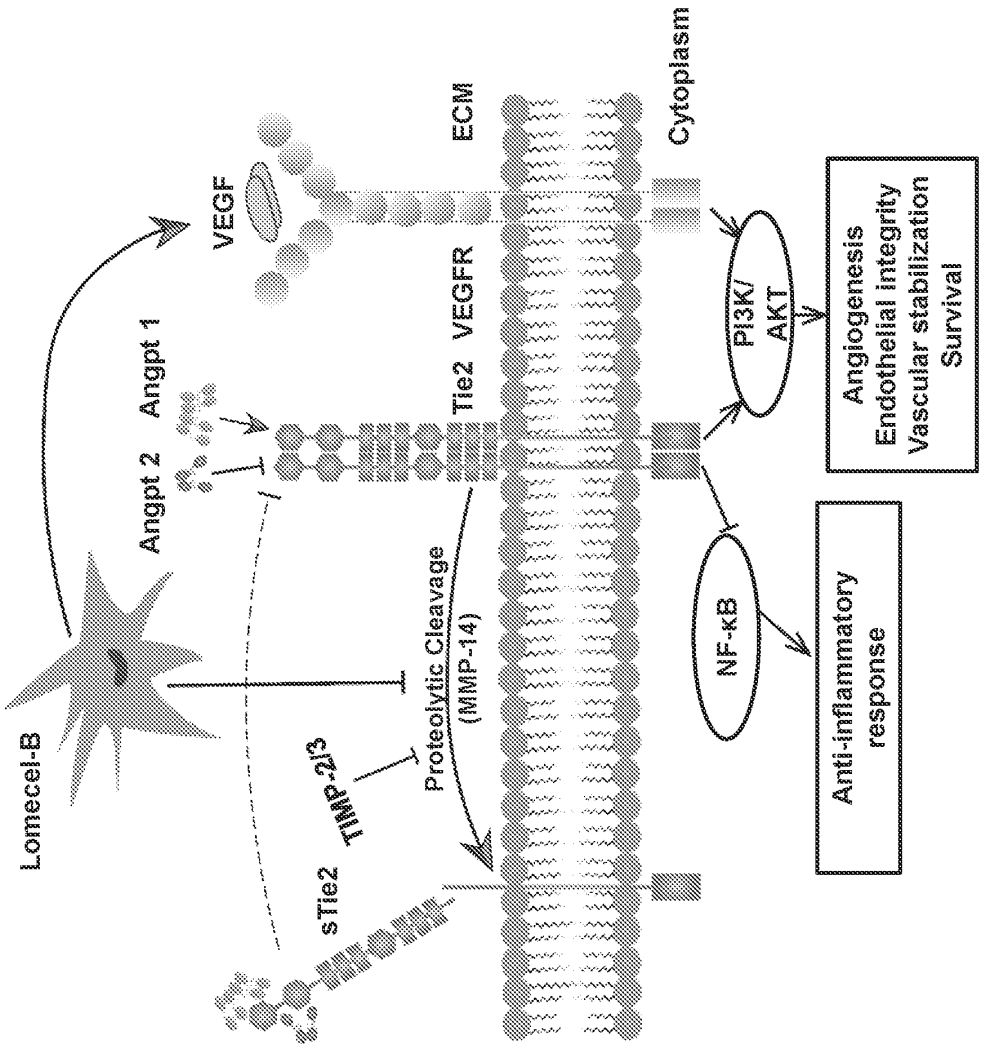

Lomecel-B
Angpt 2
Angpt 1
VEGF
ECM
Cytoplasm
Tie2
VEGFR
Proteolytic Cleavage
(MMP-14)
TIMP-2/3
sTie2
PI3K/
AKT
NF-κB
Angiogenesis
Endothelial integrity
Vascular stabilization
Survival
Anti-inflammatory
response

FIG. 1

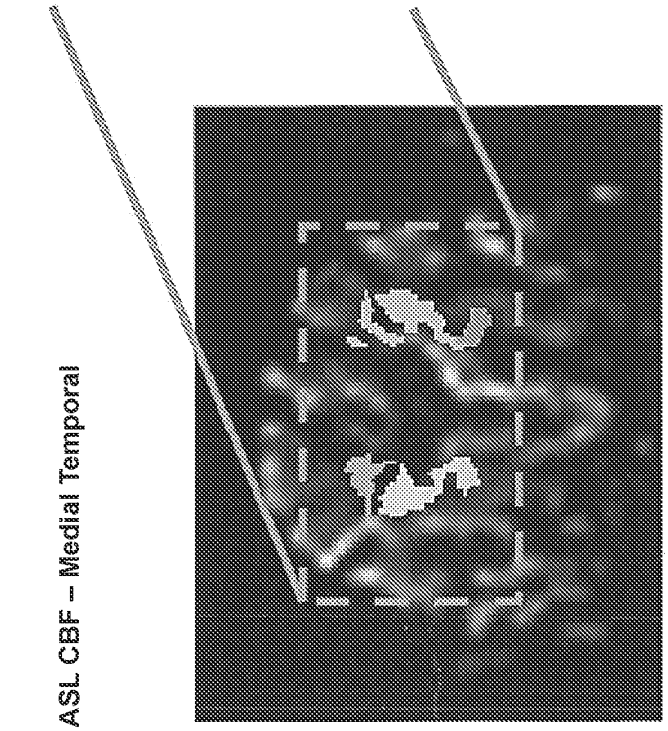



FIG. 2B

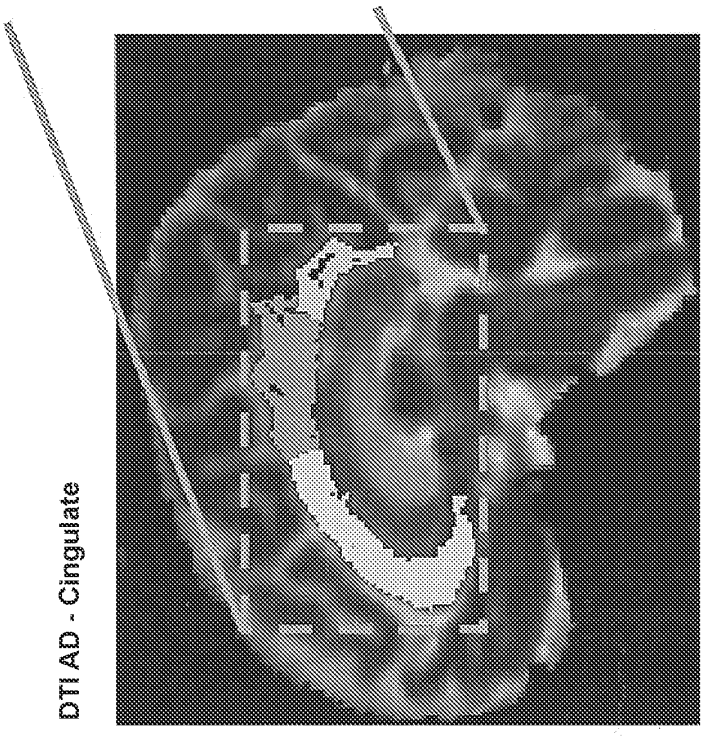



FIG. 2A

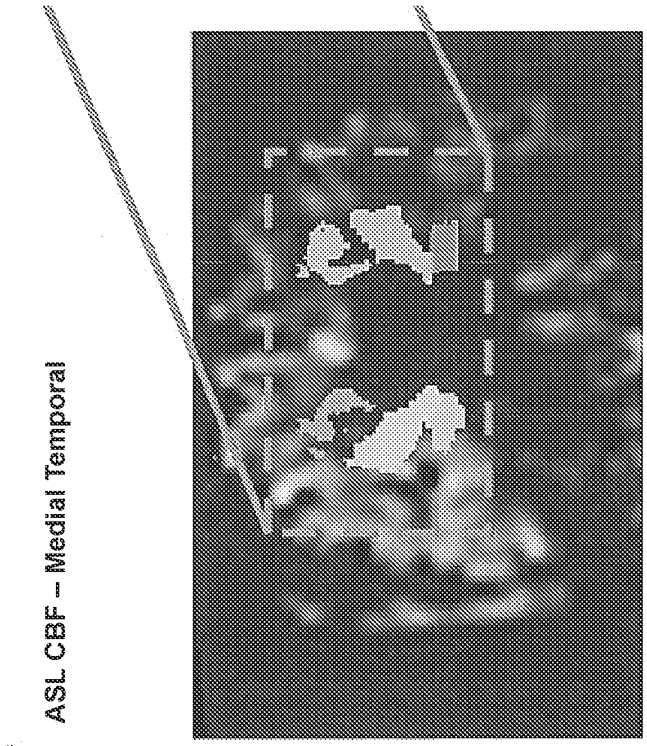



FIG. 2D

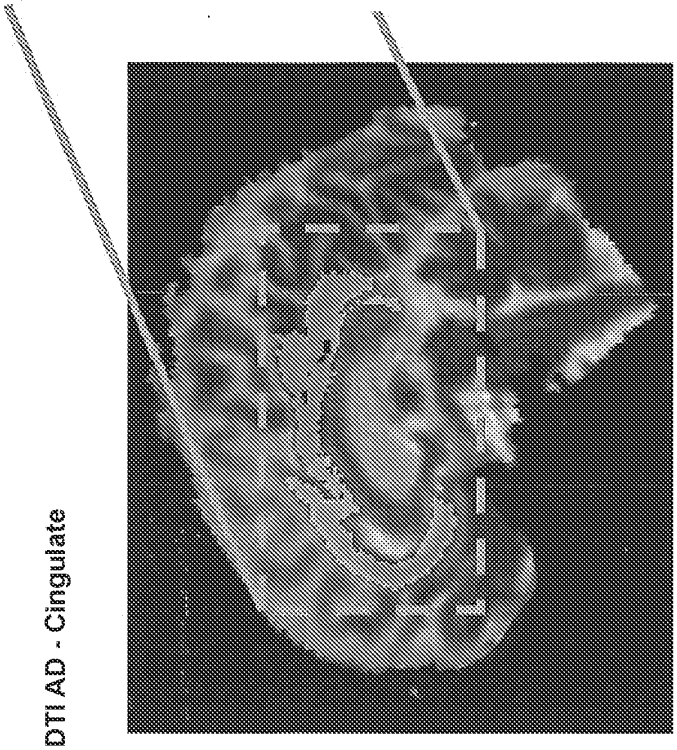
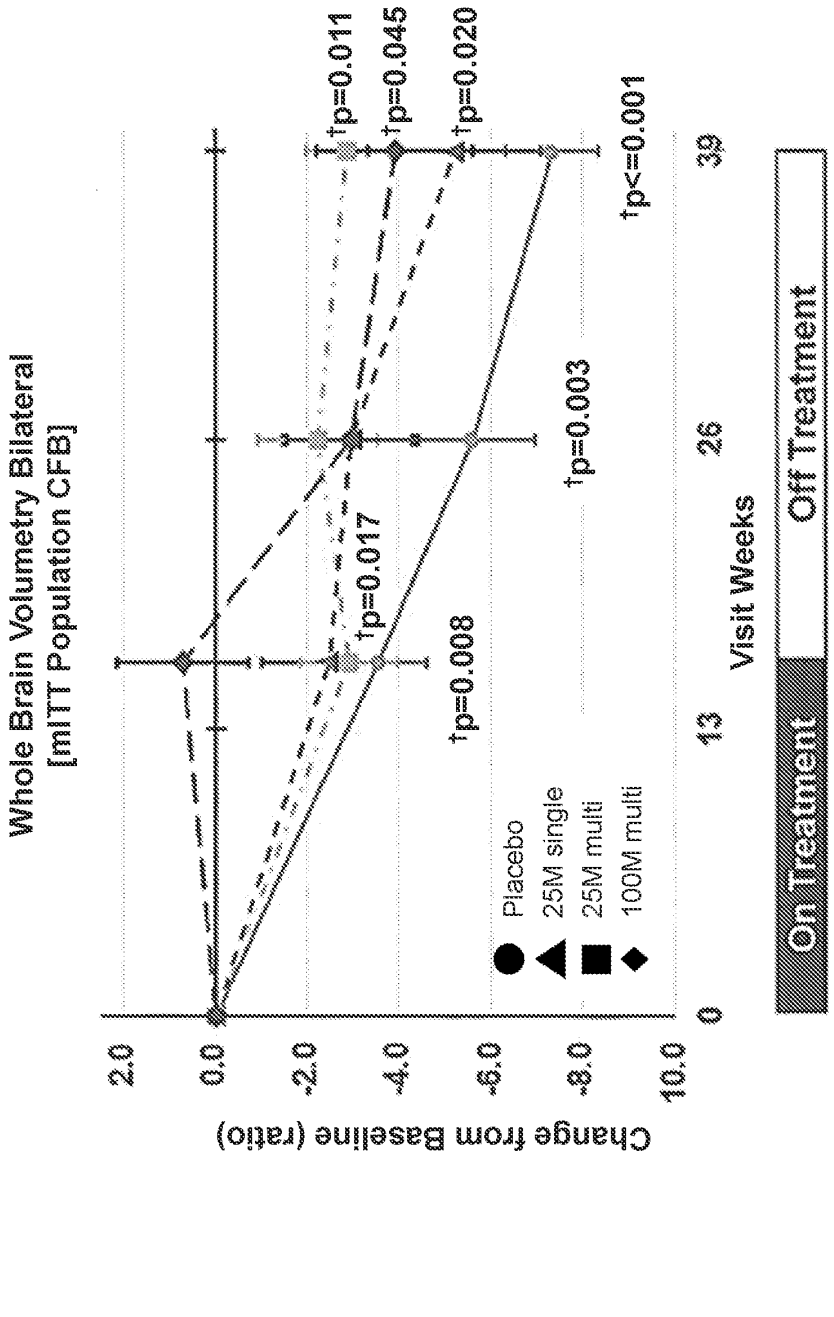
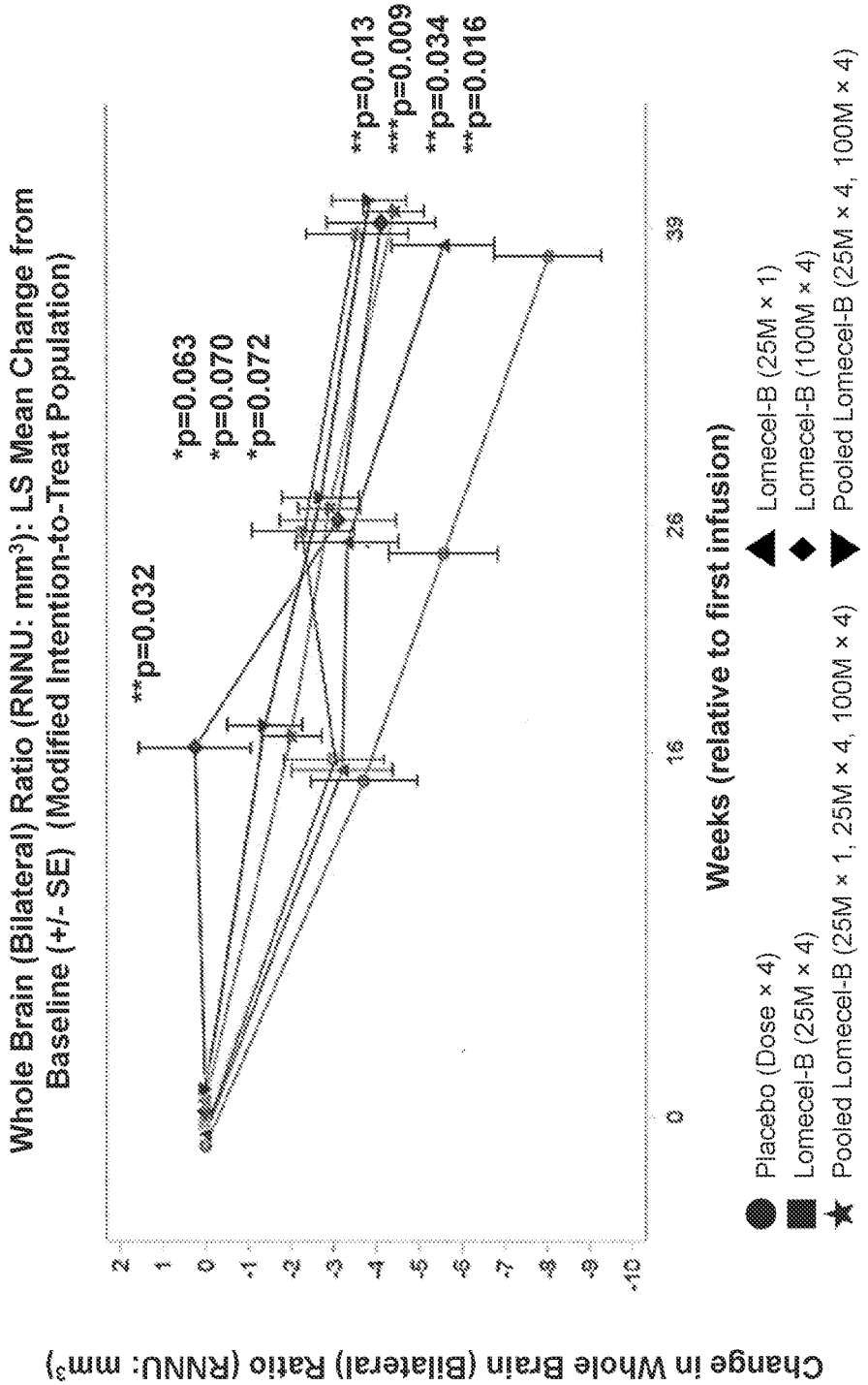



FIG. 2C



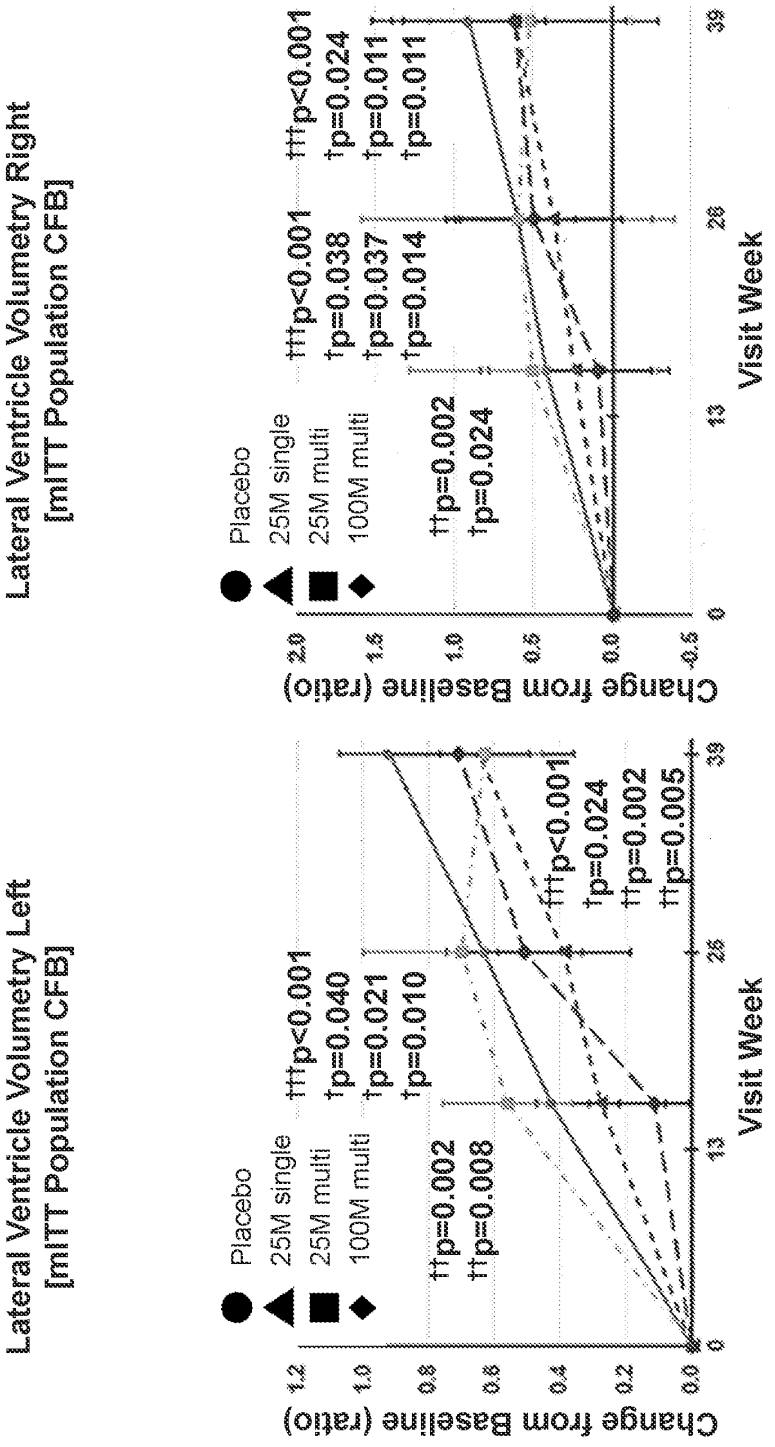

†p<0.5, ††p<0.01, †††p<0.001: significant intragroup change from baseline.

FIG. 3A




Statistical significance is indicated as follows: *p<0.1, **p<0.05, ***p<0.01, and ****p<0.001.

FIG. 3B




*p<0.5, **p<0.01, ***p<0.001: significant intergroup change versus placebo from baseline
†p<0.5, ††p<0.01, †††p<0.001: significant intragroup change from baseline

FIG. 4A

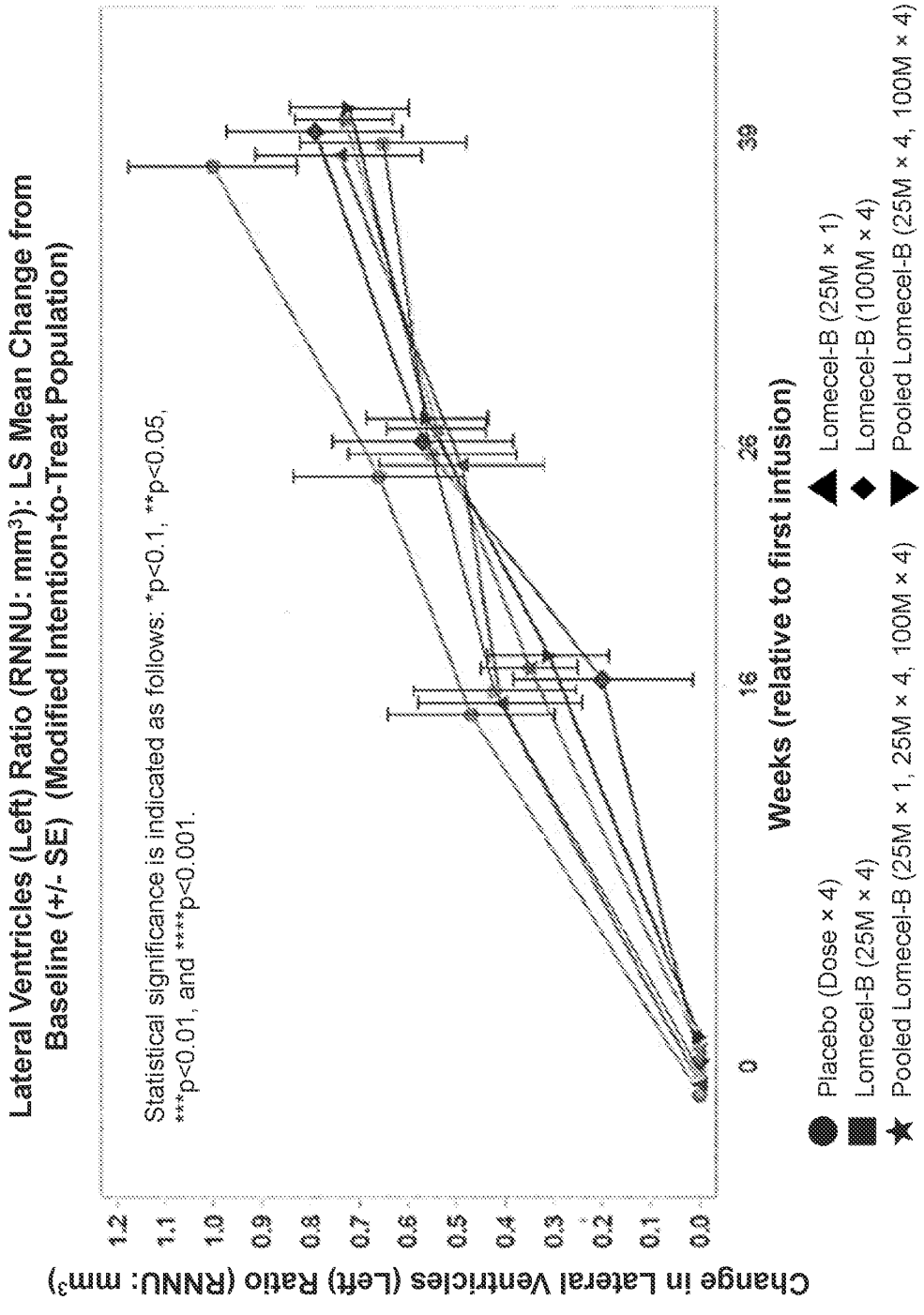

Lateral Ventricles (Left) Ratio (RNNU: mm³): LS Mean Change from Baseline (+/- SE) (Modified Intention-to-Treat Population)
Statistical significance is indicated as follows: *p<0.1, **p<0.05, ***p<0.01, and ****p<0.001.
Change in Lateral Ventricles (Left) Ratio (RNNU: mm³)
1.2
1.1
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0
16
26
39
Weeks (relative to first infusion)
Placebo (Dose × 4)
Lomecel-B (25M × 4)
Pooled Lomecel-B (25M × 1, 25M × 4, 100M × 4)
Lomecel-B (25M × 1)
Lomecel-B (100M × 4)
Pooled Lomecel-B (25M × 4, 100M × 4)

FIG. 4B

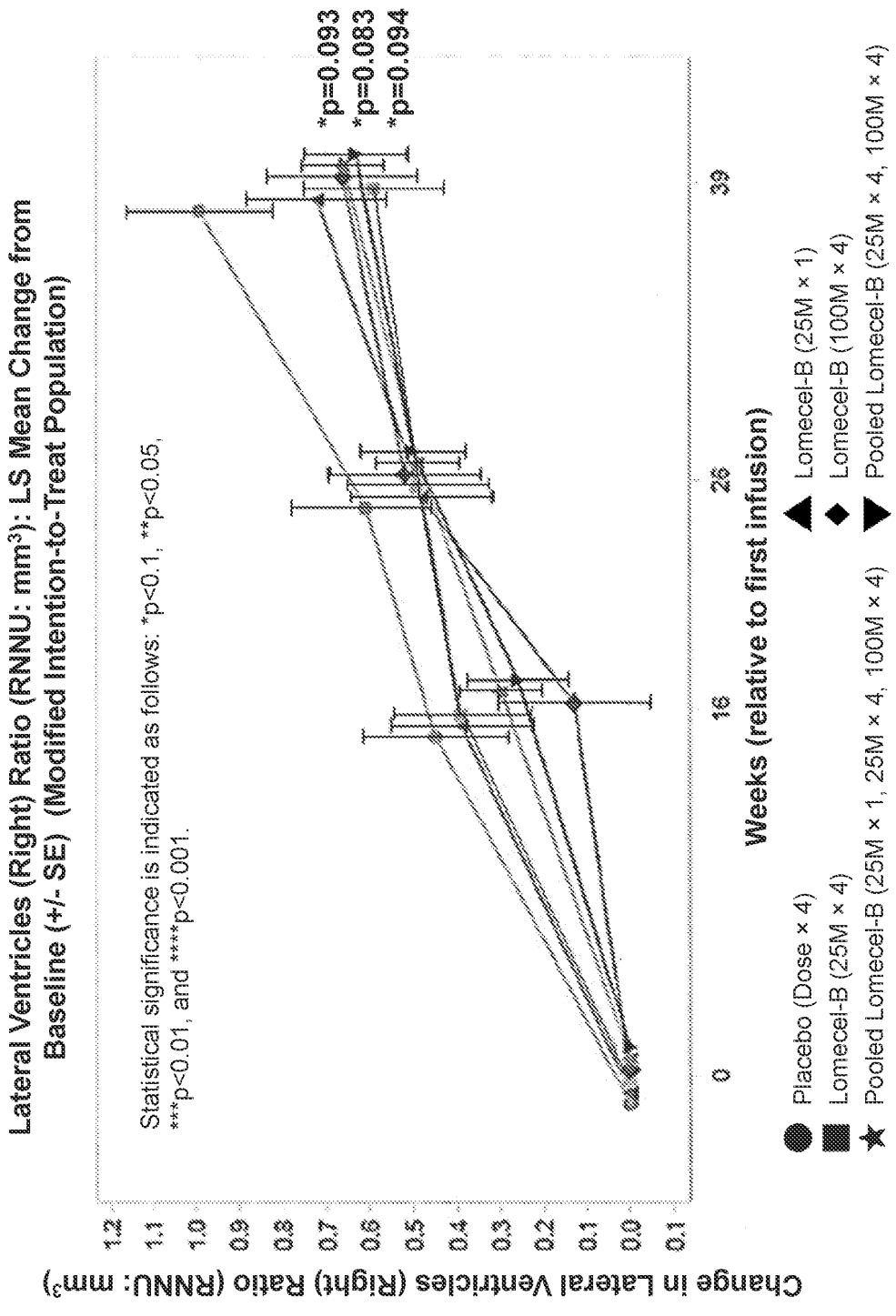

Lateral Ventricles (Right) Ratio (RNNU: mm³): LS Mean Change from Baseline (+/- SE) (Modified Intention-to-Treat Population)
Statistical significance is indicated as follows: *p<0.1, **p<0.05, ***p<0.01, and ****p<0.001.
*p=0.093
*p=0.083
*p=0.094
Change in Lateral Ventricles (Right) Ratio (RNNU: mm³)
1.2
1.1
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
-0.1
0
16
26
39
Weeks (relative to first infusion)
Placebo (Dose × 4)
Lomecel-B (25M × 4)
Pooled Lomecel-B (25M × 1, 25M × 4, 100M × 4)
Lomecel-B (25M × 1)
Lomecel-B (100M × 4)
Pooled Lomecel-B (25M × 4, 100M × 4)

FIG. 4C

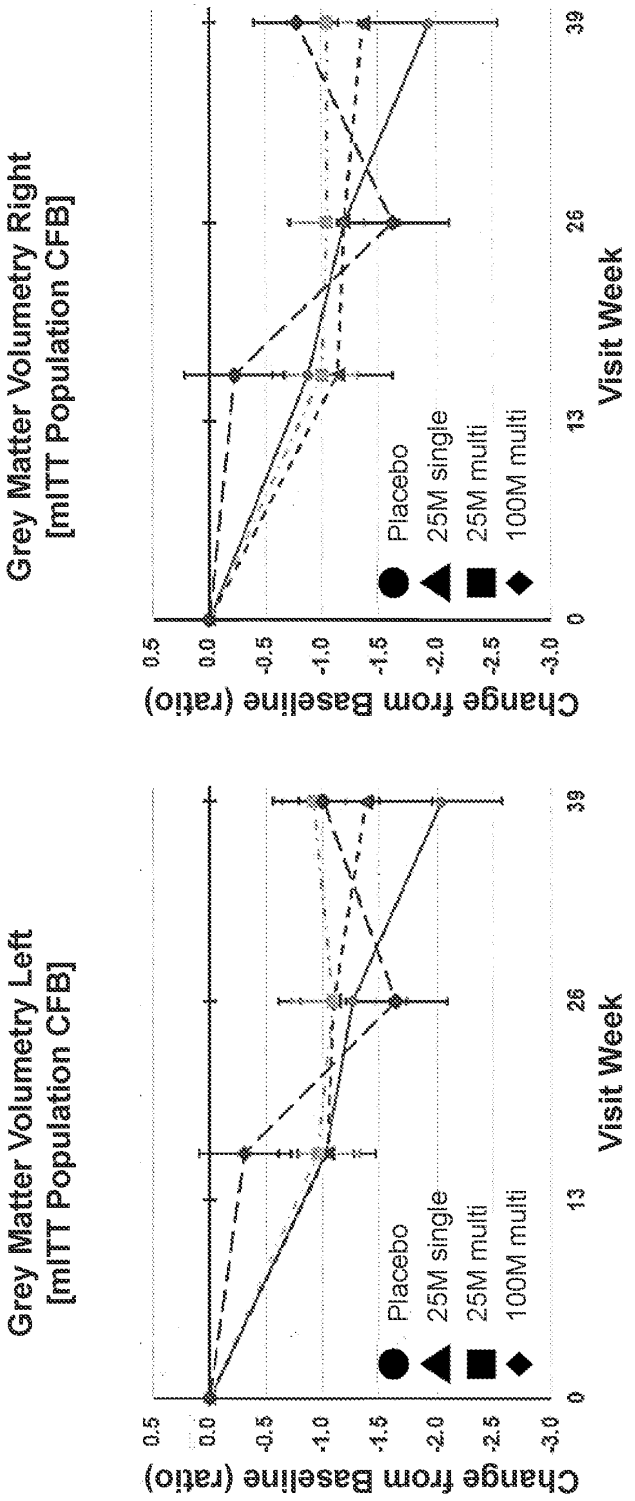

Grey Matter Volumetry Left
[mITT Population CFB]
Change from Baseline (ratio)
0.5
0.0
-0.5
-1.0
-1.5
-2.0
-2.5
-3.0
0
13
26
39
Visit Week
Placebo
25M single
25M multi
100M multi
Grey Matter Volumetry Right
[mITT Population CFB]
Change from Baseline (ratio)
0.5
0.0
-0.5
-1.0
-1.5
-2.0
-2.5
-3.0
0
13
26
39
Visit Week
Placebo
25M single
25M multi
100M multi

FIG. 5A

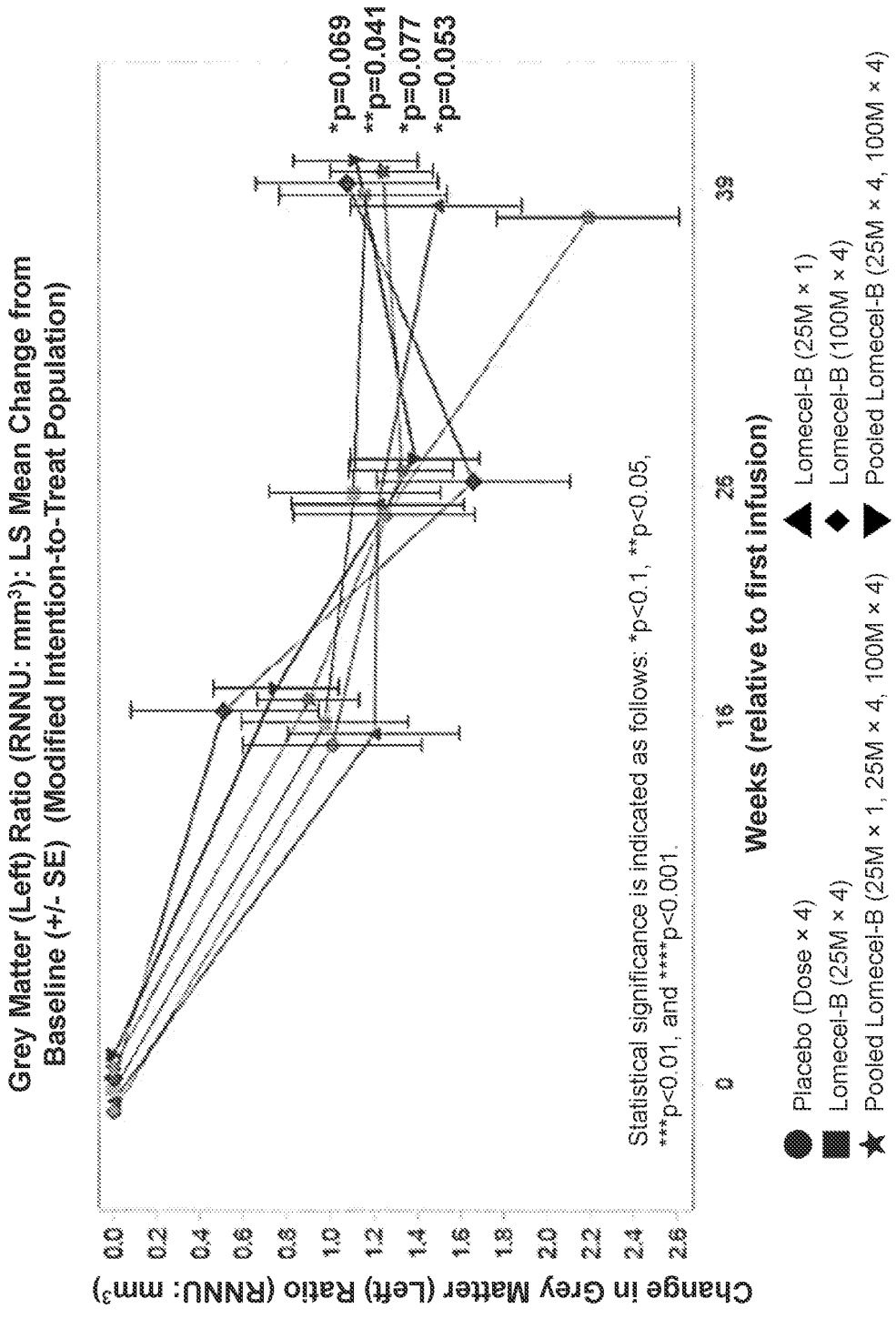

Grey Matter (Left) Ratio (RNNU: mm³): LS Mean Change from Baseline (+/- SE) (Modified Intention-to-Treat Population)
*p=0.069
**p=0.041
*p=0.077
*p=0.053
Statistical significance is indicated as follows: *p<0.1, **p<0.05, ***p<0.01, and ****p<0.001.
Change in Grey Matter (Left) Ratio (RNNU: mm³)
0.0
0.2
0.4
0.6
0.8
1.0
1.2
1.4
1.6
1.8
2.0
2.2
2.4
2.6
0
16
26
39
Weeks (relative to first infusion)
Placebo (Dose × 4)
Lomecel-B (25M × 4)
Pooled Lomecel-B (25M × 1, 25M × 4, 100M × 4)
Lomecel-B (25M × 1)
Lomecel-B (100M × 4)
Pooled Lomecel-B (25M × 4, 100M × 4)

FIG. 5B

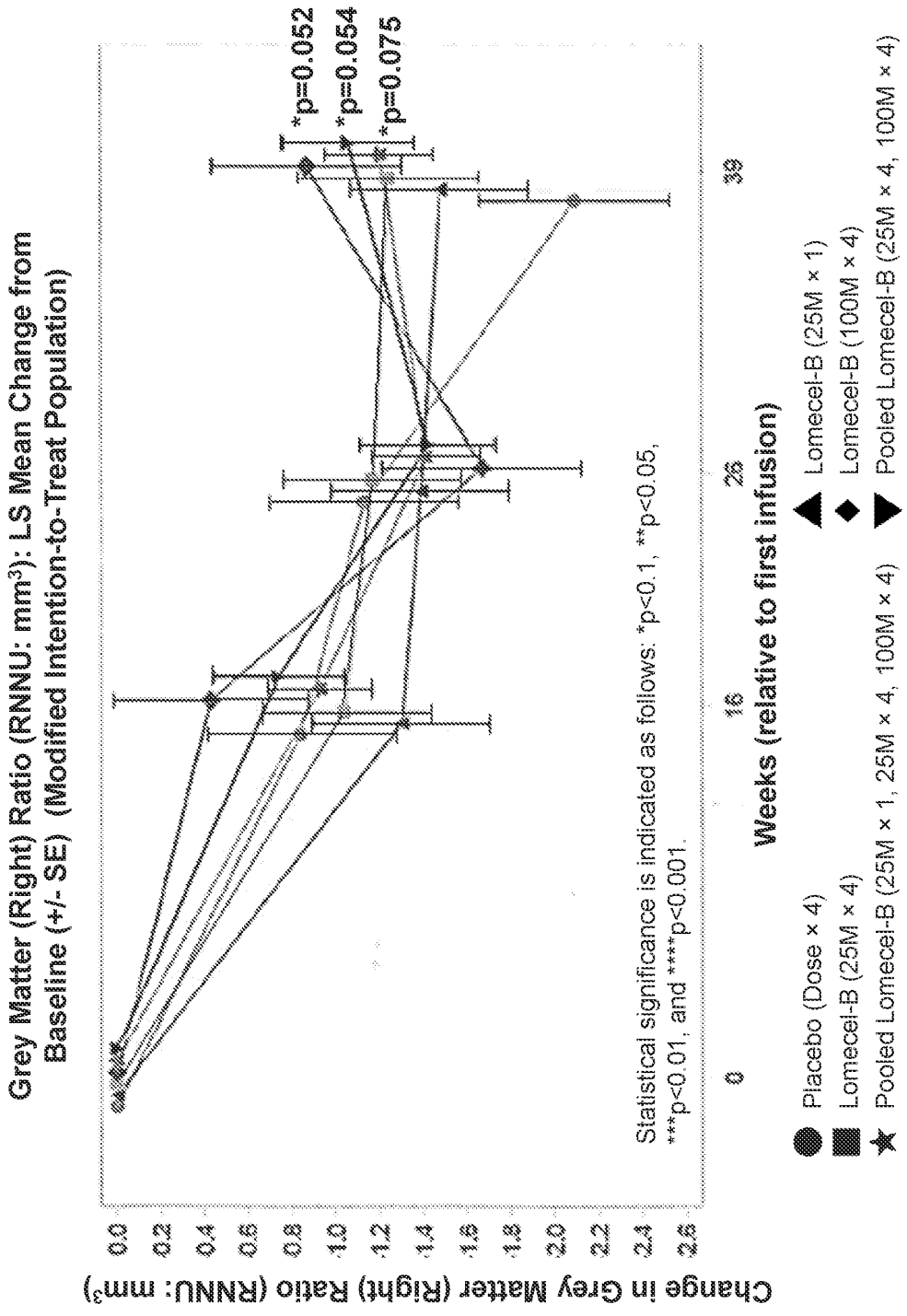
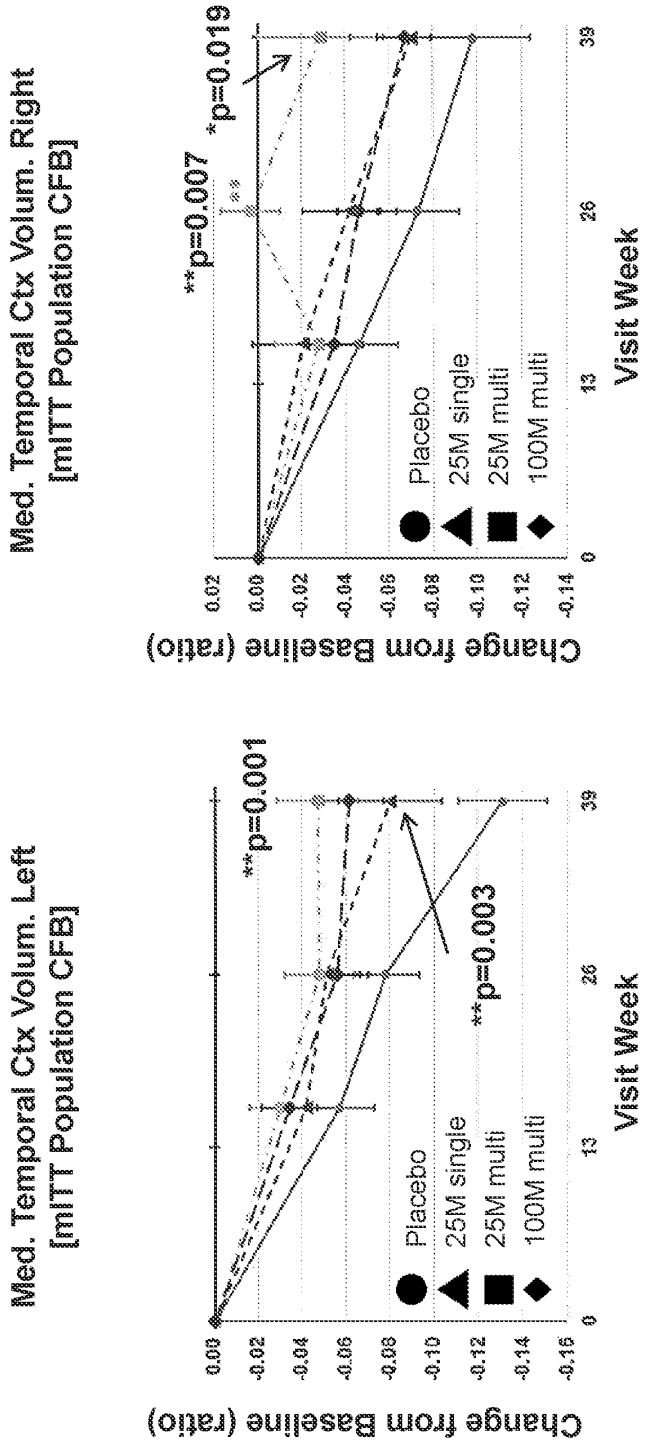

Grey Matter (Right) Ratio (RNNU: mm3): LS Mean Change from Baseline (+/- SE) (Modified Intention-to-Treat Population)
Change in Grey Matter (Right) Ratio (RNNU: mm3)
0.0
0.2
0.4
0.6
0.8
1.0
1.2
1.4
1.6
1.8
2.0
2.2
2.4
2.6
*p=0.052
*p=0.054
*p=0.075
Statistical significance is indicated as follows: *p<0.1, **p<0.05, ***p<0.01, and ****p<0.001.
0
16
26
39
Weeks (relative to first infusion)
Placebo (Dose × 4)
Lomecel-B (25M × 4)
Pooled Lomecel-B (25M × 1, 25M × 4, 100M × 4)
Lomecel-B (25M × 1)
Lomecel-B (100M × 4)
Pooled Lomecel-B (25M × 4, 100M × 4)

FIG. 5C




*p<0.5, **p<0.01, ***p<0.001: significant intergroup change versus placebo from baseline
†p<0.5, ††p<0.01, †††p<0.001: significant intragroup change from baseline

FIG. 6A

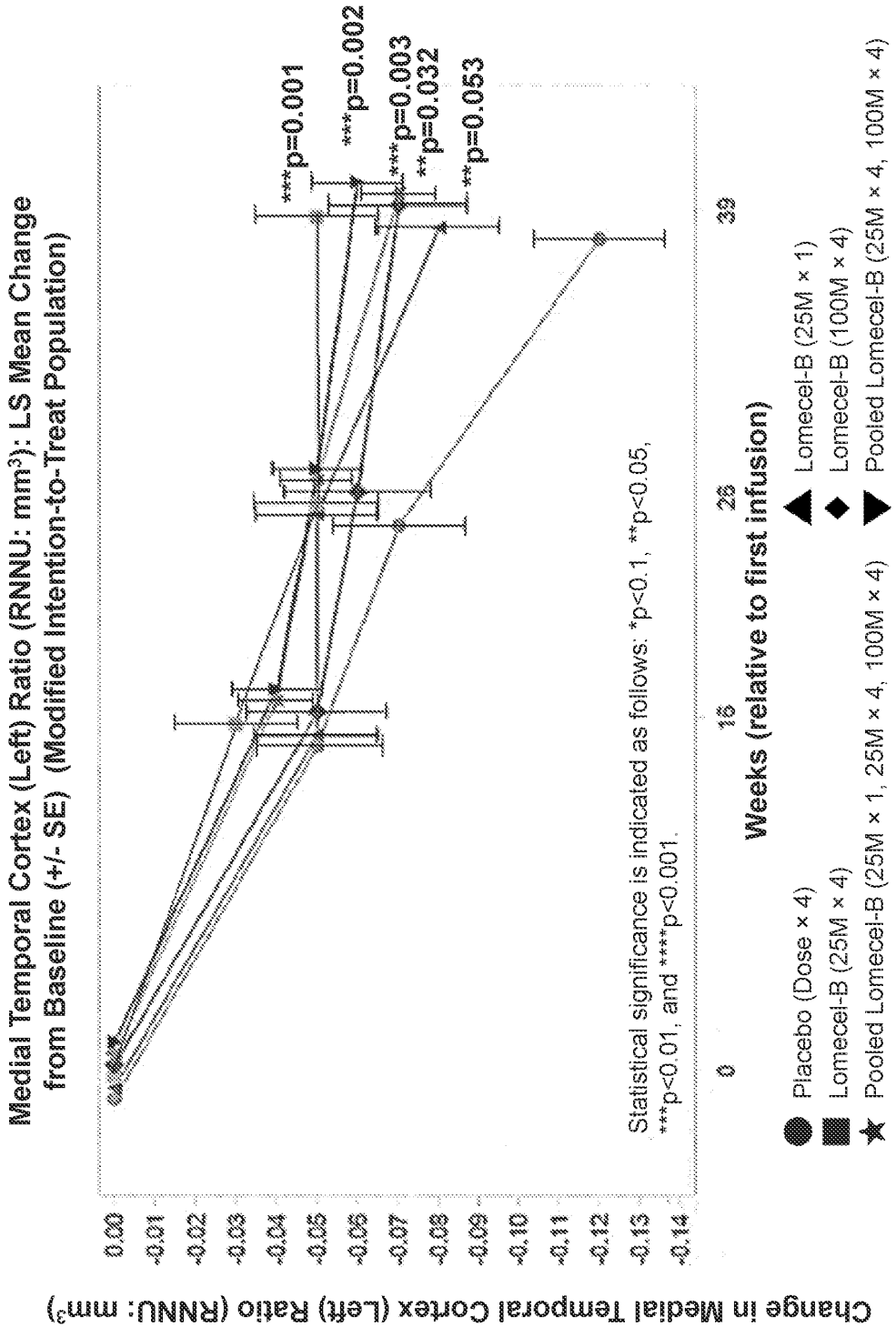

Medial Temporal Cortex (Left) Ratio (RNNU: mm³): LS Mean Change from Baseline (+/- SE) (Modified Intention-to-Treat Population)
Change in Medial Temporal Cortex (Left) Ratio (RNNU: mm³)
0.00
-0.01
-0.02
-0.03
-0.04
-0.05
-0.06
-0.07
-0.08
-0.09
-0.10
-0.11
-0.12
-0.13
-0.14
***p=0.001
***p=0.002
***p=0.003
**p=0.032
**p=0.053
Statistical significance is indicated as follows: *p<0.1, **p<0.05, ***p<0.01, and ****p<0.001.
0
16
26
39
Weeks (relative to first infusion)
Placebo (Dose × 4)
Lomecel-B (25M × 4)
Pooled Lomecel-B (25M × 1, 25M × 4, 100M × 4)
Lomecel-B (25M × 1)
Lomecel-B (100M × 4)
Pooled Lomecel-B (25M × 4, 100M × 4)

FIG. 6B

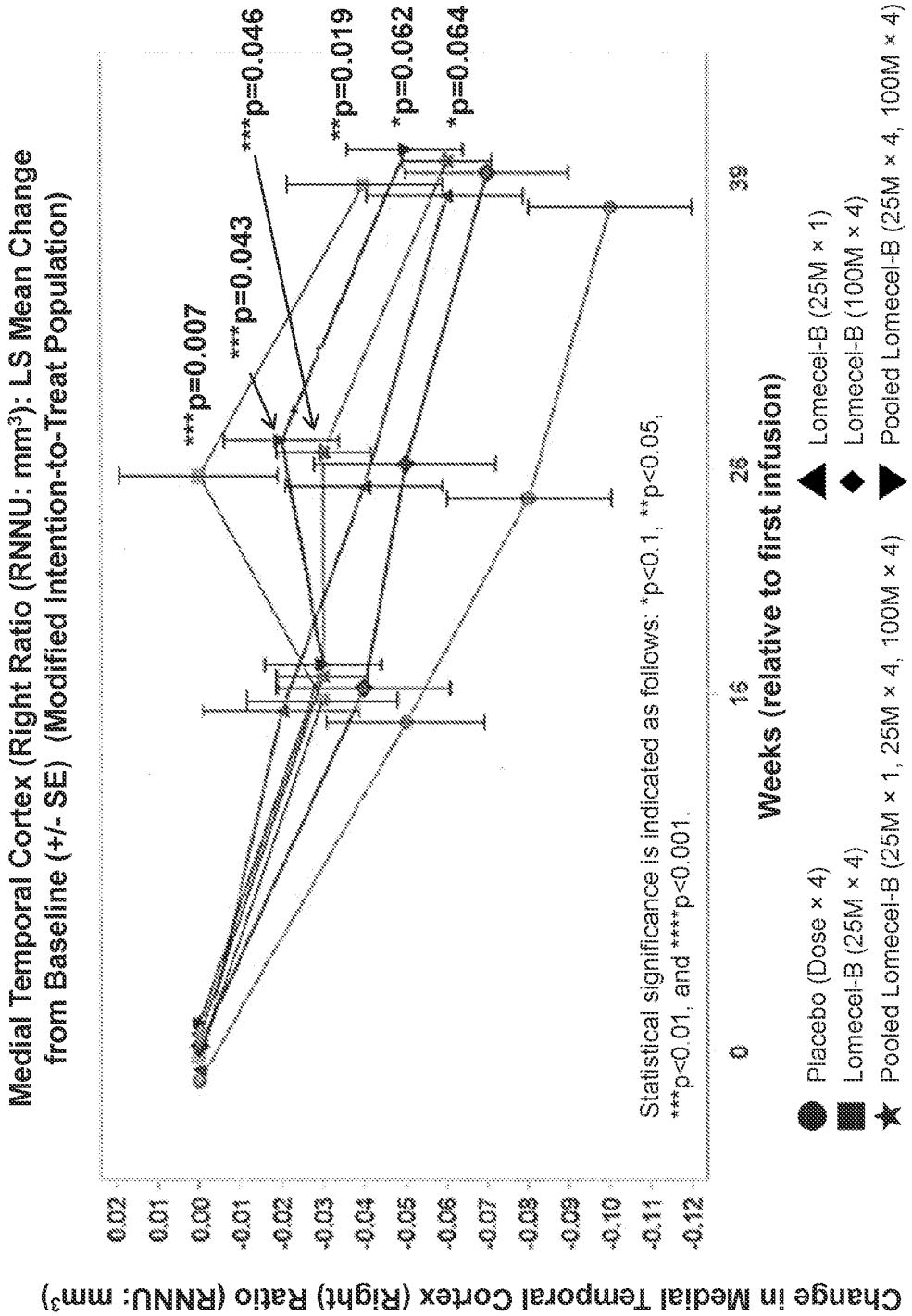
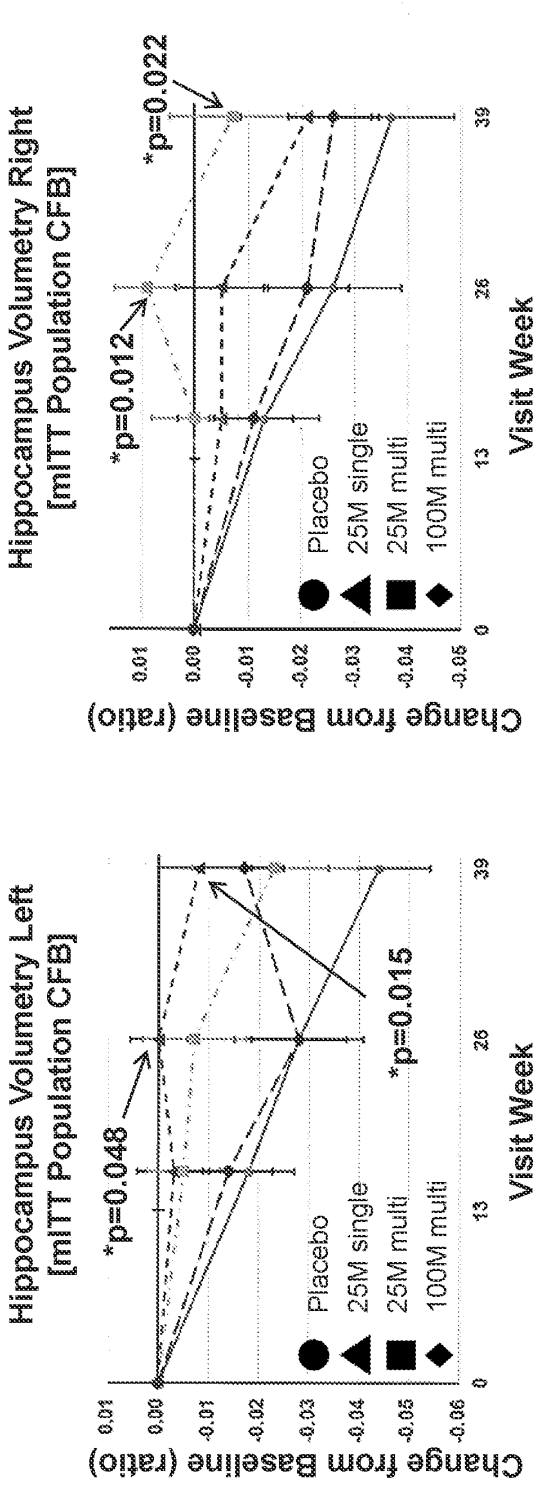

Medial Temporal Cortex (Right Ratio (RNNU: mm3): LS Mean Change from Baseline (+/- SE) (Modified Intention-to-Treat Population)
***p=0.007
***p=0.043
***p=0.046
**p=0.019
*p=0.062
*p=0.064
Statistical significance is indicated as follows: *p<0.1, **p<0.05, ***p<0.01, and ****p<0.001.
Change in Medial Temporal Cortex (Right) Ratio (RNNU: mm3)
0.02
0.01
0.00
-0.01
-0.02
-0.03
-0.04
-0.05
-0.06
-0.07
-0.08
-0.09
-0.10
-0.11
-0.12
0
16
26
39
Weeks (relative to first infusion)
Placebo (Dose × 4)
Lomecel-B (25M × 4)
Pooled Lomecel-B (25M × 1, 25M × 4, 100M × 4)
Lomecel-B (25M × 1)
Lomecel-B (100M × 4)
Pooled Lomecel-B (25M × 4, 100M × 4)

FIG. 6C




*p<0.5, **p<0.01, ***p<0.001: significant intergroup change versus placebo from baseline
†p<0.5, ††p<0.01, †††p<0.001: significant intragroup change from baseline

FIG. 7A

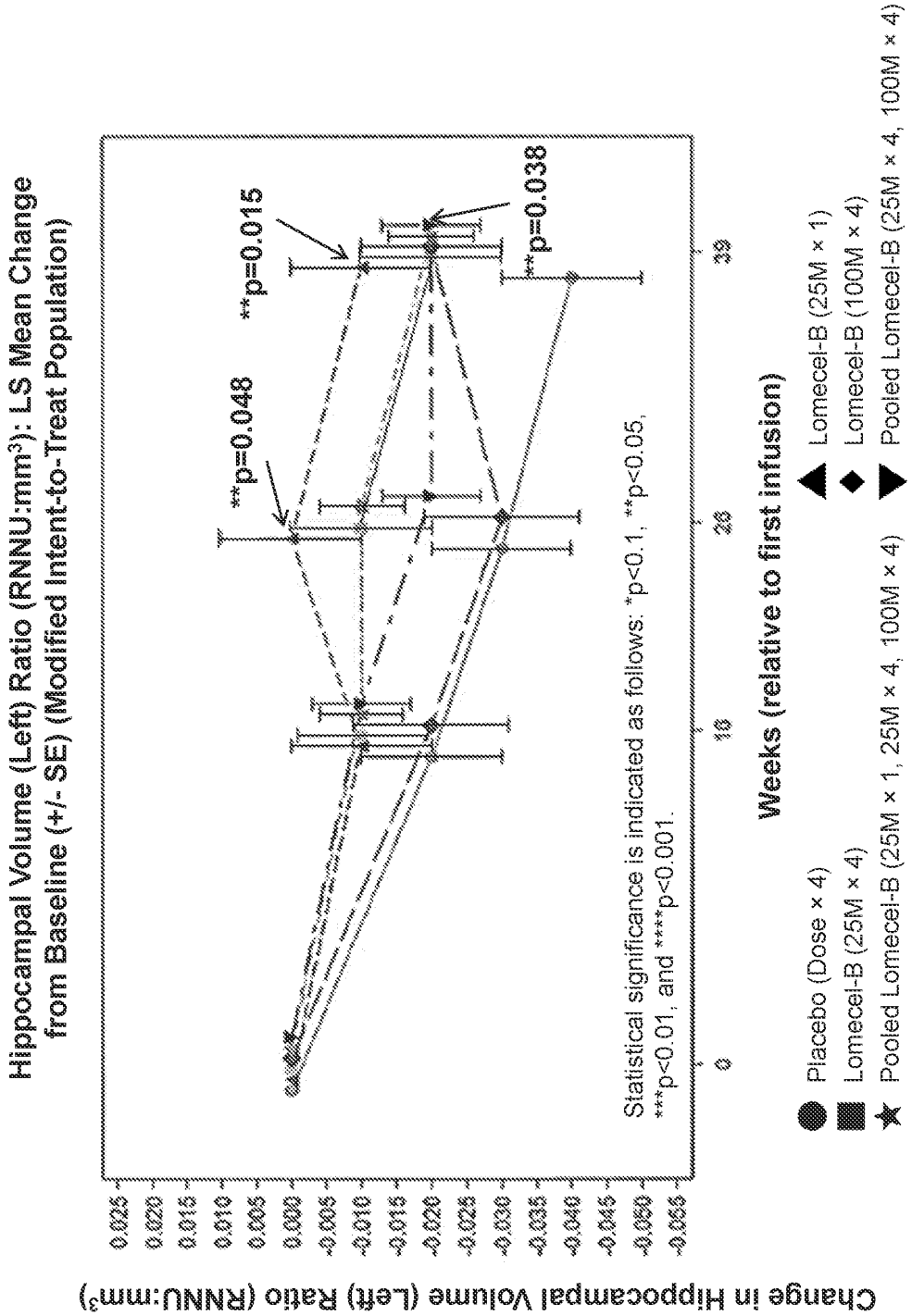

Hippocampal Volume (Left) Ratio (RNNU:mm³): LS Mean Change from Baseline (+/- SE) (Modified Intent-to-Treat Population)
**p=0.048
**p=0.015
**p=0.038
Statistical significance is indicated as follows: *p<0.1, **p<0.05, ***p<0.01, and ****p<0.001.
Change in Hippocampal Volume (Left) Ratio (RNNU:mm³)
0.025
0.020
0.015
0.010
0.005
0.000
-0.005
-0.010
-0.015
-0.020
-0.025
-0.030
-0.035
-0.040
-0.045
-0.050
-0.055
0
16
28
39
Weeks (relative to first infusion)
Placebo (Dose × 4)
Lomecel-B (25M × 4)
Pooled Lomecel-B (25M × 1, 25M × 4, 100M × 4)
Lomecel-B (25M × 1)
Lomecel-B (100M × 4)
Pooled Lomecel-B (25M × 4, 100M × 4)

FIG. 7B

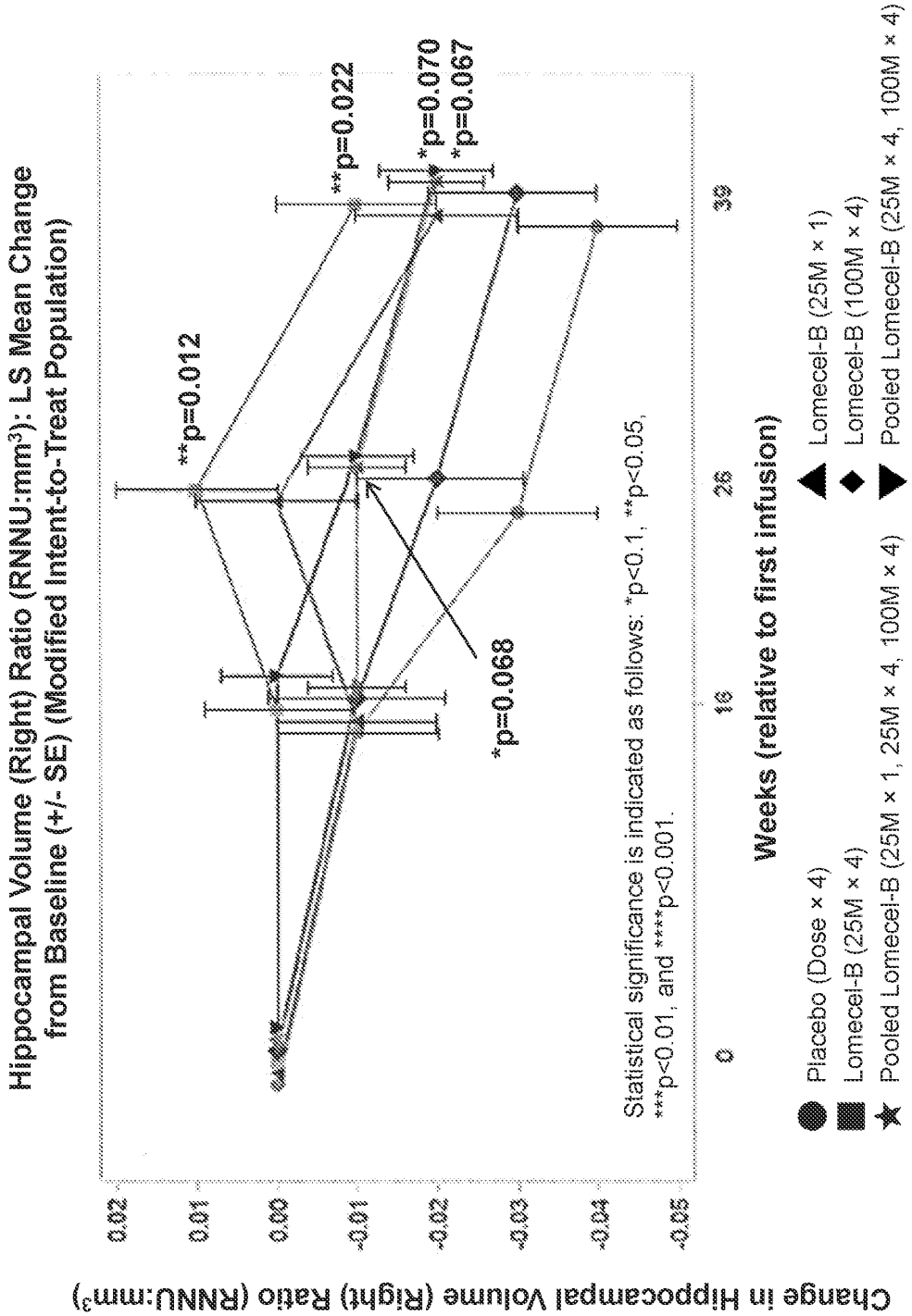
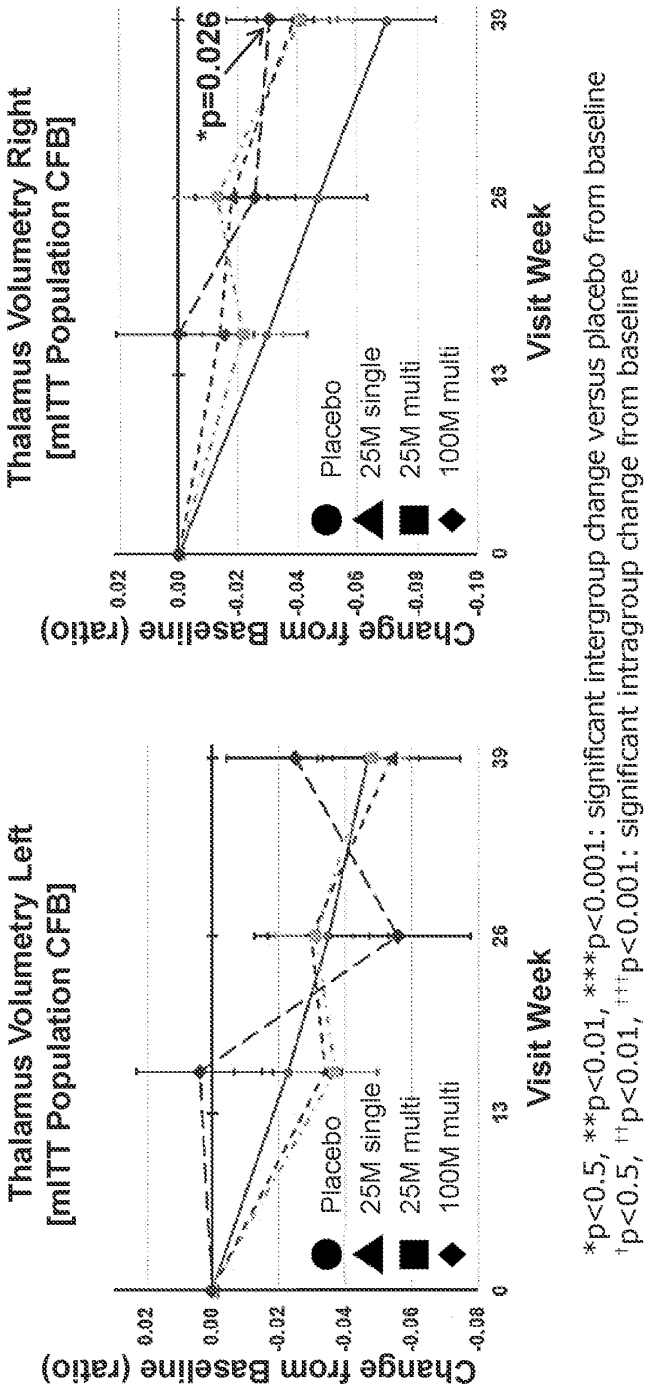

Hippocampal Volume (Right) Ratio (RNNU:mm³): LS Mean Change from Baseline (+/- SE) (Modified Intent-to-Treat Population)
Change in Hippocampal Volume (Right) Ratio (RNNU:mm³)
0.02
0.01
0.00
-0.01
-0.02
-0.03
-0.04
-0.05
0
13
26
39
Weeks (relative to first infusion)
**p=0.012
**p=0.022
*p=0.070
*p=0.067
*p=0.068
Statistical significance is indicated as follows: *p<0.1, **p<0.05, ***p<0.01, and ****p<0.001.
Placebo (Dose × 4)
Lomecel-B (25M × 4)
Pooled Lomecel-B (25M × 1, 25M × 4, 100M × 4)
Lomecel-B (25M × 1)
Lomecel-B (100M × 4)
Pooled Lomecel-B (25M × 4, 100M × 4)

FIG. 7C




*p<0.5, **p<0.01, ***p<0.001: significant intergroup change versus placebo from baseline
†p<0.5, ††p<0.01, †††p<0.001: significant intragroup change from baseline

FIG. 8A

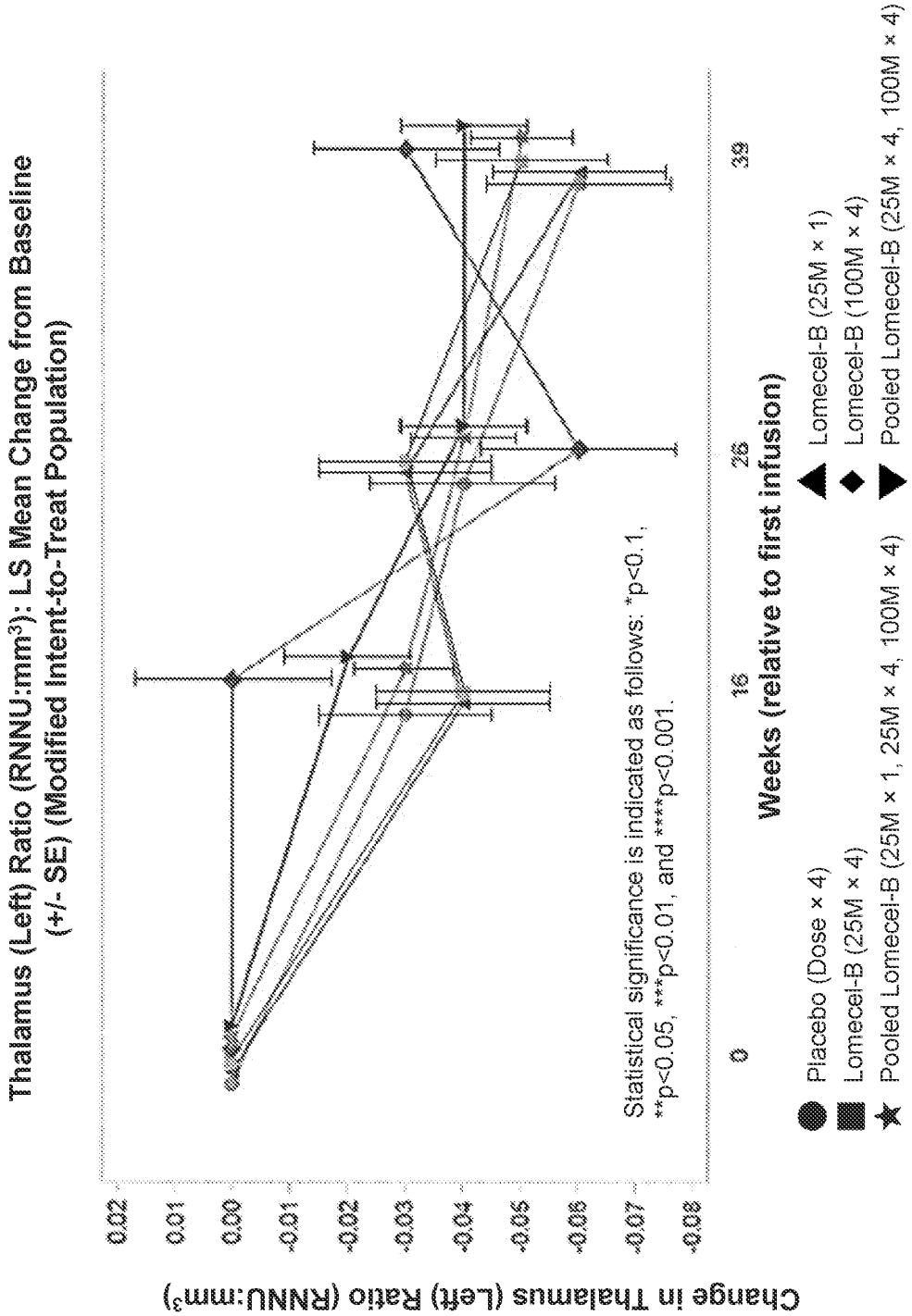

Thalamus (Left) Ratio (RNNU:mm³): LS Mean Change from Baseline
(+/- SE) (Modified Intent-to-Treat Population)
Change in Thalamus (Left) Ratio (RNNU:mm³)
0.02
0.01
0.00
-0.01
-0.02
-0.03
-0.04
-0.05
-0.06
-0.07
-0.08
0
16
26
39
Weeks (relative to first infusion)
Statistical significance is indicated as follows: *p<0.1,
**p<0.05, ***p<0.01, and ****p<0.001.
Placebo (Dose × 4)
Lomecel-B (25M × 4)
Pooled Lomecel-B (25M × 1, 25M × 4, 100M × 4)
Lomecel-B (25M × 1)
Lomecel-B (100M × 4)
Pooled Lomecel-B (25M × 4, 100M × 4)

FIG. 8B

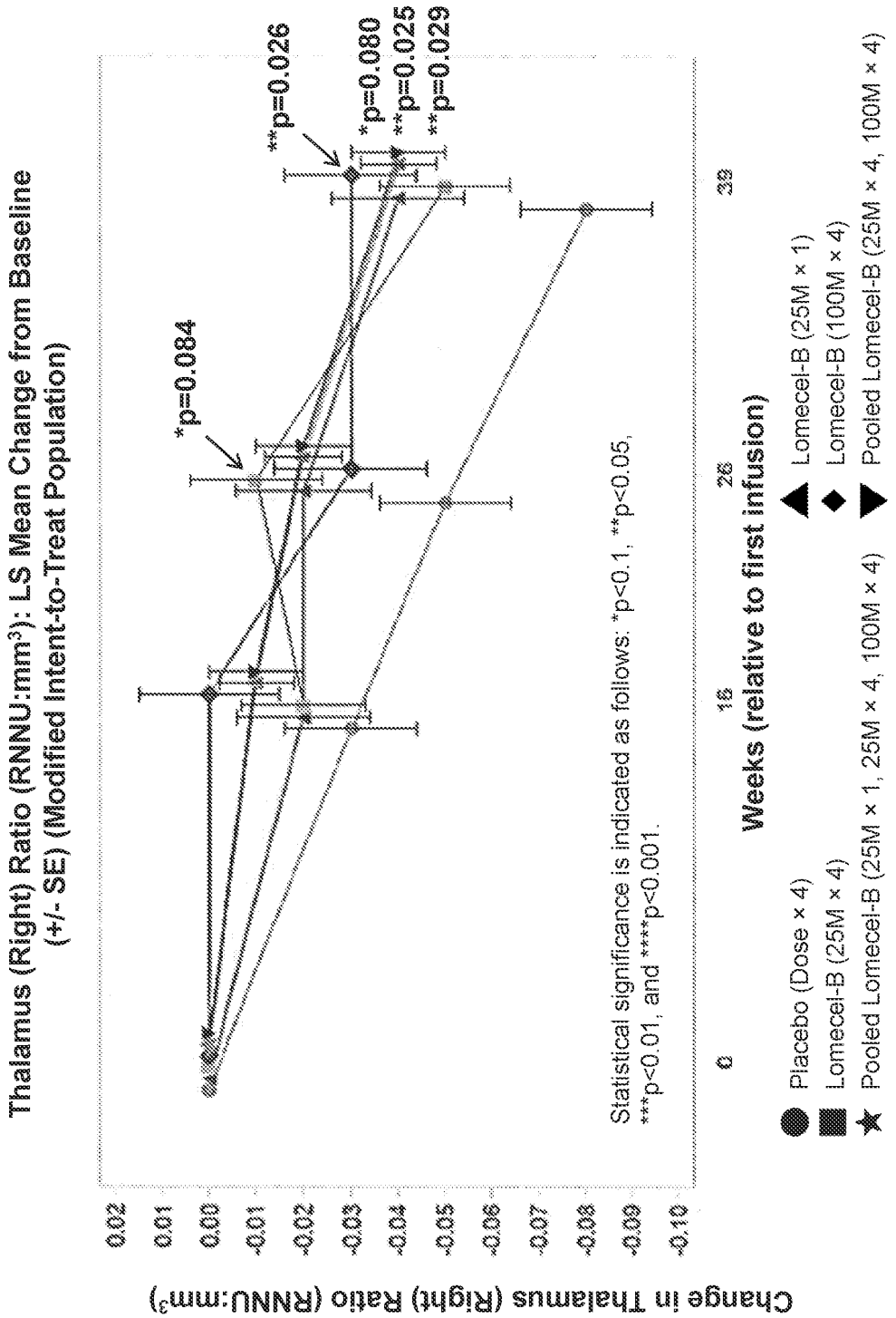
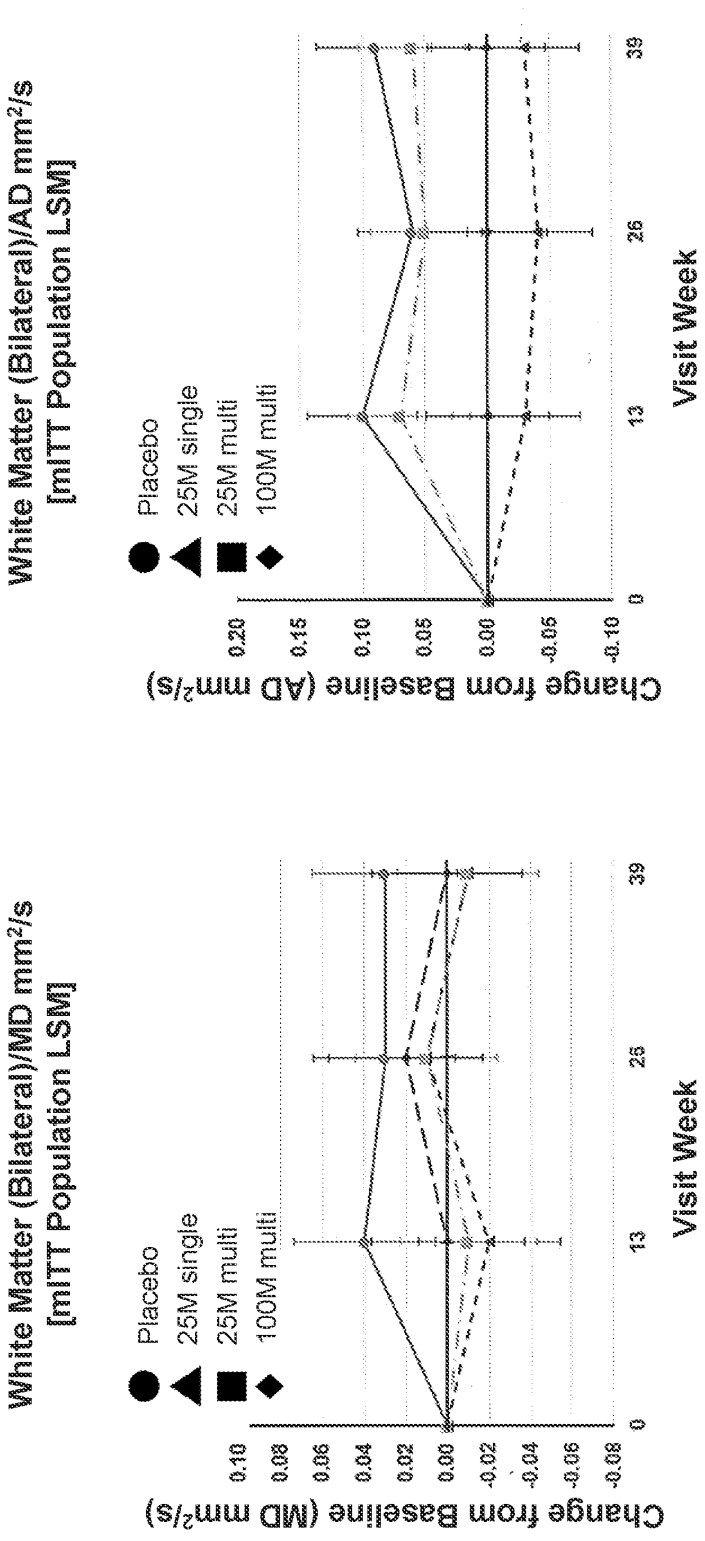
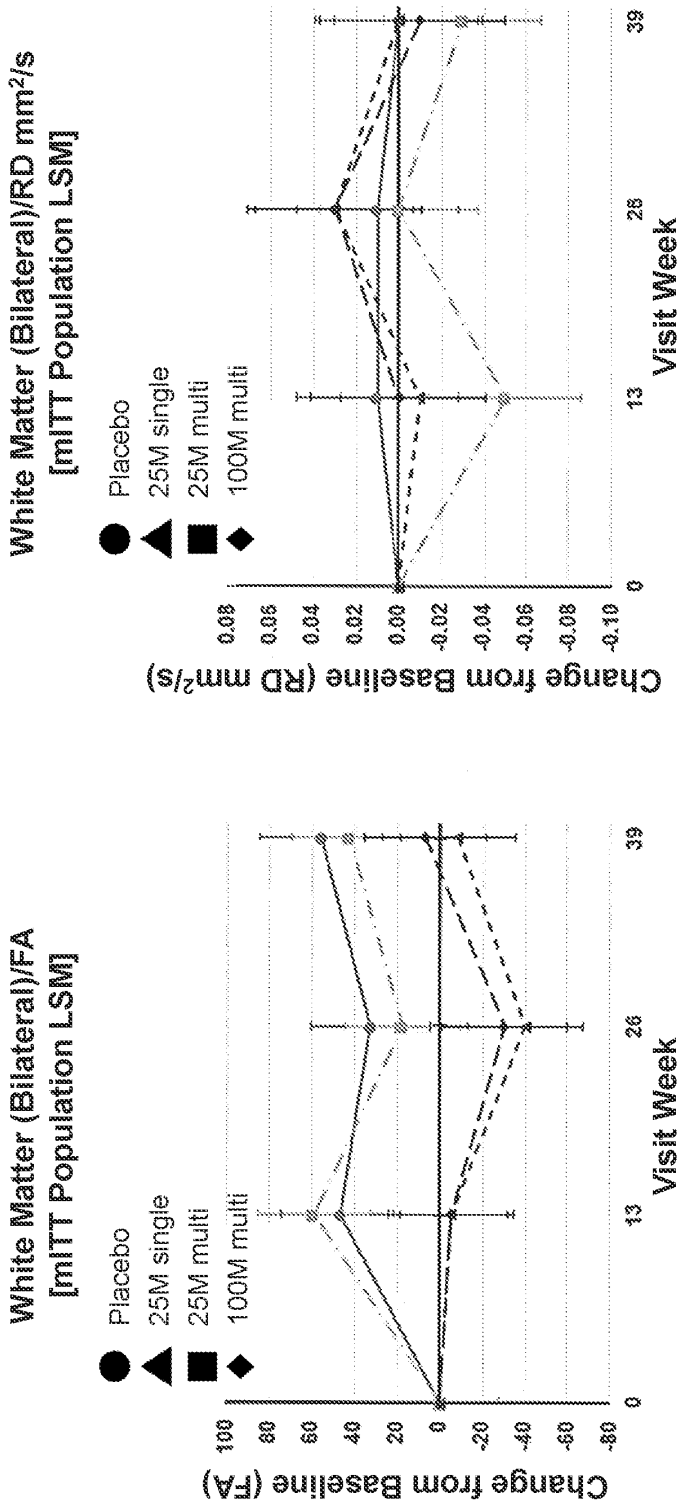

Thalamus (Right) Ratio (RNNU:mm³): LS Mean Change from Baseline
(+/- SE) (Modified Intent-to-Treat Population)
*p=0.084
**p=0.026
*p=0.080
**p=0.025
**p=0.029
Statistical significance is indicated as follows: *p<0.1, **p<0.05,
***p<0.01, and ****p<0.001.
Change in Thalamus (Right) Ratio (RNNU:mm³)
0.02
0.01
0.00
-0.01
-0.02
-0.03
-0.04
-0.05
-0.06
-0.07
-0.08
-0.09
-0.10
0
13
26
39
Weeks (relative to first infusion)
Placebo (Dose × 4)
Lomecel-B (25M × 4)
Pooled Lomecel-B (25M × 1, 25M × 4, 100M × 4)
Lomecel-B (25M × 1)
Lomecel-B (100M × 4)
Pooled Lomecel-B (25M × 4, 100M × 4)

FIG. 8C



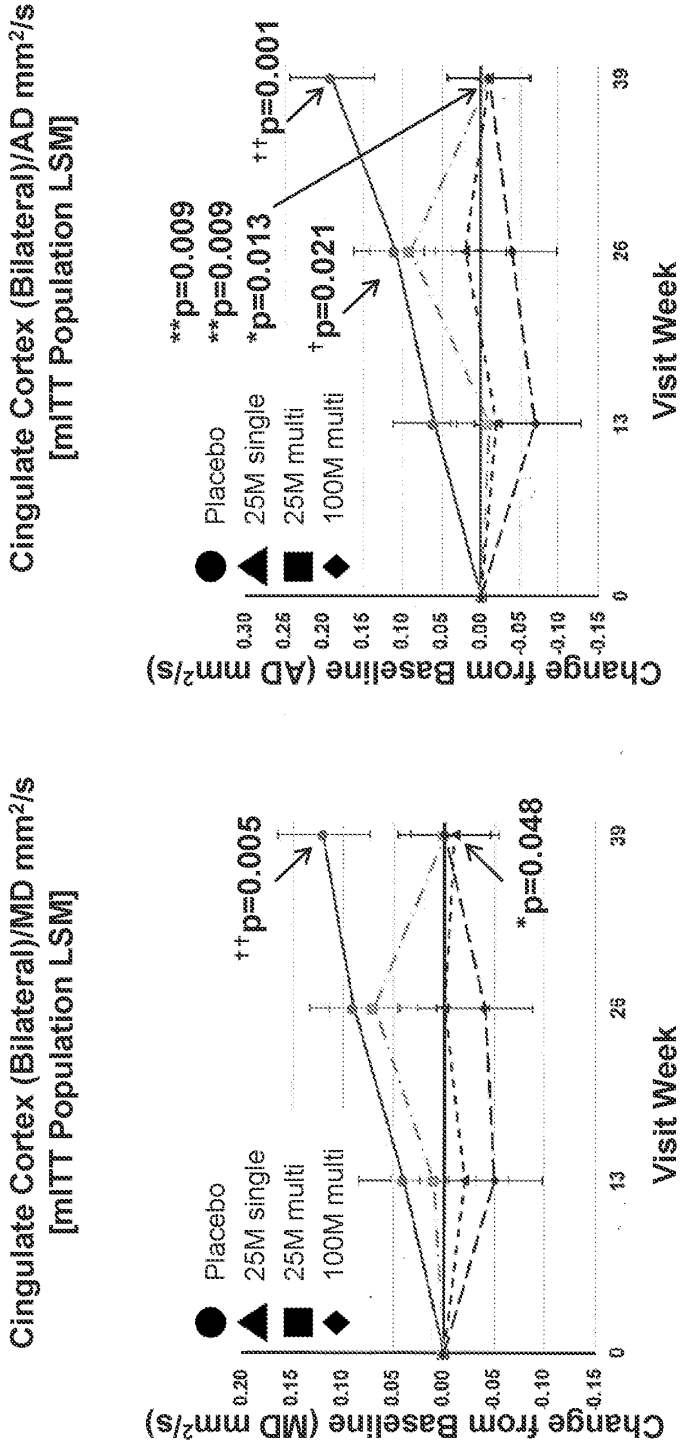

*p<0.5, **p<0.01, ***p<0.001: significant intergroup change versus placebo from baseline
†p<0.5, ††p<0.01, †††p<0.001: significant intragroup change from baseline

FIG. 9A




*p<0.5, **p<0.01, ***p<0.001: significant intergroup change versus placebo from baseline
†p<0.5, ††p<0.01, †††p<0.001: significant intragroup change from baseline

FIG. 9B




*p<0.5, **p<0.01, ***p<0.001: significant intergroup change versus placebo from baseline
†p<0.5, ††p<0.01, †††p<0.001: significant intragroup change from baseline

FIG. 9C

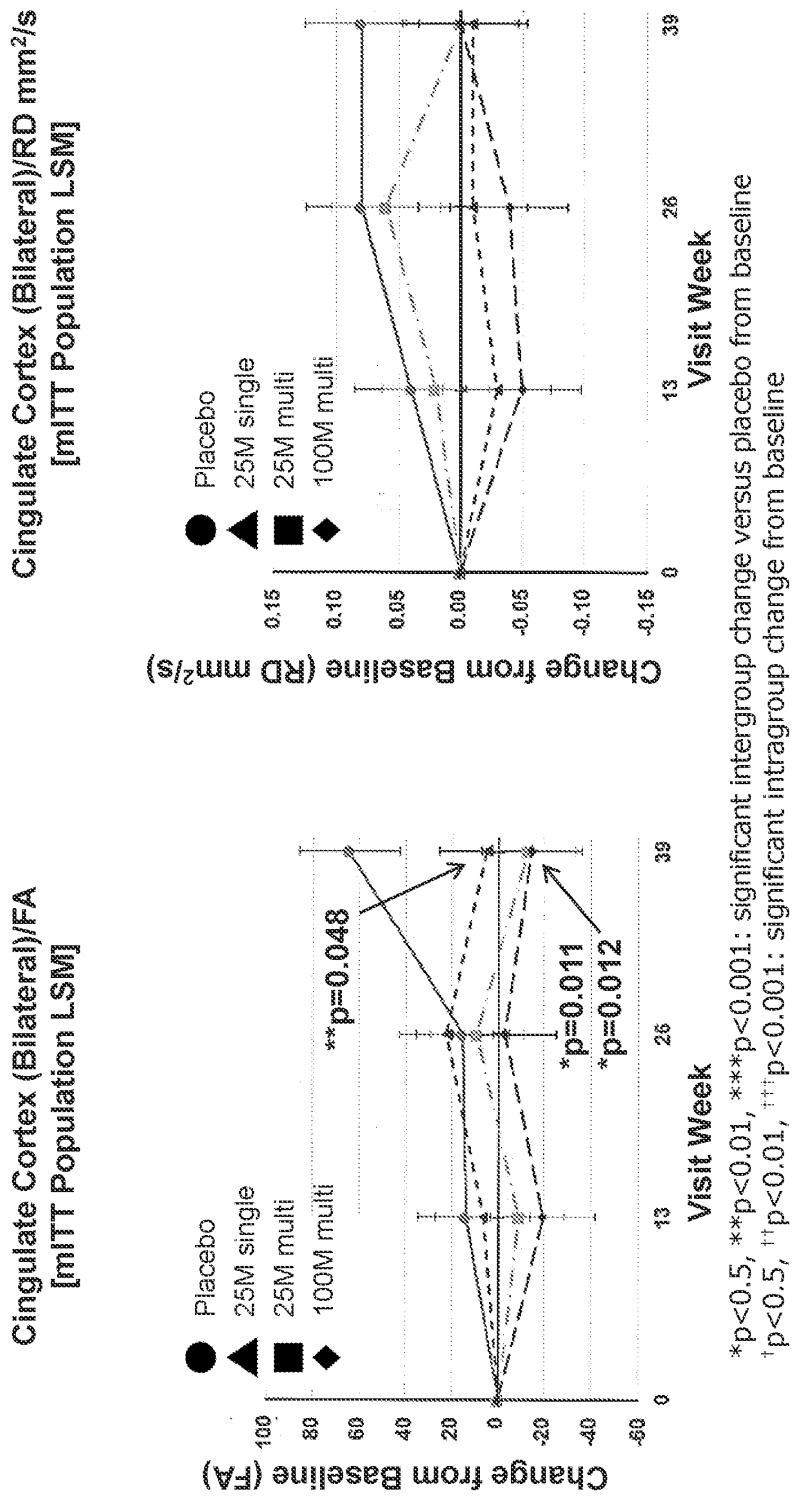
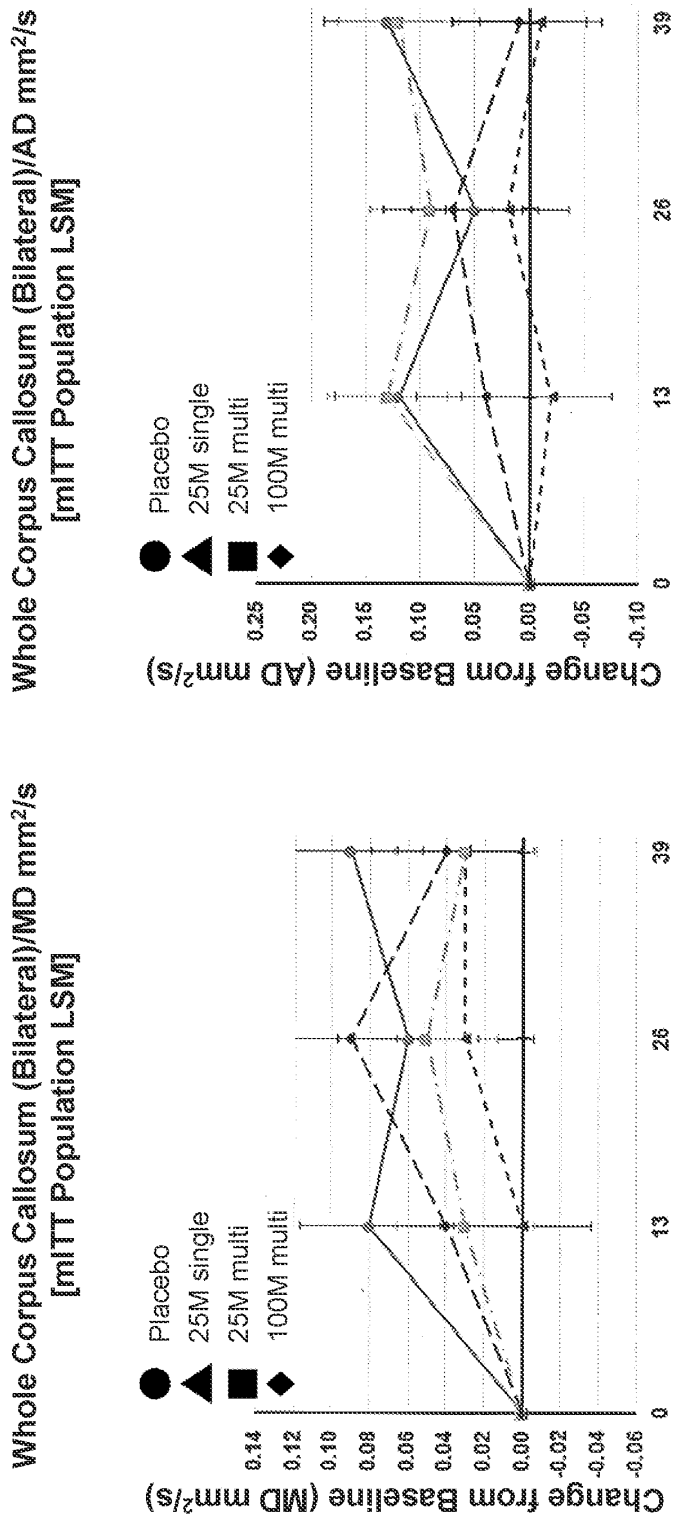
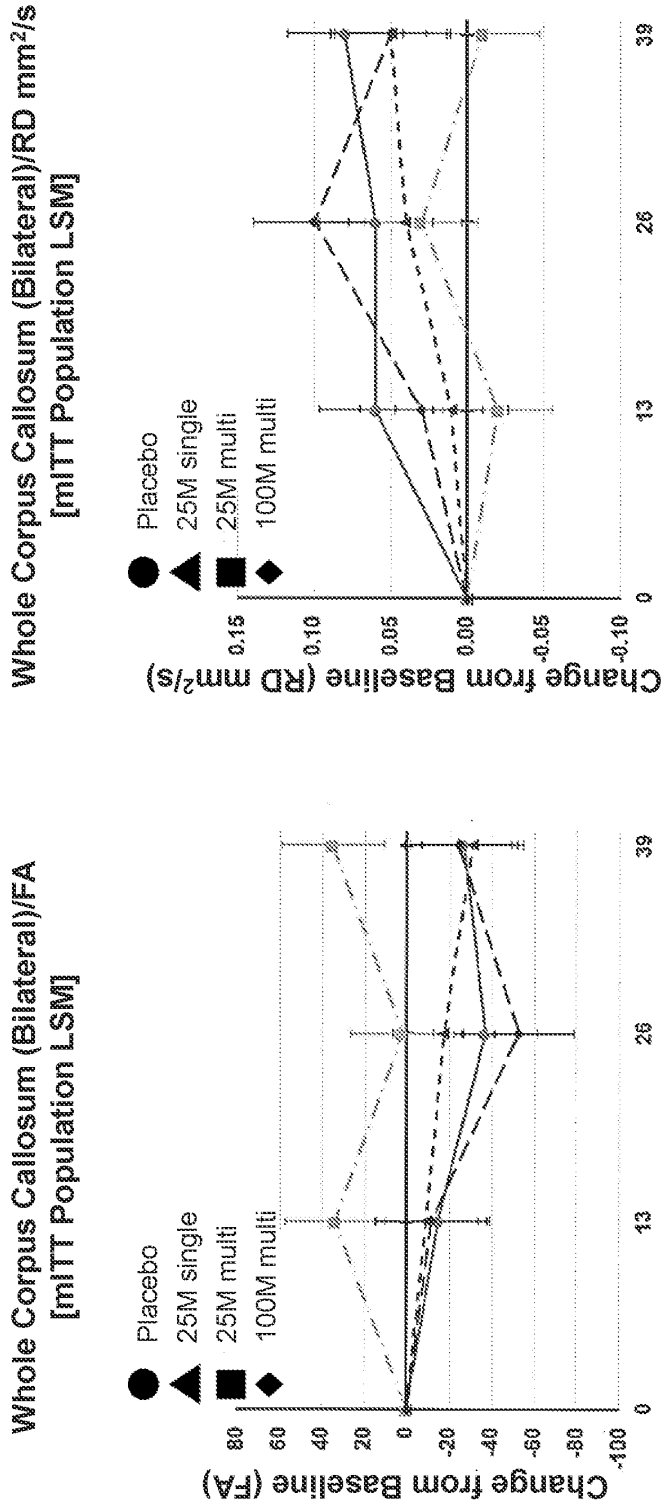

Cingulate Cortex (Bilateral)/FA
[mITT Population LSM]
Change from Baseline (FA)
Placebo
25M single
25M multi
100M multi
**p=0.048
*p=0.011
*p=0.012
Visit Week
Cingulate Cortex (Bilateral)/RD mm²/s
[mITT Population LSM]
Change from Baseline (RD mm²/s)
Placebo
25M single
25M multi
100M multi
Visit Week
*p<0.5, **p<0.01, ***p<0.001: significant intergroup change versus placebo from baseline
†p<0.5, ††p<0.01, †††p<0.001: significant intragroup change from baseline

FIG. 9D




*p<0.5, **p<0.01, ***p<0.001: significant intergroup change versus placebo from baseline
†p<0.5, ††p<0.01, †††p<0.001: significant intragroup change from baseline

FIG. 9E




*p<0.5, **p<0.01, ***p<0.001: significant intergroup change versus placebo from baseline
†p<0.5, ††p<0.01, †††p<0.001: significant intragroup change from baseline

FIG. 9F

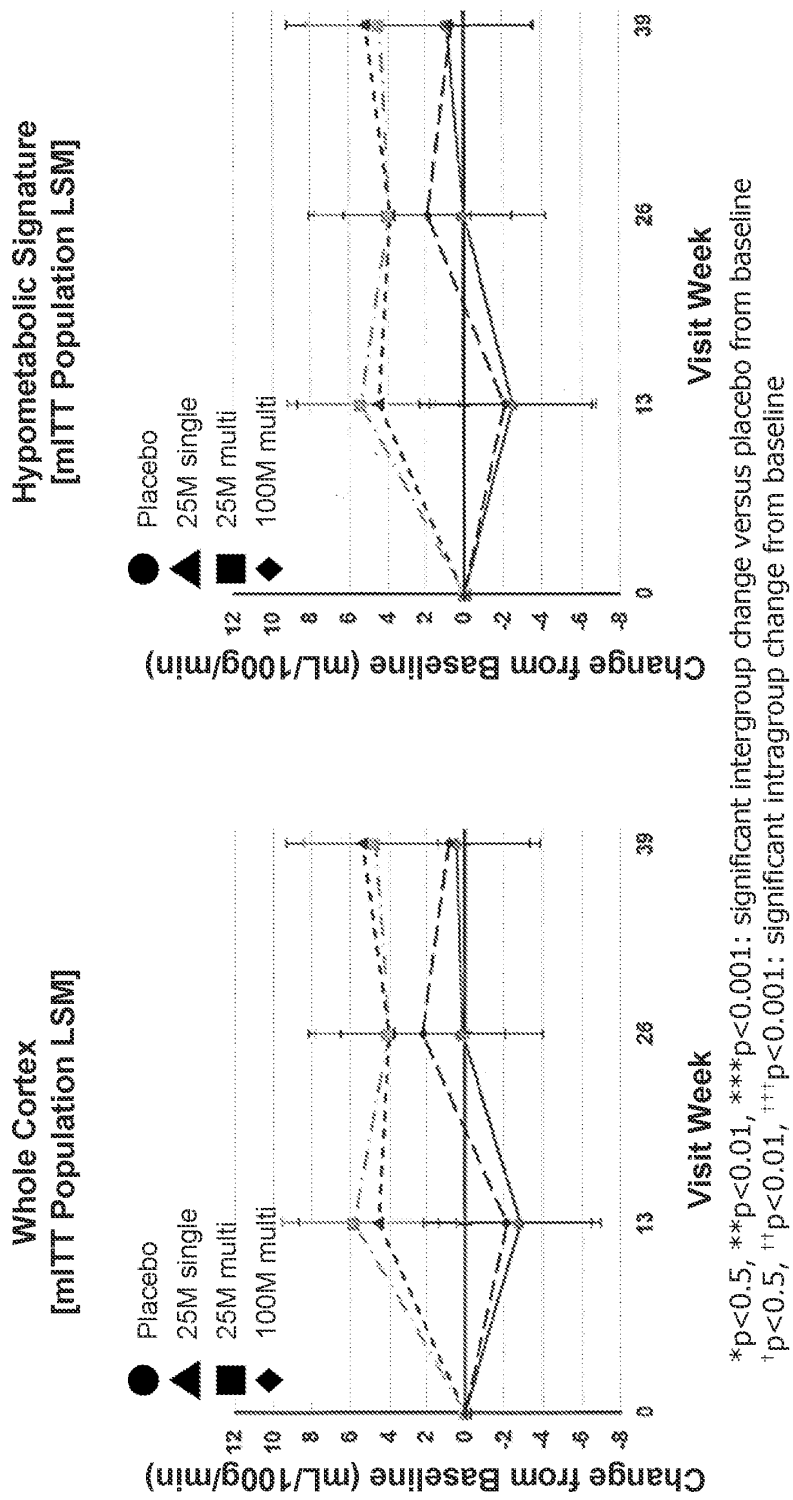

Whole Cortex
[mITT Population LSM]
Hypometabolic Signature
[mITT Population LSM]
Placebo
25M single
25M multi
100M multi
Change from Baseline (mL/100g/min)
Visit Week
12
10
8
6
4
2
0
-2
-4
-6
-8
0
13
26
28
39
*p<0.5, **p<0.01, ***p<0.001: significant intergroup change versus placebo from baseline
†p<0.5, ††p<0.01, †††p<0.001: significant intragroup change from baseline

FIG. 10A

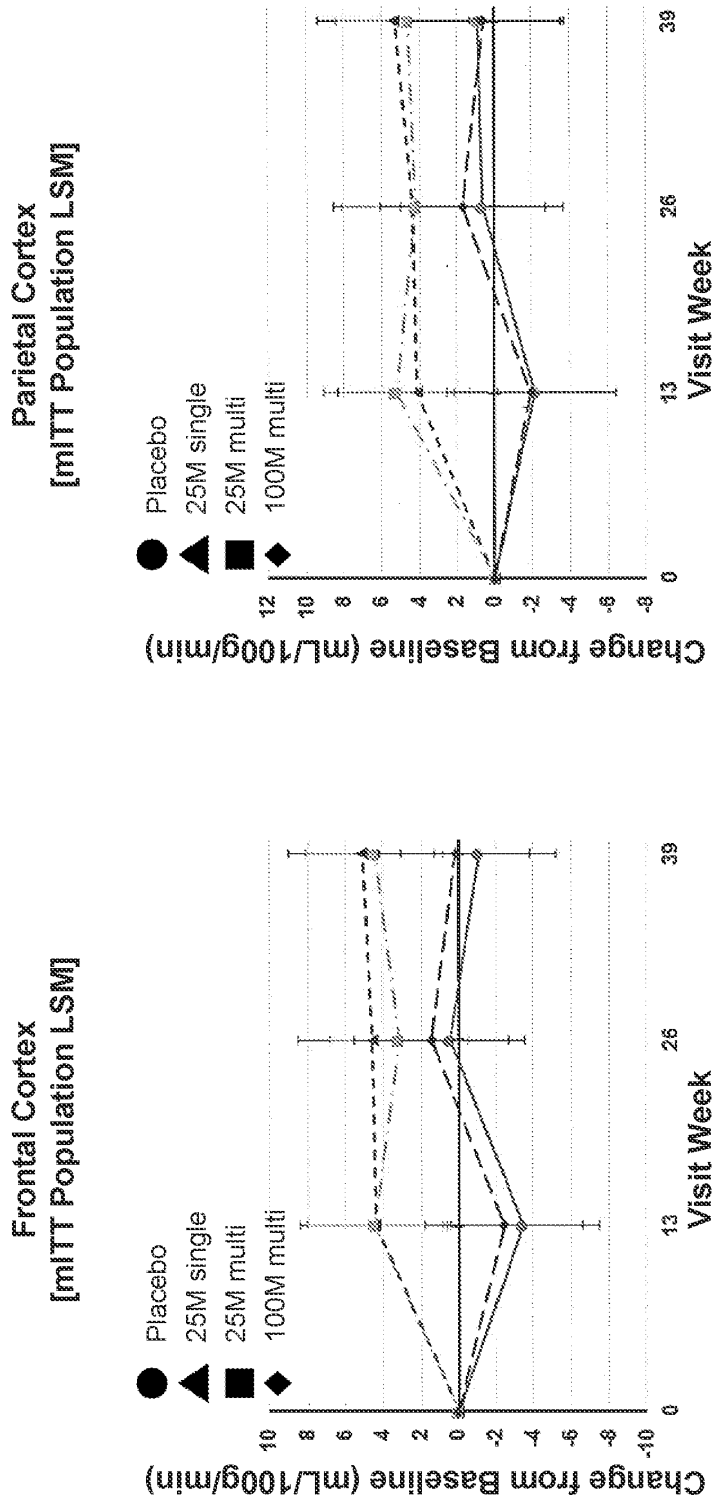

Frontal Cortex
[mITT Population LSM]
Placebo
25M single
25M multi
100M multi
Change from Baseline (mL/100g/min)
Visit Week
Parietal Cortex
[mITT Population LSM]
Placebo
25M single
25M multi
100M multi
Change from Baseline (mL/100g/min)
Visit Week
*p<0.5, **p<0.01, ***p<0.001: significant intergroup change versus placebo from baseline
†p<0.5, ††p<0.01, †††p<0.001: significant intragroup change from baseline

FIG. 10B

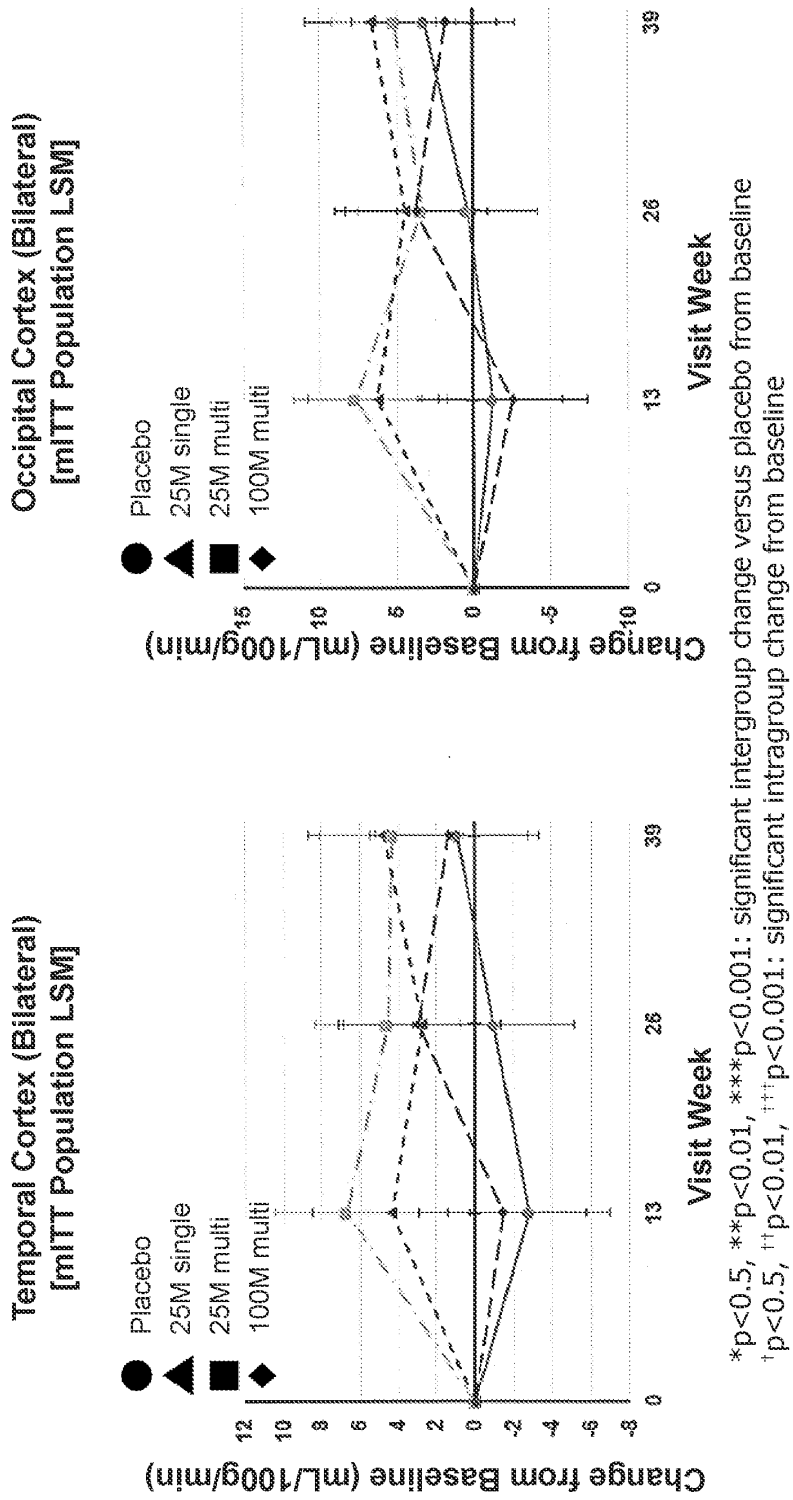

Occipital Cortex (Bilateral)
[mITT Population LSM]
Placebo
25M single
25M multi
100M multi
Change from Baseline (mL/100g/min)
Visit Week
Temporal Cortex (Bilateral)
[mITT Population LSM]
Placebo
25M single
25M multi
100M multi
Change from Baseline (mL/100g/min)
Visit Week
*p<0.5, **p<0.01, ***p<0.001: significant intergroup change versus placebo from baseline
†p<0.5, ††p<0.01, †††p<0.001: significant intragroup change from baseline

FIG. 10C

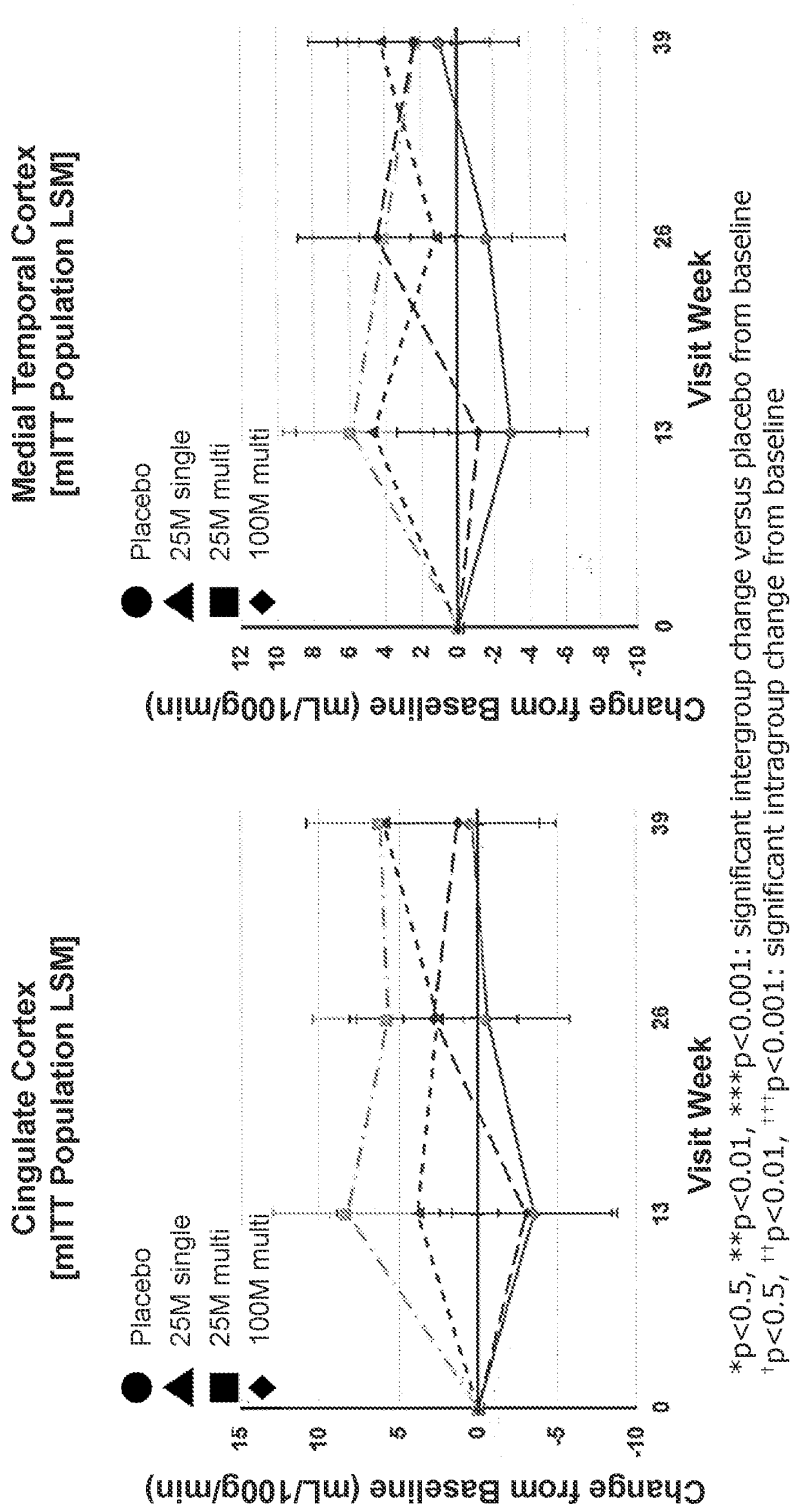

Cingulate Cortex
[mITT Population LSM]
Placebo
25M single
25M multi
100M multi
Change from Baseline (mL/100g/min)
Visit Week
Medial Temporal Cortex
[mITT Population LSM]
Placebo
25M single
25M multi
100M multi
Change from Baseline (mL/100g/min)
Visit Week
*p<0.5, **p<0.01, ***p<0.001: significant intergroup change versus placebo from baseline
†p<0.5, ††p<0.01, †††p<0.001: significant intragroup change from baseline

FIG. 10D

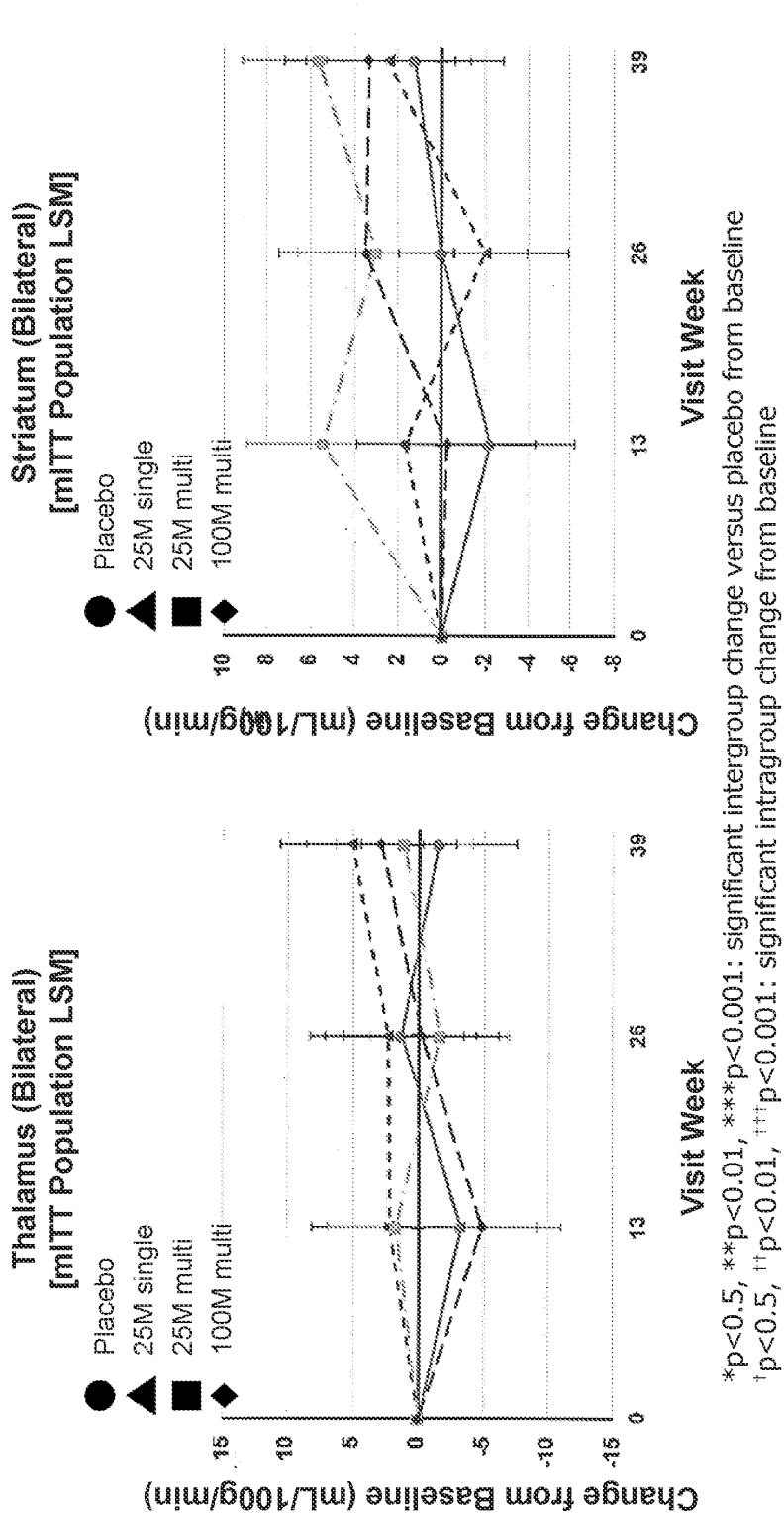
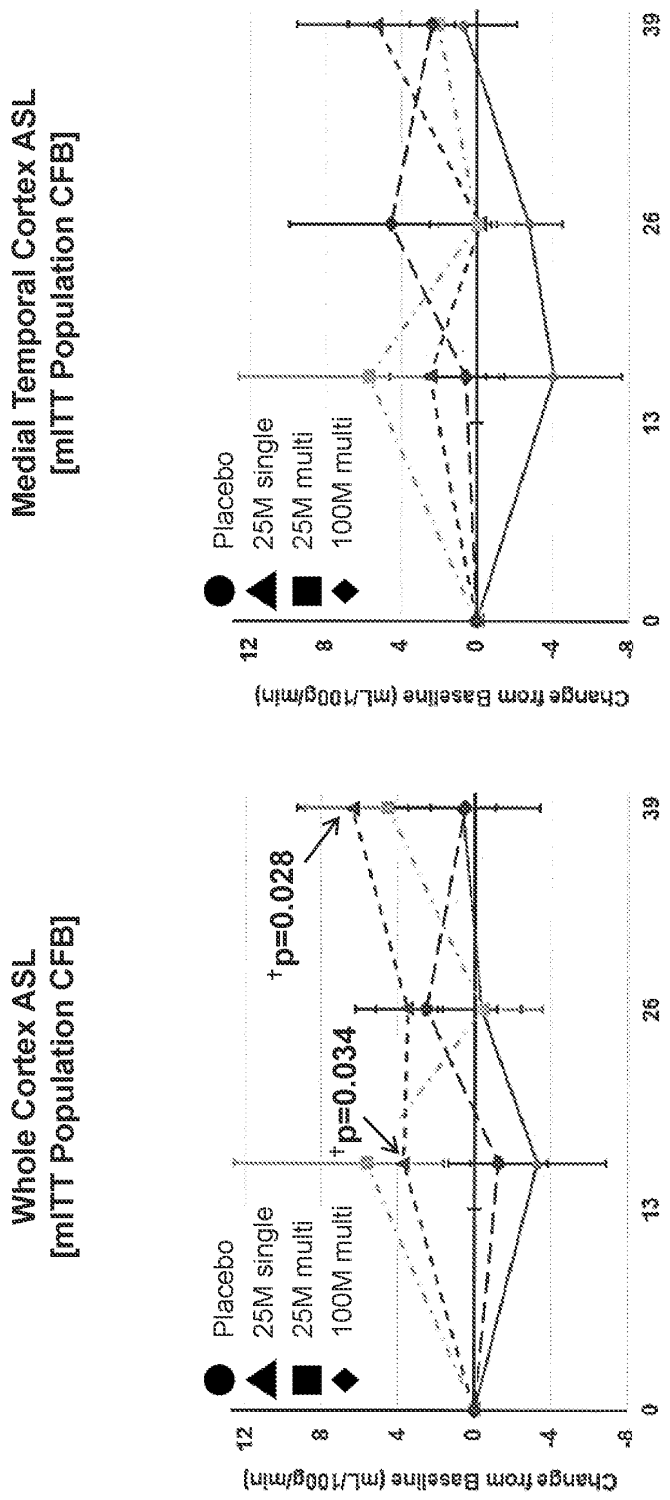

Striatum (Bilateral)
[mITT Population LSM]
Placebo
25M single
25M multi
100M multi
Change from Baseline (mL/100g/min)
Visit Week
Thalamus (Bilateral)
[mITT Population LSM]
Placebo
25M single
25M multi
100M multi
Change from Baseline (mL/100g/min)
Visit Week
*p<0.5, **p<0.01, ***p<0.001: significant intergroup change versus placebo from baseline
†p<0.5, ††p<0.01, †††p<0.001: significant intragroup change from baseline

FIG. 10E




*p<0.5, **p<0.01, ***p<0.001: significant intergroup change versus placebo from baseline
†p<0.5, ††p<0.01, †††p<0.001: significant intragroup change from baseline

FIG. 10F

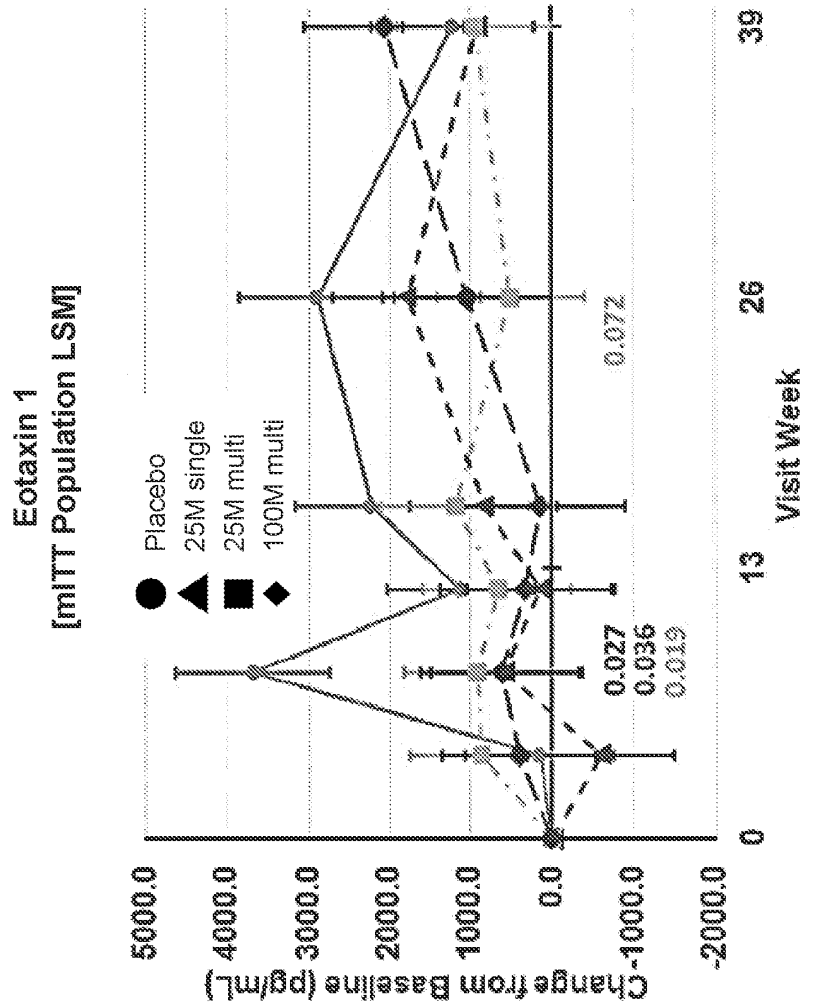

Eotaxin 1
[mITT Population LSM]
Placebo
25M single
25M multi
100M multi
Change from Baseline (pg/mL)
5000.0
4000.0
3000.0
2000.0
1000.0
0.0
-1000.0
-2000.0
0
13
26
39
Visit Week
0.027
0.036
0.019
0.072

FIG. 11A

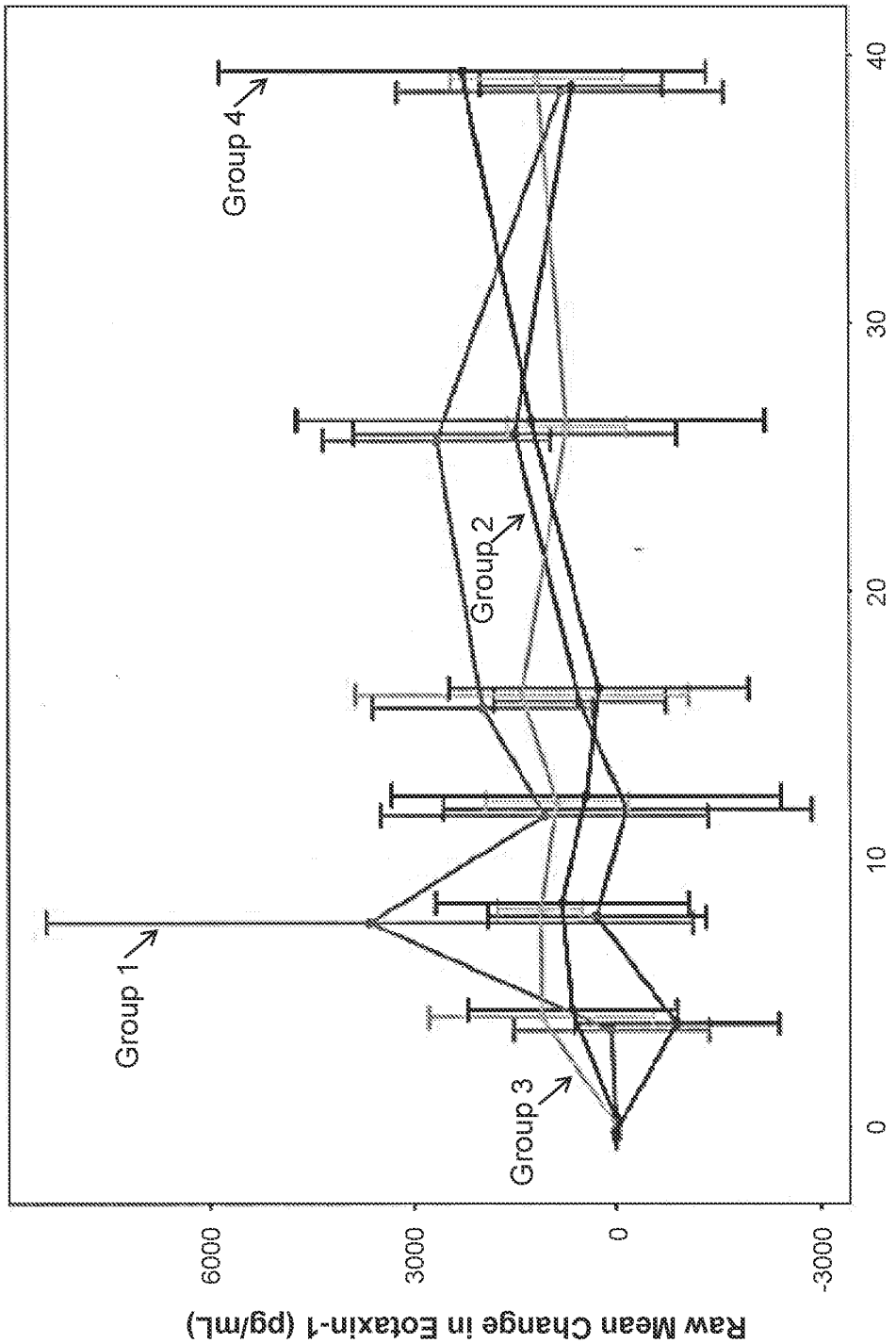

Raw Mean Change in Eotaxin-1 (pg/mL)
6000
3000
0
-3000
0
10
20
30
40
Group 1
Group 2
Group 3
Group 4

FIG. 11B

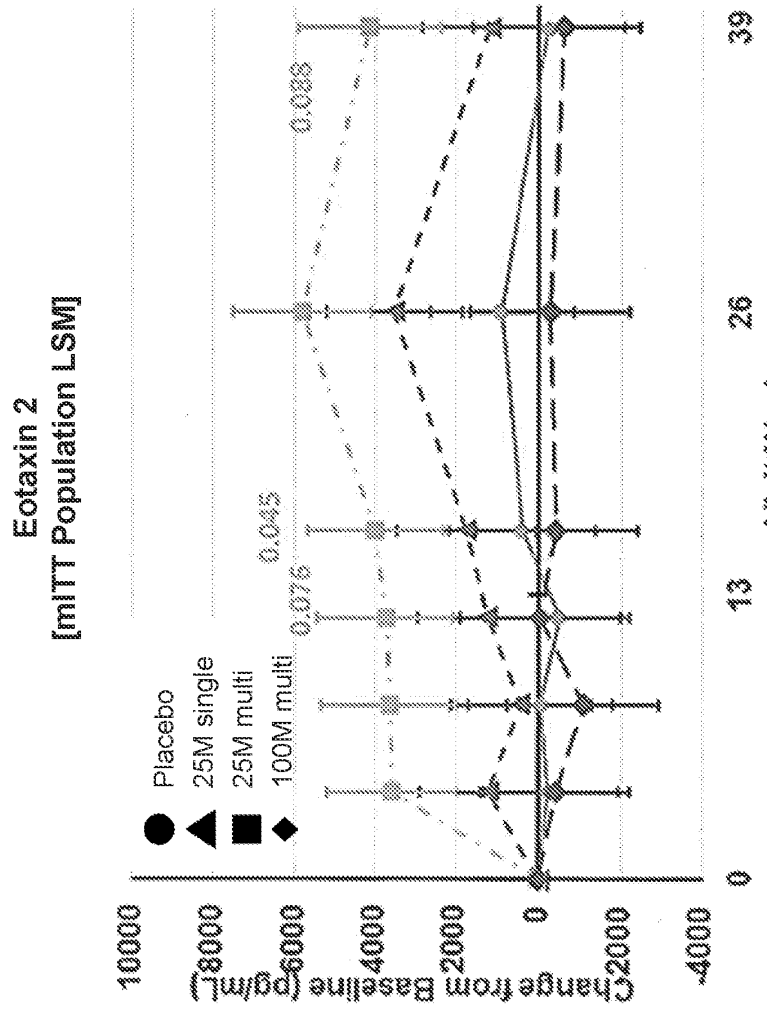

Eotaxin 2
[mITT Population LSM]
Placebo
25M single
25M multi
100M multi
0.076
0.043
0.033
Change from Baseline (pg/mL)
10000
8000
6000
4000
2000
0
-2000
-4000
0
13
26
39
Visit Week

FIG. 11C

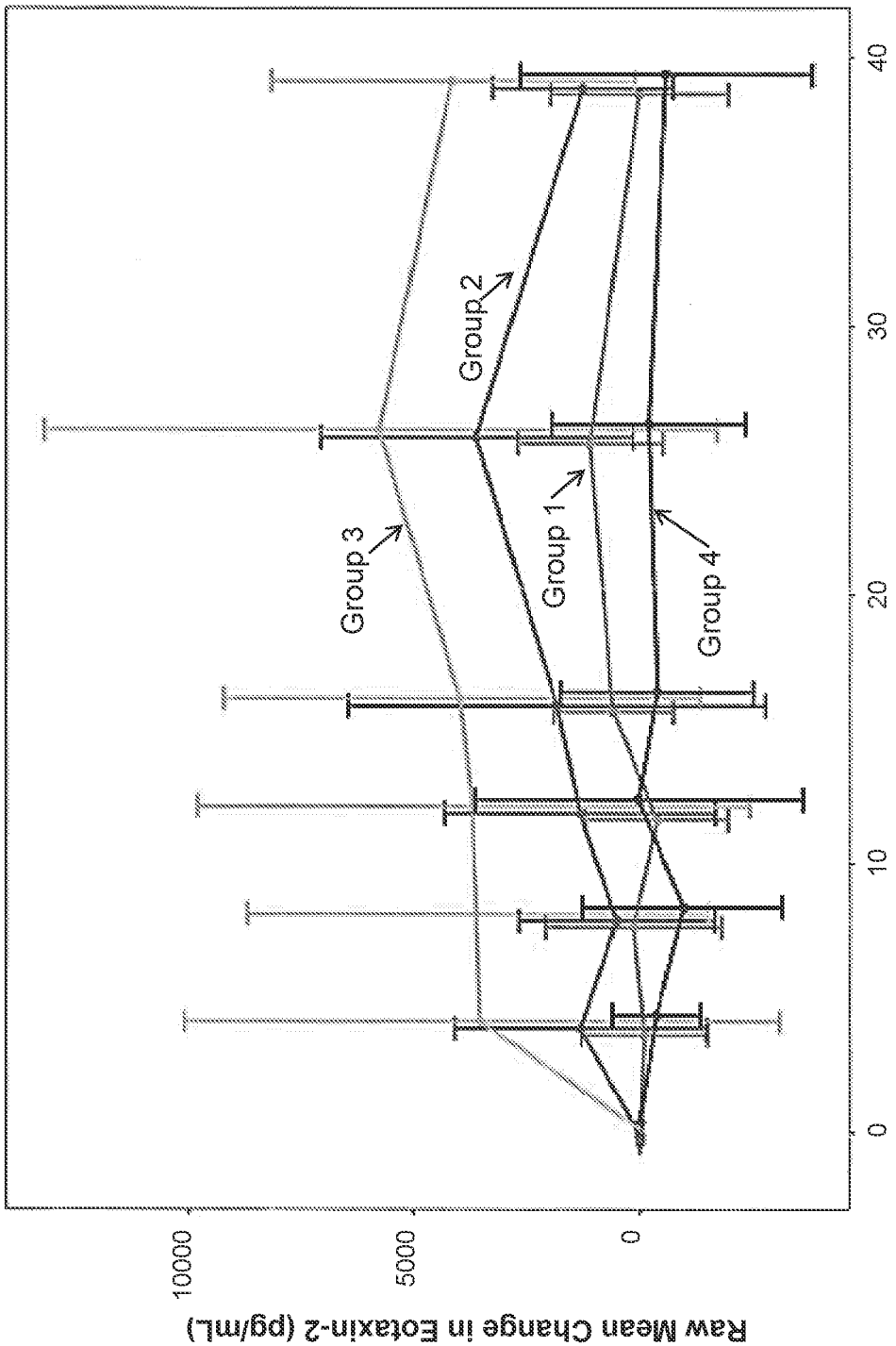

Raw Mean Change in Eotaxin-2 (pg/mL)
10000
5000
0
0
10
20
30
40
Group 1
Group 2
Group 3
Group 4

FIG. 11D

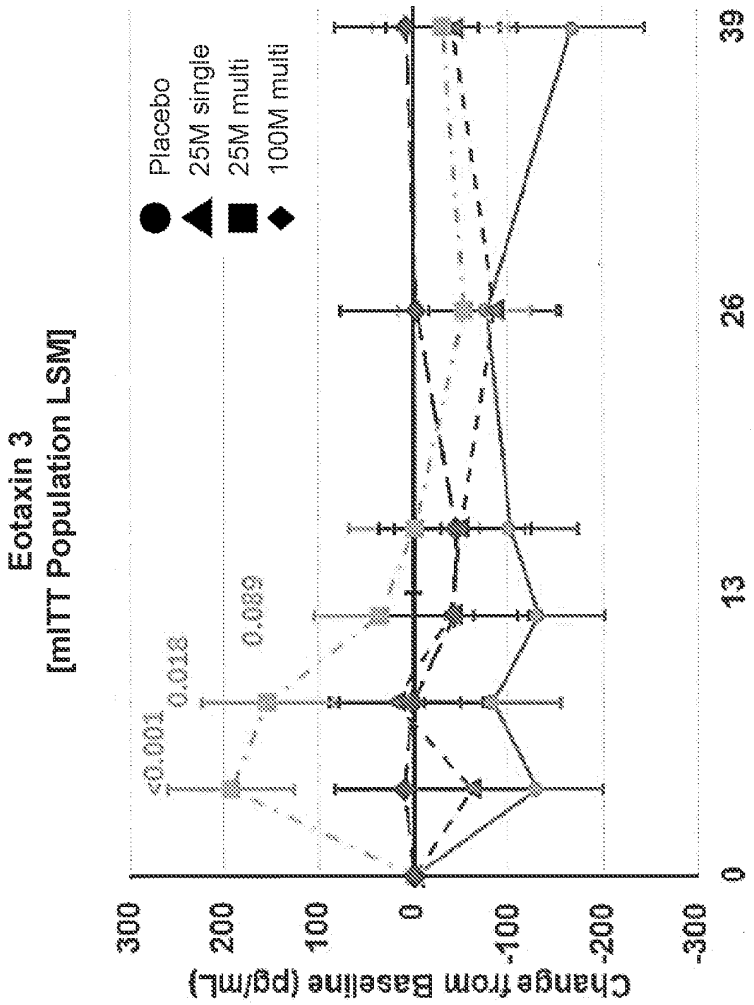

Eotaxin 3
[mITT Population LSM]
Placebo
25M single
25M multi
100M multi
<0.001
0.018
0.089
300
200
100
0
-100
-200
-300
Change from Baseline (pg/mL)
0
13
26
39
Visit Week

FIG. 11E

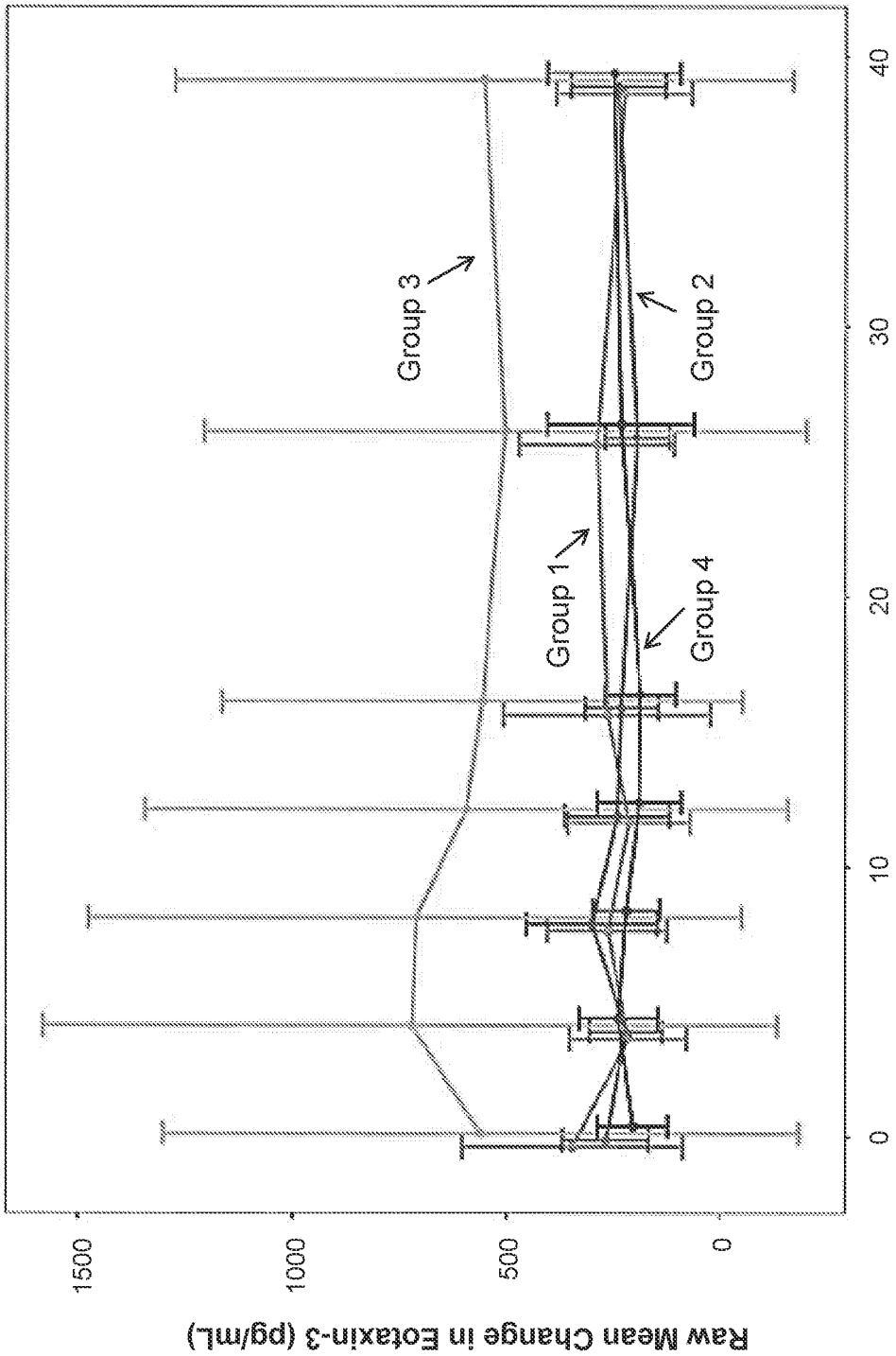

Raw Mean Change in Eotaxin-3 (pg/mL)
1500
1000
500
0
0
10
20
30
40
Group 1
Group 2
Group 3
Group 4

FIG. 11F

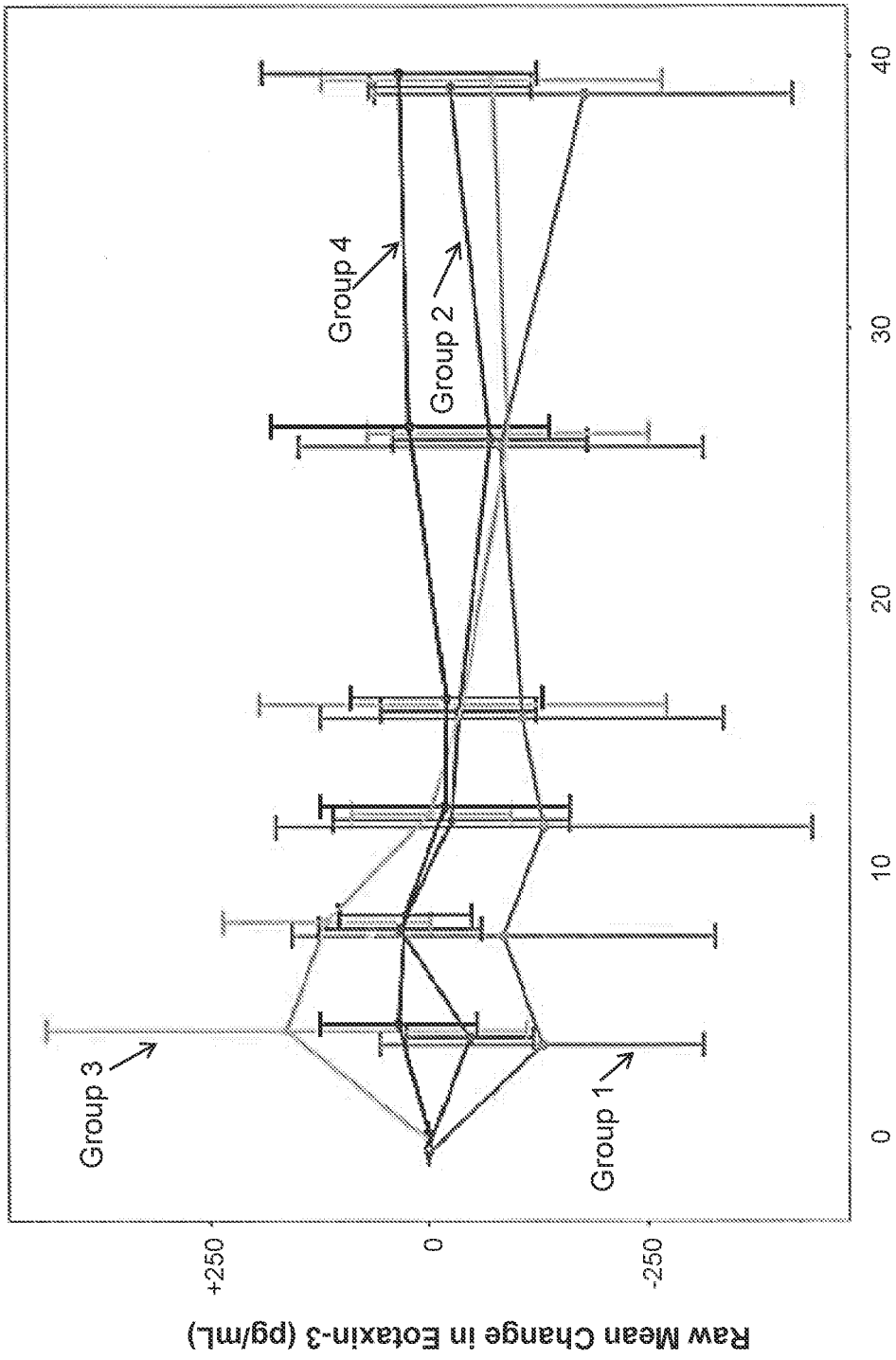

Raw Mean Change in Eotaxin-3 (pg/mL)
+250
0
-250
0
10
20
30
40
Group 1
Group 2
Group 3
Group 4

FIG. 11G

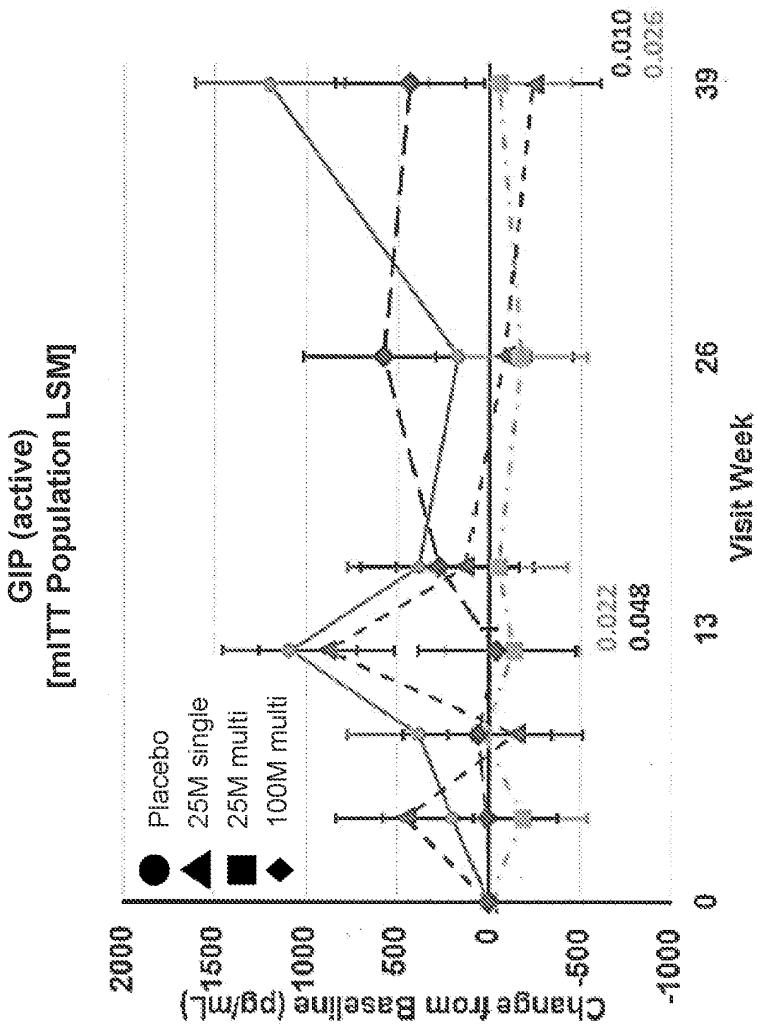

GIP (active)
[mITT Population LSM]
Placebo
25M single
25M multi
100M multi
Change from Baseline (pg/mL)
2000
1500
1000
500
0
-500
-1000
0
13
26
39
Visit Week
0.022
0.048
0.010
0.026

FIG. 12A

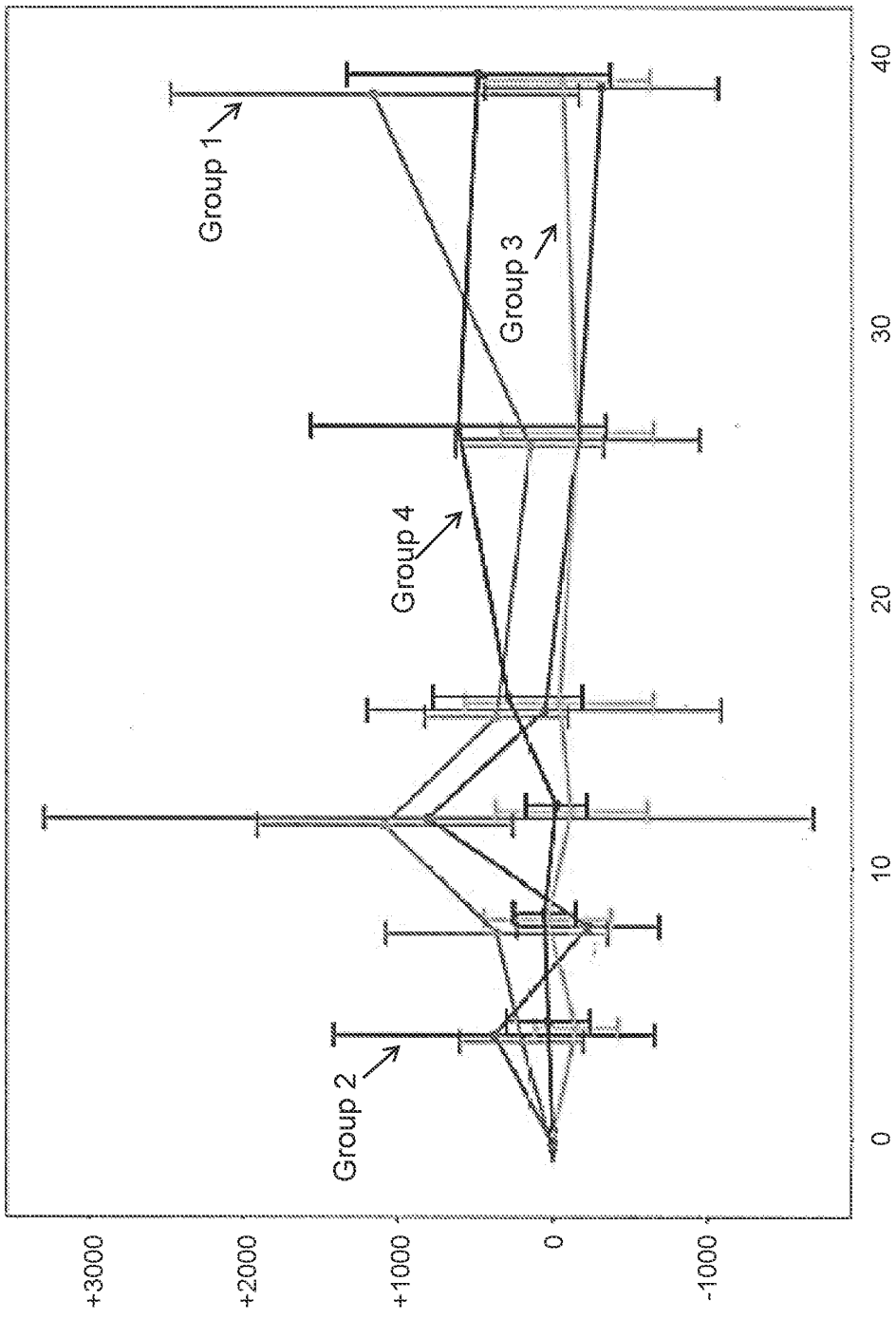

Raw Mean Change in Glucose-dep Insulinotropic Pep, Active, (pg/mL)
+3000
+2000
+1000
0
-1000
0
10
20
30
40
Group 1
Group 2
Group 3
Group 4

FIG. 12B

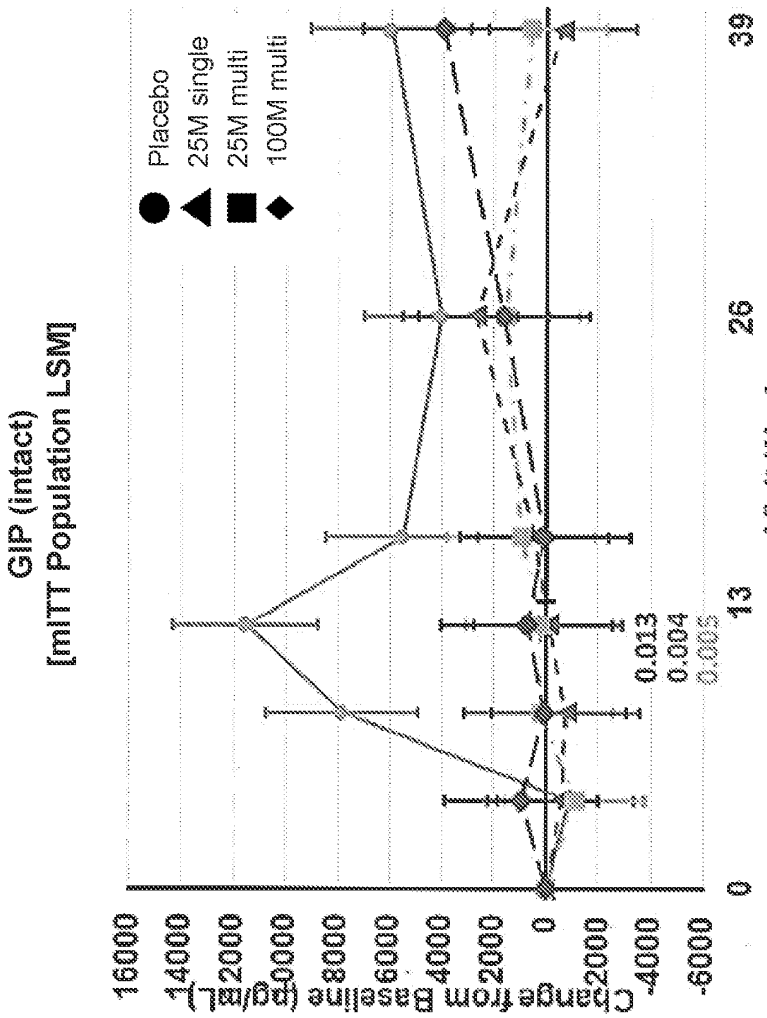

GIP (intact)
[mITT Population LSM]
Placebo
25M single
25M multi
100M multi
Change from Baseline (pg/mL)
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
-4000
-6000
0.013
0.004
0.005
0
13
26
39
Visit Week

FIG. 12C

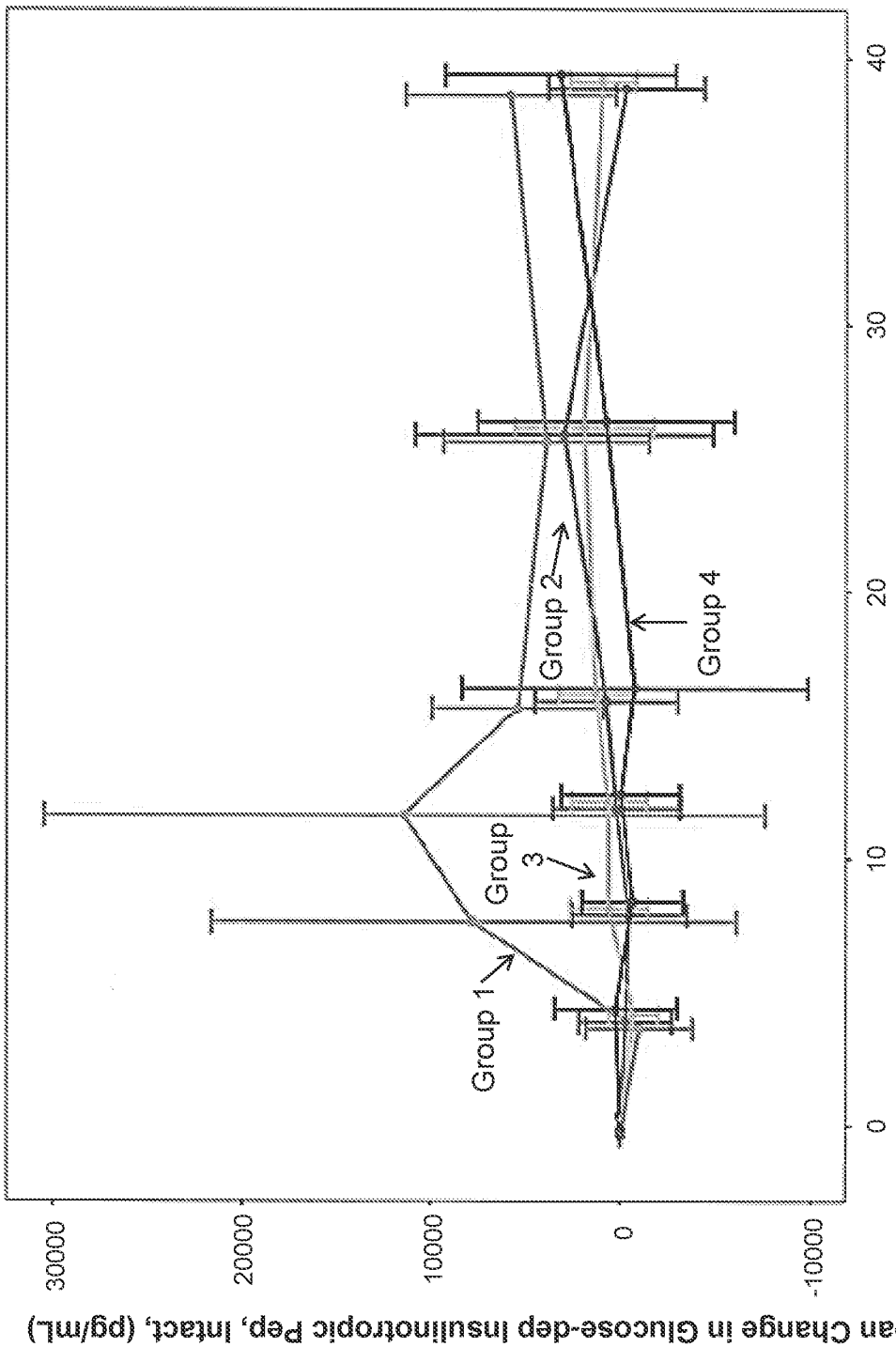

Raw Mean Change in Glucose-dep Insulinotropic Pep, Intact, (pg/mL)
30000
20000
10000
0
-10000
0
10
20
30
40
Group 1
Group 3
Group 2
Group 4

FIG. 12D

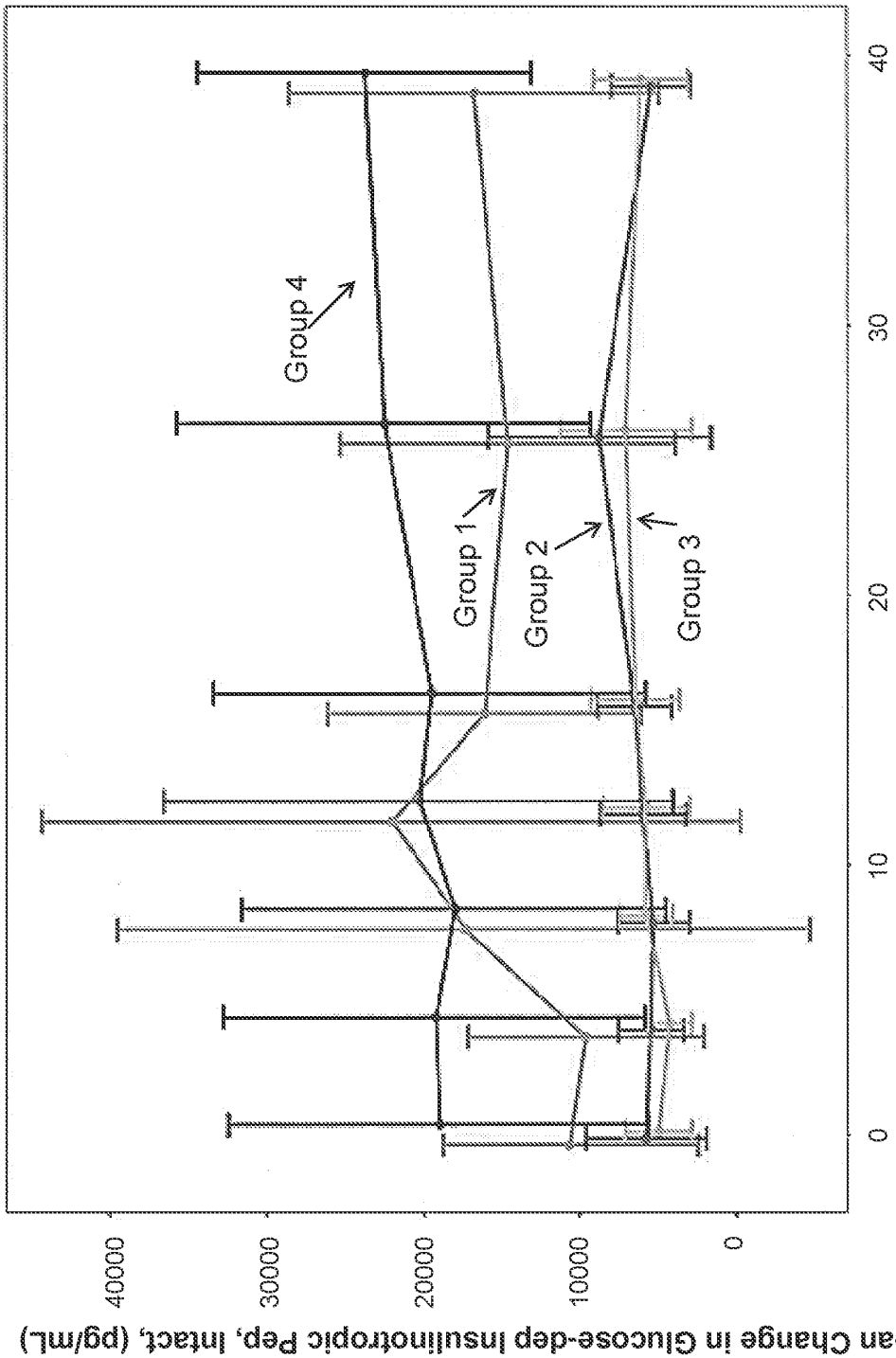

Raw Mean Change in Glucose-dep Insulinotropic Pep, Intact, (pg/mL)
40000
30000
20000
10000
0
0
10
20
30
40
Group 1
Group 2
Group 3
Group 4

FIG. 12E

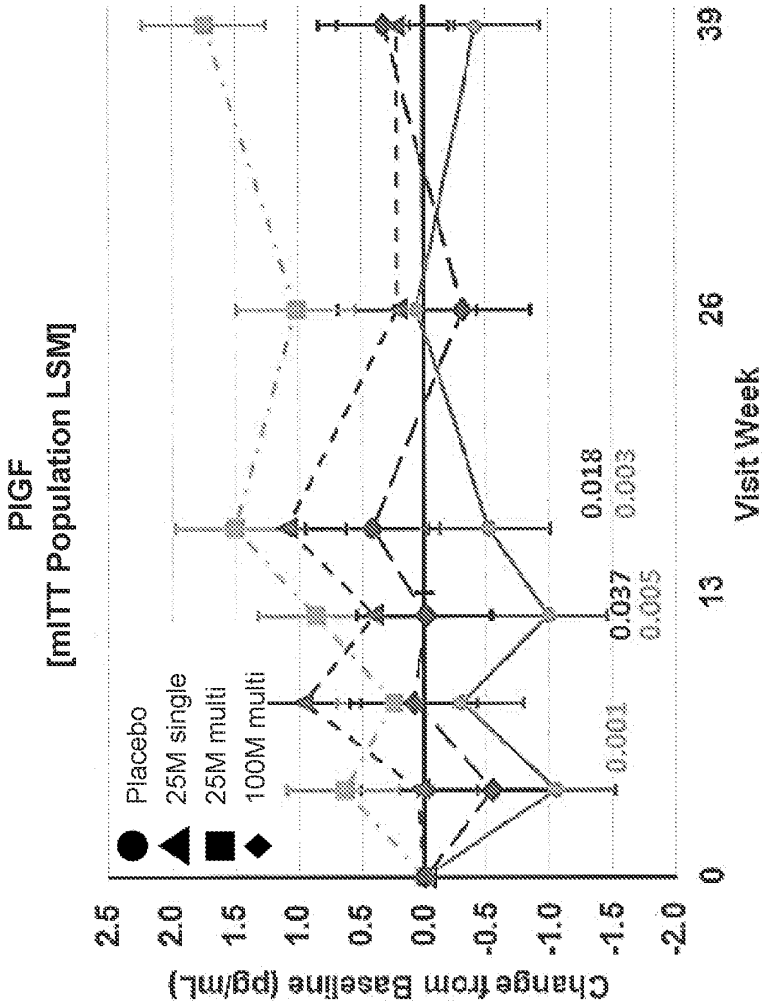

PlGF
[mITT Population LSM]
Placebo
25M single
25M multi
100M multi
Change from Baseline (pg/mL)
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
-1.5
-2.0
0
13
26
39
Visit Week
0.018
0.003
0.037
0.005
0.001

FIG. 12F

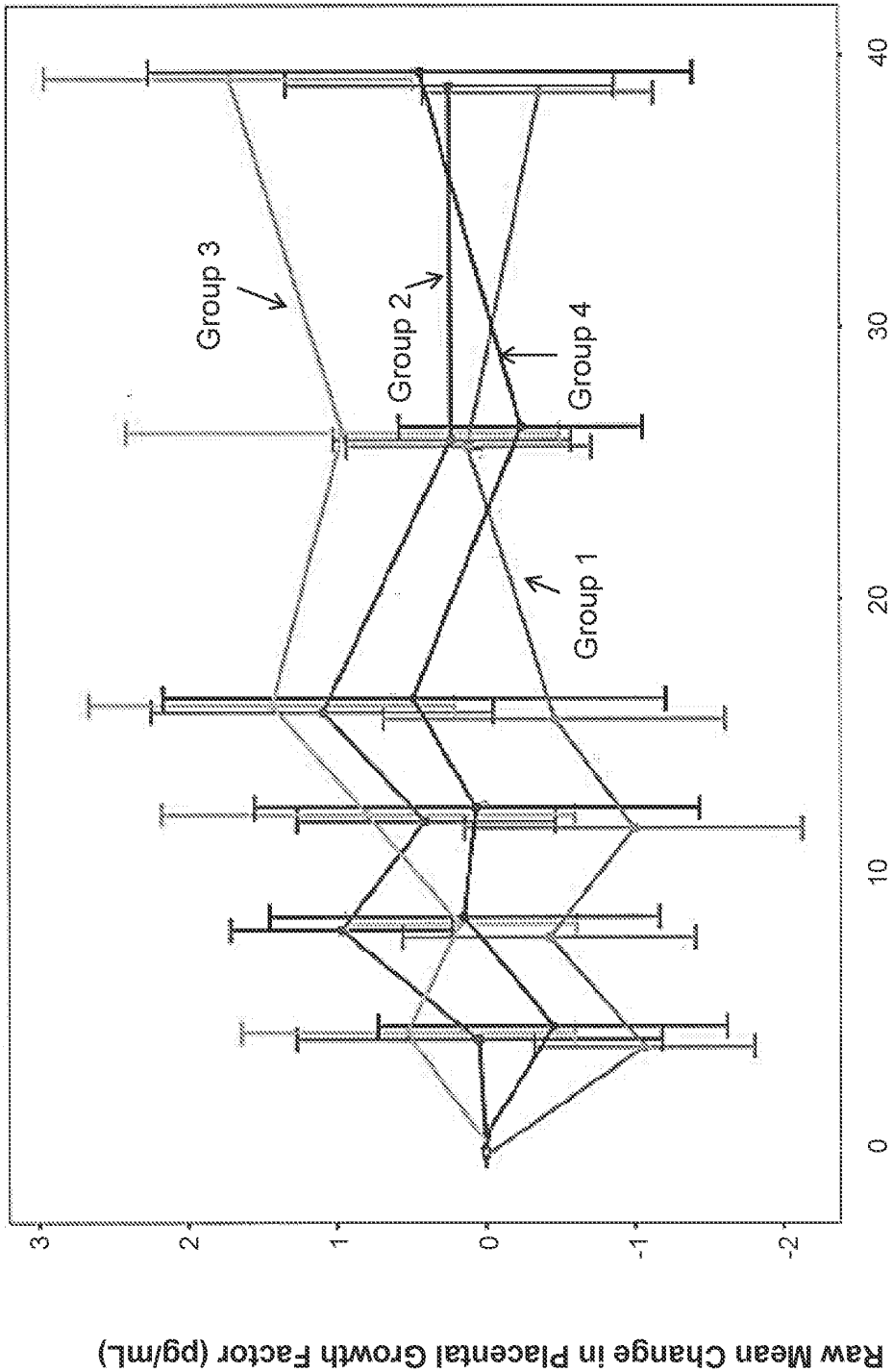

Raw Mean Change in Placental Growth Factor (pg/mL)
3
2
1
0
-1
-2
0
10
20
30
40
Group 1
Group 2
Group 3
Group 4

FIG. 12G

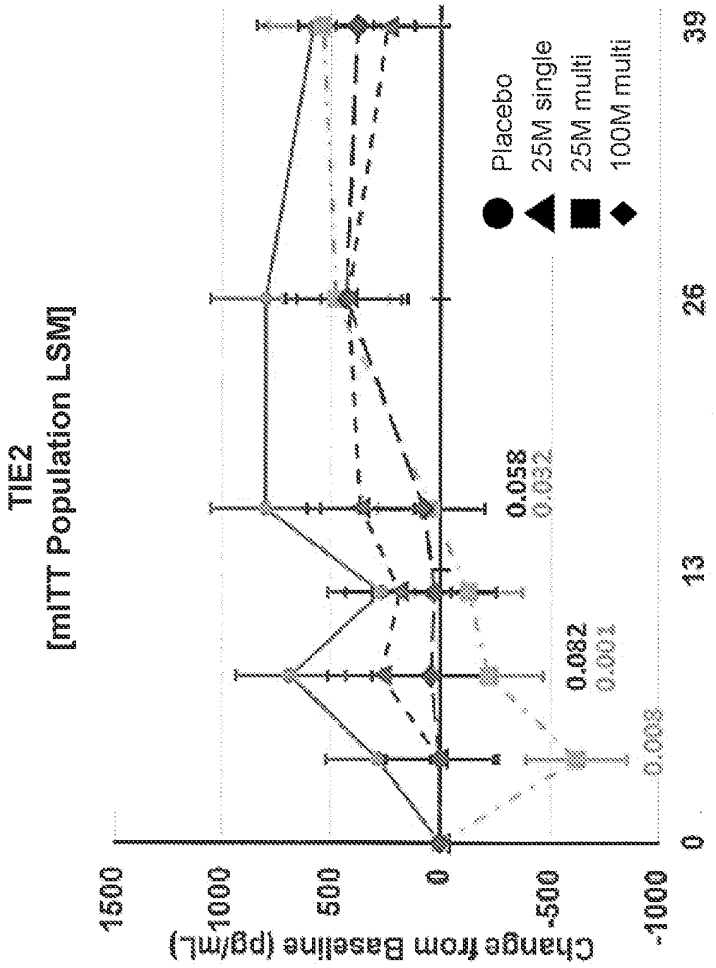

TIE2
[mITT Population LSM]
Change from Baseline (pg/mL)
1500
1000
500
0
-500
-1000
0
13
26
39
Visit Week
Placebo
25M single
25M multi
100M multi
0.058
0.032
0.082
0.001
0.008

FIG. 13A

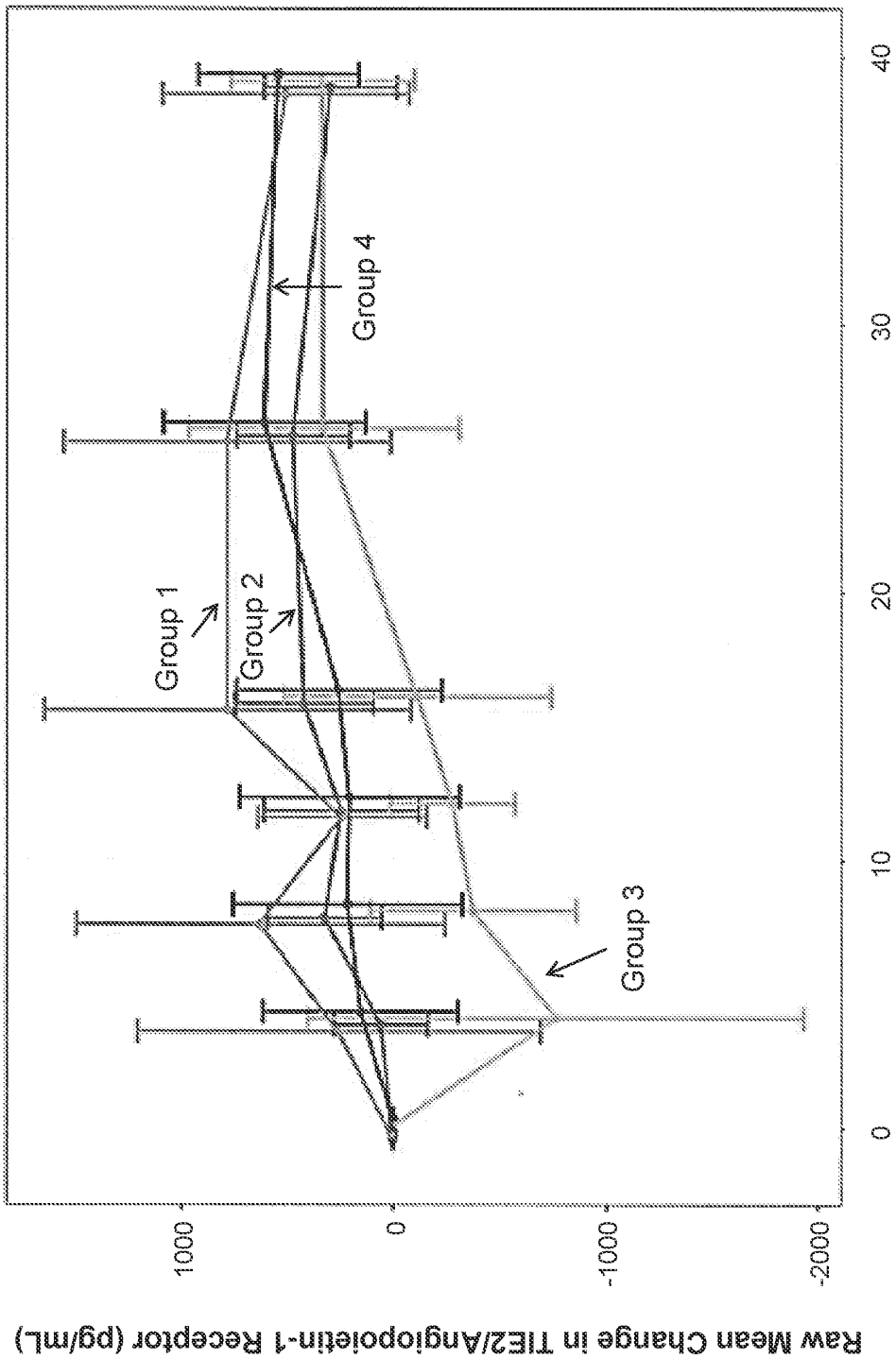

Raw Mean Change in TIE2/Angiopoietin-1 Receptor (pg/mL)
1000
0
-1000
-2000
0
10
20
30
40
Group 1
Group 2
Group 3
Group 4

FIG. 13B

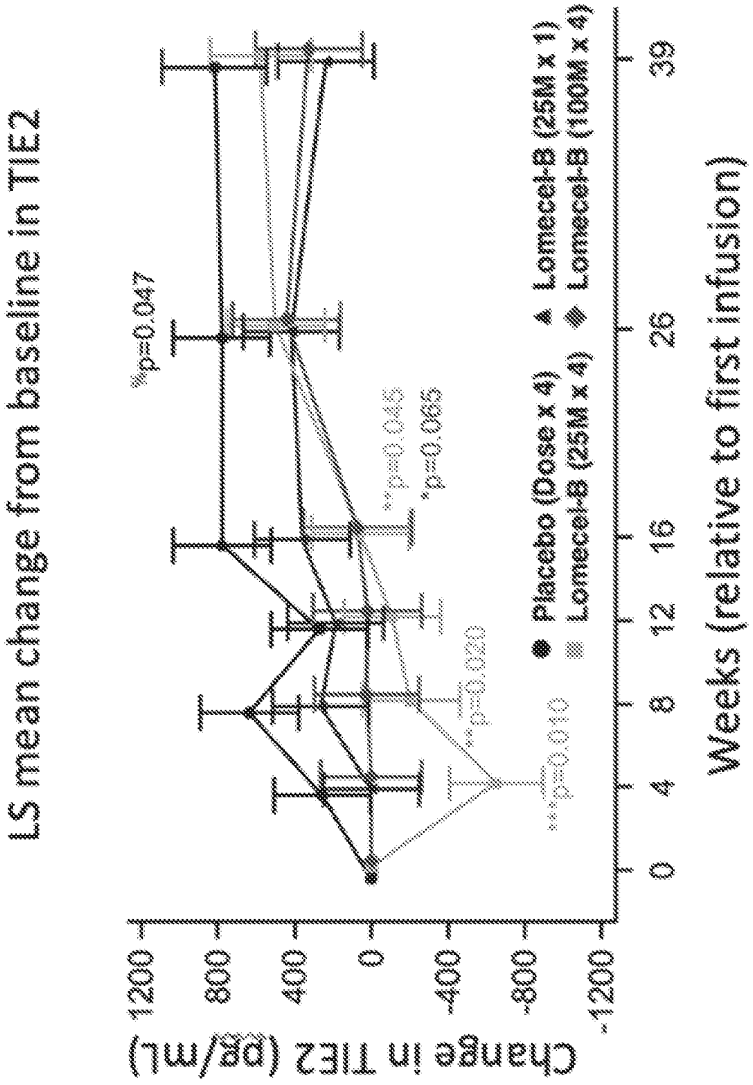
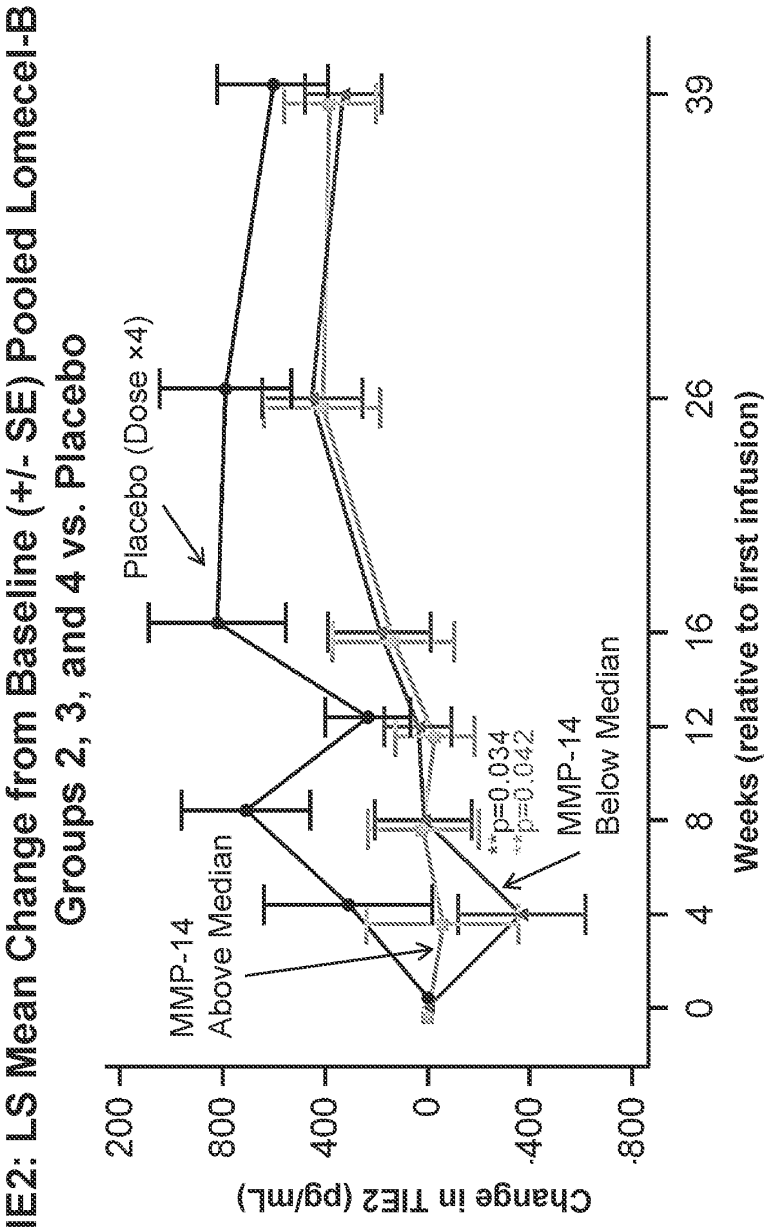
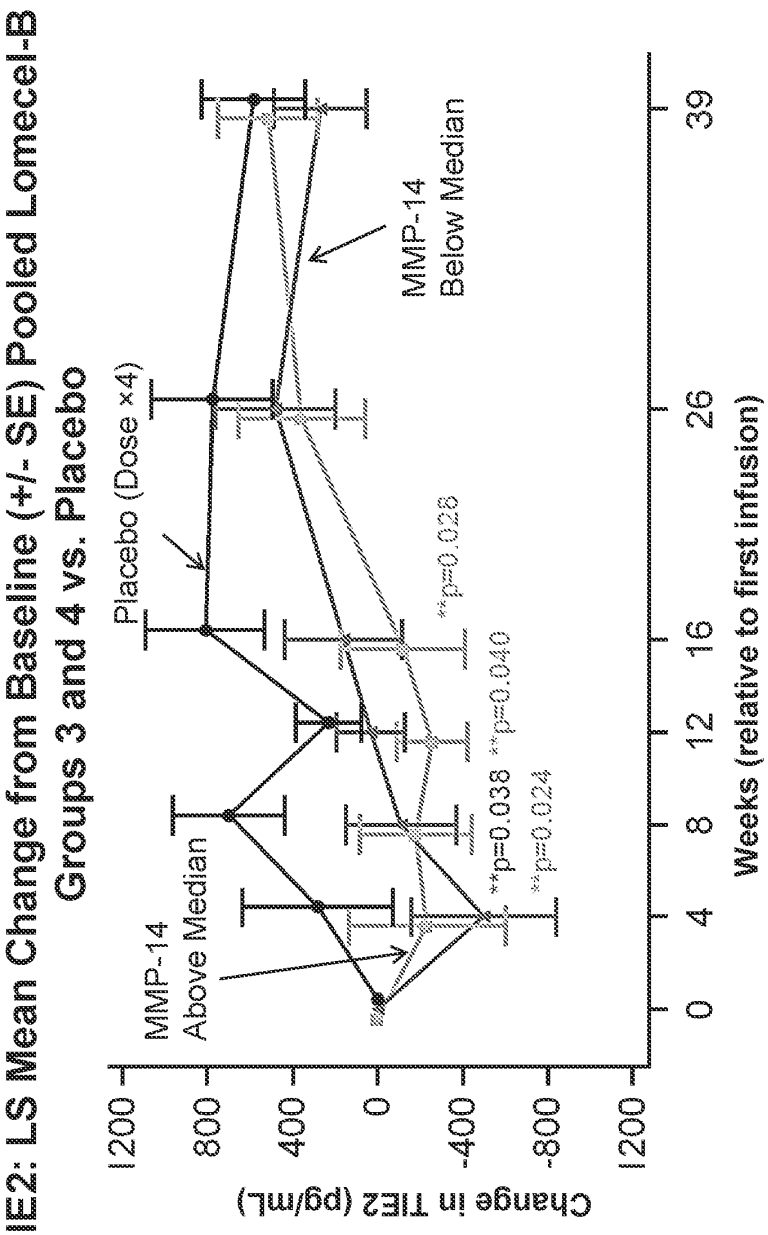

LS mean change from baseline in TIE2
Change in TIE2 (pg/mL)
1200
800
400
0
-400
-800
-1200
0
4
8
12
16
26
39
Weeks (relative to first infusion)
Placebo (Dose x 4)
Lomecel-B (25M x 1)
Lomecel-B (25M x 4)
Lomecel-B (100M x 4)
*p=0.047
*p=0.045
*p=0.065
*p=0.020
**p=0.010

FIG. 13C




Statistical significance is indicated as follows: *p<0.1, **p<0.05, ***p<0.01, ****p<0.001

FIG. 13D




Statistical significance is indicated as follows: *p<0.1, **p<0.05, ***p<0.01, ****p<0.001

FIG. 13E

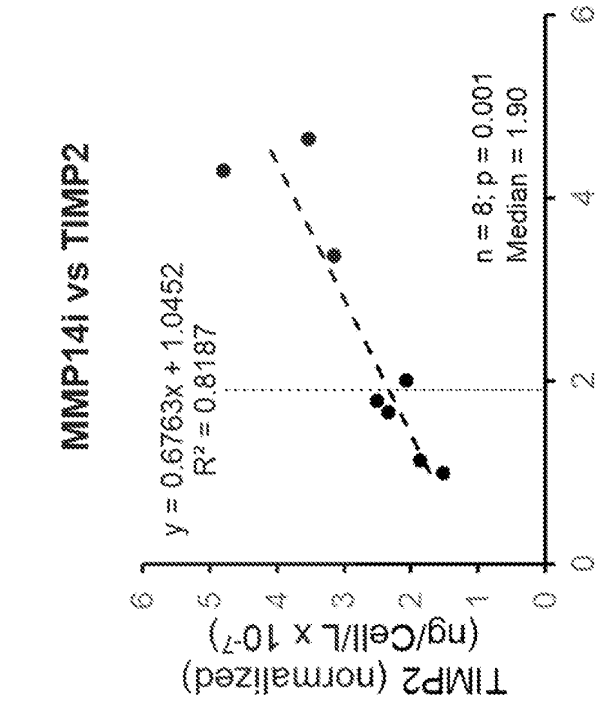



FIG. 14B

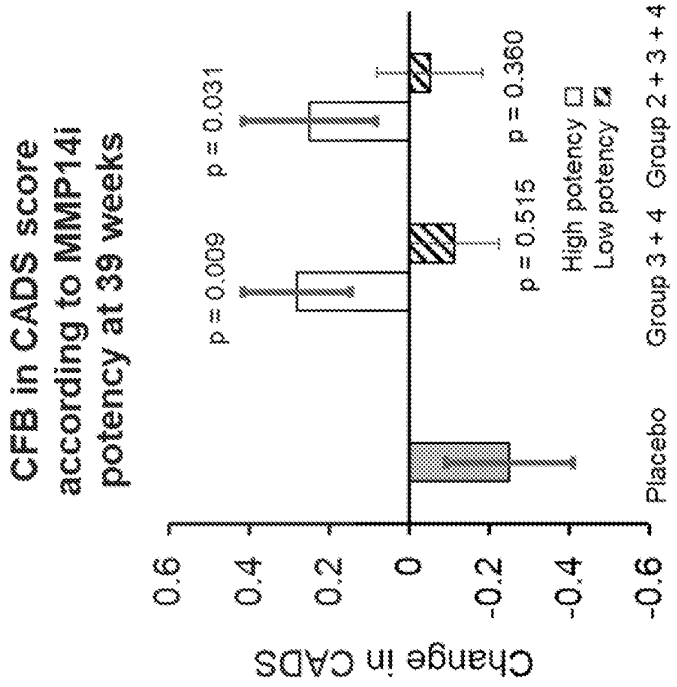



FIG. 14A

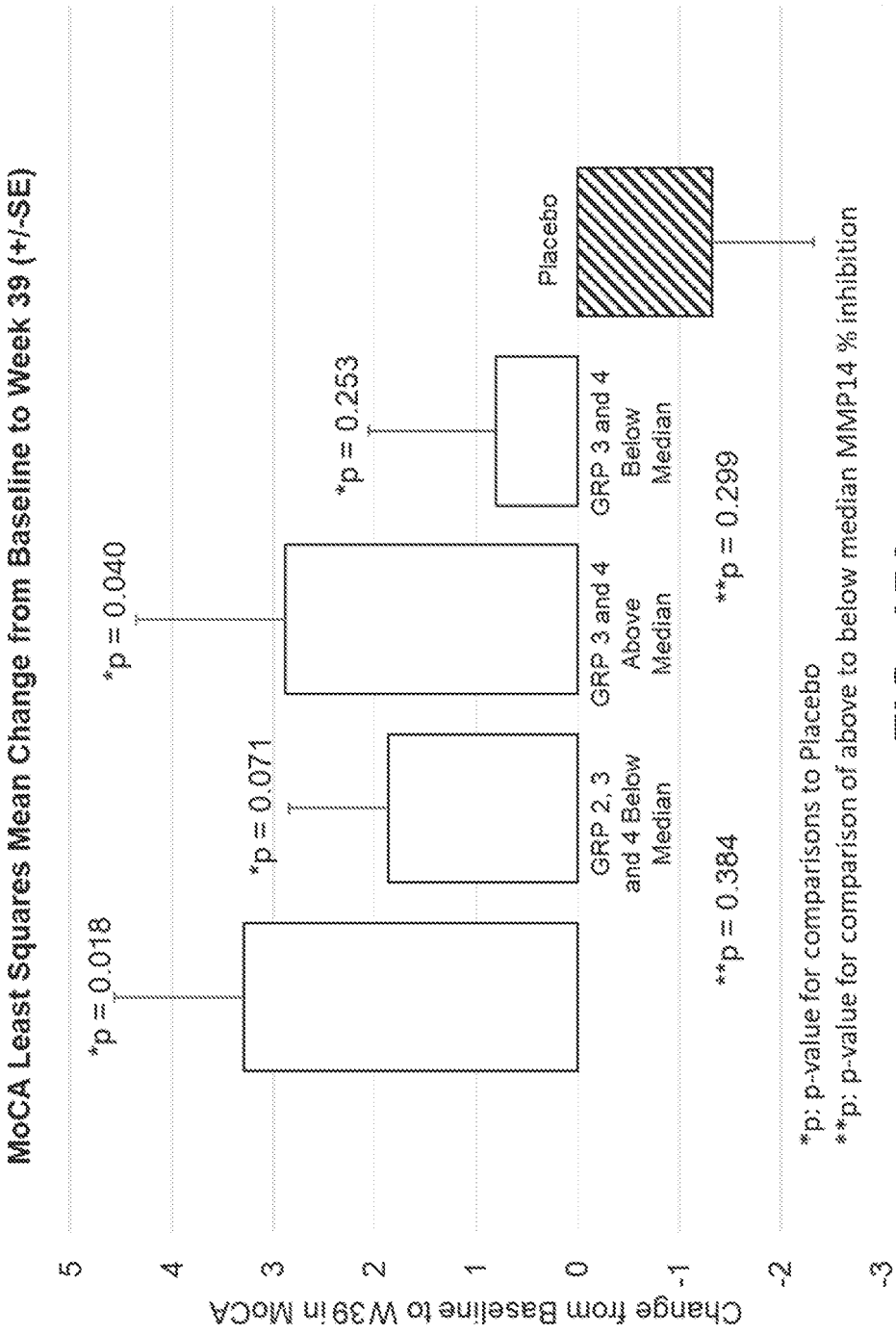

MoCA Least Squares Mean Change from Baseline to Week 39 (+/-SE)
Change from Baseline to W39 in MoCA
5
4
3
2
1
0
-1
-2
-3
*p = 0.018
*p = 0.071
*p = 0.040
*p = 0.253
**p = 0.384
**p = 0.299
GRP 2, 3 and 4 Below Median
GRP 3 and 4 Above Median
GRP 3 and 4 Below Median
Placebo
*p: p-value for comparisons to Placebo
**p: p-value for comparison of above to below median MMP14 % inhibition

FIG. 15A

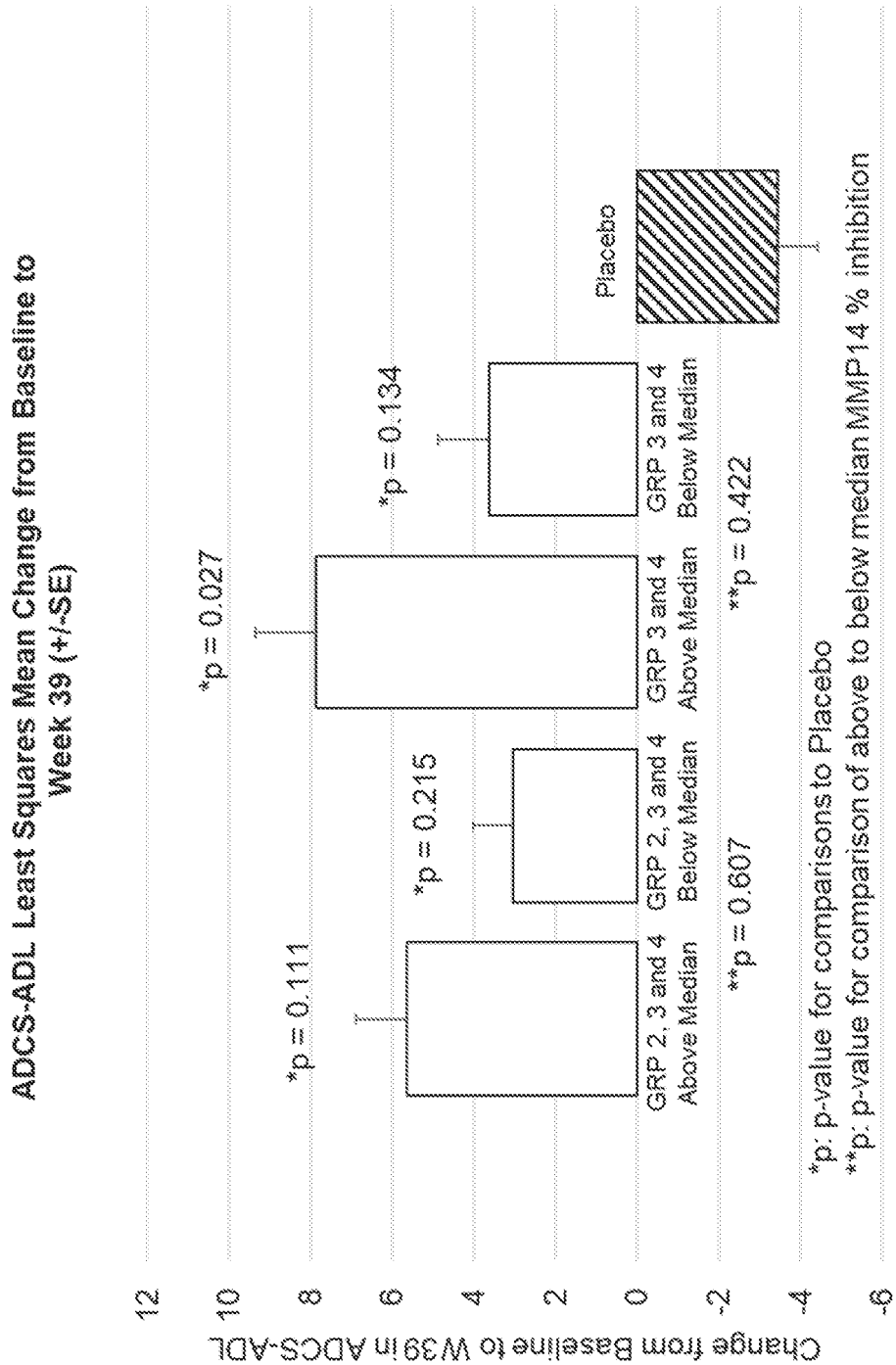

ADCS-ADL Least Squares Mean Change from Baseline to Week 39 (+/-SE)
Change from Baseline to W39 in ADCS-ADL
12
10
8
6
4
2
0
-2
-4
-6
*p = 0.111
*p = 0.027
*p = 0.215
*p = 0.134
**p = 0.607
**p = 0.422
GRP 2, 3 and 4 Above Median
GRP 2, 3 and 4 Below Median
GRP 3 and 4 Above Median
GRP 3 and 4 Below Median
Placebo
*p: p-value for comparisons to Placebo
**p: p-value for comparison of above to below median MMP14 % inhibition

FIG. 15B

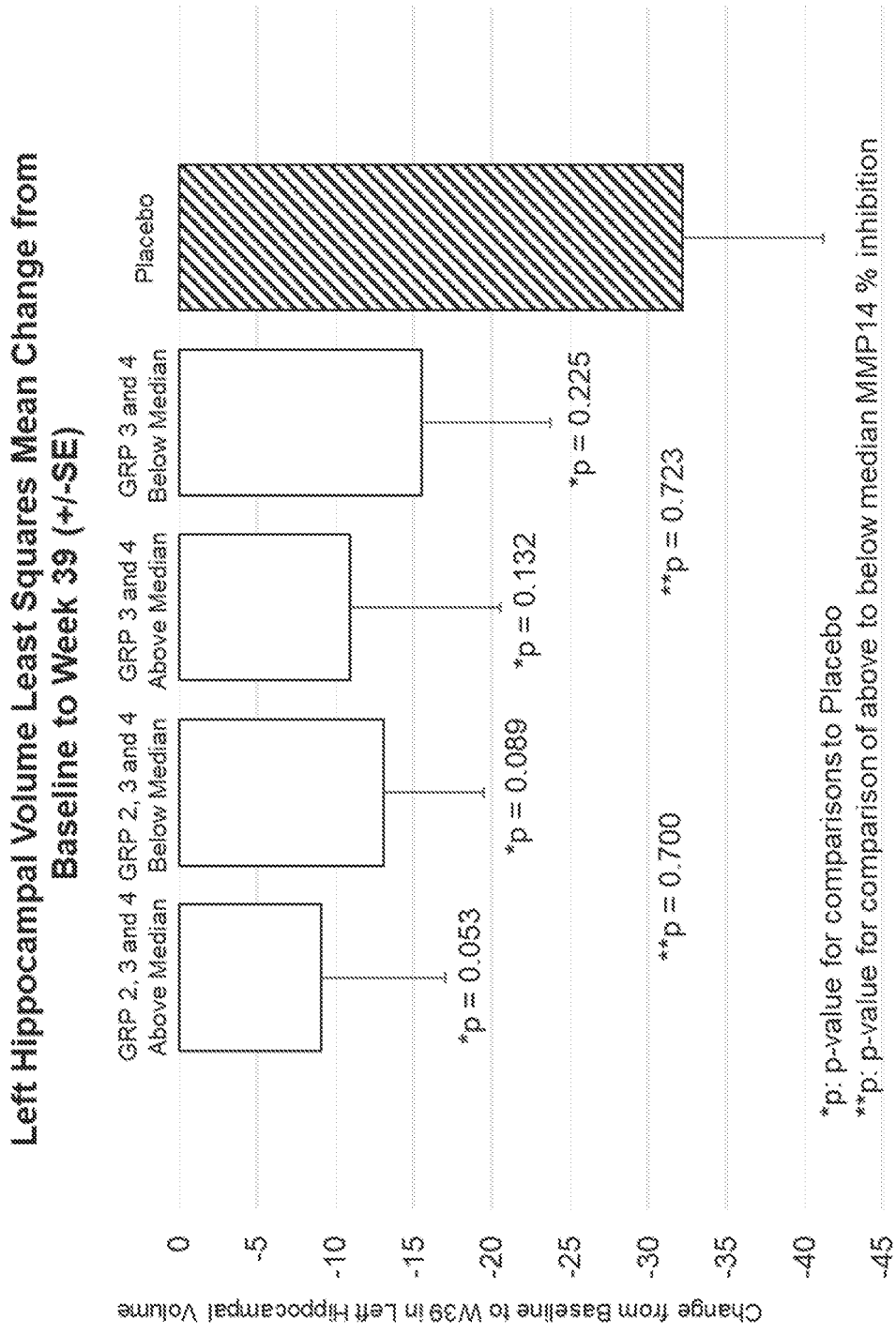
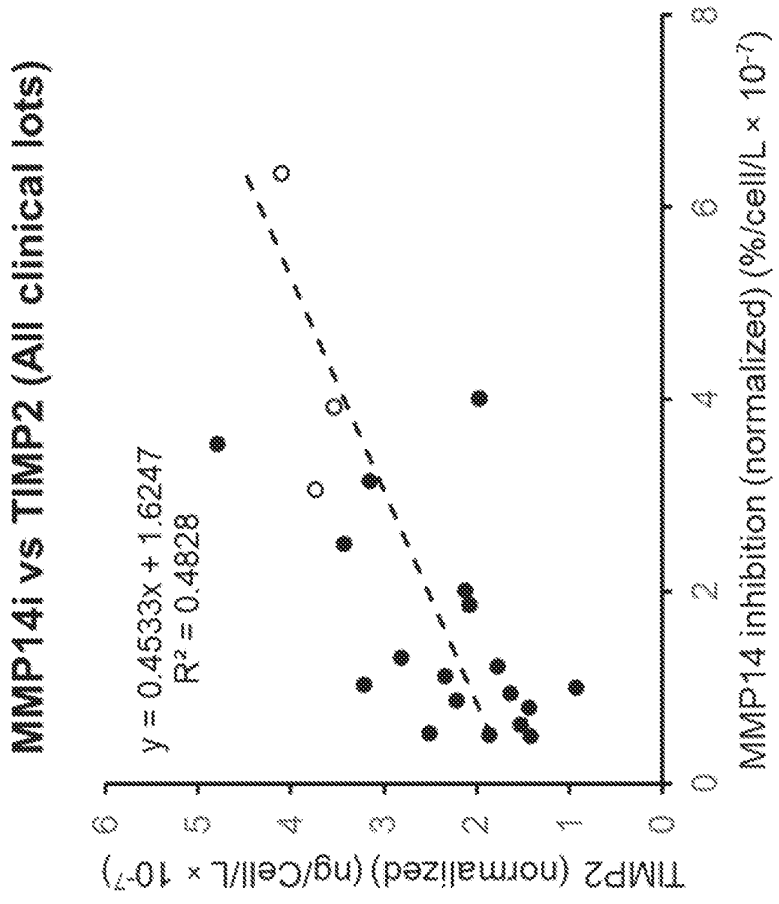
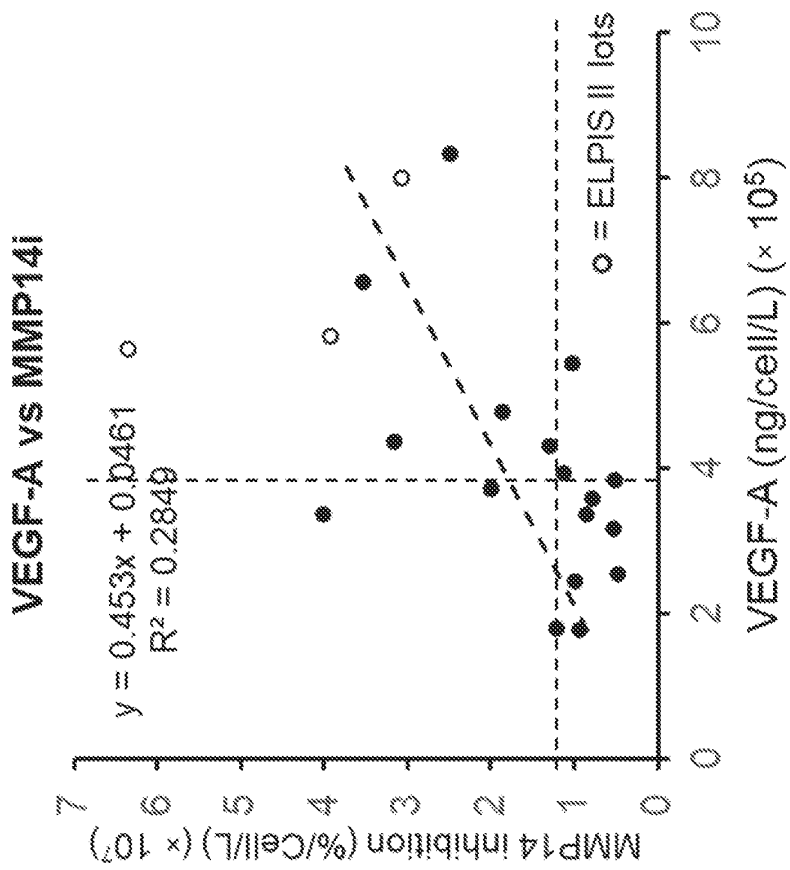

Left Hippocampal Volume Least Squares Mean Change from Baseline to Week 39 (+/-SE)
Change from Baseline to W39 in Left Hippocampal Volume
0
-5
-10
-15
-20
-25
-30
-35
-40
-45
GRP 2, 3 and 4 Above Median
GRP 2, 3 and 4 Below Median
GRP 3 and 4 Above Median
GRP 3 and 4 Below Median
Placebo
*p = 0.053
*p = 0.089
*p = 0.132
*p = 0.225
**p = 0.700
**p = 0.723
*p: p-value for comparisons to Placebo
**p: p-value for comparison of above to below median MMP14 % inhibition

FIG. 16




N = 21; p = 0.000473
MMP14i median = 1.22
TIMP2 median = 2.28

**FIG. 17A**




N = 20; p = 0.0153
MMP14i median = 1.26
VEGF-A median = 3.87

**FIG. 17B**

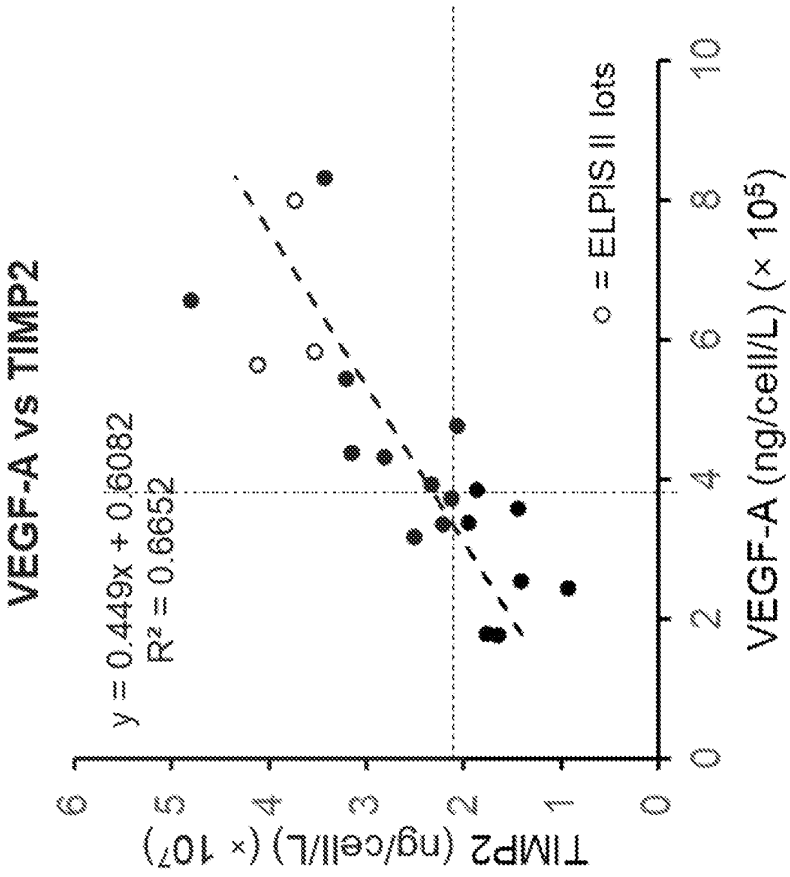

VEGF-A vs TIMP2
y = 0.449x + 0.6082
R² = 0.6652
○ = ELPIS II lots
TIMP2 (ng/cell/L) (× 10⁷)
VEGF-A (ng/cell/L) (× 10⁵)
0
1
2
3
4
5
6
0
2
4
6
8
10
N = 20; p = 0.0000117
TIMP2 median = 2.28
VEGF-A median = 3.87

FIG. 17C

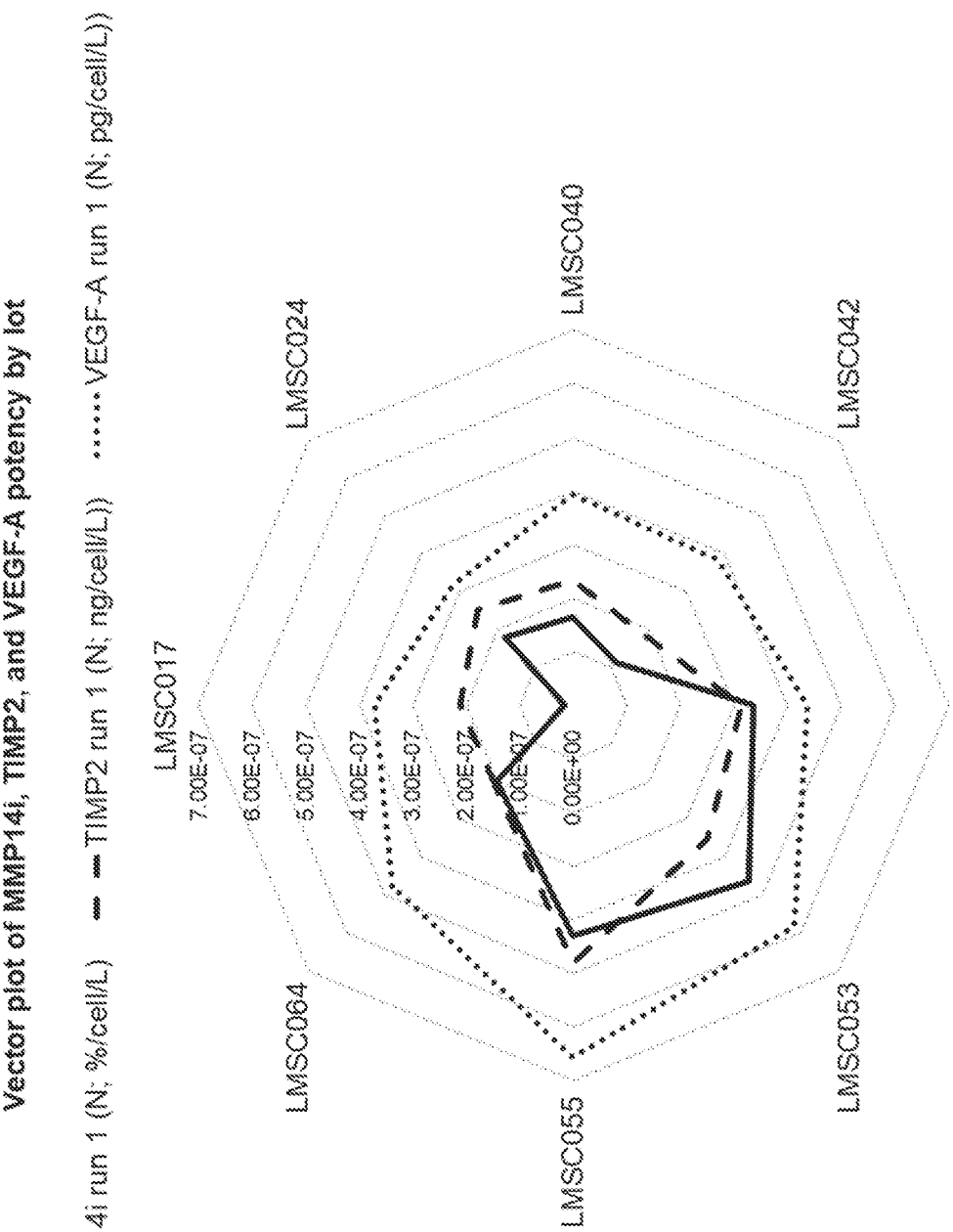

Vector plot of MMP14i, TIMP2, and VEGF-A potency by lot
MMP14i run 1 (N; %/cell/L)
TIMP2 run 1 (N; ng/cell/L))
VEGF-A run 1 (N; pg/cell/L))
LMSC017
LMSC024
LMSC040
LMSC042
LMSC045
LMSC053
LMSC055
LMSC064
7.00E-07
6.00E-07
5.00E-07
4.00E-07
3.00E-07
2.00E-07
1.00E-07
0.00E+00

FIG. 18

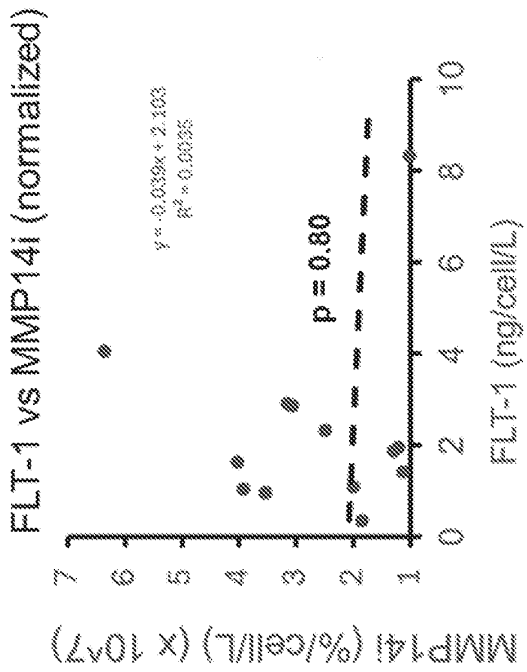



FIG. 19A

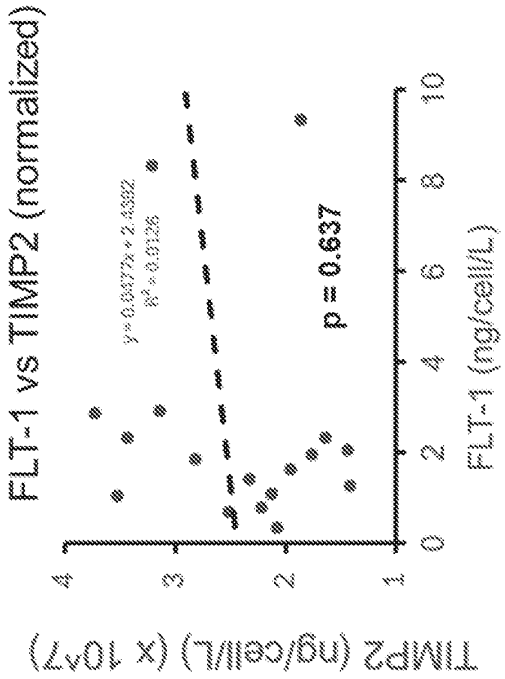
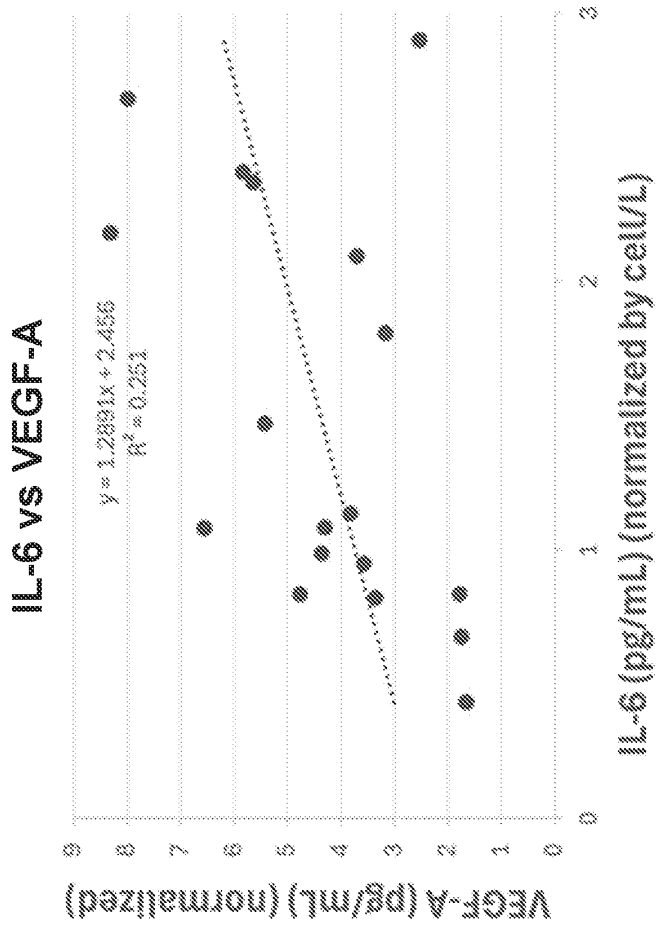



FIG. 19B




| P-value |
| --- |
| 0.01728242 |

FIG. 20A

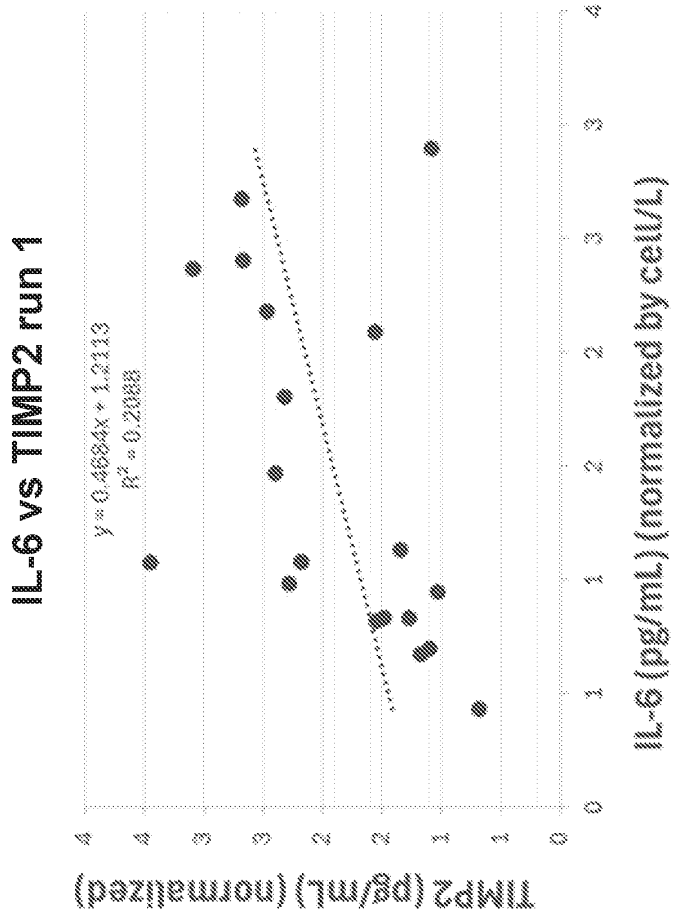

IL-6 vs TIMP2 run 1
y = 0.4884x + 1.2113
R² = 0.2088
TIMP2 (pg/mL) (normalized)
IL-6 (pg/mL) (normalized by cell/L)
P-value
0.003663176

FIG. 20B

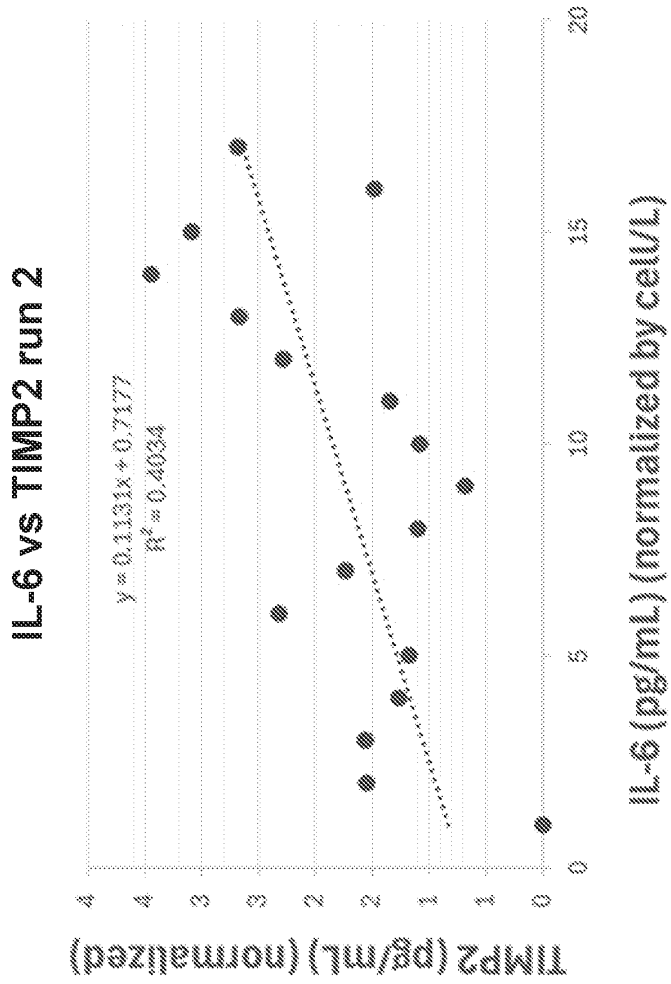
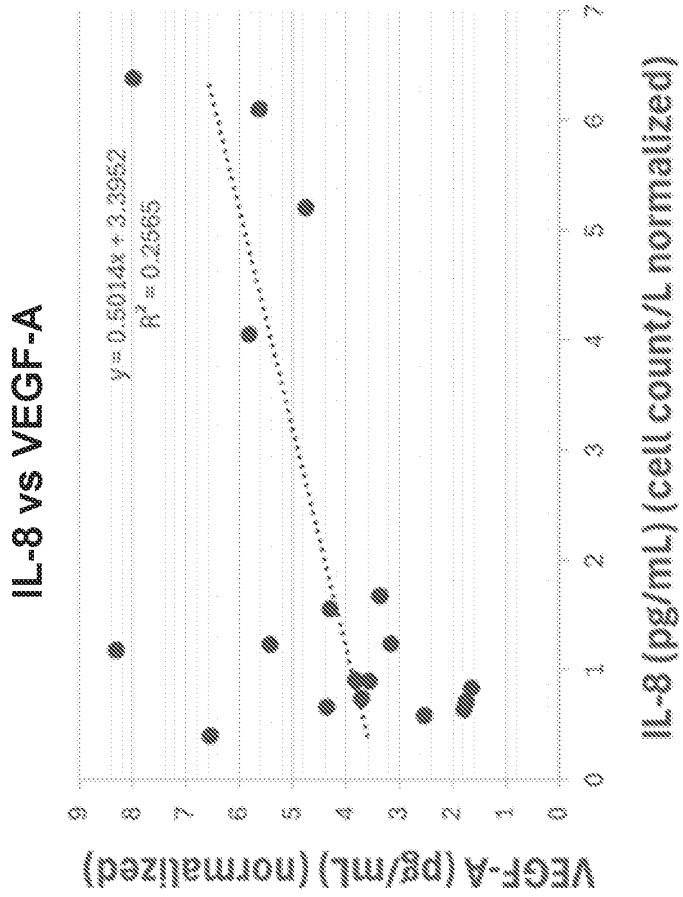

IL-6 vs TIMP2 run 2
y = 0.1131x + 0.7177
R² = 0.4034
TIMP2 (pg/mL) (normalized)
IL-6 (pg/mL) (normalized by cell/L)
0
1
2
3
4
5
10
15
20
P-value
0.0064594

FIG. 20C




| P-value |
| --- |
| 2.7474E-05 |

FIG. 21A

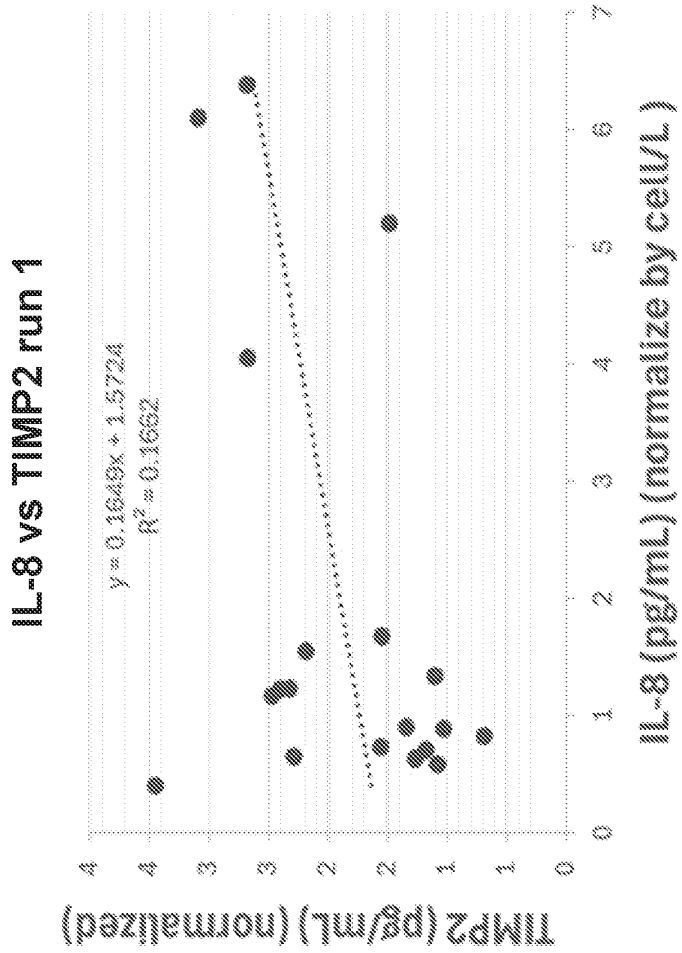

IL-8 vs TIMP2 run 1
y = 0.1649x + 1.5724
R² = 0.1662
TIMP2 (pg/mL) (normalized)
IL-8 (pg/mL) (normalize by cell/L)
0
1
2
3
4
5
6
7
P-value
5.8254E-06

FIG. 21B

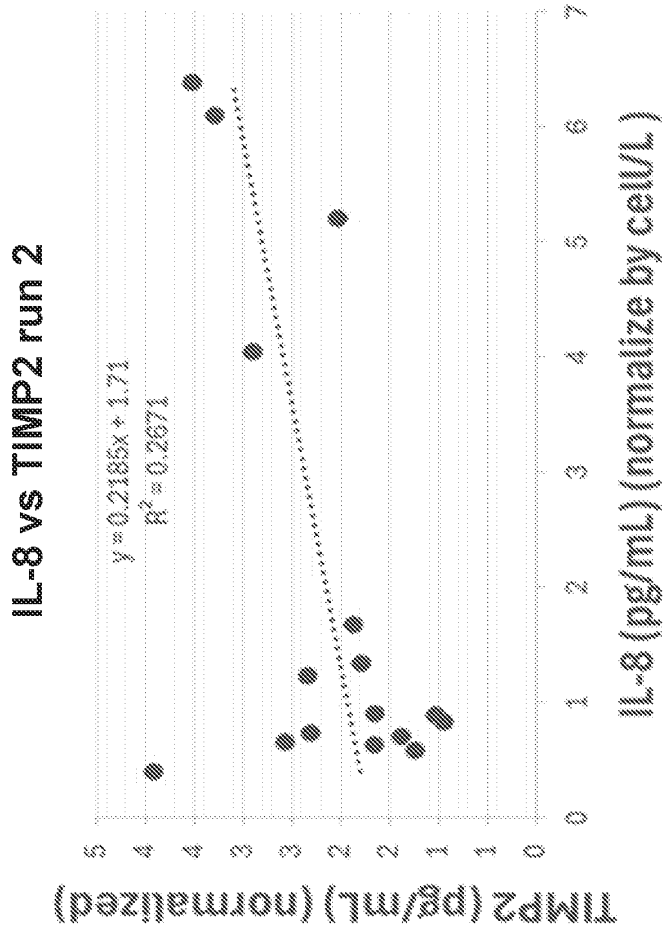

IL-8 vs TIMP2 run 2
y = 0.2185x + 1.71
R² = 0.2671
TIMP2 (pg/mL) (normalized)
IL-8 (pg/mL) (normalize by cell/L)
0
1
2
3
4
5
6
7
P-value
2.5329E-05

FIG. 21C