Figure 1A

Bispecific Antibody	Anti-VEGF binding region			Anti-DLL4 binding region		
	Heavy Chain			Heavy Chain		
	CDR1	CDR2	CDR3	CDR1	CDR2	CDR3
219R45-MB-21M18	NYWMH (SEQ ID NO:17)	DINPSNGRTSYKEKFKR (SEQ ID NO:18)	HYDDKYYPLMDY (SEQ ID NO:19)	TAYYIH (SEQ ID NO:13)	YISSYNGATNYNQKFKG (SEQ ID NO:15)	RDYDYDVGMDY (SEQ ID NO:16)
219R45-MB-21R79	NYWMH (SEQ ID NO:17)	DINPSNGRTSYKEKFKR (SEQ ID NO:18)	HYDDKYYPLMDY (SEQ ID NO:19)	TAYYIH (SEQ ID NO:13)	YIANYNRATNYNQKFKG (SEQ ID NO:14)	RDYDYDVGMDY (SEQ ID NO:16)
219R45-MB-21R75	NYWMH (SEQ ID NO:17)	DINPSNGRTSYKEKFKR (SEQ ID NO:18)	HYDDKYYPLMDY (SEQ ID NO:19)	TAYYIH (SEQ ID NO:13)	YIAGYKDATNYNQKFKG (SEQ ID NO:59)	RDYDYDVGMDY (SEQ ID NO:16)
219R45-MB-21R83	NYWMH (SEQ ID NO:17)	DINPSNGRTSYKEKFKR (SEQ ID NO:18)	HYDDKYYPLMDY (SEQ ID NO:19)	TAYYIH (SEQ ID NO:13)	YISNYNRATNYNQKFKG (SEQ ID NO:65)	RDYDYDVGMDY (SEQ ID NO:16)

Bispecific Antibody	Anti-VEGF and Anti-DLL4 binding regions		
	Light Chain		
	CDR1	CDR2	CDR3
219R45-MB-21M18	RASESVDNYGISFMK (SEQ ID NO:20)	AASNQGS (SEQ ID NO:21)	QQSKEVPWTFGG (SEQ ID NO:22)
219R45-MB-21R79	RASESVDNYGISFMK (SEQ ID NO:20)	AASNQGS (SEQ ID NO:21)	QQSKEVPWTFGG (SEQ ID NO:22)
219R45-MB-21R75	RASESVDNYGISFMK (SEQ ID NO:20)	AASNQGS (SEQ ID NO:21)	QQSKEVPWTFGG (SEQ ID NO:22)
219R45-MB-21R83	RASESVDNYGISFMK (SEQ ID NO:20)	AASNQGS (SEQ ID NO:21)	QQSKEVPWTFGG (SEQ ID NO:22)

Figure 1B

Bispecific Antibody	Anti-VEGF binding region		Anti-DLL4 binding region	
	Heavy Chain Variable Region	Light Chain Variable Region	Heavy Chain Variable Region	Light Chain Variable Region
219R45-MB-21M18	SEQ ID NO:11	SEQ ID NO:12	SEQ ID NO:9	SEQ ID NO:12
219R45-MB-21R79	SEQ ID NO:11	SEQ ID NO:12	SEQ ID NO:10	SEQ ID NO:12
219R45-MB-21R75	SEQ ID NO:11	SEQ ID NO:12	SEQ ID NO:58	SEQ ID NO:12
219R45-MB-21R83	SEQ ID NO:11	SEQ ID NO:12	SEQ ID NO:64	SEQ ID NO:12

Figure 1C

Bispecific Antibody	Anti-VEGF binding region		Anti-DLL4 binding region	
	Heavy Chain	Light Chain	Heavy Chain	Light Chain
219R45-MB-21M18	SEQ ID NO:3 SEQ ID NO:7	SEQ ID NO:4 SEQ ID NO:8	SEQ ID NO:1 SEQ ID NO:5	SEQ ID NO:4 SEQ ID NO:8
219R45-MB-21R79	SEQ ID NO:3 SEQ ID NO:7	SEQ ID NO:4 SEQ ID NO:8	SEQ ID NO:2 SEQ ID NO:6	SEQ ID NO:4 SEQ ID NO:8
219R45-MB-21R75	SEQ ID NO:3 SEQ ID NO:7	SEQ ID NO:4 SEQ ID NO:8	SEQ ID NO:57 SEQ ID NO:56	SEQ ID NO:4 SEQ ID NO:8
219R45-MB-21R83	SEQ ID NO:3 SEQ ID NO:7	SEQ ID NO:4 SEQ ID NO:8	SEQ ID NO:63 SEQ ID NO:62	SEQ ID NO:4 SEQ ID NO:8

Figure 2

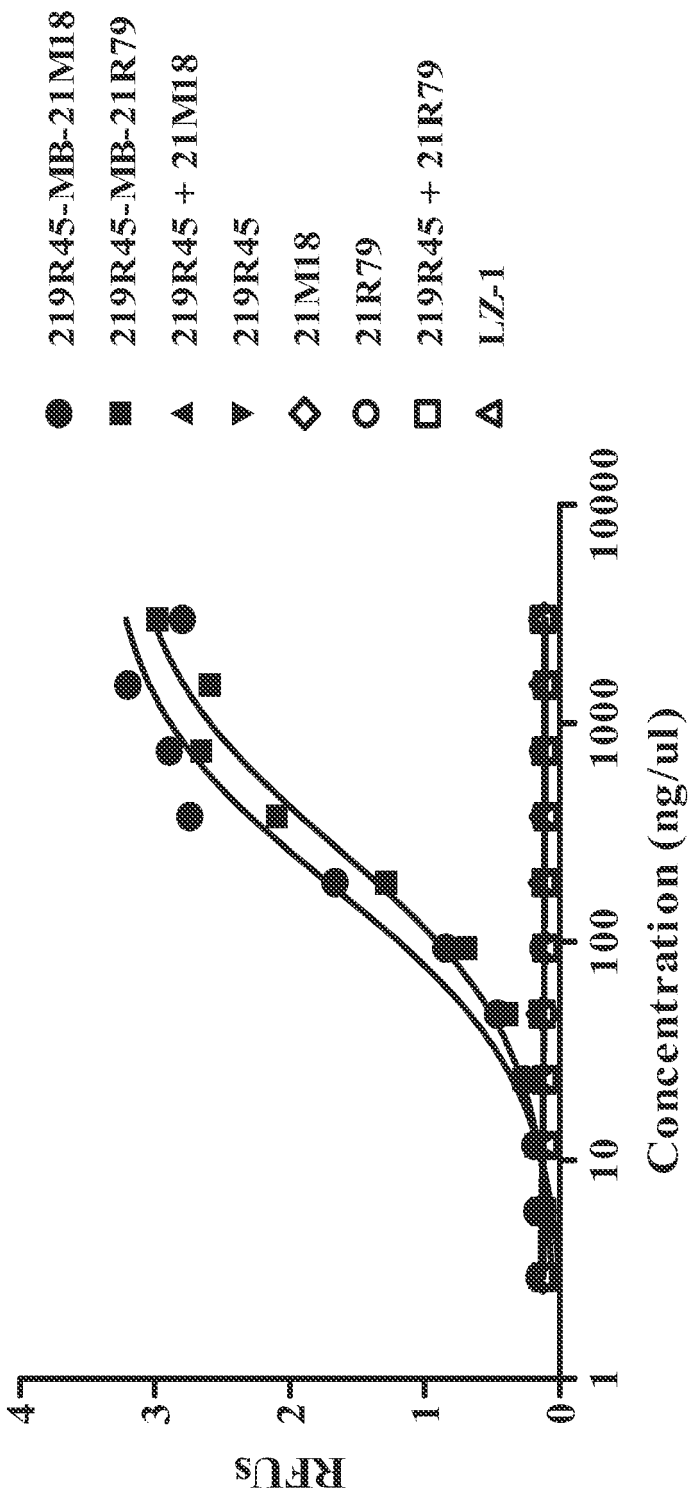

219R45-MB-21M18
219R45-MB-21R79
219R45 + 21M18
219R45
21M18
21R79
219R45 + 21R79
LZ-1
RFUs
0
1
2
3
4
1
10
100
1000
10000
Concentration (mg/ul)

Figure 3

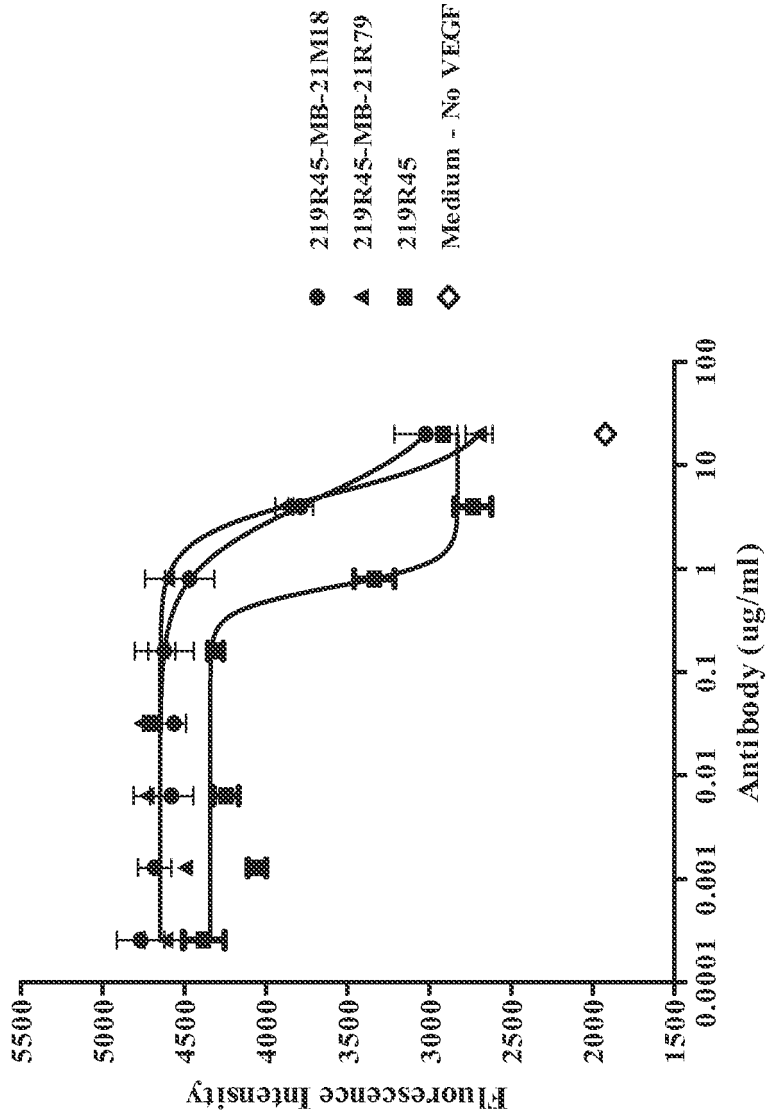

219R45-MB-21M18
219R45-MB-21R79
219R45
Medium - No VEGF
Fluorescence Intensity
5500
5000
4500
4000
3500
3000
2500
2000
1500
0.0001
0.001
0.01
0.1
1
10
100
Antibody (ug/ml)

Figure 4

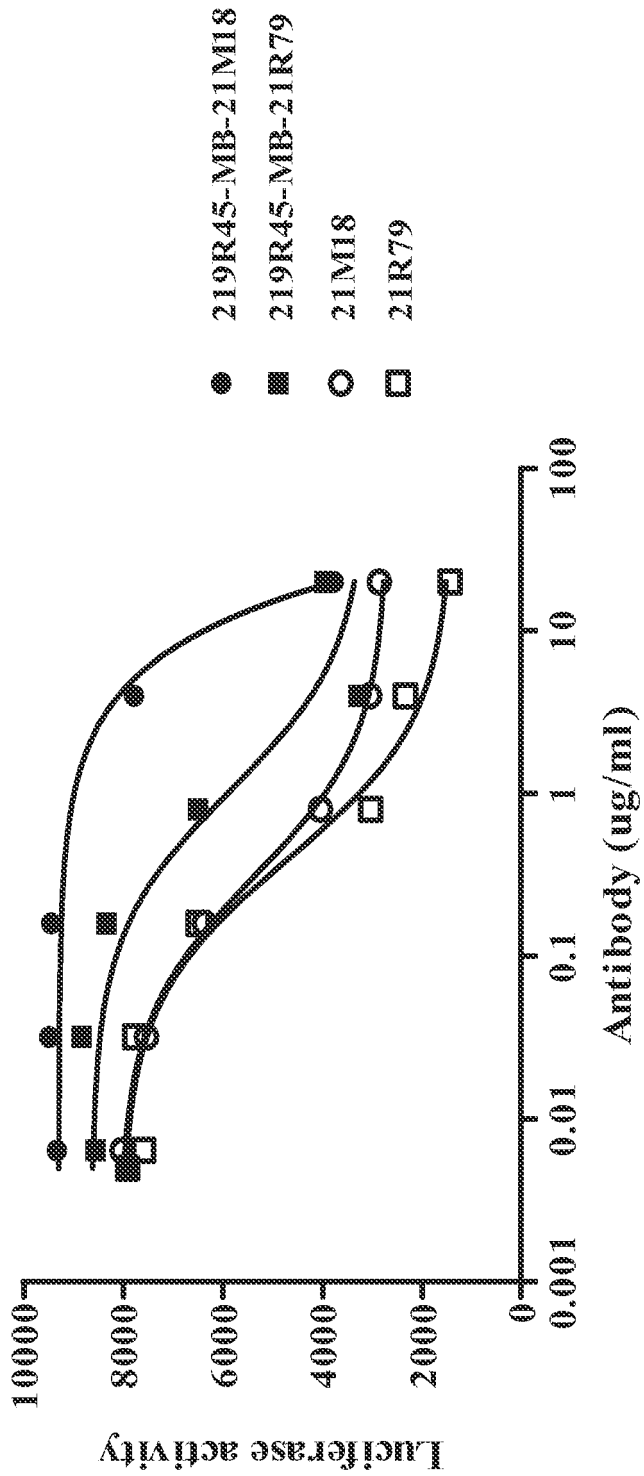

219R45-MB-21M18
219R45-MB-21R79
21M18
21R79
Luciferase activity
10000
8000
6000
4000
2000
0
0.0001
0.01
0.1
1
10
100
Antibody (ug/ml)

Figure 5

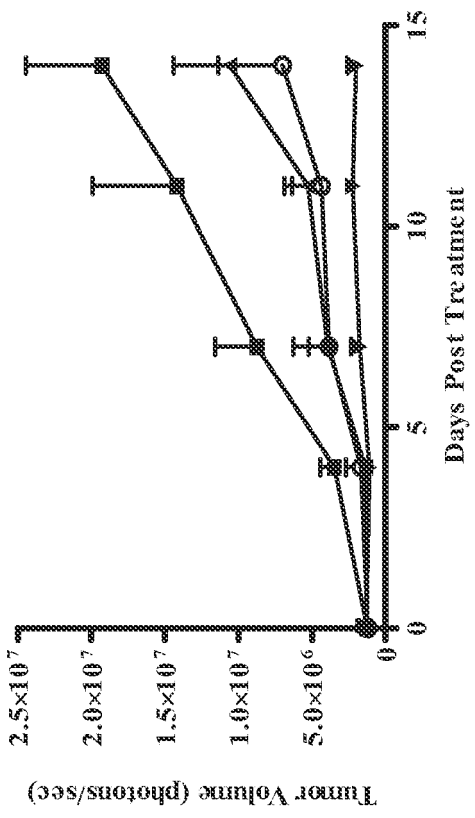

C8 – Skin graft Model
Tumor Volume (photons/sec)
2.5×10^7
2.0×10^7
1.5×10^7
1.0×10^7
5.0×10^6
0
0
5
10
15
Days Post Treatment
Control Ab
Anti-hDLL4 Ab - 21M18
Anti-VEGF Ab - bevacizumab
Anti-VEGF/DLL4 Bispecific - 219R45-MB-21M18

Figure 6

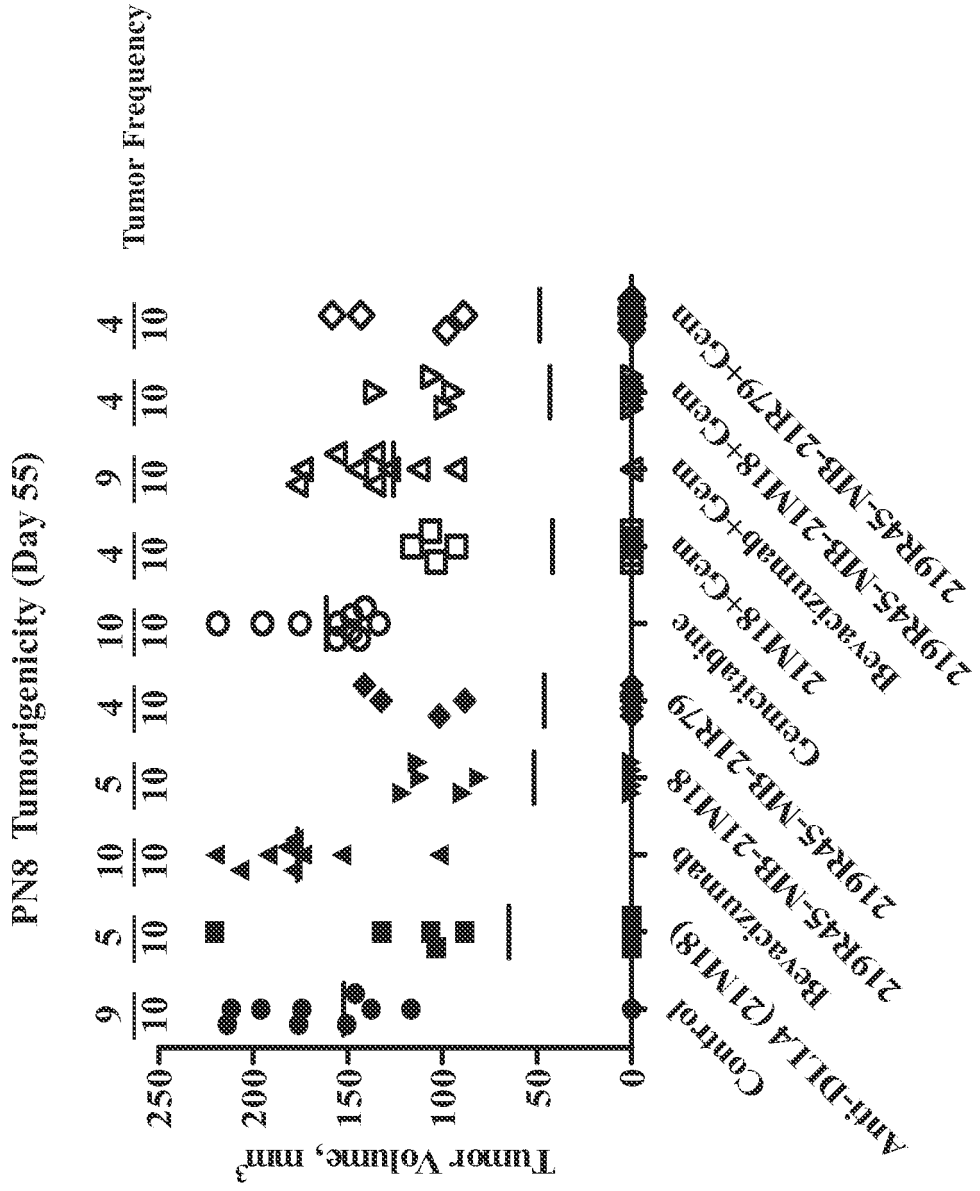

PN8 Tumorigenicity (Day 55)
Tumor Volume, mm3
250
200
150
100
50
0
Tumor Frequency
9/10
5/10
10/10
5/10
4/10
10/10
4/10
10/10
9/10
4/10
4/10
10/10
Control
Anti-DLL4 (21M18)
Bevacizumab
21R45-MB-21M18
21R45-MB-21R79
Gemcitabine
21M18+Gem
Bevacizumab+Gem
21R45-MB-21M18+Gem
21R45-MB-21R79+Gem

Figure 7

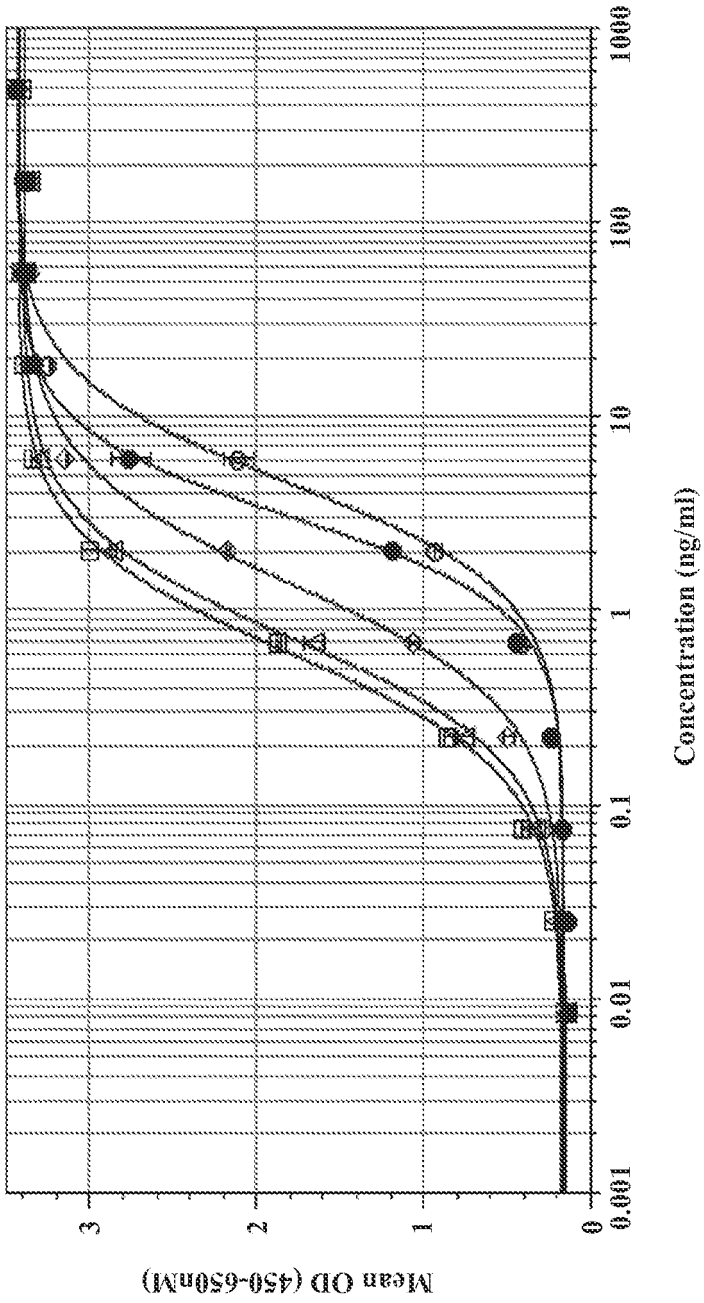

Mean OD (450-650nM)
0
1
2
3
0.001
0.01
0.1
1
10
100
1000
Concentration (ng/ml)

Figure 8

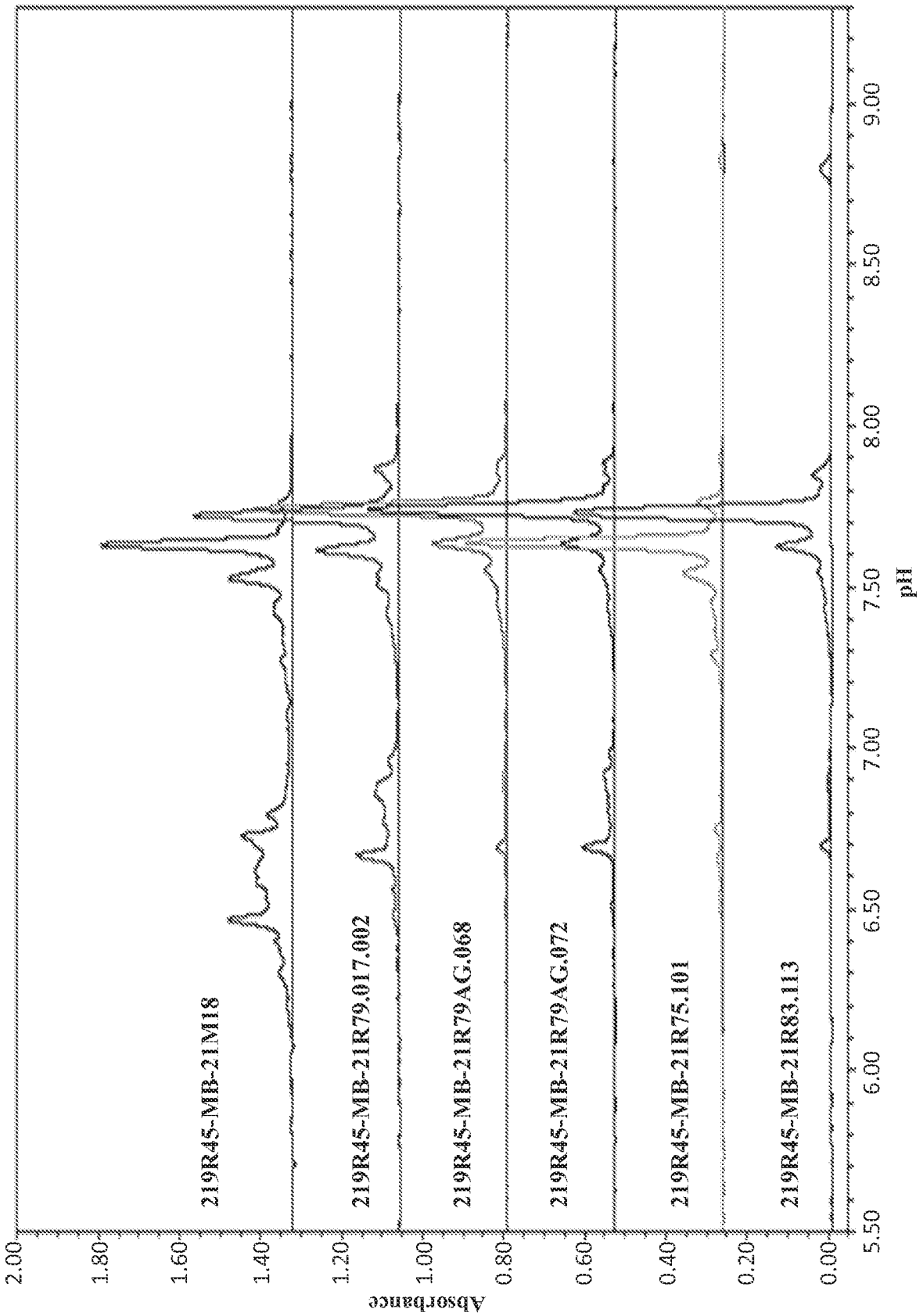

Absorbance
2.00
1.80
1.60
1.40
1.20
1.00
0.80
0.60
0.40
0.20
0.00
5.50
6.00
6.50
7.00
7.50
8.00
8.50
9.00
pH
219R45-MB-21M18
219R45-MB-21R79.017.002
219R45-MB-21R79AG.068
219R45-MB-21R79AG.072
219R45-MB-21R75.101
219R45-MB-21R83.113

Figure 9

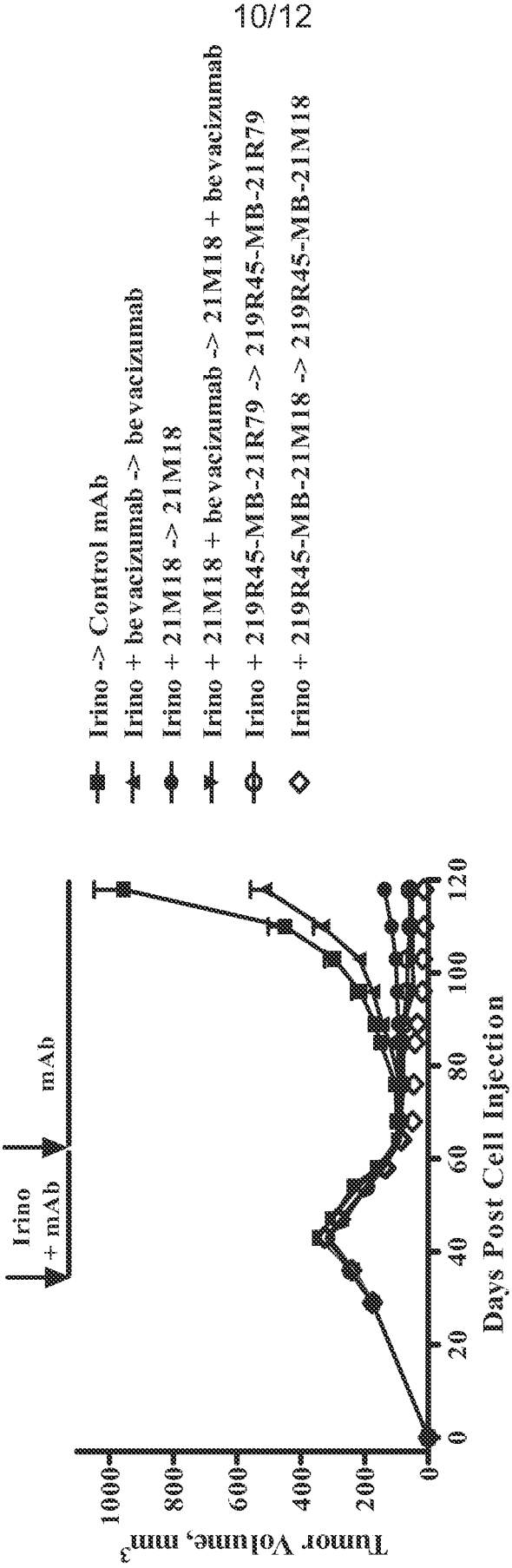

Irino + mAb
mAb
Irino -> Control mAb
Irino + bevacizumab -> bevacizumab
Irino + 21M18 -> 21M18
Irino + 21M18 + bevacizumab -> 21M18 + bevacizumab
Irino + 219R45-MB-21R79 -> 219R45-MB-21R79
Irino + 219R45-MB-21M18 -> 219R45-MB-21M18
Tumor Volume, mm3
1000
800
600
400
200
0
0
20
40
60
80
100
120
Days Post Cell Injection

Figure 10

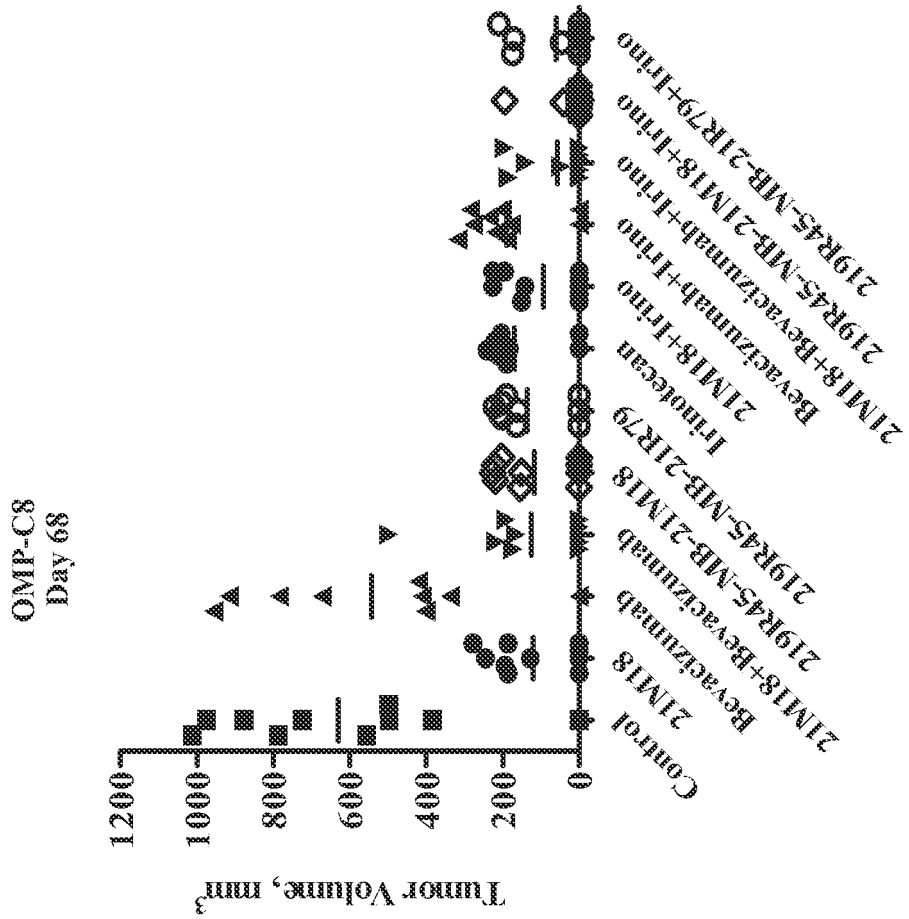
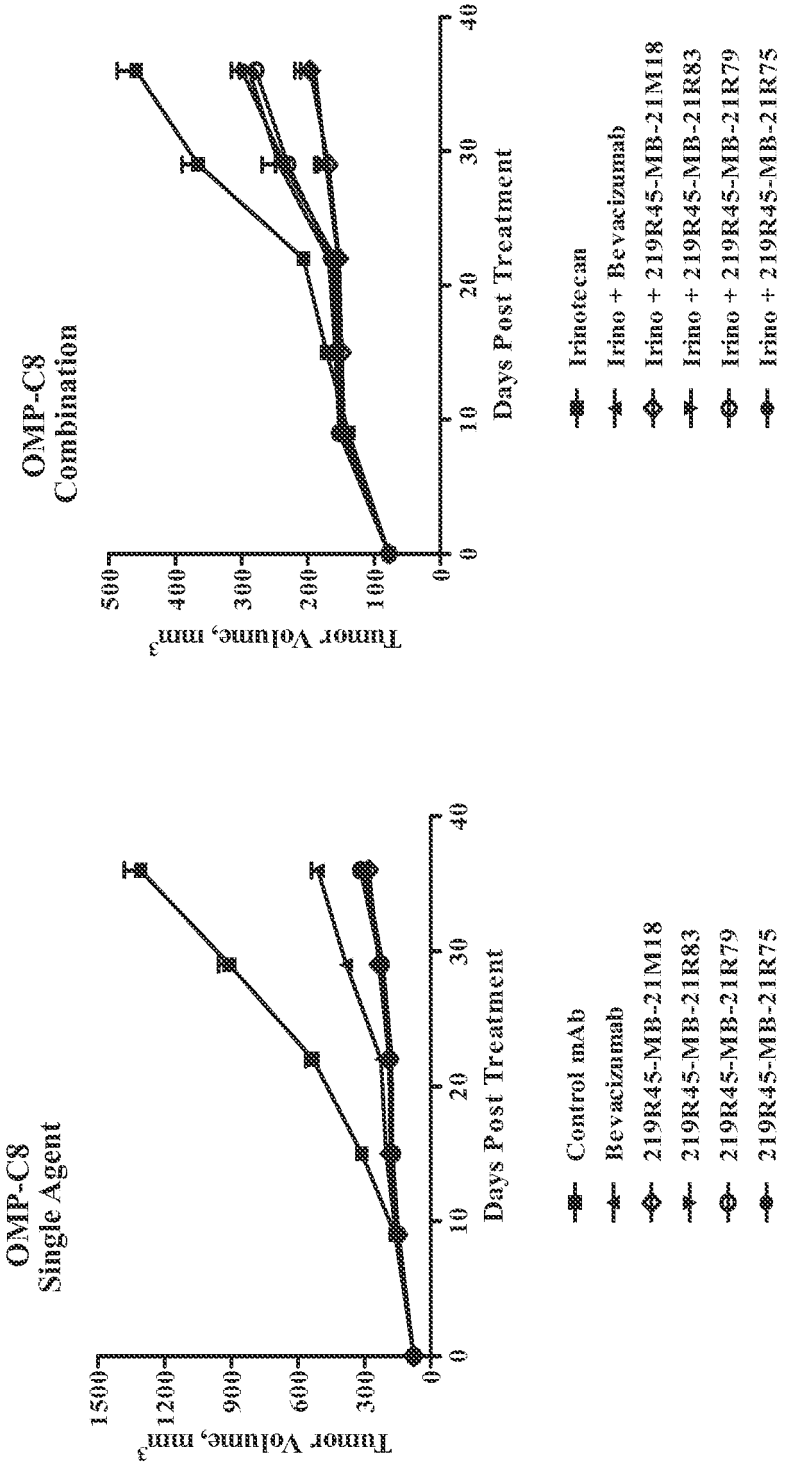

OMP-C8
Day 68
Tumor Volume, mm³
1200
1000
800
600
400
200
0
Control
21M18
Bevacizumab
21M18+Bevacizumab
21hR45-MB-21M18
21hR45-MB-21R79
Irinotecan
21M18+Irino
Bevacizumab+Irino
21M18+Bevacizumab+Irino
21hR45-MB-21M18+Irino
21hR45-MB-21R79+Irino

Figure 11


OMP-C8
Single Agent
Tumor Volume, mm3
1500
1200
900
600
300
0
0
10
20
30
40
Days Post Treatment
OMP-C8
Combination
Tumor Volume, mm3
500
400
300
200
100
0
0
10
20
30
40
Days Post Treatment
Control mAb
Bevacizumab
219R45-MB-21M18
219R45-MB-21R83
219R45-MB-21R79
219R45-MB-21R75
Irinotecan
Irino + Bevacizumab
Irino + 219R45-MB-21M18
Irino + 219R45-MB-21R83
Irino + 219R45-MB-21R79
Irino + 219R45-MB-21R75