Oral (14 days) + 400 mg Gluteal (Day 1)
	g11sim4x	20 mg Oral (Day 1) + 400 mg IM Depot Gluteal (Day 1) + 400 mg IM Depot Deltoid (Day 1)
	d1	10 mg Oral (14 days) + 400 mg Deltoid (Day 1)
	d2	20 mg Oral (14 days) + 400 mg Deltoid (Day 1)
	g1	10 mg Oral (14 days) + 400 mg Gluteal (Day 1)
	g2	20 mg Oral (14 days) + 400 mg Gluteal (Day 1)
	g3	20 mg Oral (Day 1) + 2x300 mg Gluteal (Day 1)
	g4	20 mg Oral (Day 1) + 400 + 300 mg Gluteal (Day 1)
	g5	20 mg Oral (Day 1) + 2x400 mg Gluteal (Day 1)
	d1	10 mg Oral (14 days) + 400 mg Deltoid (Day 1)
	d2	20 mg Oral (14 days) + 400 mg Deltoid (Day 1)
	d3	20 mg Oral (Day 1) + 2x300 mg Deltoid 1 (Day 1)
	d4	20 mg Oral (Day 1) + 400 + 300 mg Deltoid (Day 1)
	d5	20 mg Oral (Day 1) + 2x400 mg Deltoid (Day 1)
To compare the existing initiation regimens (g1 & g2 or d1 & d2) with other initiation regimens where 10, 20, or 30 mg Oral + 2x400 mg IM Depot were administered	g1	10 mg Oral (14 days) + 400 mg Gluteal (Day 1)
	g2	20 mg Oral (14 days) + 400 mg Gluteal (Day 1)
	g6	10 mg Oral (Day 1) + 2x400 mg Gluteal (Day 1)
	g5	20 mg Oral (Day 1) + 2x400 mg Gluteal (Day 1)
	g7	30 mg Oral (Day 1) + 2x400 mg Gluteal (Day 1)
	d1	10 mg Oral (14 days) + 400 mg Deltoid (Day 1)
	d2	20 mg Oral (14 days) + 400 mg Deltoid (Day 1)
	d6	10 mg Oral (Day 1) + 2x400 mg Deltoid (Day 1)
	d5	20 mg Oral (Day 1) + 2x400 mg Deltoid (Day 1)
	d7	30 mg Oral (Day 1) + 2x400 mg Deltoid (Day 1)
To show separate contribution from oral and IM Depot formulation (one or two injections) to the initiation regimens	g8	20 mg Oral (Day 1)
	g10	400 mg Gluteal (Day 1)
	d10	400 mg Deltoid (Day 1)
	g8	20 mg Oral (Day 1)
	g9	2x400 mg Gluteal (Day 1)
	g8	20 mg Oral (Day 1)
	d9	2x400 mg Deltoid (Day 1)

FIG. 3A

[Fig. 3B]

Table 2.7.2.5.1-1 Purpose and Description of Simulations

Simulation Purpose	Number	Simulation Scenario
To show Cmax distribution and PK profiles following alternate initiation regimens with 2x300 mg or 2x400 mg IM Depot doses compared between the poor and extensive CYP2D6 metabolizers	g5	20 mg Oral (Day 1) + 2x400 mg Gluteal (Day 1) [EM]
	g5p	20 mg Oral (Day 1) + 2x400 mg Gluteal (Day 1) [PM]
	g11	20 mg Oral (Day 1) + 2x300 mg Gluteal (Day 1) [PM]
	d5	20 mg Oral (Day 1) + 2x400 mg Deltoid (Day 1) [EM]
	d5p	20 mg Oral (Day 1) + 2x400 mg Deltoid (Day 1) [PM]
	d11	20 mg Oral (Day 1) + 2x300 mg Deltoid (Day 1) [PM]
To compare PK profile between the existing initiation regimen and the initiation regimen with 20mg oral + 2x400 IM Depot dose when administered in subjects who were already stabilized on oral aripiprazole (10 -30 mg) before initiating treatment with the IM Depot formulation	g12	10 mg Oral (ss) + 10 mg Oral (14 days) + 400 mg Gluteal (Day 1)
	g14	10 mg Oral (ss) + 20 mg Oral (Day 1) + 2x400 mg Gluteal (Day 1)
	g13	20 mg Oral (ss) + 20 mg Oral (14 days) + 400 mg Gluteal (Day 1)
	g15	20mg Oral (ss) + 20 mg Oral (Day 1) + 2x400 mg Gluteal (Day 1)
	g5x	30 mg Oral (ss) + 20 mg Oral (14 days) + 400 mg Gluteal (Day 1)
	g13x	30mg Oral (ss) + 20 mg Oral (Day 1) + 2x400 mg Gluteal (Day 1)
	d12	10 mg Oral (ss) + 10 mg Oral (14 days) + 400 mg Deltoid (Day 1)
	d14	10 mg Oral (ss) + 20 mg Oral (Day 1) + 2x400 mg Deltoid (Day 1)
	d13	20 mg Oral (ss) + 20 mg Oral (14 days) + 400 mg Deltoid (Day 1)
	d15	20mg Oral (ss) + 20 mg Oral (Day 1) + 2x400 mg Deltoid (Day 1)
	d5x	30 mg Oral (ss) + 20 mg Oral (14 days) + 400 mg Deltoid (Day 1)
	d13x	30mg Oral (ss) + 20 mg Oral (Day 1) + 2x400 mg Deltoid (Day 1)
To compare PK profile between the existing initiation regimen and the initiation regimen with 20 mg oral + 2x300 or 2x400 mg IM Depot dose in subjects who were already stabilized on oral aripiprazole (30 mg [EM] or 15 mg [PM]) before initiating treatment with the IM Depot formulation	g5x	30 mg Oral (ss) + 20 mg Oral (1 day) + 400 mg Gluteal (Day 1) [EM]
	g5px2	15 mg Oral (ss) + 20 mg Oral (Day 1) + 2x400 mg Gluteal (Day 1) [PM]
	g11x2	15 mg Oral (ss) + 20 mg Oral (Day 1) + 2x300 mg Gluteal (Day 1) [PM]
	d5x	30 mg Oral (ss) + 20 mg Oral (1 day) + 400 mg Deltoid (Day 1) [EM]
	d5px2	15 mg Oral (ss) + 20 mg Oral (Day 1) + 2x400 mg Deltoid (Day 1) [PM]
	d11x2	15 mg Oral (ss) + 20 mg Oral (Day 1) + 2x300 mg Deltoid (Day 1) [PM]

FIG. 3B

[Fig. 3C]

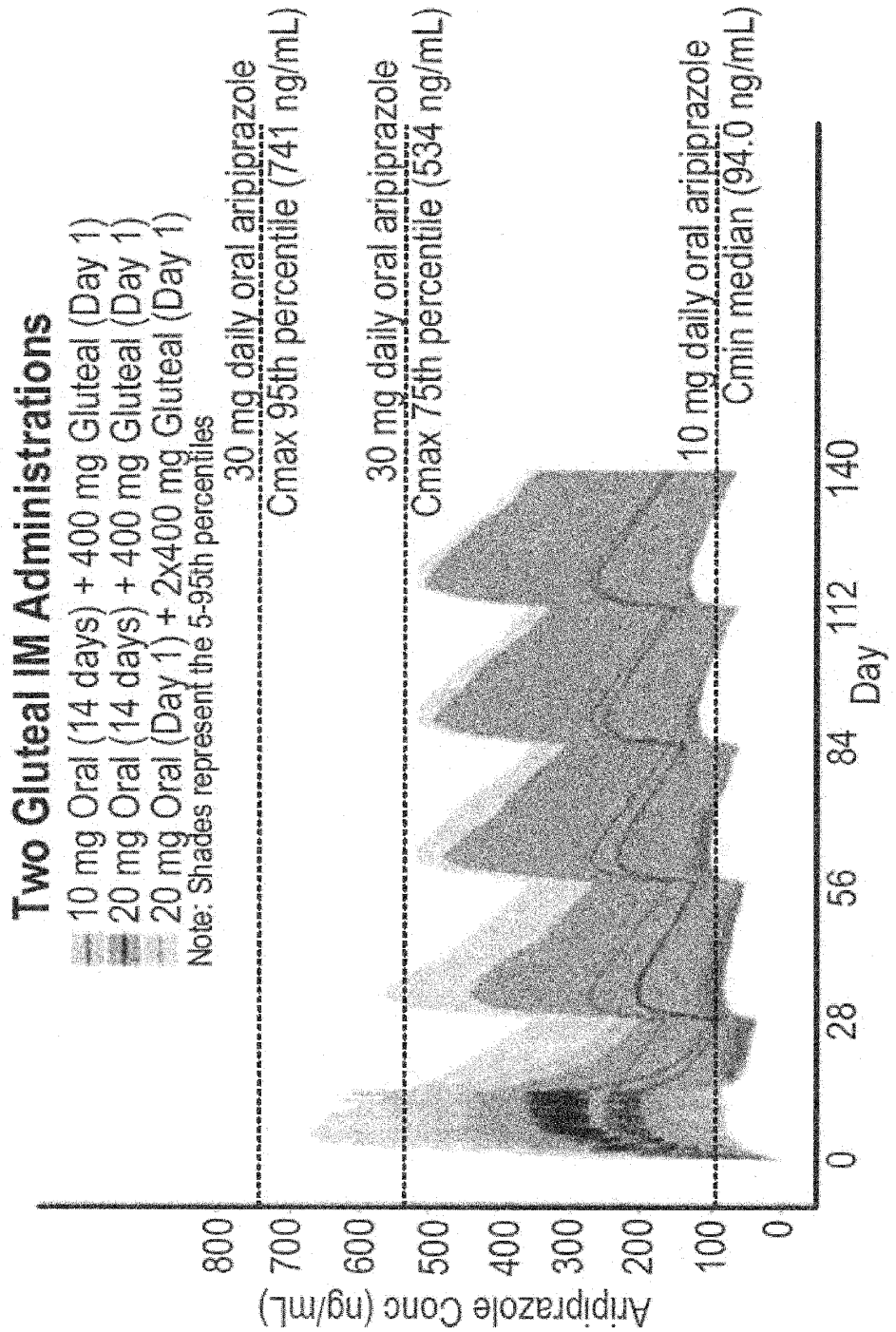
Table 2.7.2.5.1-1 Purpose and Description of Simulations

Simulation Purpose	Number	Simulation Scenario
To compare PK profile between the existing initiation regimen and the initiation regimen with 20 mg oral + 2x300 or 2x400 mg IM Depot dose in subjects who were already stabilized on oral aripiprazole (20 mg [EM] or 10 mg [PM]) before initiating treatment with the IM Depot formulation	g15	20 mg Oral (ss) + 20 mg Oral (1 day) + 400 mg Gluteal (Day 1) [EM]
	g5px3	10 mg Oral (ss) + 20 mg Oral (Day 1) + 2x400 mg Gluteal (Day 1) [PM]
	g11x3	10 mg Oral (ss) + 20 mg Oral (Day 1) + 2x300 mg Gluteal (Day 1) [PM]
	d15	20 mg Oral (ss) + 20 mg Oral (1 day) + 400 mg Deltoid (Day 1) [EM]
	d5px3	10 mg Oral (ss) + 20 mg Oral (Day 1) + 2x400 mg Deltoid (Day 1) [PM]
	d11x3	10 mg Oral (ss) + 20 mg Oral (Day 1) + 2x300 mg Deltoid (Day 1) [PM]
To compare PK following initiation and re-initiation with 20 mg oral + 2x400 mg IM Depot dose (an alternative initiation regimen) vs the existing initiation regimen when the second or third IM Depot dose was missed, and it has been 5 weeks since the last IM Depot dose	g19	Missed 2nd Dose- Re-initiation with 20 mg oral (Day 1) + 2x400 mg IM (Day 1) [Gluteal]
	g20	Missed 2nd Dose- Re-initiation with 20 mg oral (14 days) + 400 mg IM (Day 1) [Gluteal]
	g21	Missed 3rd Dose- Re-initiation with 20 mg oral (Day 1) + 2x400 mg IM (Day 1) [Gluteal]
	g22	Missed 3rd Dose- Re-initiation with 20 mg oral (14 days) + 400 mg IM (Day 1) [Gluteal]
	d19	Missed 2nd Dose- Re-initiation with 20 mg oral (Day 1) + 2x400 mg IM (Day 1) [Deltoid]
	d20	Missed 2nd Dose- Re-initiation with 20 mg oral (14 days) + 400 mg IM (Day 1) [Deltoid]
	d21	Missed 3rd Dose- Re-initiation with 20 mg oral (Day 1) + 2x400 mg IM (Day 1) [Deltoid]
	d22	Missed 3rd Dose- Re-initiation with 20 mg oral (14 days) + 400 mg IM (Day 1) [Deltoid]
To compare PK following initiation and reinitiation with 20 mg oral + 2 x 400 mg IM depot dose (an alternative initiation regimen) vs the existing initiation regimen when the fourth or a steady state IM depot dose was missed, and it has been 6 weeks since the last IM depot dose To compare PK following initiation and re-initiation with 20 mg oral + 2x400 mg IM Depot dose (an alternative initiation regimen) vs the existing initiation regimen when the fourth or a steady state IM Depot dose was missed, and it has been 6 weeks since the last IM Depot dose	g23	Missed 4th Dose- Re-initiation with 20 mg oral (Day 1) + 2x400 mg IM (Day 1) [Gluteal]
	g24	Missed 4th Dose- Re-initiation with 20 mg oral (14 days) + 400 mg IM (Day 1) [Gluteal]
	g25	Missed ss Dose- Re-initiation with 20 mg oral (Day 1) + 2x400 mg IM (Day 1) [Gluteal]
	g26	Missed ss Dose- Re-initiation with 20 mg oral (14 days) + 400 mg IM (Day 1) [Gluteal]
	d23	Missed 4th Dose- Re-initiation with 20 mg oral (Day 1) + 2x400 mg IM (Day 1) [Deltoid]
	d24	Missed 4th Dose- Re-initiation with 20 mg oral (14 days) + 400 mg IM (Day 1) [Deltoid]
	d25	Missed ss Dose- Re-initiation with 20 mg oral (Day 1) + 2x400 mg IM (Day 1) [Deltoid]
	d26	Missed ss Dose- Re-initiation with 20 mg oral (14 days) + 400 mg IM (Day 1) [Deltoid]

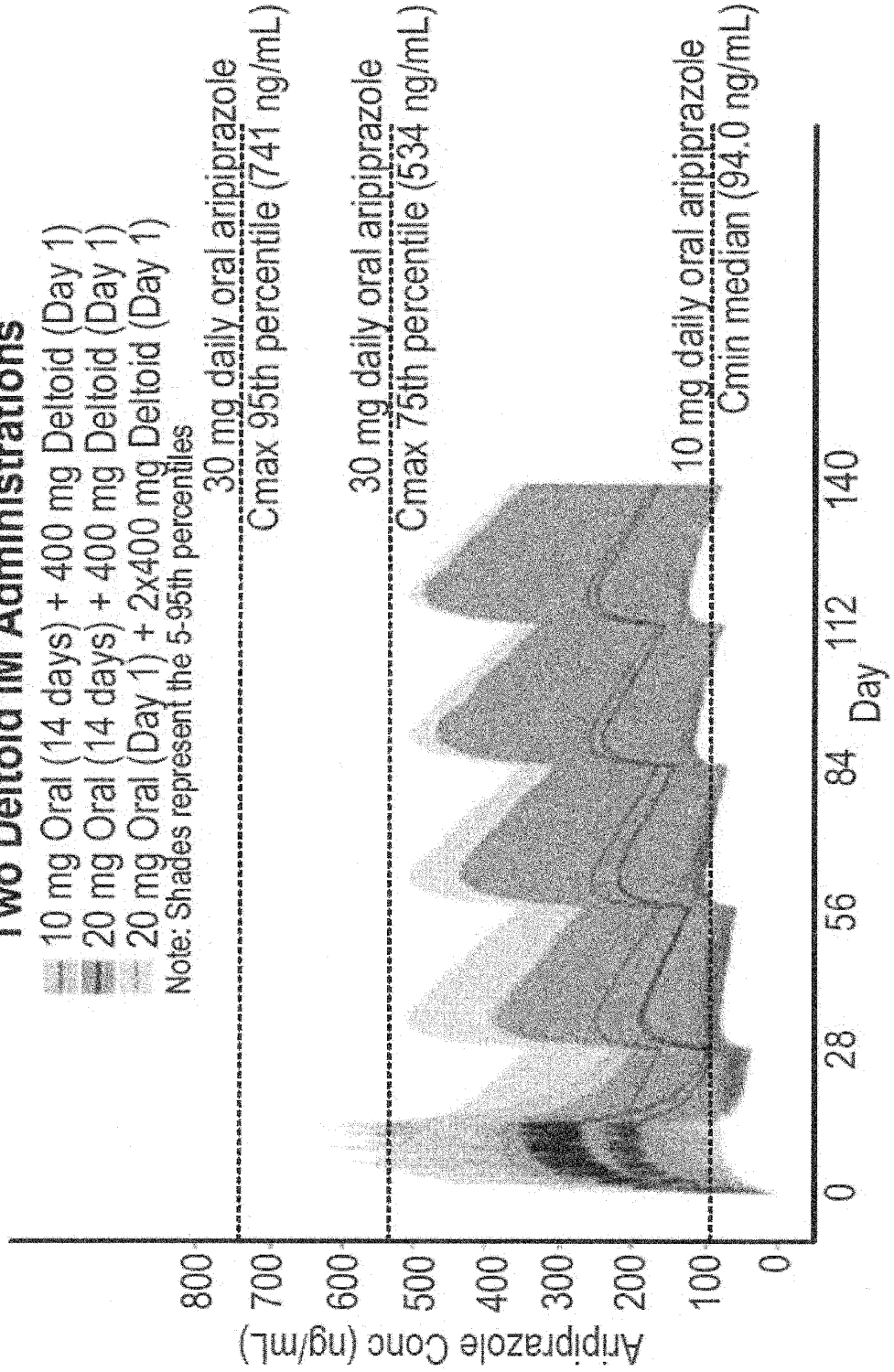
FIG. 3C

[Fig. 4A]

FIG. 4A


Two Gluteal IM Administrations
10 mg Oral (14 days) + 400 mg Gluteal (Day 1)
20 mg Oral (14 days) + 400 mg Gluteal (Day 1)
20 mg Oral (Day 1) + 2x400 mg Gluteal (Day 1)
Note: Shades represent the 5-95th percentiles
30 mg daily oral aripiprazole
Cmax 95th percentile (741 ng/mL)
30 mg daily oral aripiprazole
Cmax 75th percentile (534 ng/mL)
10 mg daily oral aripiprazole
Cmin median (94.0 ng/mL)
Aripiprazole Conc (ng/mL)
800
700
600
500
400
300
200
100
0
0
28
56
84
112
140
Day

[Fig. 4B]


FIG. 4B
Two Deltoid IM Administrations
10 mg Oral (14 days) + 400 mg Deltoid (Day 1)
20 mg Oral (14 days) + 400 mg Deltoid (Day 1)
20 mg Oral (Day 1) + 2x400 mg Deltoid (Day 1)
Note: Shades represent the 5-95th percentiles
30 mg daily oral aripiprazole
Cmax 95th percentile (741 ng/mL)
30 mg daily oral aripiprazole
Cmax 75th percentile (534 ng/mL)
10 mg daily oral aripiprazole
Cmin median (94.0 ng/mL)
Aripiprazole Conc (ng/mL)
800
700
600
500
400
300
200
100
0
0
28
56
84
112
140
Day

[Fig. 4C]

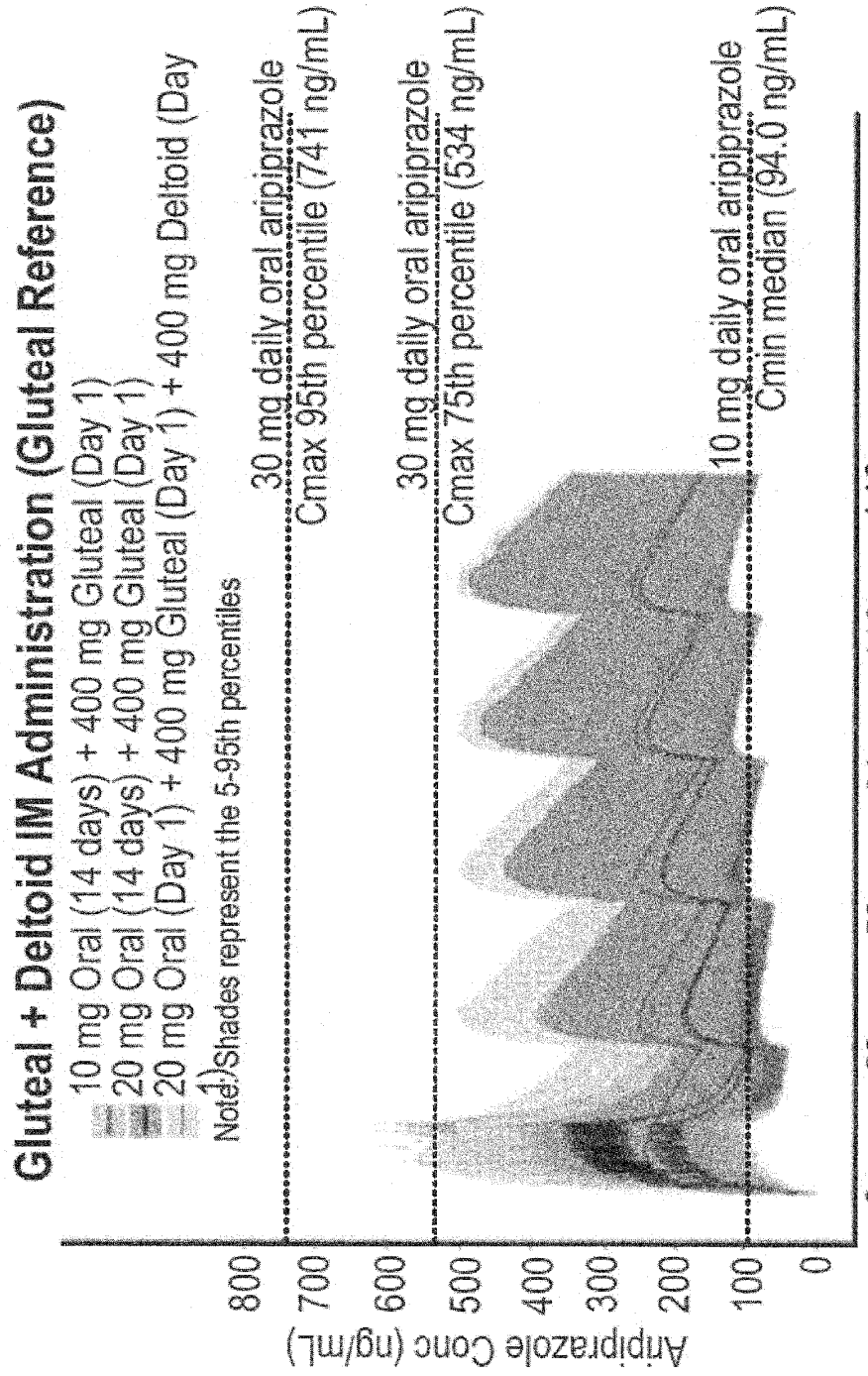

Gluteal + Deltoid IM Administration (Gluteal Reference)
10 mg Oral (14 days) + 400 mg Gluteal (Day 1)
20 mg Oral (14 days) + 400 mg Gluteal (Day 1)
20 mg Oral (Day 1) + 400 mg Gluteal (Day 1) + 400 mg Deltoid (Day 1)
Note: Shades represent the 5-95th percentiles
30 mg daily oral aripiprazole
Cmax 95th percentile (741 ng/mL)
30 mg daily oral aripiprazole
Cmax 75th percentile (534 ng/mL)
10 mg daily oral aripiprazole
Cmin median (94.0 ng/mL)
Aripiprazole Conc (ng/mL)
800
700
600
500
400
300
200
100
0
0
28
56
84
112
140
Day

FIG. 4C

[Fig. 4D]

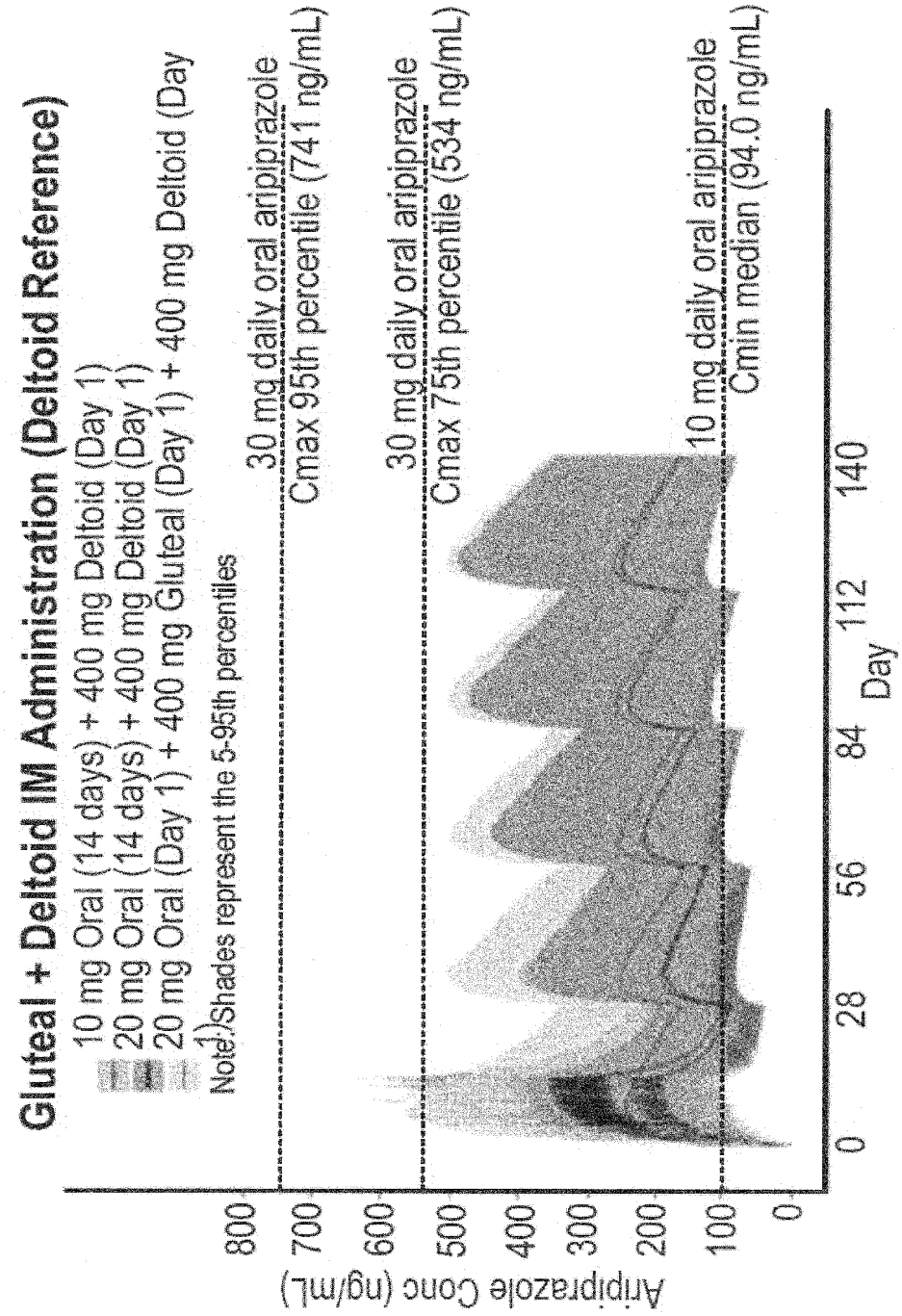

Gluteal + Deltoid IM Administration (Deltoid Reference)
10 mg Oral (14 days) + 400 mg Deltoid (Day 1)
20 mg Oral (14 days) + 400 mg Deltoid (Day 1)
20 mg Oral (Day 1) + 400 mg Gluteal (Day 1) + 400 mg Deltoid (Day 1)
Note: Shades represent the 5-95th percentiles
30 mg daily oral aripiprazole
Cmax 95th percentile (741 ng/mL)
30 mg daily oral aripiprazole
Cmax 75th percentile (534 ng/mL)
10 mg daily oral aripiprazole
Cmin median (94.0 ng/mL)
Aripiprazole Conc (ng/mL)
800
700
600
500
400
300
200
100
0
0
28
56
84
112
140
Day

FIG. 4D

[Fig. 5A]

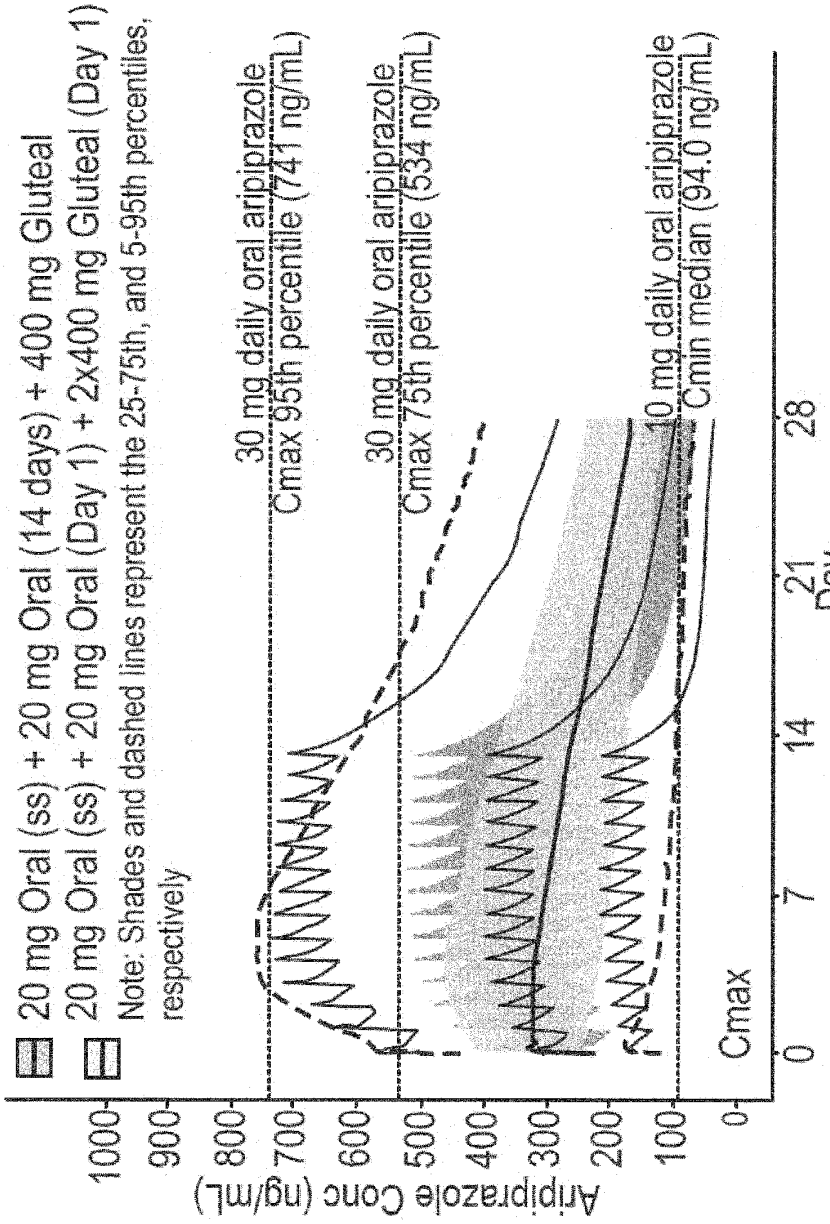

Gluteal IM Administration
20 mg Oral (ss) + 20 mg Oral (14 days) + 400 mg Gluteal
20 mg Oral (ss) + 20 mg Oral (Day 1) + 2x400 mg Gluteal (Day 1)
Note: Shades and dashed lines represent the 25-75th, and 5-95th percentiles, respectively
30 mg daily oral aripiprazole
Cmax 95th percentile (741 ng/mL)
30 mg daily oral aripiprazole
Cmax 75th percentile (534 ng/mL)
10 mg daily oral aripiprazole
Cmin median (94.0 ng/mL)
Cmax
Aripiprazole Conc (ng/mL)
1000
900
800
700
600
500
400
300
200
100
0
0
7
14
21
28
Day

FIG. 5A

[Fig. 5B]

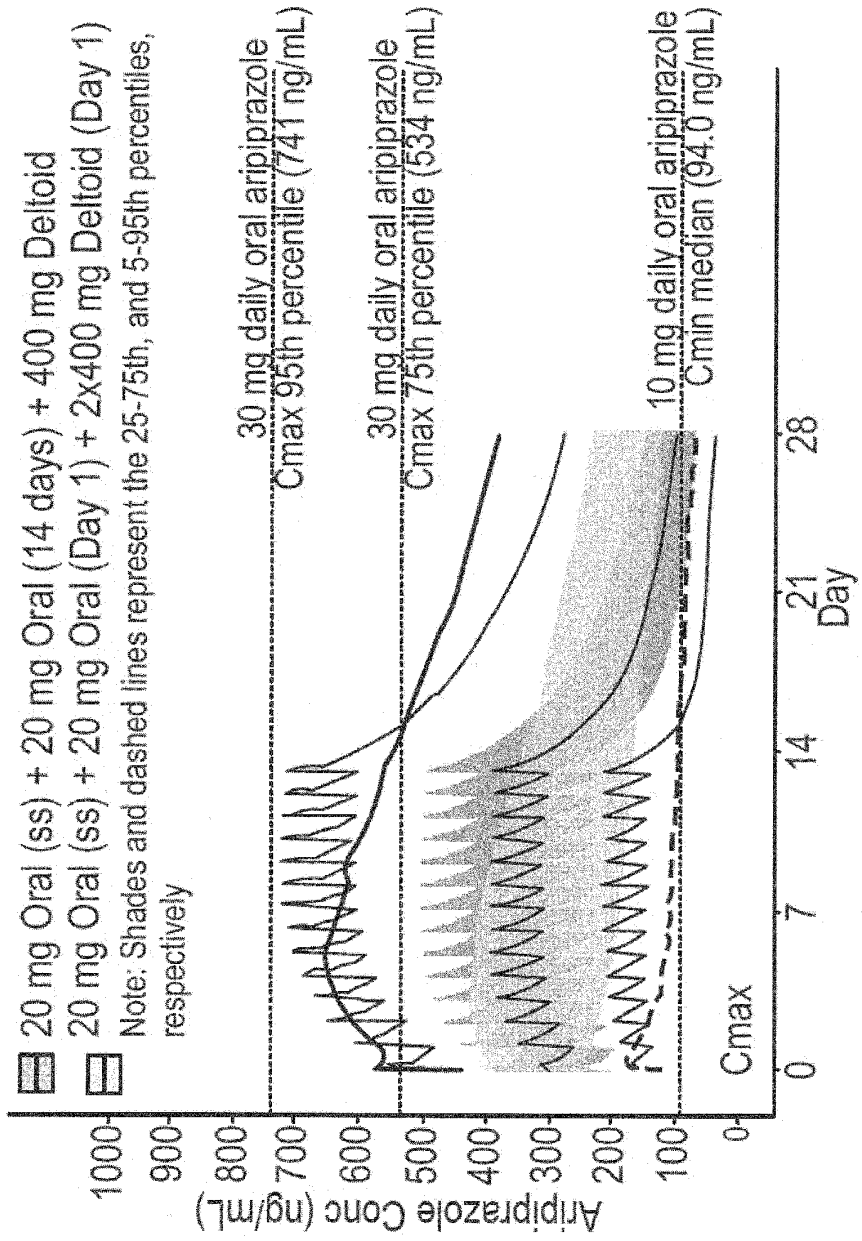

Deltoid IM Administration
20 mg Oral (ss) + 20 mg Oral (14 days) + 400 mg Deltoid
20 mg Oral (ss) + 20 mg Oral (Day 1) + 2x400 mg Deltoid (Day 1)
Note: Shades and dashed lines represent the 25-75th, and 5-95th percentiles, respectively
30 mg daily oral aripiprazole Cmax 95th percentile (741 ng/mL)
30 mg daily oral aripiprazole Cmax 75th percentile (534 ng/mL)
10 mg daily oral aripiprazole Cmin median (94.0 ng/mL)
Cmax
Aripiprazole Conc (ng/mL)
1000
900
800
700
600
500
400
300
200
100
0
0
7
14
21
28
Day

FIG. 5B

[Fig. 6A]

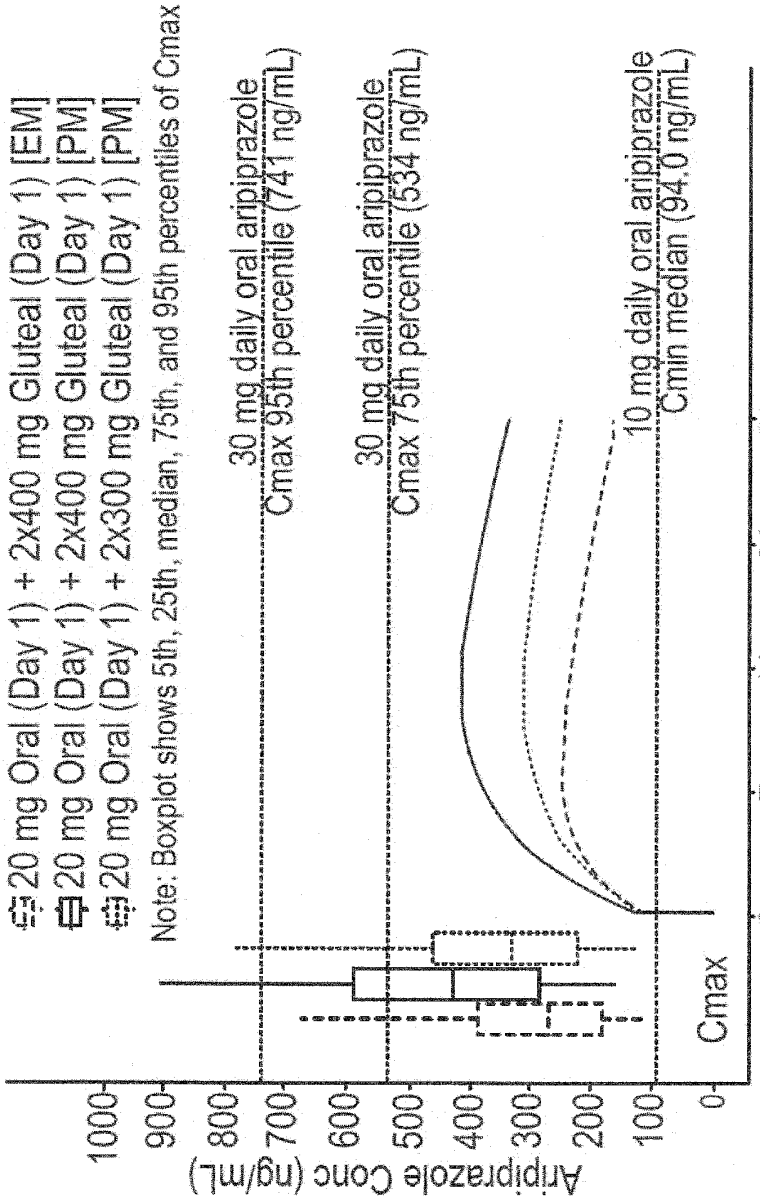

Gluteal IM Administration
20 mg Oral (Day 1) + 2x400 mg Gluteal (Day 1) [EM]
20 mg Oral (Day 1) + 2x400 mg Gluteal (Day 1) [PM]
20 mg Oral (Day 1) + 2x300 mg Gluteal (Day 1) [PM]
Note: Boxplot shows 5th, 25th, median, 75th, and 95th percentiles of Cmax
30 mg daily oral aripiprazole
Cmax 95th percentile (741 ng/mL)
30 mg daily oral aripiprazole
Cmax 75th percentile (534 ng/mL)
10 mg daily oral aripiprazole
Cmin median (94.0 ng/mL)
Cmax
Aripiprazole Conc (ng/mL)
1000
900
800
700
600
500
400
300
200
100
0
0
7
14
21
28
Day

FIG. 6A

[Fig. 6B]

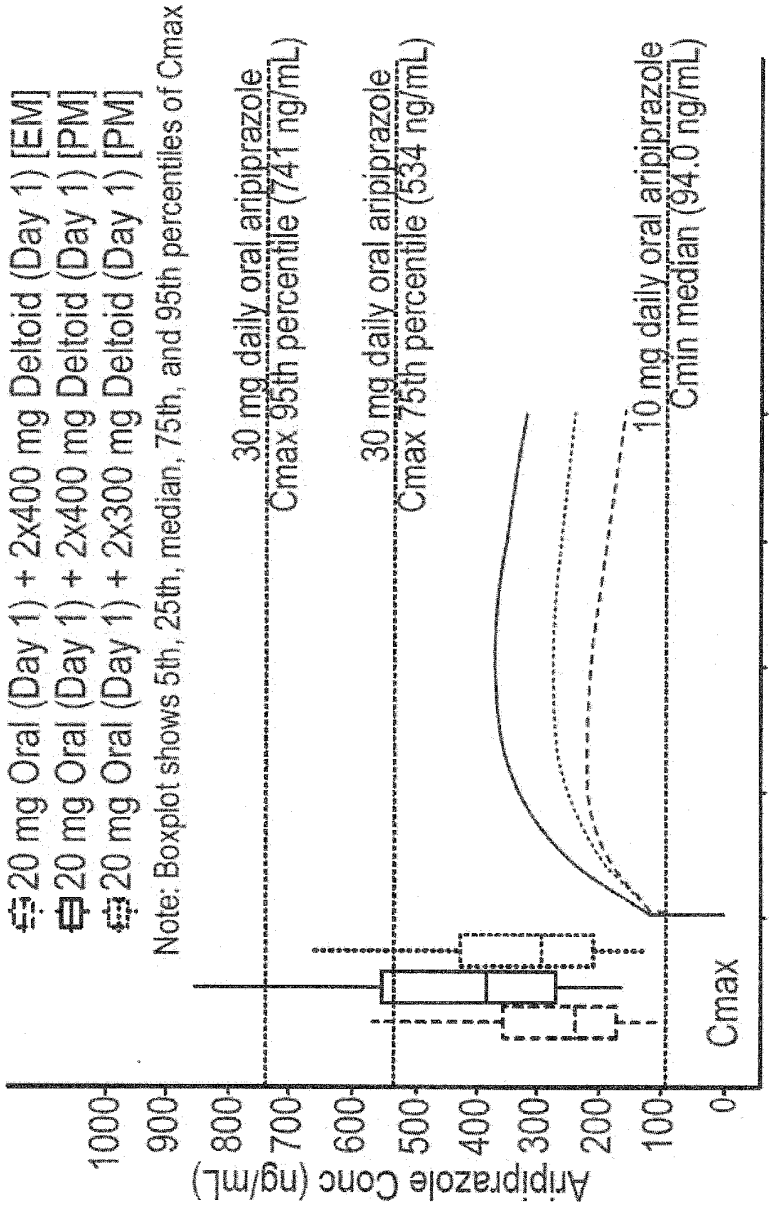

Deltoid IM Administration
20 mg Oral (Day 1) + 2x400 mg Deltoid (Day 1) [EM]
20 mg Oral (Day 1) + 2x400 mg Deltoid (Day 1) [PM]
20 mg Oral (Day 1) + 2x300 mg Deltoid (Day 1) [PM]
Note: Boxplot shows 5th, 25th, median, 75th, and 95th percentiles of Cmax
30 mg daily oral aripiprazole
Cmax 95th percentile (741 ng/mL)
30 mg daily oral aripiprazole
Cmax 75th percentile (534 ng/mL)
10 mg daily oral aripiprazole
Cmin median (94.0 ng/mL)
Cmax
Aripiprazole Conc (ng/mL)
1000
900
800
700
600
500
400
300
200
100
0
0
7
14
21
28
Day

FIG. 6B

[Fig. 7A]

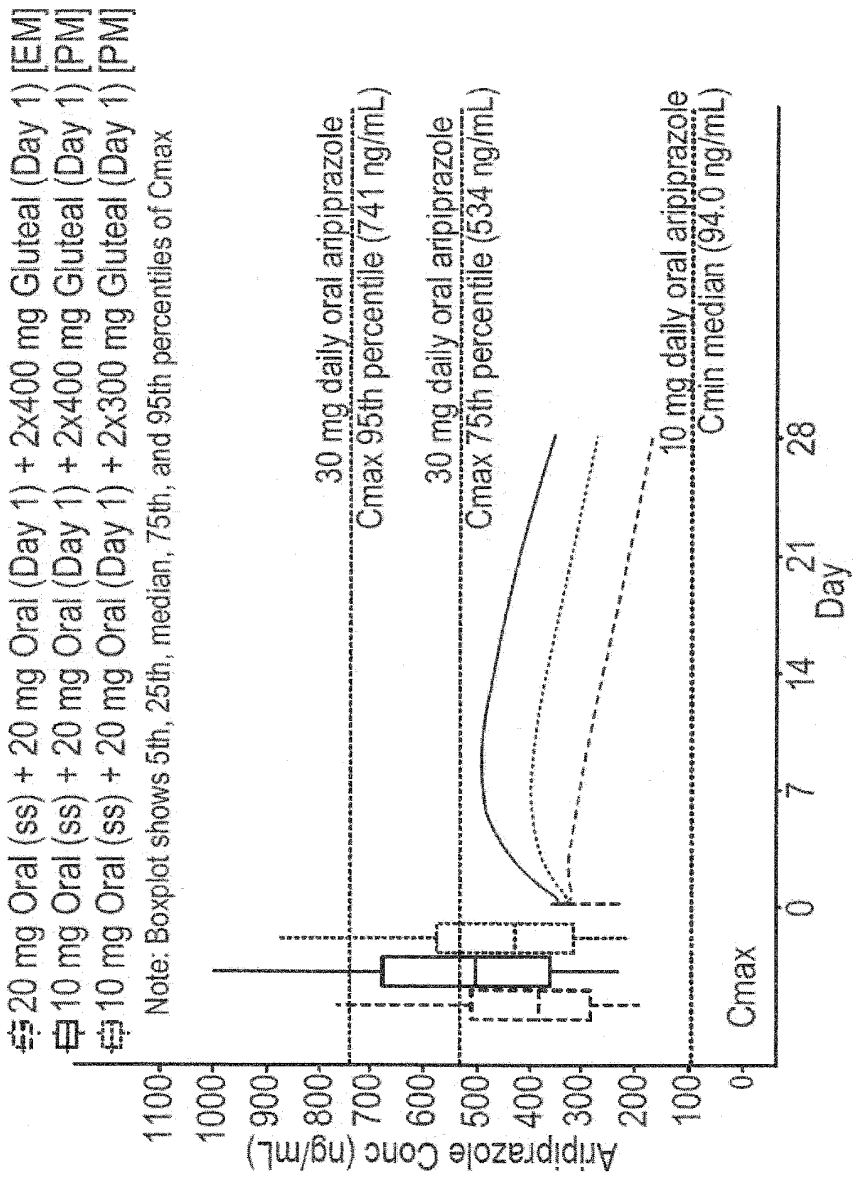

Gluteal IM Administration
20 mg Oral (ss) + 20 mg Oral (Day 1) + 2x400 mg Gluteal (Day 1) [EM]
10 mg Oral (ss) + 20 mg Oral (Day 1) + 2x400 mg Gluteal (Day 1) [PM]
10 mg Oral (ss) + 20 mg Oral (Day 1) + 2x300 mg Gluteal (Day 1) [PM]
Note: Boxplot shows 5th, 25th, median, 75th, and 95th percentiles of Cmax
30 mg daily oral aripiprazole
Cmax 95th percentile (741 ng/mL)
30 mg daily oral aripiprazole
Cmax 75th percentile (534 ng/mL)
10 mg daily oral aripiprazole
Cmin median (94.0 ng/mL)
Aripiprazole Conc (ng/mL)
1100
1000
900
800
700
600
500
400
300
200
100
0
Cmax
0
7
14
21
28
Day

FIG. 7A

[Fig. 7B]

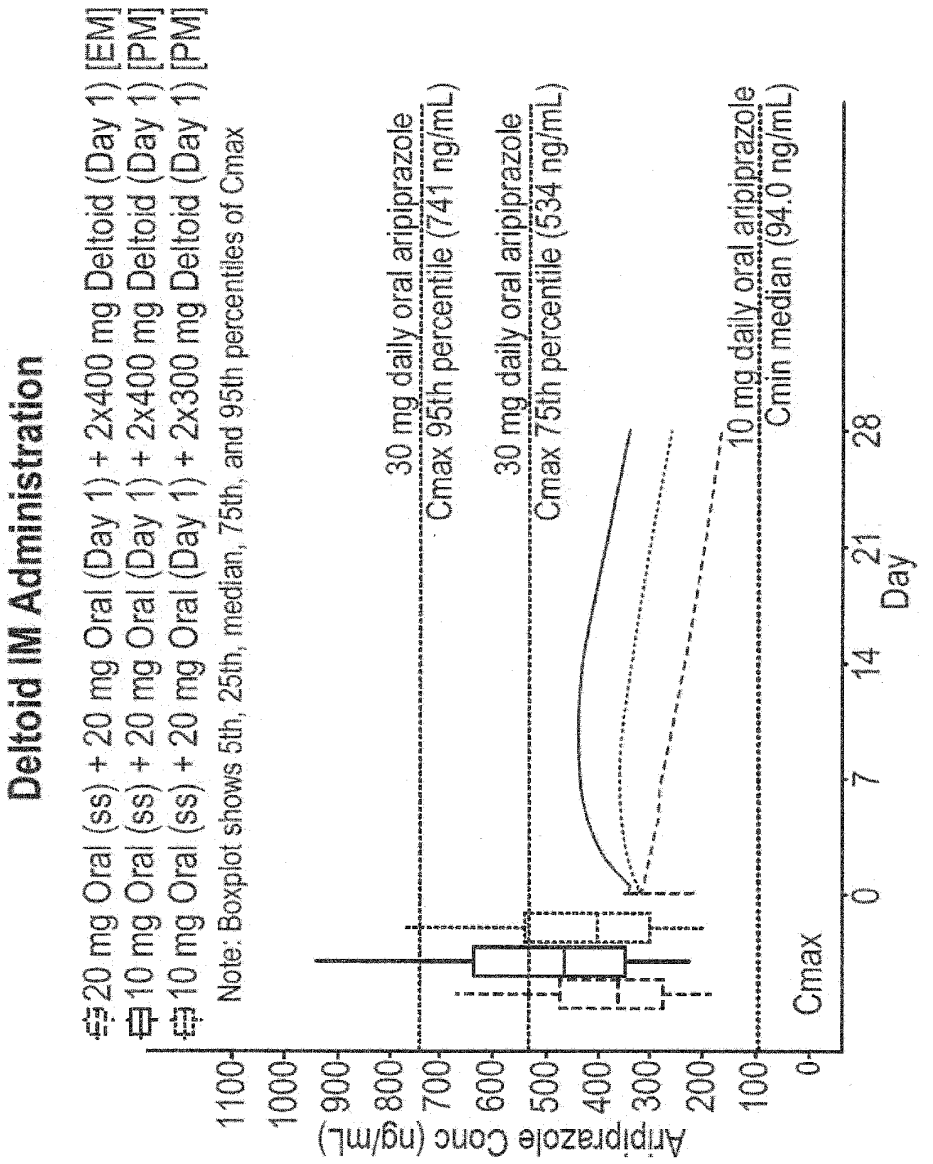
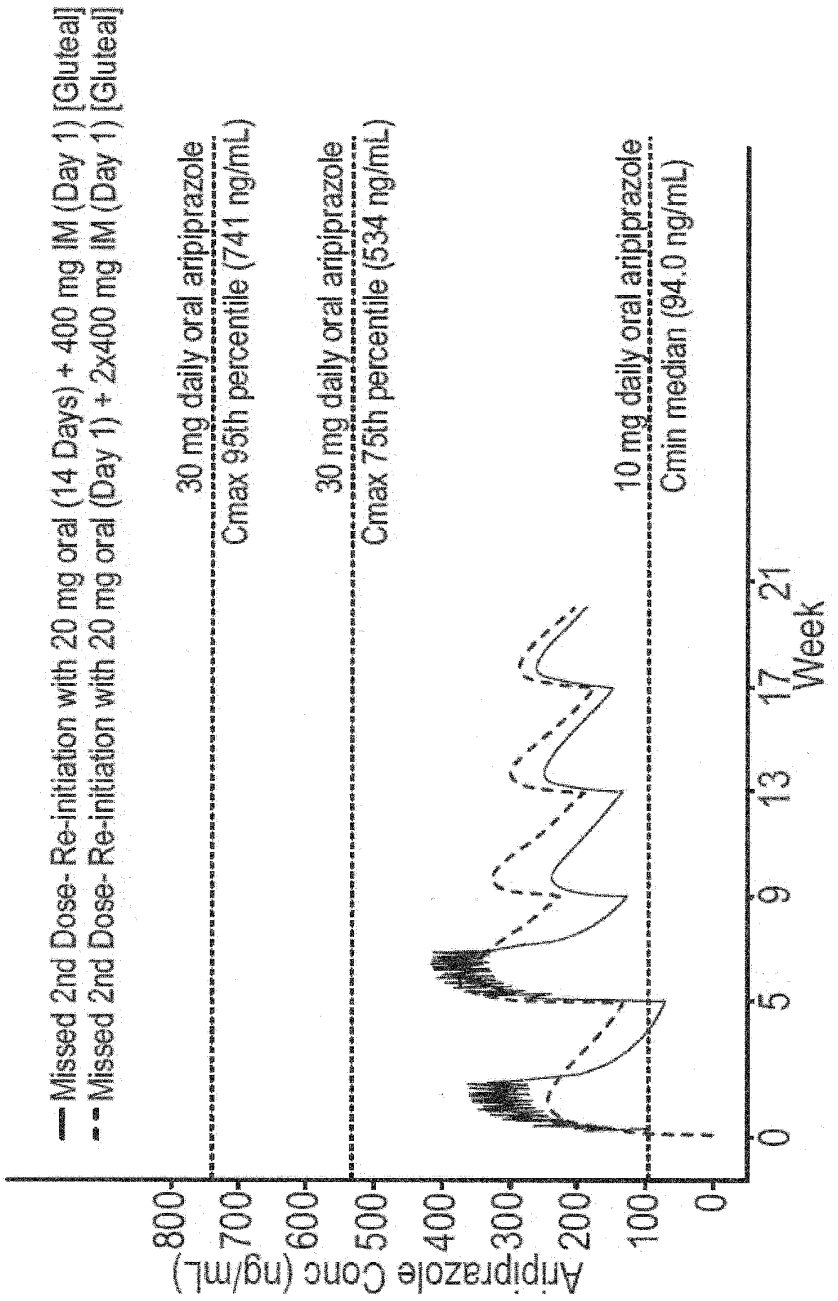

Deltoid IM Administration
20 mg Oral (ss) + 20 mg Oral (Day 1) + 2x400 mg Deltoid (Day 1) [EM]
10 mg Oral (ss) + 20 mg Oral (Day 1) + 2x400 mg Deltoid (Day 1) [PM]
10 mg Oral (ss) + 20 mg Oral (Day 1) + 2x300 mg Deltoid (Day 1) [PM]
Note: Boxplot shows 5th, 25th, median, 75th, and 95th percentiles of Cmax
30 mg daily oral aripiprazole
Cmax 95th percentile (741 ng/mL)
30 mg daily oral aripiprazole
Cmax 75th percentile (534 ng/mL)
10 mg daily oral aripiprazole
Cmin median (94.0 ng/mL)
Aripiprazole Conc (ng/mL)
1100
1000
900
800
700
600
500
400
300
200
100
0
Cmax
0
7
14
21
28
Day

FIG. 7B

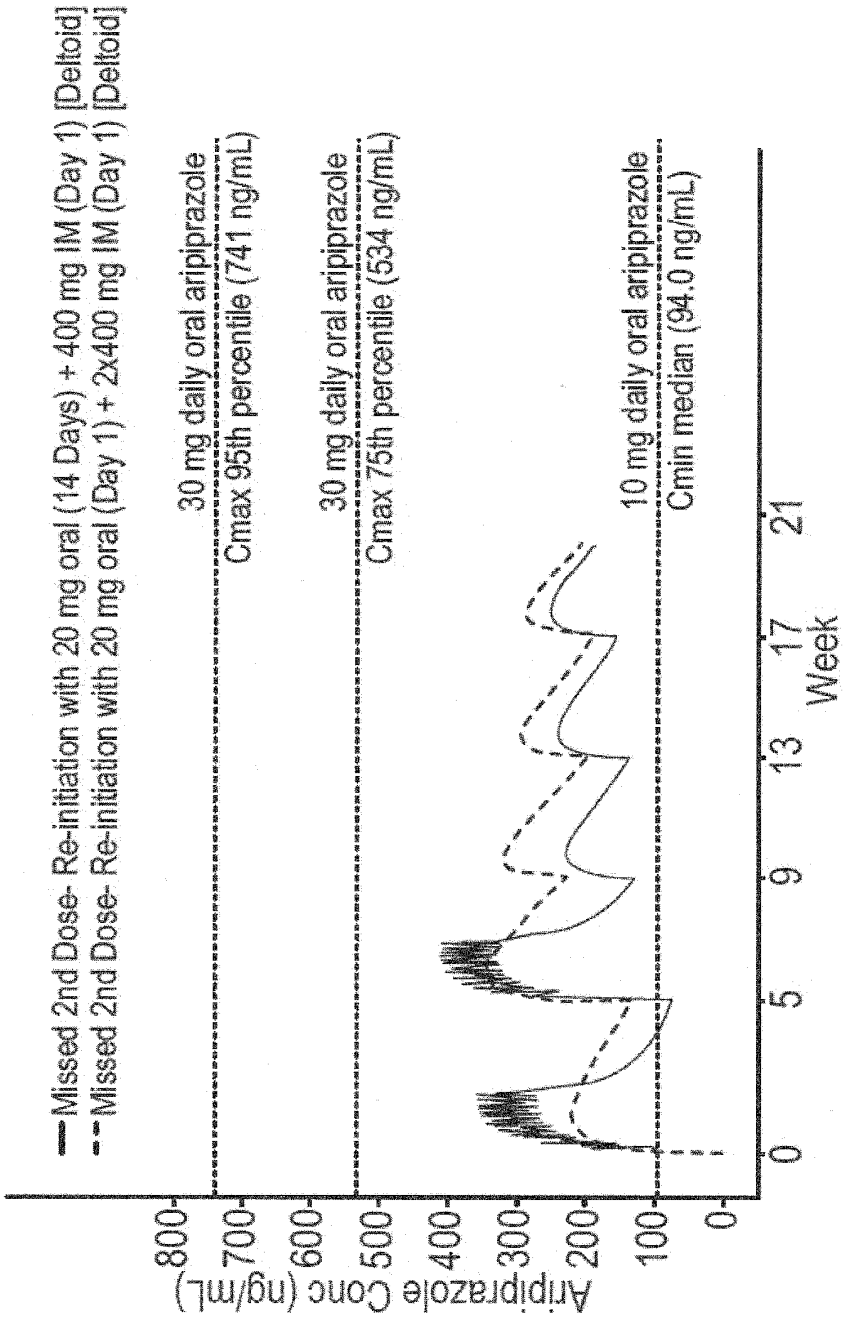
[Fig. 8A]

FIG. 8A


Missed 2nd Gluteal IM Administration
Missed 2nd Dose- Re-initiation with 20 mg oral (14 Days) + 400 mg IM (Day 1) [Gluteal]
Missed 2nd Dose- Re-initiation with 20 mg oral (Day 1) + 2x400 mg IM (Day 1) [Gluteal]
30 mg daily oral aripiprazole
Cmax 95th percentile (741 ng/mL)
30 mg daily oral aripiprazole
Cmax 75th percentile (534 ng/mL)
10 mg daily oral aripiprazole
Cmin median (94.0 ng/mL)
Aripiprazole Conc (ng/mL)
800
700
600
500
400
300
200
100
0
0
5
9
13
17
21
Week

[Fig. 8B]

FIG. 8B


Missed 2nd Deltoid IM Administration
Missed 2nd Dose- Re-initiation with 20 mg oral (14 Days) + 400 mg IM (Day 1) [Deltoid]
Missed 2nd Dose- Re-initiation with 20 mg oral (Day 1) + 2x400 mg IM (Day 1) [Deltoid]
30 mg daily oral aripiprazole
Cmax 95th percentile (741 ng/mL)
30 mg daily oral aripiprazole
Cmax 75th percentile (534 ng/mL)
10 mg daily oral aripiprazole
Cmin median (94.0 ng/mL)
Aripiprazole Conc (ng/mL)
0
100
200
300
400
500
600
700
800
0
5
9
13
17
21
Week

[Fig. 8C]

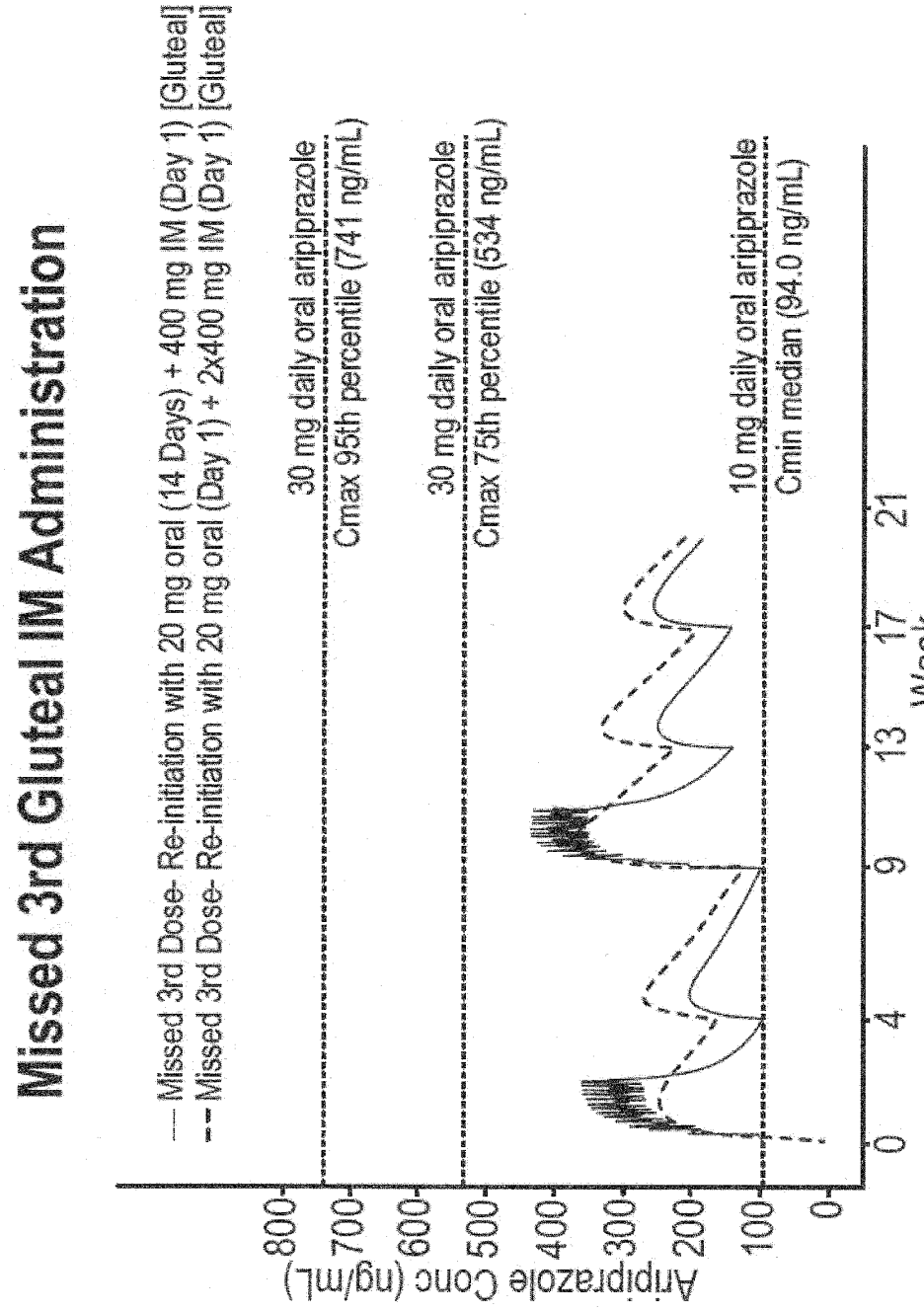

Missed 3rd Gluteal IM Administration
Missed 3rd Dose- Re-initiation with 20 mg oral (14 Days) + 400 mg IM (Day 1) [Gluteal]
Missed 3rd Dose- Re-initiation with 20 mg oral (Day 1) + 2x400 mg IM (Day 1) [Gluteal]
30 mg daily oral aripiprazole
Cmax 95th percentile (741 ng/mL)
30 mg daily oral aripiprazole
Cmax 75th percentile (534 ng/mL)
10 mg daily oral aripiprazole
Cmin median (94.0 ng/mL)
Aripiprazole Conc (ng/mL)
0
100
200
300
400
500
600
700
800
0
4
9
13
17
21
Week

FIG. 8C

[Fig. 8D]

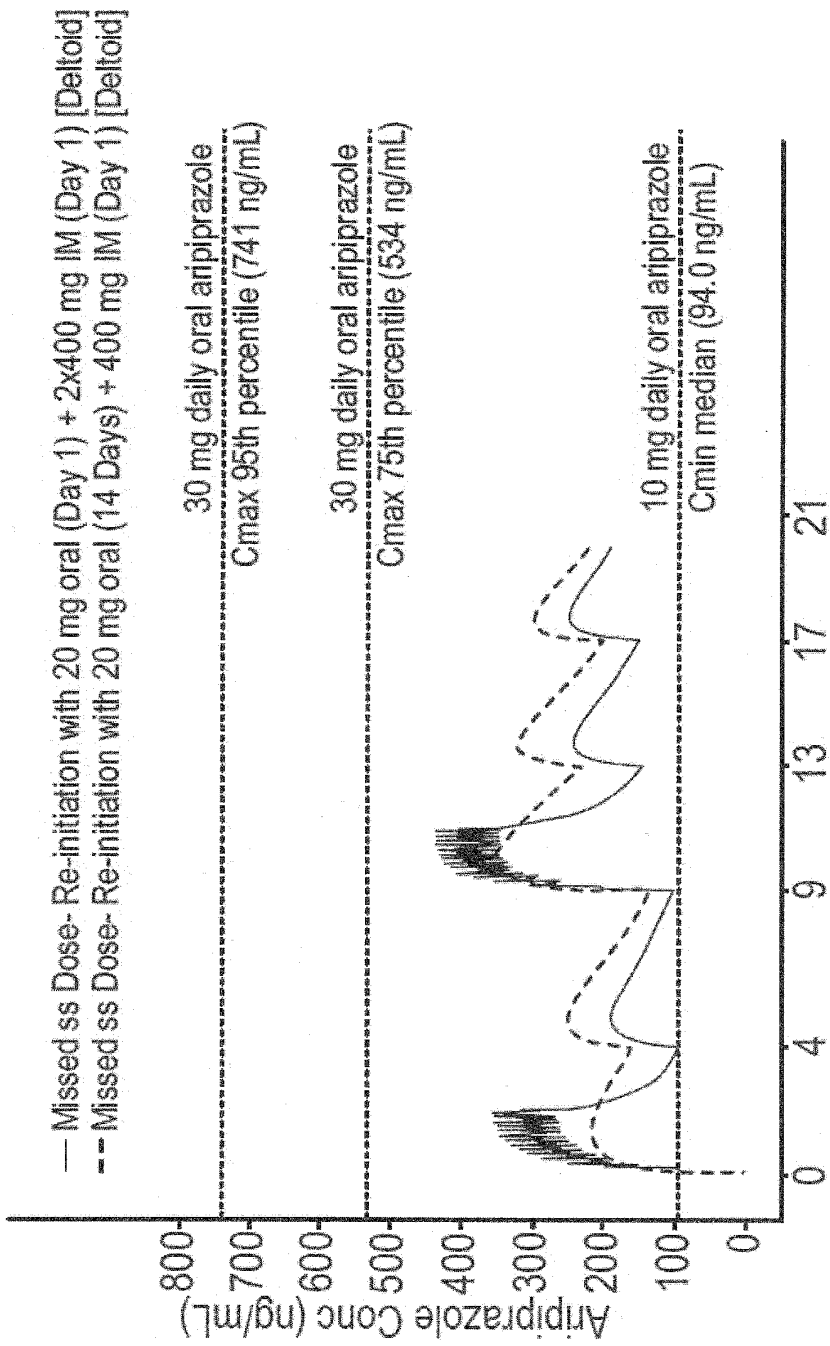
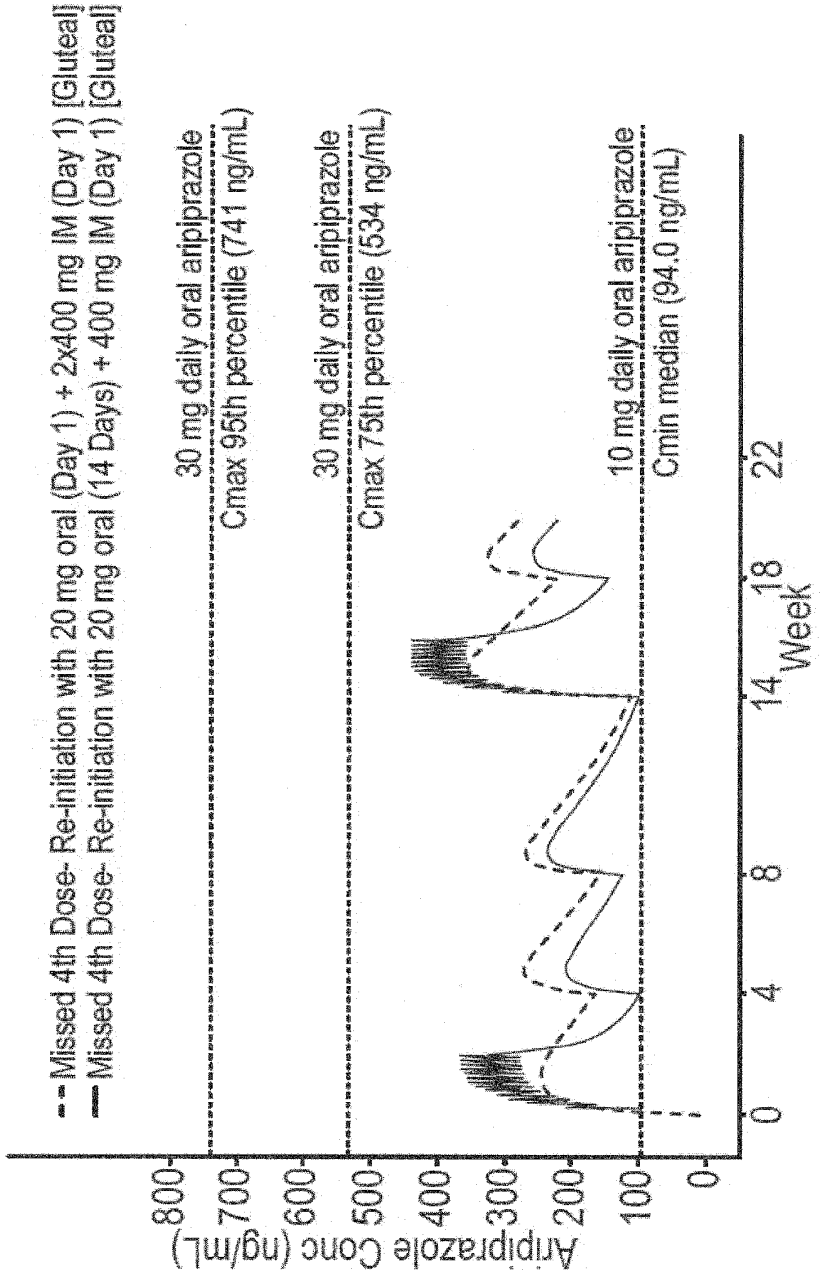

Missed 3rd Deltoid IM Administration
— Missed ss Dose- Re-initiation with 20 mg oral (Day 1) + 2x400 mg IM (Day 1) [Deltoid]
-- Missed ss Dose- Re-initiation with 20 mg oral (14 Days) + 400 mg IM (Day 1) [Deltoid]
30 mg daily oral aripiprazole
Cmax 95th percentile (741 ng/mL)
30 mg daily oral aripiprazole
Cmax 75th percentile (534 ng/mL)
10 mg daily oral aripiprazole
Cmin median (94.0 ng/mL)
Aripiprazole Conc (ng/mL)
800
700
600
500
400
300
200
100
0
0
4
9
13
17
21
Week

FIG. 8D

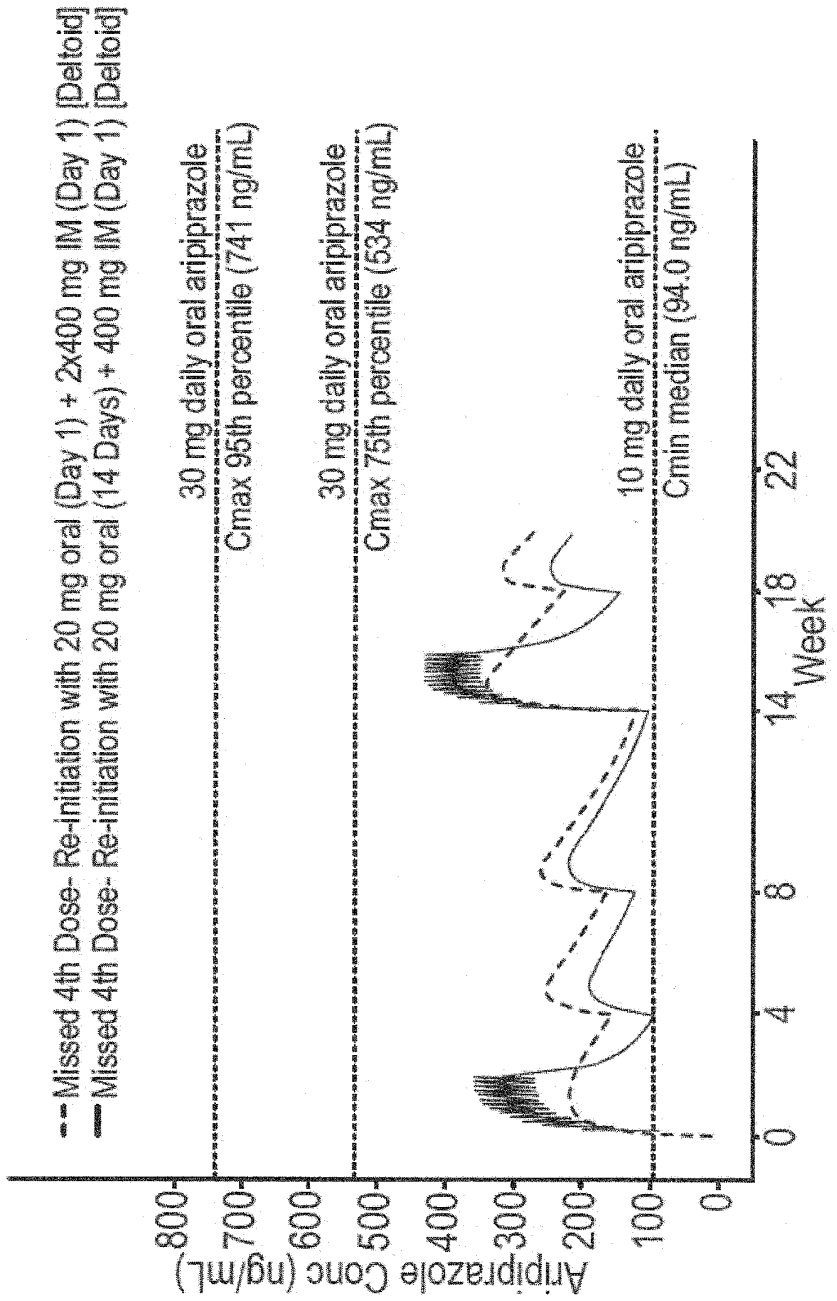
[Fig. 9A]

FIG. 9A


Missed 4th Gluteal IM Administration
Missed 4th Dose- Re-initiation with 20 mg oral (Day 1) + 2x400 mg IM (Day 1) [Gluteal]
Missed 4th Dose- Re-initiation with 20 mg oral (14 Days) + 400 mg IM (Day 1) [Gluteal]
30 mg daily oral aripiprazole
Cmax 95th percentile (741 ng/mL)
30 mg daily oral aripiprazole
Cmax 75th percentile (534 ng/mL)
10 mg daily oral aripiprazole
Cmin median (94.0 ng/mL)
Aripiprazole Conc (ng/mL)
0
100
200
300
400
500
600
700
800
0
4
8
14
18
22
Week

[Fig. 9B]

FIG. 9B


Missed 4th Deltoid IM Administration
Missed 4th Dose- Re-initiation with 20 mg oral (Day 1) + 2x400 mg IM (Day 1) [Deltoid]
Missed 4th Dose- Re-initiation with 20 mg oral (14 Days) + 400 mg IM (Day 1) [Deltoid]
30 mg daily oral aripiprazole
Cmax 95th percentile (741 ng/mL)
30 mg daily oral aripiprazole
Cmax 75th percentile (534 ng/mL)
10 mg daily oral aripiprazole
Cmin median (94.0 ng/mL)
Aripiprazole Conc (ng/mL)
800
700
600
500
400
300
200
100
0
0
4
8
14
18
22
Week

[Fig. 9C]

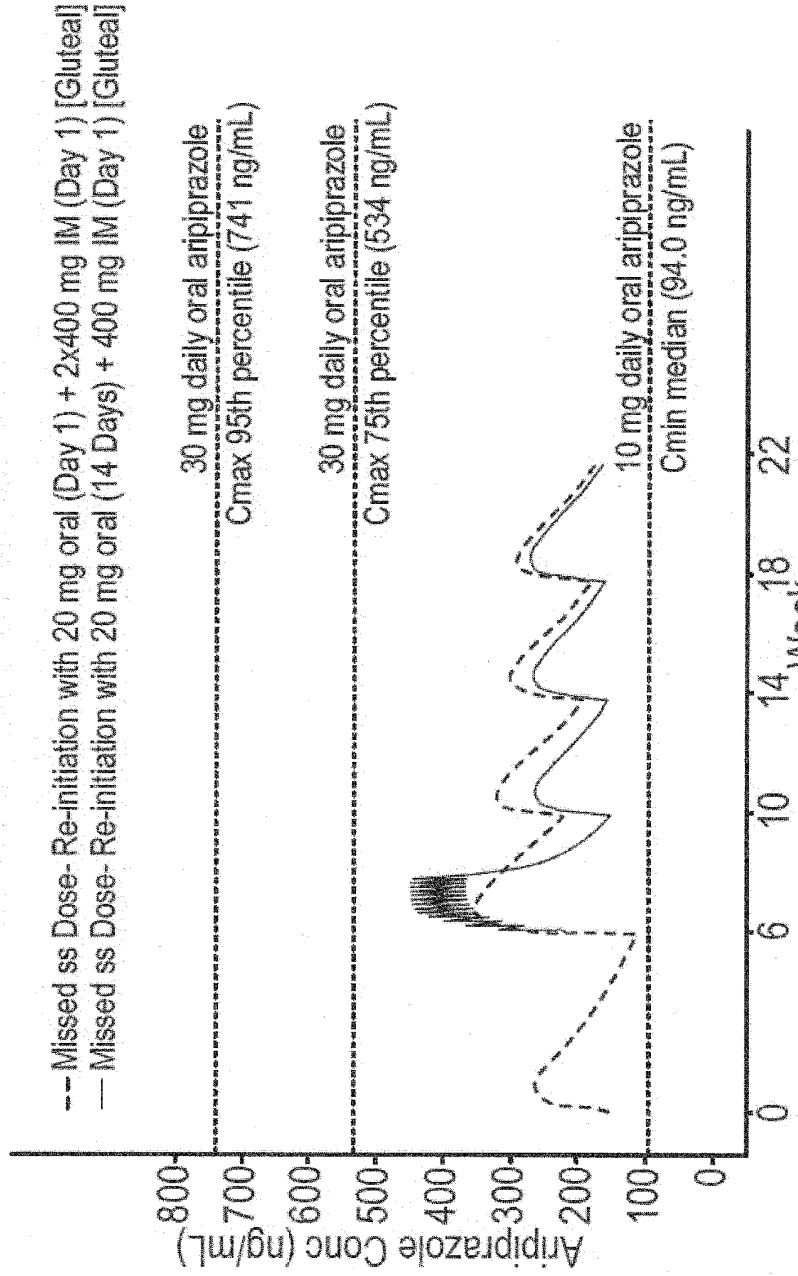

Missed 5th (Steady-State)
Gluteal IM Administration
-- Missed ss Dose- Re-initiation with 20 mg oral (Day 1) + 2x400 mg IM (Day 1) [Gluteal]
— Missed ss Dose- Re-initiation with 20 mg oral (14 Days) + 400 mg IM (Day 1) [Gluteal]
30 mg daily oral aripiprazole
Cmax 95th percentile (741 ng/mL)
30 mg daily oral aripiprazole
Cmax 75th percentile (534 ng/mL)
10 mg daily oral aripiprazole
Cmin median (94.0 ng/mL)
Aripiprazole Conc (ng/mL)
800
700
600
500
400
300
200
100
0
0
6
10
14
18
22
Week

FIG. 9C

[Fig. 9D]

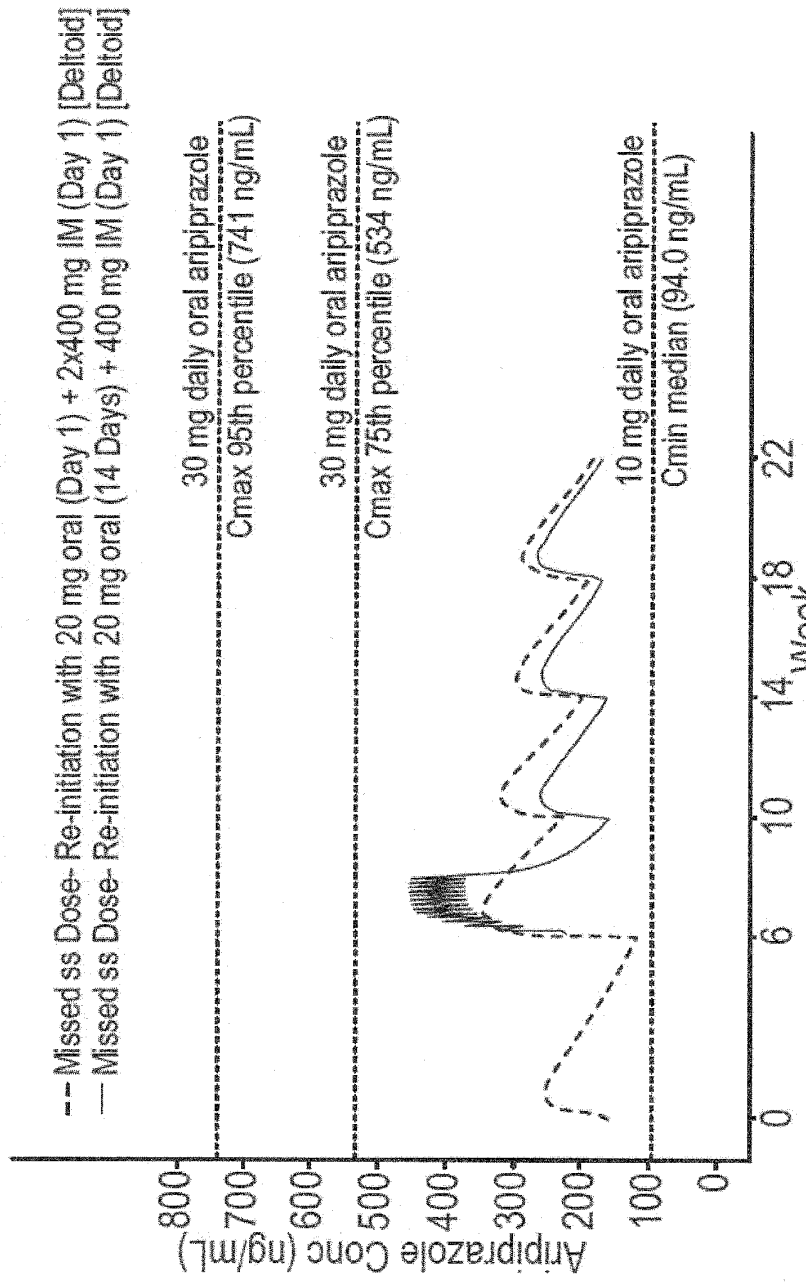

Missed 5th (Steady-State)
Deltoid IM Administration
-- Missed ss Dose- Re-initiation with 20 mg oral (Day 1) + 2x400 mg IM (Day 1) [Deltoid]
— Missed ss Dose- Re-initiation with 20 mg oral (14 Days) + 400 mg IM (Day 1) [Deltoid]
30 mg daily oral aripiprazole
Cmax 95th percentile (741 ng/mL)
30 mg daily oral aripiprazole
Cmax 75th percentile (534 ng/mL)
10 mg daily oral aripiprazole
Cmin median (94.0 ng/mL)
Aripiprazole Conc (ng/mL)
800
700
600
500
400
300
200
100
0
0
6
10
14
18
22
Week

FIG. 9D

[Fig. 10]

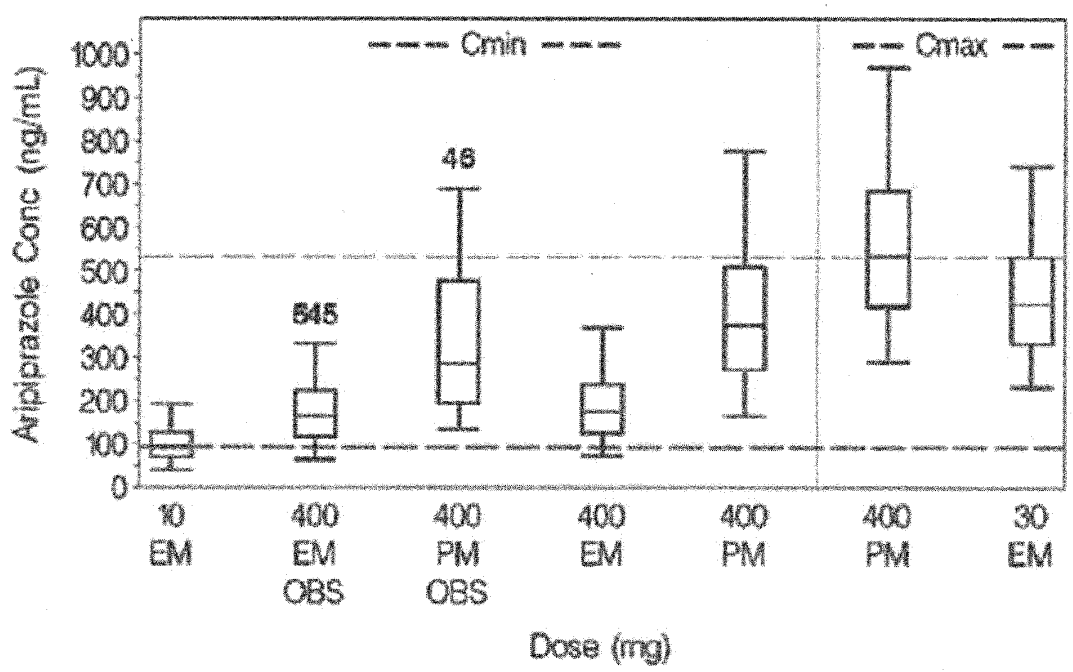

Cmin
Cmax
Aripiprazole Conc (ng/mL)
1000
900
800
700
600
500
400
300
200
100
0
46
545
10 EM
400 EM OBS
400 PM OBS
400 EM
400 PM
400 PM
30 EM
Dose (mg)

FIG. 10

[Fig. 11]

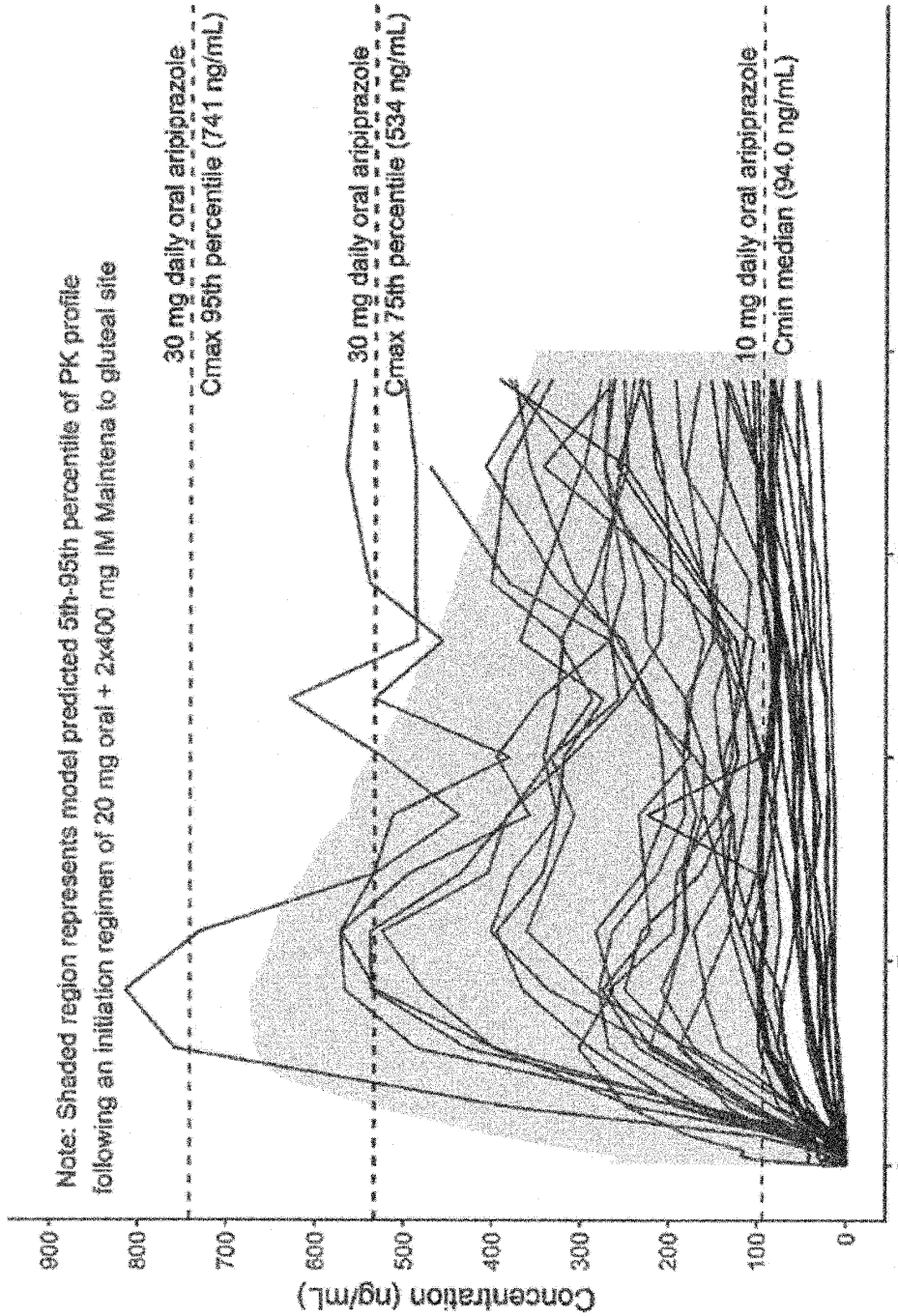

Note: Shaded region represents model predicted 5th-95th percentile of PK profile
following an initiation regimen of 20 mg oral + 2x400 mg IM Maintena to gluteal site
30 mg daily oral aripiprazole
Cmax 95th percentile (741 ng/mL)
30 mg daily oral aripiprazole
Cmax 75th percentile (534 ng/mL)
10 mg daily oral aripiprazole
Cmin median (94.0 ng/mL)
Concentration (ng/mL)
900
800
700
600
500
400
300
200
100
0
0
7
14
21
28
Time (Day)

FIG. 11

[Fig. 12]

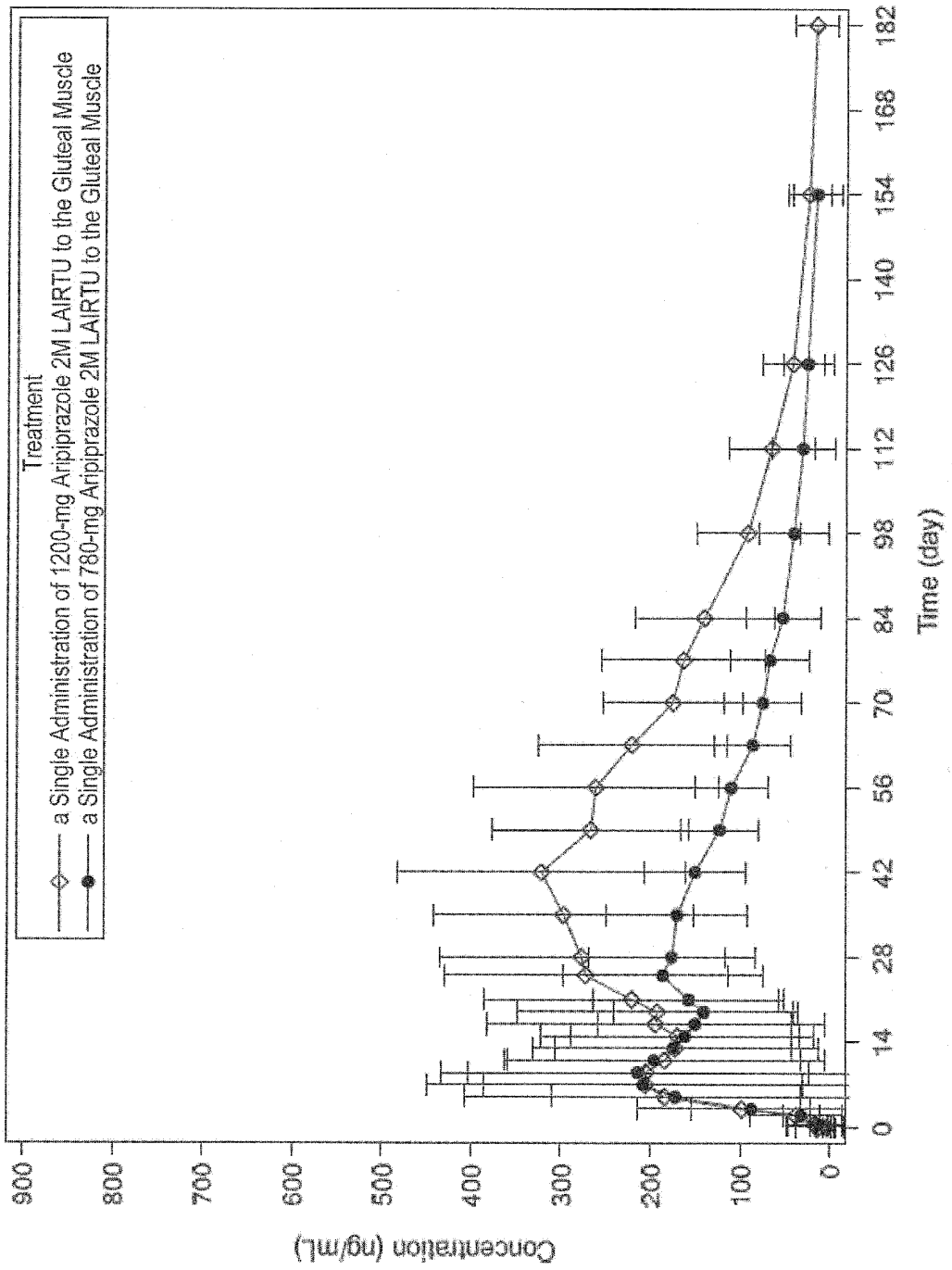

Treatment
a Single Administration of 1200-mg Aripiprazole 2M LAIRTU to the Gluteal Muscle
a Single Administration of 780-mg Aripiprazole 2M LAIRTU to the Gluteal Muscle
Concentration (ng/mL)
0
100
200
300
400
500
600
700
800
900
Time (day)
0
14
28
42
56
70
84
98
112
126
140
154
168
182

FIG. 12

[Fig. 13]

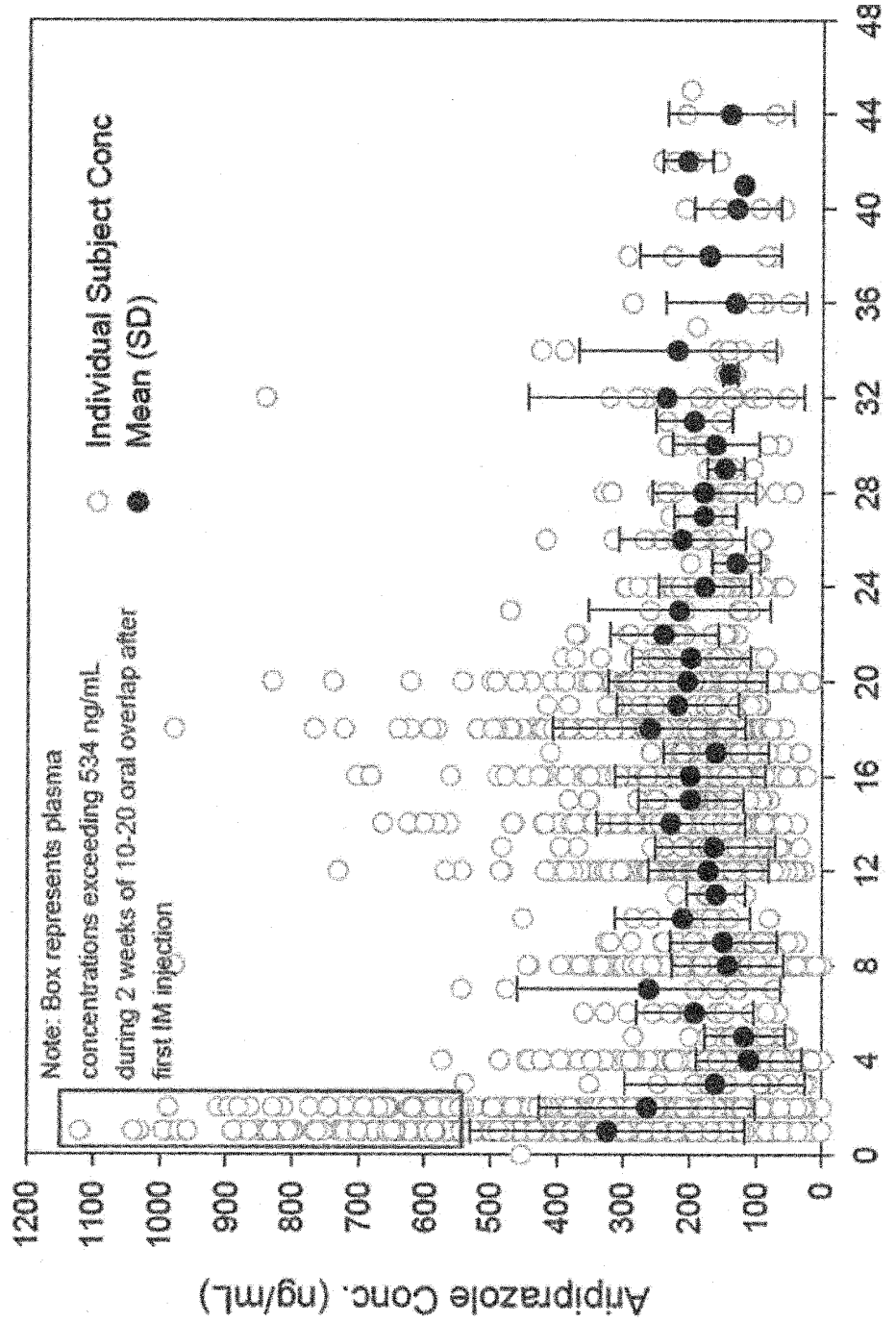

Aripiprazole Conc. (ng/mL)
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
Time After First Injection (Weeks)
0
4
8
12
16
20
24
28
32
36
40
44
48
Individual Subject Conc
Mean (SD)
Note: Box represents plasma concentrations exceeding 534 ng/mL during 2 weeks of 10-20 oral overlap after first IM injection

FIG. 13