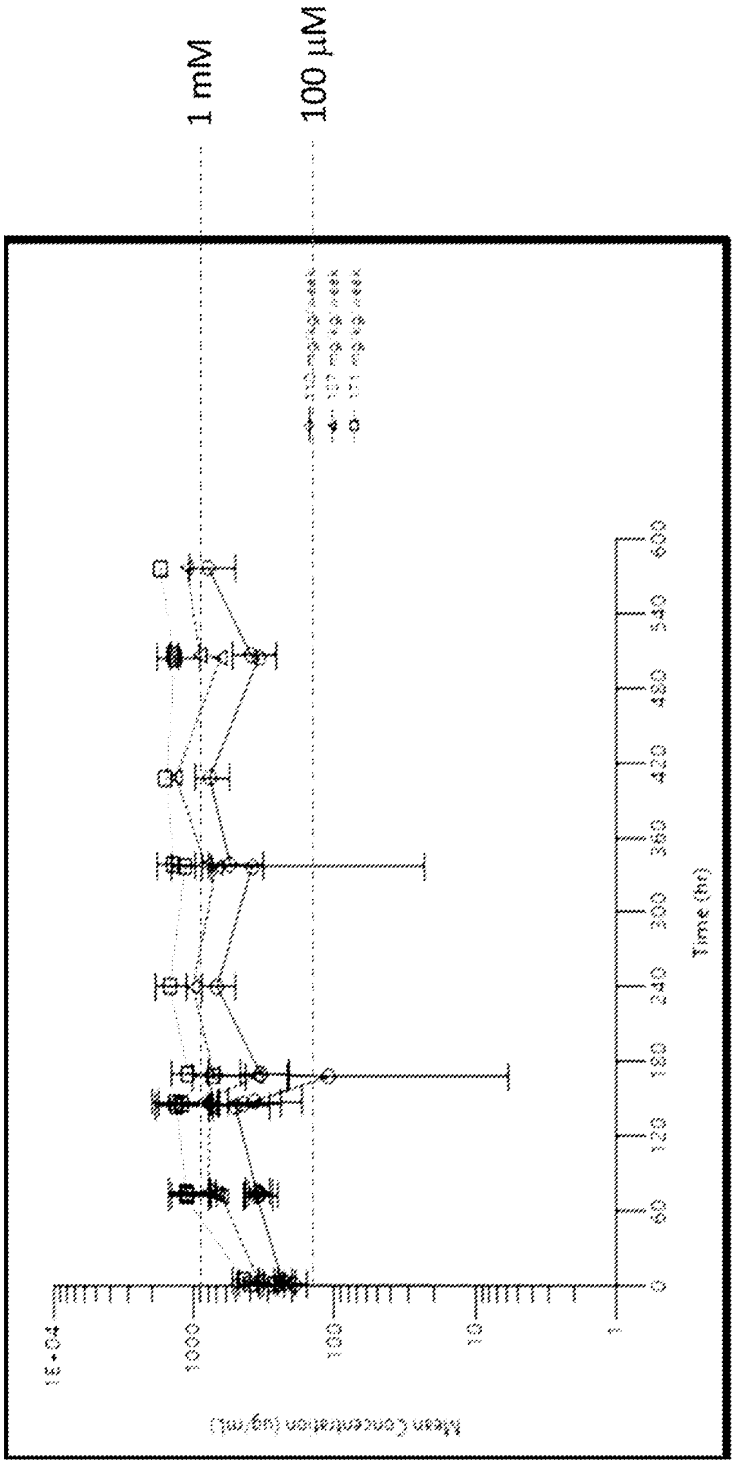
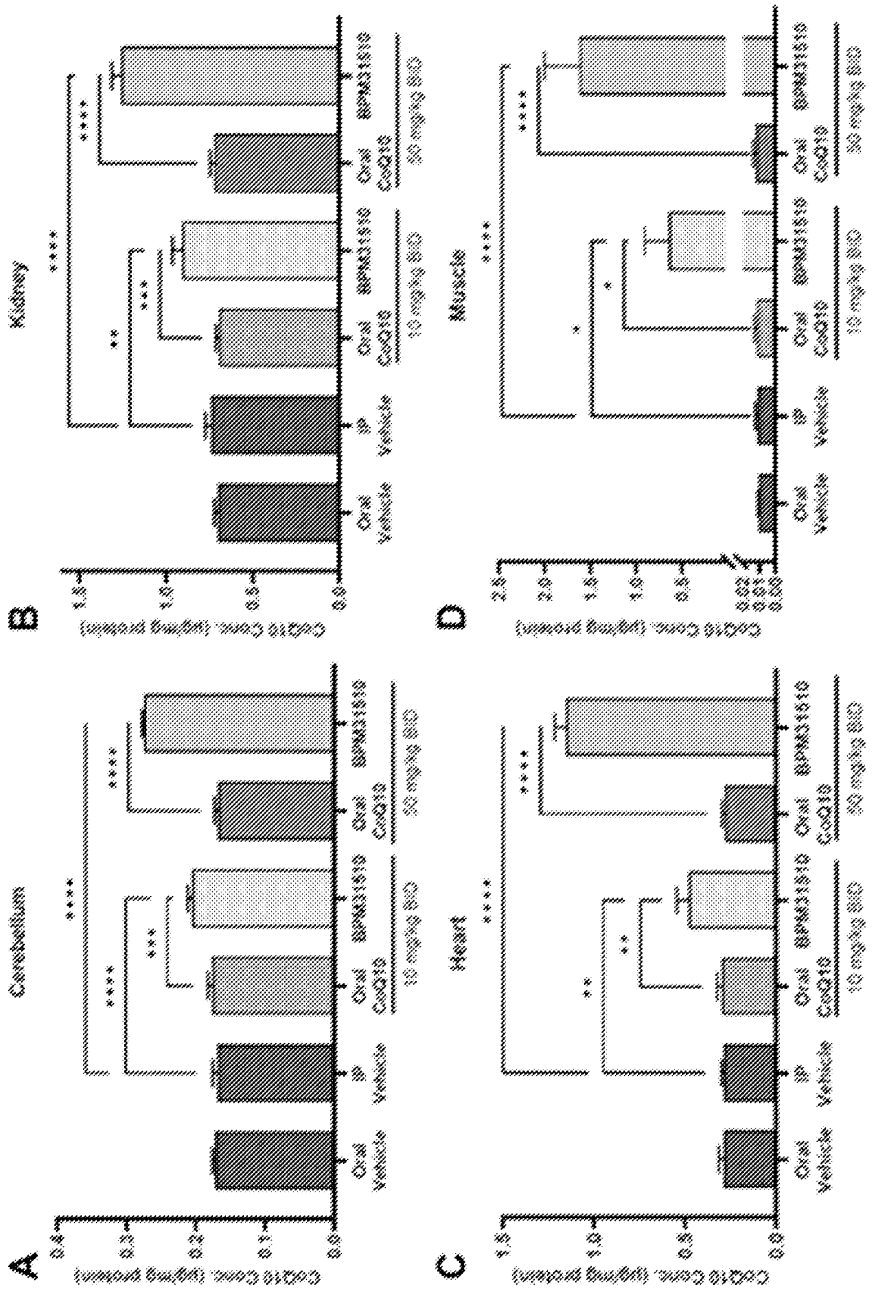
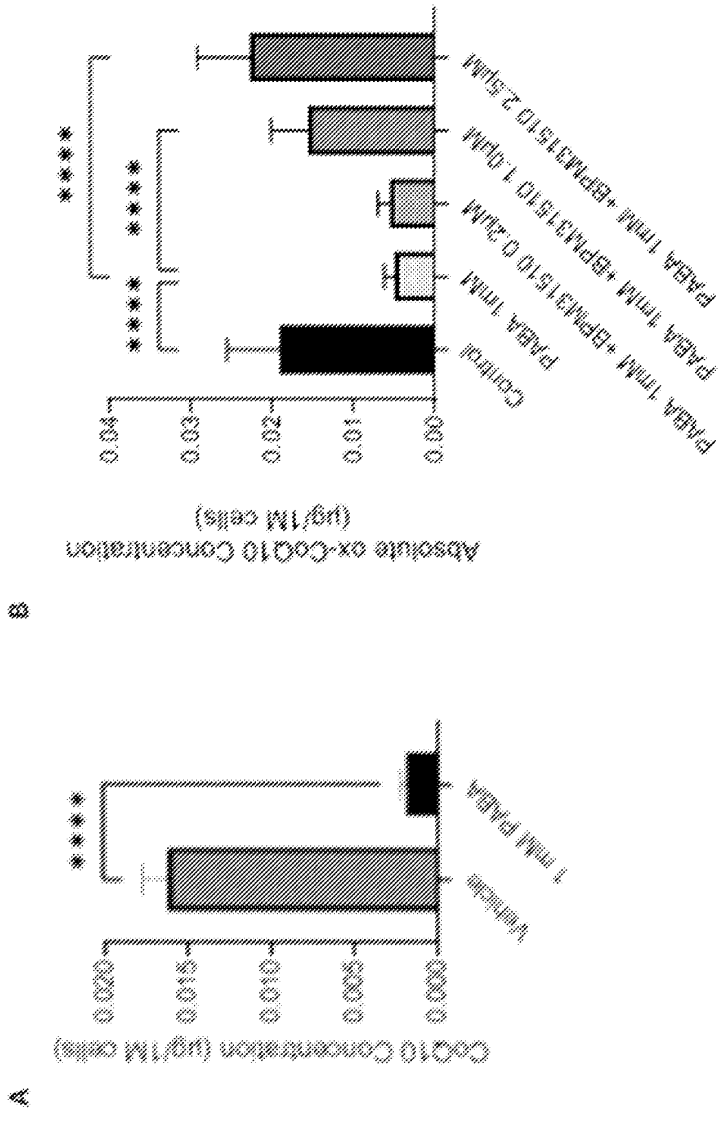

1 mM
100 µM
10 mg/kg
3 mg/kg
1 mg/kg
Time (hr)
0
60
120
180
240
300
360
420
480
540
600
1
10
100
1000
1E+04
Eltrombopag Concentration (ug/mL)

FIG. 1


A
Cerebellum
B
Kidney
C
Heart
D
Muscle
CoQ10 Conc. (ug/mg protein)
Oral Vehicle
IP Vehicle
Oral CoQ10 10 mg/kg BID
Oral BPM31510 10 mg/kg BID
Oral CoQ10 50 mg/kg BID
Oral BPM31510 50 mg/kg BID

FIGS. 2A-2D


B
Absolute ox-CoQ10 Concentration
(pg/1M cells)
0.04
0.03
0.02
0.01
0.00
Control
PAβA 1mM
PAβA 1mM +EPA:DHA 15:10 0.2μM
PAβA 1mM +EPA:DHA 15:10 1.0μM
PAβA 1mM +EPA:DHA 15:10 2.5μM
****
****
****
A
CoQ10 Concentration (pg/1M cells)
0.020
0.015
0.010
0.005
0.000
Vehicle
1 mM PAβA
****

FIGS. 3A-3B

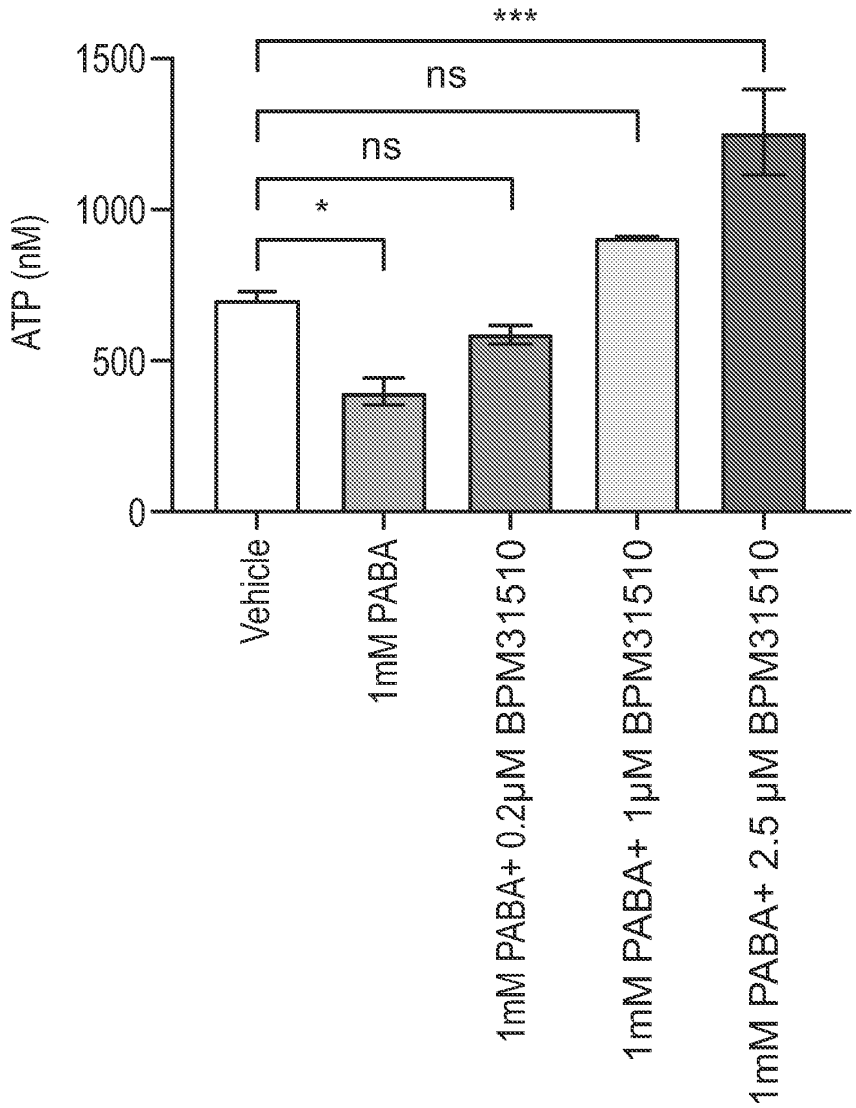

***
ns
ns
*
1500
1000
500
0
ATP (nM)
Vehicle
1mM PABA
1mM PABA+ 0.2µM BPM31510
1mM PABA+ 1µM BPM31510
1mM PABA+ 2.5 µM BPM31510

FIG. 4

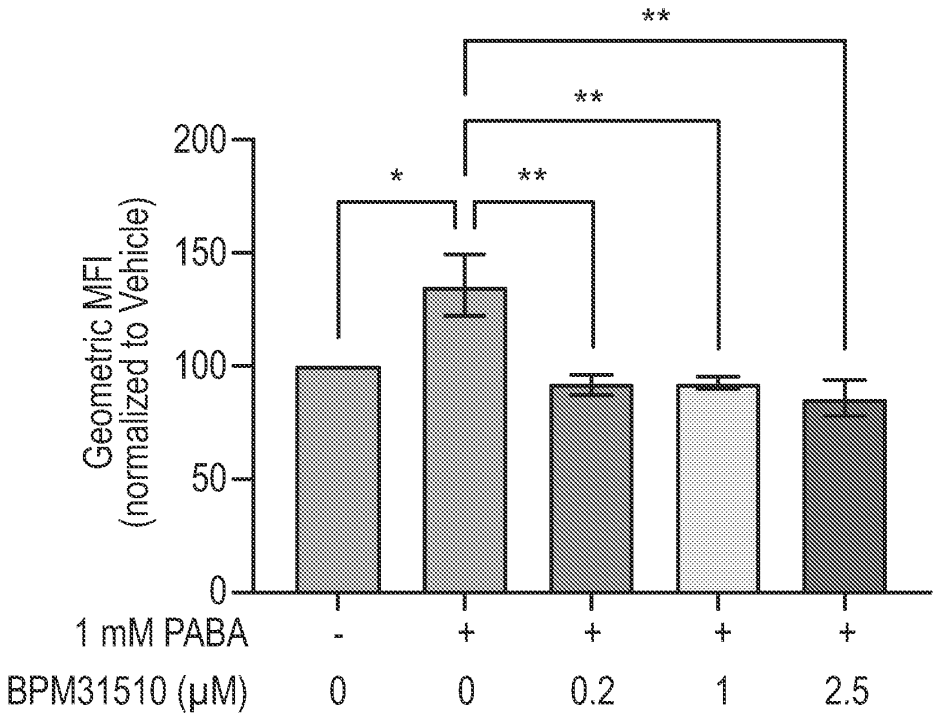

**
**
*
**
200
150
100
50
0
Geometric MFI
(normalized to Vehicle)
1 mM PABA
-
+
+
+
+
BPM31510 (μM)
0
0
0.2
1
2.5

FIG. 5

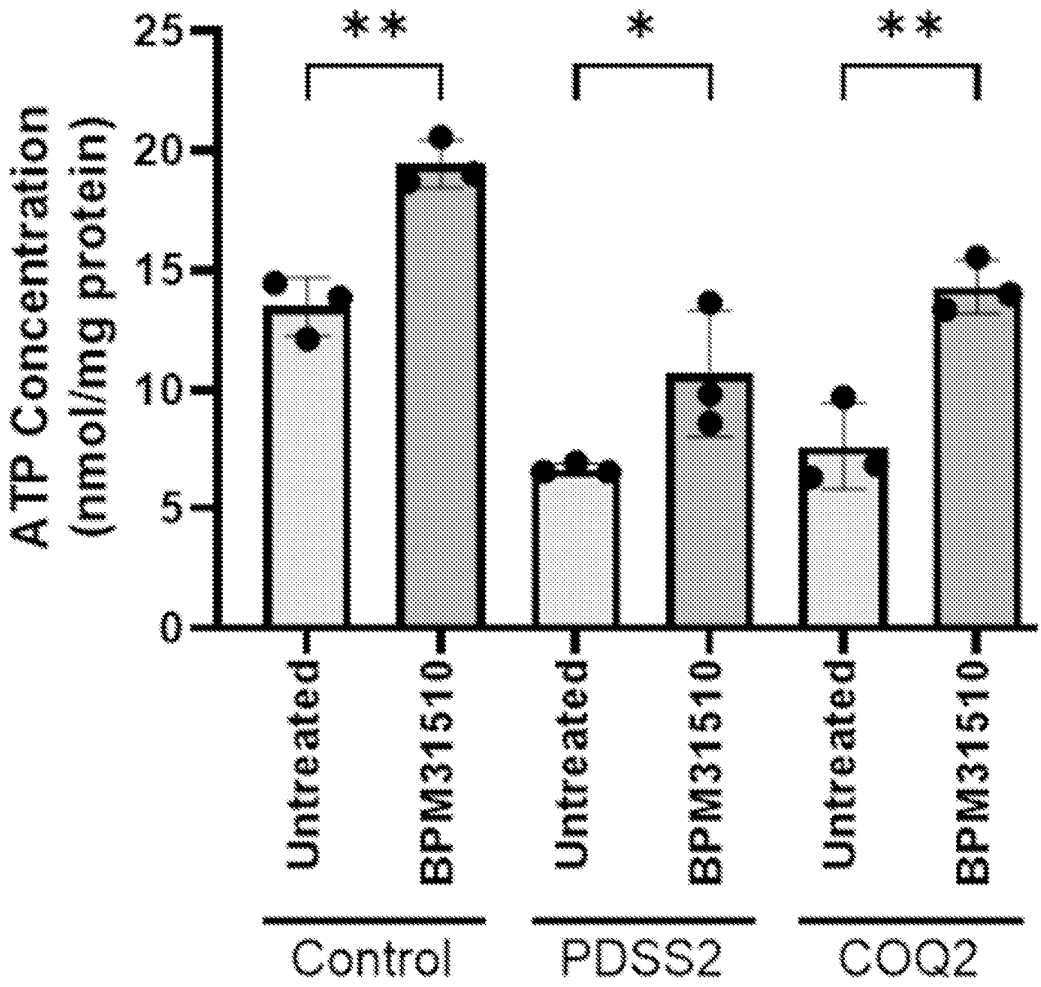

ATP Concentration
(nmol/mg protein)
25
20
15
10
5
0
**
*
**
Untreated
BPM31510
Untreated
BPM31510
Untreated
BPM31510
Control
PDSS2
COQ2

FIG. 6

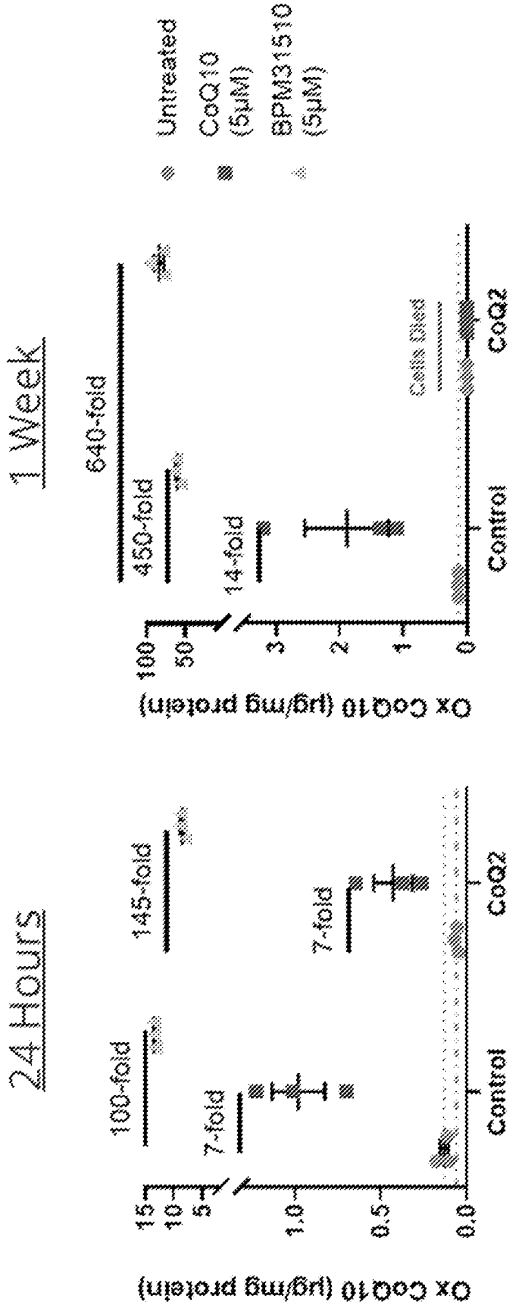

24 Hours
1 Week
Ox CoQ10 (µg/mg protein)
15
10
5
1.0
0.5
0.0
100-fold
7-fold
145-fold
7-fold
Control
CoQ2
Ox CoQ10 (µg/mg protein)
100
50
3
2
1
0
640-fold
450-fold
14-fold
Cells Died
Control
CoQ2
Untreated
CoQ10 (5µM)
BPM31510 (5µM)

FIG. 7

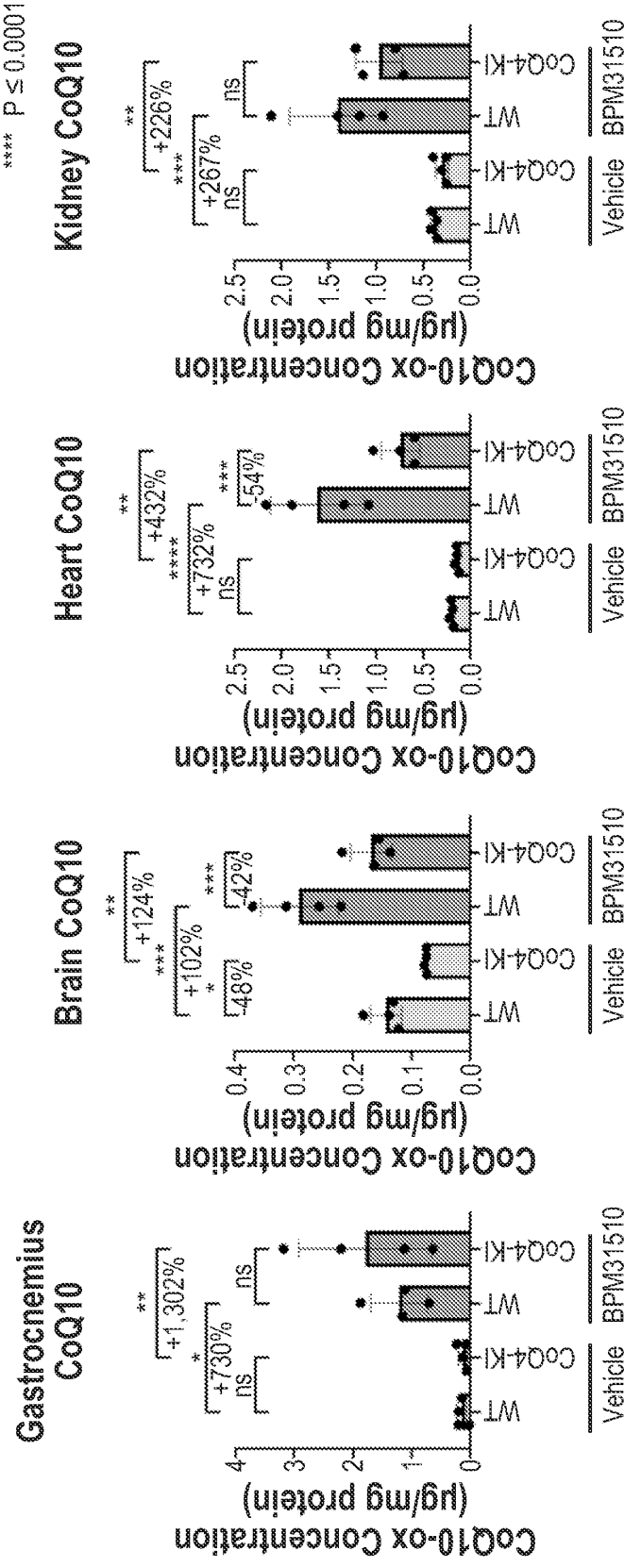

Gastrocnemius CoQ10
Brain CoQ10
Heart CoQ10
Kidney CoQ10
CoQ10-ox Concentration (µg/mg protein)
Vehicle
BPM31510
WT
CoQ4-KI
ns
*
**
***
****
+730%
+1,302%
+48%
+102%
+124%
+42%
+732%
+432%
+54%
+267%
+226%
P > 0.05
P ≤ 0.05
P ≤ 0.01
P ≤ 0.001
P ≤ 0.0001

FIG. 8

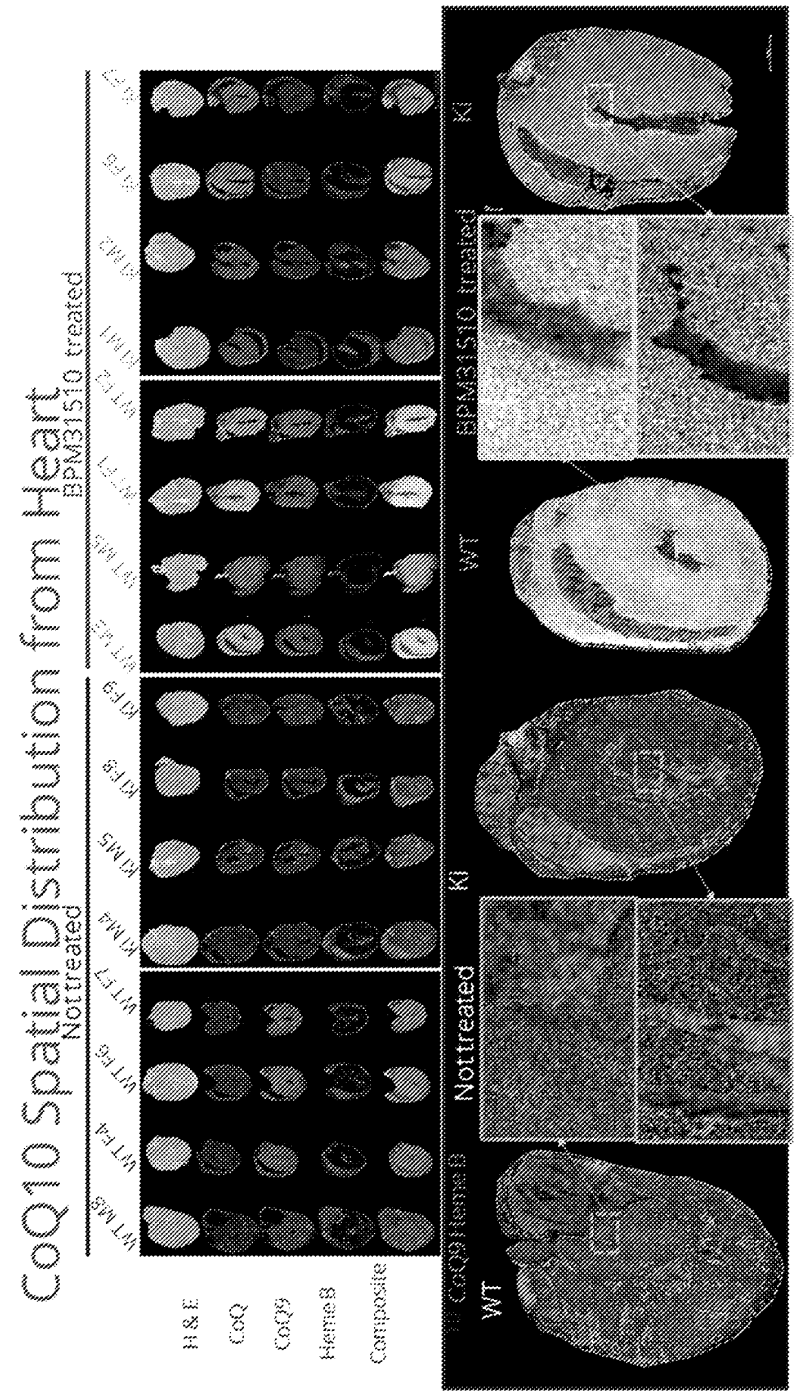
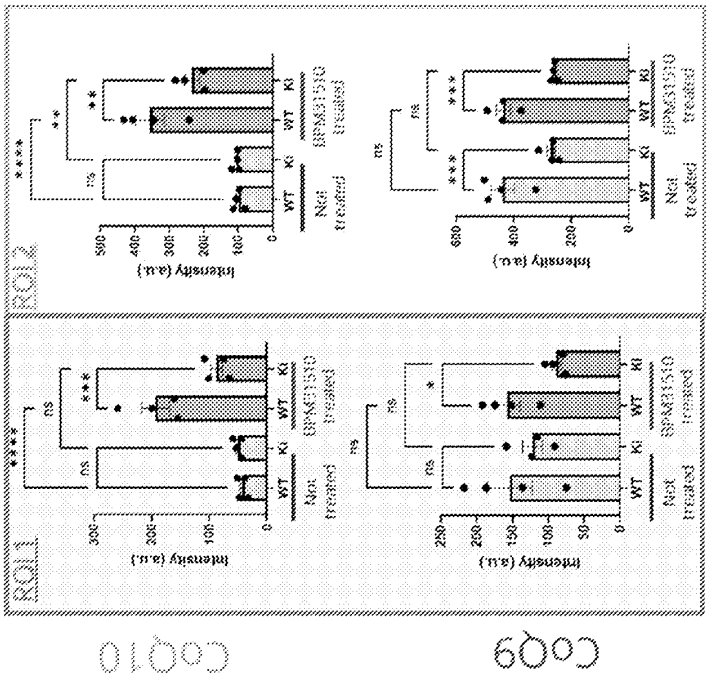

CoQ10 Spatial Distribution from Heart
Nottreated
BPM31510 treated
H & E
CoQ
CoQ9
Heme B
Composite
WT
Nottreated
Ki
WT
BPM31510 treated
Ki

FIG. 9


ROI 1
ROI 2
Intensity (a.u.)
WT
KI
Not treated
BPM31510 treated
Coq9
Coq10


ROI 1- Vascular enriched
ROI 2- Tissue

FIG. 10

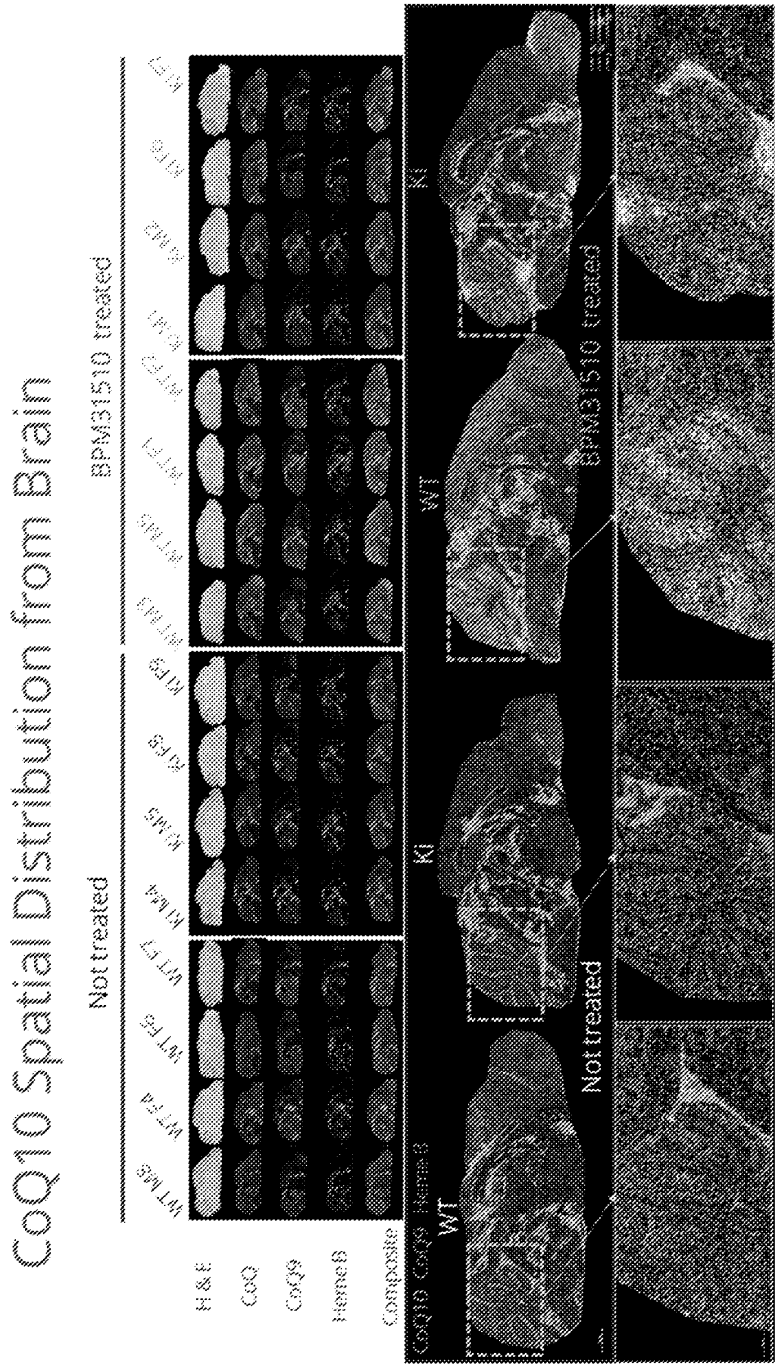

CoQ10 Spatial Distribution from Brain
Not treated
BPM31510 treated
H & E
CoQ
CoQ9
Heme B
Composite
WT
Ki
Not treated
BPM31510 treated

FIG. 11

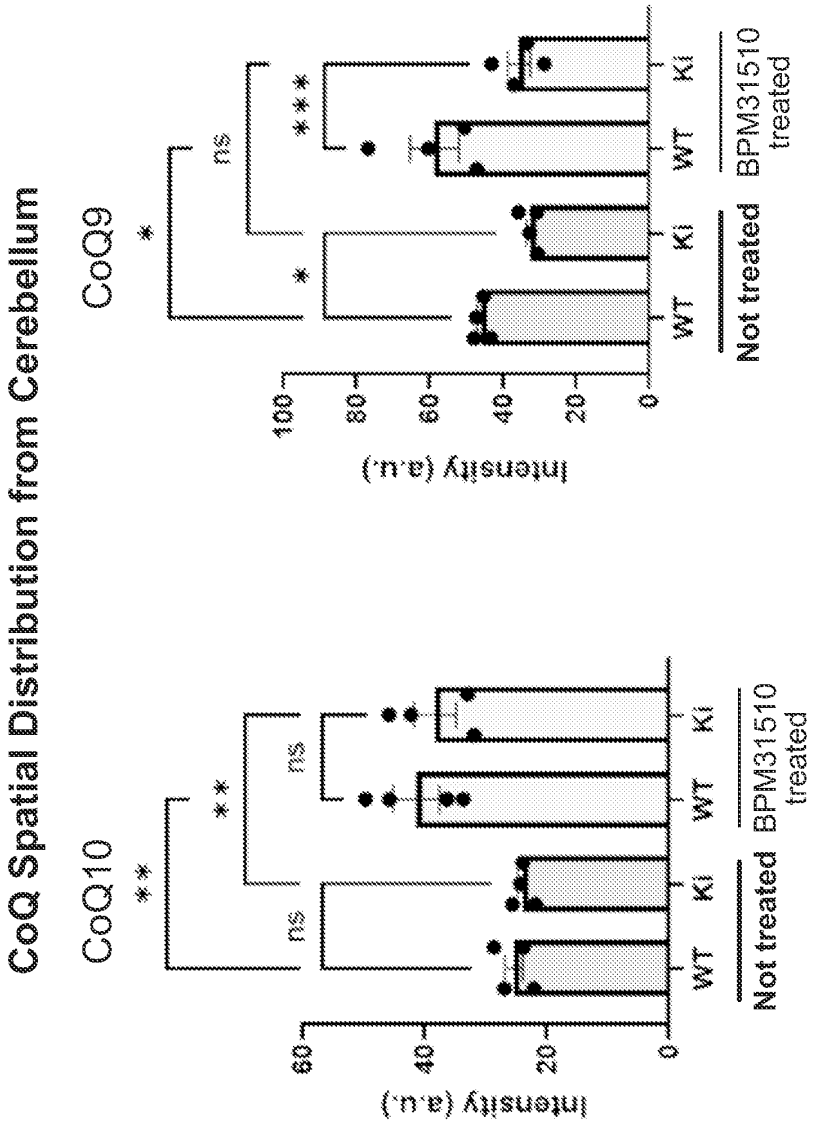

CoQ Spatial Distribution from Cerebellum
CoQ10
CoQ9
Intensity (a.u.)
0
20
40
60
80
100
WT
Ki
WT
Ki
Not treated
BPM31510 treated
ns
*
**
***

FIG. 12

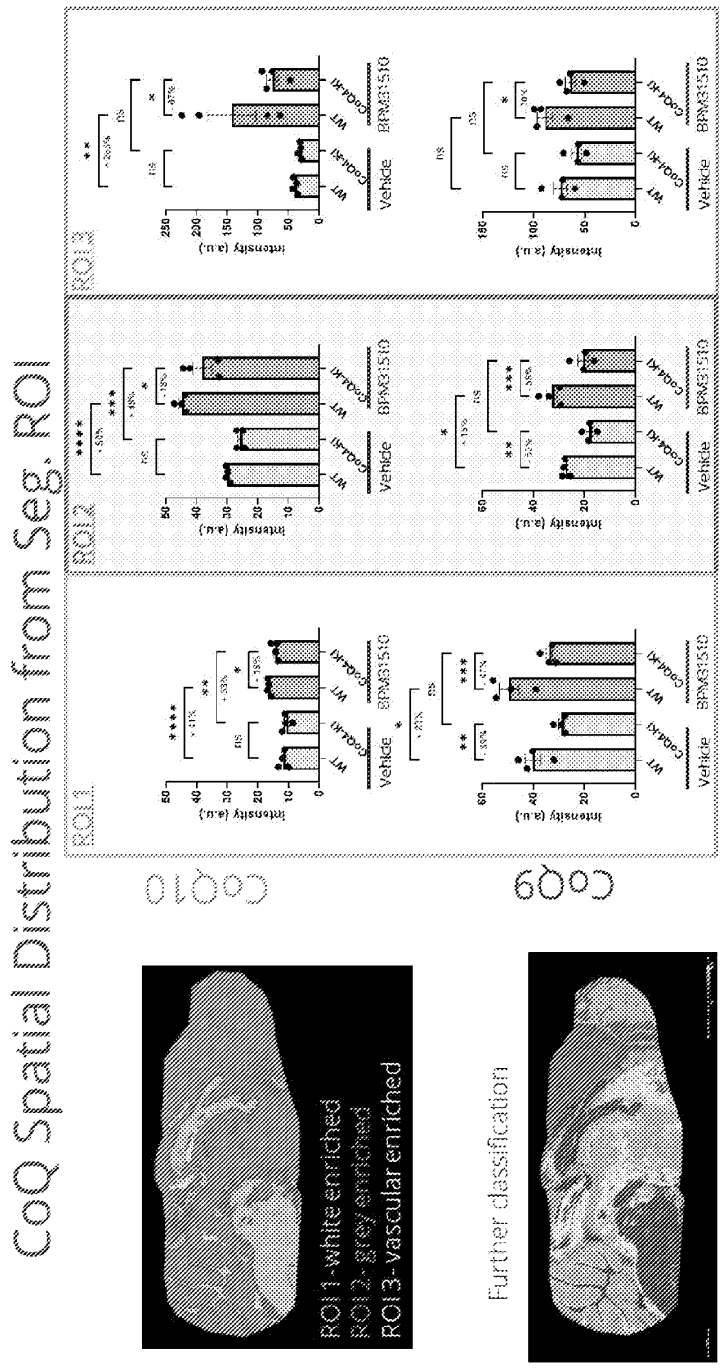

CoQ Spatial Distribution from Seg. ROI
ROI 1-white enriched
ROI 2- grey enriched
ROI 3- vascular enriched
Further classification
CoQ9
CoQ10
ROI 1
ROI 2
ROI 3
Intensity (a.u.)
Vehicle
BPM31510
WT
Cox4i-KI

FIG. 13

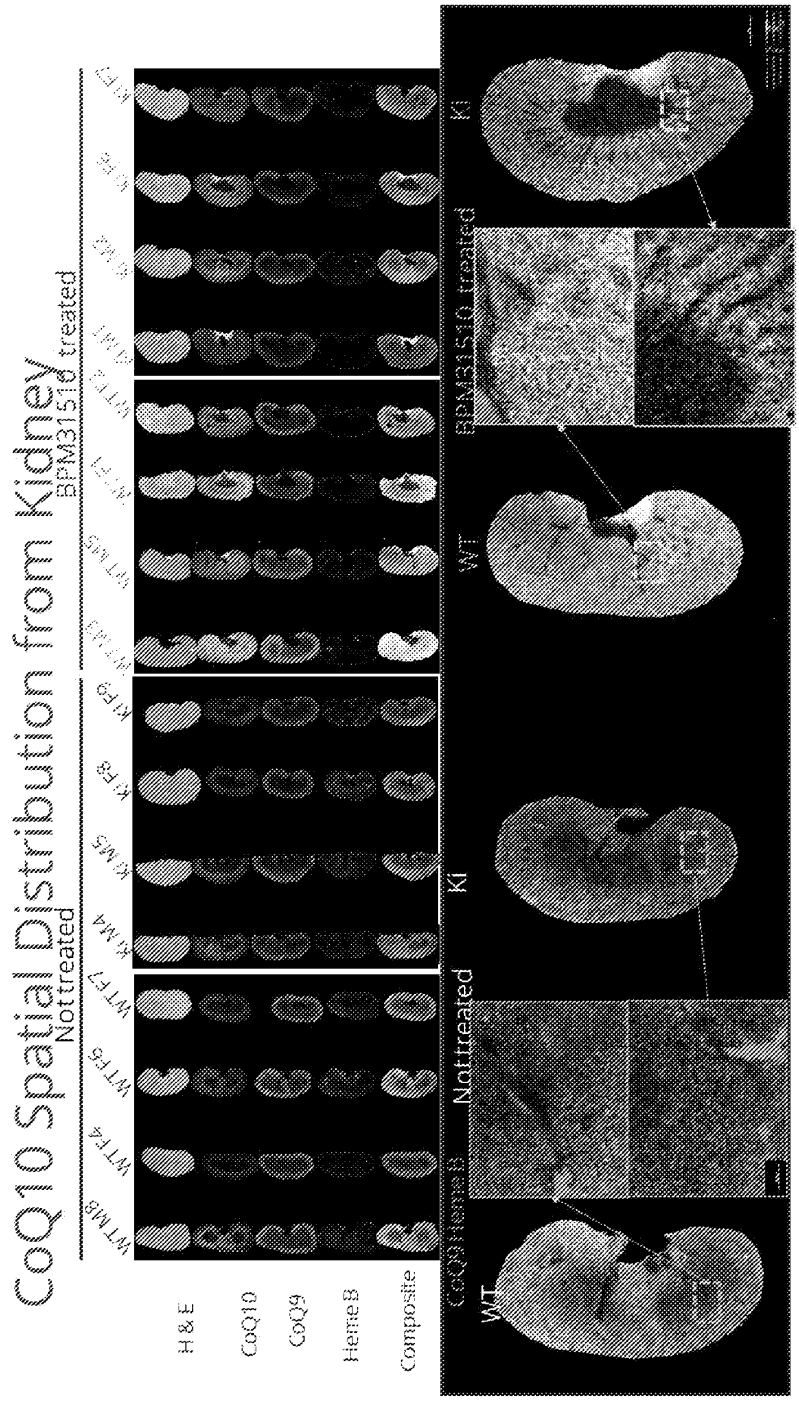

CoQ10 Spatial Distribution from Kidney
Not treated
BPM31510 treated
H & E
CoQ10
CoQ9
Heme B
Composite
WT
Ki
Not treated
BPM31510 treated

FIG. 14

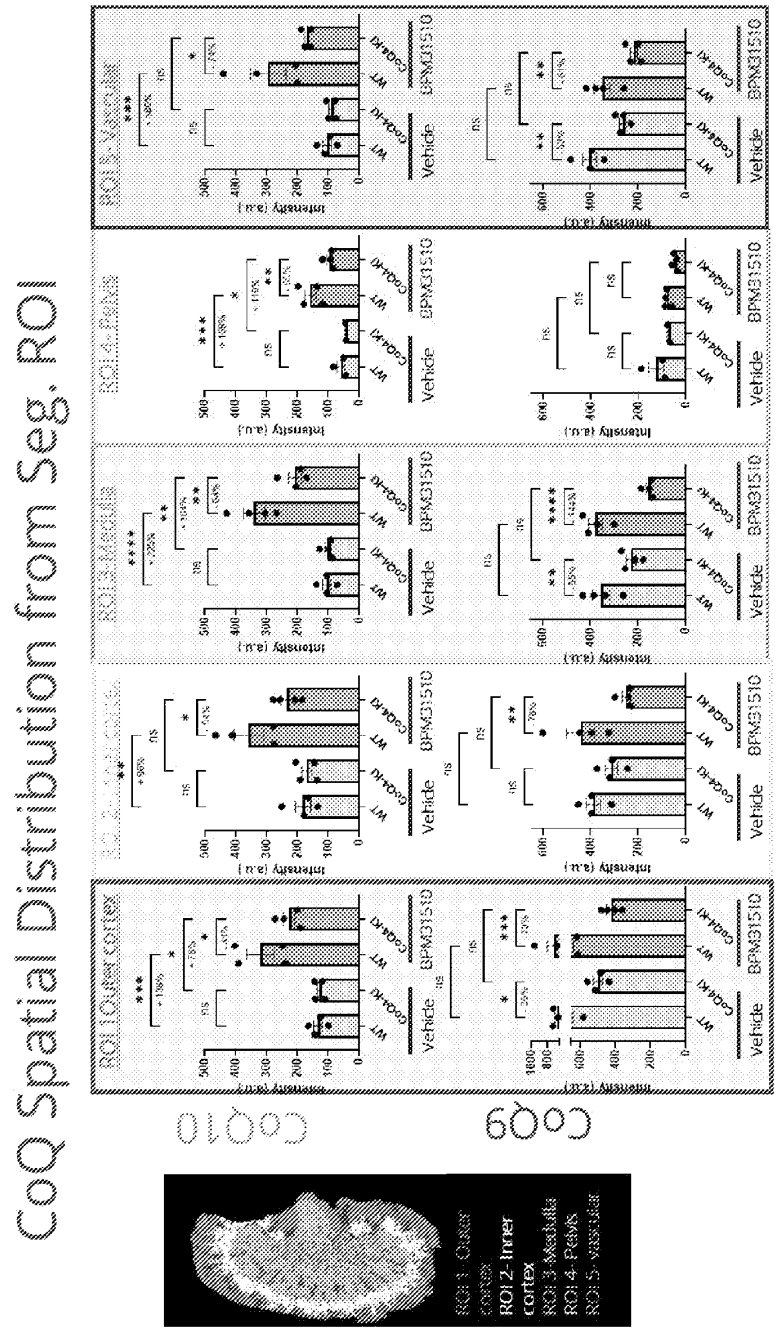

CoQ Spatial Distribution from Seg. ROI
CoQ10
CoQ9
ROI 1- Outer cortex
ROI 2- Inner cortex
ROI 3- Medulla
ROI 4- Pelvis
ROI 5- vascular
ROI 1 Outer cortex
ROI 2 Inner cortex
ROI 3 Medulla
ROI 4 Pelvis
ROI 5 Vascular
Intensity (a.u.)
Vehicle
BPM31510
WT
Coq4-/-

FIG. 15

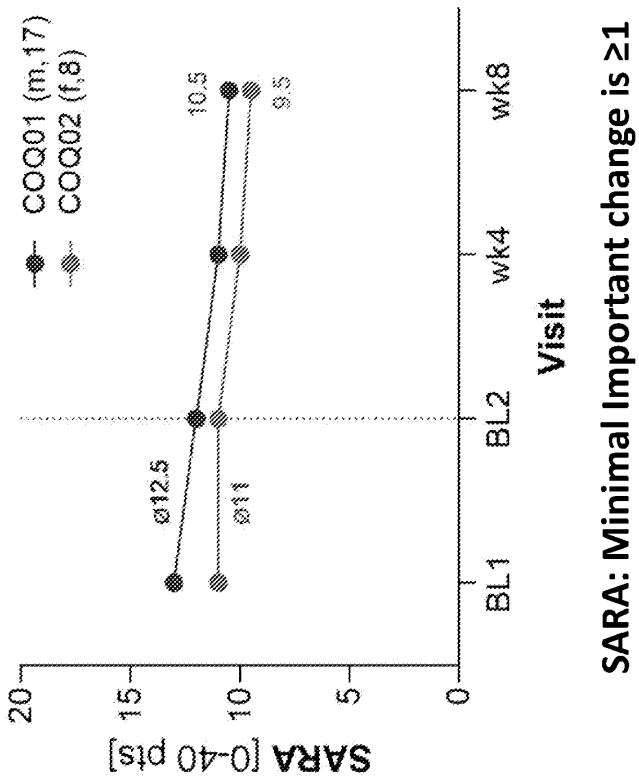

COQ01 (m,17)
COQ02 (f,8)
SARA [0-40 pts]
20
15
10
5
0
ø12.5
ø11
10.5
9.5
BL1
BL2
wk4
wk8
Visit
SARA: Minimal Important change is ≥1

FIG. 16

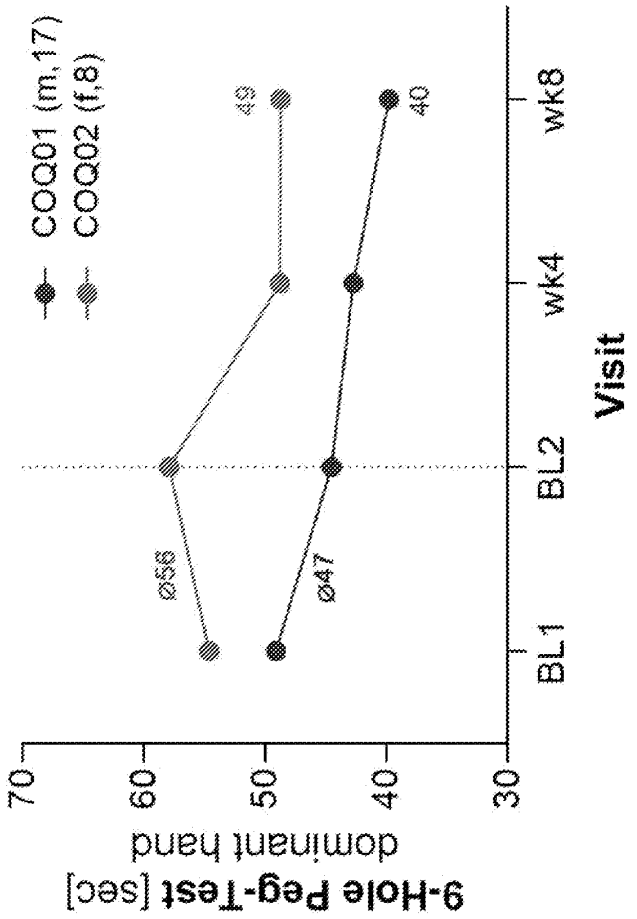

COQ01 (m,17)
COQ02 (f,8)
9-Hole Peg-Test [sec]
dominant hand
70
60
50
40
30
BL1
BL2
wk4
wk8
Visit
ø56
ø47
49
40

FIG. 17

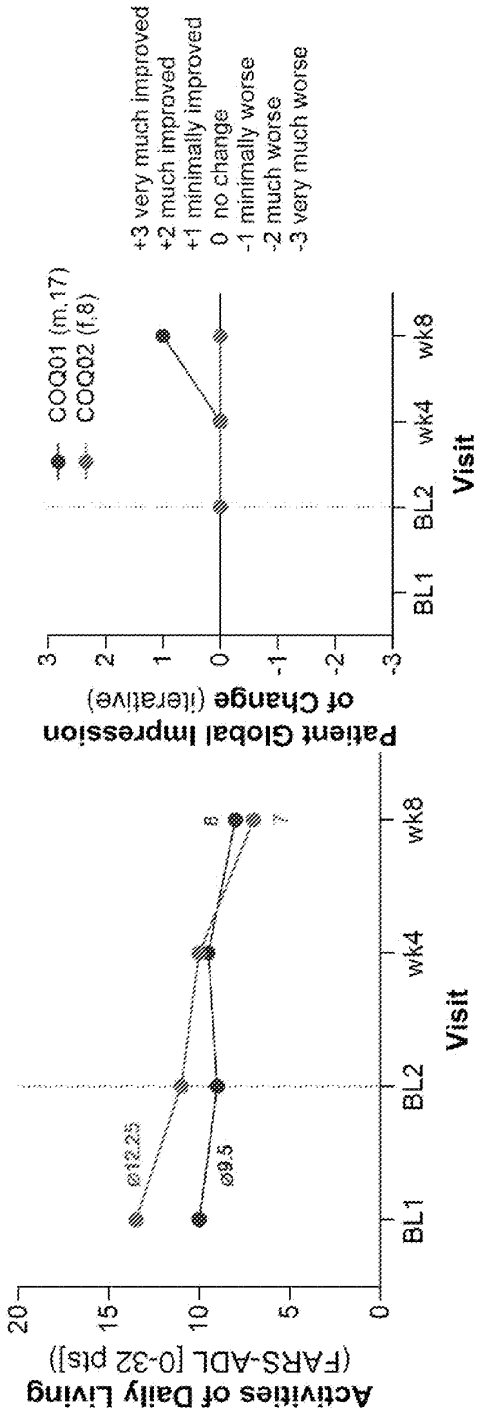

Activities of Daily Living
(FARS-ADL [0-32 pts])
20
15
10
5
0
BL1
BL2
wk4
wk8
Visit
Patient Global Impression
of Change (Iterative)
3
2
1
0
-1
-2
-3
COQ01 (m,17)
COQ02 (f,8)
+3 very much improved
+2 much improved
+1 minimally improved
0 no change
-1 minimally worse
-2 much worse
-3 very much worse

FIG. 18

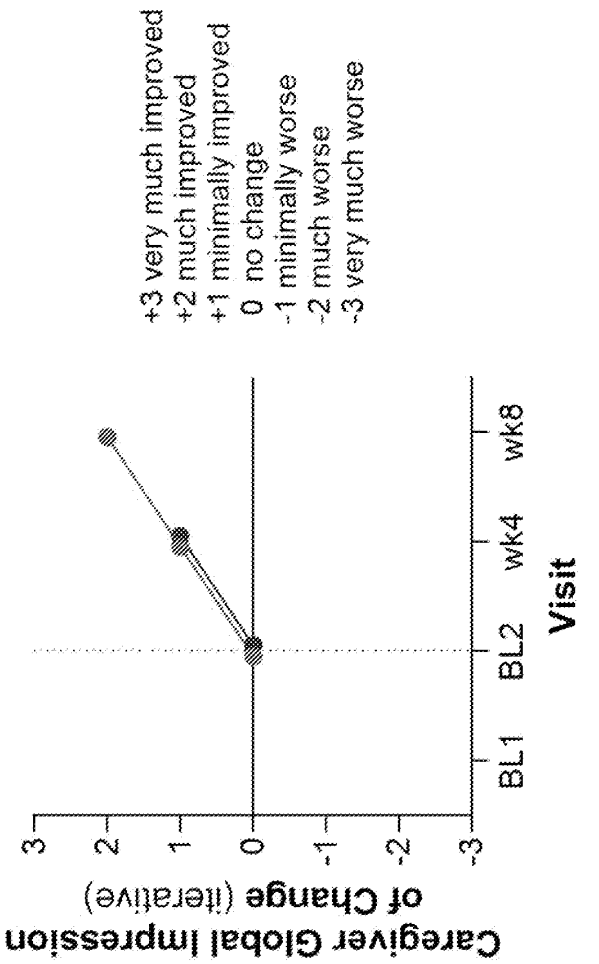

Caregiver Global Impression
of Change (Iterative)
3
2
1
0
-1
-2
-3
BL1
BL2
wk4
wk8
Visit
+3 very much improved
+2 much improved
+1 minimally improved
0 no change
-1 minimally worse
-2 much worse
-3 very much worse

FIG. 19

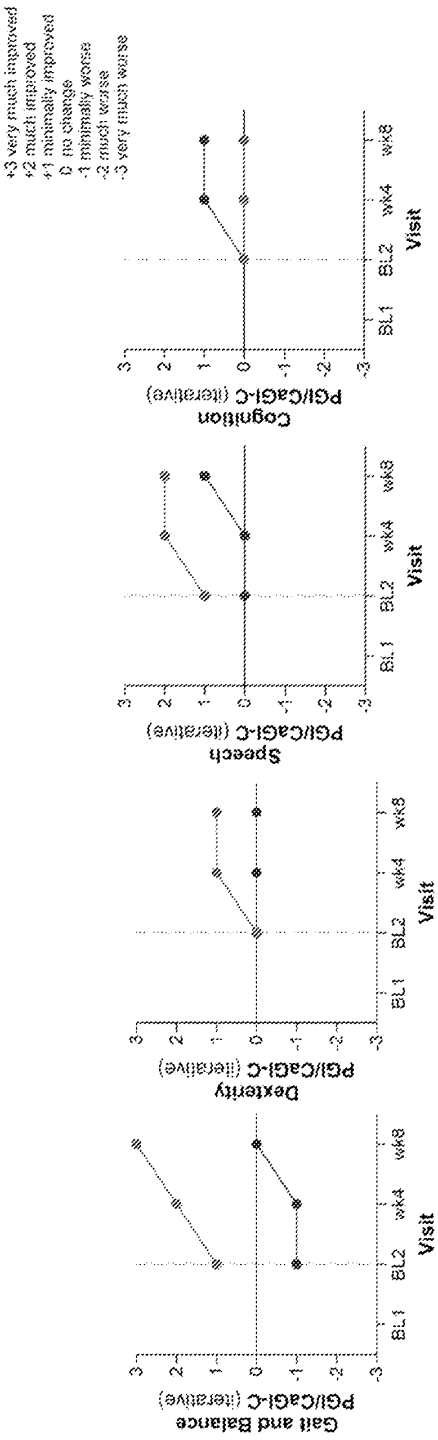

+3 very much improved
+2 much improved
+1 minimally improved
0 no change
-1 minimally worse
-2 much worse
-3 very much worse
Gait and Balance
PGI/CaGI-C (iterative)
Dexterity
PGI/CaGI-C (iterative)
Speech
PGI/CaGI-C (iterative)
Cognition
PGI/CaGI-C (iterative)
3
2
1
0
-1
-2
-3
BL1
BL2
wk4
wk8
Visit

FIG. 20

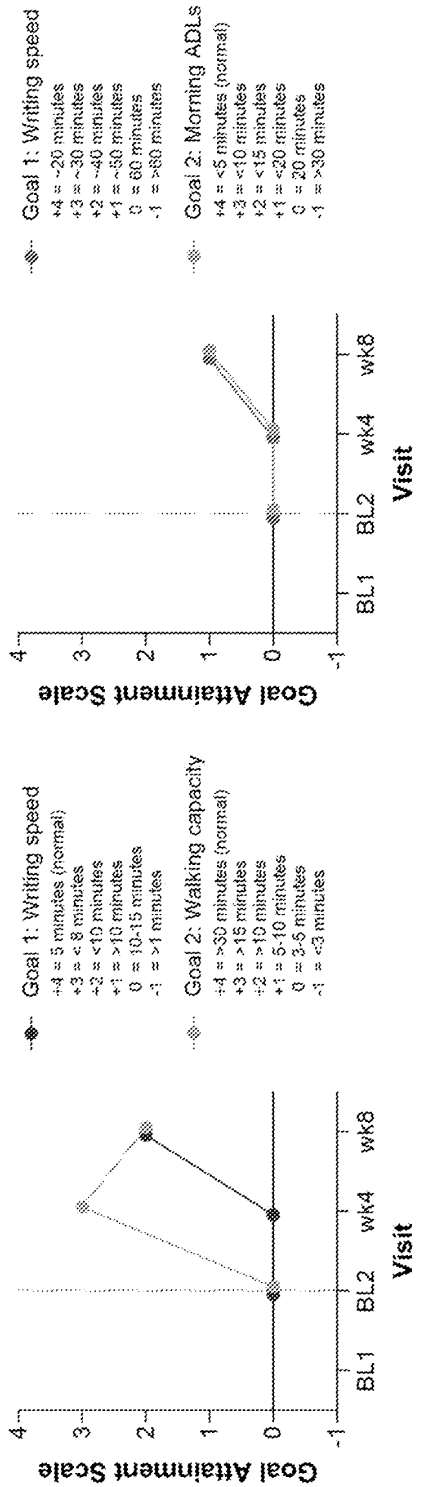

Goal 1: Writing speed
+4 = 5 minutes (normal)
+3 = < 8 minutes
+2 = <10 minutes
+1 = >10 minutes
0 = 10-15 minutes
-1 = >1 minutes
Goal 2: Walking capacity
+4 = >30 minutes (normal)
+3 = >15 minutes
+2 = >10 minutes
+1 = 5-10 minutes
0 = 3-5 minutes
-1 = <3 minutes
Goal Attainment Scale
4
3
2
1
0
-1
BL1
BL2
wk4
wk8
Visit
Goal 1: Writing speed
+4 = ~20 minutes
+3 = ~30 minutes
+2 = ~40 minutes
+1 = ~50 minutes
0 = 60 minutes
-1 = >60 minutes
Goal 2: Morning ADLs
+4 = <5 minutes (normal)
+3 = <10 minutes
+2 = <15 minutes
+1 = <20 minutes
0 = 20 minutes
-1 = >30 minutes
Goal Attainment Scale
4
3
2
1
0
-1
BL1
BL2
wk4
wk8
Visit

FIG. 21