Figure 1A

RSPO1

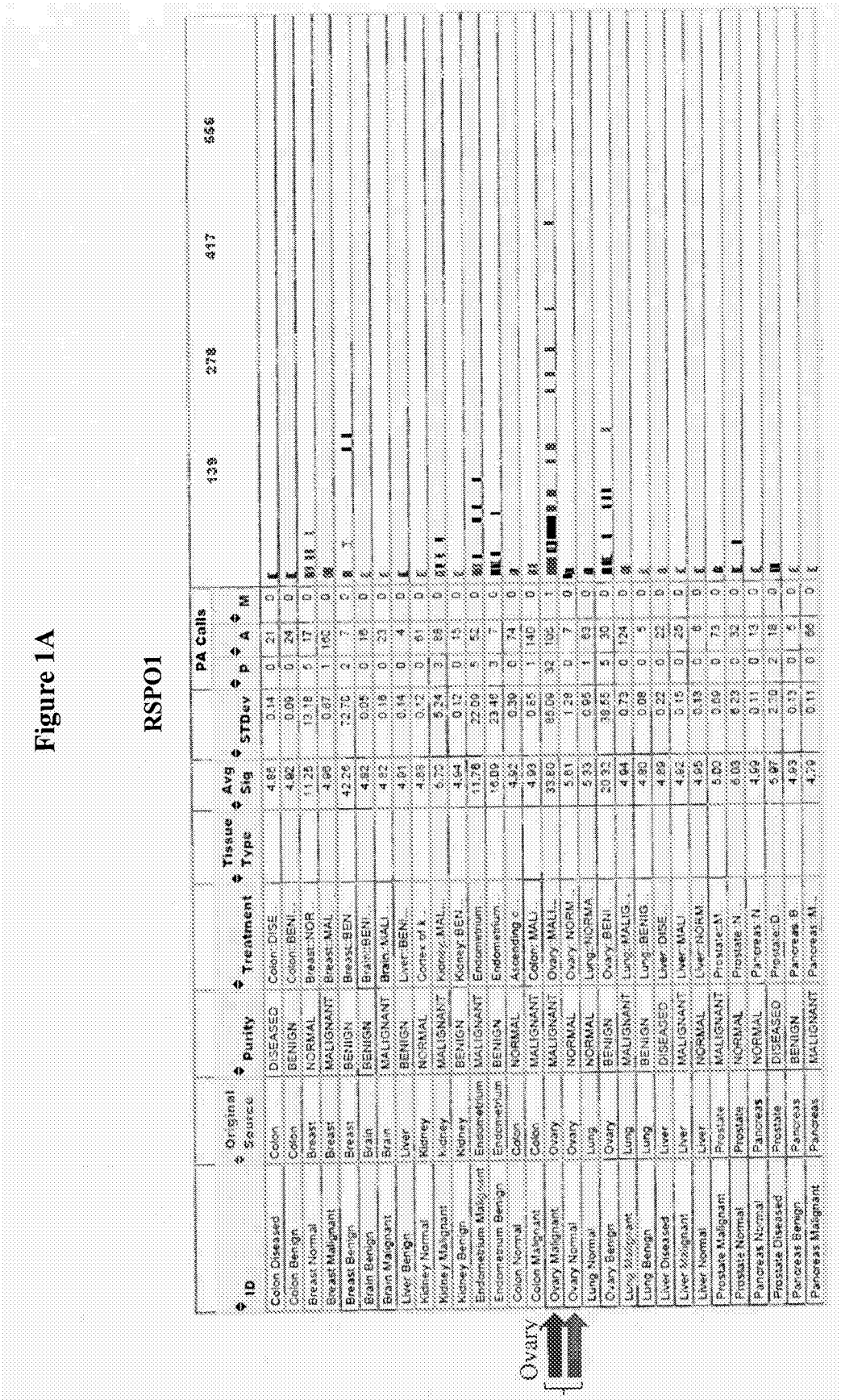
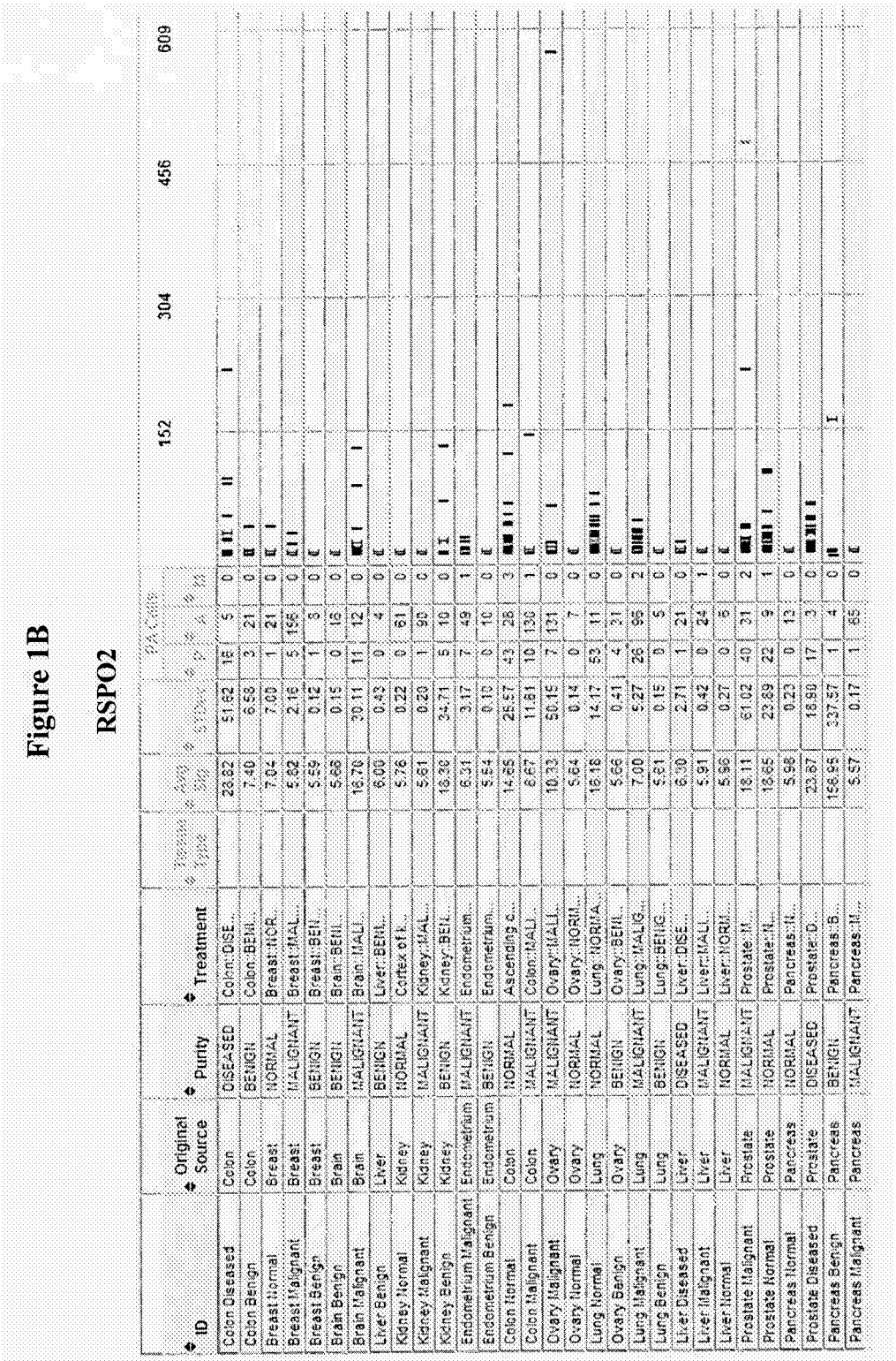


**Figure 1B**

**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

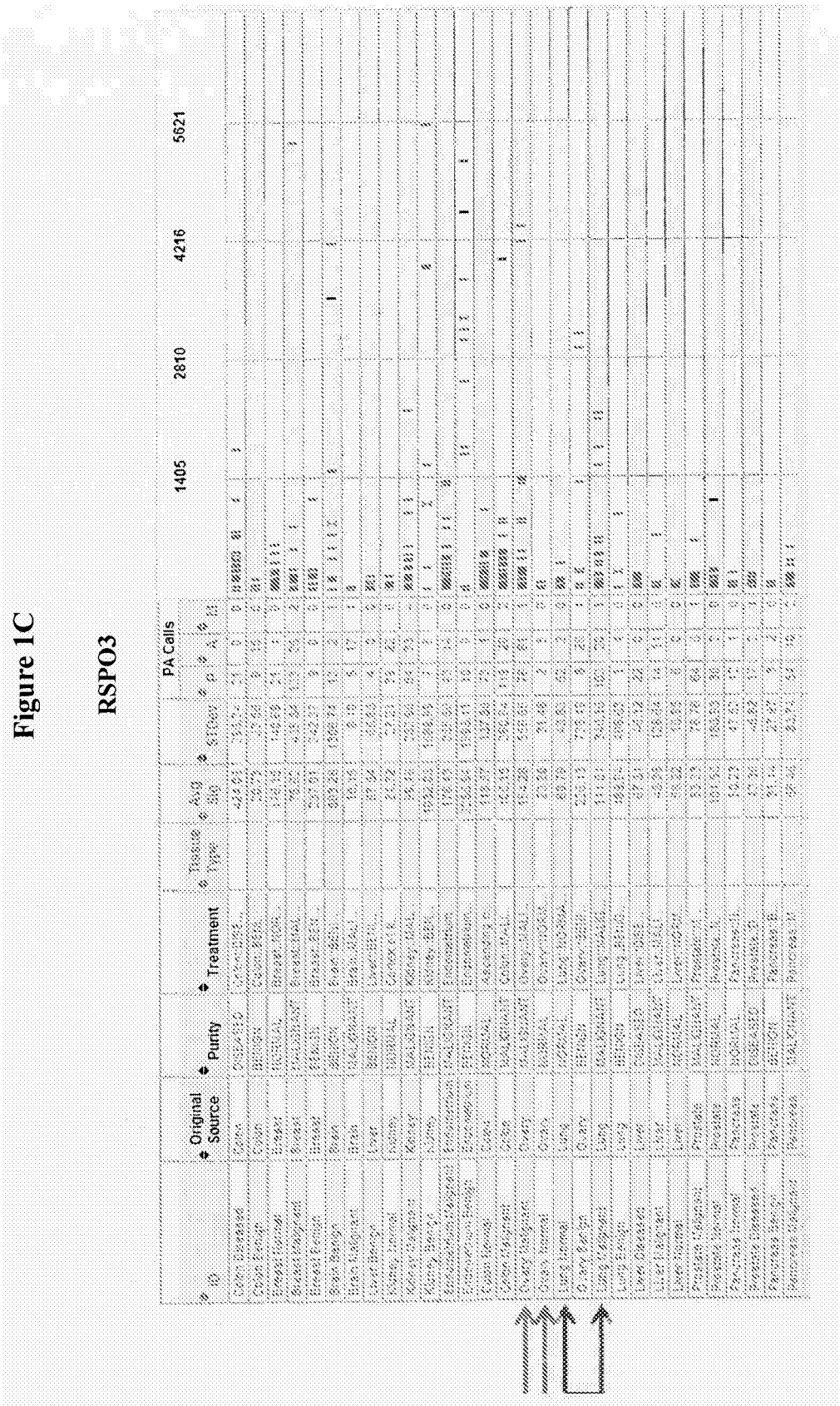


Figure 2

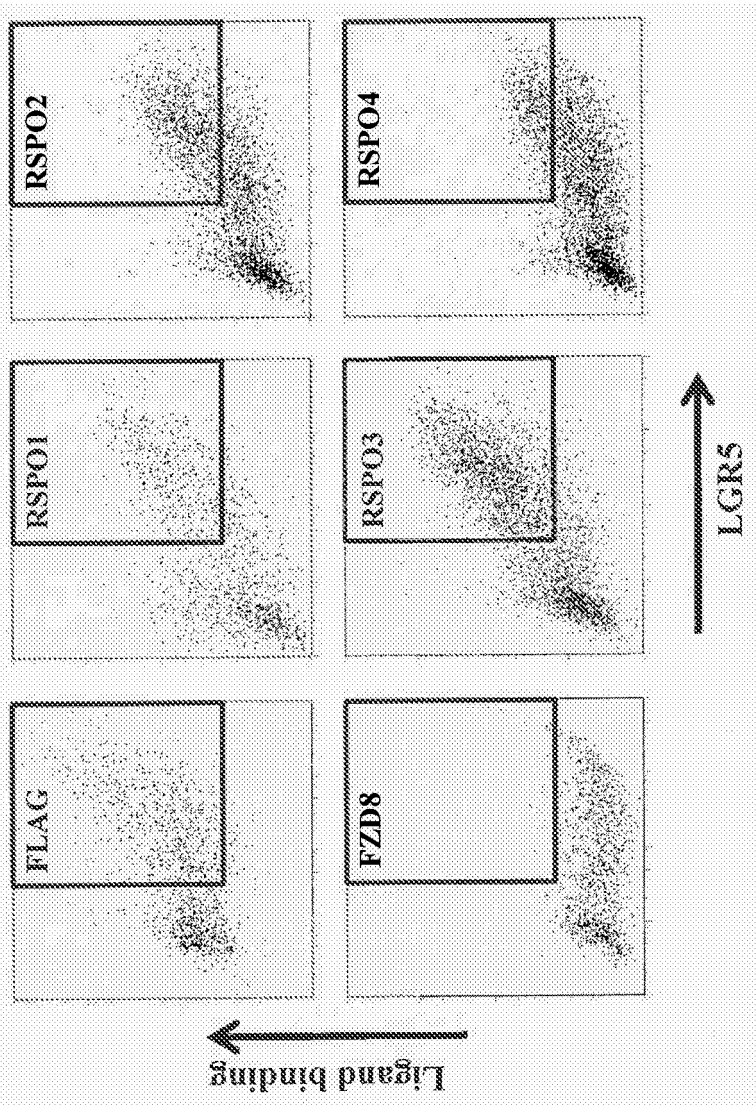


Figure 3

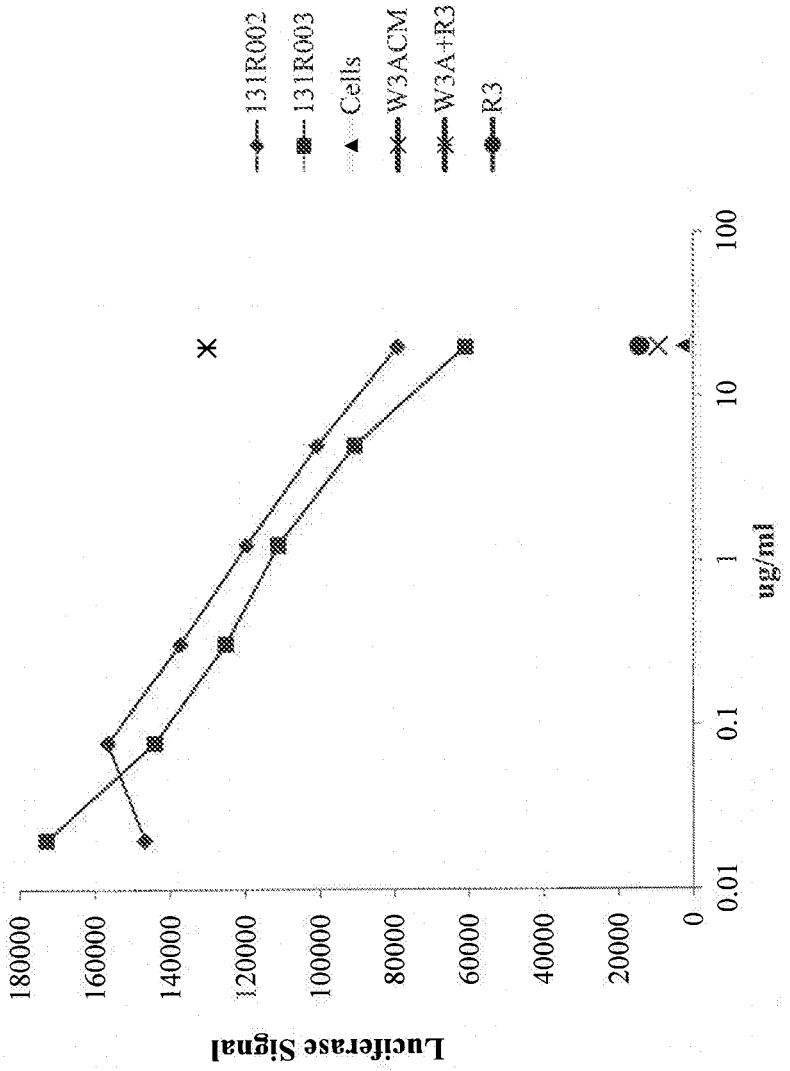

131R002
131R003
Cells
W3ACM
W3A+R3
R3
Luciferase Signal
180000
160000
140000
120000
100000
80000
60000
40000
20000
0
0.01
0.1
1
10
100
ug/ml

Figure 4

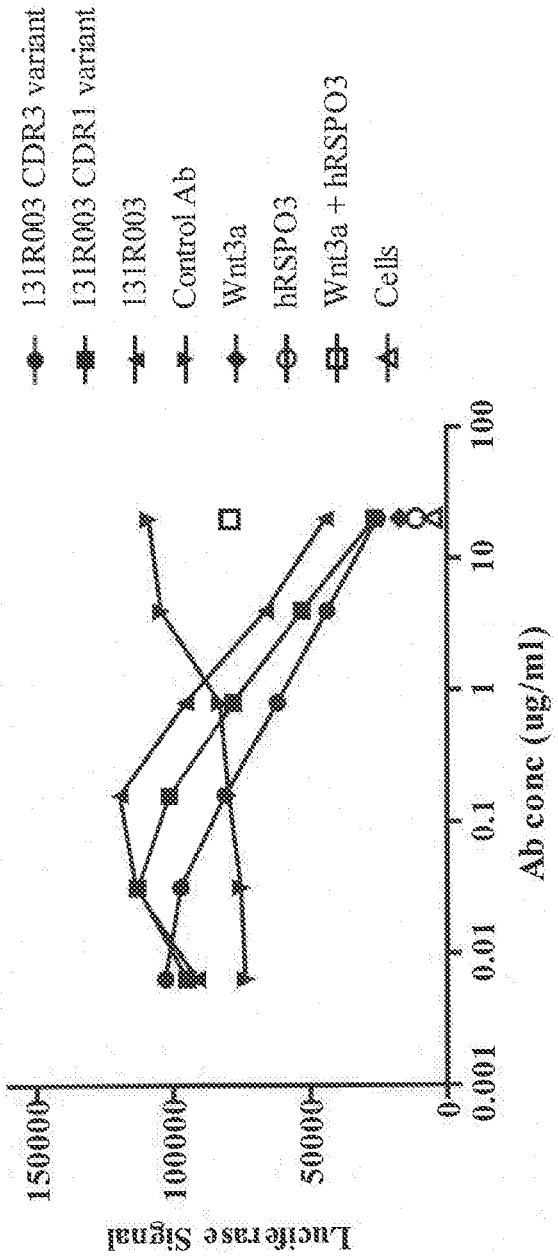

131R003 CDR3 variant
131R003 CDR1 variant
131R003
Control Ab
Wnt3a
hRSPO3
Wnt3a + hRSPO3
Cells
Luciferase Signal
150000
100000
50000
0
0.001
0.01
0.1
1
10
100
Ab conc (ug/ml)

Figure 5

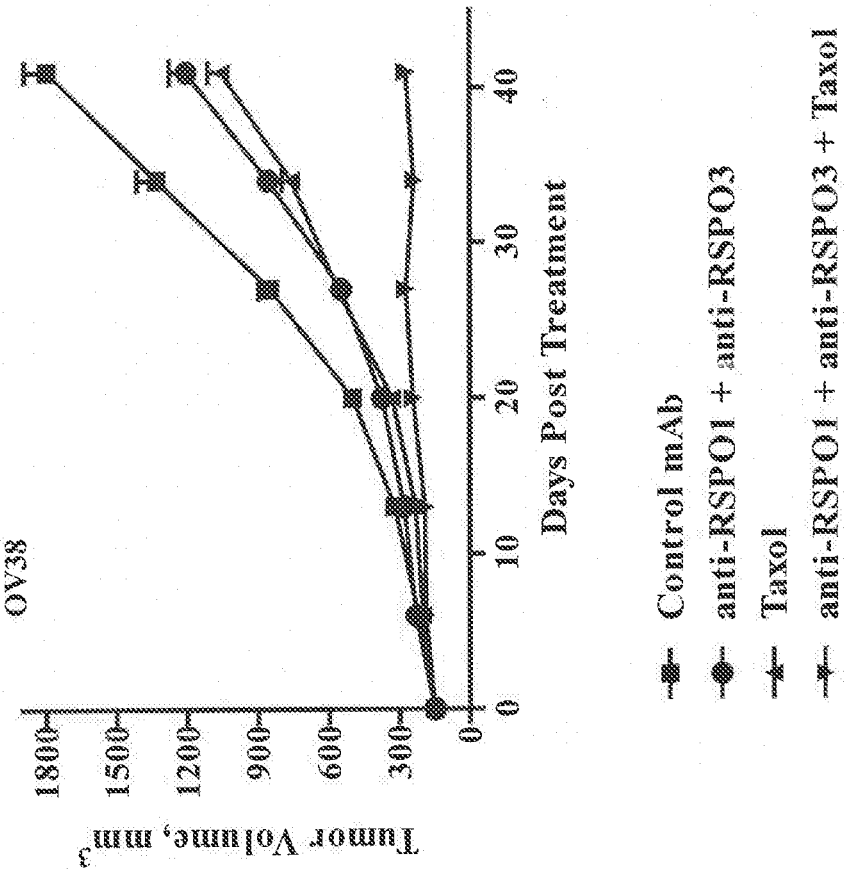

OV38
Tumor Volume, mm3
1800
1500
1200
900
600
300
0
0
10
20
30
40
Days Post Treatment
Control mAb
anti-RSPO1 + anti-RSPO3
Taxol
anti-RSPO1 + anti-RSPO3 + Taxol

Figure 6

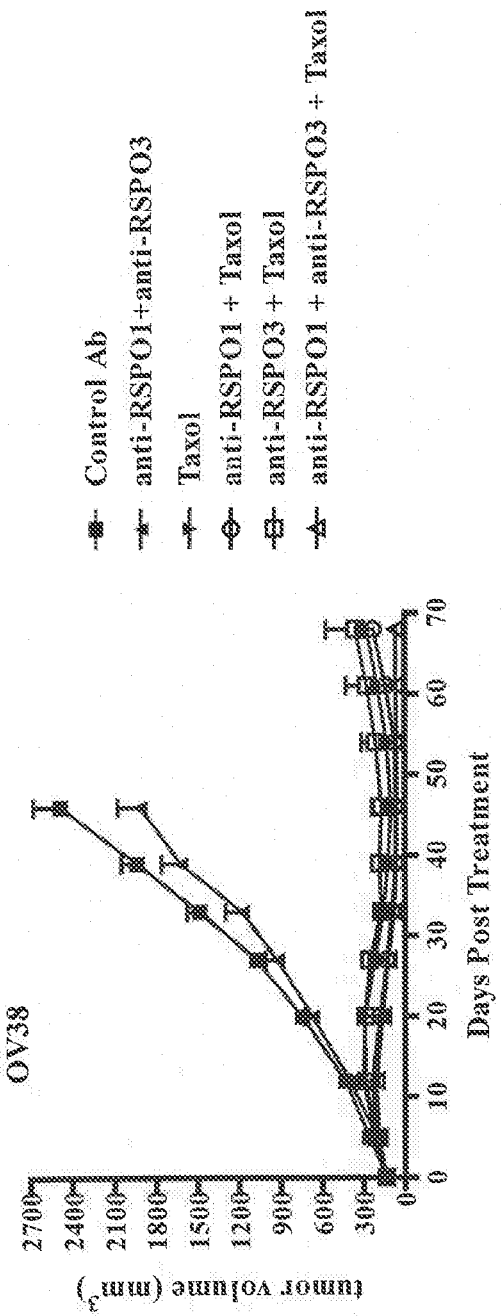

Control Ab
anti-RSPO1+anti-RSPO3
Taxol
anti-RSPO1 + Taxol
anti-RSPO3 + Taxol
anti-RSPO1 + anti-RSPO3 + Taxol
OV38
tumor volume (mm3)
2700
2400
2100
1800
1500
1200
900
600
300
0
0
10
20
30
40
50
60
70
Days Post Treatment

Figure 7

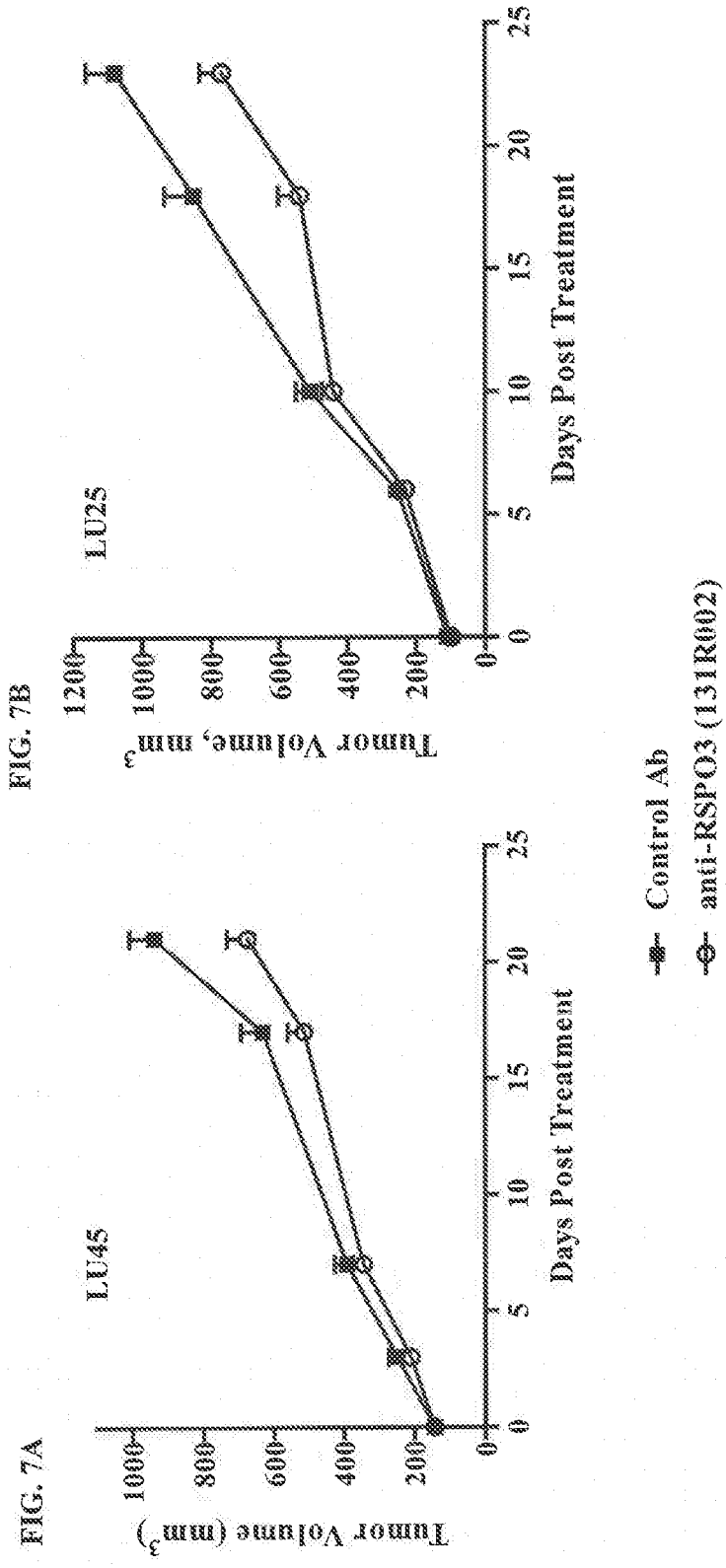

FIG. 7A
LU45
Tumor Volume (mm3)
1000
800
600
400
200
0
0
5
10
15
20
25
Days Post Treatment
FIG. 7B
LU25
Tumor Volume, mm3
1200
1000
800
600
400
200
0
0
5
10
15
20
25
Days Post Treatment
Control Ab
anti-RSPO3 (131R0002)

Figure 8

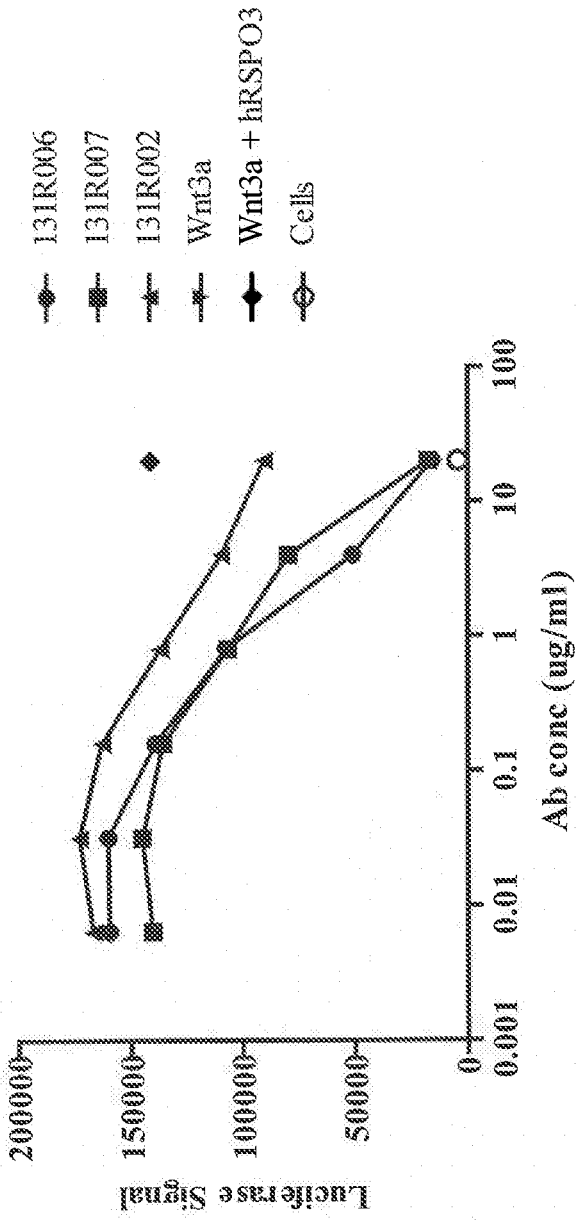

131R006
131R007
131R002
Wnt3a
Wnt3a + hRSPO3
Cells
Luciferase Signal
200000
150000
100000
50000
0
0.001
0.01
0.1
1
10
100
Ab conc (ug/ml)

**Figure 9**

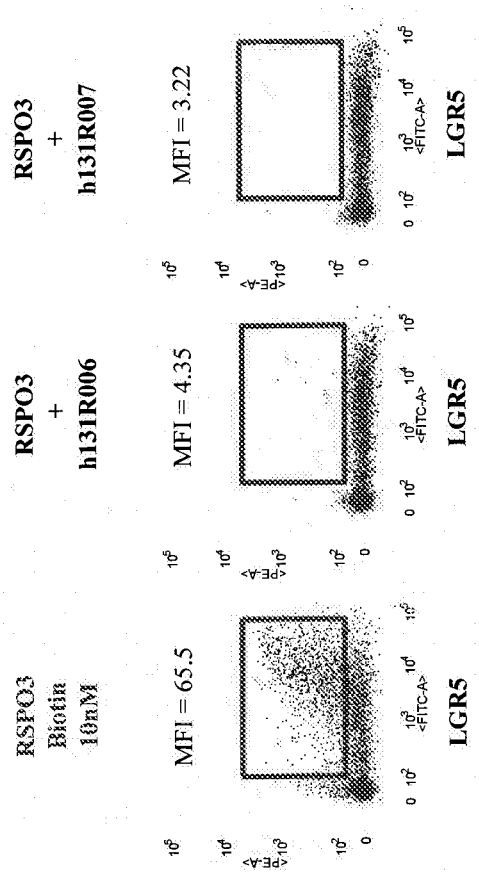

RSPO3
Biotin
10nM
MFI = 65.5
LGR5
RSPO3
+
h131R006
MFI = 4.35
LGR5
RSPO3
+
h131R007
MFI = 3.22
LGR5

Figure 10

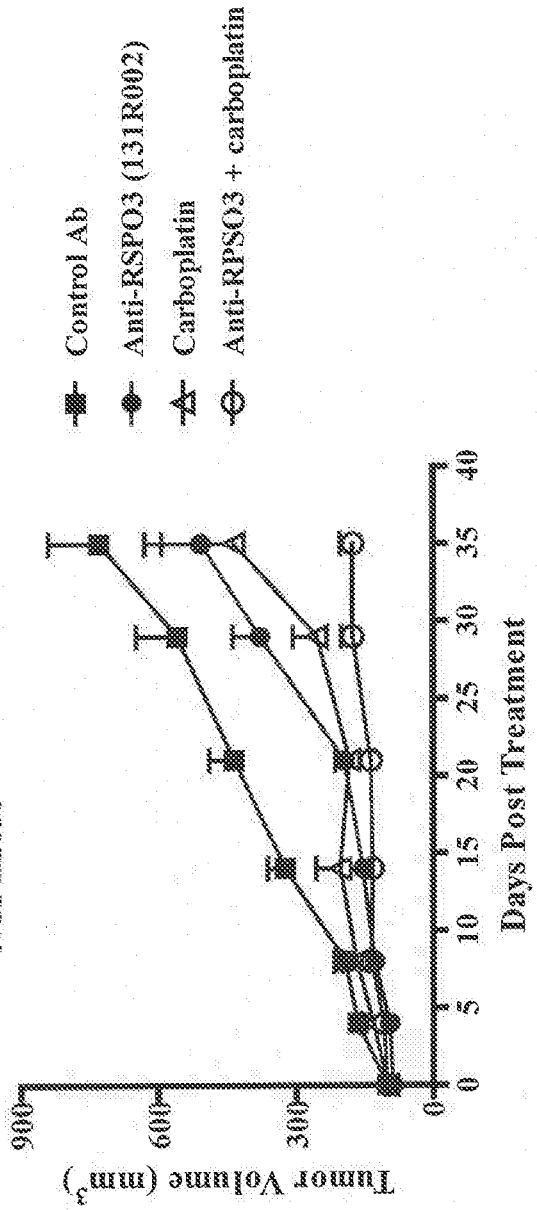

Control Ab
Anti-RSPO3 (131R002)
Carboplatin
Anti-RPSO3 + carboplatin
NCI-H2030
Tumor Volume (mm3)
900
600
300
0
0
5
10
15
20
25
30
35
40
Days Post Treatment

Figure 11

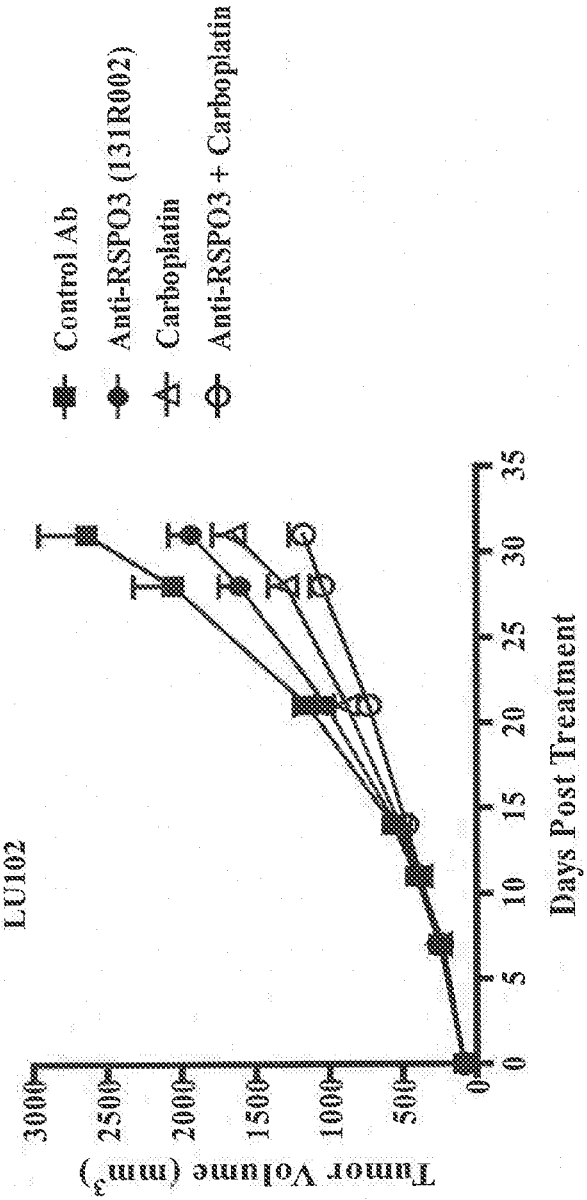



FIG. 11A

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

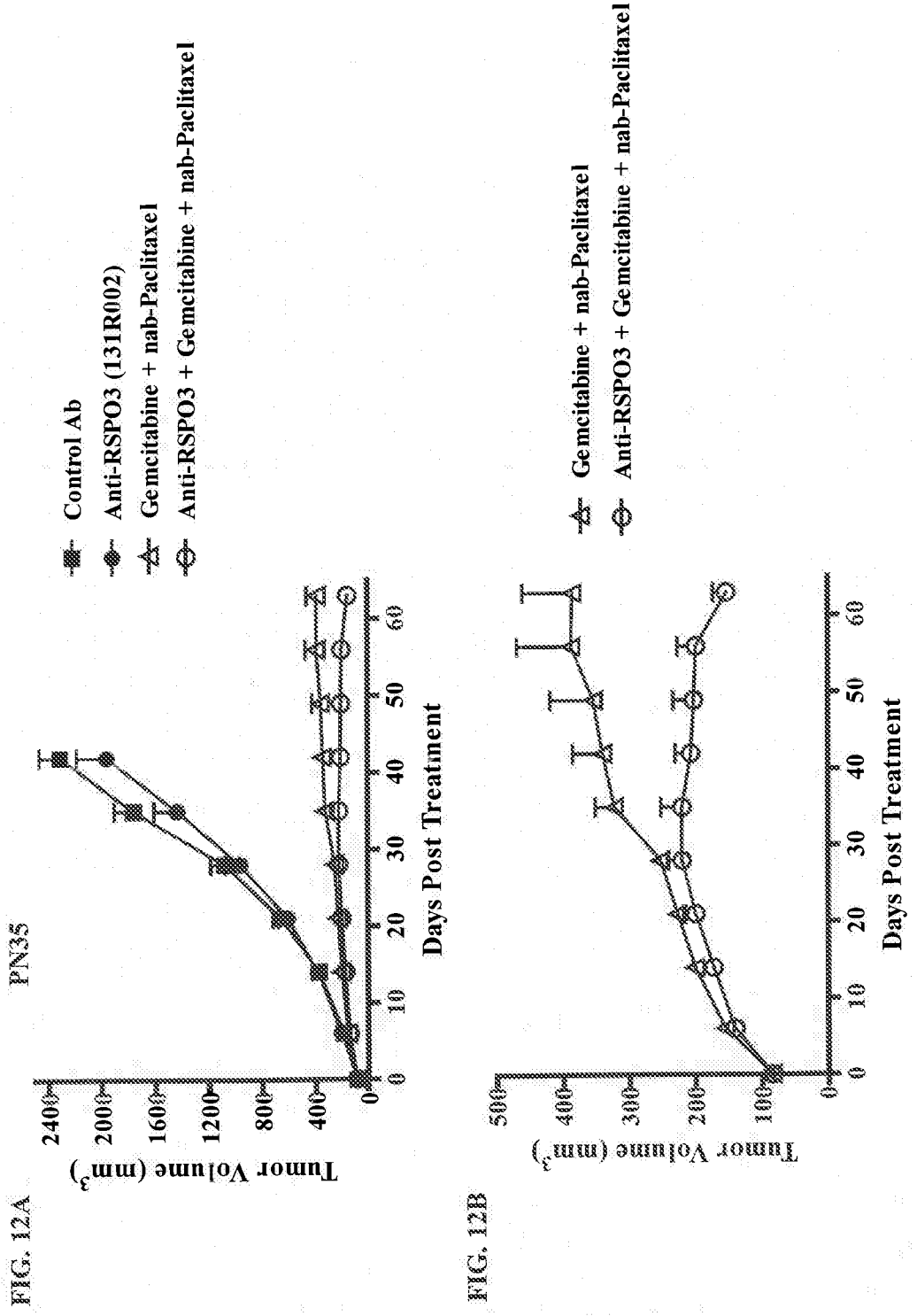



FIG. 12A

FIG. 12B

Figure 13

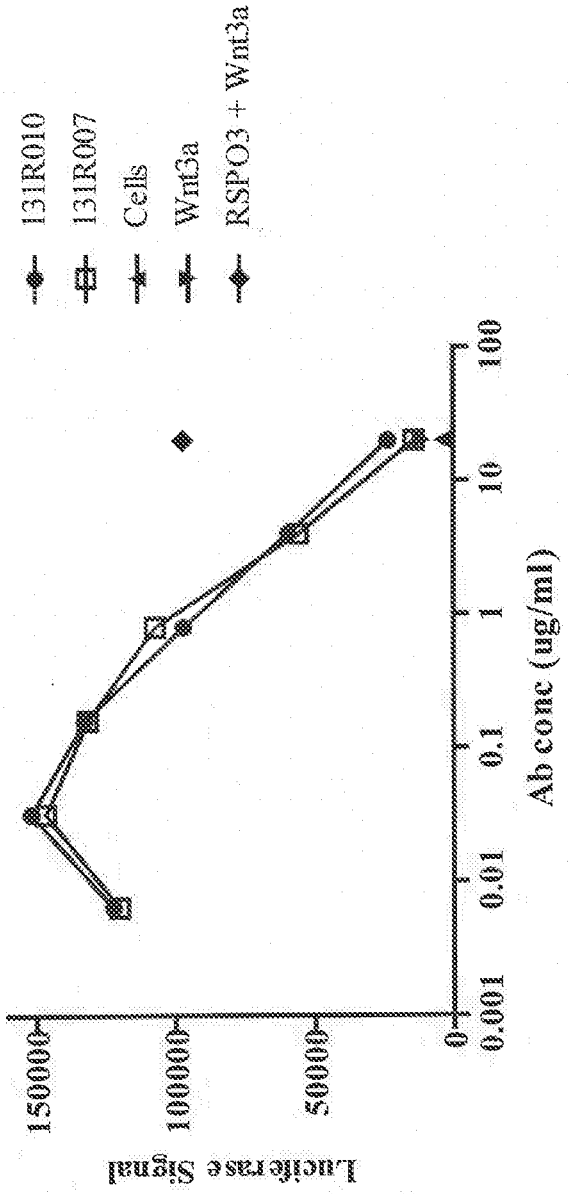
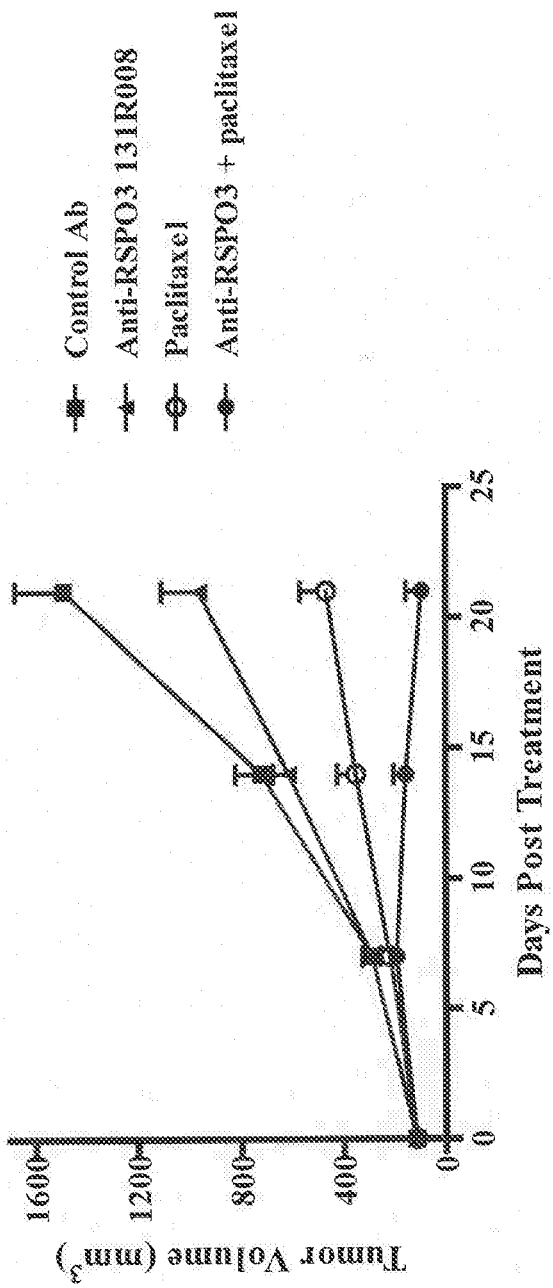

131R010
131R007
Cells
Wnt3a
RSPO3 + Wnt3a
Luciferase Signal
150000
100000
50000
0
0.001
0.01
0.1
1
10
100
Ab conc (ug/ml)

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