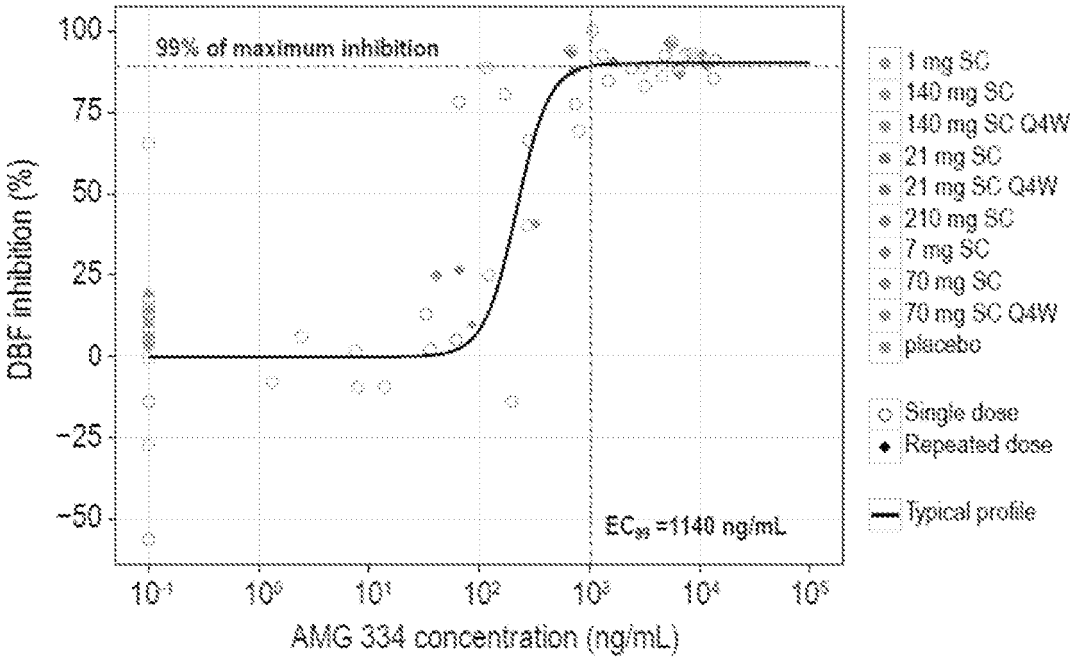
Serum AMG 334 Concentration and DBF Inhibition Relationship



Parameter	Mean Estimate	95% CI
Max inhibition (%)	90.2	(90, 92)
EC_{50} (ng/mL)	218	(49, 387)
Sigmoidal coefficient	2.94	(1.04, 4.82)

FIG. 1

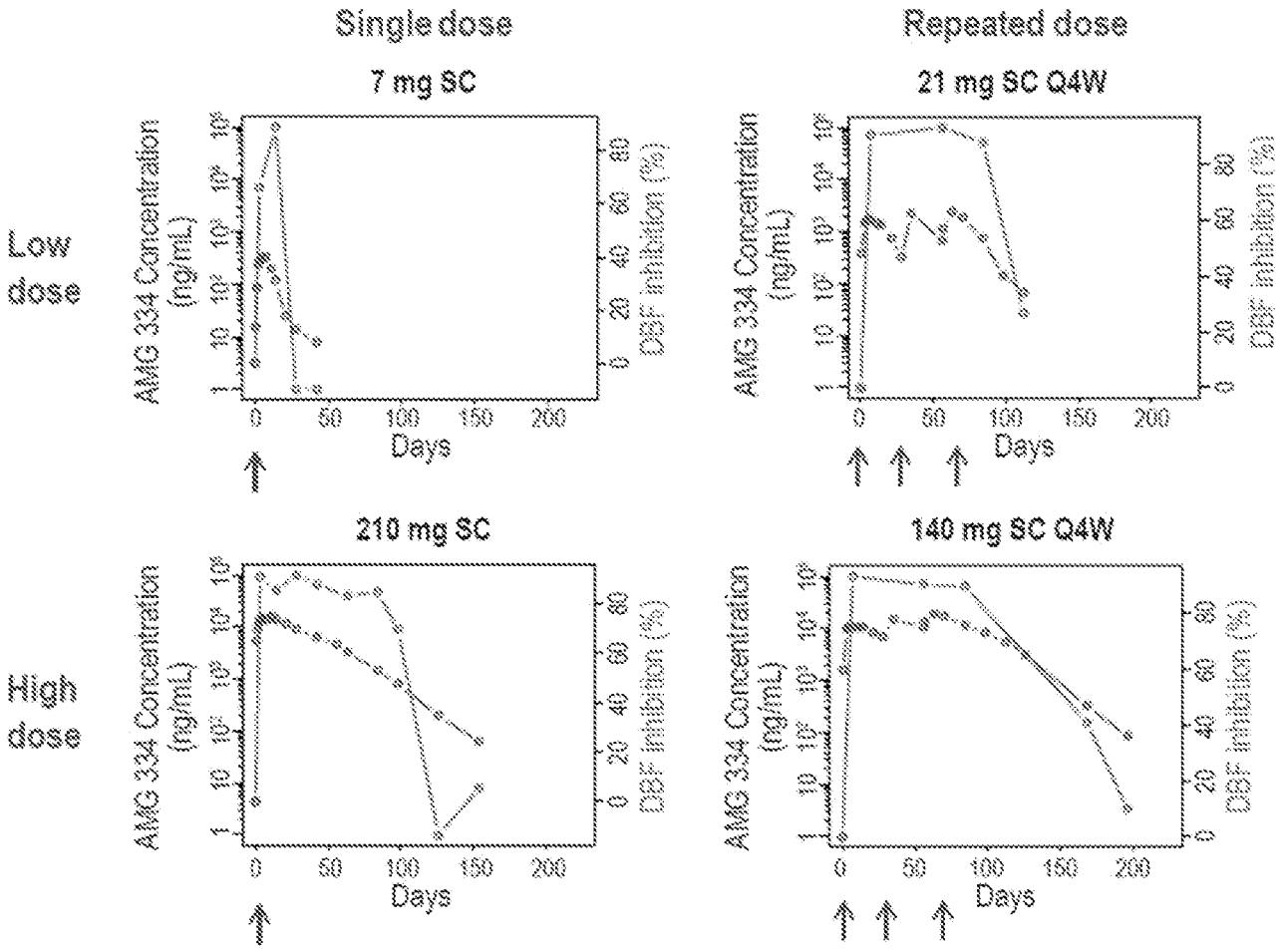

Single dose
Repeated dose
7 mg SC
21 mg SC Q4W
210 mg SC
140 mg SC Q4W
Low dose
High dose
AMG 334 Concentration (ng/mL)
DBF inhibition (%)
Days

FIG. 2

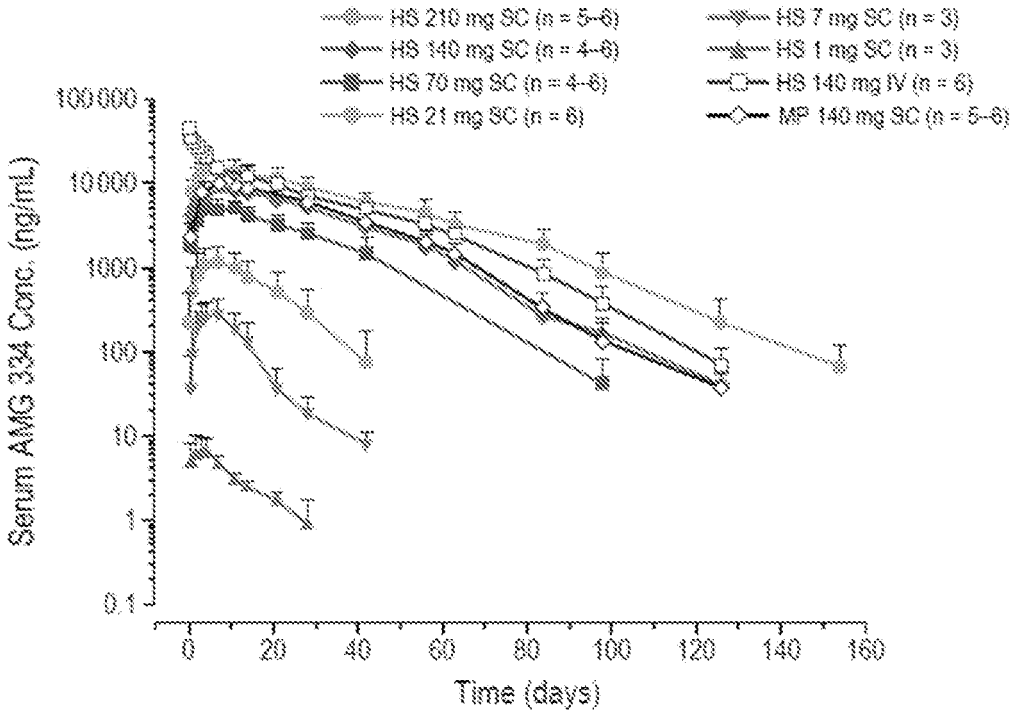

HS 210 mg SC (n = 5–6)
HS 140 mg SC (n = 4–6)
HS 70 mg SC (n = 4–6)
HS 21 mg SC (n = 6)
HS 7 mg SC (n = 3)
HS 1 mg SC (n = 3)
HS 140 mg IV (n = 6)
MP 140 mg SC (n = 5–6)
Serum AMG 334 Conc. (ng/mL)
100 000
10 000
1000
100
10
1
0.1
0
20
40
60
80
100
120
140
160
Time (days)

FIG. 3A

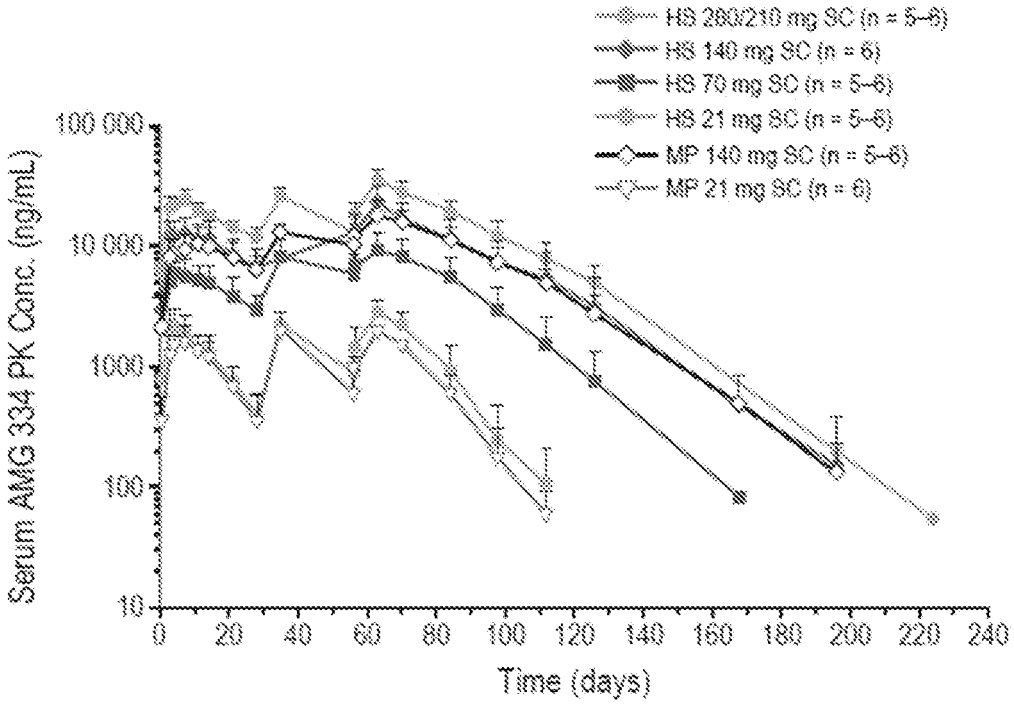

HS 280/210 mg SC (n = 5–6)
HS 140 mg SC (n = 6)
HS 70 mg SC (n = 5–6)
HS 21 mg SC (n = 5–6)
MP 140 mg SC (n = 5–6)
MP 21 mg SC (n = 6)
Serum AMG 334 PK Conc. (ng/mL)
100 000
10 000
1000
100
10
0
20
40
60
80
100
120
140
160
180
200
220
240
Time (days)

FIG. 3B

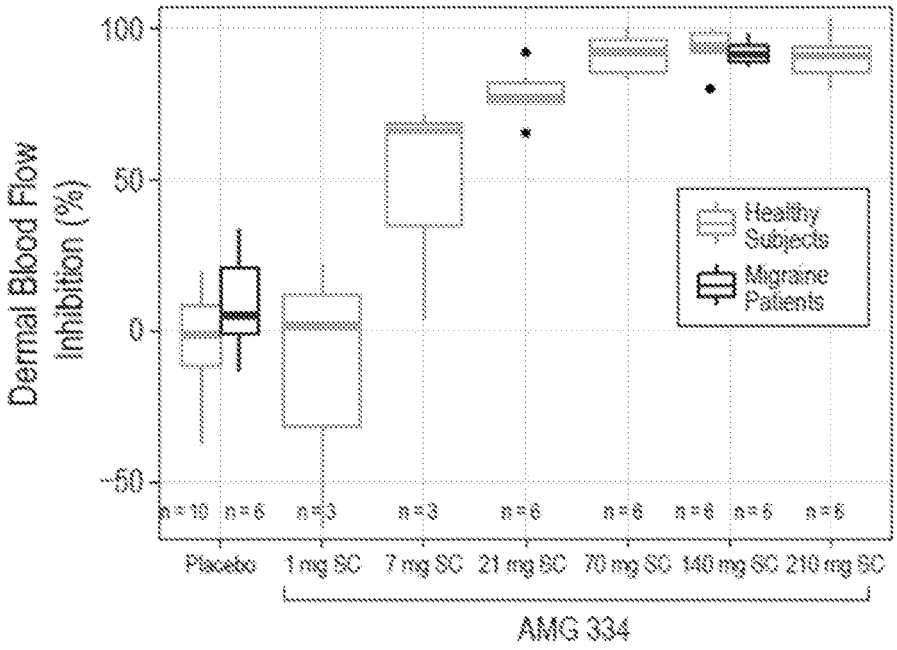

Dermal Blood Flow Inhibition (%)
100
50
0
-50
Healthy Subjects
Migraine Patients
n = 10 n = 6 n = 3 n = 3 n = 6 n = 6 n = 6 n = 6 n = 6
Placebo
1 mg SC
7 mg SC
21 mg SC
70 mg SC
140 mg SC
210 mg SC
AMG 334

FIG. 4A

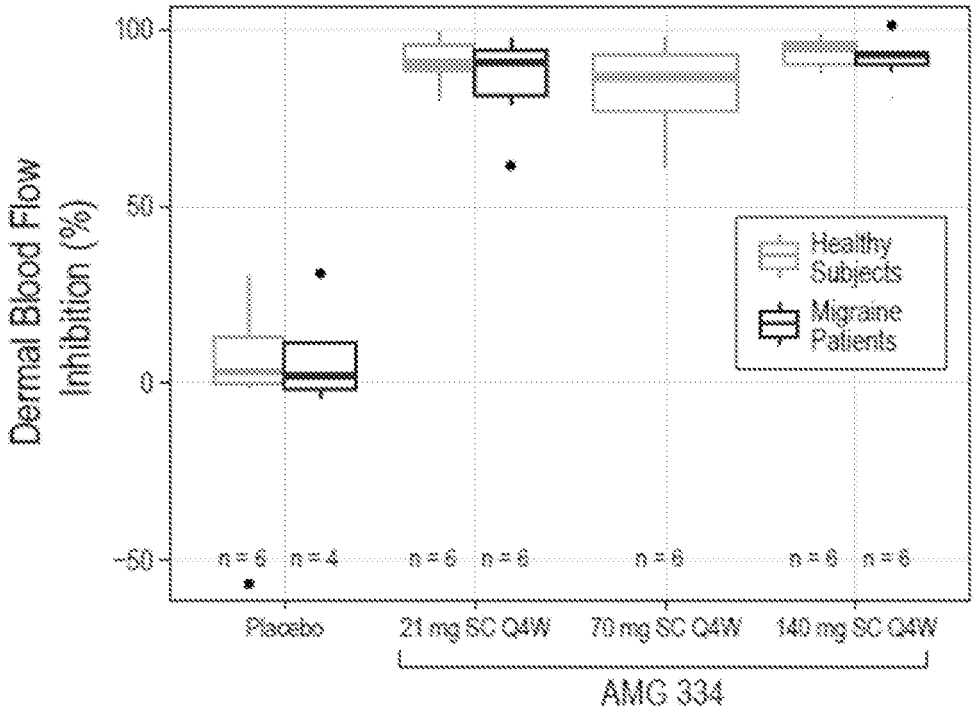
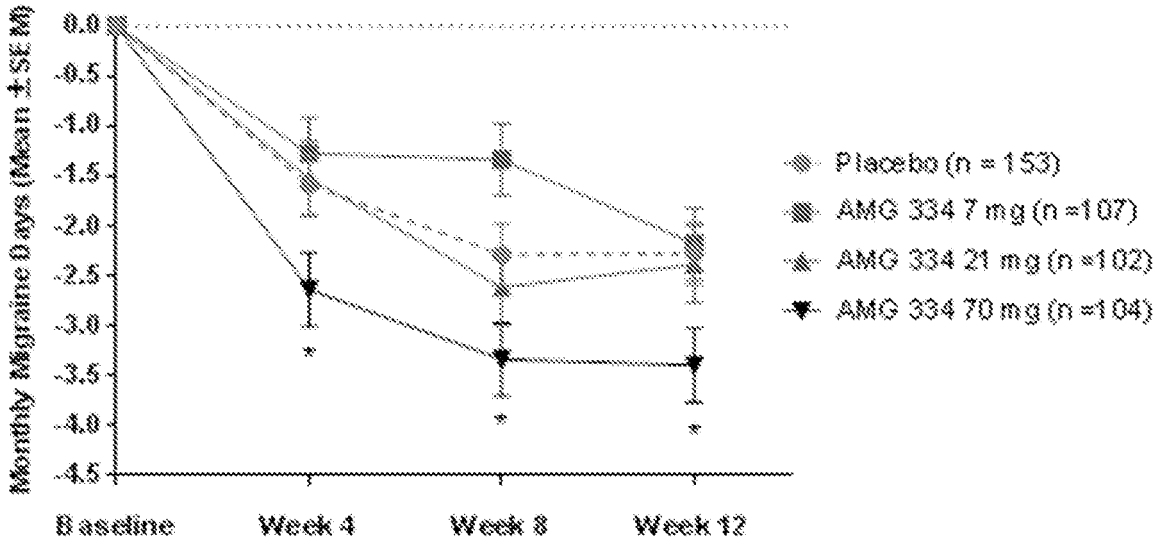

Dermal Blood Flow Inhibition (%)
100
50
0
-50
Healthy Subjects
Migraine Patients
n = 6 n = 4 n = 6 n = 6 n = 6 n = 6 n = 6
Placebo
21 mg SC Q4W
70 mg SC Q4W
140 mg SC Q4W
AMG 334

FIG. 4B

Change From Baseline in Mean Monthly Migraine Days



* $P < 0.05$, n=number of subjects in analysis set

FIG. 5

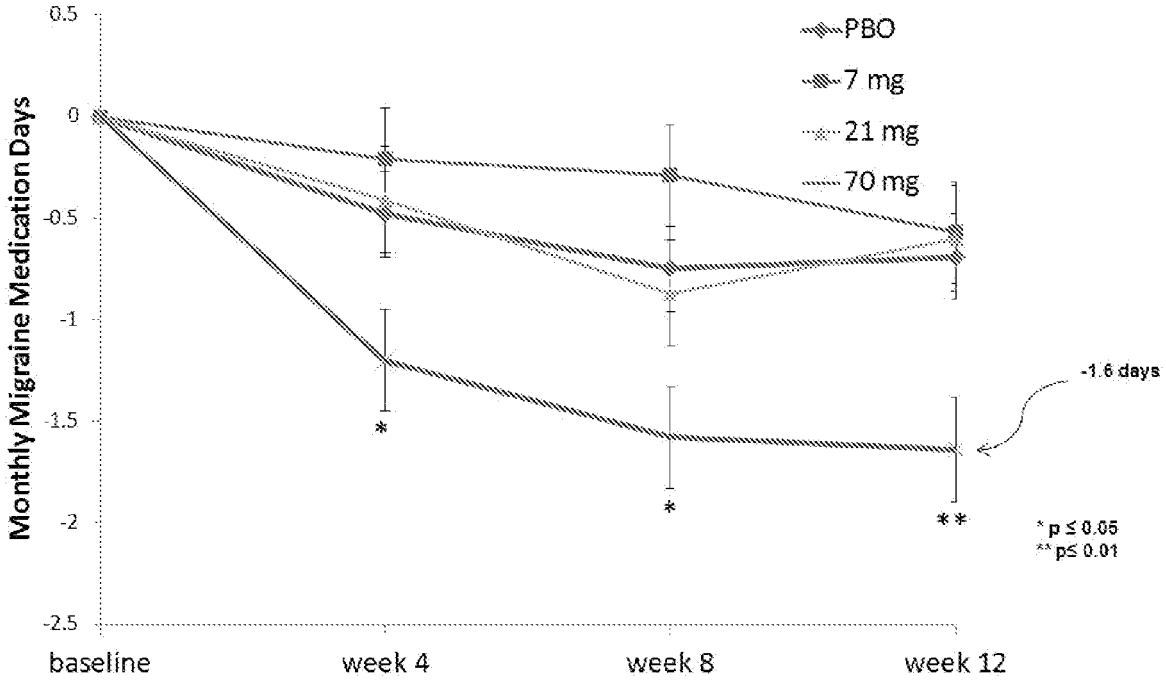

0.5
0
-0.5
-1
-1.5
-2
-2.5
Monthly Migraine Medication Days
PBO
7 mg
21 mg
70 mg
-1.6 days
*
*
**
* p ≤ 0.05
** p≤ 0.01
baseline
week 4
week 8
week 12

FIG. 6

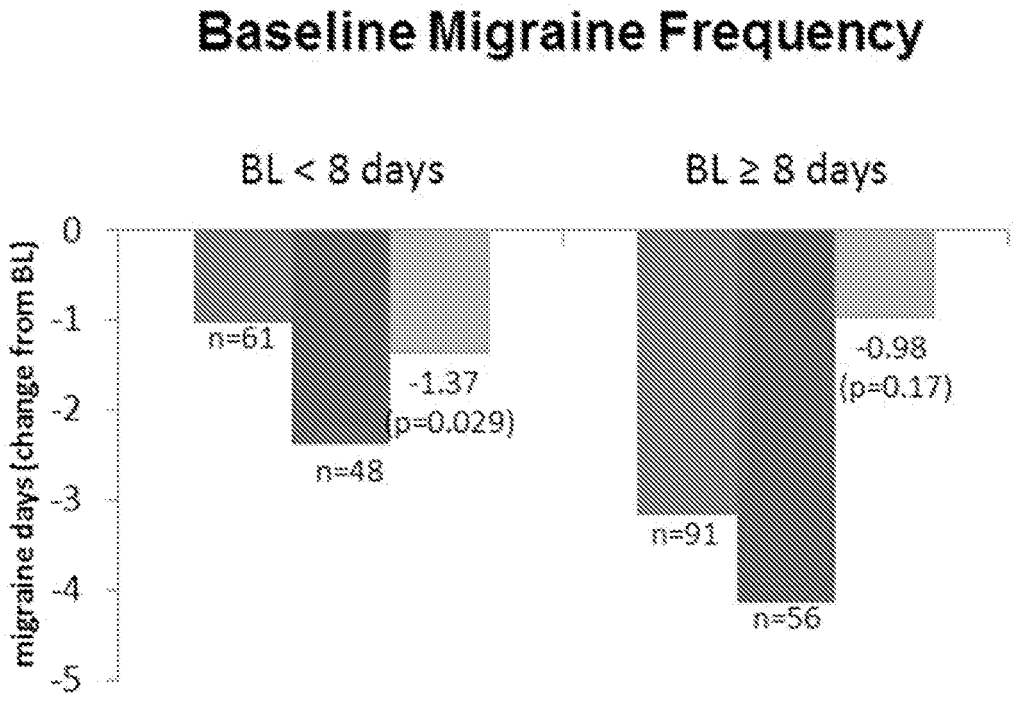

Baseline Migraine Frequency
BL < 8 days
BL ≥ 8 days
migraine days (change from BL)
0
-1
-2
-3
-4
-5
n=61
n=48
-1.37
(p=0.029)
n=91
n=56
-0.98
(p=0.17)

FIG. 7A

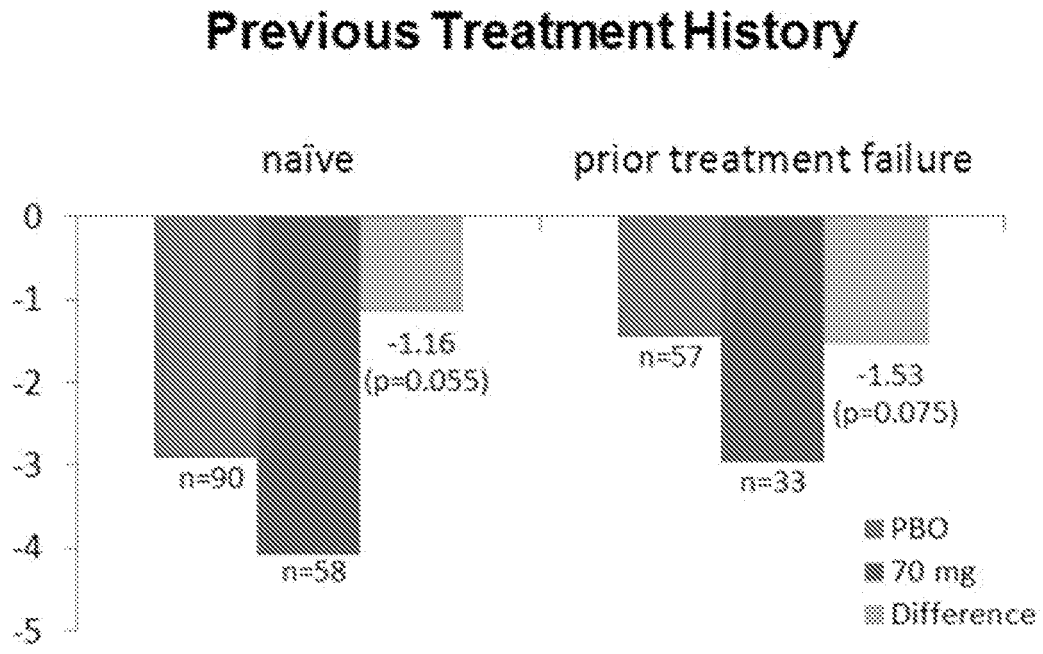

Previous Treatment History
naïve
prior treatment failure
0
-1
-2
-3
-4
-5
n=90
n=58
-1.16
(p=0.055)
n=57
n=33
-1.53
(p=0.075)
PBO
70 mg
Difference

FIG. 7B

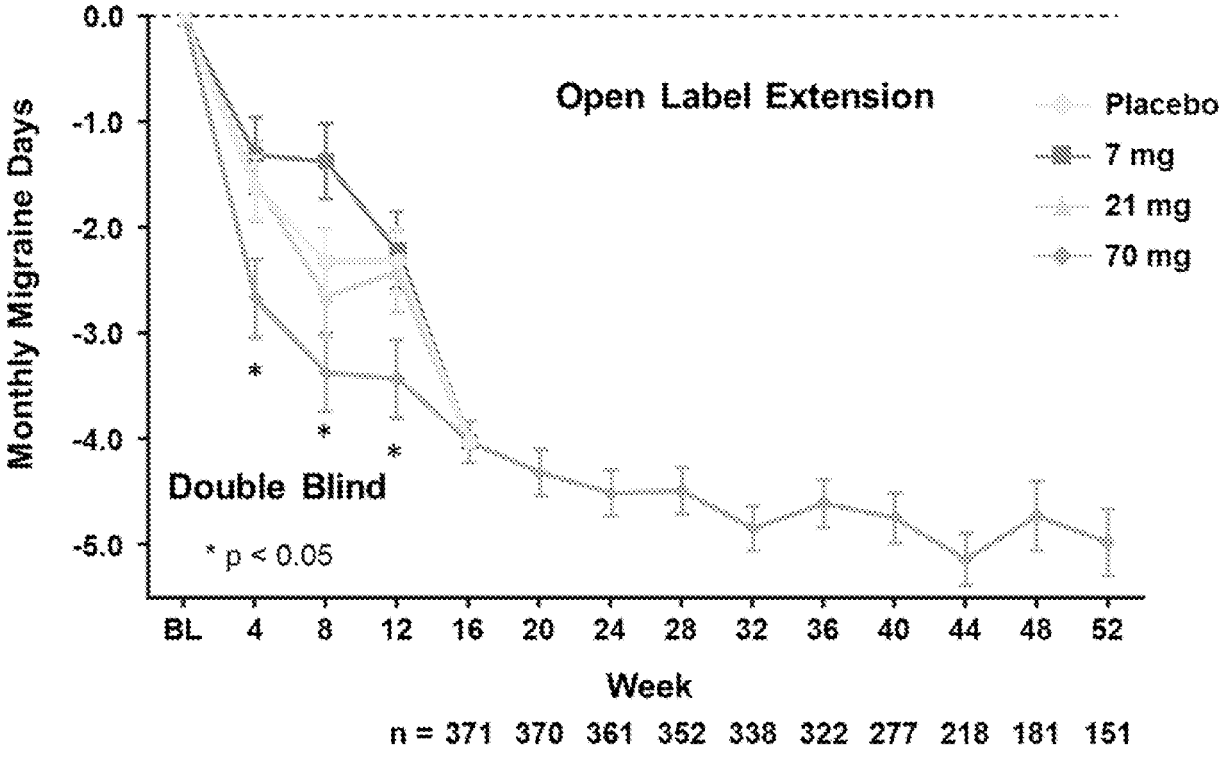

Monthly Migraine Days
0.0
-1.0
-2.0
-3.0
-4.0
-5.0
Open Label Extension
Placebo
7 mg
21 mg
70 mg
Double Blind
* p < 0.05
BL 4 8 12 16 20 24 28 32 36 40 44 48 52
Week
n = 371 370 361 352 338 322 277 218 181 151

FIG. 8

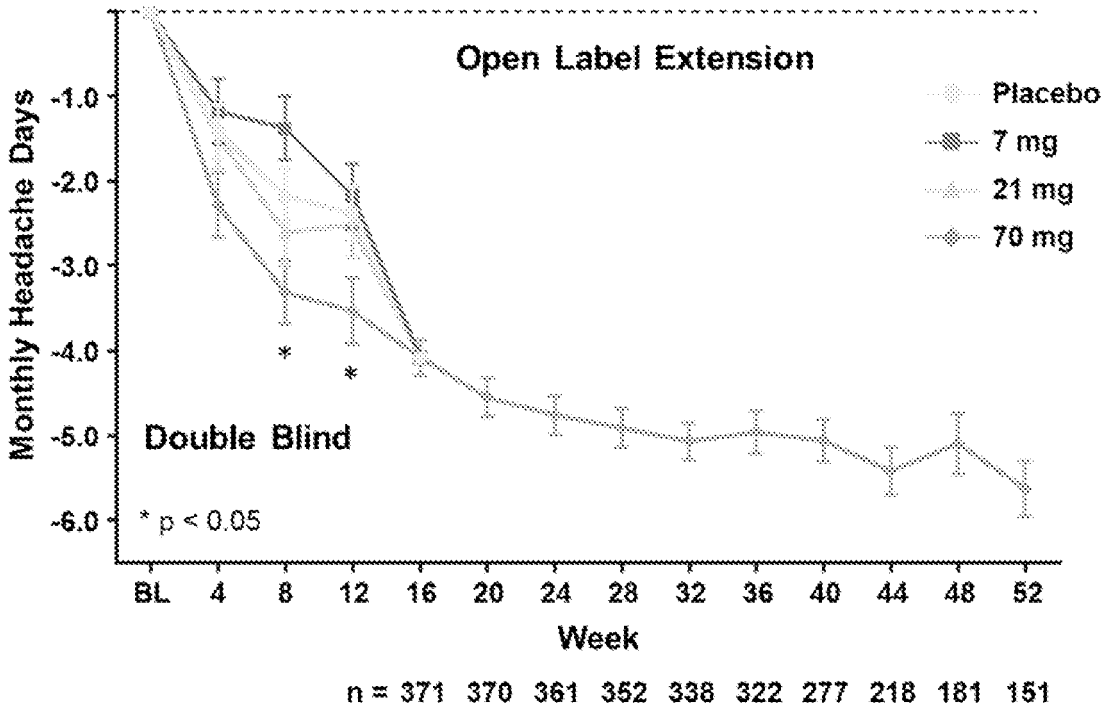

Open Label Extension
Placebo
7 mg
21 mg
70 mg
Monthly Headache Days
-1.0
-2.0
-3.0
-4.0
-5.0
-6.0
Double Blind
* p < 0.05
BL 4 8 12 16 20 24 28 32 36 40 44 48 52
Week
n = 371 370 361 352 338 322 277 218 181 151

FIG. 9A

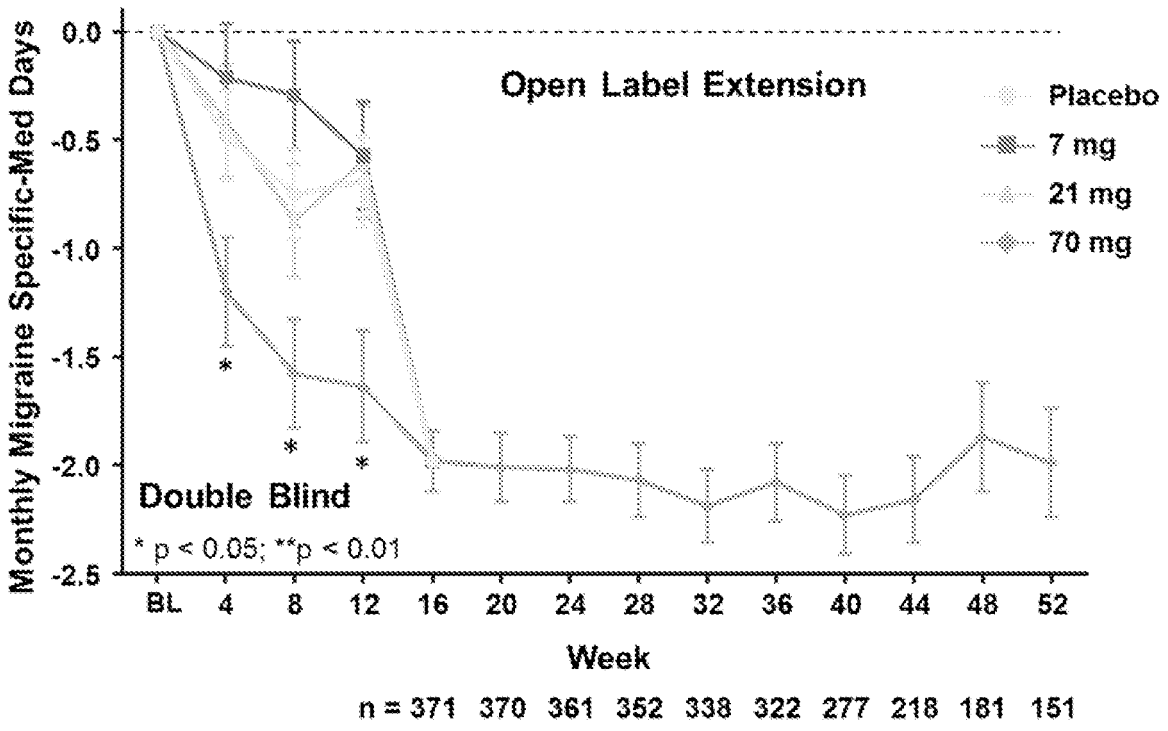

Open Label Extension
Placebo
7 mg
21 mg
70 mg
Monthly Migraine Specific-Med Days
0.0
-0.5
-1.0
-1.5
-2.0
-2.5
Double Blind
* p < 0.05; **p < 0.01
BL 4 8 12 16 20 24 28 32 36 40 44 48 52
Week
n = 371 370 361 352 338 322 277 218 181 151

FIG. 9B