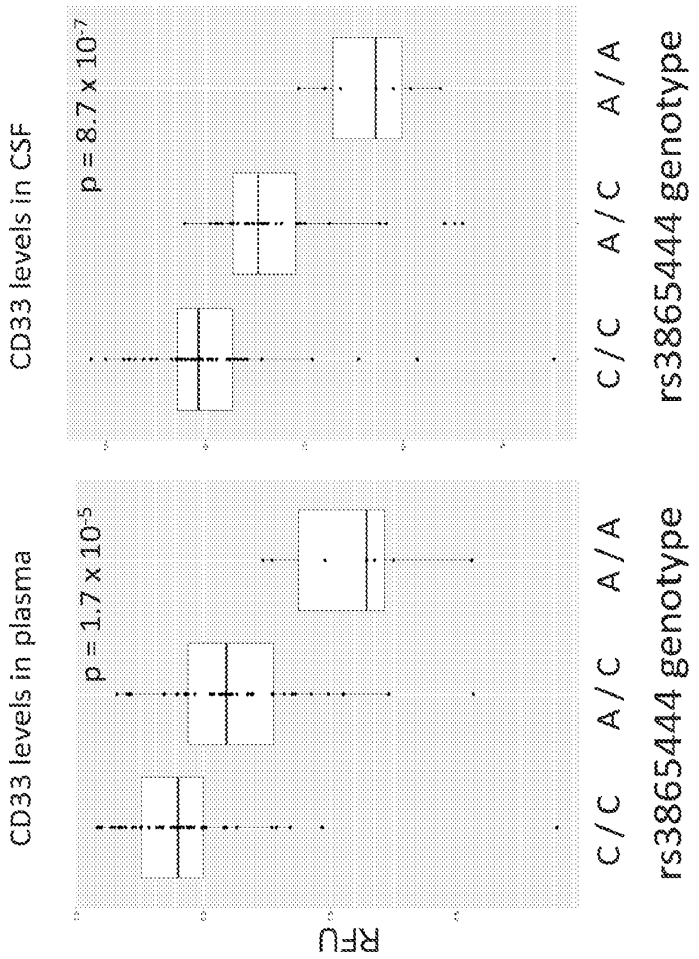
CD33 levels in plasma
p = 1,7 x 10-5
RFU
C/C A/C A/A
rs3865444 genotype
CD33 levels in CSF
p = 8.7 x 10-7
C/C A/C A/A
rs3865444 genotype

FIG. 1

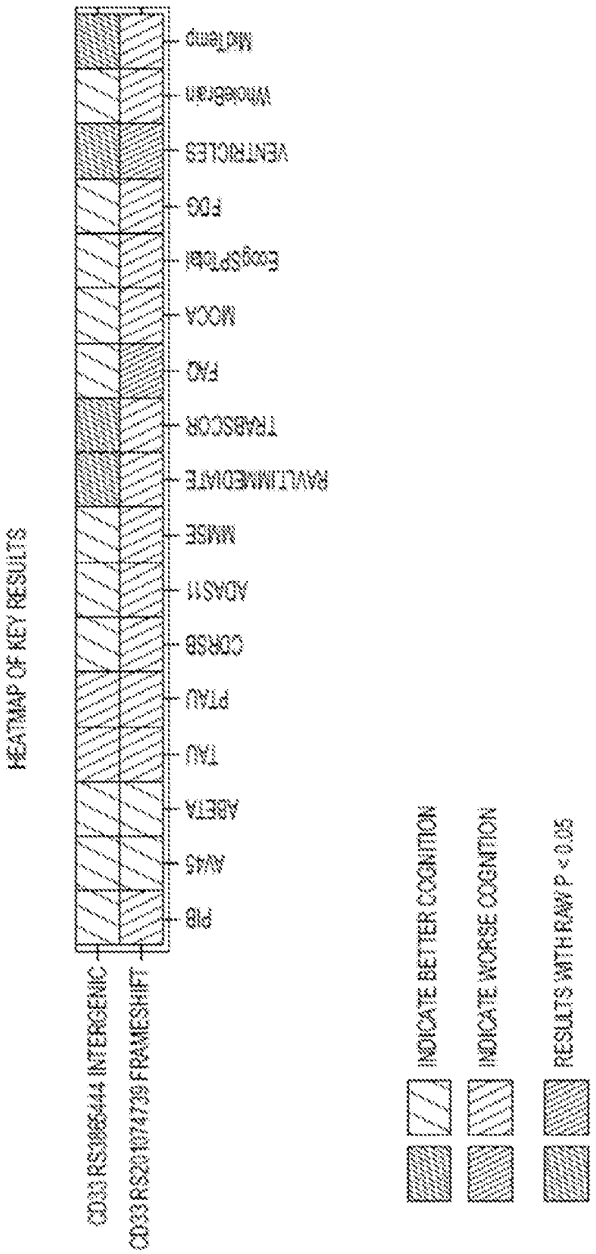
HEATMAP OF KEY RESULTS
CD33 RS3865444 INTERGENIC
CD33 RS2071747 FRAMESHIFT
PIB
AV45
ABETA
TAU
PTAU
CDRSB
ADAS11
MMSE
RAVLTIMMEDIATE
TRABSCOR
FAQ
MOCA
EcogSPTotal
FDG
VENTRICLES
WholeBrain
HippoTemp
INDICATE BETTER COGNITION
INDICATE WORSE COGNITION
RESULTS WITH RAW P < 0.05

FIG. 2

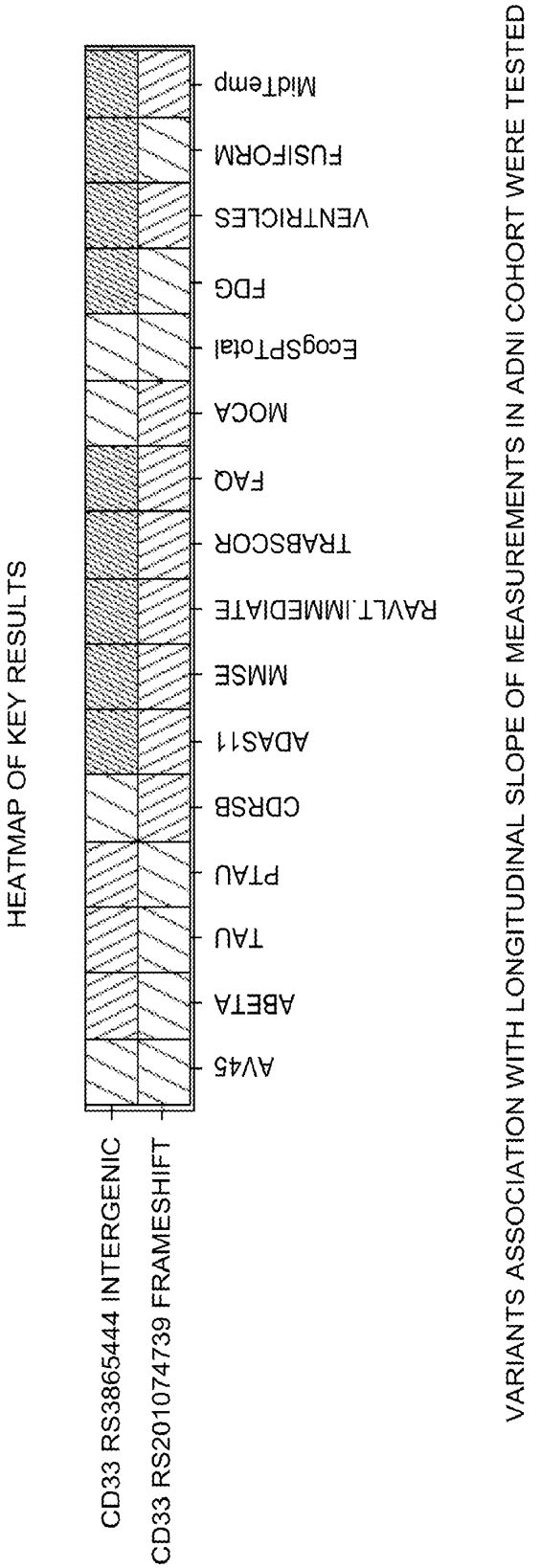
HEATMAP OF KEY RESULTS
CD33 RS3865444 INTERGENIC
CD33 RS201074739 FRAMESHIFT
AV45
ABETA
TAU
PTAU
CDRSB
ADAS11
MMSE
RAVLT_IMMEDIATE
TRABSCOR
FAQ
MOCA
EcogSPTotal
FDG
VENTRICLES
FUSIFORM
MidTemp
VARIANTS ASSOCIATION WITH LONGITUDINAL SLOPE OF MEASUREMENTS IN ADNI COHORT WERE TESTED
INDICATE BENEFICIAL
INDICATE DELETERIOUS
RESULTS WITH RAW P <0.05

FIG. 3

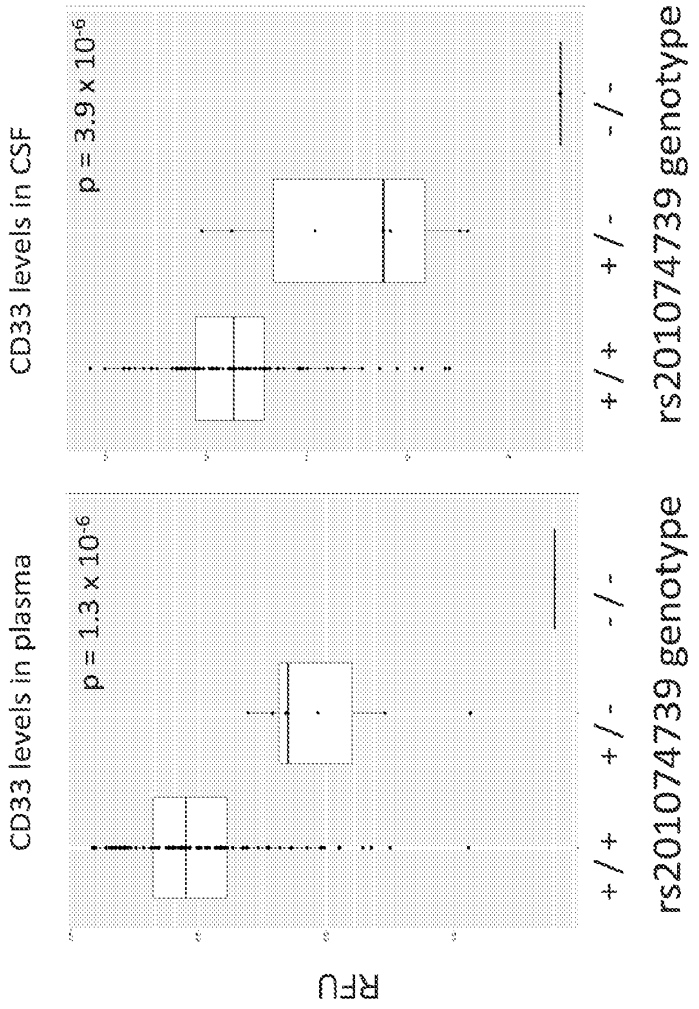
CD33 levels in plasma
p = 1.3 x 10-6
CD33 levels in CSF
p = 3.9 x 10-6
RFU
+ / +
+ / -
- / -
rs201074739 genotype
rs201074739 genotype

FIG. 4

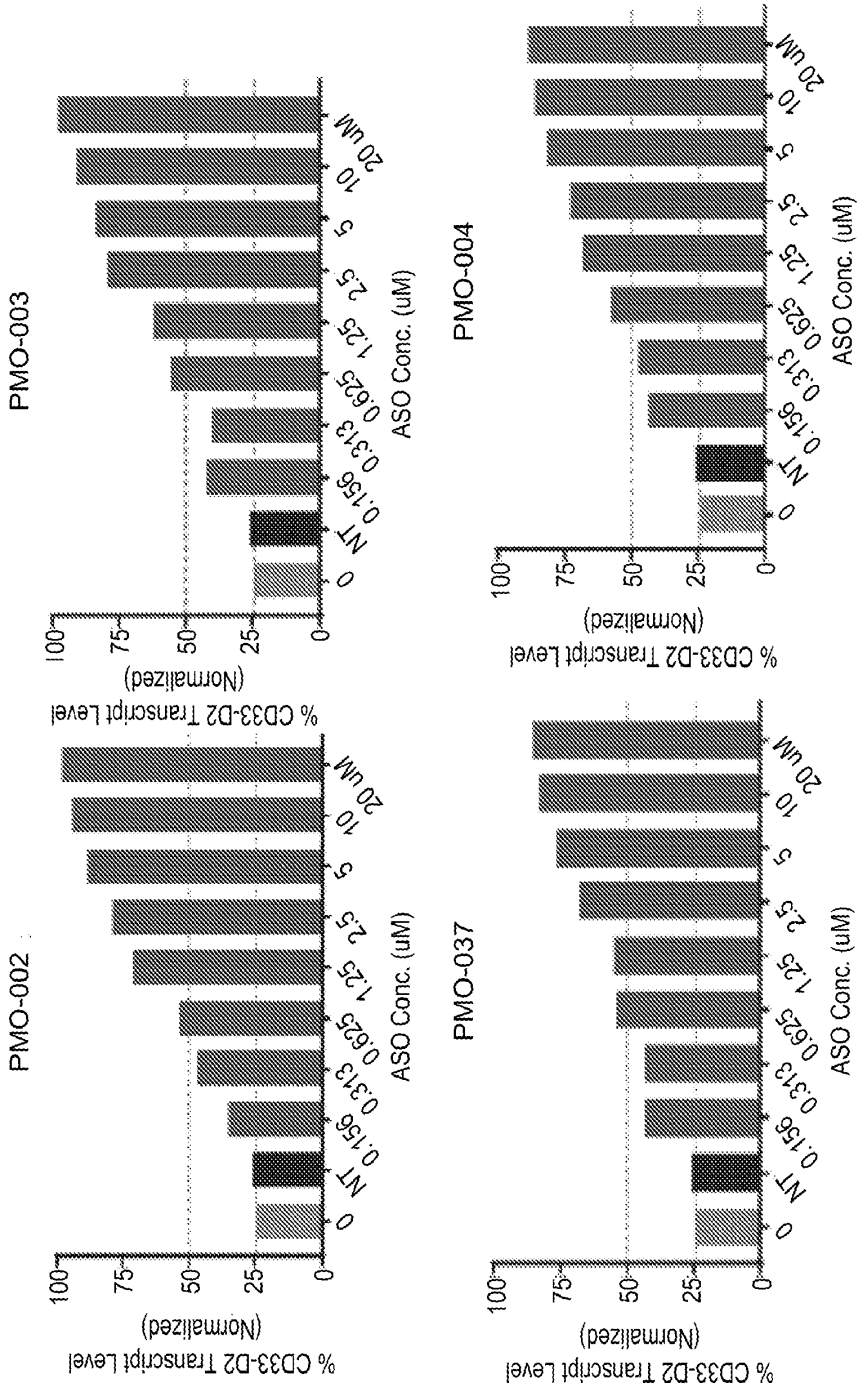
PMO-003
PMO-004
PMO-002
PMO-037
% CD33-D2 Transcript Level (Normalized)
ASO Conc. (uM)
0
NT
0.156
0.313
0.625
1.25
2.5
5
10
20 uM
100
75
50
25
0

FIG. 5

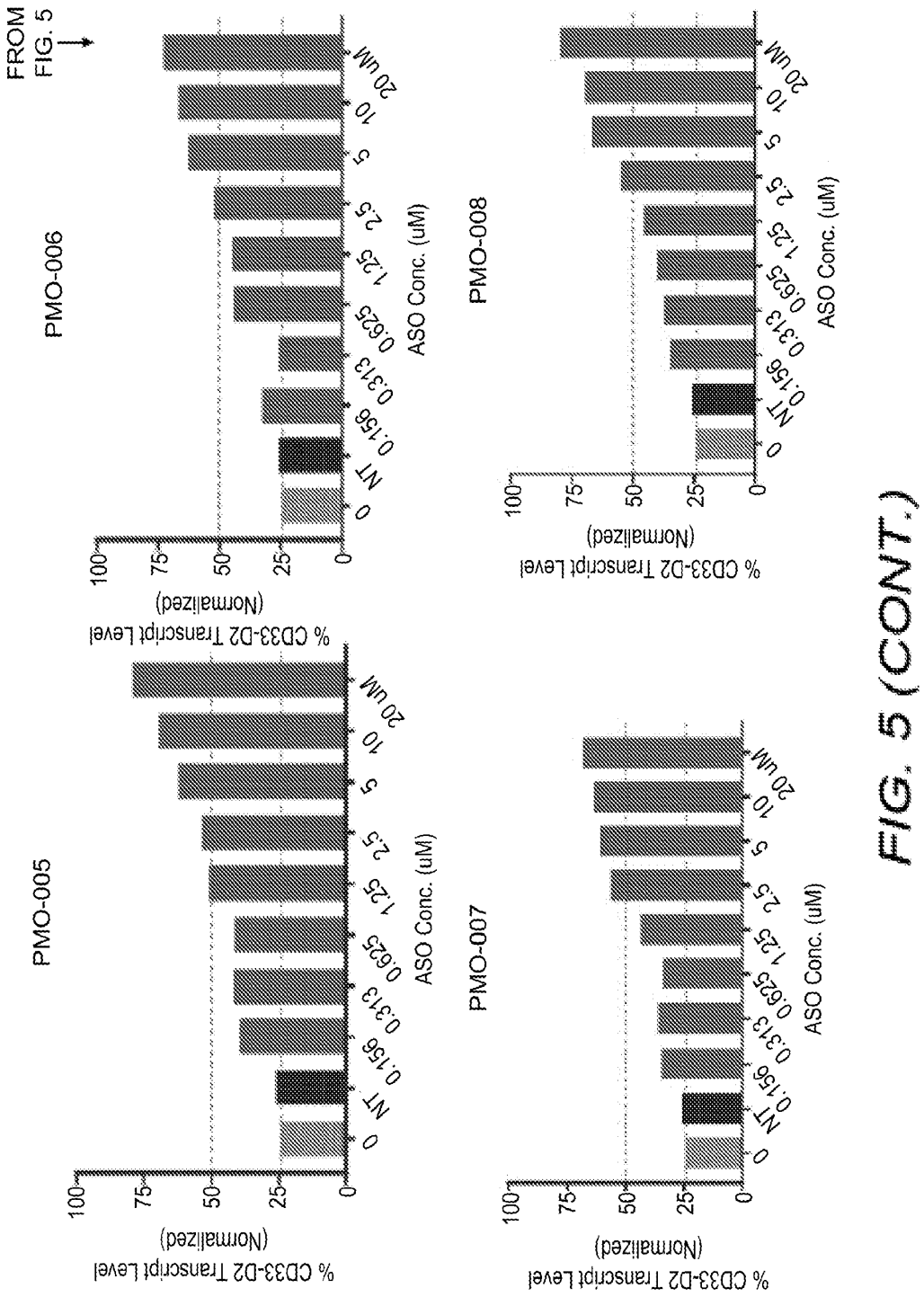
FROM FIG. 5
PMO-006
PMO-008
PMO-005
PMO-007
% CD33-D2 Transcript Level (Normalized)
ASO Conc. (uM)
0
NT
0.156
0.313
0.625
1.25
2.5
5
10
20 uM
0
25
50
75
100

FIG. 5 (CONT.)

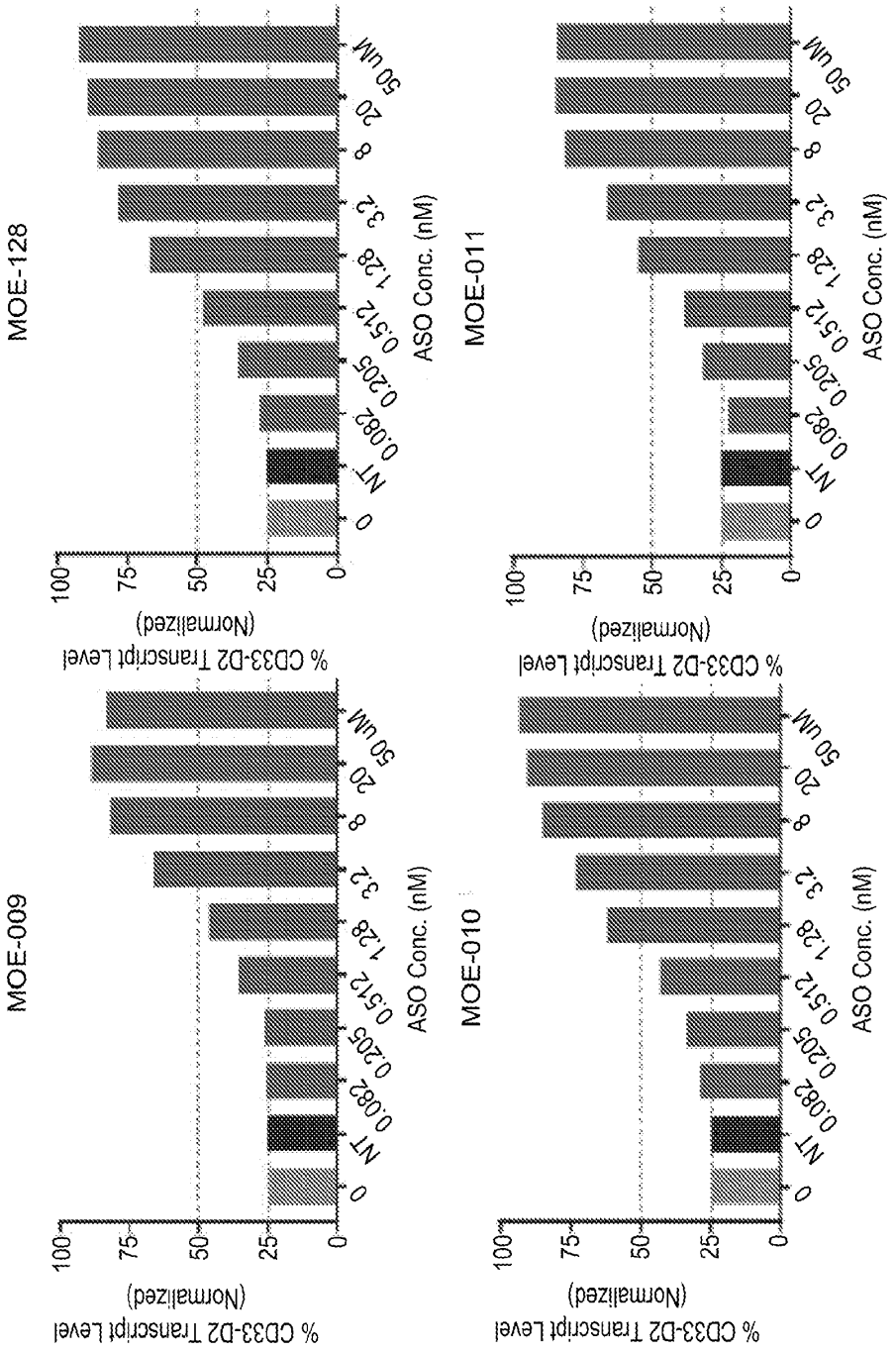
MOE-128
MOE-011
MOE-009
MOE-010
% CD33-D2 Transcript Level (Normalized)
ASO Conc. (nM)
0
NT
0.082
0.205
0.512
1.28
3.2
8
20
50 uM
100
75
50
25
0

FIG. 6

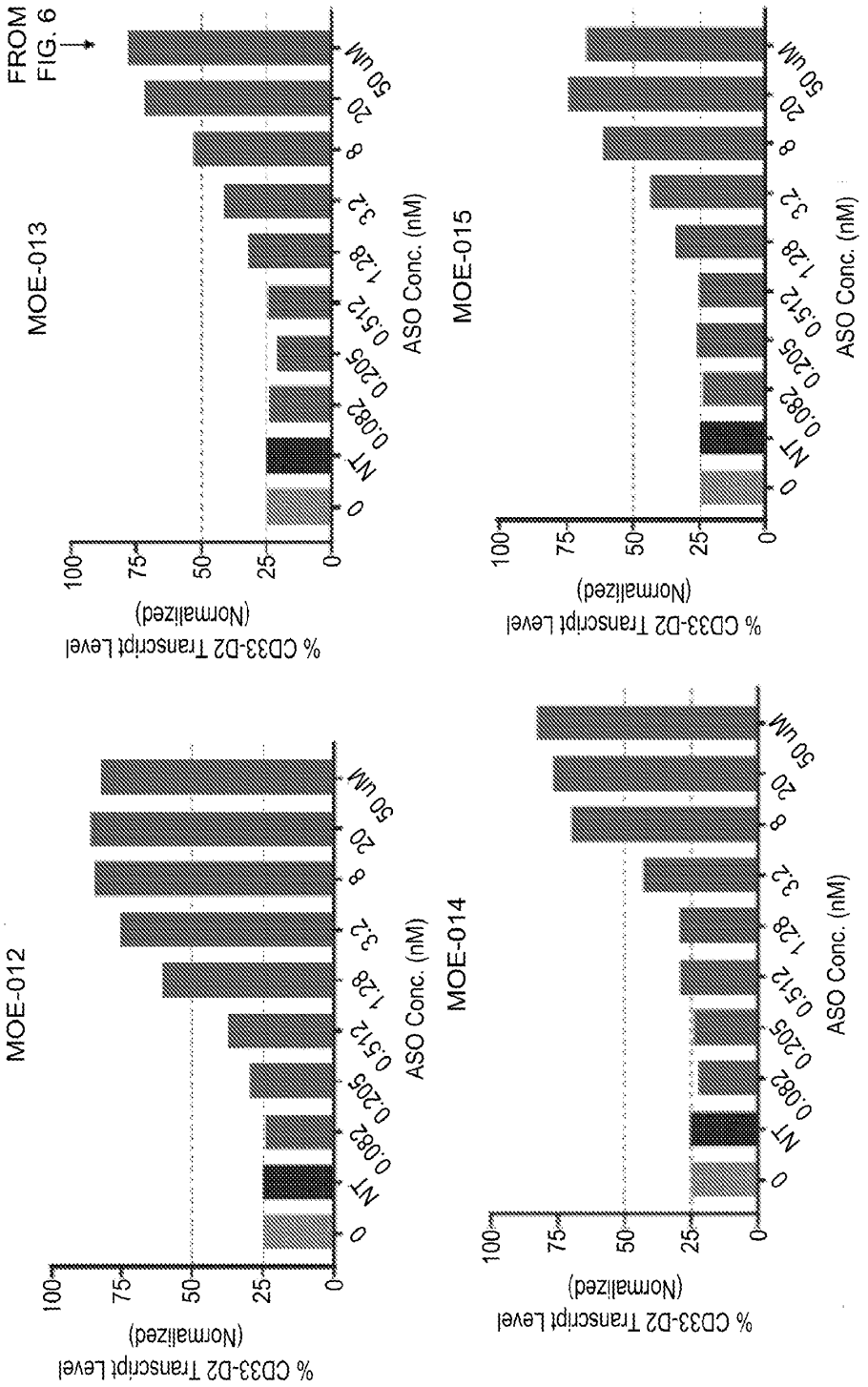
FROM FIG. 6
MOE-013
MOE-015
MOE-012
MOE-014
% CD33-D2 Transcript Level (Normalized)
ASO Conc. (nM)
0
NT
0.082
0.205
0.512
1.28
3.2
8
20
50 uM
100
75
50
25
0

FIG. 6 (CONT.)

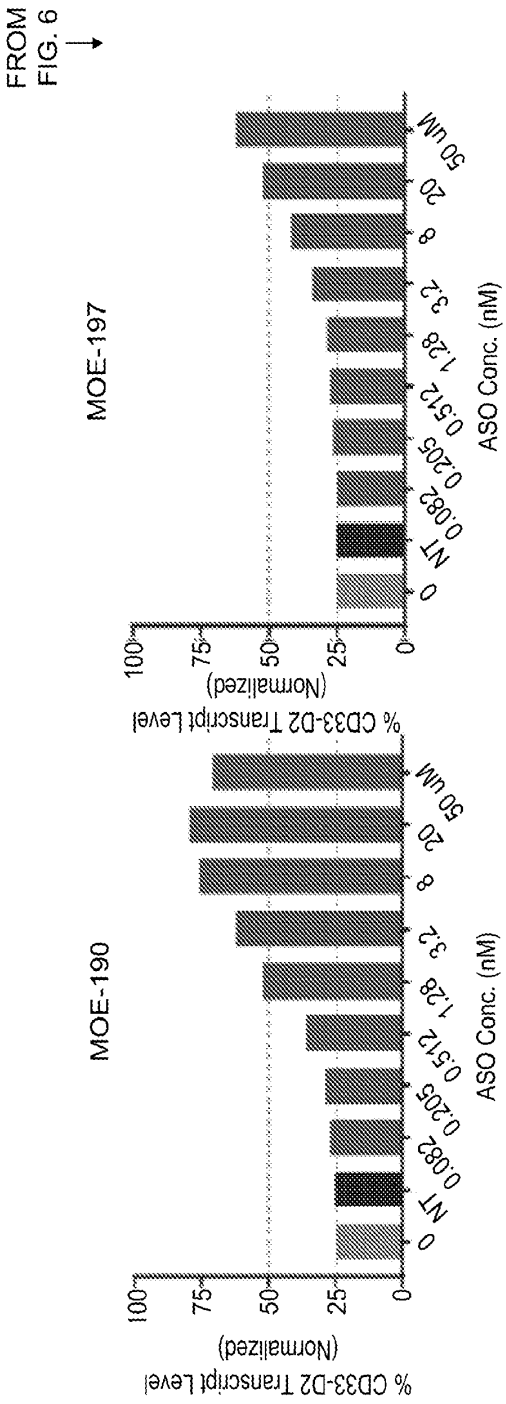
FROM FIG. 6
MOE-197
% CD33-D2 Transcript Level (Normalized)
100
75
50
25
0
0
NT
0.082
0.205
0.512
1.28
3.2
8
20
50 uM
ASO Conc. (nM)
MOE-190
% CD33-D2 Transcript Level (Normalized)
100
75
50
25
0
0
NT
0.082
0.205
0.512
1.28
3.2
8
20
50 uM
ASO Conc. (nM)

FIG. 6 (CONT.)

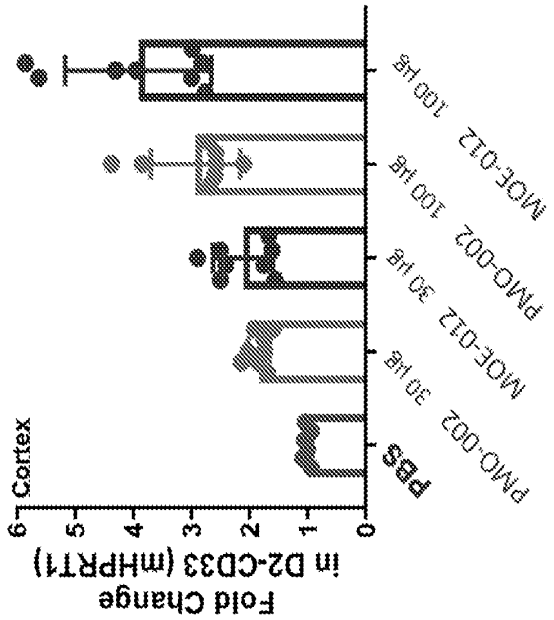
Cortex
Fold Change
in D2-CD33 (mHPRT1)
0
1
2
3
4
5
6
PBS
PMO-002 30 uE
MOE-012 30 uE
PMO-002 100 uE
MOE-012 100 uE

FIG. 8

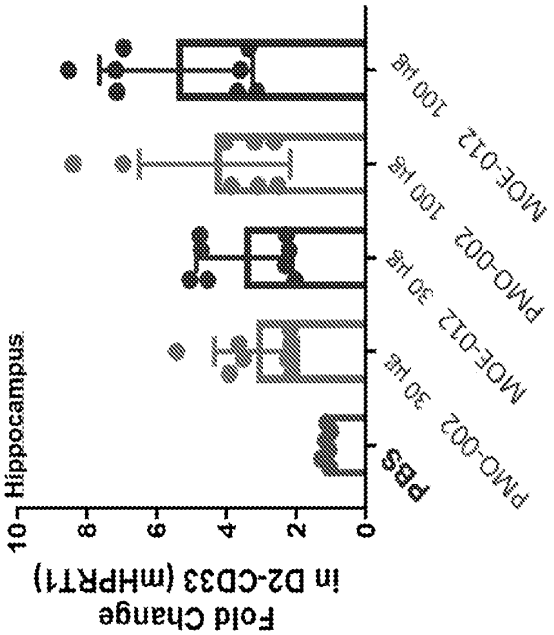
Hippocampus
Fold Change
in D2-CD33 (mHPRT1)
0
2
4
6
8
10
PBS
PMO-002 30 uE
MOE-012 30 uE
PMO-002 100 uE
MOE-012 100 uE

FIG. 7

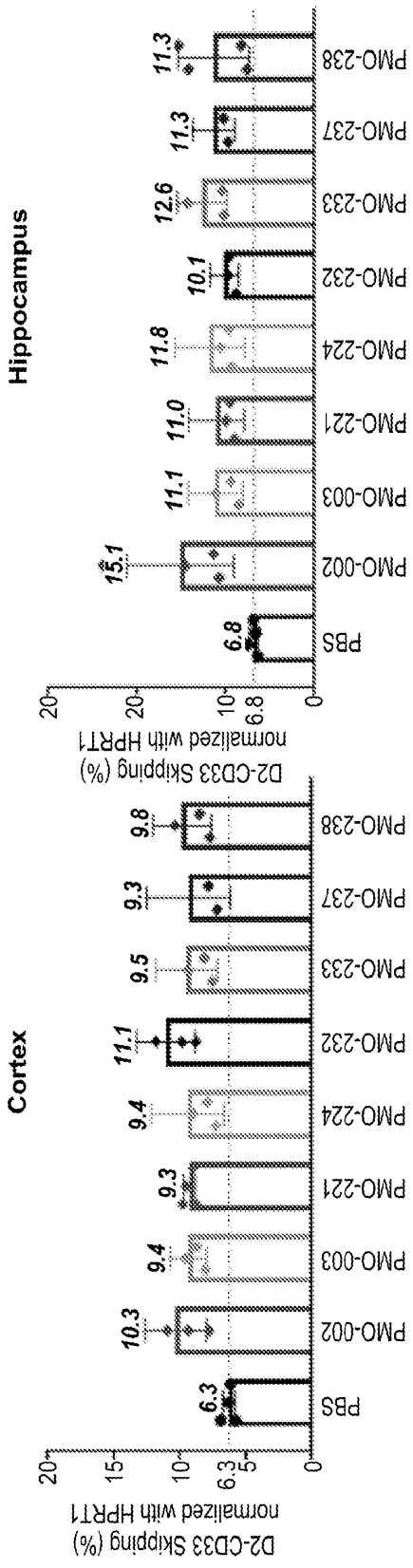
Hippocampus
D2-CD33 Skipping (%)
normalized with HPRT1
20
20
10
6.8
0
PBS
PMO-002
PMO-003
PMO-221
PMO-224
PMO-232
PMO-233
PMO-237
PMO-238
6.8
15.1
11.1
11.0
11.8
10.1
12.6
11.3
11.3
Cortex
D2-CD33 Skipping (%)
normalized with HPRT1
20
15
10
6.3
5
0
PBS
PMO-002
PMO-003
PMO-221
PMO-224
PMO-232
PMO-233
PMO-237
PMO-238
6.3
10.3
9.4
9.3
9.4
11.1
9.5
9.3
9.8

FIG. 9

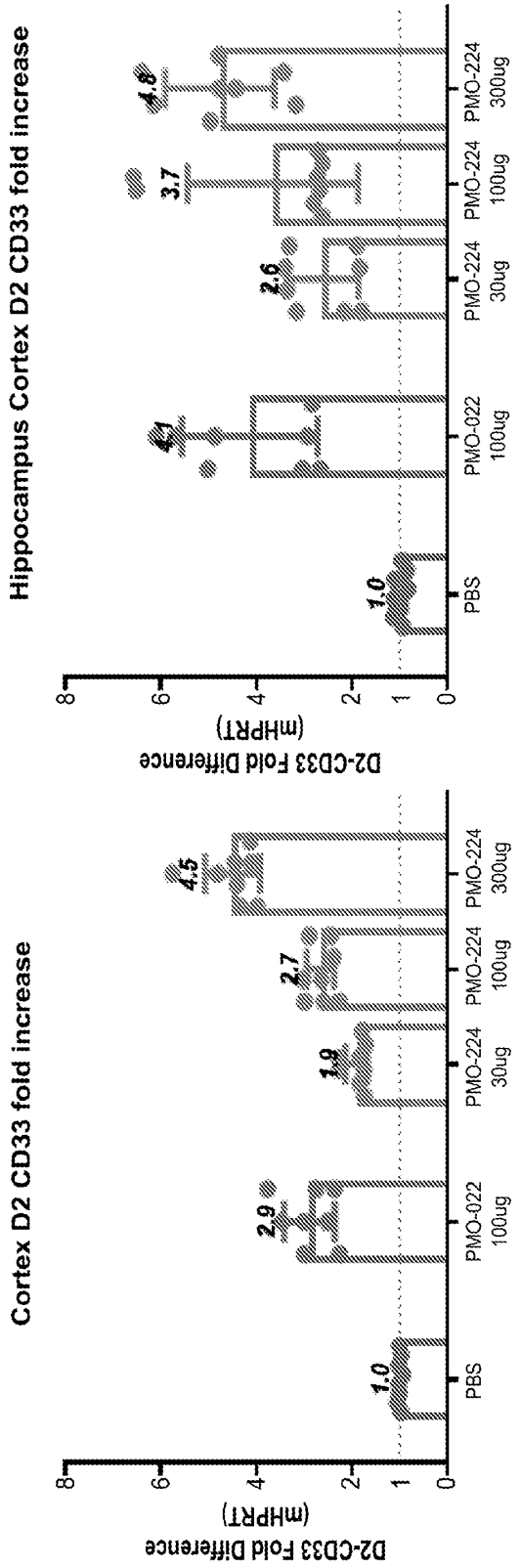
Hippocampus Cortex D2 CD33 fold increase
D2-CD33 Fold Difference (mHPRT)
0
1
2
4
6
8
1.0
4.1
2.6
3.7
4.8
PBS
PMO-022 100ug
PMO-224 30ug
PMO-224 100ug
PMO-224 300ug
Cortex D2 CD33 fold increase
D2-CD33 Fold Difference (mHPRT)
0
1
2
4
6
8
1.0
2.9
1.9
2.7
4.5
PBS
PMO-022 100ug
PMO-224 30ug
PMO-224 100ug
PMO-224 300ug

FIG. 10

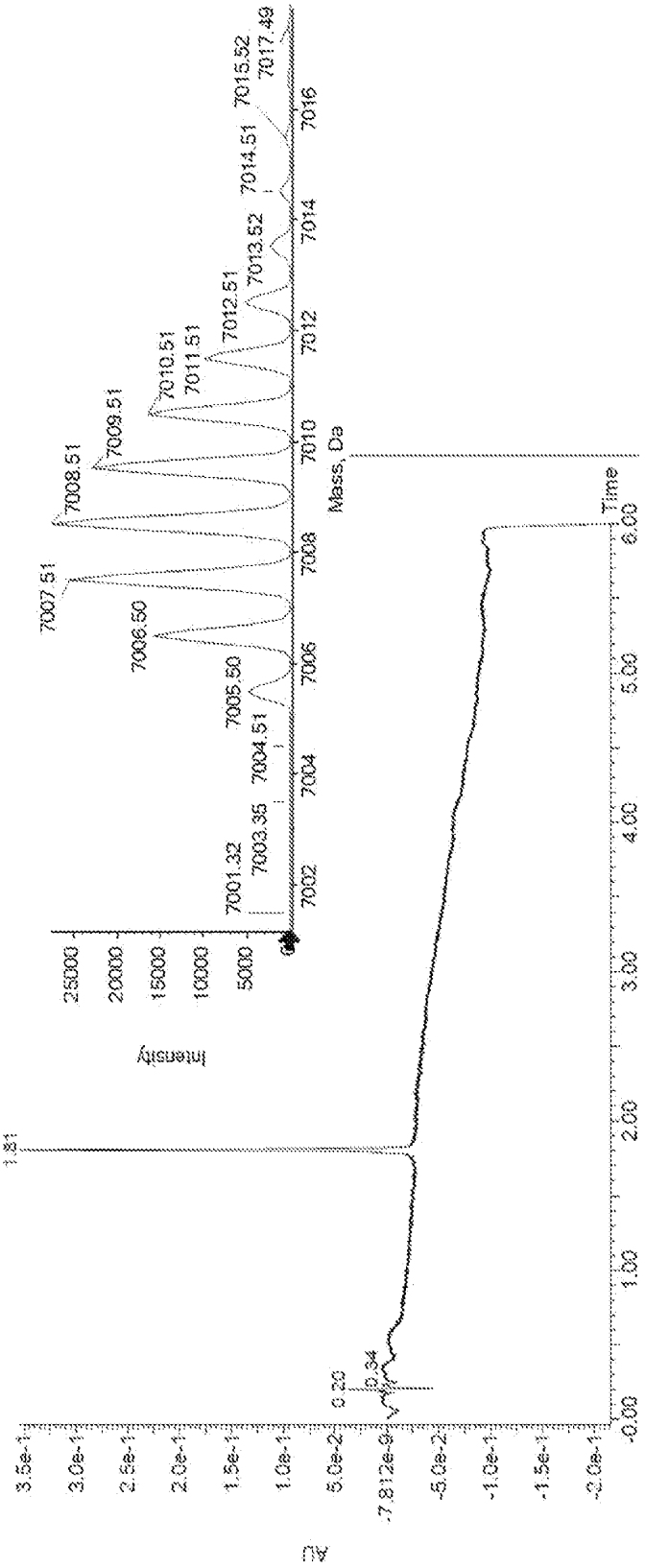
AU
Time
Mass, Da
Intensity
1.81
0.20
0.34
7.812e-9
7001.32
7003.35
7004.51
7005.50
7006.50
7007.51
7008.51
7009.51
7010.51
7011.51
7012.51
7013.52
7014.51
7015.52
7017.49

FIG. 11

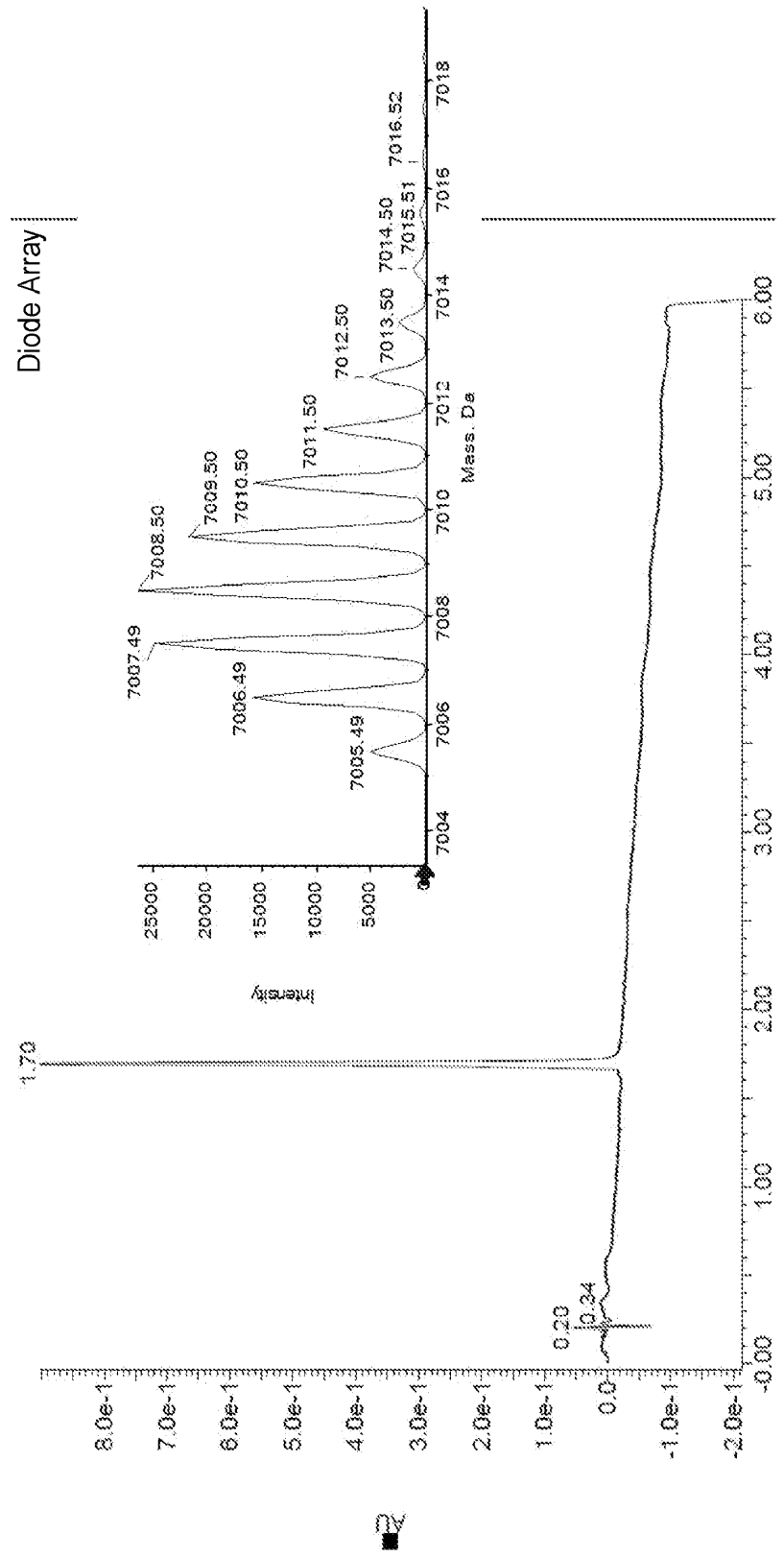
Diode Array
1.70
0.20
0.24
8.0e-1
7.0e-1
6.0e-1
5.0e-1
4.0e-1
3.0e-1
2.0e-1
1.0e-1
0.0
-1.0e-1
-2.0e-1
AU
-0.00
1.00
2.00
3.00
4.00
5.00
6.00
Min
7004
7005.49
7006
7006.49
7007.49
7008
7008.50
7009.50
7010
7010.50
7011.50
7012
7012.50
7013.50
7014
7014.50
7015
7015.51
7016.52
7018
Mass, Da
Intensity
25000
20000
15000
10000
5000
0

FIG. 12

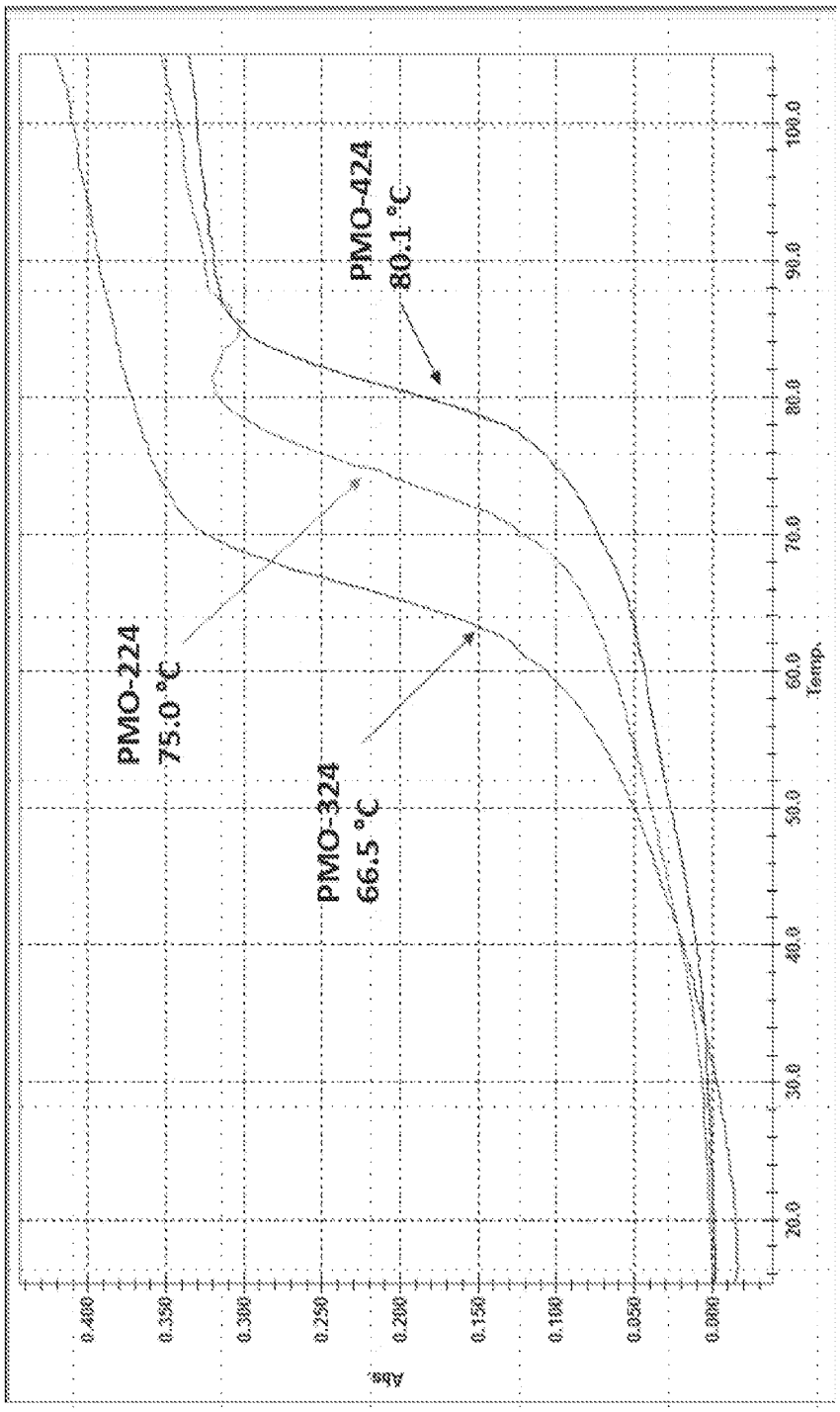
PMO-424
80.1 °C
PMO-224
75.0 °C
PMO-324
66.5 °C
Abs
Temp.
0.400
0.350
0.300
0.250
0.200
0.150
0.100
0.050
0.000
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0

FIG. 13

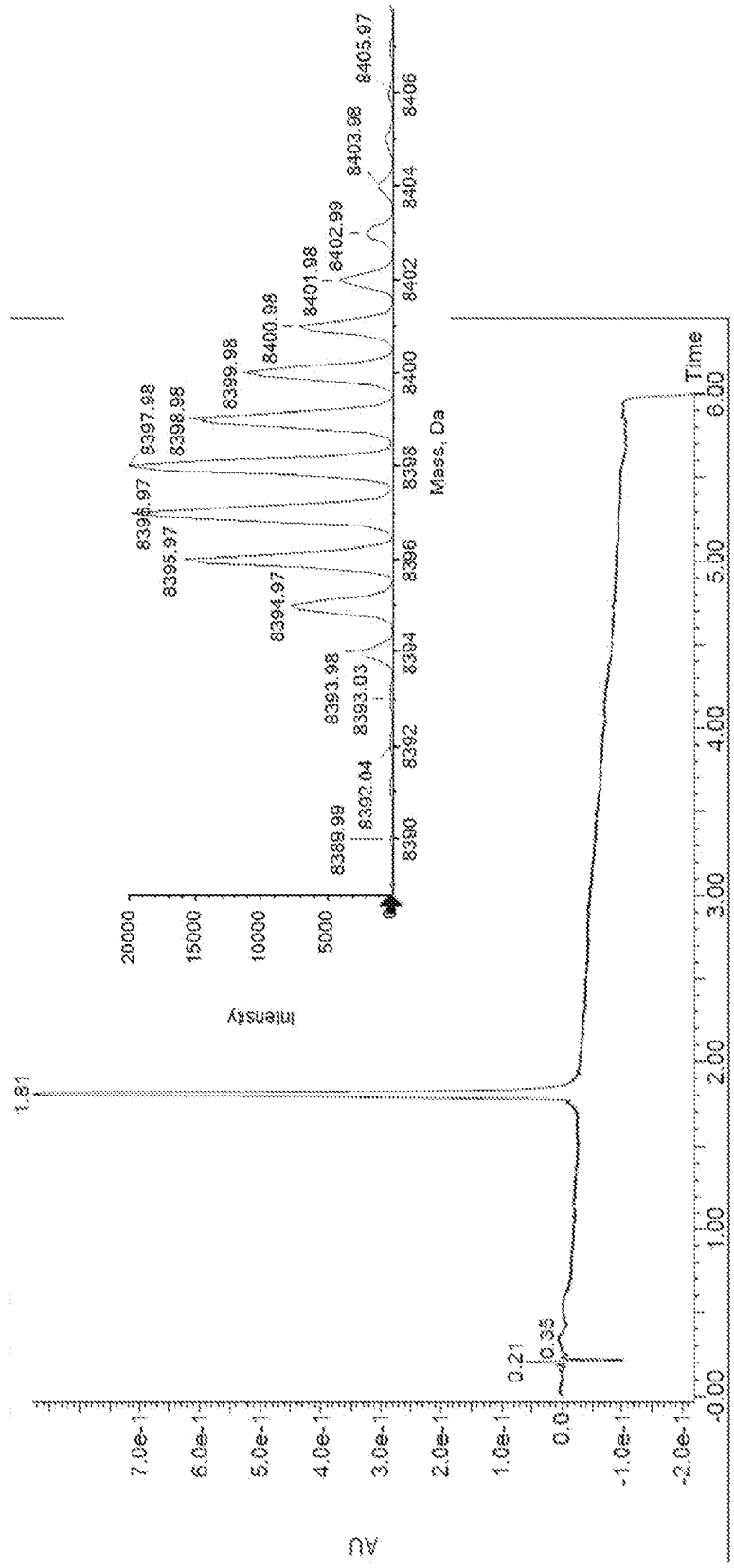
AU
Time
Mass, Da
Intensity
1.81
0.21
0.35
8388.99
8392.04
8393.03
8393.98
8394.97
8395.97
8396.97
8397.98
8398.98
8399.98
8400.98
8401.98
8402.99
8403.98
8405.97

FIG. 14

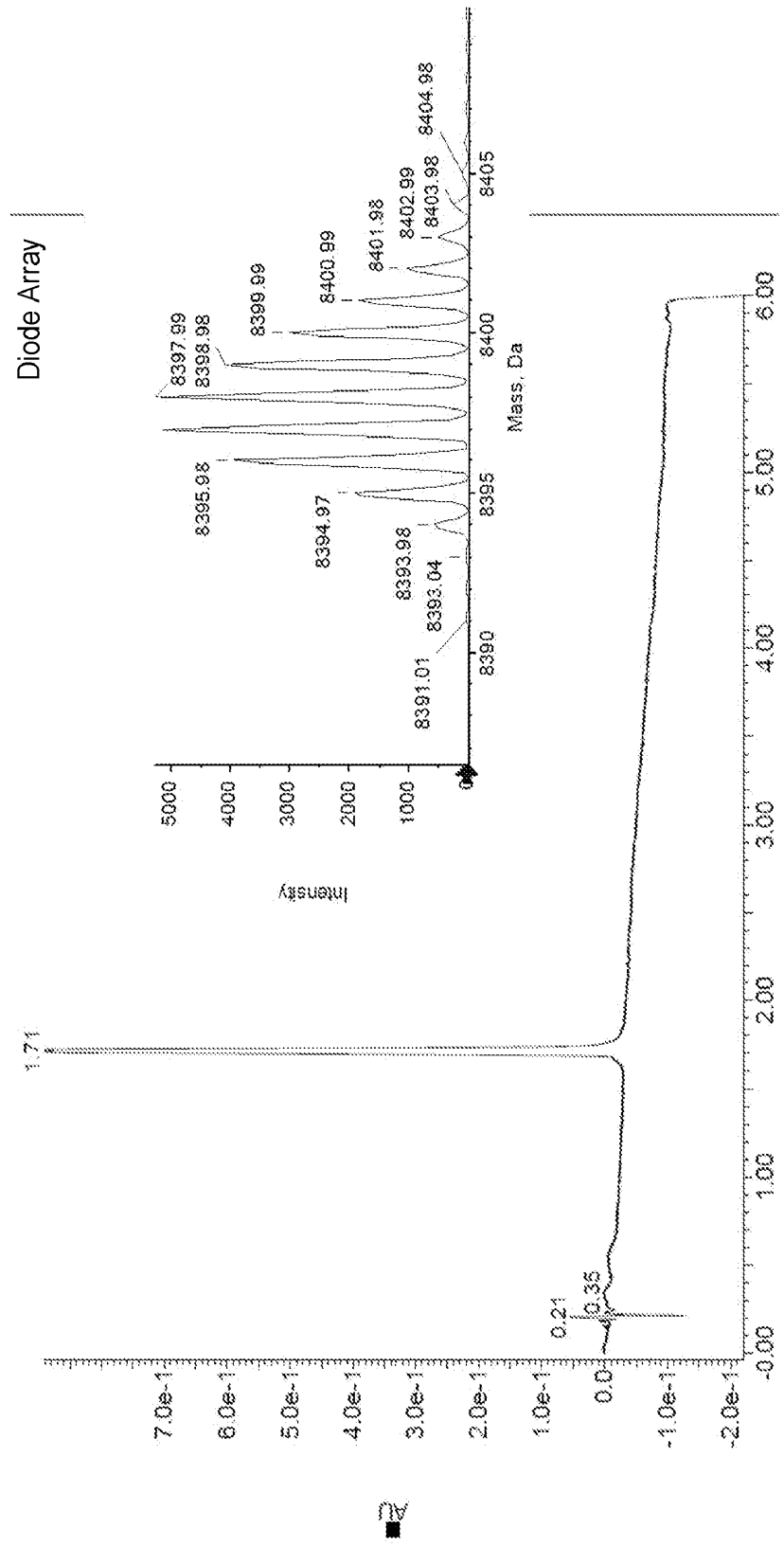
Diode Array
1.71
0.21
0.35
AU
7.0e-1
6.0e-1
5.0e-1
4.0e-1
3.0e-1
2.0e-1
1.0e-1
0.0
-1.0e-1
-2.0e-1
-0.00
1.00
2.00
3.00
4.00
5.00
6.00
Intensity
5000
4000
3000
2000
1000
0
8390
8395
8400
8405
Mass, Da
8391.01
8393.04
8393.98
8394.97
8395.98
8397.99
8398.98
8399.99
8400.99
8401.98
8402.99
8403.98
8404.98

FIG. 15

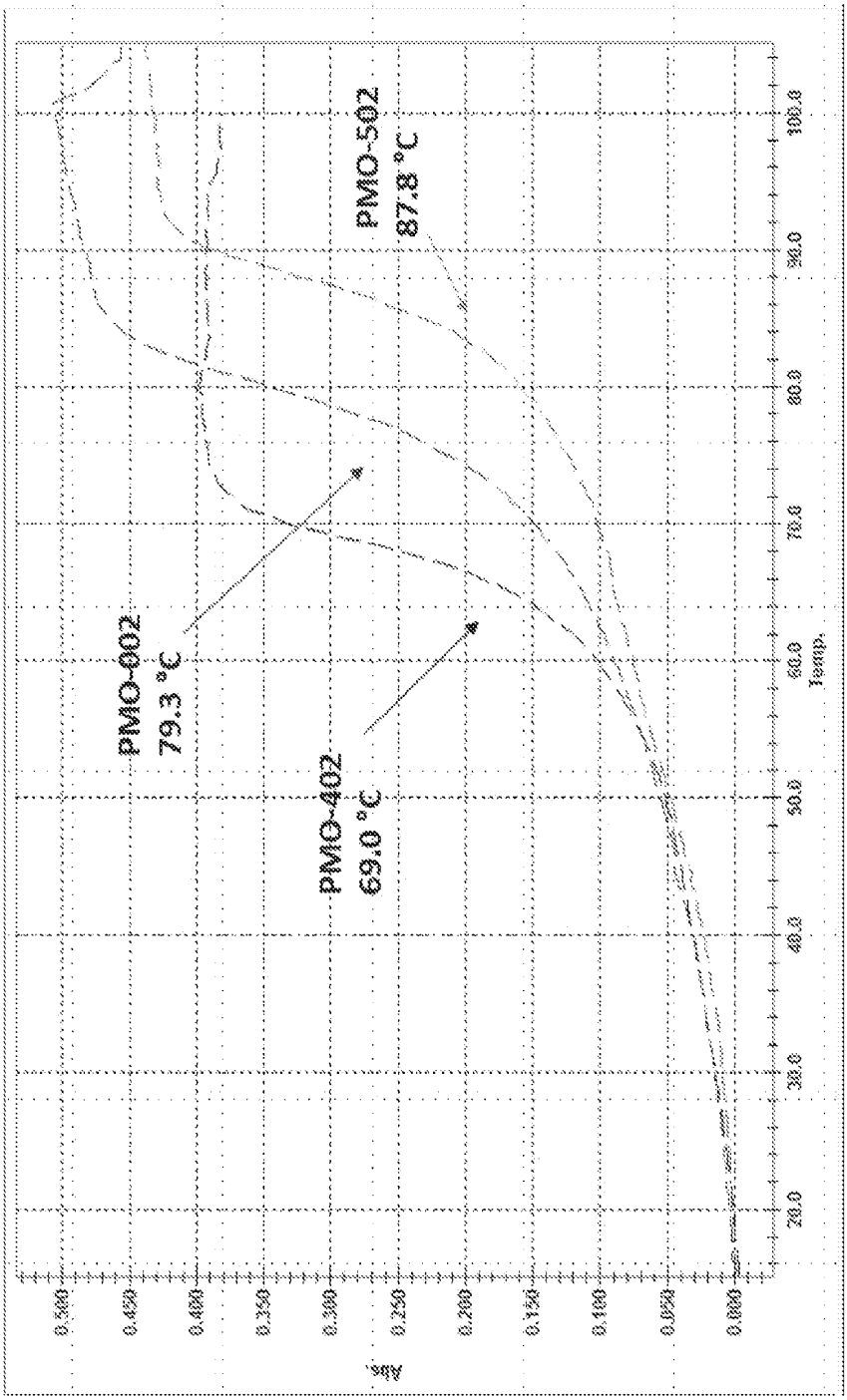
PMO-502
87.8 °C
PMO-002
79.3 °C
PMO-402
69.0 °C
Abs
Temp.
0.500
0.450
0.400
0.350
0.300
0.250
0.200
0.150
0.100
0.050
0.000
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0

FIG. 16

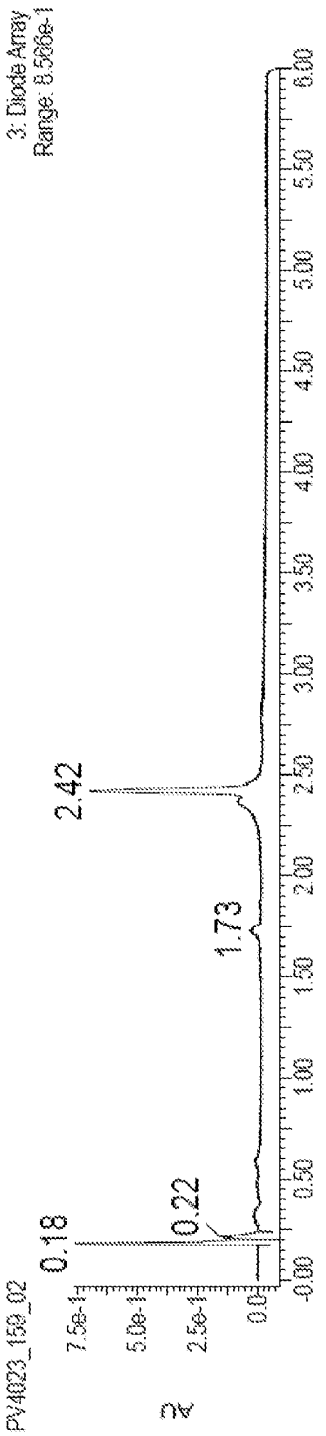
3: Diode Array
Range: 8.598e-1
PV4023_159_02
0.18
0.22
1.73
2.42
mAU
7.5e-1
5.0e-1
2.5e-1
0.0
-0.00
0.50
1.00
1.50
2.00
2.50
3.00
3.50
4.00
4.50
5.00
5.50
6.00

FIG. 17

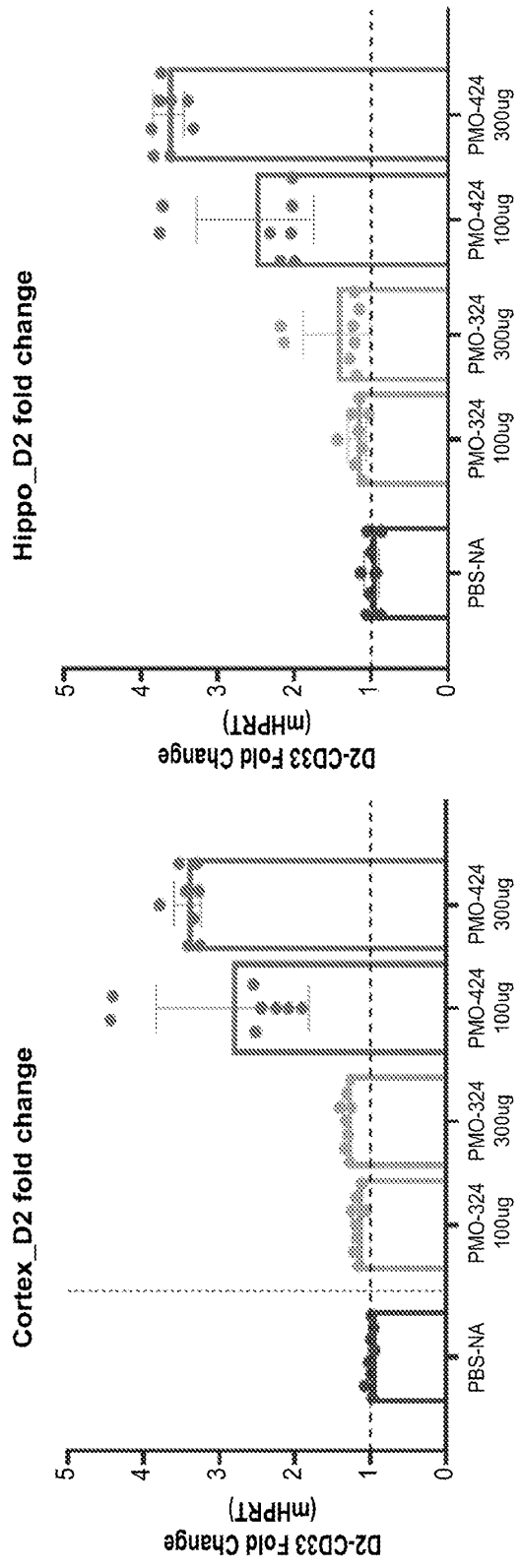
Hippo_D2 fold change
D2-CD33 Fold Change (mHPRT)
0
1
2
3
4
5
PBS-NA
PMO-324 100ug
PMO-324 300ug
PMO-424 100ug
PMO-424 300ug
Cortex_D2 fold change
D2-CD33 Fold Change (mHPRT)
0
1
2
3
4
5
PBS-NA
PMO-324 100ug
PMO-324 300ug
PMO-424 100ug
PMO-424 300ug

FIG. 18

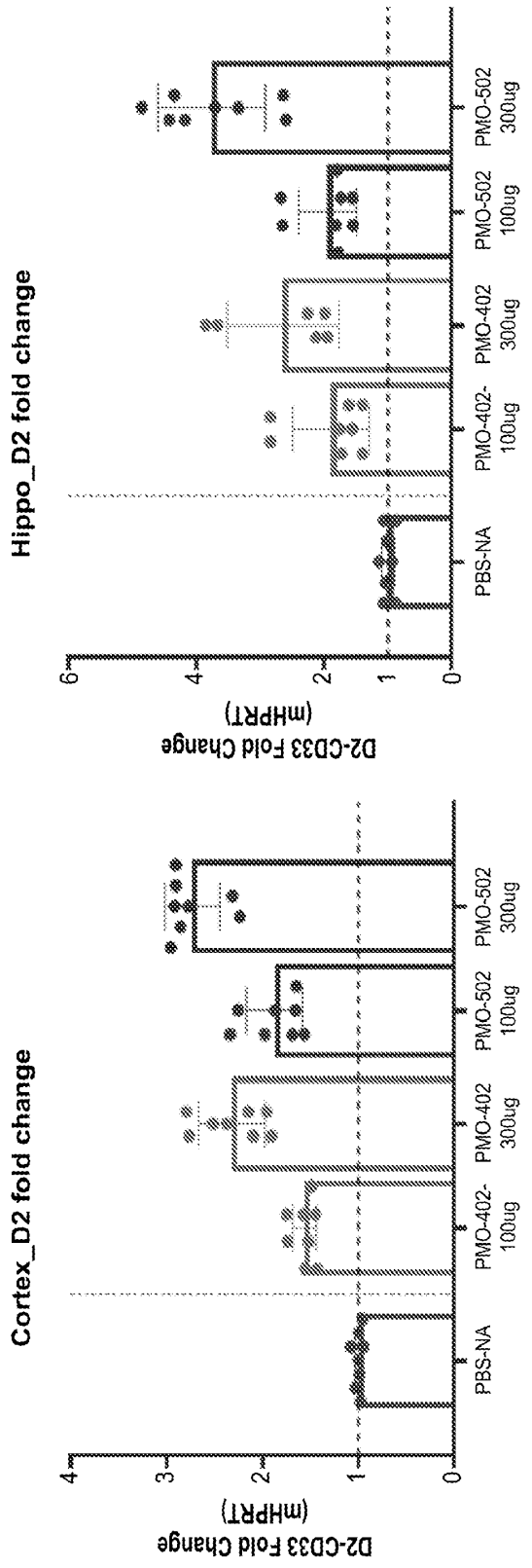
Hippo_D2 fold change
D2-CD33 Fold Change (mHPRT)
0
1
2
4
6
PBS-NA
PMO-402-100ug
PMO-402 300ug
PMO-502 100ug
PMO-502 300ug
Cortex_D2 fold change
D2-CD33 Fold Change (mHPRT)
0
1
2
3
4
PBS-NA
PMO-402-100ug
PMO-402 300ug
PMO-502 100ug
PMO-502 300ug

FIG. 19

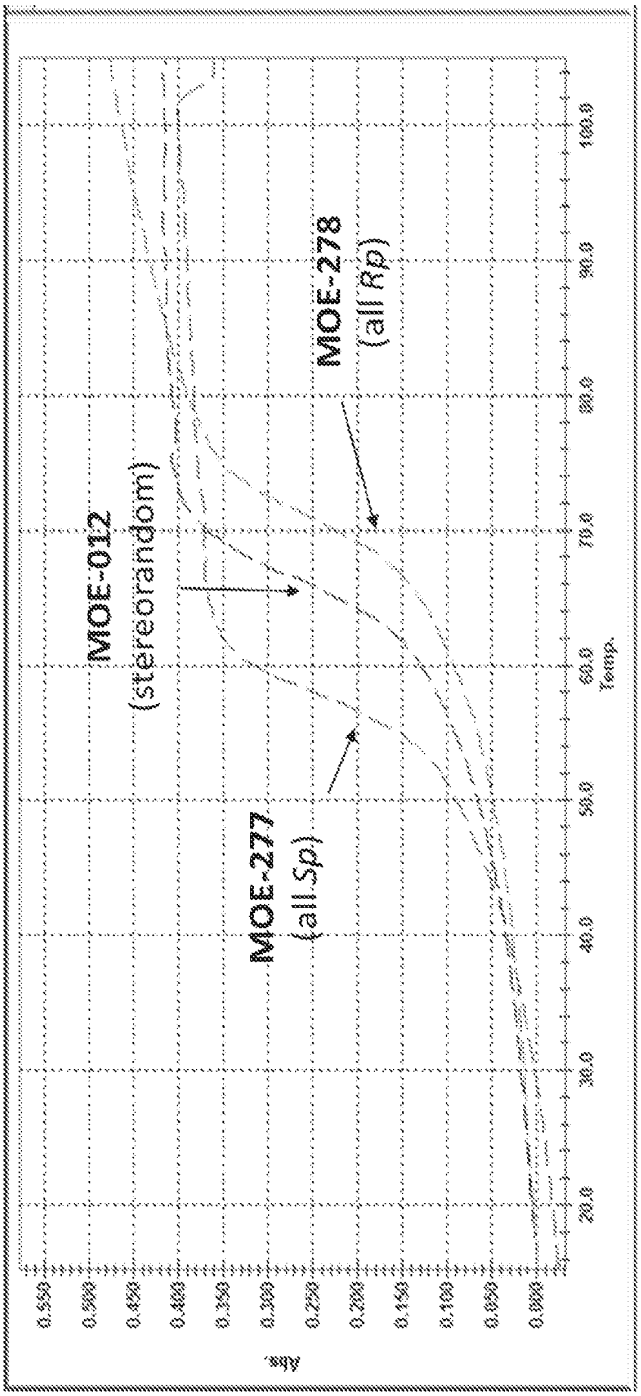

FIG. 20

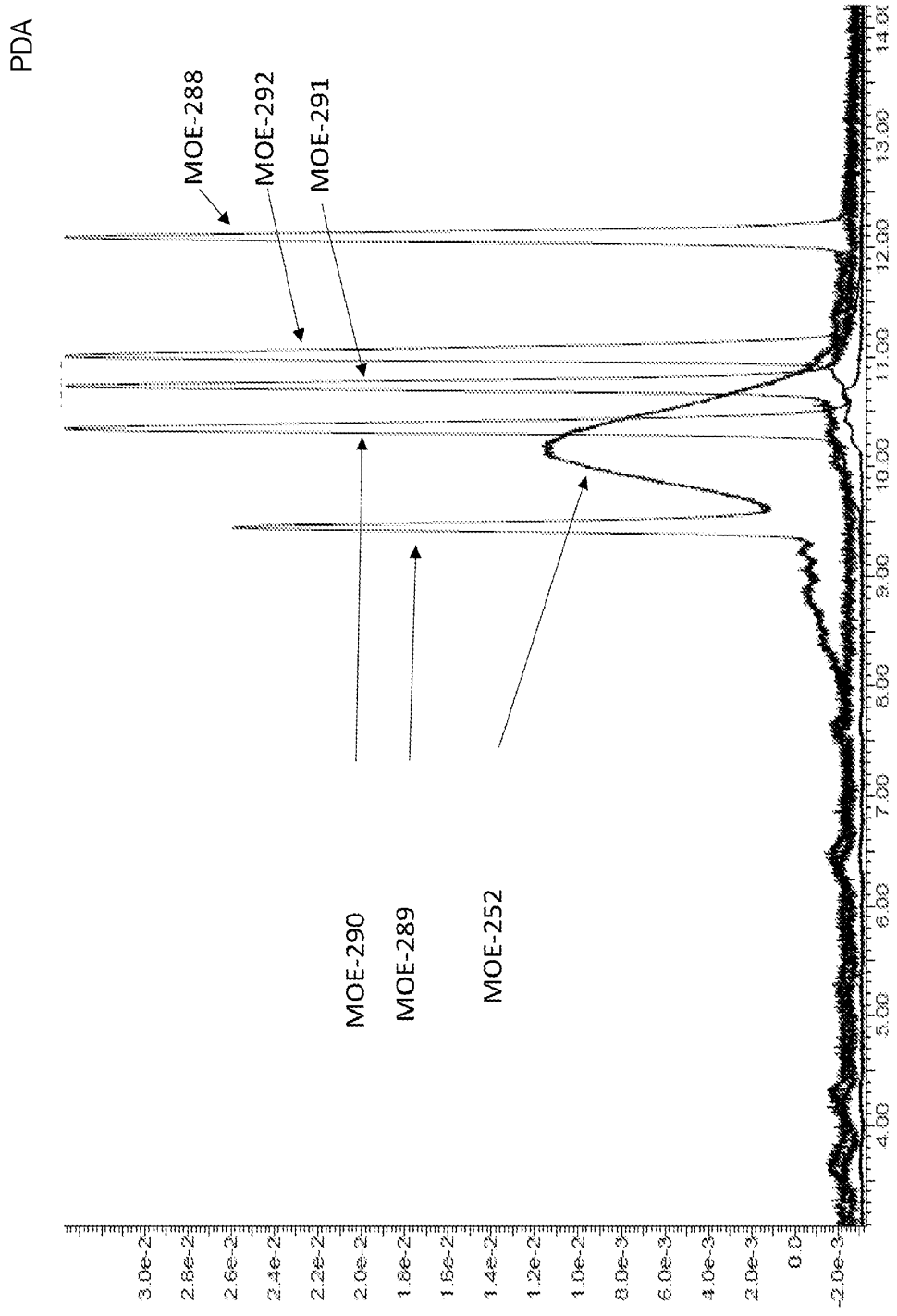
PDA
MOE-288
MOE-292
MOE-291
MOE-290
MOE-289
MOE-252
3.0e-2
2.8e-2
2.6e-2
2.4e-2
2.2e-2
2.0e-2
1.8e-2
1.6e-2
1.4e-2
1.2e-2
1.0e-2
8.0e-3
6.0e-3
4.0e-3
2.0e-3
0.0
-2.0e-3
4.00
5.00
6.00
7.00
8.00
9.00
10.00
11.00
12.00
13.00
14.00

FIG. 21

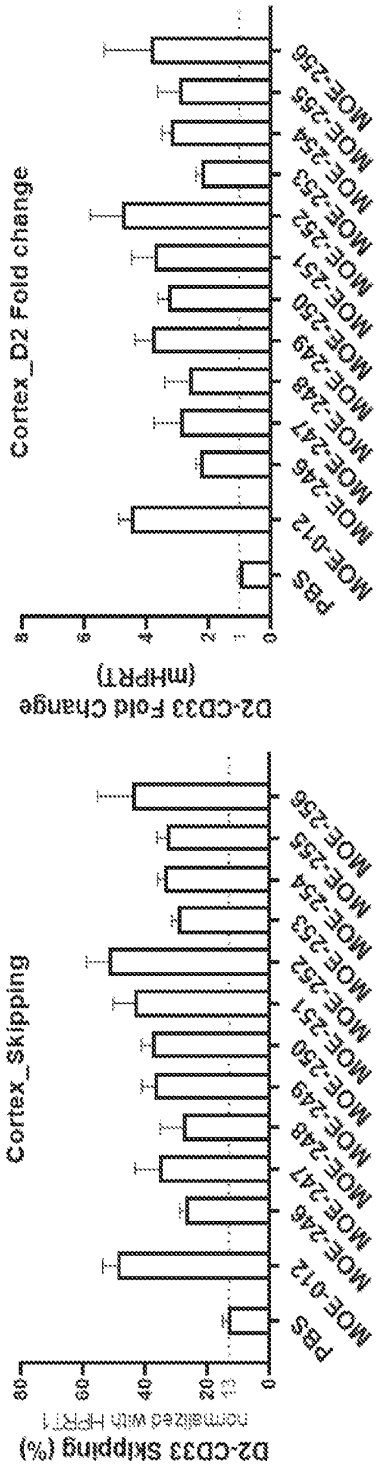
Cortex_D2 Fold change
D2-CD33 Fold Change (mHPRT)
0
2
4
6
8
PBS
MOE-012
MOE-246
MOE-247
MOE-248
MOE-249
MOE-250
MOE-251
MOE-252
MOE-253
MOE-254
MOE-255
MOE-256
Cortex_Skipping
D2-CD33 Skipping (%) normalized with HPRT1
0
20
40
60
80
PBS
MOE-012
MOE-246
MOE-247
MOE-248
MOE-249
MOE-250
MOE-251
MOE-252
MOE-253
MOE-254
MOE-255
MOE-256

FIG. 22

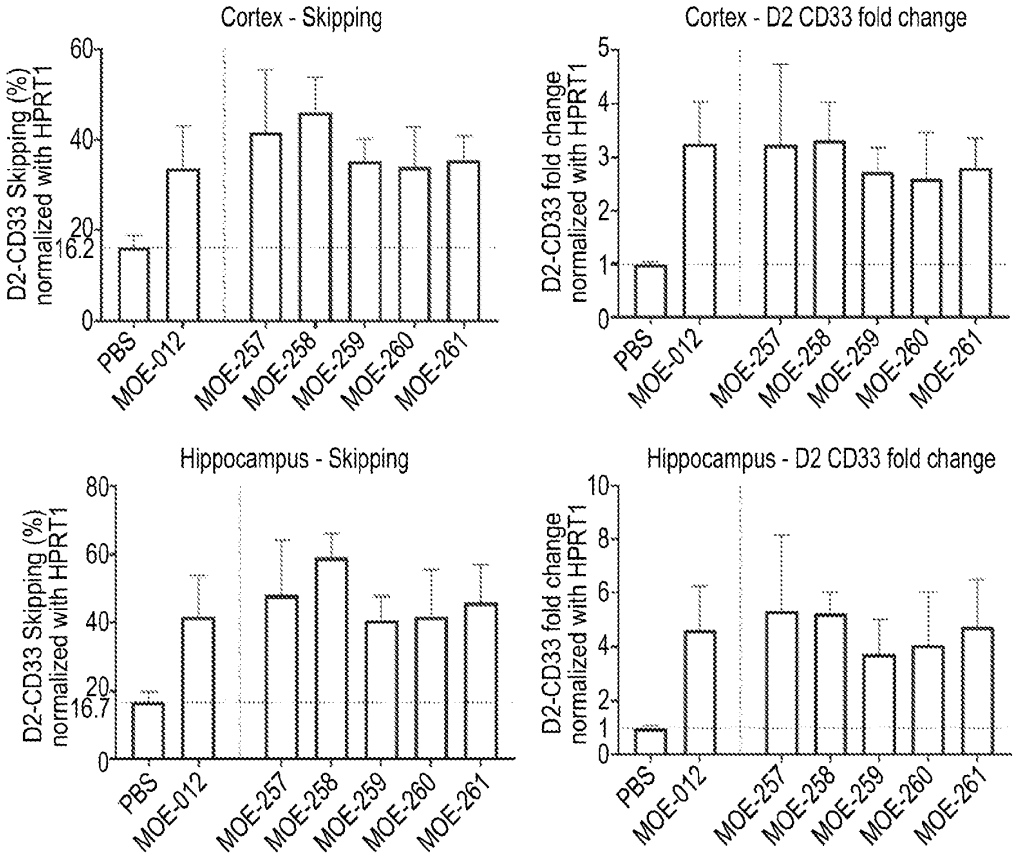
Cortex - Skipping
D2-CD33 Skipping (%) normalized with HPRT1
60
40
20
16.2
0
PBS
MOE-012
MOE-257
MOE-258
MOE-259
MOE-260
MOE-261
Cortex - D2 CD33 fold change
D2-CD33 fold change normalized with HPRT1
5
4
3
2
1
0
PBS
MOE-012
MOE-257
MOE-258
MOE-259
MOE-260
MOE-261
Hippocampus - Skipping
D2-CD33 Skipping (%) normalized with HPRT1
80
60
40
20
16.7
0
PBS
MOE-012
MOE-257
MOE-258
MOE-259
MOE-260
MOE-261
Hippocampus - D2 CD33 fold change
D2-CD33 fold change normalized with HPRT1
10
8
6
4
2
1
0
PBS
MOE-012
MOE-257
MOE-258
MOE-259
MOE-260
MOE-261

FIG. 23

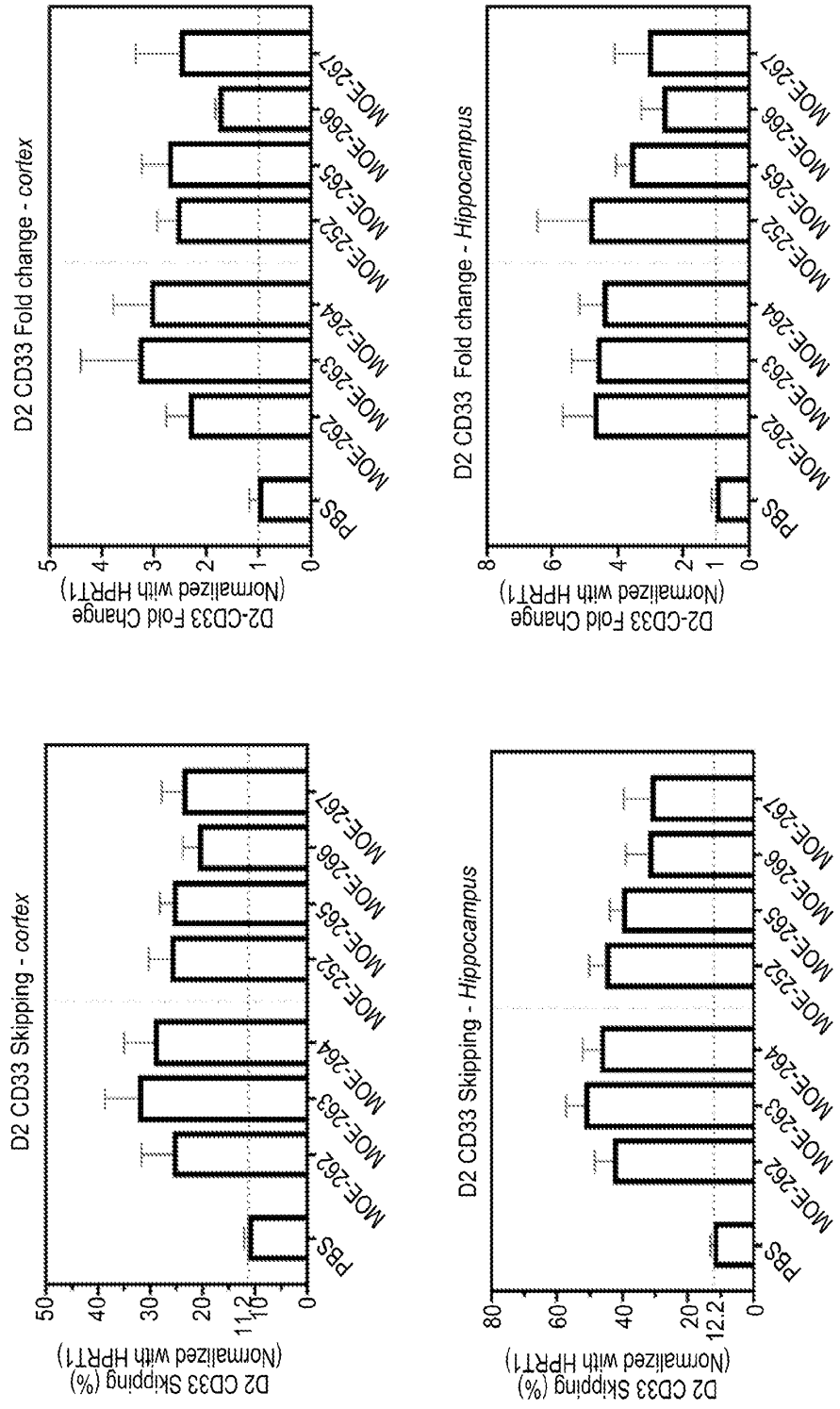
D2 CD33 Fold change - cortex
D2-CD33 Fold Change (Normalized with HPRT1)
PBS
MOE-262
MOE-263
MOE-264
MOE-252
MOE-265
MOE-266
MOE-267
D2 CD33 Fold change - Hippocampus
D2-CD33 Fold Change (Normalized with HPRT1)
D2 CD33 Skipping - cortex
D2 CD33 Skipping (%) (Normalized with HPRT1)
11.2
D2 CD33 Skipping - Hippocampus
D2 CD33 Skipping (%) (Normalized with HPRT1)
12.2

FIG. 24

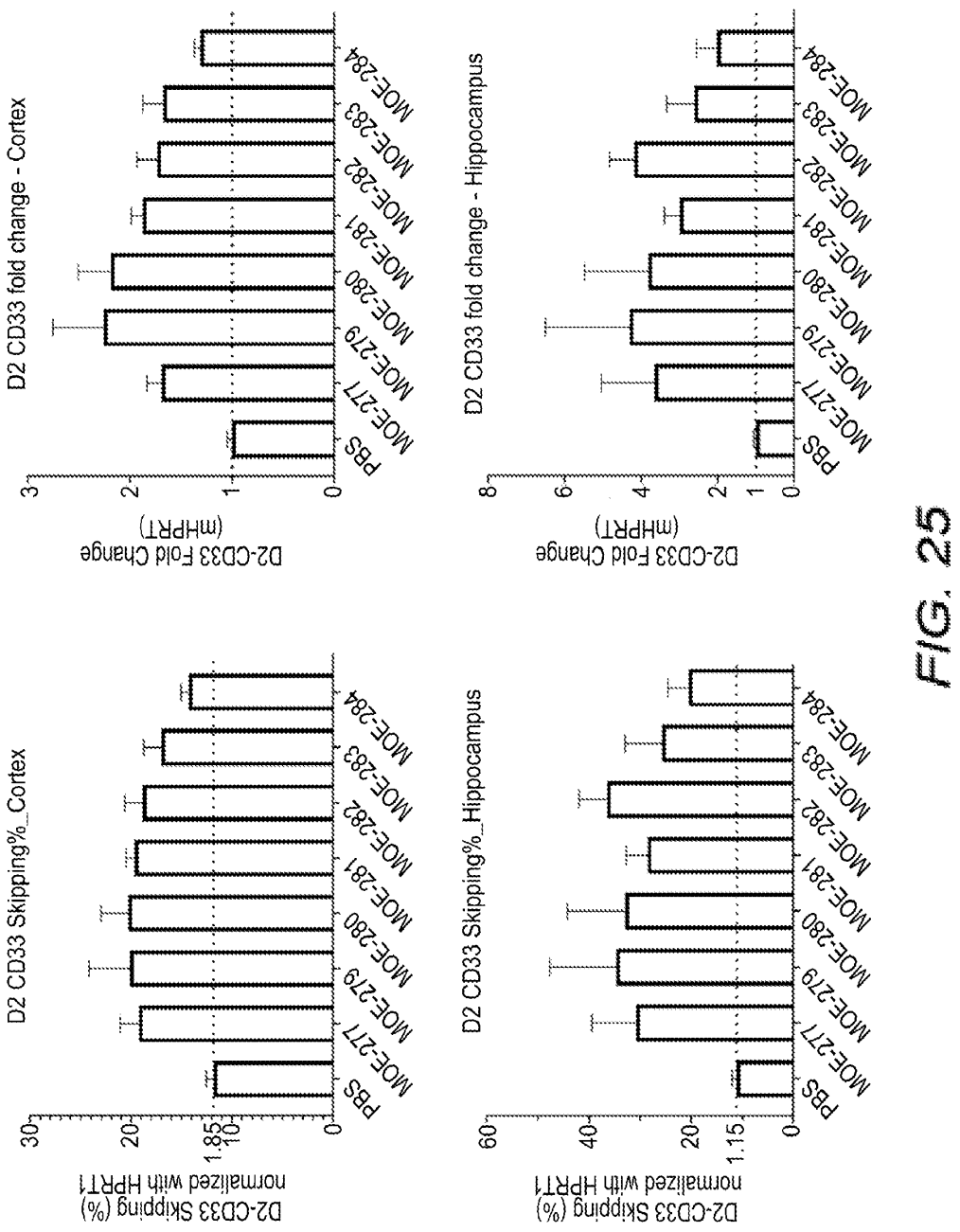
D2 CD33 fold change - Cortex
D2-CD33 Fold Change (mHPRT)
D2 CD33 fold change - Hippocampus
D2-CD33 Fold Change (mHPRT)
D2 CD33 Skipping%_Cortex
D2-CD33 Skipping (%) normalized with HPRT1
D2 CD33 Skipping%_Hippocampus
D2-CD33 Skipping (%) normalized with HPRT1
PBS
MOE-277
MOE-279
MOE-280
MOE-281
MOE-282
MOE-283
MOE-284

FIG. 25

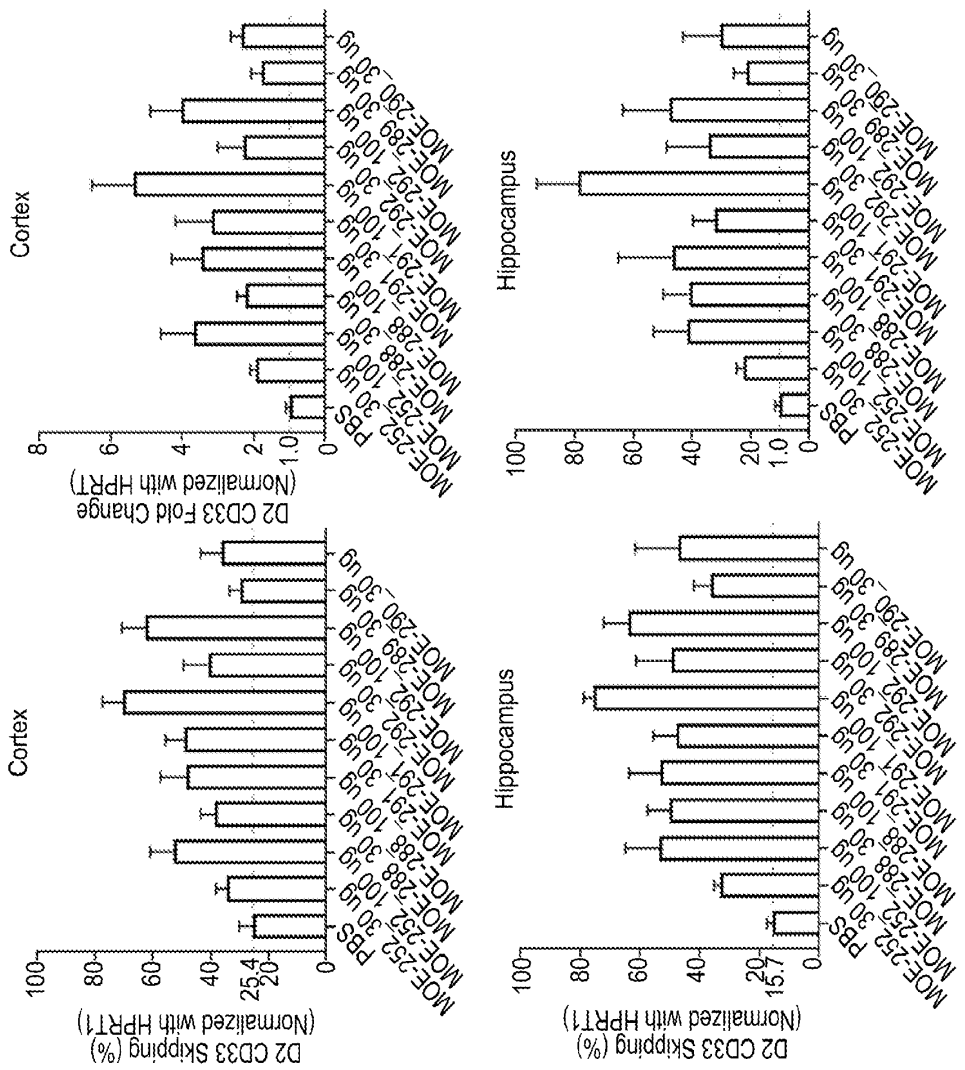
Cortex
D2 CD33 Fold Change (Normalized with HPRT)
Cortex
D2 CD33 Skipping (%) (Normalized with HPRT1)
Hippocampus
Hippocampus
PBS
MOE-252 30 ug
MOE-252 100 ug
MOE-288 30 ug
MOE-288 100 ug
MOE-291 30 ug
MOE-291 100 ug
MOE-292 30 ug
MOE-292 100 ug
MOE-289 30 ug
MOE-290 30 ug

FIG. 26

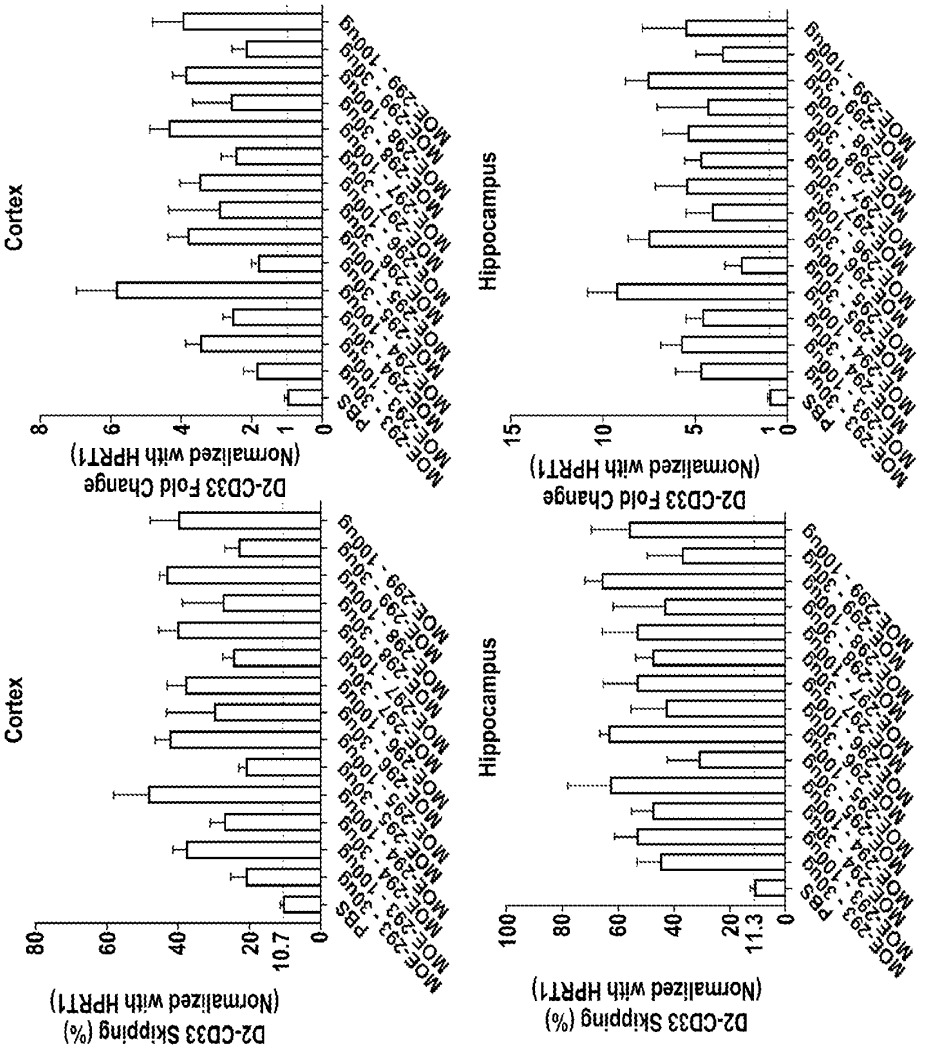
Cortex
D2-CD33 Fold Change
(Normalized with HPRT1)
Cortex
D2-CD33 Skipping (%)
(Normalized with HPRT1)
Hippocampus
D2-CD33 Fold Change
(Normalized with HPRT1)
Hippocampus
D2-CD33 Skipping (%)
(Normalized with HPRT1)
PBS
MOE-293 - 30uM
MOE-293 - 100uM
MOE-294 - 30uM
MOE-294 - 100uM
MOE-295 - 30uM
MOE-295 - 100uM
MOE-296 - 30uM
MOE-296 - 100uM
MOE-297 - 30uM
MOE-297 - 100uM
MOE-298 - 30uM
MOE-298 - 100uM
MOE-299 - 30uM
MOE-299 - 100uM

FIG. 27

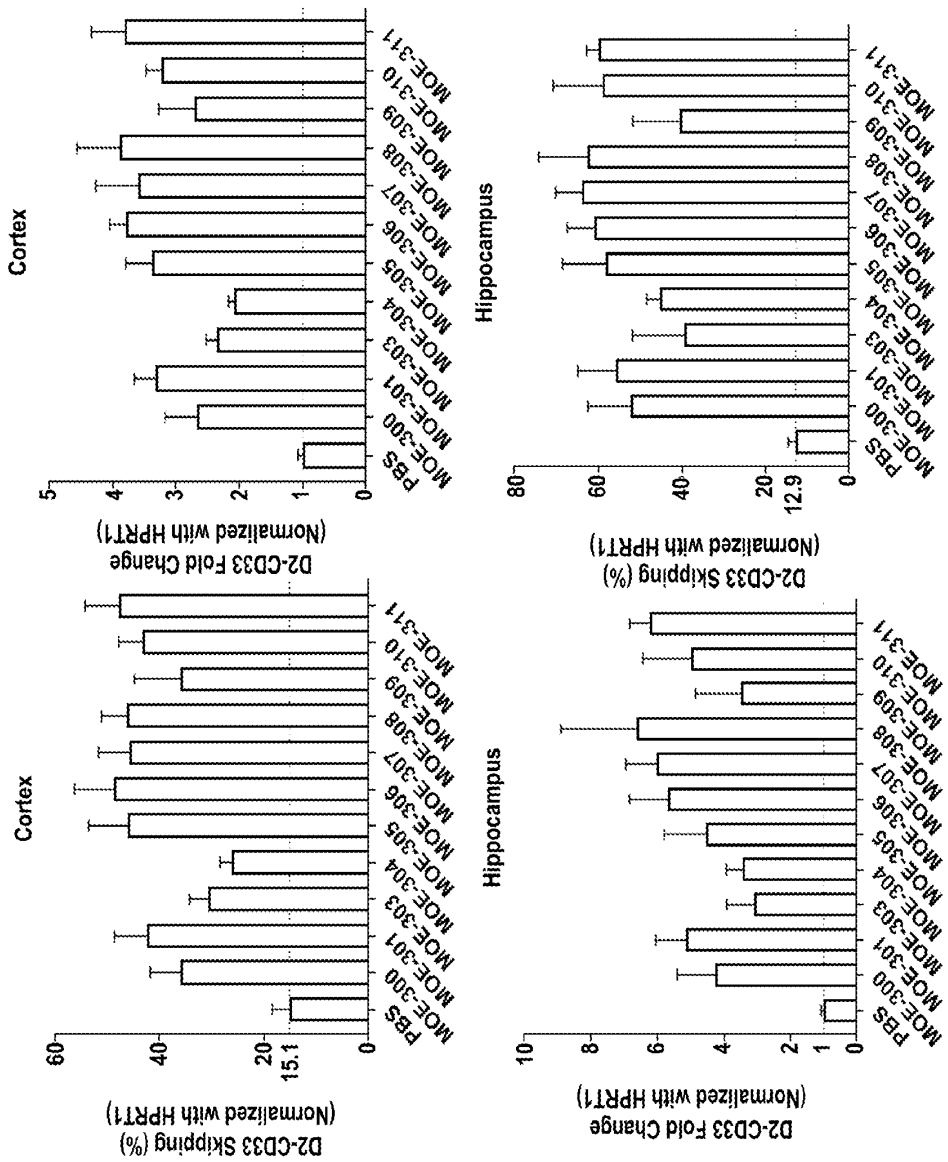
Cortex
D2-CD33 Fold Change
(Normalized with HPRT1)
PBS
MOE-300
MOE-301
MOE-303
MOE-304
MOE-305
MOE-306
MOE-307
MOE-308
MOE-309
MOE-310
MOE-311
Hippocampus
D2-CD33 Skipping (%)
(Normalized with HPRT1)
12.9
Cortex
D2-CD33 Skipping (%)
(Normalized with HPRT1)
15.1
Hippocampus
D2-CD33 Fold Change
(Normalized with HPRT1)

FIG. 28

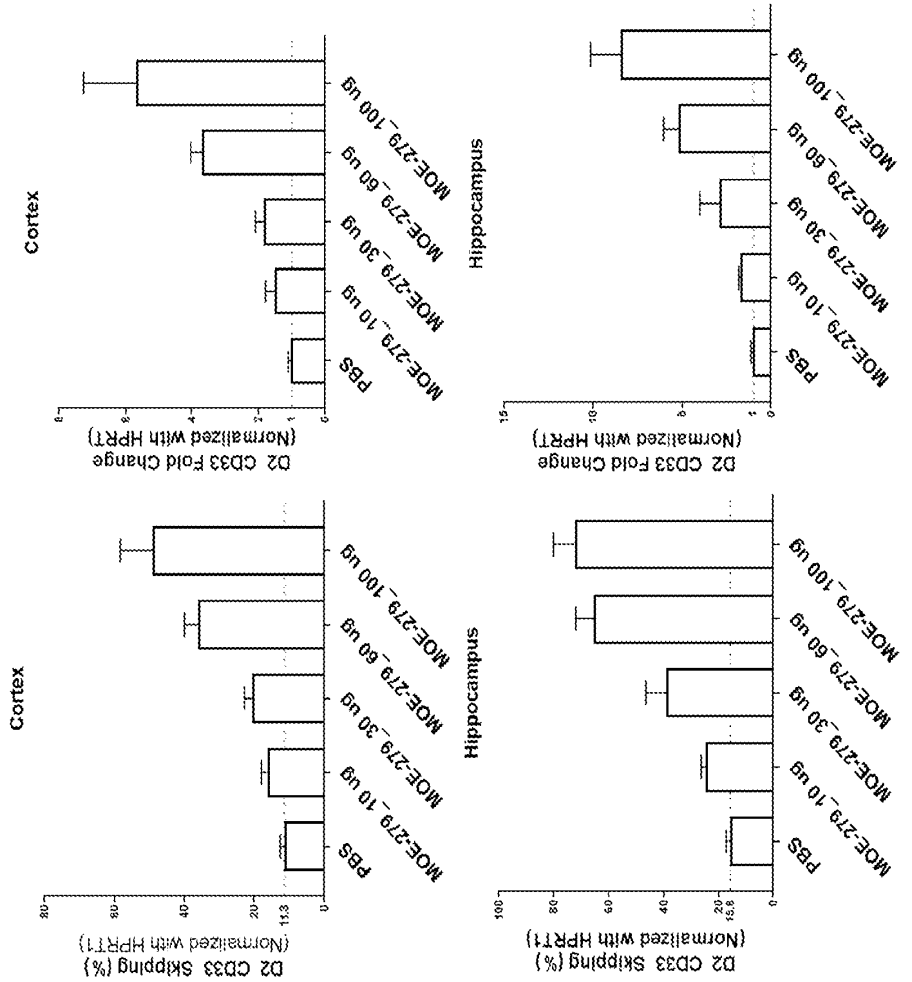
Cortex
Hippocampus
D2 CD33 Fold Change (Normalized with HPRT)
D2 CD33 Skipping (%) (Normalized with HPRT1)
PBS
MOE-279_10 ug
MOE-279_30 ug
MOE-279_60 ug
MOE-279_100 ug

FIG. 29

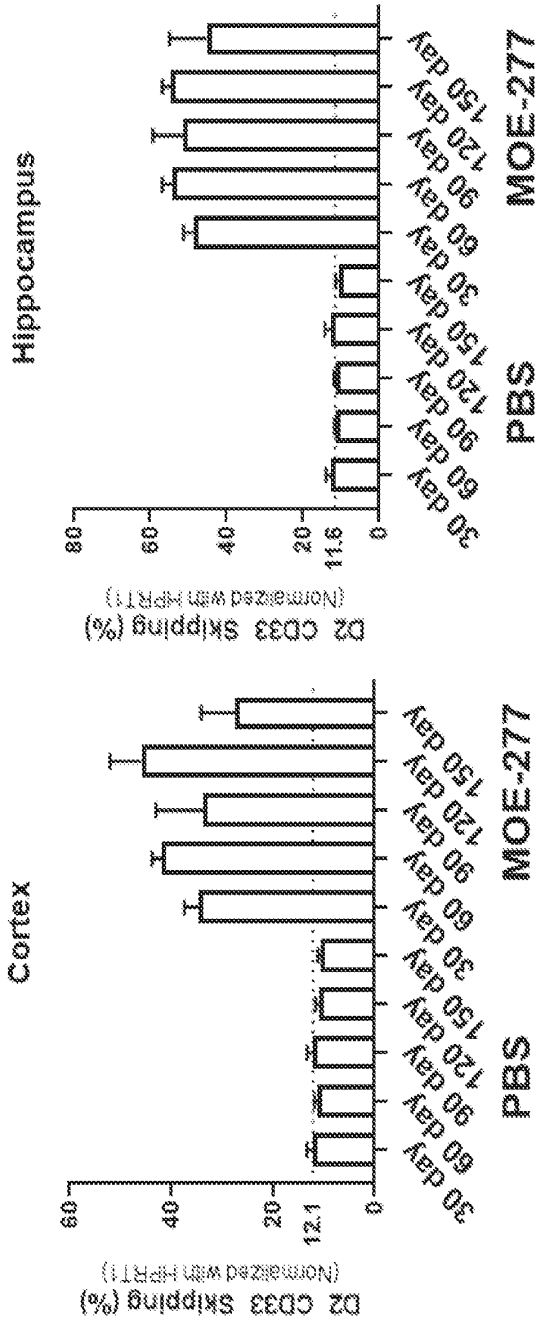
Hippocampus
D2 CD33 Skipping (%)
(Normalized with HPRT1)
80
60
40
20
11.6
0
30 day
60 day
90 day
120 day
150 day
30 day
60 day
90 day
120 day
150 day
PBS
MOE-277
Cortex
D2 CD33 Skipping (%)
(Normalized with HPRT1)
60
40
20
12.1
0
30 day
60 day
90 day
120 day
150 day
30 day
60 day
90 day
120 day
150 day
PBS
MOE-277

FIG. 30

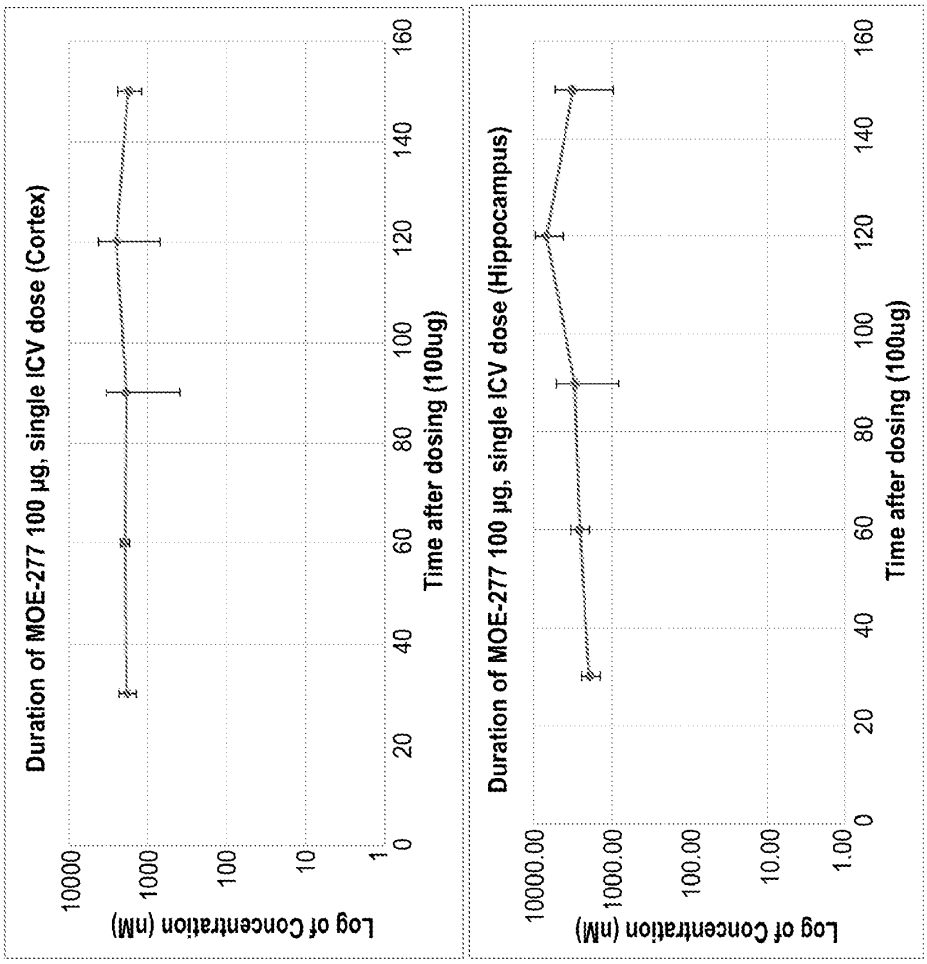
Duration of MOE-277 100 µg, single ICV dose (Cortex)
Log of Concentration (nM)
10000
1000
100
10
1
0
20
40
60
80
100
120
140
160
Time after dosing (100ug)
Duration of MOE-277 100 µg, single ICV dose (Hippocampus)
Log of Concentration (nM)
10000.00
1000.00
100.00
10.00
1.00
0
20
40
60
80
100
120
140
160
Time after dosing (100ug)

FIG. 31