Figure 1A

RSPO1

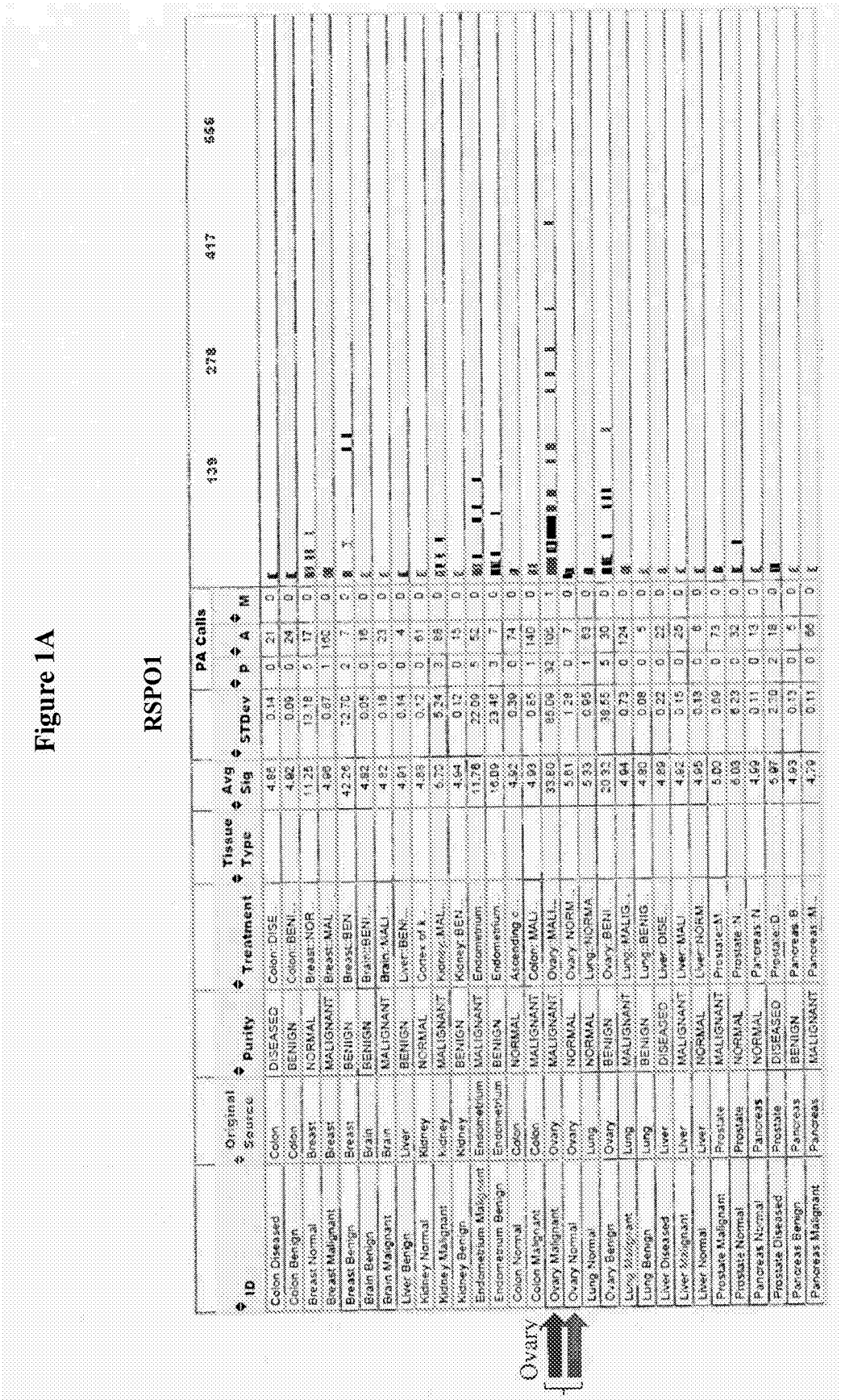
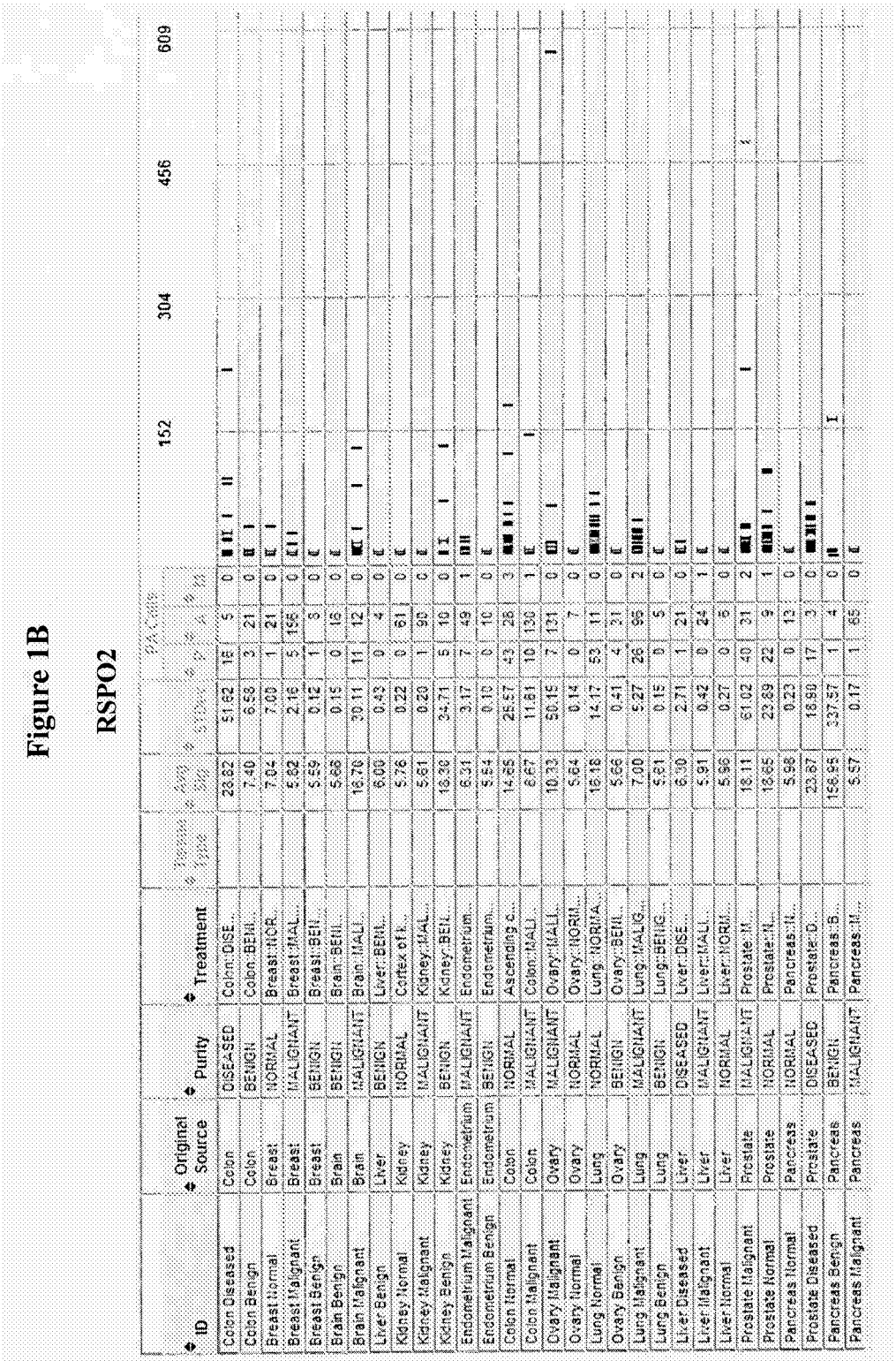


Figure 1B

RSPO2



ID	Original Source	Purity	Treatment	Tissue Type	Average Expression	Standard Deviation	Expression Value	Count	Percentile
Colon Diseased	Colon	DISEASED	Colon::DISE...		23.82	51.62	16	5	0
Colon Benign	Colon	BENIGN	Colon::BENI...		7.40	6.58	3	21	0
Breast Normal	Breast	NORMAL	Breast::NOR...		7.04	7.00	1	21	0
Breast Malignant	Breast	MALIGNANT	Breast::MAL...		5.62	2.16	5	155	0
Breast Benign	Breast	BENIGN	Breast::BEN...		5.59	0.12	1	5	0
Brain Benign	Brain	BENIGN	Brain::BENI...		5.68	0.15	0	16	0
Brain Malignant	Brain	MALIGNANT	Brain::MALI...		16.76	30.11	11	12	0
Liver Benign	Liver	BENIGN	Liver::BENI...		6.00	0.43	0	4	0
Kidney Normal	Kidney	NORMAL	Cortex et k...		5.76	0.22	0	61	0
Kidney Malignant	Kidney	MALIGNANT	Kidney::MAL...		5.81	0.20	1	90	0
Kidney Benign	Kidney	BENIGN	Kidney::BEN...		16.38	34.71	5	10	0
Endometrium Malignant	Endometrium	MALIGNANT	Endometrium...		6.31	3.17	7	49	1
Endometrium Benign	Endometrium	BENIGN	Endometrium...		5.64	0.10	0	10	0
Colon Normal	Colon	NORMAL	Ascending c...		14.65	25.57	43	28	3
Colon Malignant	Colon	MALIGNANT	Colon::MALI...		8.67	11.81	10	130	1
Ovary Malignant	Ovary	MALIGNANT	Ovary::MALI...		10.33	50.15	7	131	0
Ovary Normal	Ovary	NORMAL	Ovary::NORM...		5.64	0.14	0	7	0
Lung Normal	Lung	NORMAL	Lung::NORMA...		16.16	14.17	53	11	0
Ovary Benign	Ovary	BENIGN	Ovary::BENI...		5.66	0.41	4	31	0
Lung Malignant	Lung	MALIGNANT	Lung::MALIG...		7.00	5.27	26	95	2
Lung Benign	Lung	BENIGN	Lung::BENIG...		5.61	0.15	0	5	0
Liver Diseased	Liver	DISEASED	Liver::DISE...		6.30	2.71	1	21	0
Liver Malignant	Liver	MALIGNANT	Liver::MALI...		5.91	0.42	0	24	1
Liver Normal	Liver	NORMAL	Liver::NORM...		5.96	0.27	0	6	0
Prostate Malignant	Prostate	MALIGNANT	Prostate::M...		18.11	61.02	40	31	2
Prostate Normal	Prostate	NORMAL	Prostate::N...		18.65	23.89	22	9	1
Pancreas Normal	Pancreas	NORMAL	Pancreas::N...		5.98	0.23	0	13	0
Prostate Diseased	Prostate	DISEASED	Prostate::D...		23.87	18.80	17	3	0
Pancreas Benign	Pancreas	BENIGN	Pancreas::B...		158.95	337.57	1	4	0
Pancreas Malignant	Pancreas	MALIGNANT	Pancreas::M...		5.57	0.17	1	65	0

Figure 1C

RSPO3

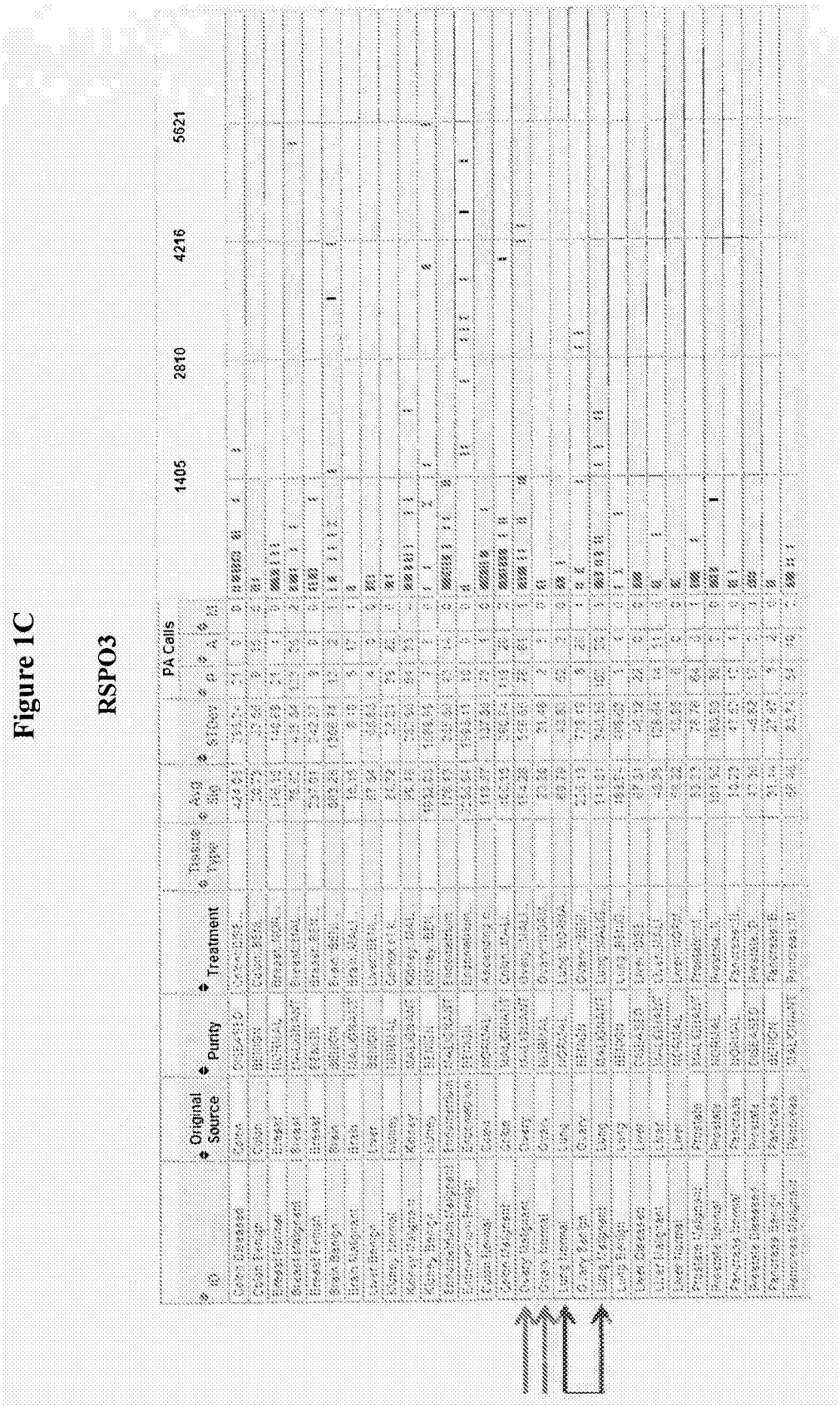


Figure 2

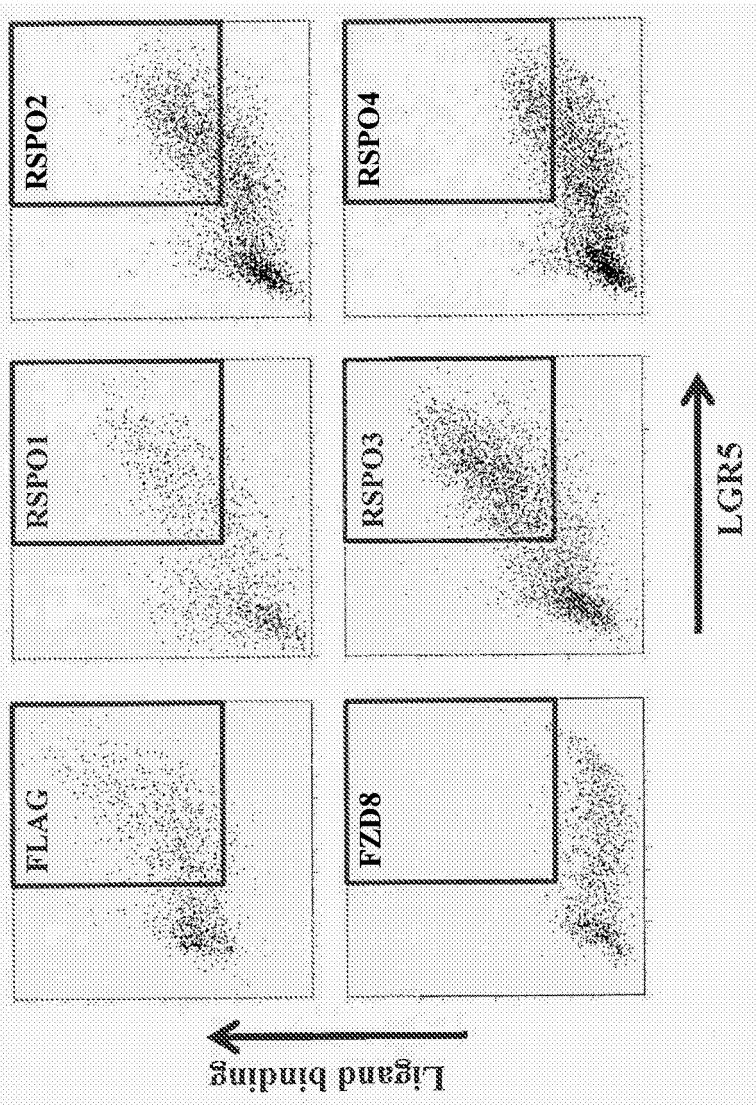


Figure 3

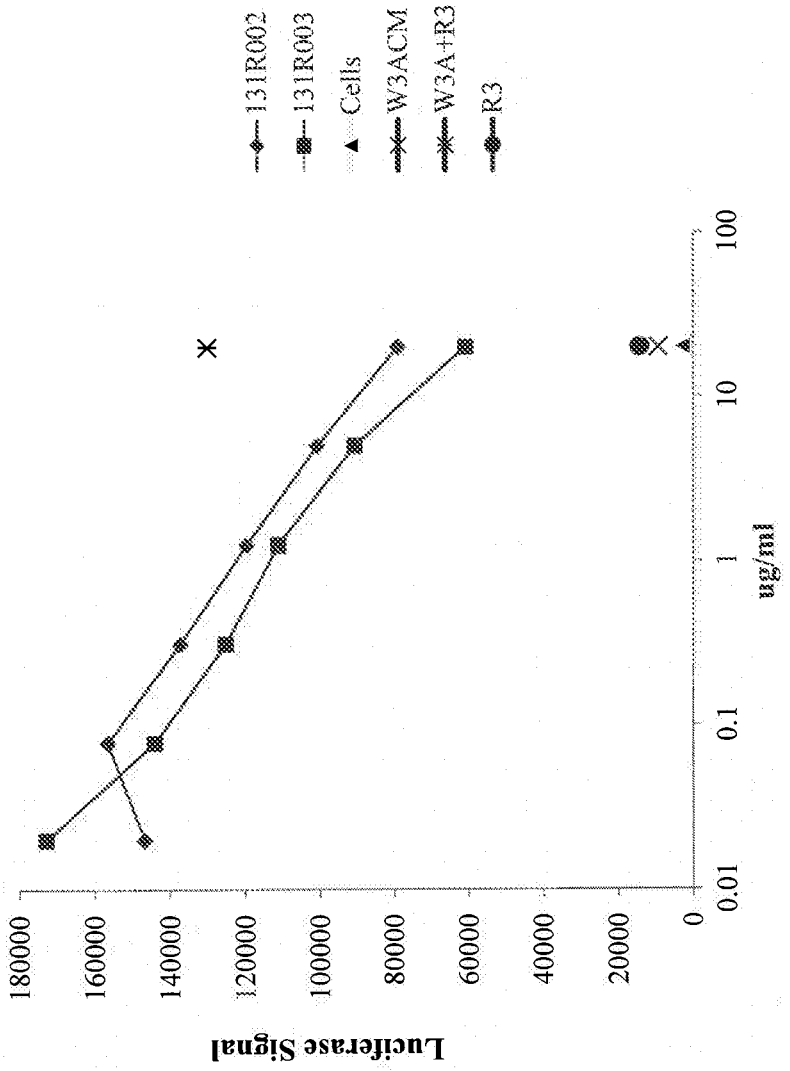

131R002
131R003
Cells
W3ACM
W3A+R3
R3
Luciferase Signal
180000
160000
140000
120000
100000
80000
60000
40000
20000
0
0.01
0.1
1
10
100
ug/ml

Figure 4

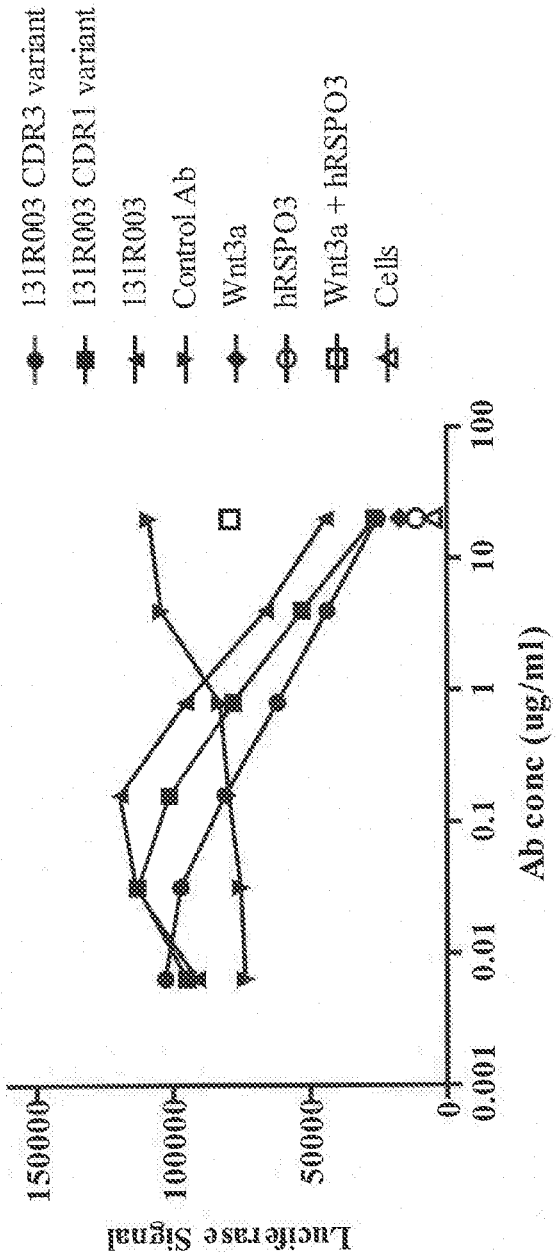

131R003 CDR3 variant
131R003 CDR1 variant
131R003
Control Ab
Wnt3a
hRSPO3
Wnt3a + hRSPO3
Cells
Luciferase Signal
150000
100000
50000
0
0.001
0.01
0.1
1
10
100
Ab conc (ug/ml)

Figure 5

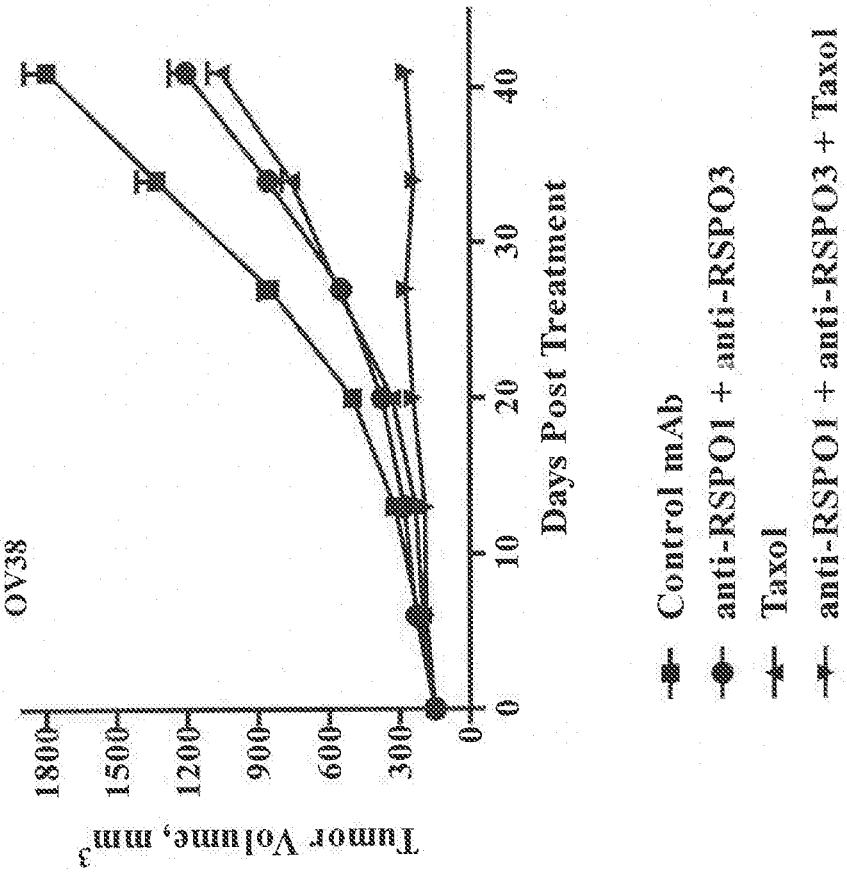

OV38
Tumor Volume, mm3
1800
1500
1200
900
600
300
0
0
10
20
30
40
Days Post Treatment
Control mAb
anti-RSPO1 + anti-RSPO3
Taxol
anti-RSPO1 + anti-RSPO3 + Taxol

Figure 6

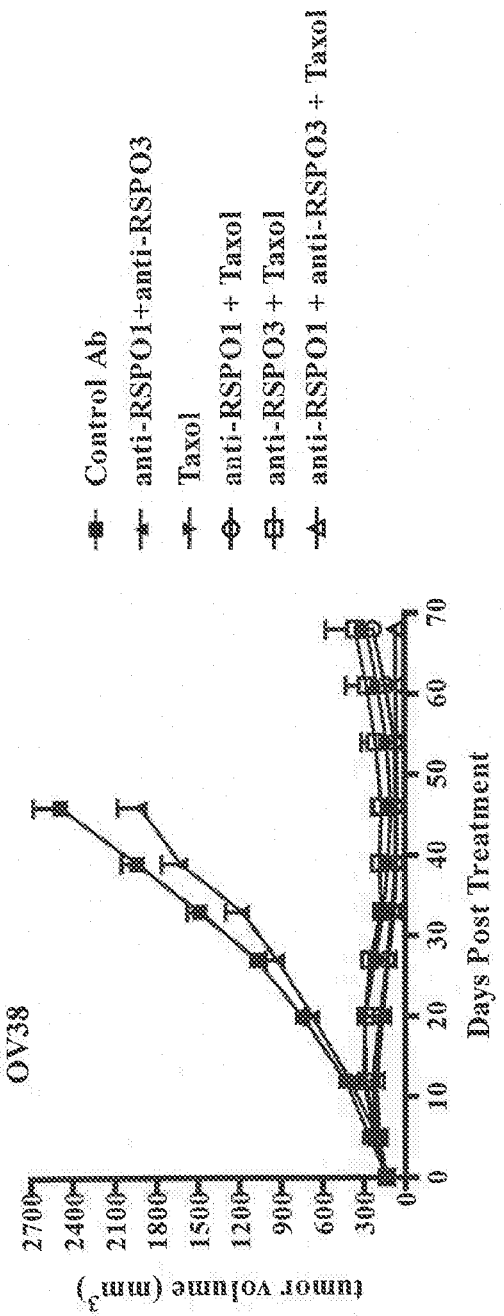

Control Ab
anti-RSPO1+anti-RSPO3
Taxol
anti-RSPO1 + Taxol
anti-RSPO3 + Taxol
anti-RSPO1 + anti-RSPO3 + Taxol
OV38
tumor volume (mm3)
2700
2400
2100
1800
1500
1200
900
600
300
0
0
10
20
30
40
50
60
70
Days Post Treatment

Figure 7

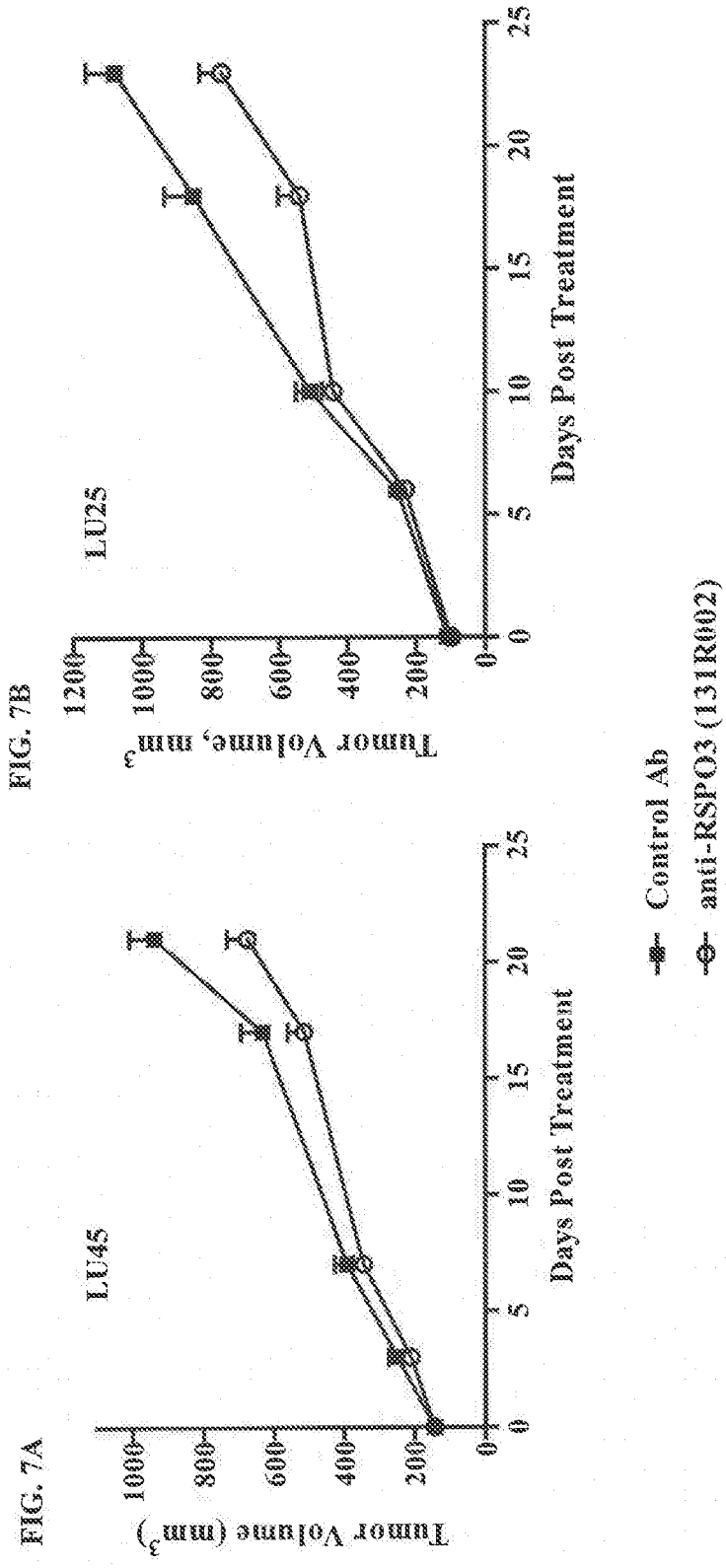

FIG. 7A
LU45
Tumor Volume (mm3)
1000
800
600
400
200
0
0
5
10
15
20
25
Days Post Treatment
FIG. 7B
LU25
Tumor Volume, mm3
1200
1000
800
600
400
200
0
0
5
10
15
20
25
Days Post Treatment
Control Ab
anti-RSPO3 (131R0002)

Figure 8

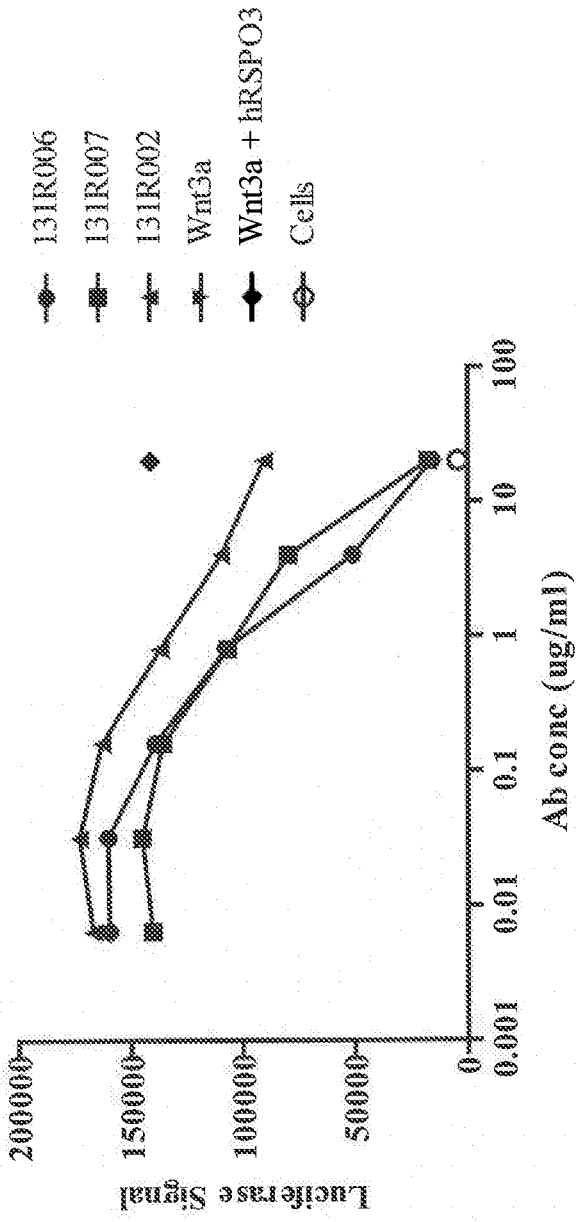

131R006
131R007
131R002
Wnt3a
Wnt3a + hRSPO3
Cells
Luciferase Signal
200000
150000
100000
50000
0
0.001
0.01
0.1
1
10
100
Ab conc (ug/ml)

Figure 9

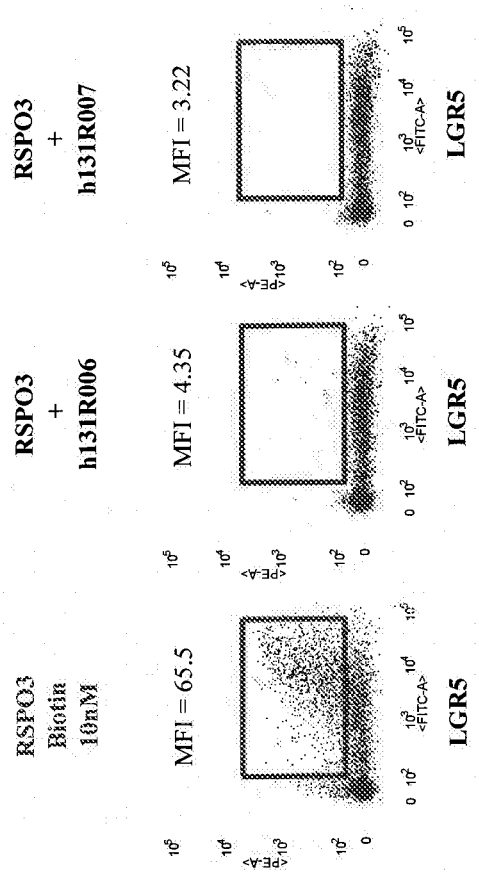

RSPO3
Biotin
10nM
MFI = 65.5
LGR5
RSPO3
+
h131R006
MFI = 4.35
LGR5
RSPO3
+
h131R007
MFI = 3.22
LGR5

Figure 10

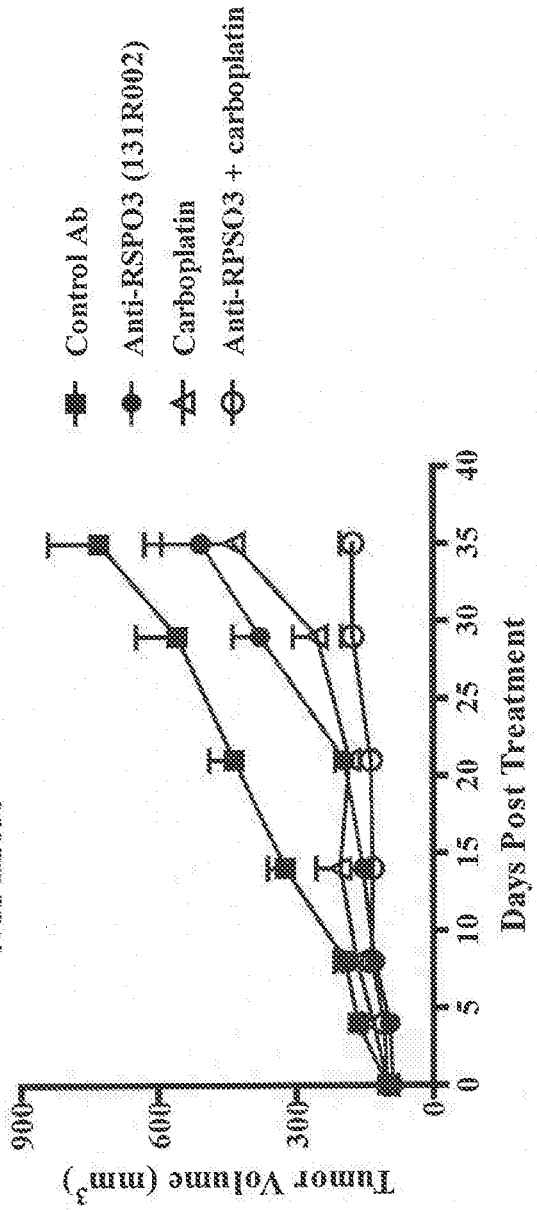

Control Ab
Anti-RSPO3 (131R002)
Carboplatin
Anti-RPSO3 + carboplatin
NCI-H2030
Tumor Volume (mm3)
900
600
300
0
0
5
10
15
20
25
30
35
40
Days Post Treatment

Figure 11

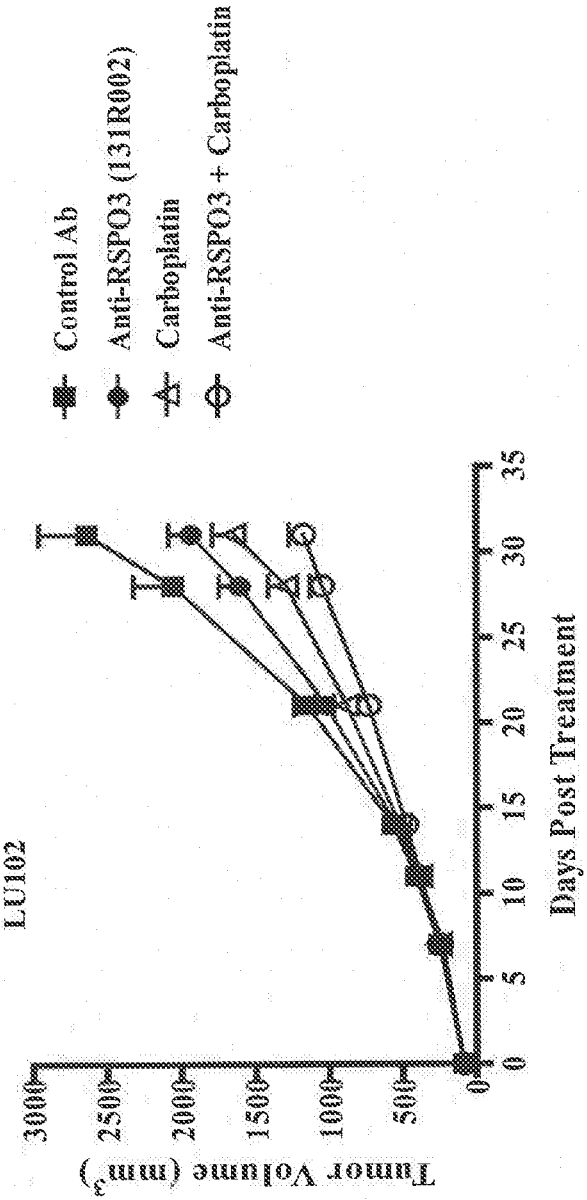


FIG. 11A

Figure 11

FIG. 11B

Anti-RSPO3 antibody as single agent

Geneset	SIZE	p-val
OMP_DLL4_UP	88	0.00E+00
WEINBERG_ES_1	371	7.30E-03
OMP_NEWCSC_UP	66	8.32E-03
CURATED_TGFB	200	2.23E-02
CURATED_STEMCELL	280	2.48E-02

Carboplatin as single agent

Geneset	SIZE	p-val
ASSOU_ESC_DN	69	1.43E-03

Anti-RSPO3 antibody + Carboplatin

Geneset	SIZE	p-val
BATLLE_HU_PROLIFERATION	184	0.00E+00
TIAN_GBM_CD133_UP	83	0.00E+00
NEVINS_CSR	85	0.00E+00
OMP_CD201+_HIGH	240	0.00E+00
WONG_EMBRYONIC_STEM_CELL_CORE	329	0.00E+00
WEINBERG_PROLIFERATION	147	0.00E+00
WEINBERG_ES_1	371	0.00E+00
RICKMAN_TUMOR_DIFFERENTIATED_W	106	0.00E+00
WEINBERG_OCT4_TARGETS	286	1.33E-02
MILANO_GSI_RAT_DN	57	1.66E-02
WEINBERG_ES_2	35	2.34E-02
PN_CD201_LOGIT18	18	4.71E-02

Figure 12

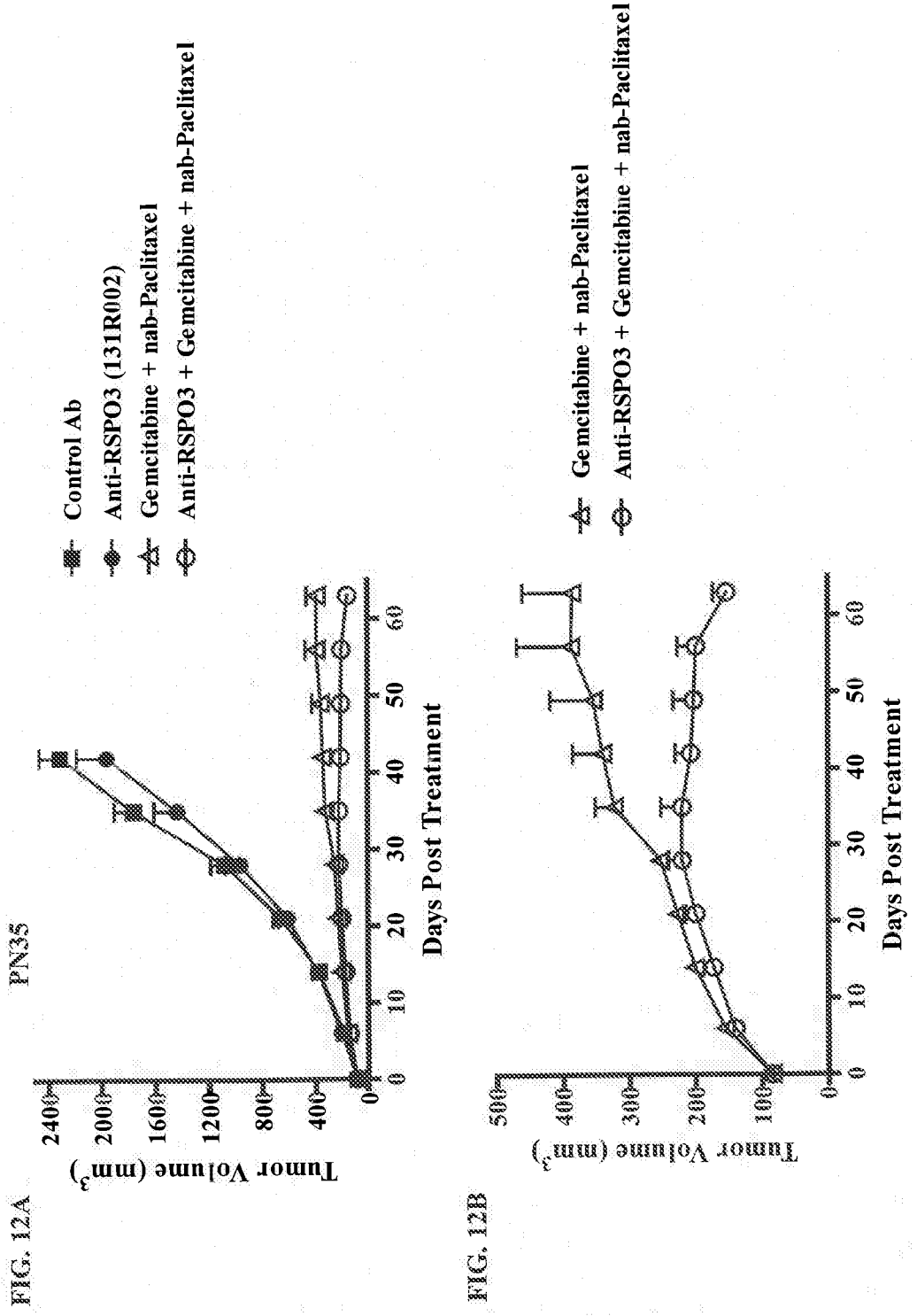


FIG. 12A

FIG. 12B

Figure 13

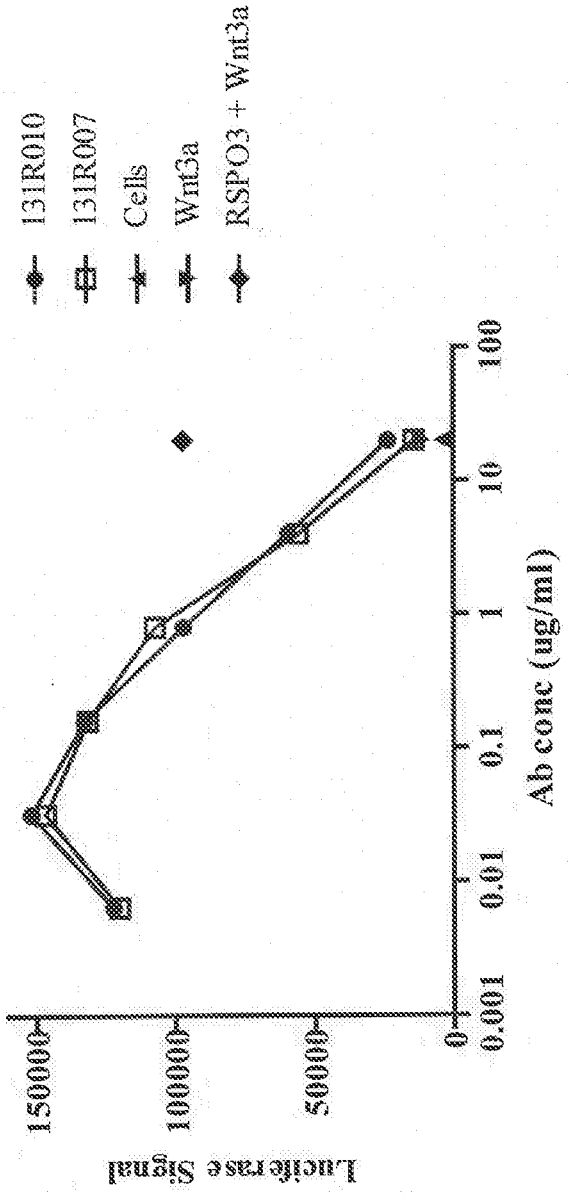
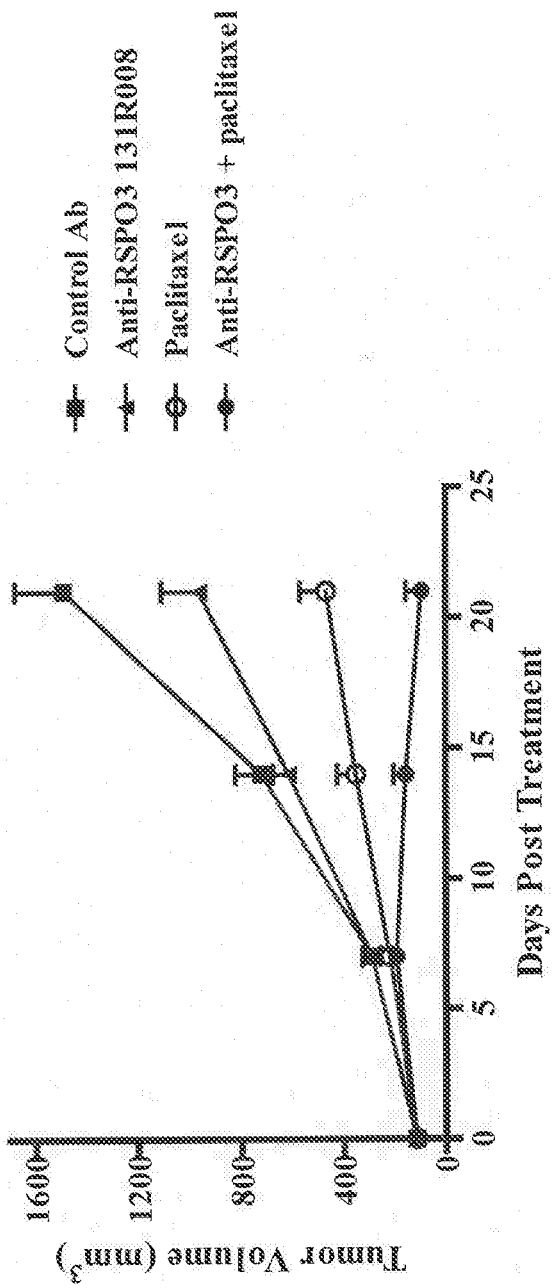

131R010
131R007
Cells
Wnt3a
RSPO3 + Wnt3a
Luciferase Signal
150000
100000
50000
0
0.001
0.01
0.1
1
10
100
Ab conc (ug/ml)

Figure 14


Control Ab
Anti-RSPO3 131R008
Paclitaxel
Anti-RSPO3 + paclitaxel
Tumor Volume (mm3)
1600
1200
800
400
0
0
5
10
15
20
25
Days Post Treatment