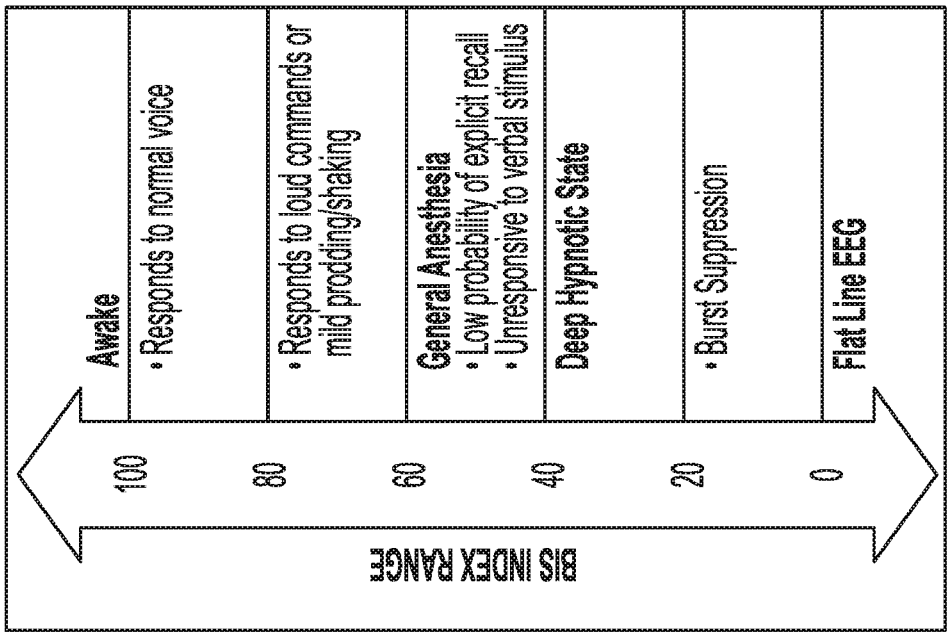

BIS INDEX RANGE
100
80
60
40
20
0
Awake
• Responds to normal voice
• Responds to loud commands or mild prodding/shaking
General Anesthesia
• Low probability of explicit recall
• Unresponsive to verbal stimulus
Deep Hypnotic State
• Burst Suppression
Flat Line EEG

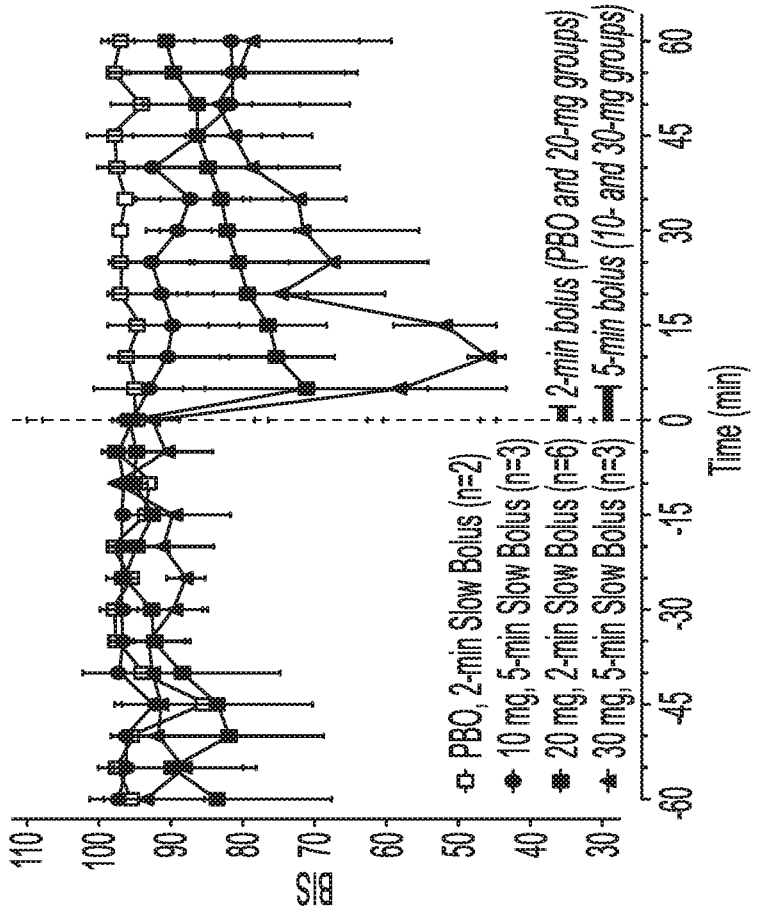

BIS
110
100
90
80
70
60
50
40
30
-60
-45
-30
-15
0
15
30
45
60
Time (min)
PBO, 2-min Slow Bolus (n=2)
10 mg, 5-min Slow Bolus (n=3)
20 mg, 2-min Slow Bolus (n=6)
30 mg, 5-min Slow Bolus (n=3)
2-min bolus (PBO and 20-mg groups)
5-min bolus (10- and 30-mg groups)

FIG. 1

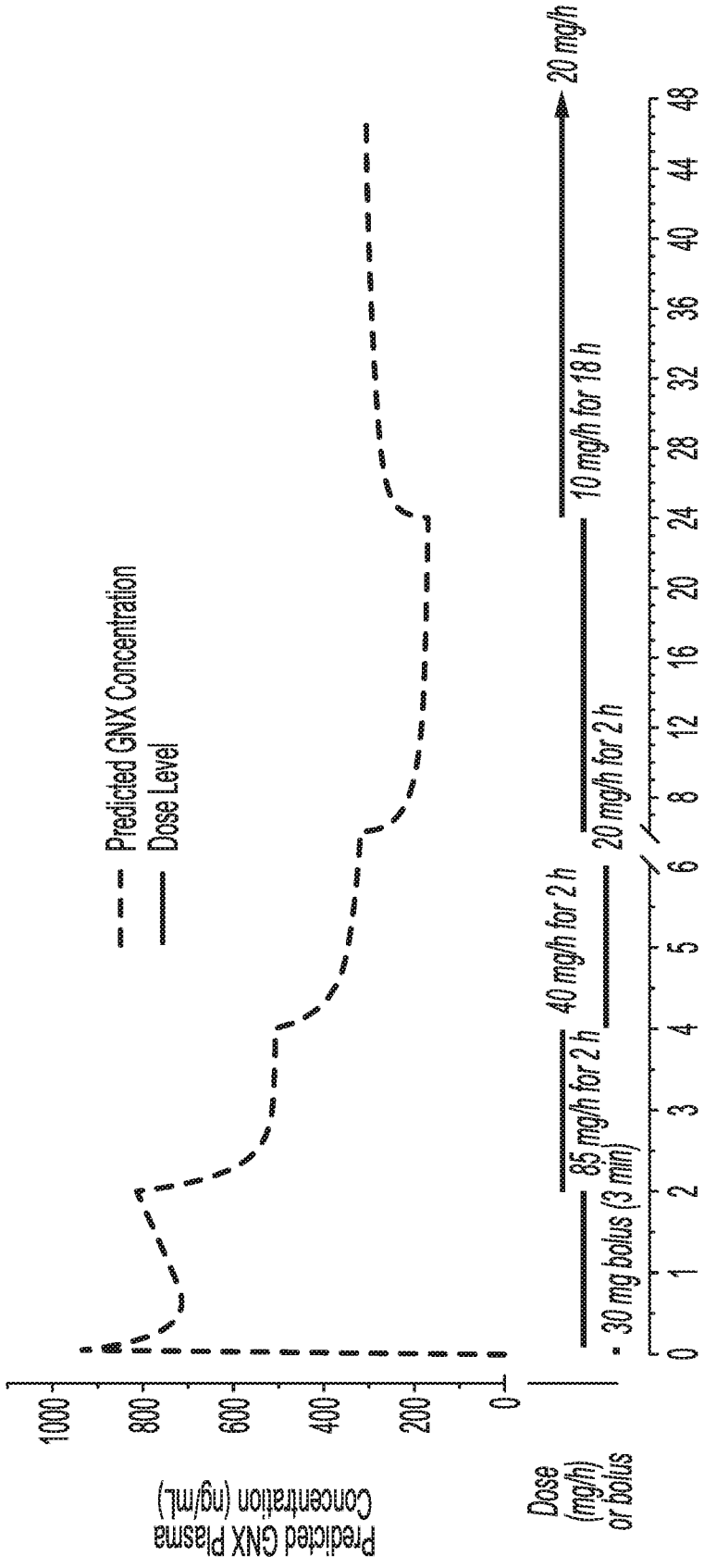

Predicted GNX Concentration
Dose Level
Predicted GNX Plasma Concentration (ng/mL)
1000
800
600
400
200
0
Dose (mg/h) or bolus
30 mg bolus (3 min)
85 mg/h for 2 h
40 mg/h for 2 h
20 mg/h for 2 h
10 mg/h for 18 h
20 mg/h
0 1 2 3 4 5 6 8 12 16 20 24 28 32 36 40 44 48
Time (h)

FIG. 2

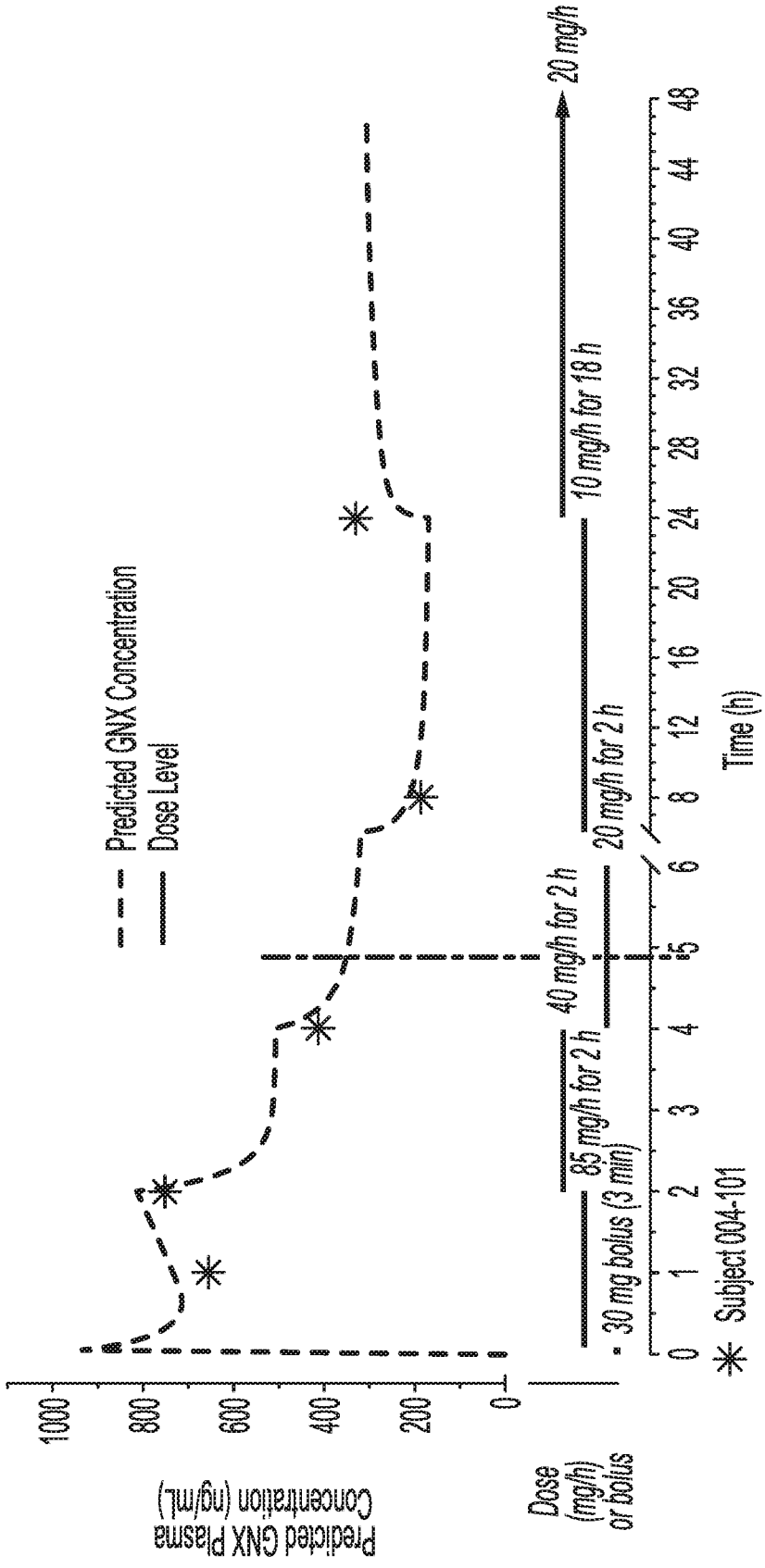

Predicted GNX Concentration
Dose Level
Predicted GNX Plasma Concentration (ng/mL)
1000
800
600
400
200
0
Dose (mg/h) or bolus
30 mg bolus (3 min)
85 mg/h for 2 h
40 mg/h for 2 h
20 mg/h for 2 h
10 mg/h for 18 h
20 mg/h
Time (h)
0 1 2 3 4 5 6 8 12 16 20 24 28 32 36 40 44 48
Subject 004-101

FIG. 3

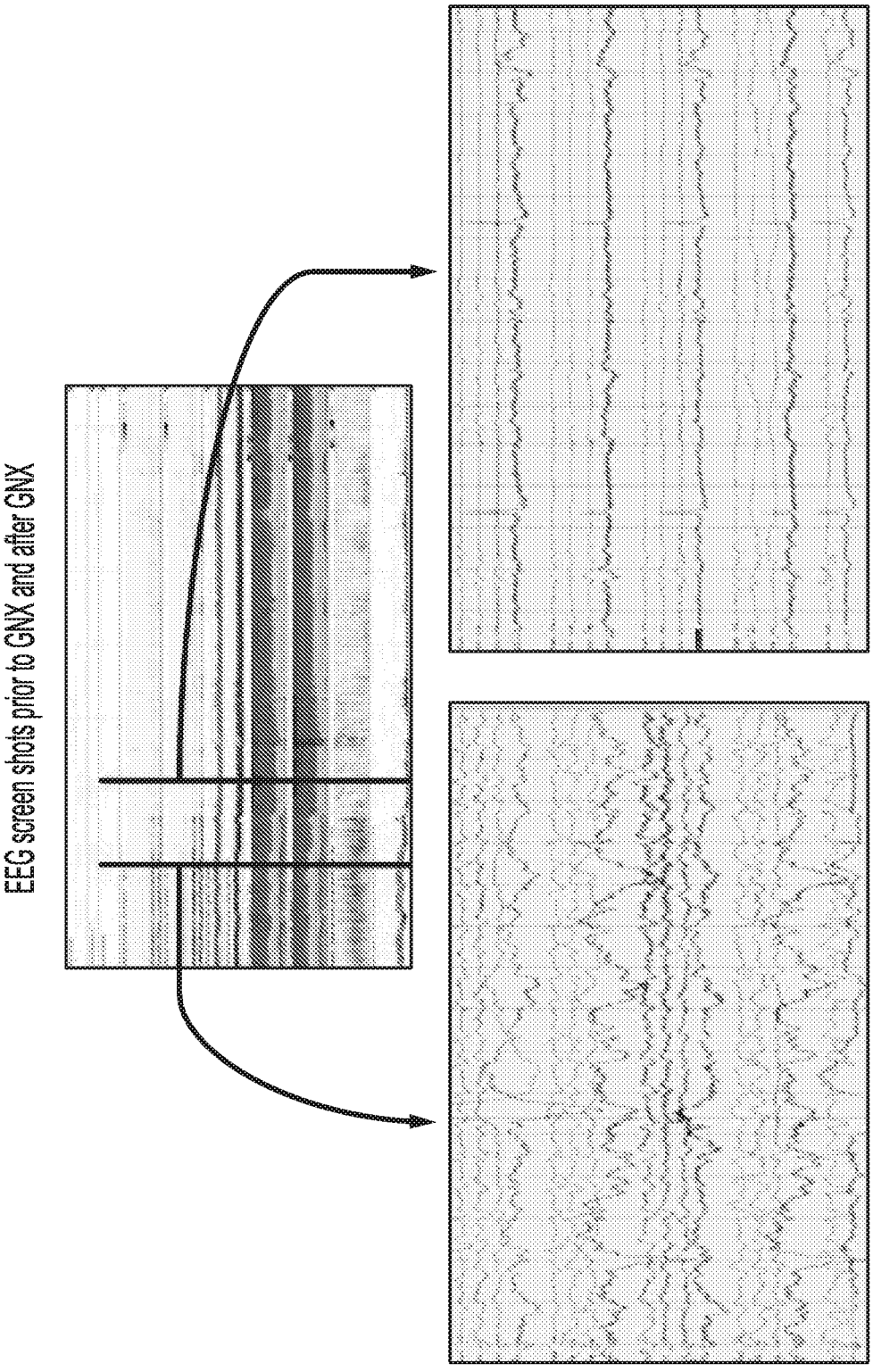



FIG. 4

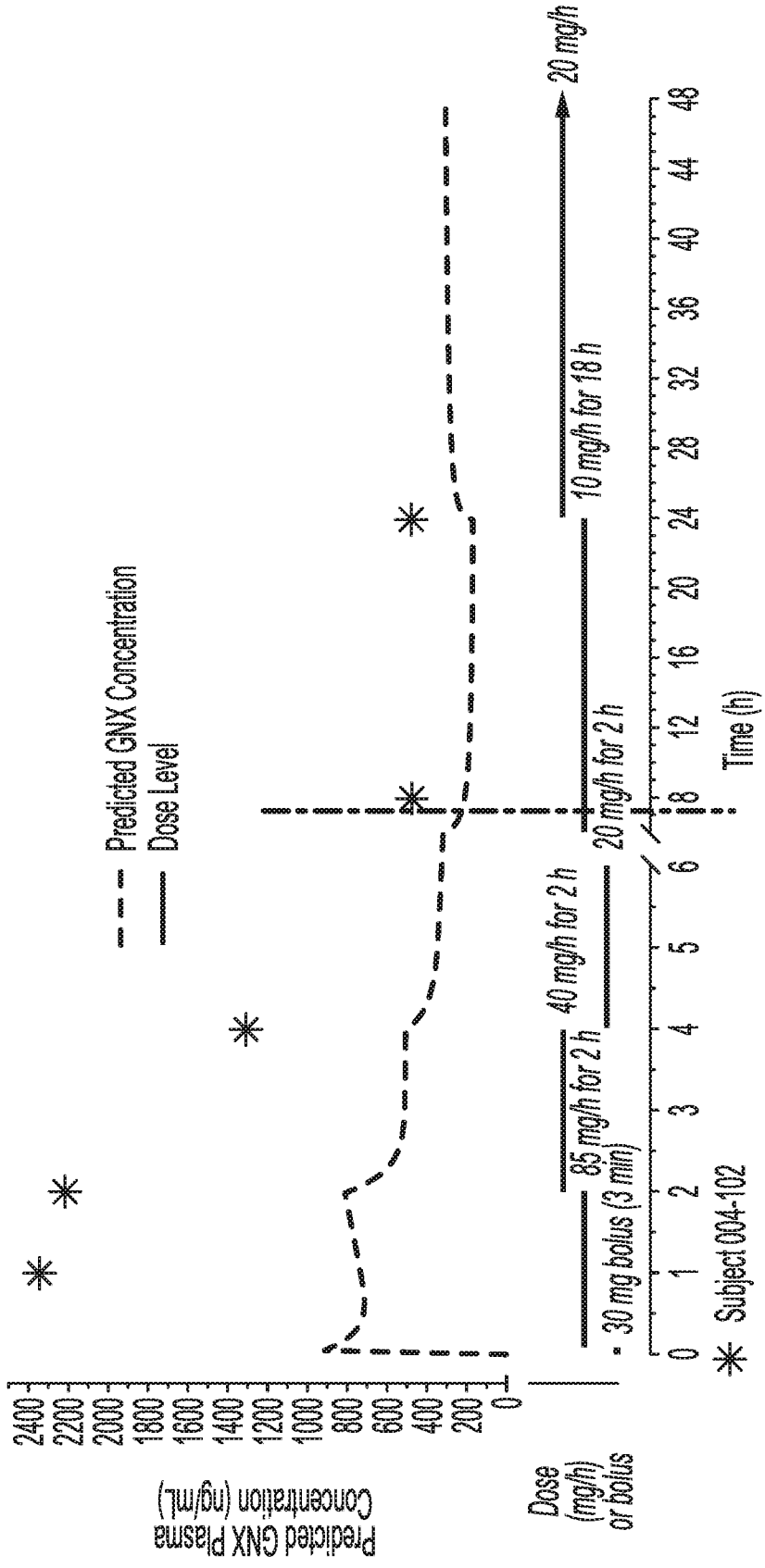

Predicted GNX Concentration
Dose Level
Predicted GNX Plasma Concentration (ng/mL)
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
Dose (mg/h) or bolus
30 mg bolus (3 min)
85 mg/h for 2 h
40 mg/h for 2 h
20 mg/h for 2 h
10 mg/h for 18 h
20 mg/h
Time (h)
0 1 2 3 4 5 6 8 12 16 20 24 28 32 36 40 44 48
Subject 004-102

FIG. 5

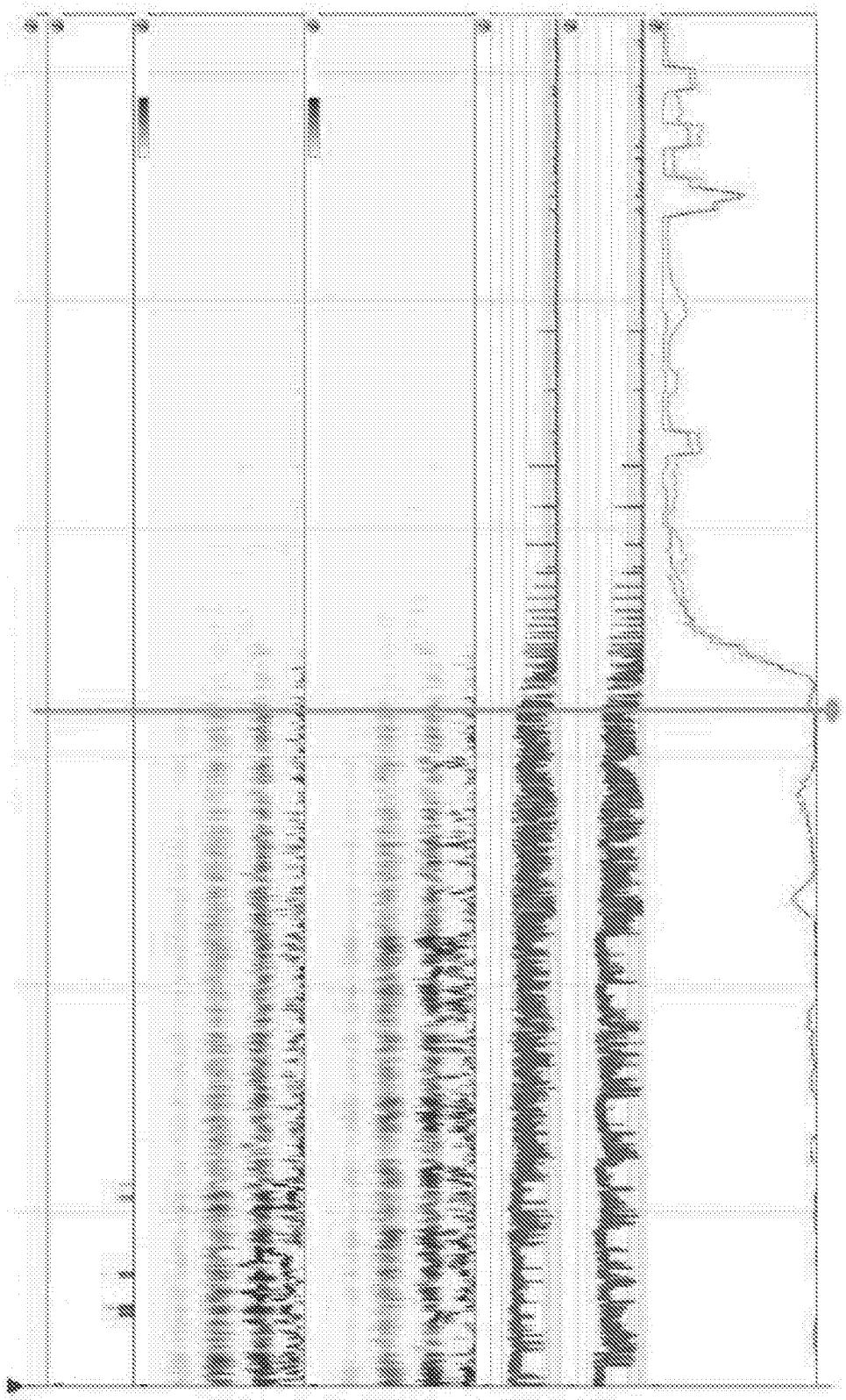



FIG. 6

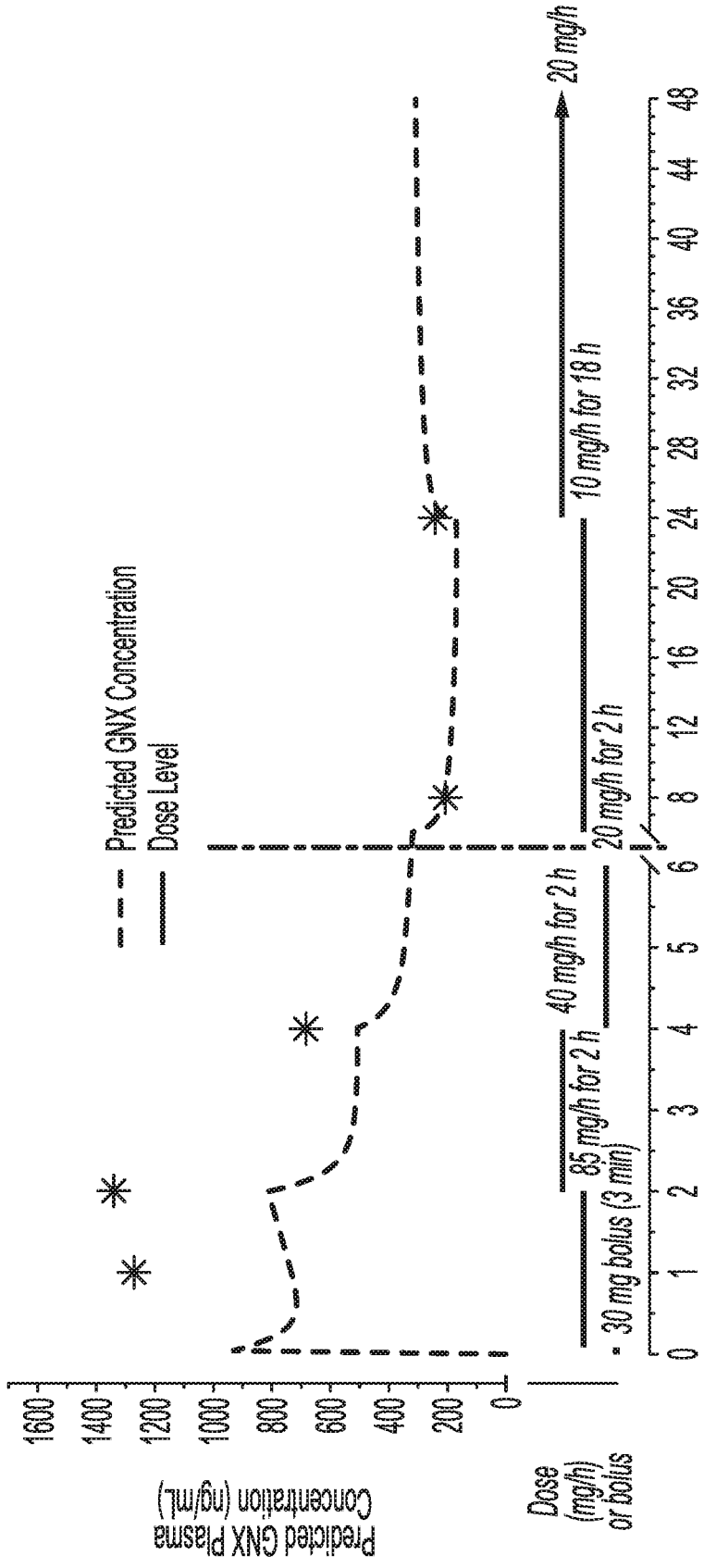

Predicted GNX Concentration
Dose Level
Predicted GNX Plasma Concentration (ng/mL)
1600
1400
1200
1000
800
600
400
200
0
Dose (mg/h) or bolus
30 mg bolus (3 min)
85 mg/h for 2 h
40 mg/h for 2 h
20 mg/h for 2 h
10 mg/h for 18 h
20 mg/h
Time (h)
0 1 2 3 4 5 6 8 12 16 20 24 28 32 36 40 44 48
Subject 006-101

FIG. 7

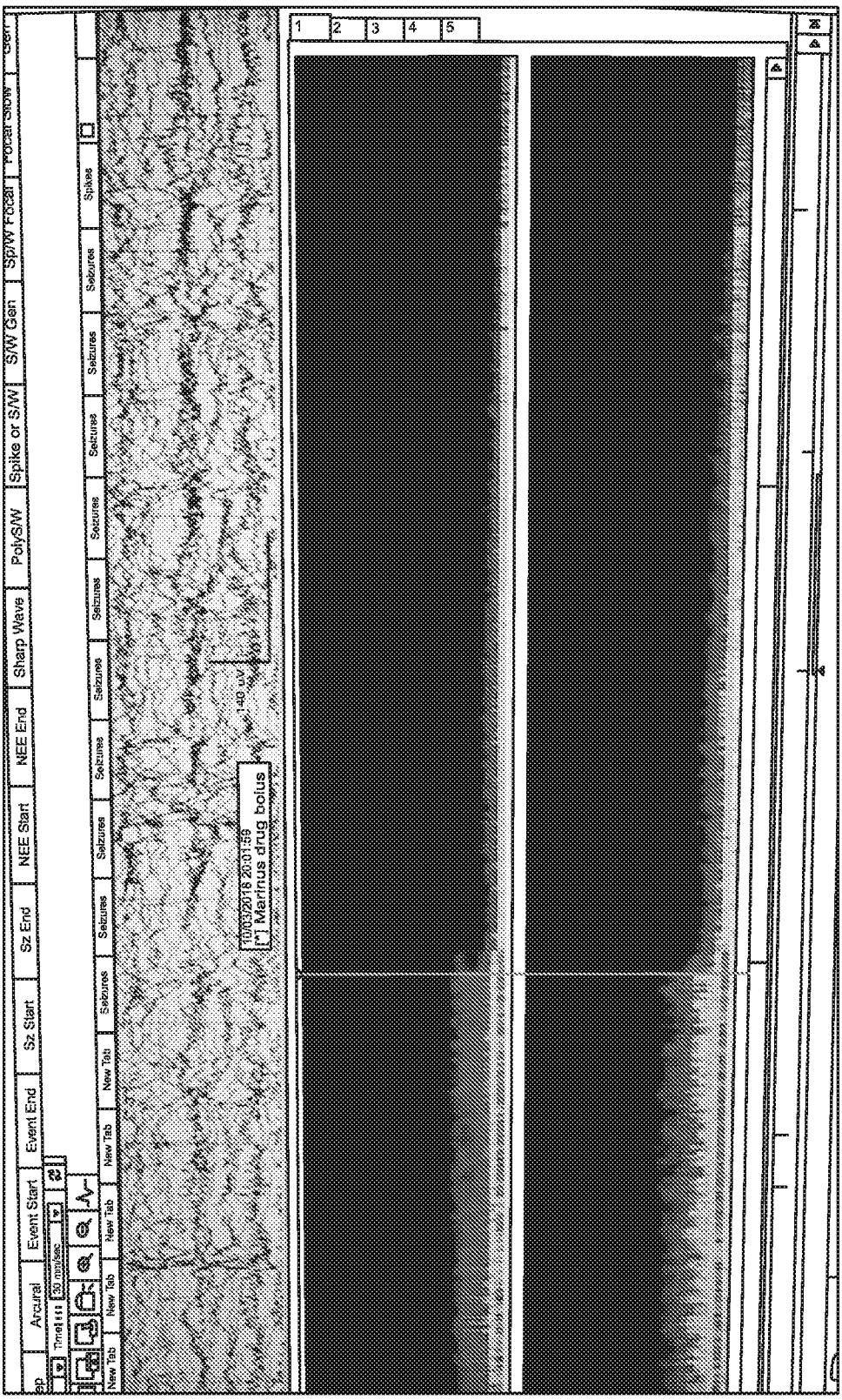

Arousal
Event Start
Event End
Sz Start
Sz End
NEE Start
NEE End
Sharp Waves
PolySW
Spike or S/W
S/W Gen
Sp/W Focal
Focal Slows
Seizures
Spikes
New Tab
10/03/2018 20:01:56
Marinus drug bolus
1
2
3
4
5

FIG. 8

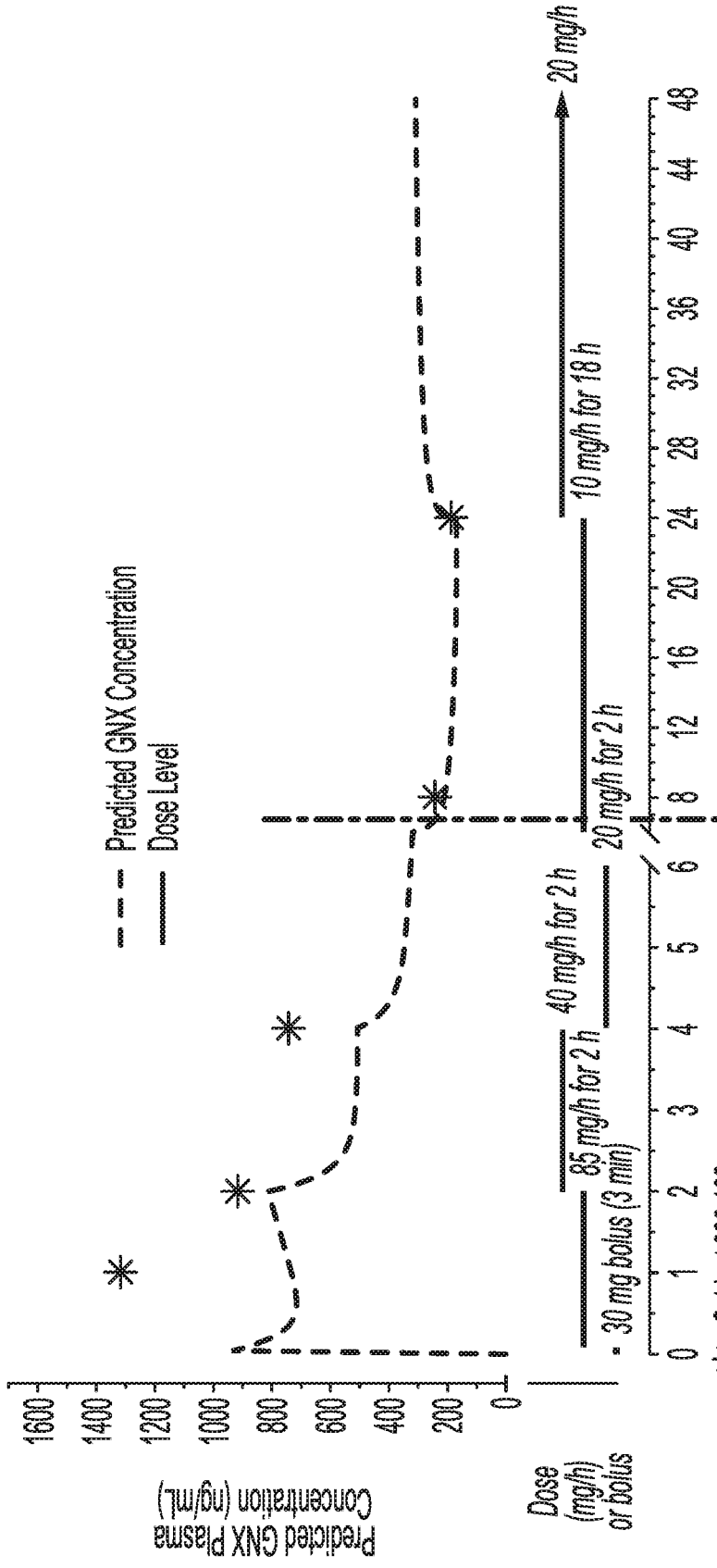

Predicted GNX Concentration
Dose Level
Predicted GNX Plasma Concentration (ng/mL)
1600
1400
1200
1000
800
600
400
200
0
Dose (mg/h) or bolus
30 mg bolus (3 min)
85 mg/h for 2 h
40 mg/h for 2 h
20 mg/h for 2 h
10 mg/h for 18 h
20 mg/h
Time (h)
0 1 2 3 4 5 6 8 12 16 20 24 28 32 36 40 44 48
Subject 006-102

FIG. 9

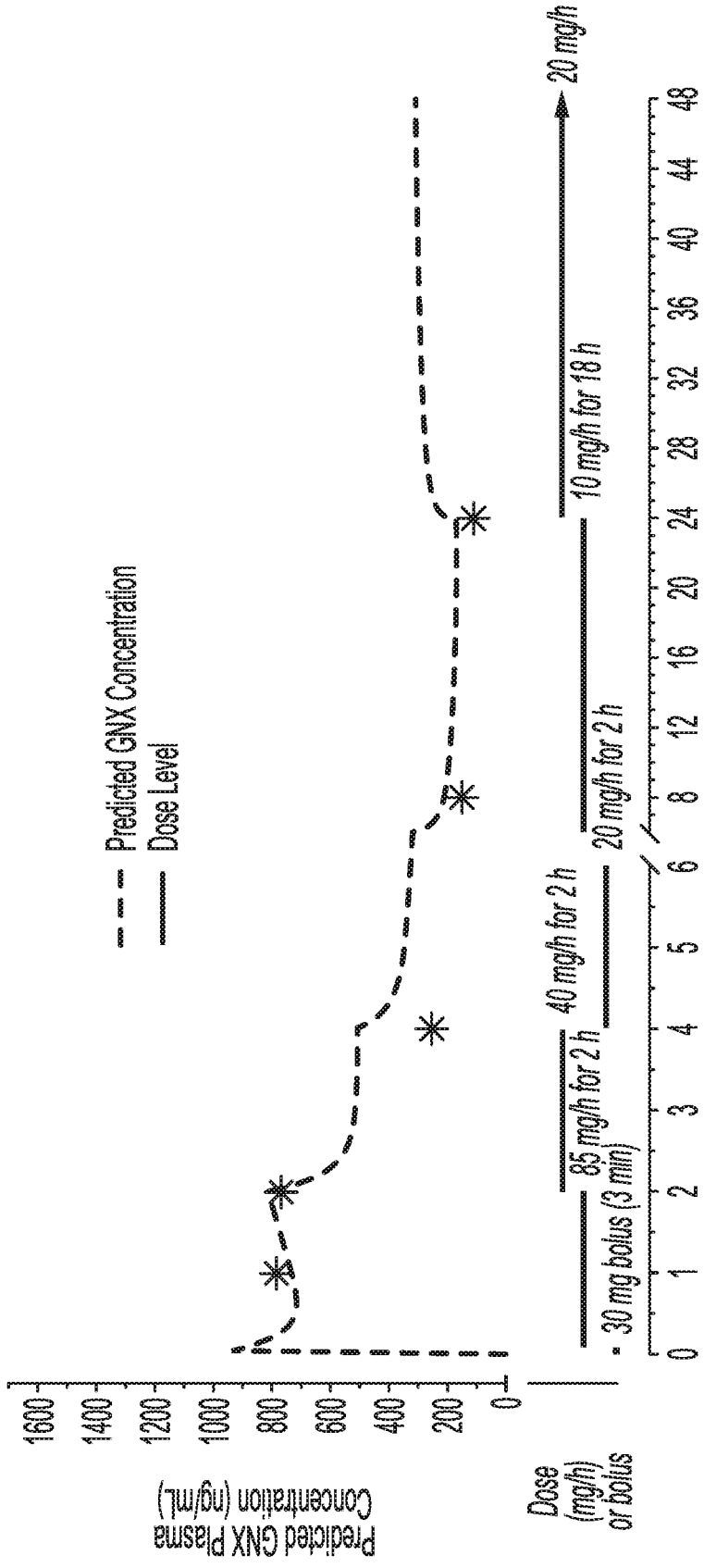

Predicted GNX Concentration
Dose Level
Predicted GNX Plasma Concentration (ng/mL)
1600
1400
1200
1000
800
600
400
200
0
Dose (mg/h) or bolus
30 mg bolus (3 min)
85 mg/h for 2 h
40 mg/h for 2 h
20 mg/h for 2 h
10 mg/h for 18 h
20 mg/h
Time (h)
0 1 2 3 4 5 6 8 12 16 20 24 28 32 36 40 44 48
Subject 015-101

FIG. 10

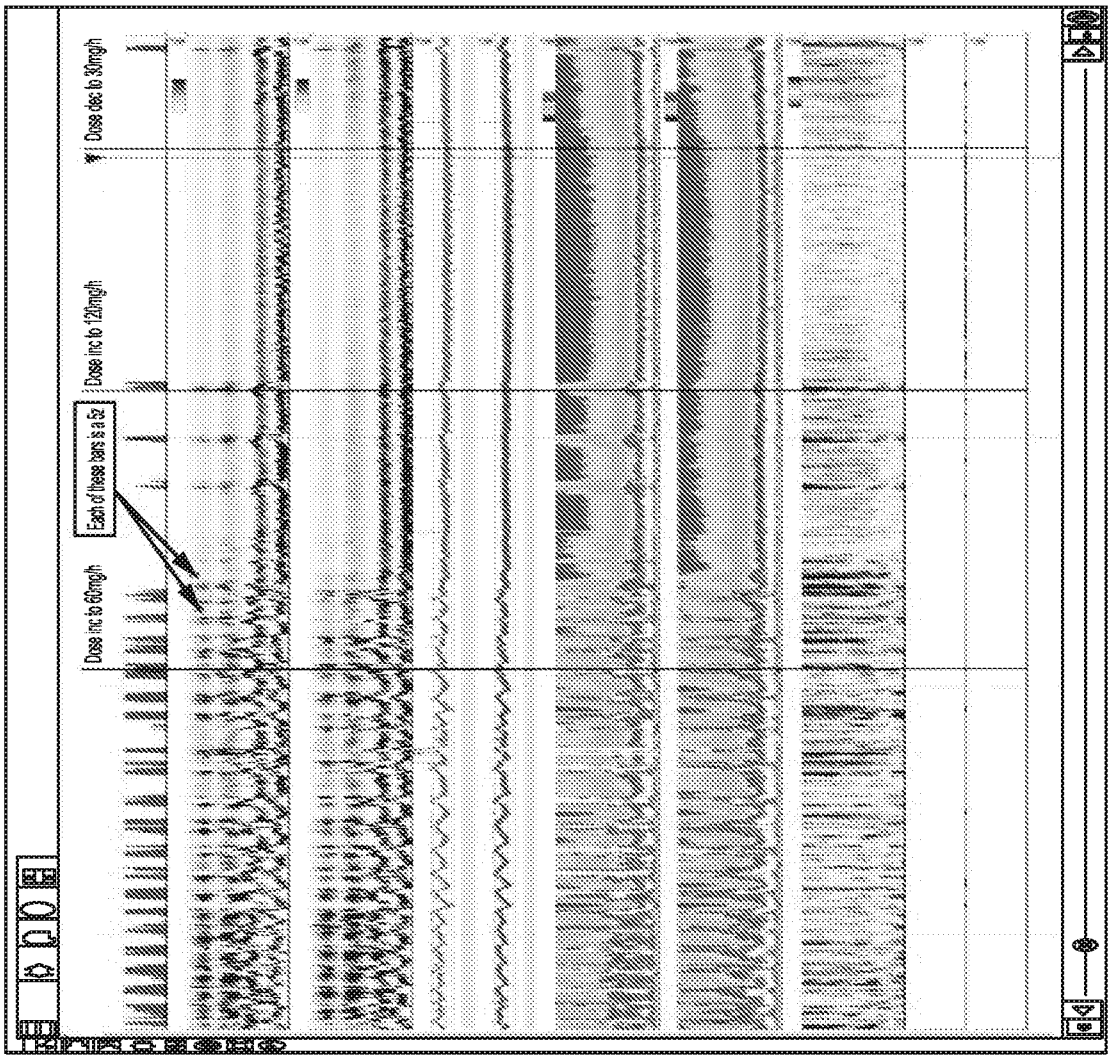

Dose inc to 60mg/h
Each of these bars is a 5s
Dose inc to 120mg/h
Dose dec to 30mg/h

FIG. 11

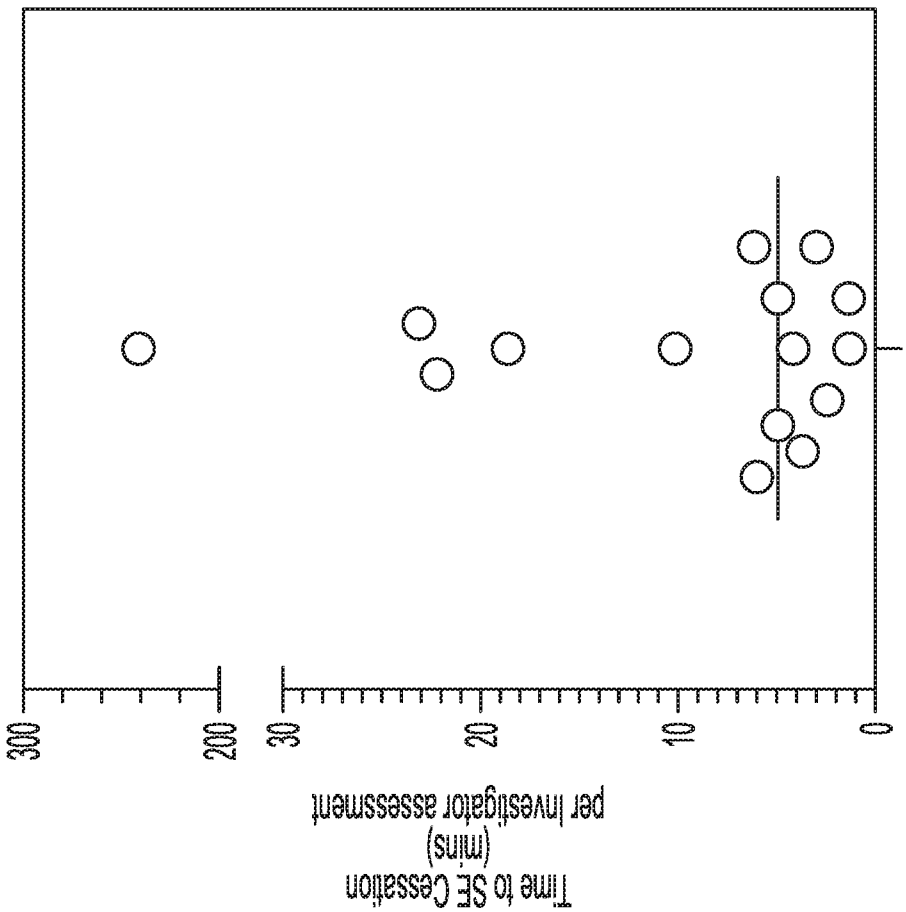

Time to SE Cessation
(mins)
per Investigator assessment
300
200
30
20
10
0

FIG. 12

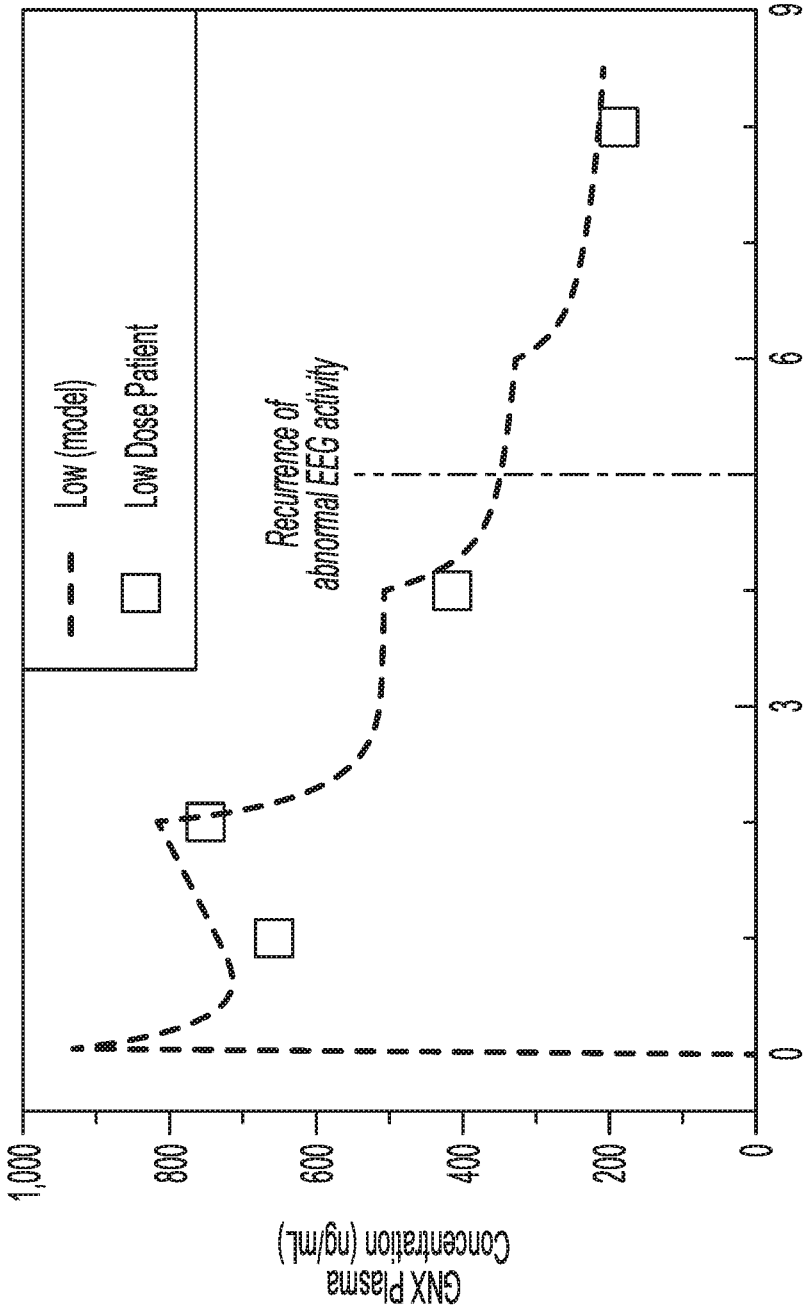

Low (model)
Low Dose Patient
Recurrence of abnormal EEG activity
GNX Plasma Concentration (ng/mL)
1,000
800
600
400
200
0
0
3
6
9
Time (hrs)

FIG. 13A

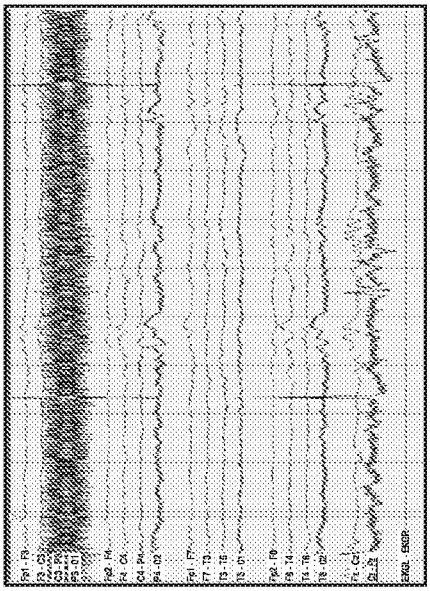


FIG. 13D

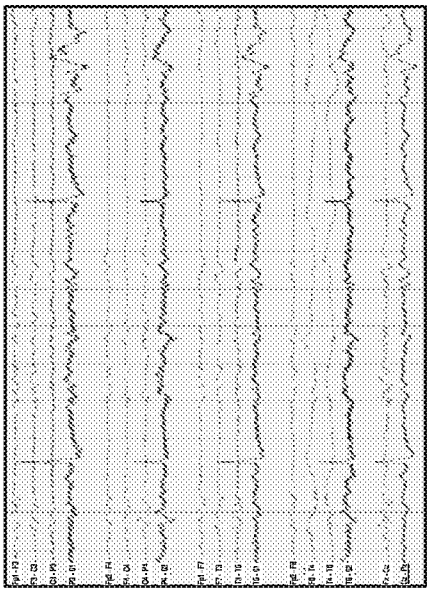


FIG. 13C

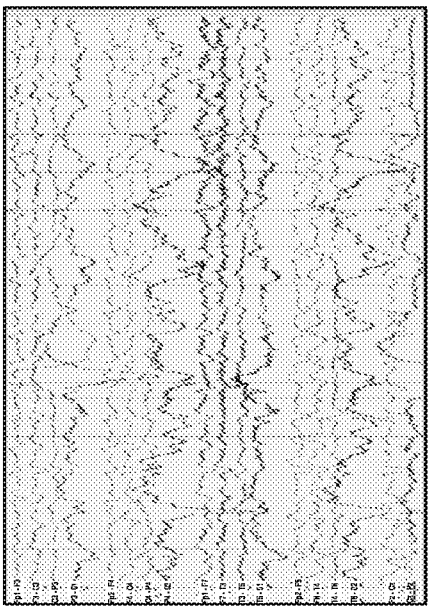


FIG. 13B

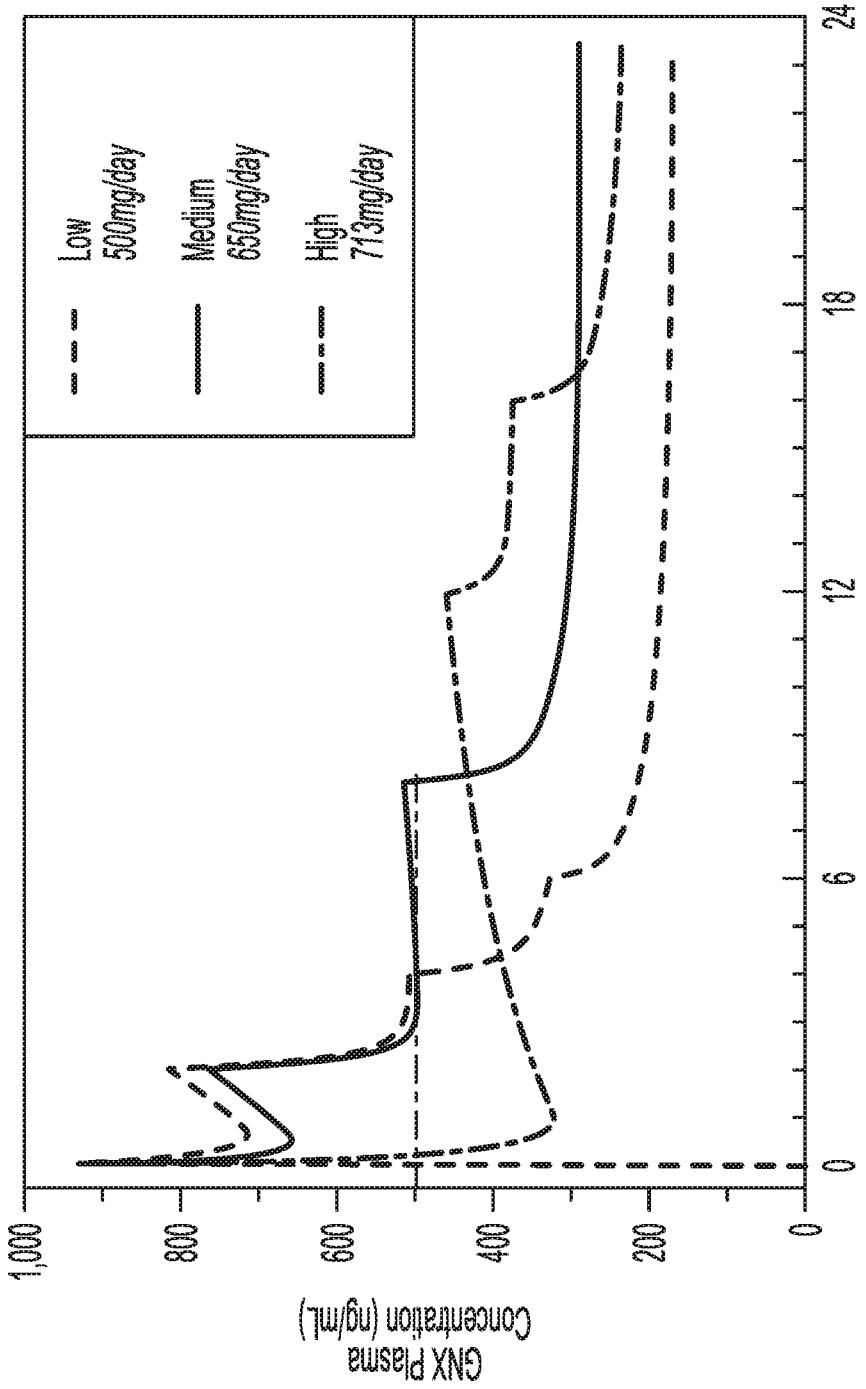

Low
500mg/day
Medium
650mg/day
High
713mg/day
GNX Plasma
Concentration (ng/mL)
1,000
800
600
400
200
0
0
6
12
18
24
Time (hrs)

FIG. 14

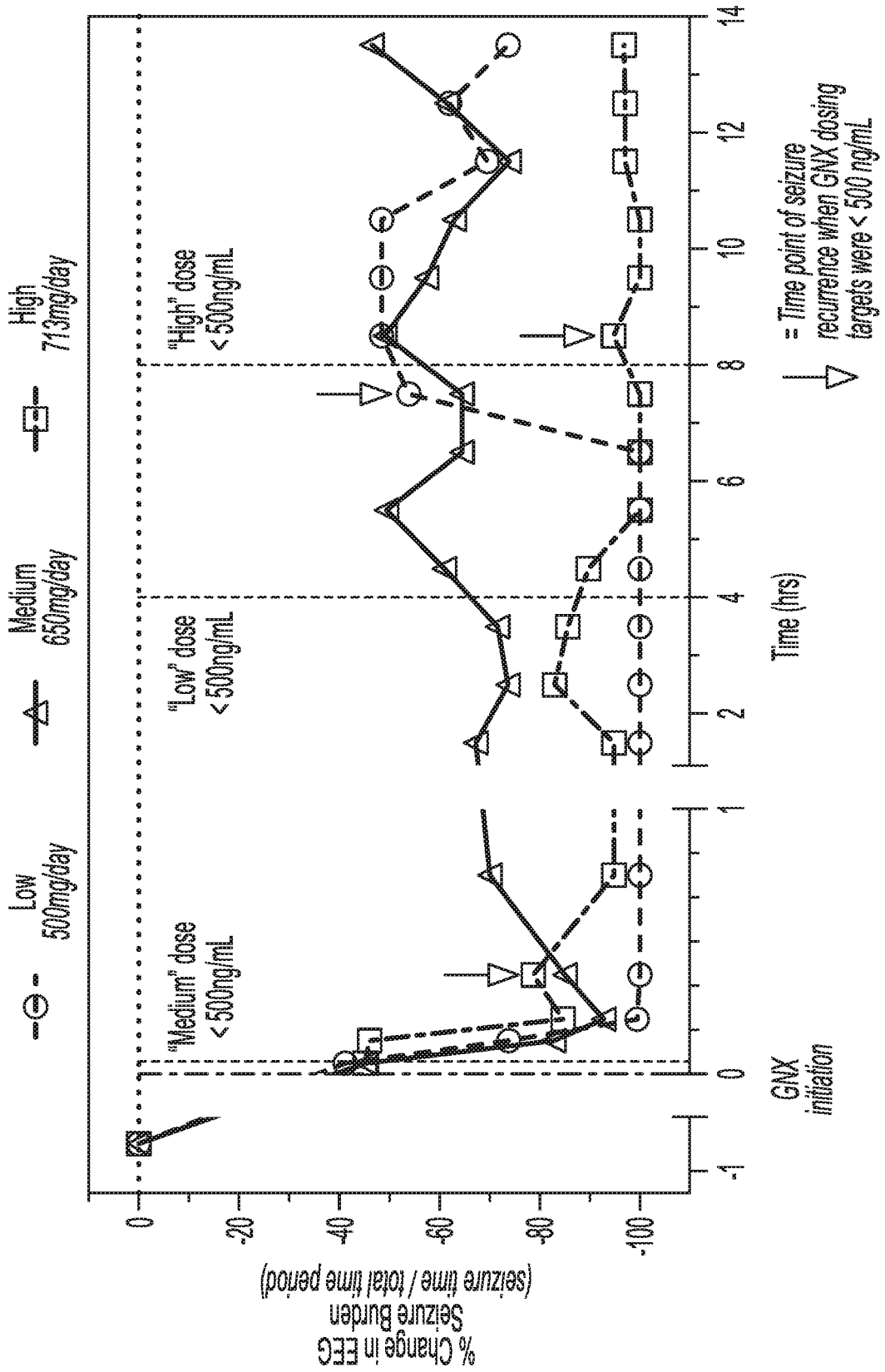

Low
500mg/day
Medium
650mg/day
High
713mg/day
"Medium" dose
< 500ng/mL
"Low" dose
< 500ng/mL
"High" dose
< 500ng/mL
% Change in EEG
Seizure Burden
(seizure time / total time period)
0
-20
-40
-60
-80
-100
-1
0
1
2
4
6
8
10
12
14
GNX
initiation
Time (hrs)
= Time point of seizure
recurrence when GNX dosing
targets were < 500 ng/mL

FIG. 15