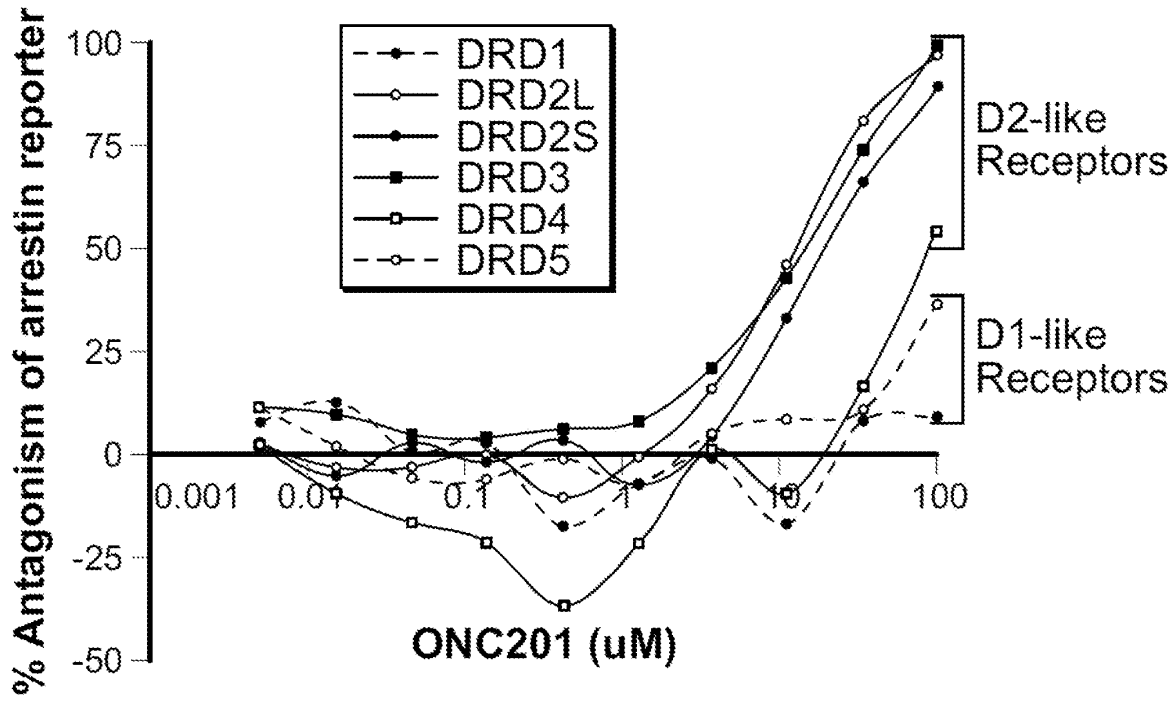
Figure 1


% Antagonism of arrestin reporter
100
75
50
25
0
-25
-50
0.001
0.01
0.1
1
10
100
ONC201 (uM)
DRD1
DRD2L
DRD2S
DRD3
DRD4
DRD5
D2-like Receptors
D1-like Receptors

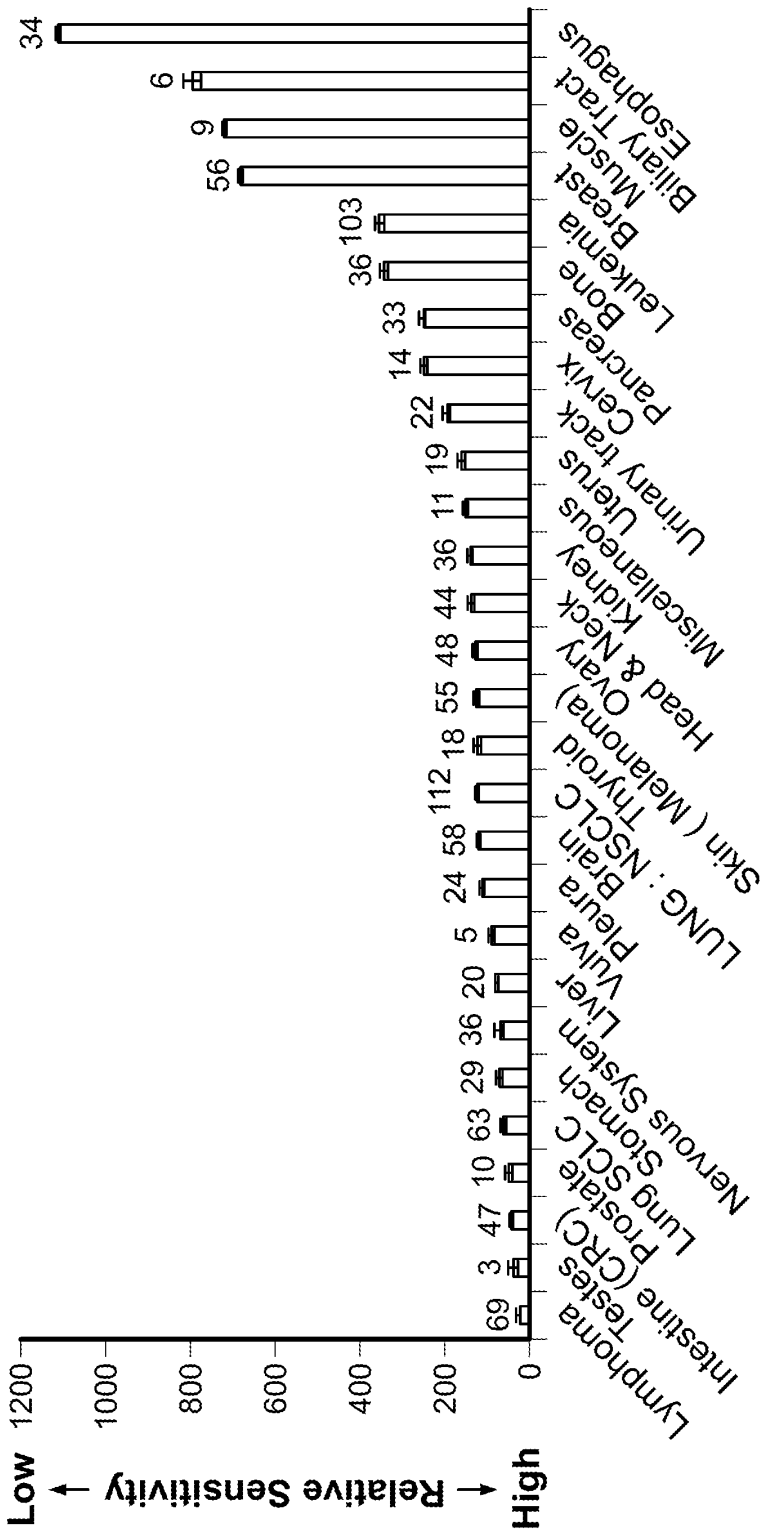
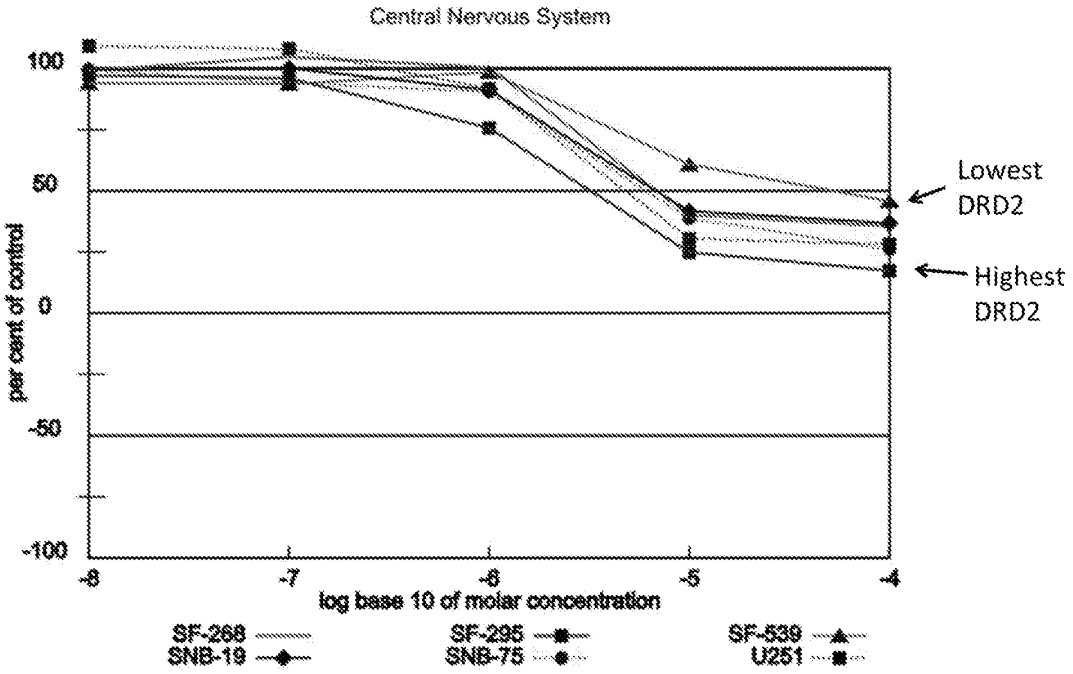

Low
Relative Sensitivity
High
1200
1000
800
600
400
200
0
69
3
47
10
63
29
36
20
5
24
58
112
18
55
48
44
36
11
19
22
14
33
36
103
56
9
6
34
Testes
Intestine (CRC)
Prostate
Lung SCLC
Stomach
Nervous System
Liver
Vulva
Pleura
Brain
LUNG : NSCLC
Thyroid
Skin (Melanoma)
Ovary
Head & Neck
Kidney
Miscellaneous
Uterus
Urinary tract
Cervix
Pancreas
Bone
Leukemia
Breast
Muscle
Biliary Tract
Esophagus

Figure 2

Figure 3

A


Central Nervous System
100
50
0
-50
-100
per cent of control
-8
-7
-6
-5
-4
log base 10 of molar concentration
Lowest DRD2
Highest DRD2
SF-268
SNB-19
SF-295
SNB-75
SF-539
U251

B

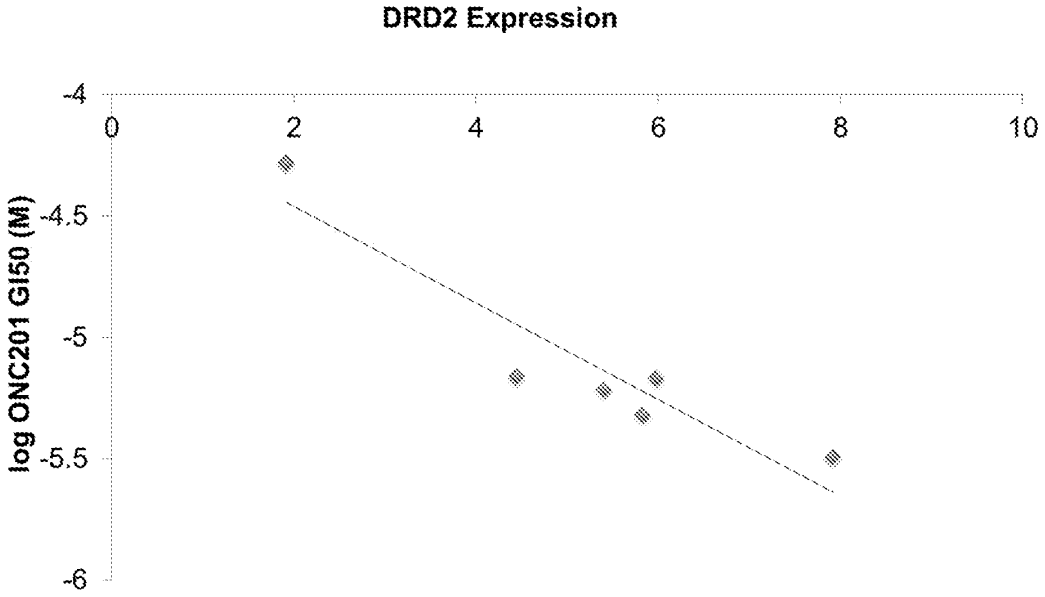
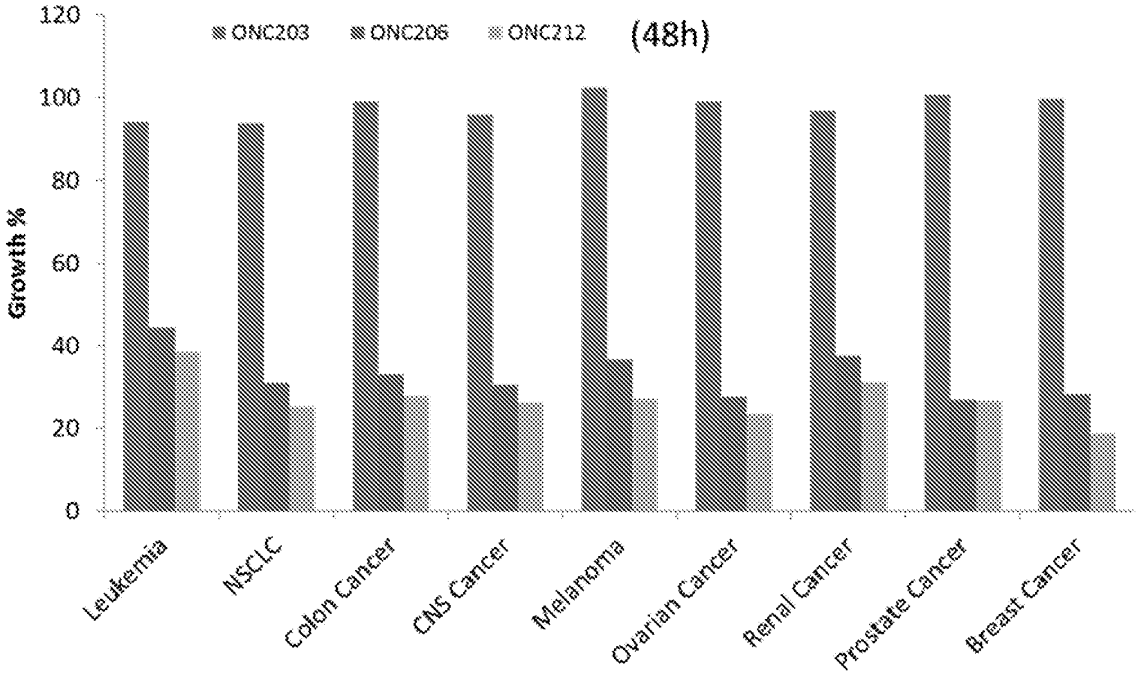

DRD2 Expression
-4
0
2
4
6
8
10
-4.5
-5
-5.5
-6
log ONC201 GI50 (M)

Figure 4


120
100
80
60
40
20
0
Growth %
ONC203
ONC206
ONC212
(48h)
Leukemia
NSCLC
Colon Cancer
CNS Cancer
Melanoma
Ovarian Cancer
Renal Cancer
Prostate Cancer
Breast Cancer

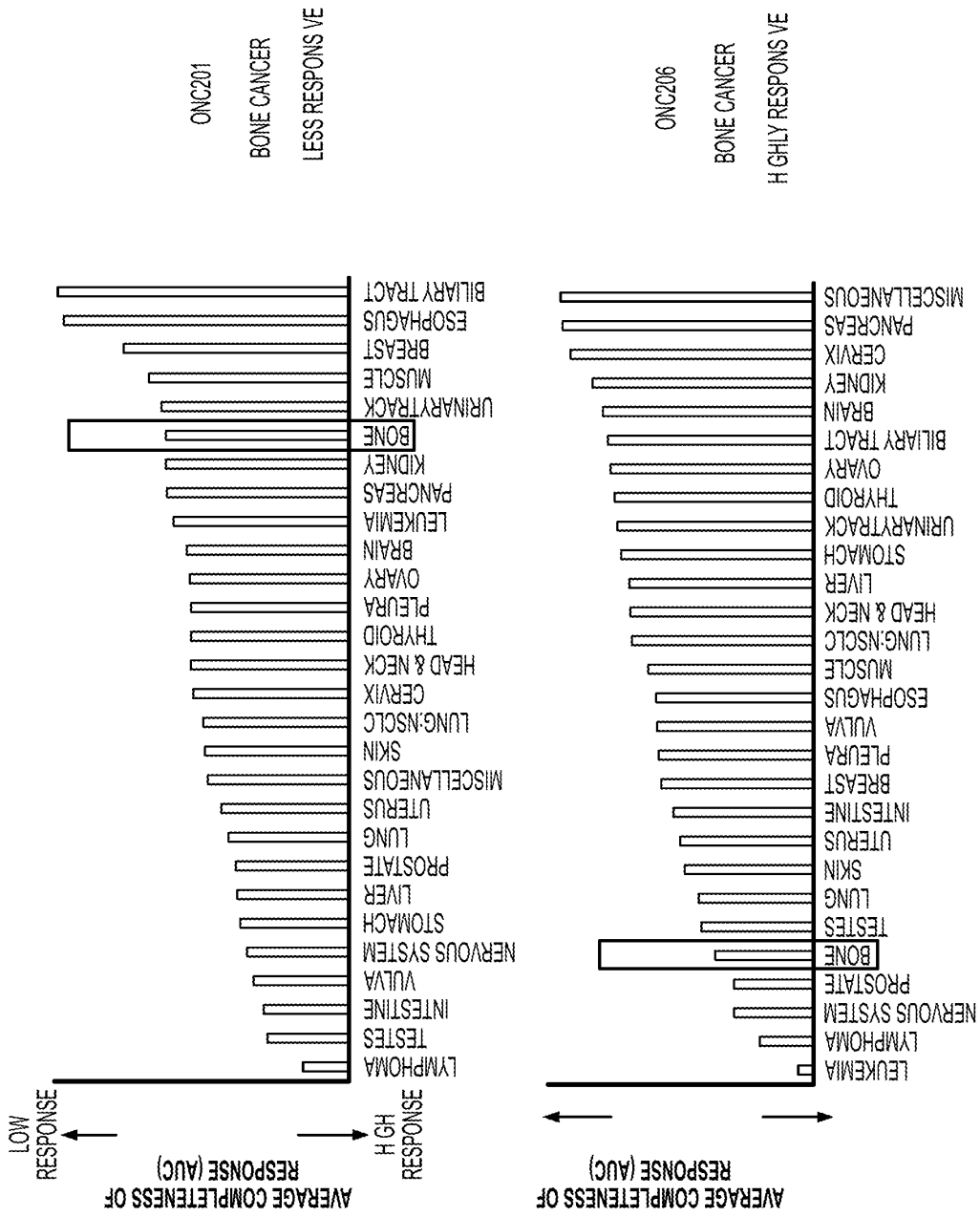
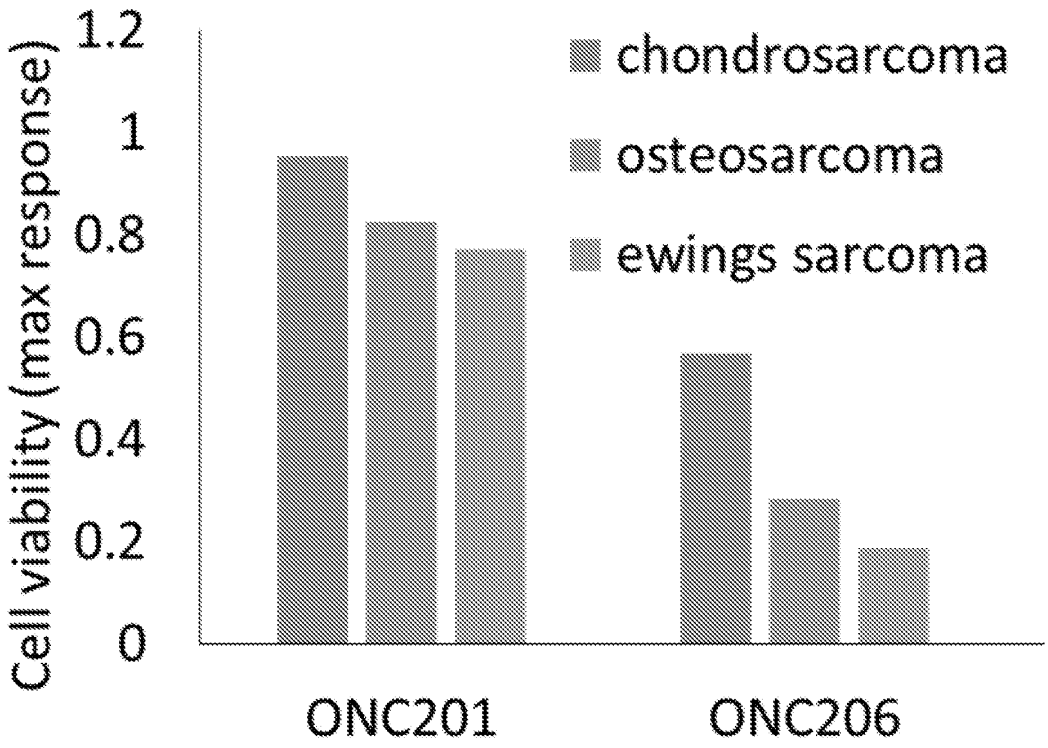
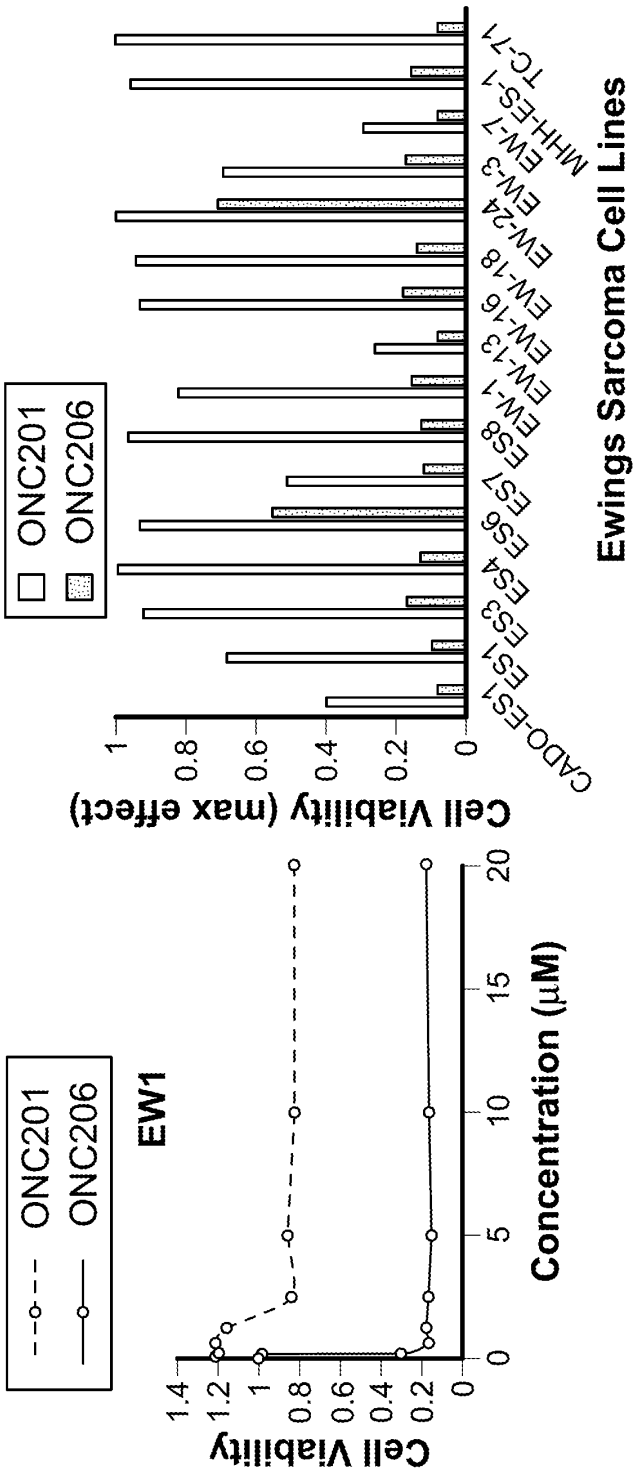

ONC201
BONE CANCER
LESS RESPONS VE
LYMPHOMA
TESTES
INTESTINE
VULVA
NERVOUS SYSTEM
STOMACH
LIVER
PROSTATE
LUNG
UTERUS
MISCELLANEOUS
SKIN
LUNG:NSCLC
CERVIX
HEAD & NECK
THYROID
PLEURA
OVARY
BRAIN
LEUKEMIA
PANCREAS
KIDNEY
BONE
URINARYTRACK
MUSCLE
BREAST
ESOPHAGUS
BILIARY TRACT
LOW RESPONSE
H GH RESPONSE
AVERAGE COMPLETENESS OF RESPONSE (AUC)
ONC206
BONE CANCER
H GHLY RESPONS VE
LEUKEMIA
LYMPHOMA
NERVOUS SYSTEM
PROSTATE
BONE
TESTES
LUNG
SKIN
UTERUS
INTESTINE
BREAST
PLEURA
VULVA
ESOPHAGUS
MUSCLE
LUNG:NSCLC
HEAD & NECK
LIVER
STOMACH
URINARYTRACK
THYROID
OVARY
BILIARY TRACT
BRAIN
KIDNEY
CERVIX
PANCREAS
MISCELLANEOUS
AVERAGE COMPLETENESS OF RESPONSE (AUC)

Figure 6


Cell viability (max response)
1.2
1
0.8
0.6
0.4
0.2
0
chondrosarcoma
osteosarcoma
ewings sarcoma
ONC201
ONC206


ONC201
ONC206
EW1
Cell Viability
1.4
1.2
1
0.8
0.6
0.4
0.2
0
0
5
10
15
20
Concentration (μM)
ONC201
ONC206
Cell Viability (max effect)
1
0.8
0.6
0.4
0.2
0
CADO-ES1
ES1
ES3
ES4
ES6
ES7
ES8
EW-1
EW-13
EW-16
EW-18
EW-24
EW-3
EW-7
MHH-ES-1
TC-71
Ewings Sarcoma Cell Lines

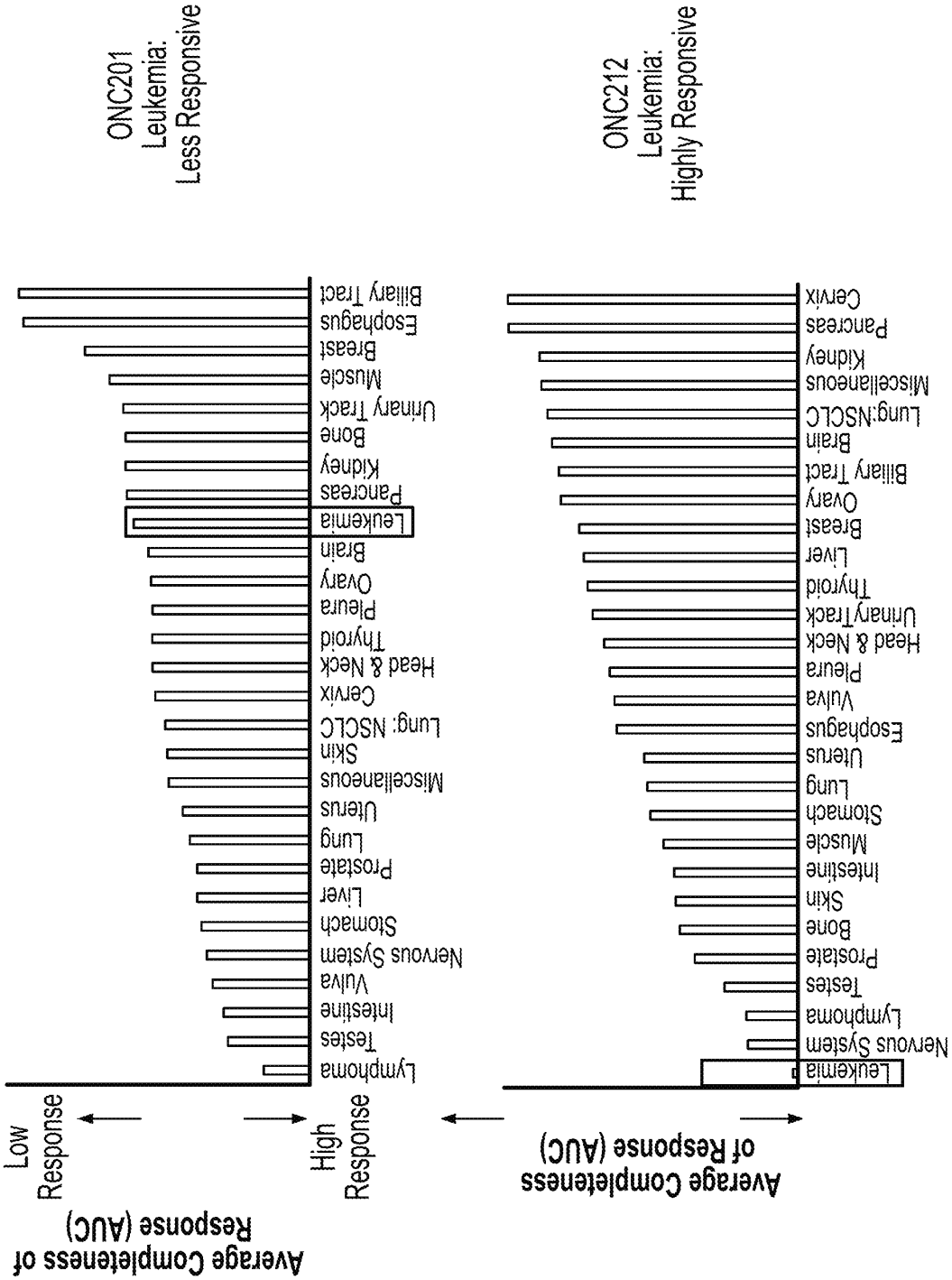
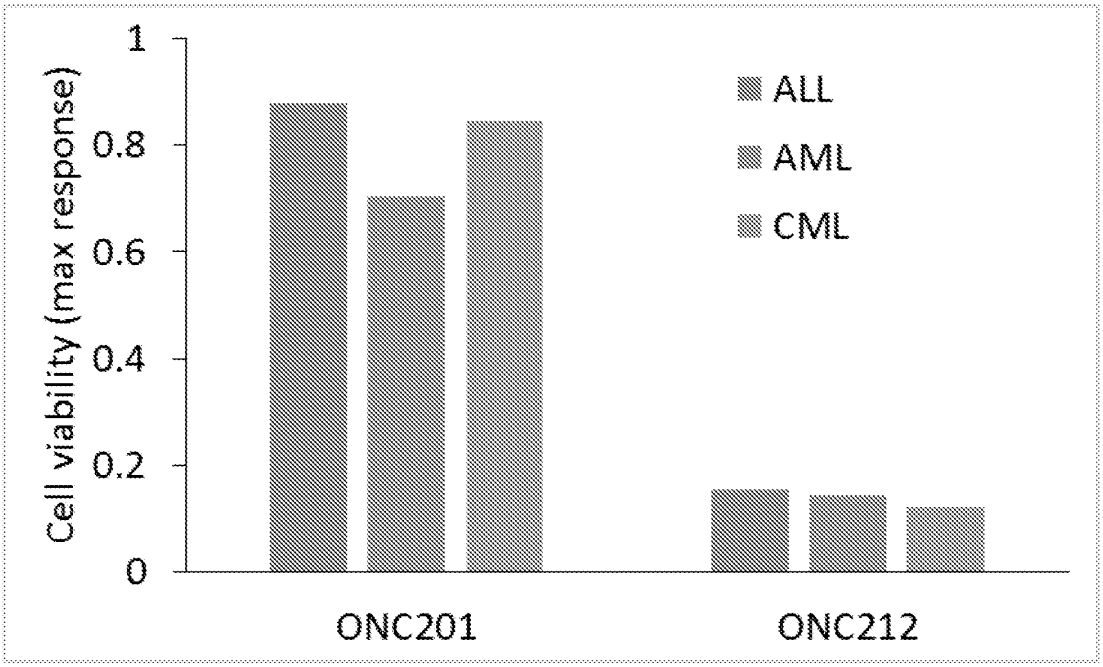
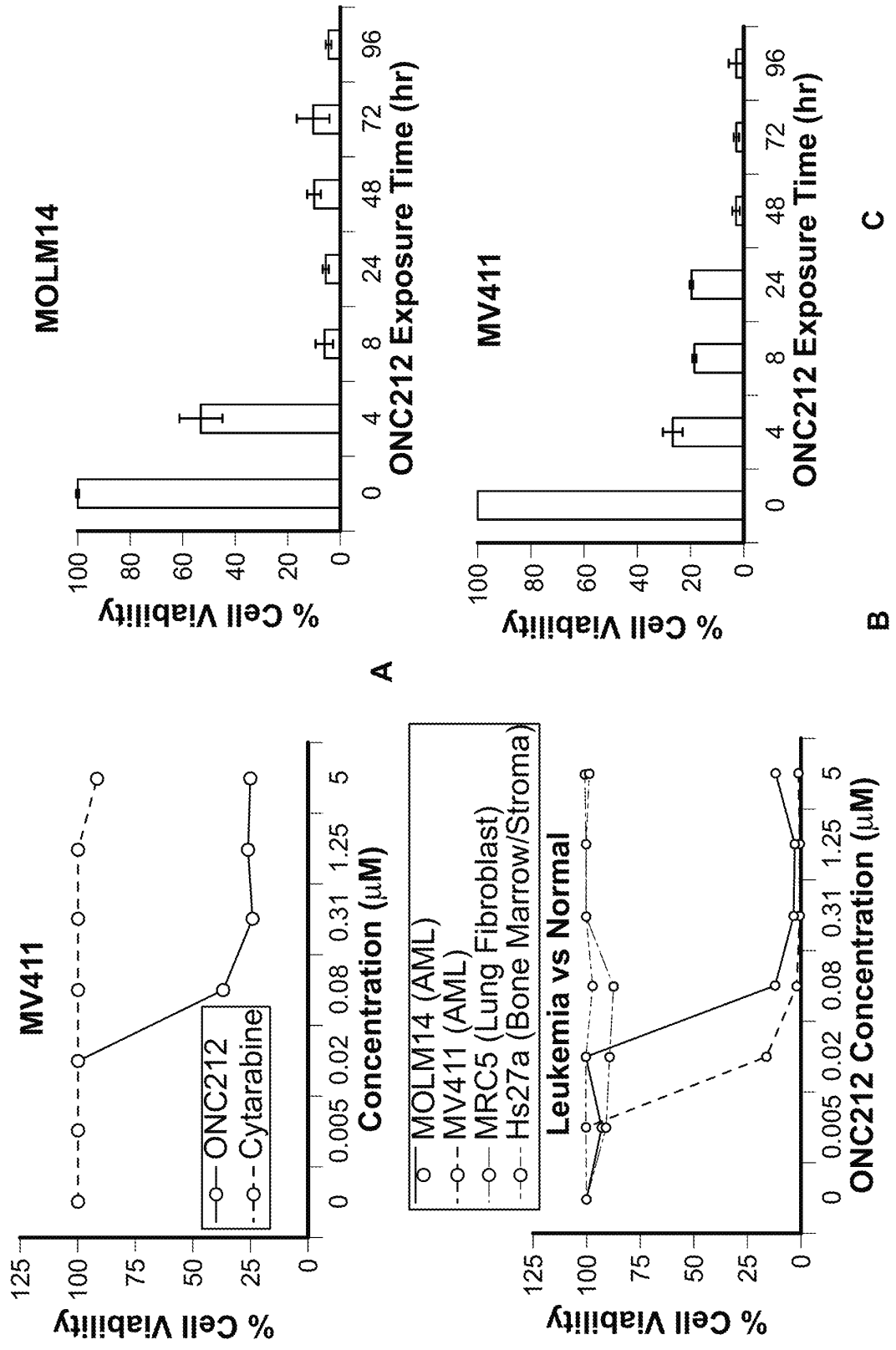
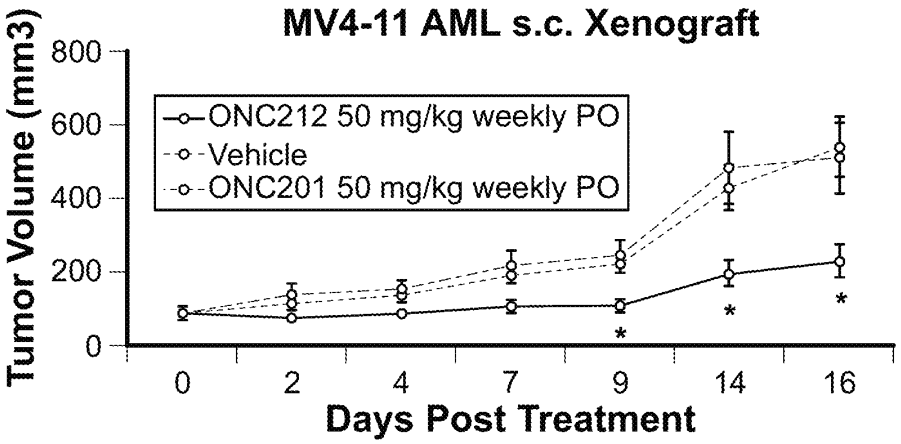

ONC201
Leukemia:
Less Responsive
ONC212
Leukemia:
Highly Responsive
Average Completeness of Response (AUC)
Low Response
High Response
Lymphoma
Testes
Intestine
Vulva
Nervous System
Stomach
Liver
Prostate
Lung
Uterus
Miscellaneous
Skin
Lung: NSCLC
Cervix
Head & Neck
Thyroid
Pleura
Ovary
Brain
Leukemia
Pancreas
Kidney
Bone
Urinary Track
Muscle
Breast
Esophagus
Biliary Tract
Leukemia
Nervous System
Lymphoma
Testes
Prostate
Bone
Skin
Intestine
Muscle
Stomach
Lung
Uterus
Esophagus
Vulva
Pleura
Head & Neck
Urinary Track
Thyroid
Liver
Breast
Ovary
Biliary Tract
Brain
Lung:NSCLC
Miscellaneous
Kidney
Pancreas
Cervix

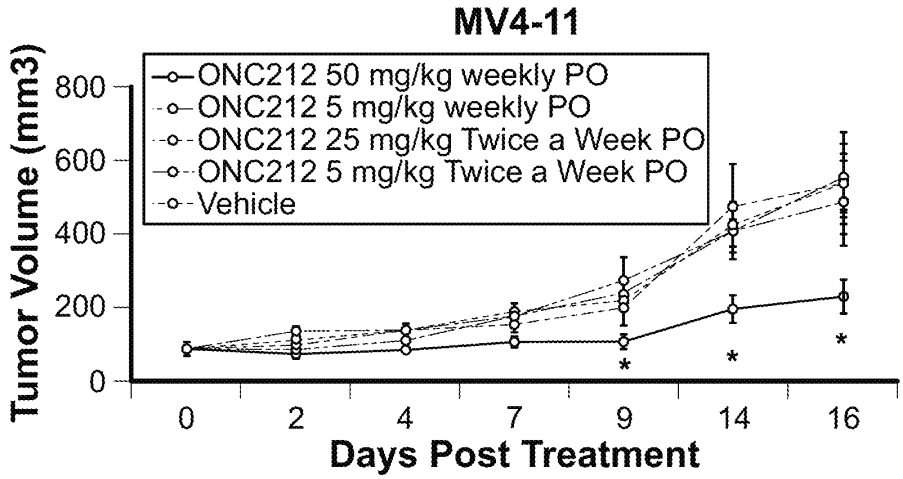
Figure 9


Cell viability (max response)
1
0.8
0.6
0.4
0.2
0
ALL
AML
CML
ONC201
ONC212

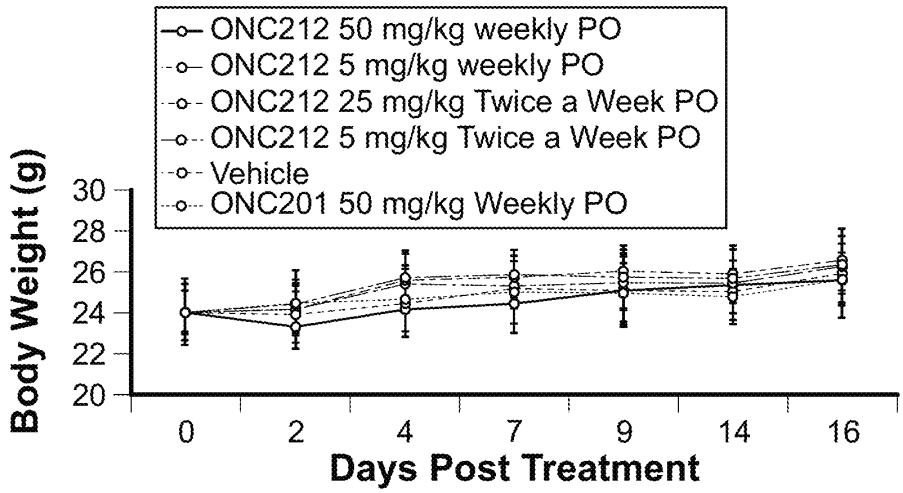

MOLM14
% Cell Viability
ONC212 Exposure Time (hr)
A
MV411
% Cell Viability
ONC212 Exposure Time (hr)
B
C
MV411
% Cell Viability
ONC212
Cytarabine
Concentration (μM)
Leukemia vs Normal
MOLM14 (AML)
MV411 (AML)
MRC5 (Lung Fibroblast)
Hs27a (Bone Marrow/Stroma)
% Cell Viability
ONC212 Concentration (μM)


MV4-11 AML s.c. Xenograft
Tumor Volume (mm3)
800
600
400
200
0
ONC212 50 mg/kg weekly PO
Vehicle
ONC201 50 mg/kg weekly PO
*
*
*
0
2
4
7
9
14
16
Days Post Treatment

A

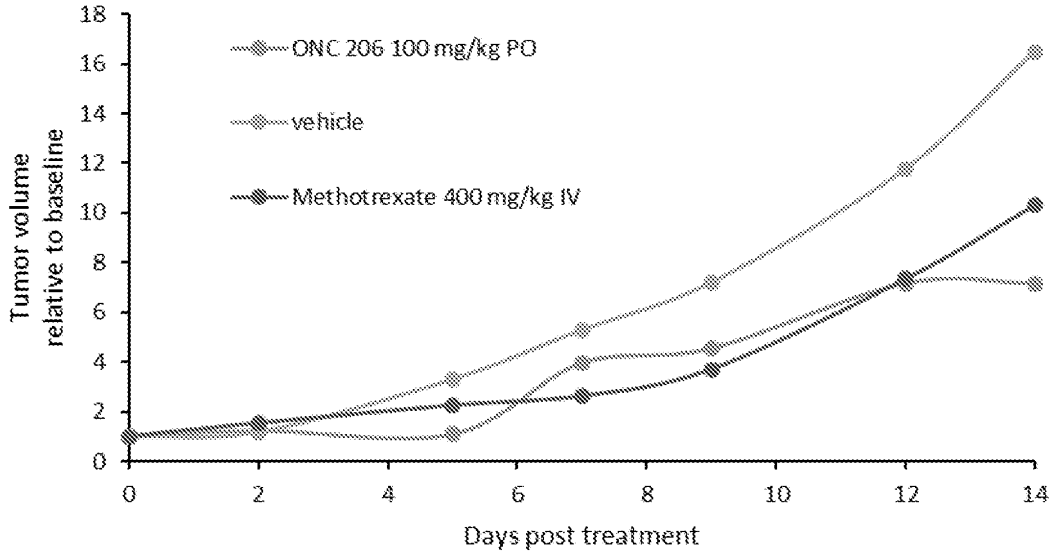

MV4-11
Tumor Volume (mm3)
800
600
400
200
0
ONC212 50 mg/kg weekly PO
ONC212 5 mg/kg weekly PO
ONC212 25 mg/kg Twice a Week PO
ONC212 5 mg/kg Twice a Week PO
Vehicle
*
*
*
0
2
4
7
9
14
16
Days Post Treatment

B

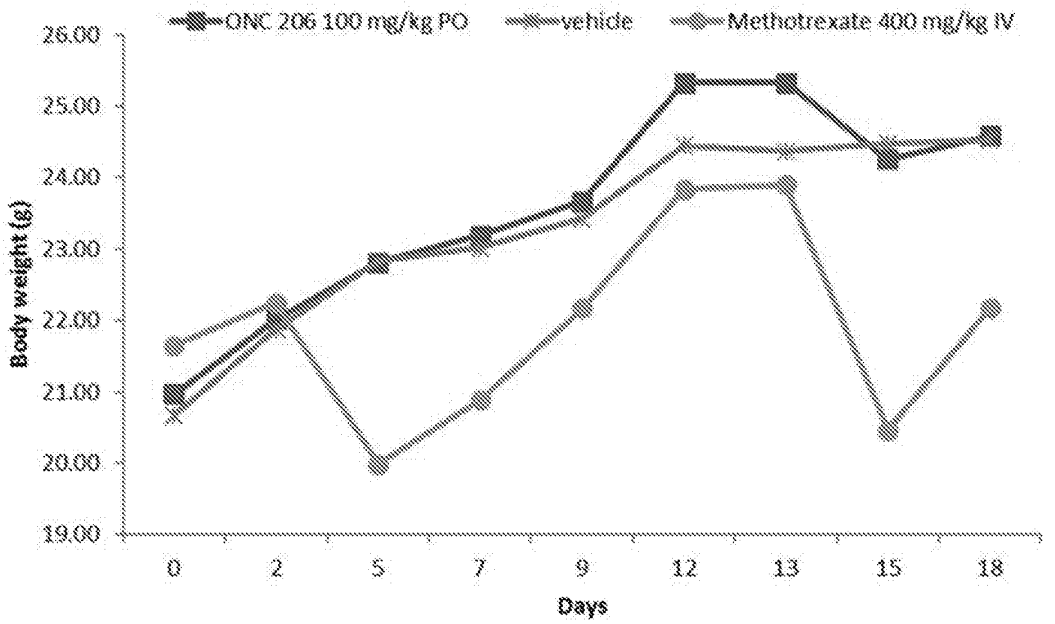

Body Weight (g)
30
28
26
24
22
20
ONC212 50 mg/kg weekly PO
ONC212 5 mg/kg weekly PO
ONC212 25 mg/kg Twice a Week PO
ONC212 5 mg/kg Twice a Week PO
Vehicle
ONC201 50 mg/kg Weekly PO
0
2
4
7
9
14
16
Days Post Treatment

C

Figure 12


ONC 206 100 mg/kg PO
vehicle
Methotrexate 400 mg/kg IV
Tumor volume relative to baseline
Days post treatment
0
2
4
6
8
10
12
14
16
18

A


ONC 206 100 mg/kg PO
vehicle
Methotrexate 400 mg/kg IV
Body weight (g)
Days
19.00
20.00
21.00
22.00
23.00
24.00
25.00
26.00
0
2
5
7
9
12
13
15
18

B

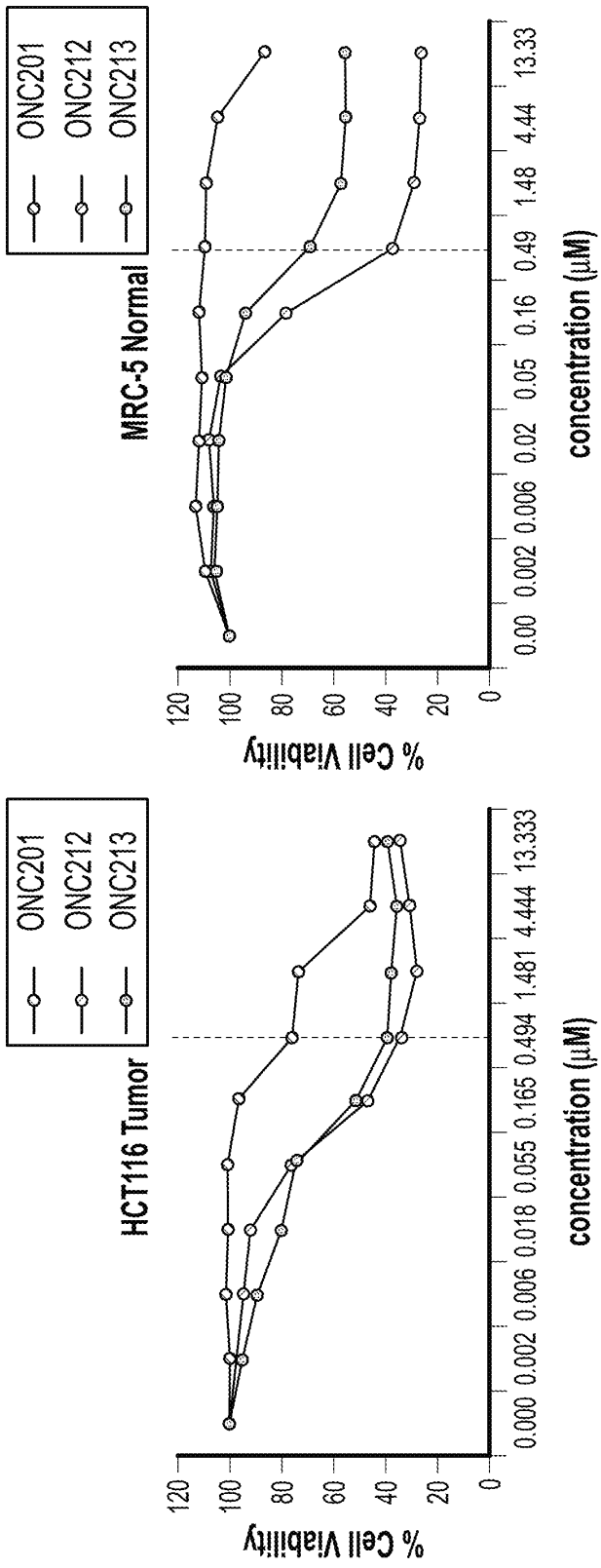

MRC-5 Normal
ONC201
ONC212
ONC213
% Cell Viability
120
100
80
60
40
20
0
0.00
0.002
0.006
0.02
0.05
0.16
0.49
1.48
4.44
13.33
concentration (µM)
HCT116 Tumor
ONC201
ONC212
ONC213
% Cell Viability
120
100
80
60
40
20
0
0.000
0.002
0.006
0.018
0.055
0.165
0.494
1.481
4.444
13.333
concentration (µM)

Figure 13

Figure 14

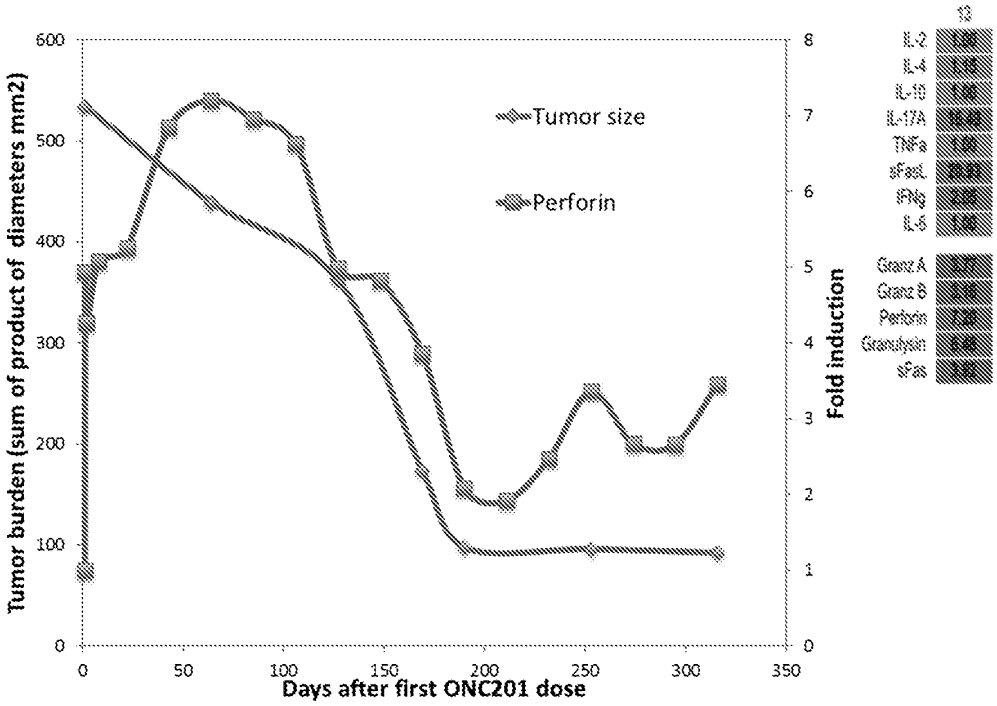

Tumor burden (sum of product of diameters mm2)
Days after first ONC201 dose
Fold induction
Tumor size
Perforin
IL-2
IL-4
IL-10
IL-17A
TNFa
sFasL
IFNg
IL-6
Granz A
Granz B
Perforin
Granulysin
sFas

Figure 15

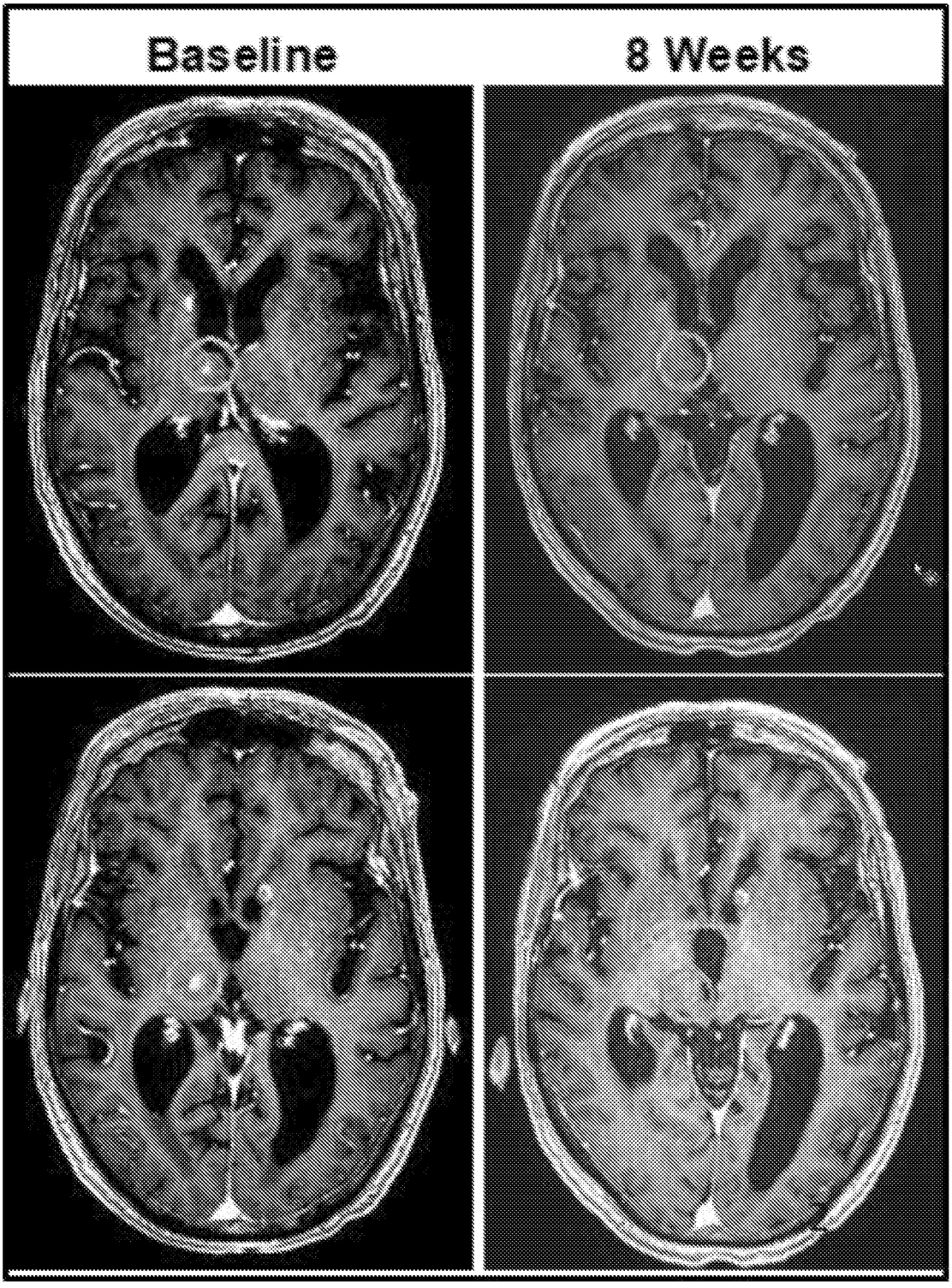


Figure 16

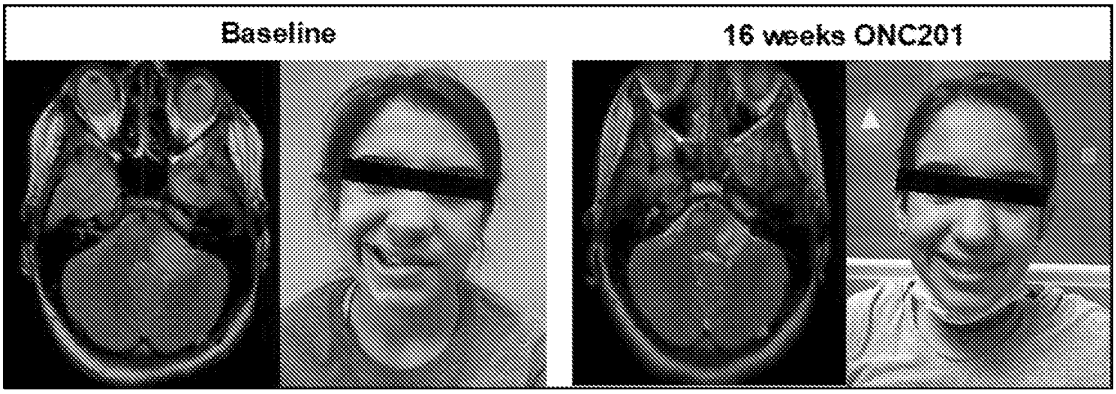
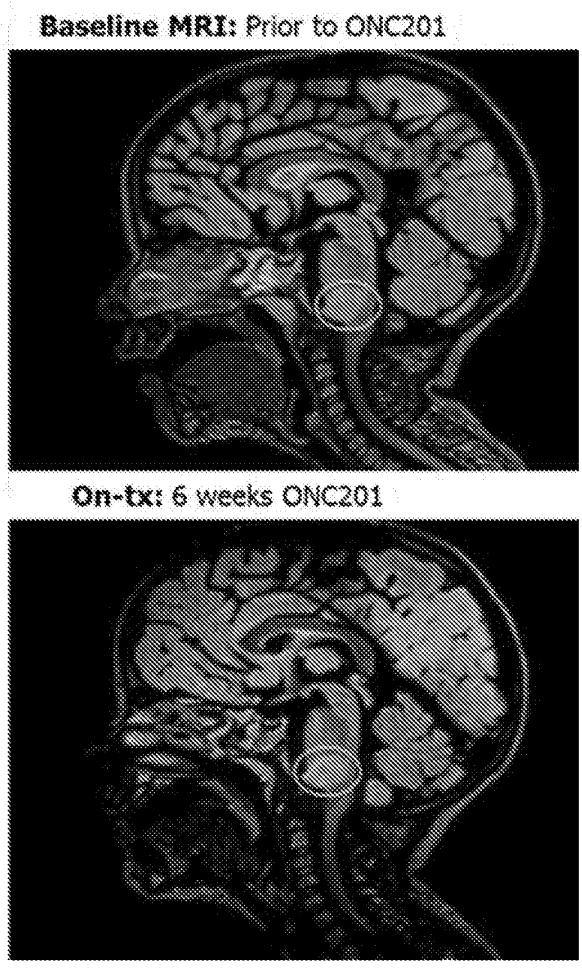


Figure 17



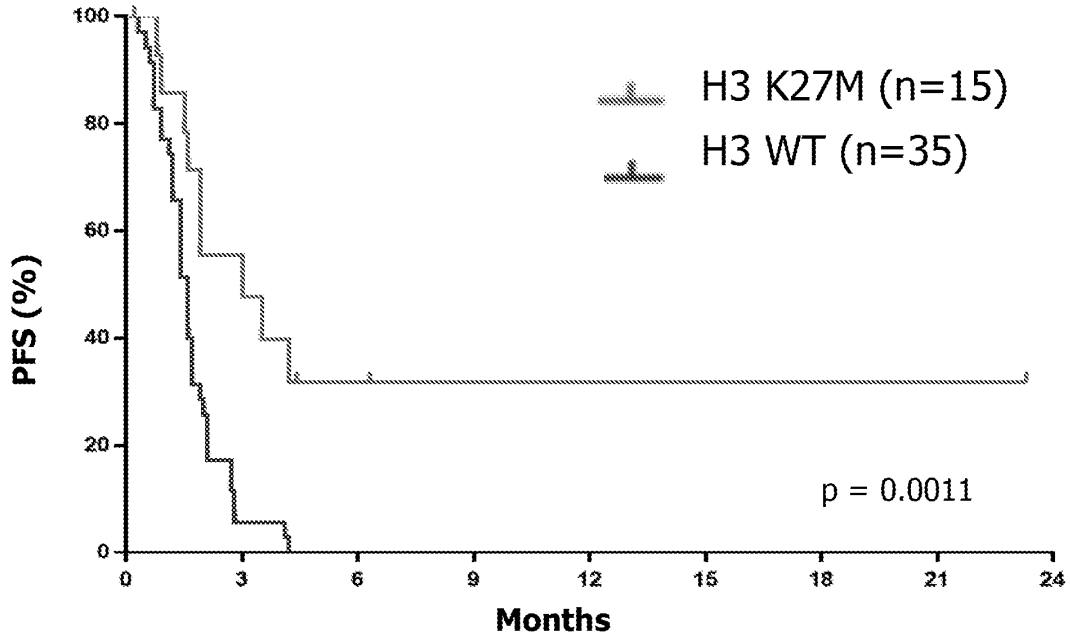

100
80
60
40
20
0
PFS (%)
0
3
6
9
12
15
18
21
24
Months
H3 K27M (n=15)
H3 WT (n=35)
p = 0.0011

Figure 18

Figure 19

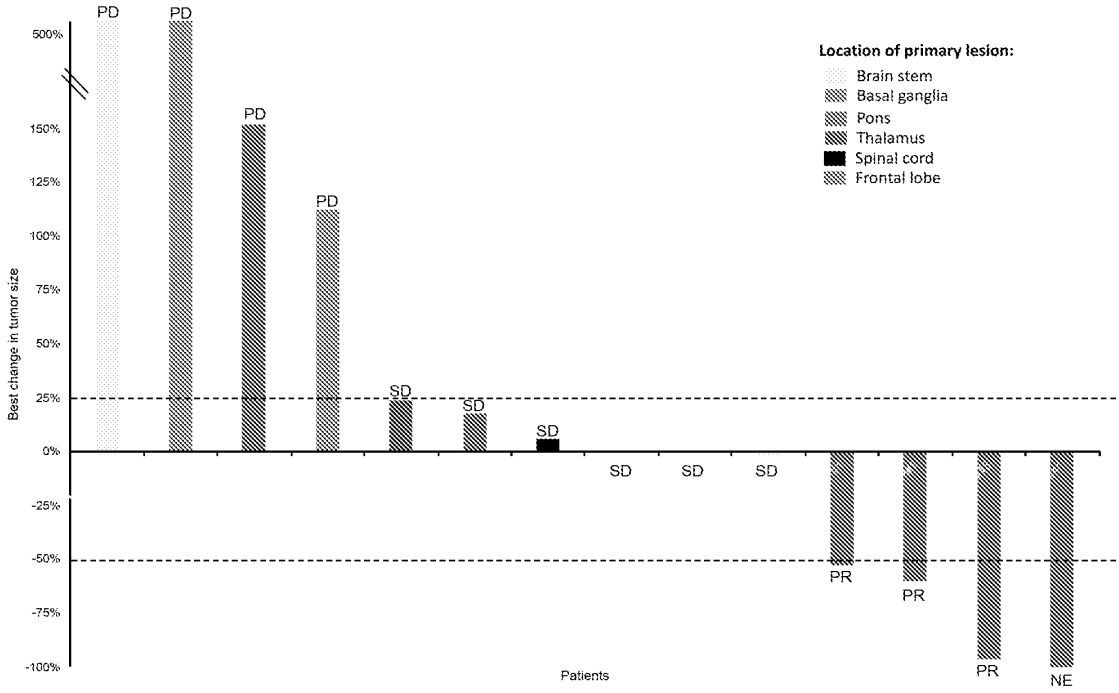
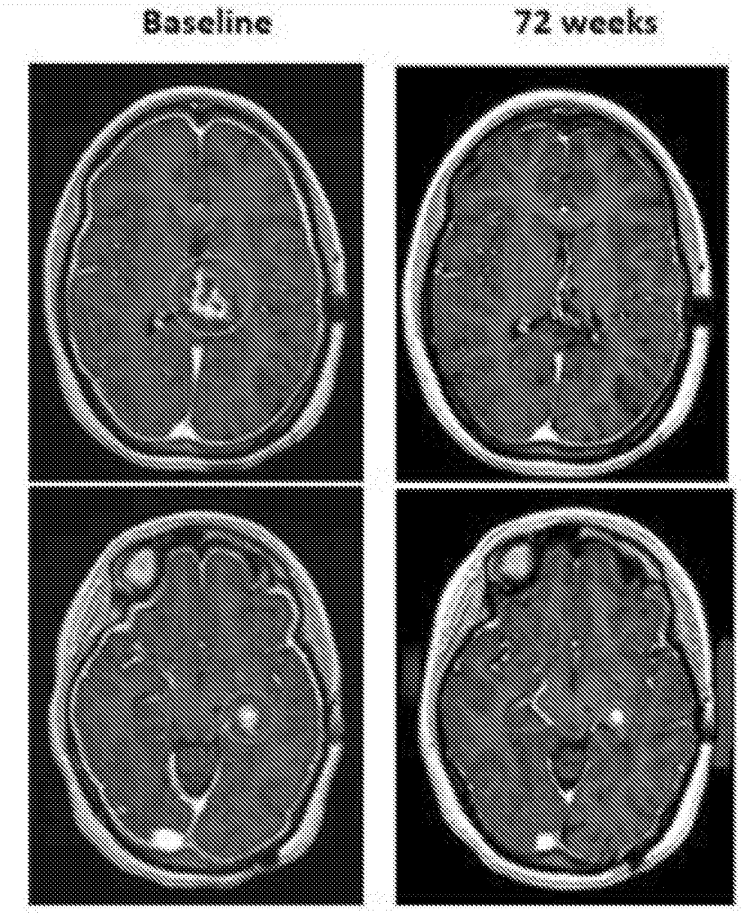

Best change in tumor size
500%
150%
125%
100%
75%
50%
25%
0%
-25%
-50%
-75%
-100%
PD
PD
PD
PD
SD
SD
SD
SD
SD
SD
PR
PR
PR
NE
Patients
Location of primary lesion:
Brain stem
Basal ganglia
Pons
Thalamus
Spinal cord
Frontal lobe

Figure 20

A


Baseline
72 weeks

B

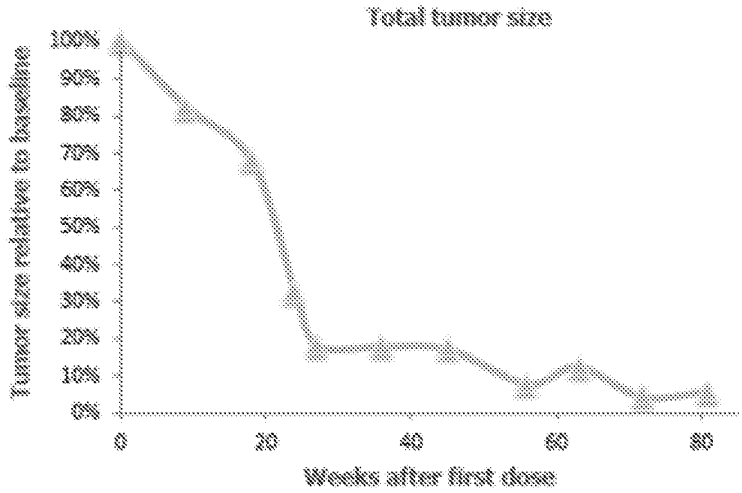

Total tumor size
Tumor size relative to baseline
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0
20
40
60
80
Weeks after first dose

Figure 21

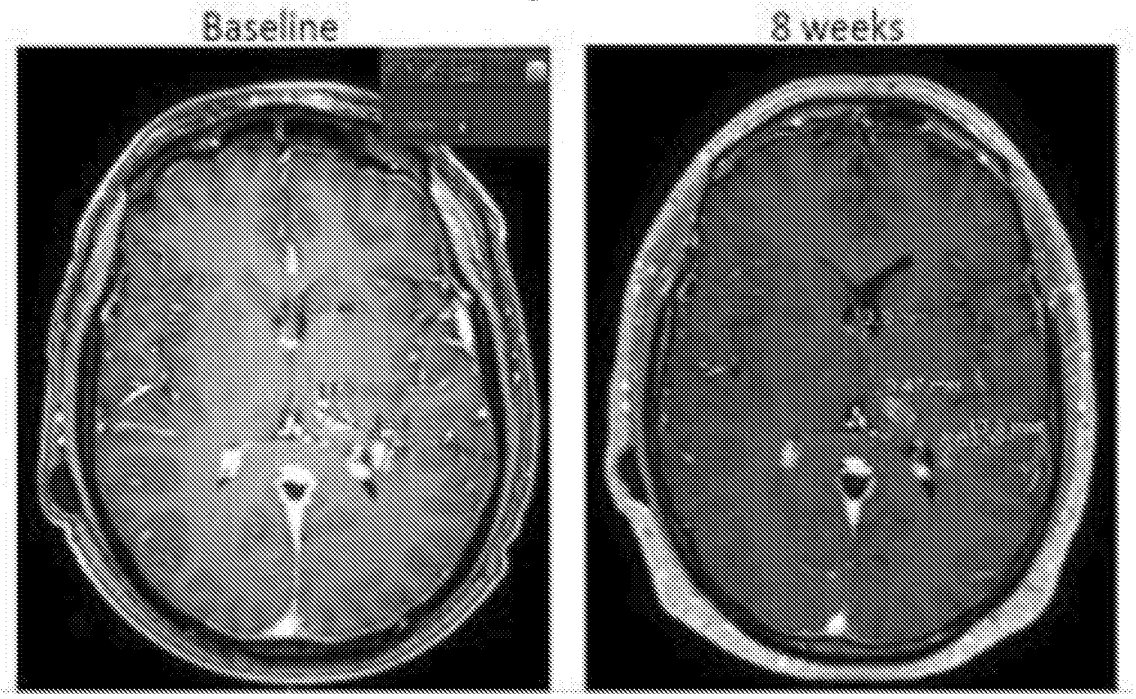


Figure 22

