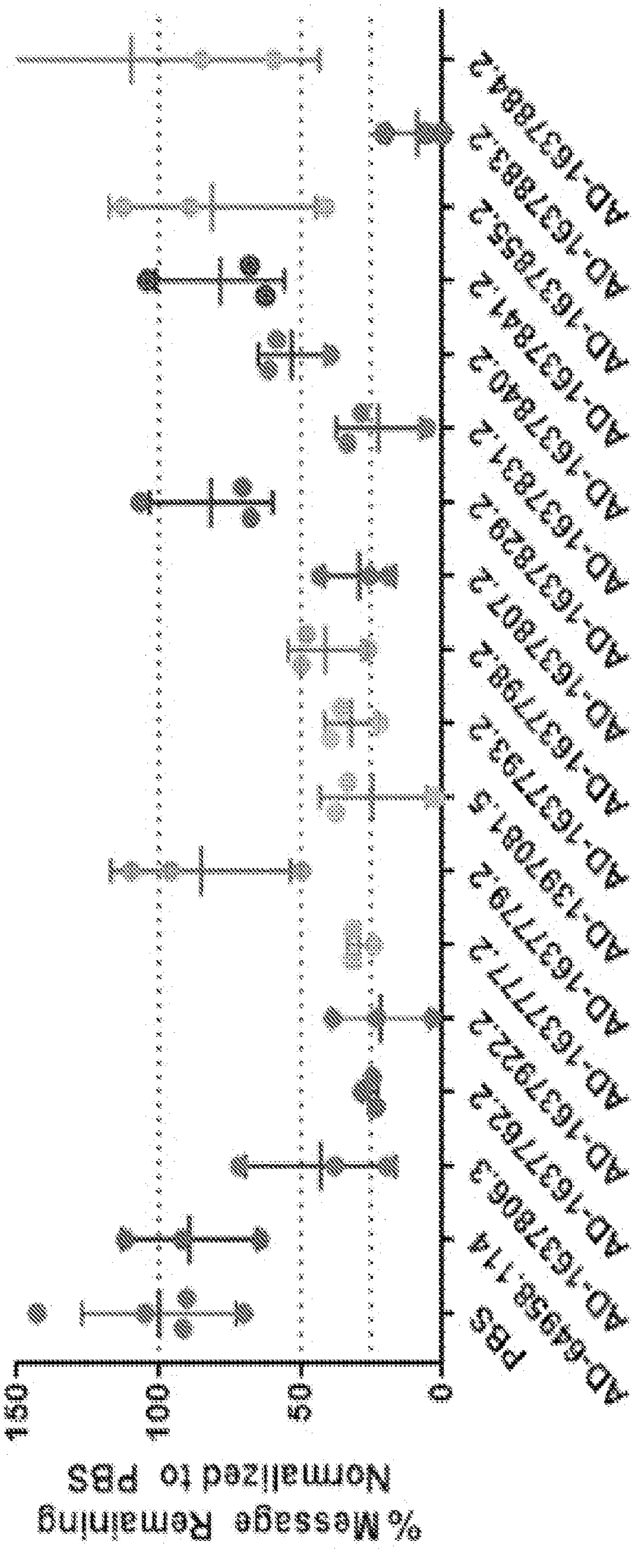
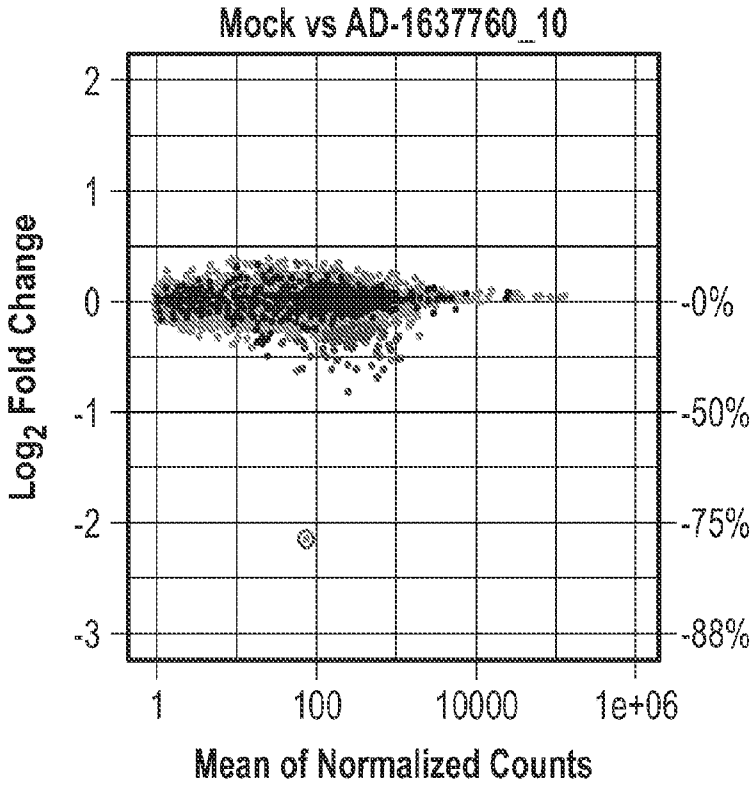

% Message Remaining
Normalized to PBS
150
100
50
0
PBS
AD-64958.114
AD-1637806.3
AD-1637762.2
AD-1637922.2
AD-1637772.2
AD-1637779.2
AD-1397081.5
AD-1637793.2
AD-1637798.2
AD-1637807.2
AD-1637829.2
AD-1637831.2
AD-1637840.2
AD-1637841.2
AD-1637855.2
AD-1637883.2
AD-1637884.2

FIG. 1


Mock vs AD-1637760_10
Log2 Fold Change
2
1
0
-1
-2
-3
-0%
-50%
-75%
-88%
1
100
10000
1e+06
Mean of Normalized Counts

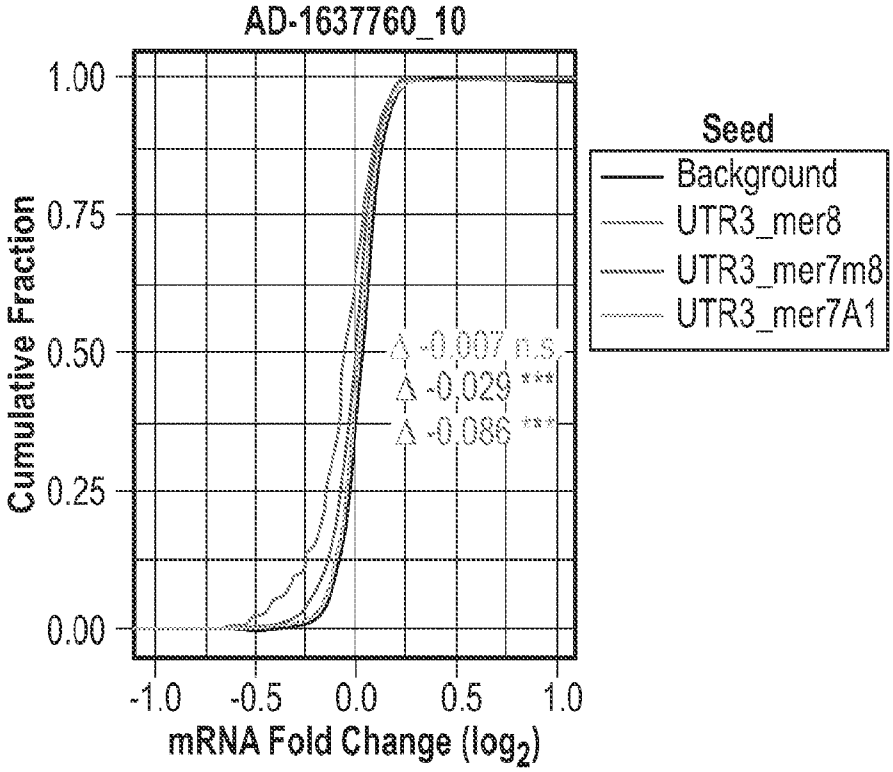
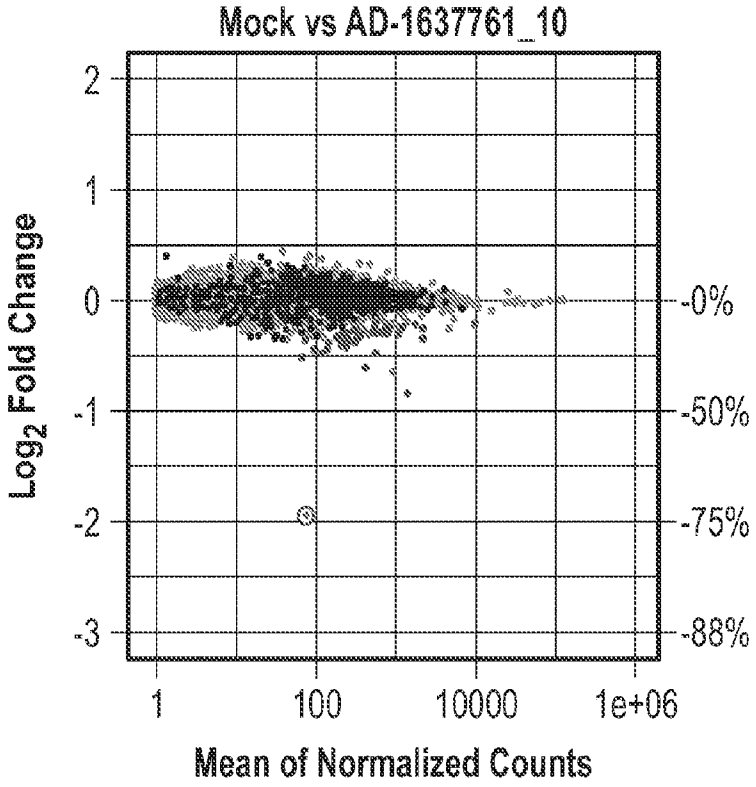

AD-1637760_10
Cumulative Fraction
1.00
0.75
0.50
0.25
0.00
-1.0
-0.5
0.0
0.5
1.0
mRNA Fold Change (log2)
Seed
Background
UTR3_mer8
UTR3_mer7m8
UTR3_mer7A1
Δ -0.007 n.s.
Δ -0.029 ***
Δ -0.086 ***

FIG. 2A



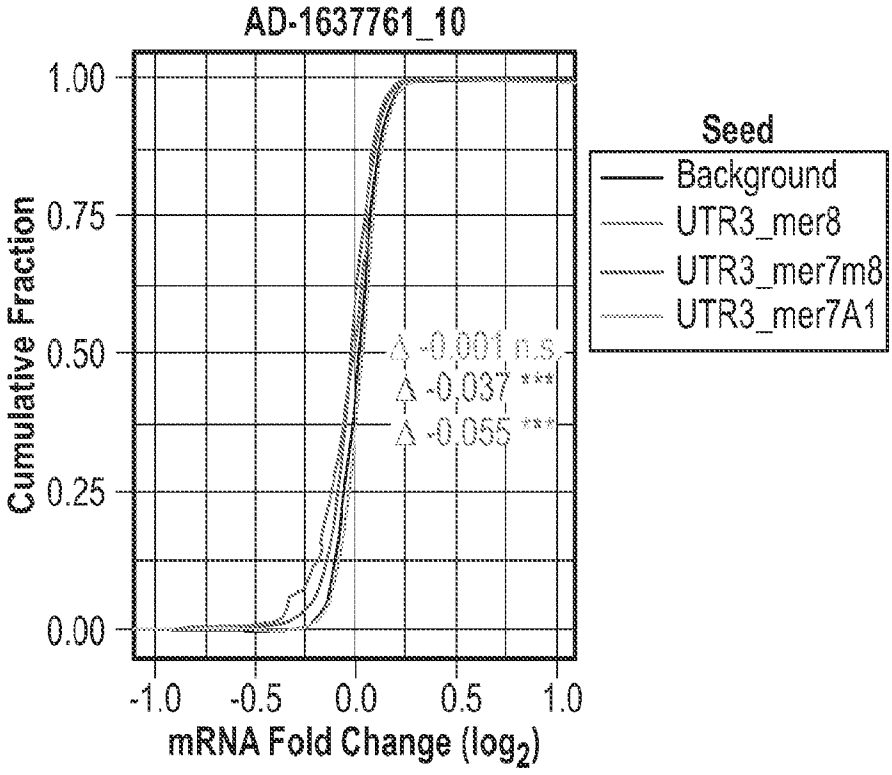
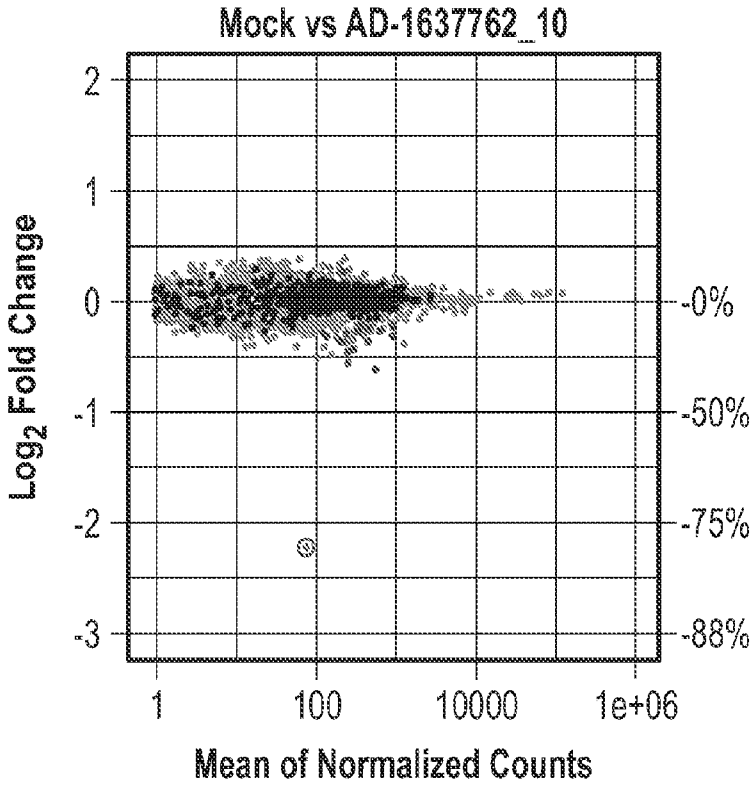


FIG. 2A
(Continued)



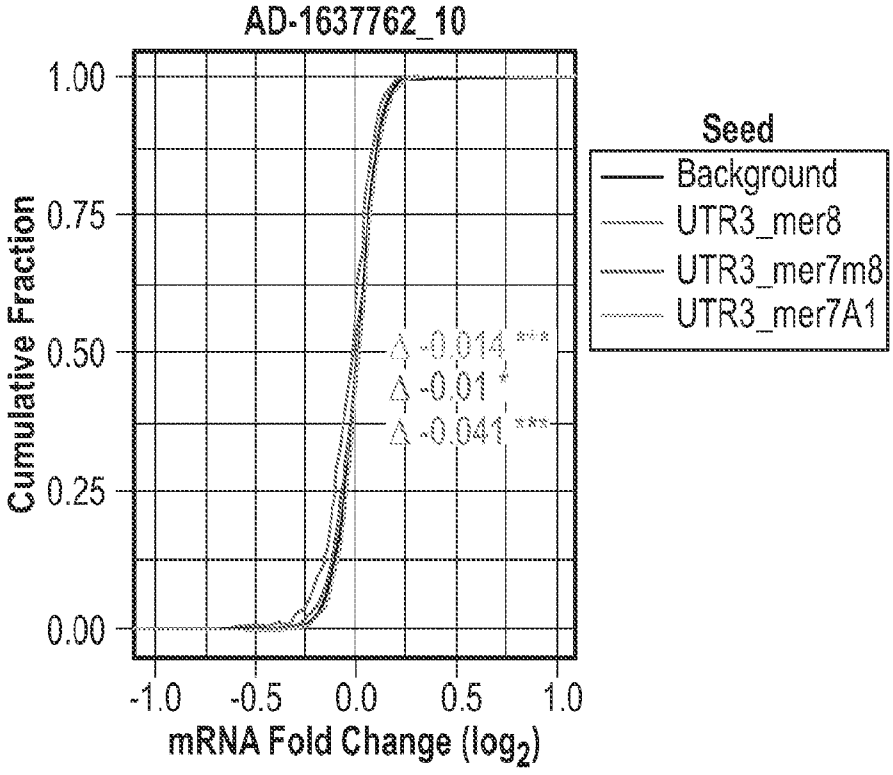
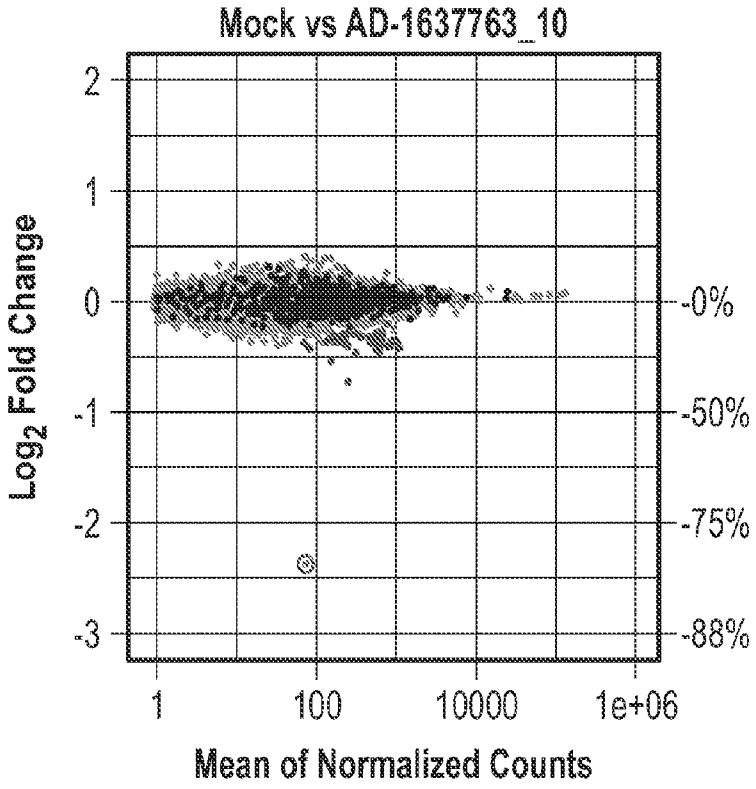


FIG. 2A
(Continued)


Mock vs AD-1637763_10
Log2 Fold Change
2
1
0
-1
-2
-3
-0%
-50%
-75%
-88%
1
100
10000
1e+06
Mean of Normalized Counts

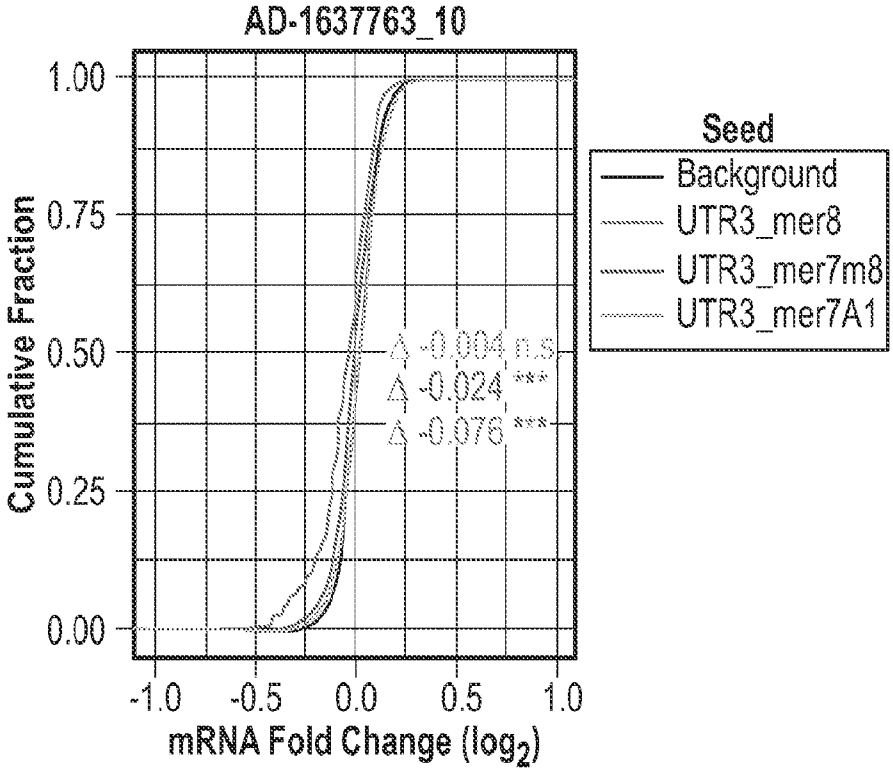
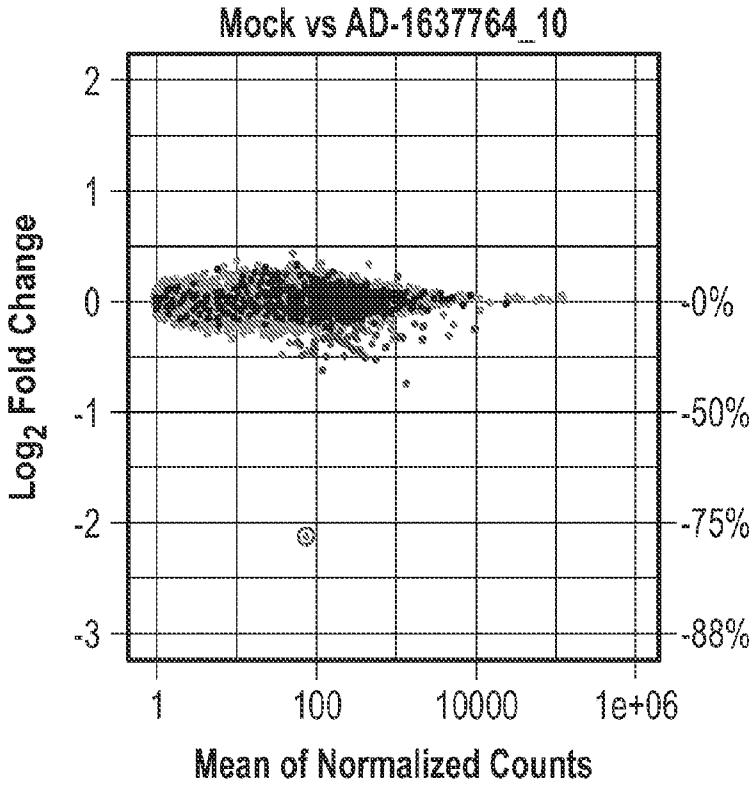

AD-1637763_10
Cumulative Fraction
1.00
0.75
0.50
0.25
0.00
-1.0
-0.5
0.0
0.5
1.0
mRNA Fold Change (log2)
Seed
Background
UTR3_mer8
UTR3_mer7m8
UTR3_mer7A1
Δ -0.004 n.s
Δ -0.024 **
Δ -0.076 ***

FIG. 2B



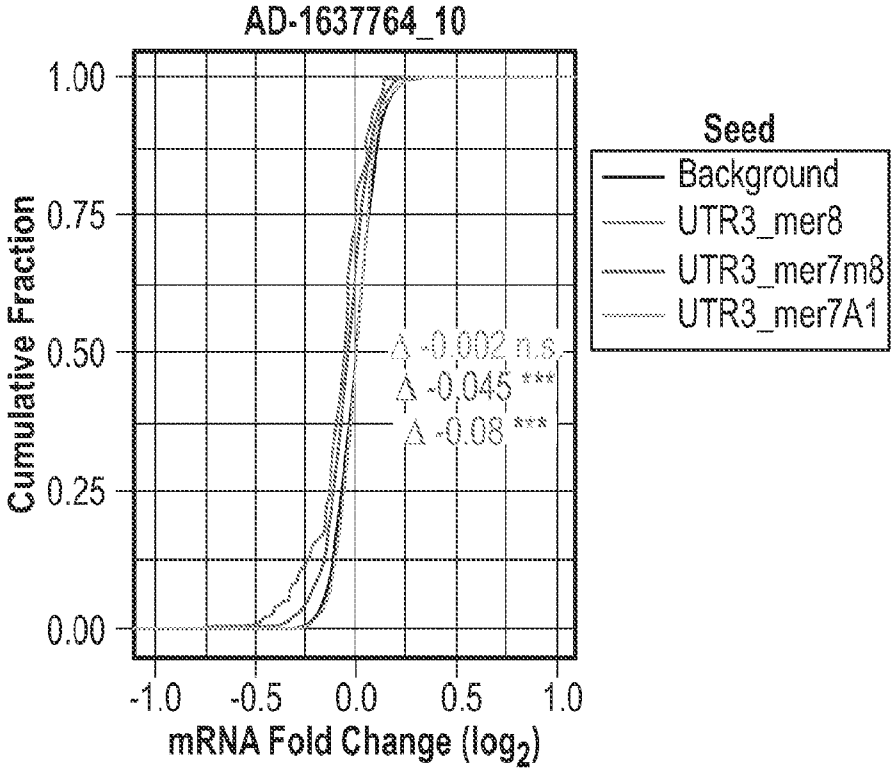
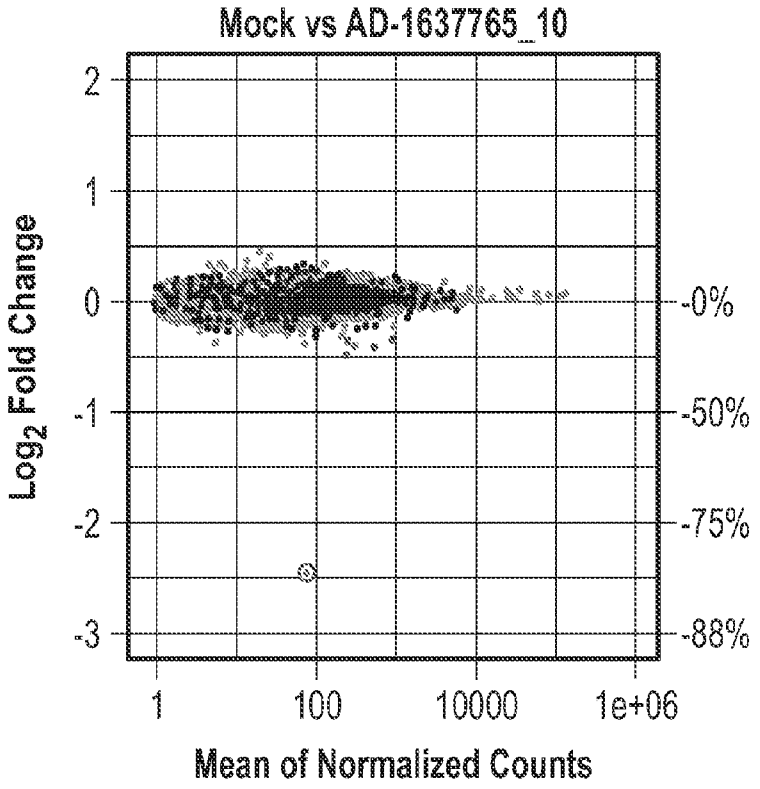


FIG. 2B
(Continued)



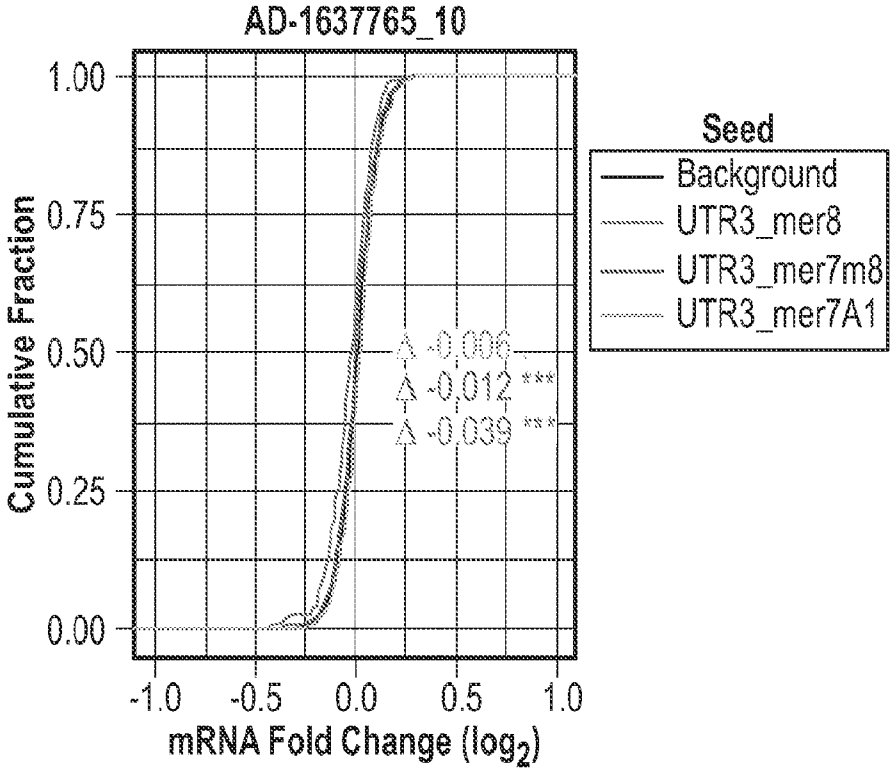


FIG. 2B
(Continued)

FIG. 3A

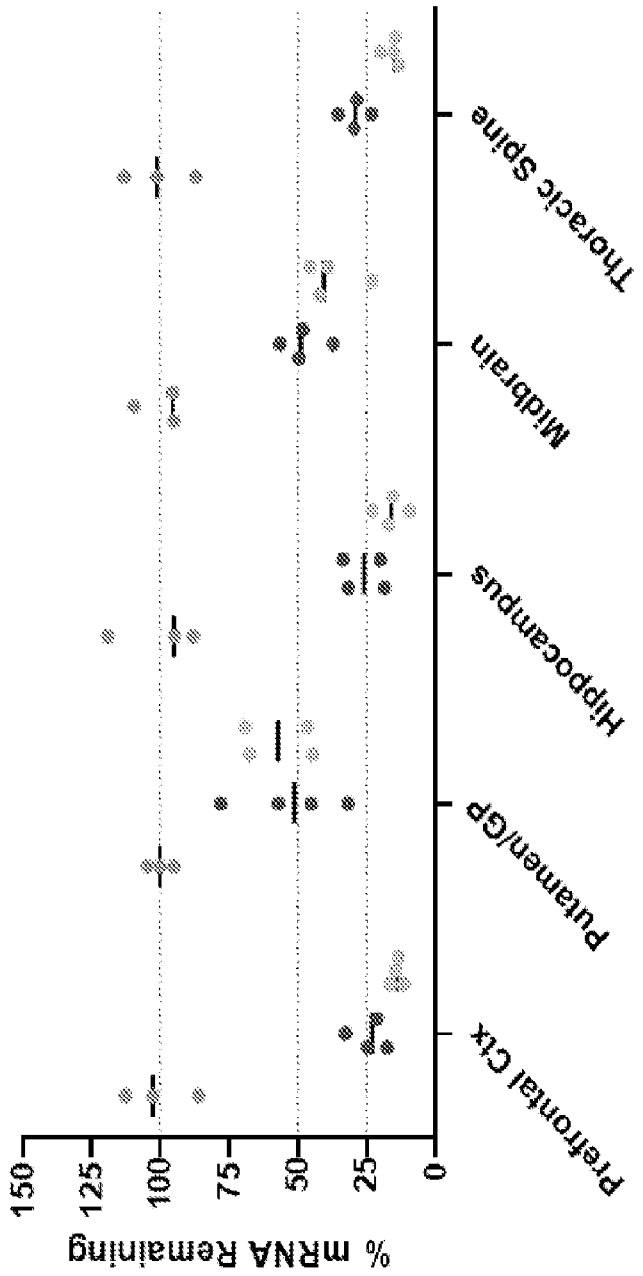

aCSF
AD-1623140
AD-1637701
% mRNA Remaining
150
125
100
75
50
25
0
Prefrontal Ctx
Putamen/GP
Hippocampus
Midbrain
Thoracic Spine

FIG. 3B

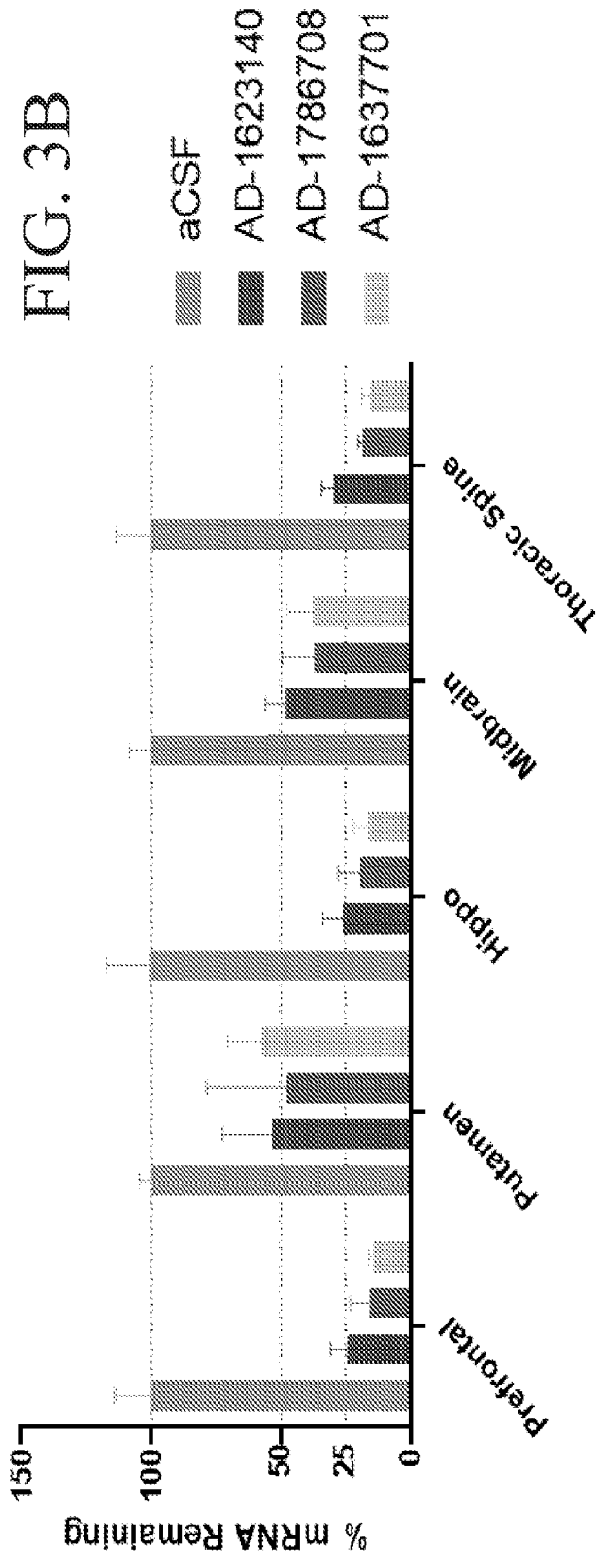

aCSF
AD-1623140
AD-1786708
AD-1637701
% mRNA Remaining
150
100
50
25
0
Prefrontal
Putamen
Hippo
Midbrain
Thoracic Spine

FIG. 4A

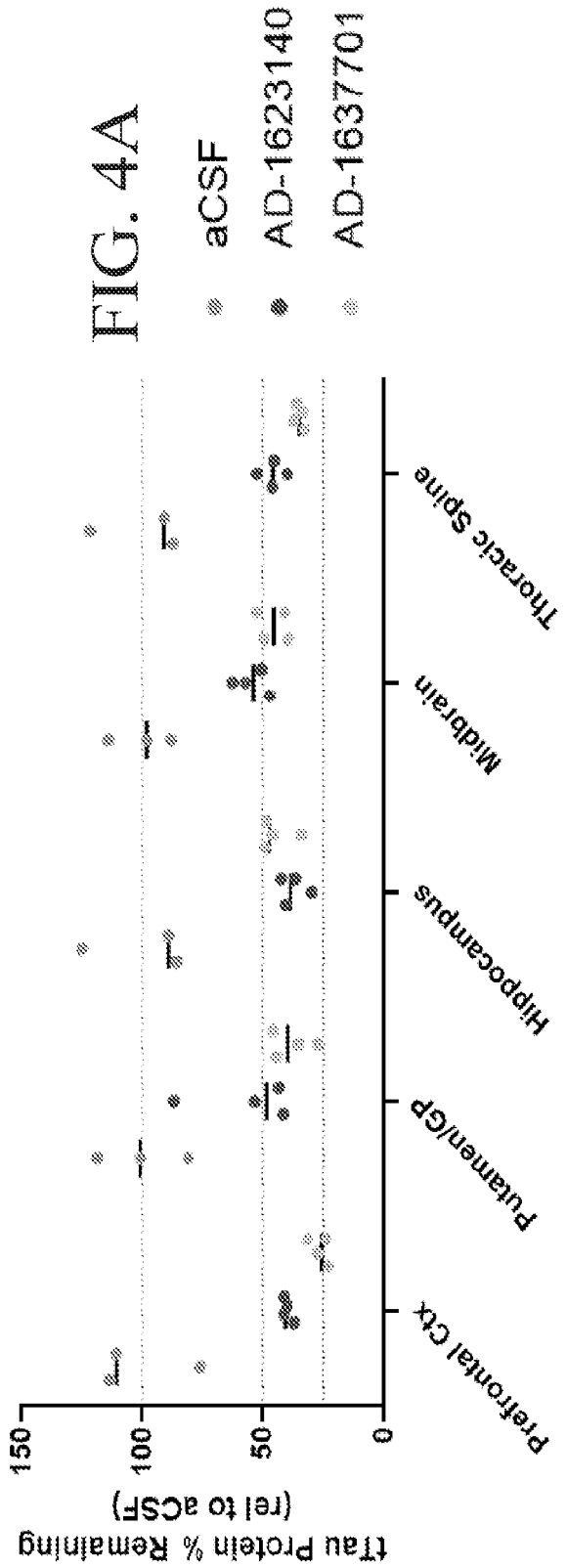

aCSF
AD-1623140
AD-1637701
tTau Protein % Remaining
(rel to aCSF)
150
100
50
0
Prefrontal Ctx
Putamen/GP
Hippocampus
Midbrain
Thoracic Spine

FIG. 4B

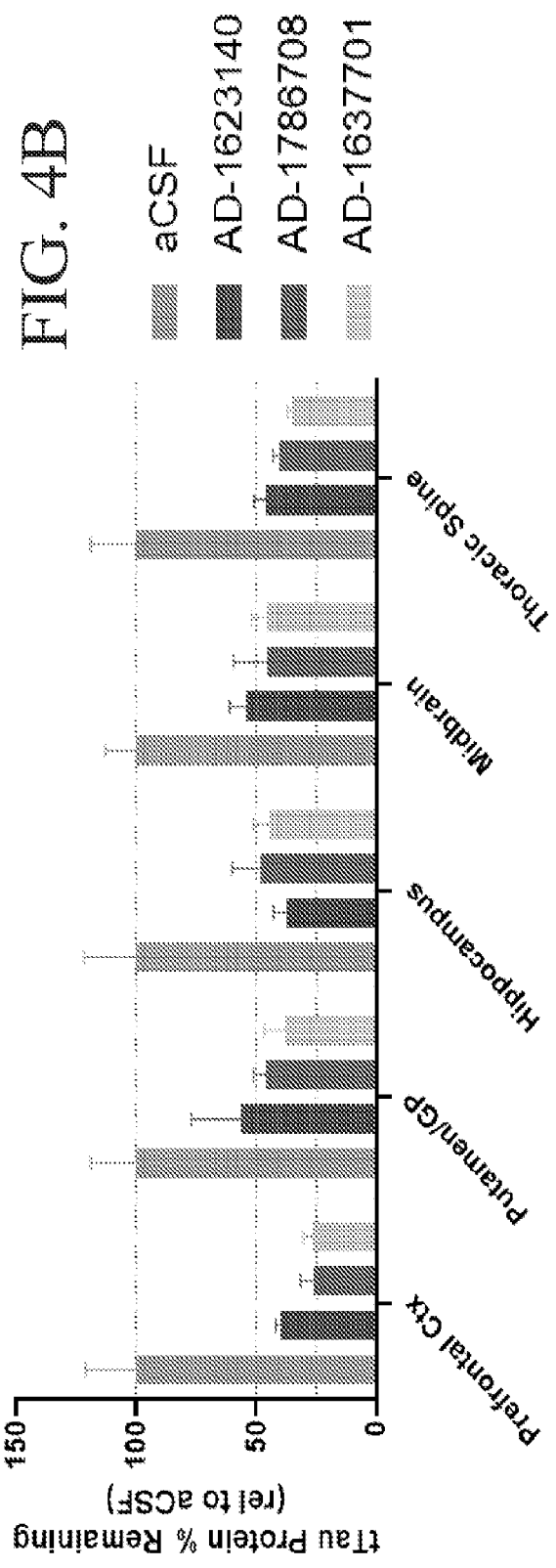

aCSF
AD-1623140
AD-1786708
AD-1637701
tTau Protein % Remaining
(rel to aCSF)
150
100
50
0
Prefrontal Ctx
Putamen/GP
Hippocampus
Midbrain
Thoracic Spine

FIG. 5

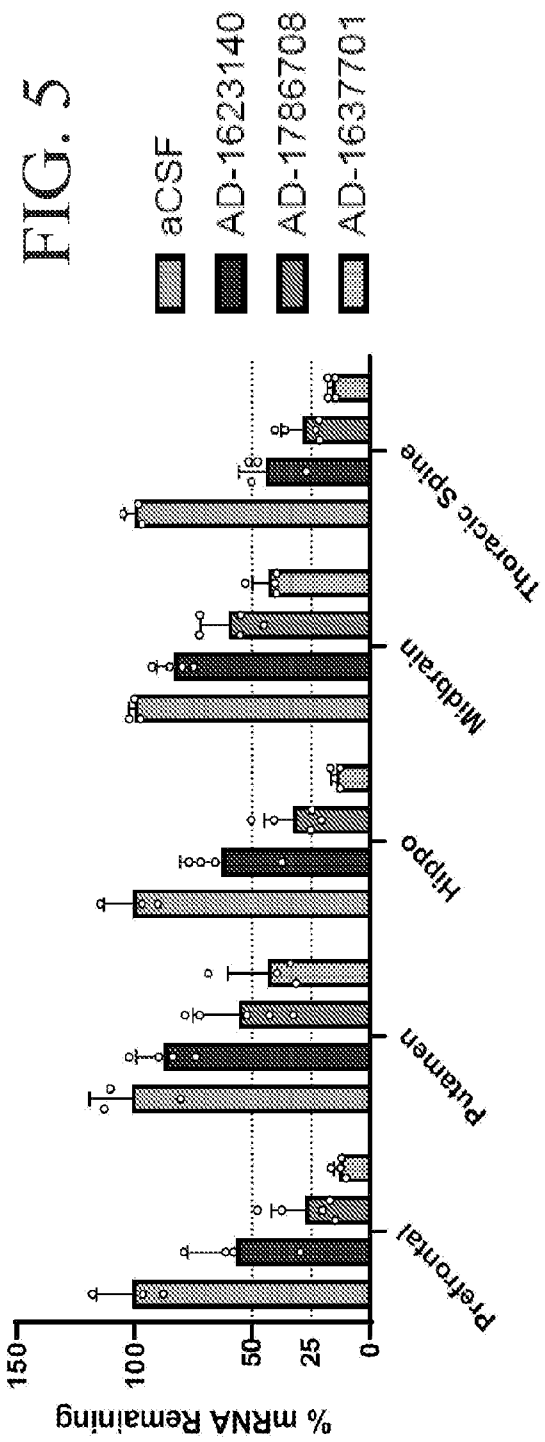
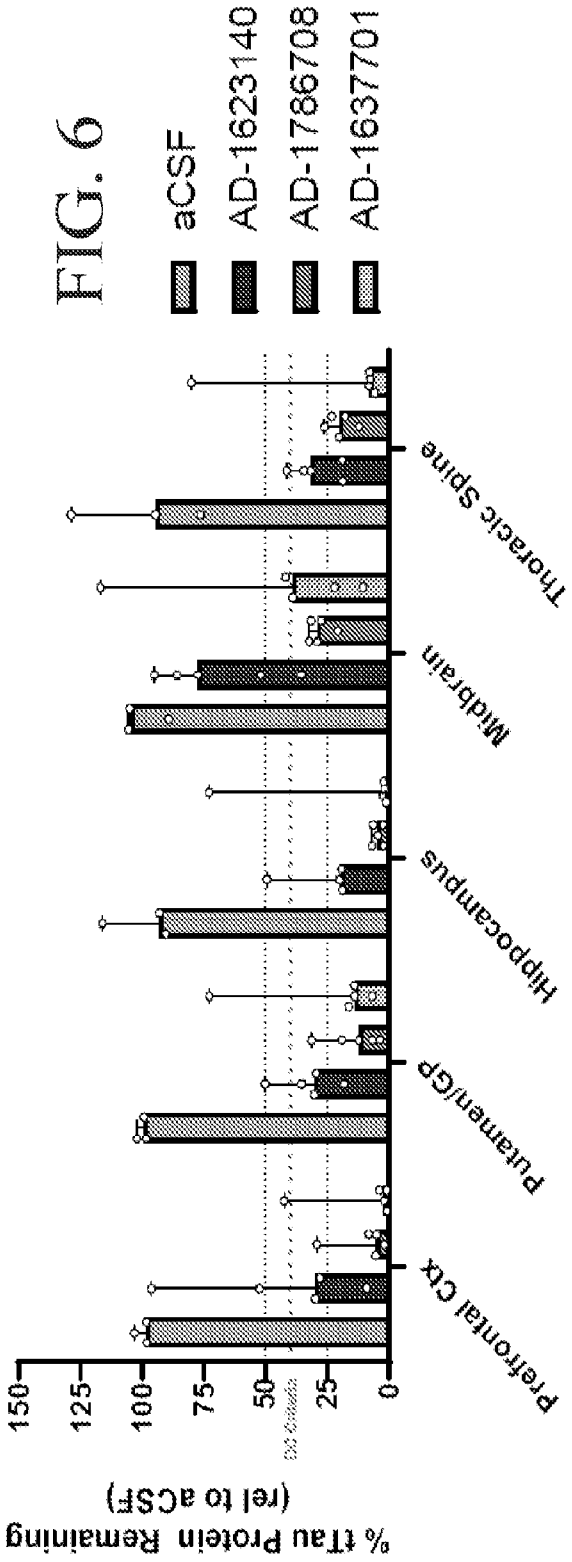

aCSF
AD-1623140
AD-1786708
AD-1637701
% mRNA Remaining
150
100
50
25
0
Prefrontal
Putamen
Hippo
Midbrain
Thoracic Spine

FIG. 6


aCSF
AD-1623140
AD-1786708
AD-1637701
% tTau Protein Remaining
(rel to aCSF)
150
125
100
75
50
25
0
Prefrontal Ctx
Putamen/GP
Hippocampus
Midbrain
Thoracic Spine

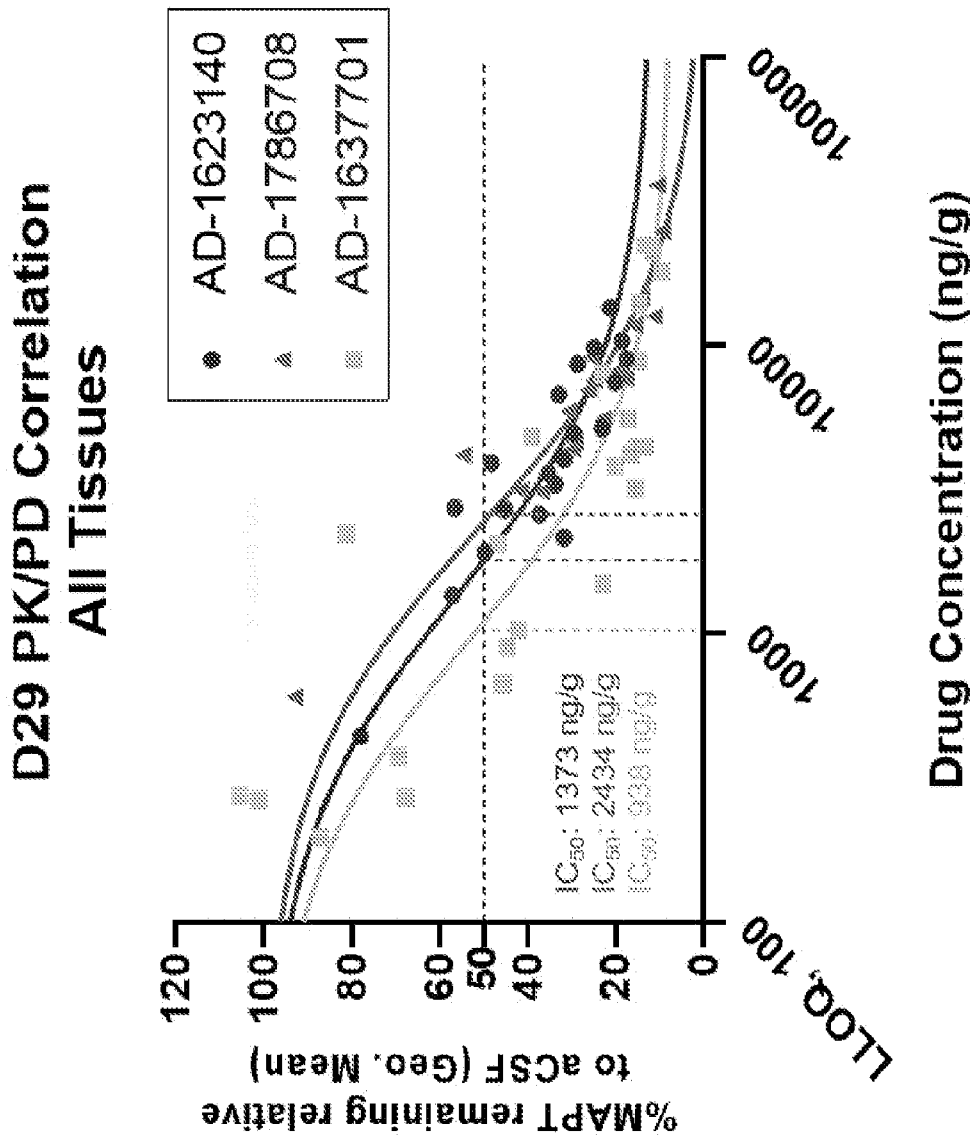

D29 PK/PD Correlation
All Tissues
AD-16231140
AD-17867708
AD-16377701
%MAPT remaining relative to aCSF (Geo. Mean)
120
100
80
60
50
40
20
0
LLOQ, 100
1000
10000
100000
Drug Concentration (ng/g)

FIG. 7A

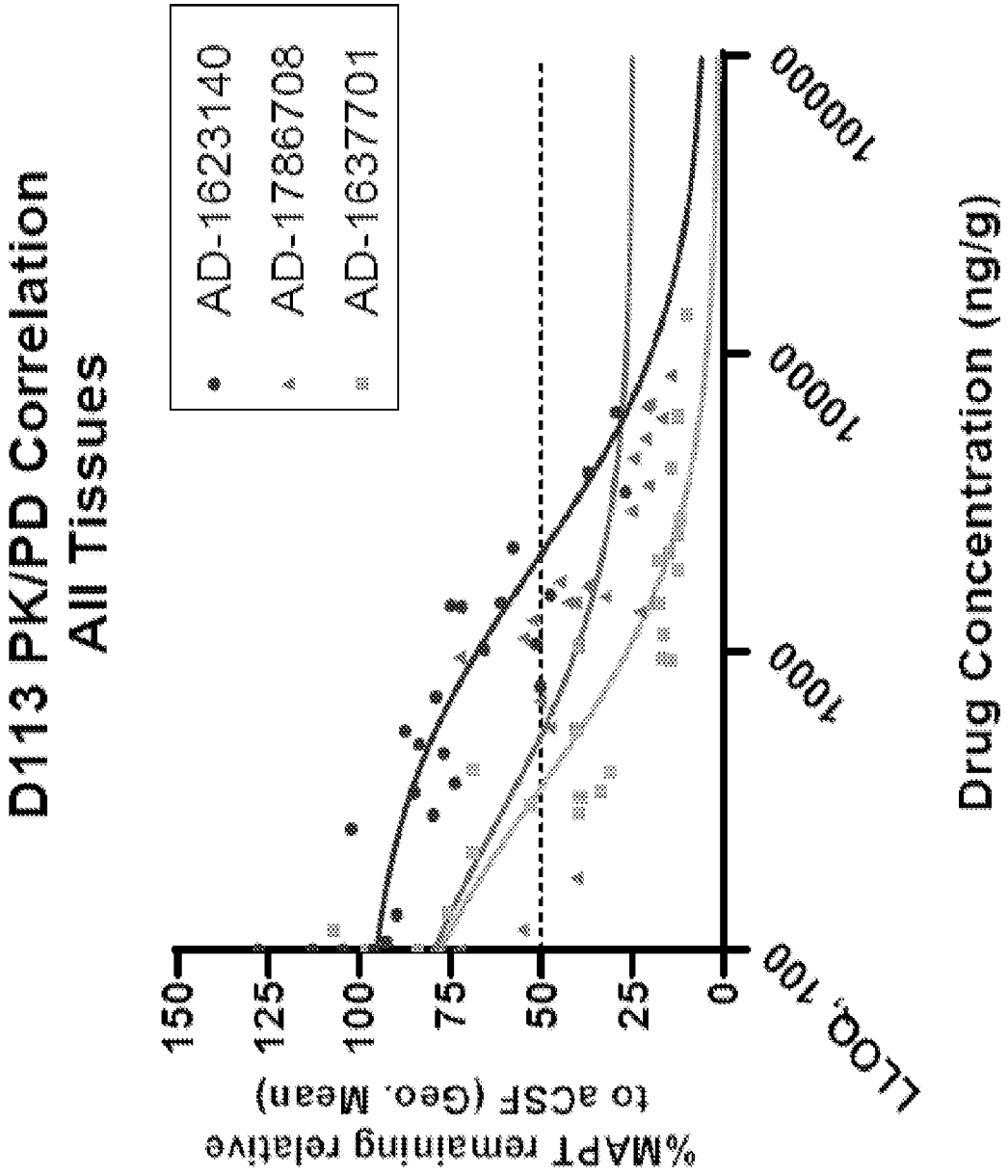

D113 PK/PD Correlation
All Tissues
AD-16231140
AD-17867708
AD-16377701
%MAPT remaining relative to aCSF (Geo. Mean)
150
125
100
75
50
25
0
LLOQ, 100
1000
10000
100000
Drug Concentration (ng/g)

FIG. 7B

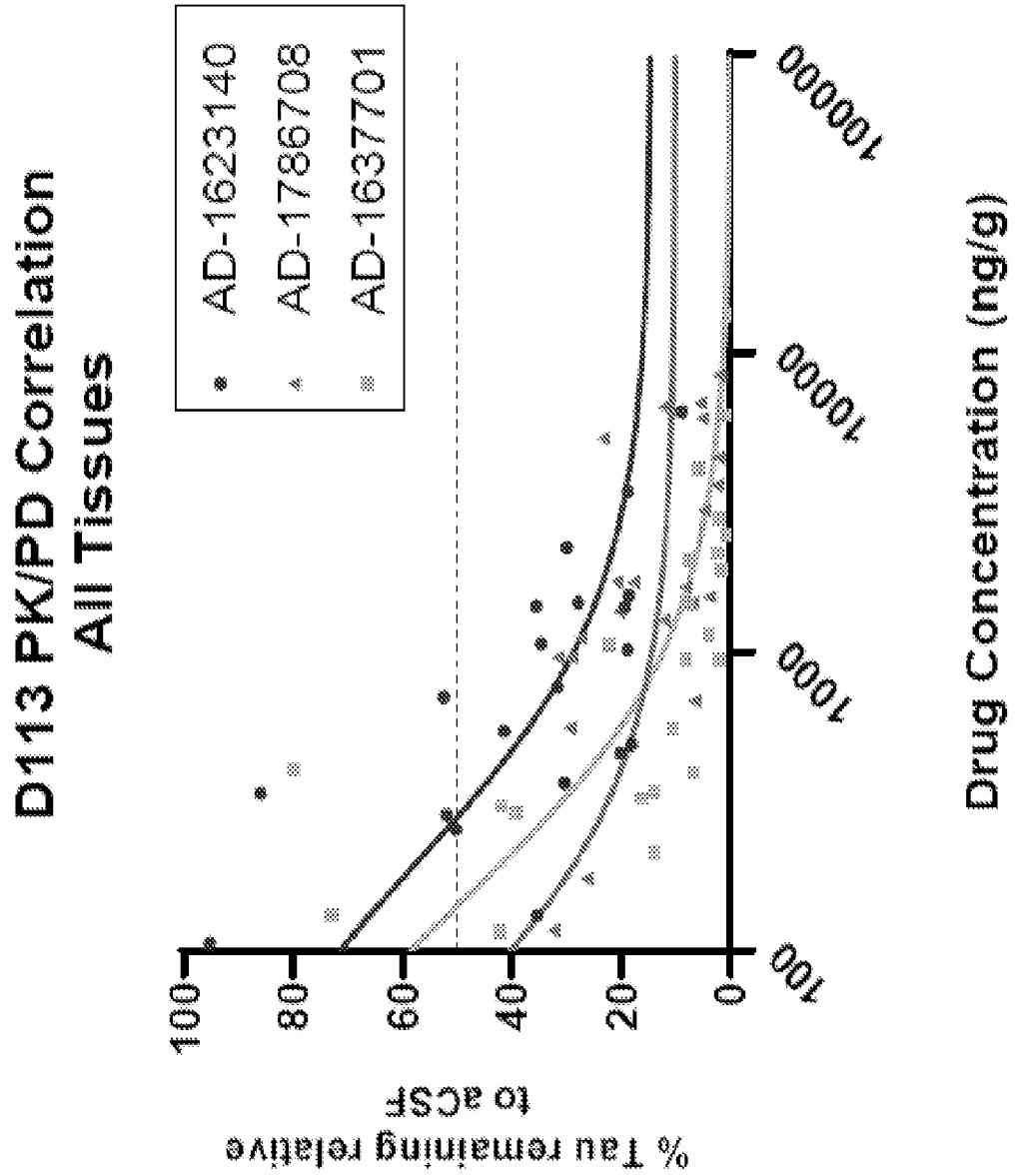

D113 PK/PD Correlation
All Tissues
AD-16231140
AD-17867708
AD-16377701
% Tau remaining relative to aCSF
100
80
60
40
20
0
100
1000
10000
100000
Drug Concentration (ng/g)

FIG. 7C