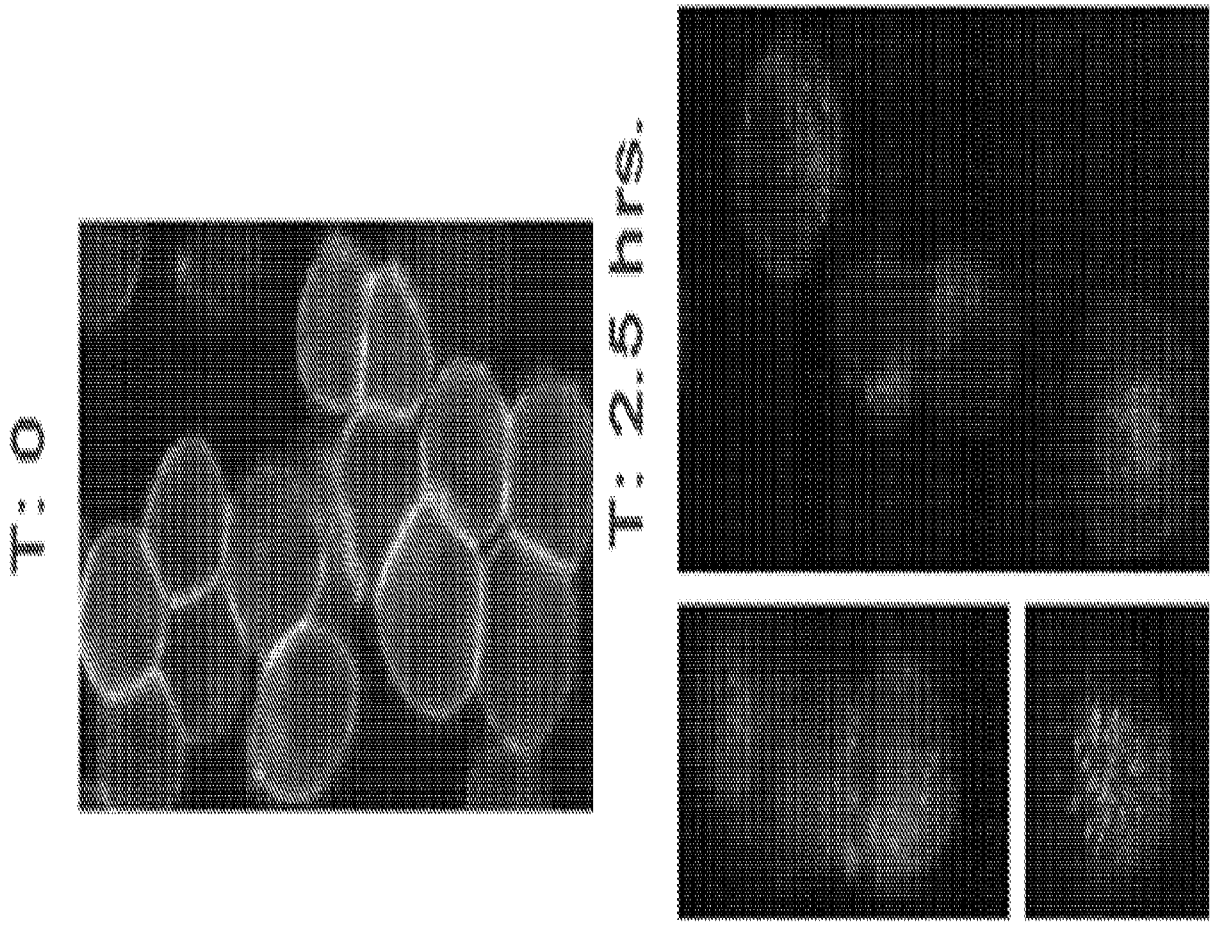


Fig. 1

Kabat #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	27a	27b	28
CL16 (original)	Q	Y	E	L	T	Q	P	P	S	-	A	S	G	T	P	G	Q	S	V	T	M	S	C	S	G	S	S	S	N	I
CL16 (GL)	Q	S	V	L	T	Q	P	P	S	-	A	S	G	T	P	G	Q	R	V	T	I	S	C	S	G	S	S	S	N	I
5H6	Q	S	V	L	T	Q	P	P	S	-	A	S	G	T	P	G	Q	R	V	T	I	S	C	S	G	S	S	S	N	I
8A3	Q	S	V	L	T	Q	P	P	S	-	A	S	G	T	P	G	Q	R	V	T	I	S	C	S	G	S	S	S	N	I
4H6	Q	S	V	L	T	Q	P	P	S	-	A	S	G	T	P	G	Q	R	V	T	I	S	C	R	G	S	S	S	N	I
6E.3	Q	S	V	L	T	Q	P	P	S	-	A	S	G	T	P	G	Q	R	V	T	I	S	C	S	G	S	L	S	N	I
2B11	Q	S	V	L	T	Q	P	P	S	-	A	S	G	T	P	G	Q	R	V	T	I	S	C	S	G	S	S	S	N	I
2D1	Q	S	V	L	T	Q	P	P	S	-	A	S	G	T	P	G	Q	R	V	T	I	S	C	S	G	S	S	S	N	I
3A6	Q	S	V	L	T	Q	P	P	S	-	A	S	G	T	P	G	Q	R	V	T	I	S	C	S	G	S	S	S	N	I
4C4	Q	S	V	L	T	Q	P	P	S	-	A	S	G	T	P	G	Q	R	V	T	I	S	C	S	G	S	S	S	N	I
																								CDR1						

Kabat #	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58
CL16 (original)	G	L	N	Y	V	S	W	Y	Q	H	L	P	G	T	A	P	K	L	L	I	S	R	N	N	Q	R	P	S	G	V
CL16 (GL)	G	L	N	Y	V	S	W	Y	Q	Q	L	P	G	T	A	P	K	L	L	I	S	R	N	N	Q	R	P	S	G	V
5H6	G	L	N	Y	V	S	W	Y	Q	Q	L	P	G	T	A	P	K	L	L	I	S	R	N	N	Q	R	P	S	G	V
8A3	G	L	N	Y	V	S	W	Y	Q	Q	L	P	G	T	A	P	K	L	L	I	S	R	N	N	Q	R	P	S	G	V
4H6	G	L	N	Y	V	S	W	Y	Q	Q	L	P	G	T	A	P	K	L	L	I	S	R	N	N	Q	R	P	S	G	V
6E.3	G	L	N	Y	V	S	W	Y	Q	Q	L	P	G	T	A	P	K	L	L	I	S	R	N	N	Q	R	P	S	G	V
2B11	G	L	N	Y	V	S	W	Y	Q	Q	L	P	G	T	A	P	K	L	L	I	S	R	N	N	Q	R	P	S	G	V
2D1	G	L	N	Y	V	S	W	Y	Q	Q	L	P	G	T	A	P	K	L	L	I	S	R	N	N	Q	R	P	S	G	V
3A6	G	L	N	Y	V	S	W	Y	Q	Q	L	P	G	T	A	P	K	L	L	I	S	R	N	N	Q	R	P	S	G	V
4C4	G	L	N	Y	V	S	W	Y	Q	Q	L	P	G	T	A	P	K	L	L	I	S	R	N	N	Q	R	P	S	G	V
																										CDR2				

Fig. 2A part I

Kabat #	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88
CL16 (original)	P	D	R	F	S	G	S	K	S	G	T	S	A	S	L	A	I	S	G	L	R	S	E	D	E	A	D	Y	Y	C
CL16 (GL)	P	D	R	F	S	G	S	K	S	G	T	S	A	S	L	A	I	S	G	L	R	S	E	D	E	A	D	Y	Y	C
5H6	P	D	R	F	S	G	S	K	S	G	T	S	A	S	L	A	I	S	G	L	R	S	E	D	E	A	D	Y	Y	C
8A3	P	D	R	F	S	G	S	K	S	G	T	S	A	S	L	A	I	S	G	L	R	S	E	D	E	A	D	Y	Y	C
4H6	P	D	R	F	S	G	S	K	S	G	T	S	A	S	L	A	I	S	G	L	R	S	E	D	E	A	D	Y	Y	C
6E.3	P	D	R	F	S	G	S	K	S	G	T	S	A	S	L	A	I	S	G	L	R	S	E	D	E	A	D	Y	Y	C
2B11	P	D	R	F	S	G	S	K	S	G	T	S	A	S	L	A	I	S	G	L	R	S	E	D	E	A	D	Y	Y	C
2D1	P	D	R	F	S	G	S	K	S	G	T	S	A	S	L	A	I	S	G	L	R	S	E	D	E	A	D	Y	Y	C
3A6	P	D	R	F	S	G	S	K	S	G	T	S	A	S	L	A	I	S	G	L	R	S	E	D	E	A	D	Y	Y	C
4C4	P	D	R	F	S	G	S	K	S	G	T	S	A	S	L	A	I	S	G	L	R	S	E	D	E	A	D	Y	Y	C

Kabat #	89	90	91	92	93	94	95	95a	95b	96	97	98	99	100	101	102	103	104	105	106	107
CL16 (original)	A	A	W	D	D	S	L	S		G	E	V	F	G	G	G	T	K	L	T	V	L
CL16 (GL)	A	A	W	D	D	S	L	S		G	E	V	F	G	G	G	T	K	L	T	V	L
5H6	A	A	W	D	D	G	L	P		G	E	V	F	G	G	G	T	K	L	T	V	L
8A3	A	A	W	D	D	S	L	I		G	E	V	F	G	G	G	T	K	L	T	V	L
4H6	A	A	W	D	D	S	L	S		G	E	V	F	G	G	G	T	K	L	T	V	L
6E.3	A	A	W	D	D	S	L	S		G	E	V	F	G	G	G	T	K	L	T	V	L
2B11	A	A	W	D	D	S	L	P		G	E	V	F	G	G	G	T	K	L	T	V	L
2D1	A	A	W	D	D	S	L	S		G	E	A	F	G	G	G	T	K	L	T	V	L
3A6	A	A	W	D	D	S	P	S		G	E	V	F	G	G	G	T	K	L	T	V	L
4C4	A	A	W	D	D	S	L	R		G	E	V	F	G	G	G	T	K	L	T	V	L

CDR3

Fig. 2A part II

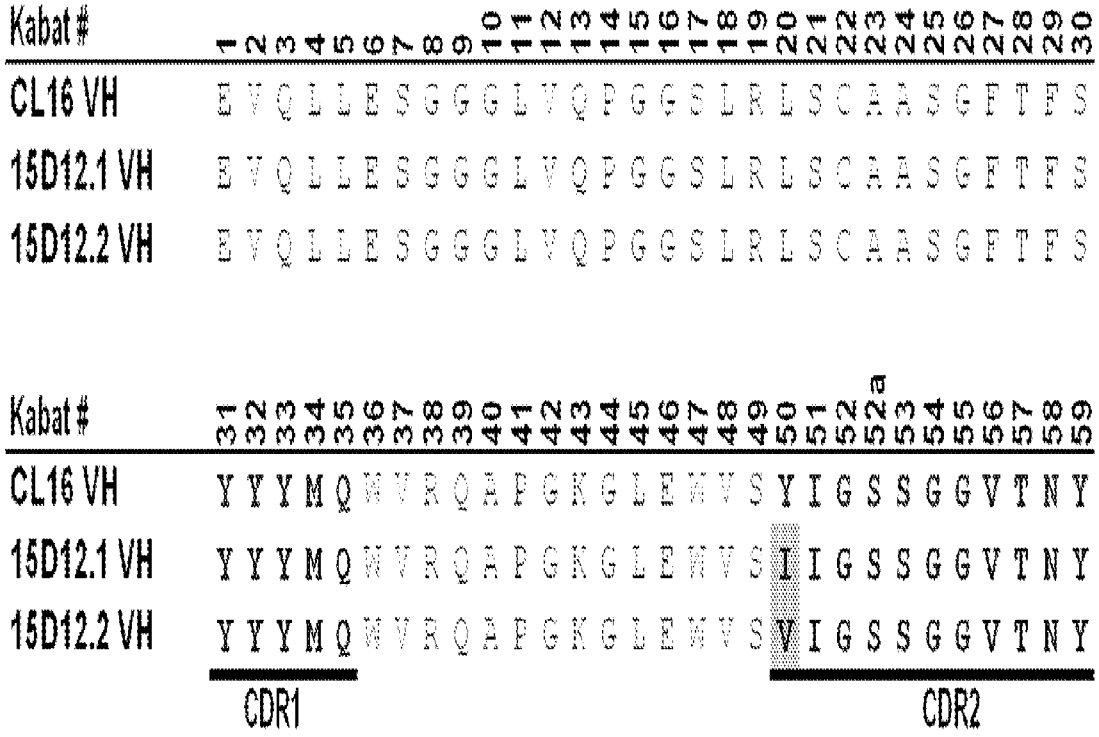

Kabat # 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30
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15D12.1 VH E V Q L L E S G G G L V Q P G G S L R L S C A A S G F T F S
15D12.2 VH E V Q L L E S G G G L V Q P G G S L R L S C A A S G F T F S
Kabat # 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 52a 53 54 55 56 57 58 59
CL16 VH Y Y Y M Q W V R Q A P G K G L E W V S Y I G S S G G V T N Y
15D12.1 VH Y Y Y M Q W V R Q A P G K G L E W V S I I G S S G G V T N Y
15D12.2 VH Y Y Y M Q W V R Q A P G K G L E W V S V I G S S G G V T N Y
CDR1
CDR2

Fig. 2B part I

Kabat #	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	82a	82b	82c	83	84	85
CL16 VH	Y	A	D	S	V	K	G	R	F	T	I	S	R	D	N	S	K	N	T	L	Y	L	Q	M	N	S	L	R	A	E
15D12.1 VH	Y	A	D	S	V	K	G	R	F	T	I	S	R	D	N	S	K	N	T	L	Y	L	Q	M	N	S	L	R	A	E
15D12.2 VH	Y	A	D	S	V	K	G	R	F	T	I	S	R	D	N	S	K	N	T	L	Y	L	Q	M	N	S	L	R	A	E

Kabat #	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100	100a	101	102	103	104	105	106	107	108	109	110	111	112	113
CL16 VH	D	T	A	V	Y	Y	C	A	R	V	G	L	G	D	A	F	D	I	W	G	Q	G	T	M	V	T	V	S	S
15D12.1 VH	D	T	A	V	Y	Y	C	A	R	V	G	L	G	D	A	F	D	I	W	G	Q	G	T	M	V	T	V	S	S
15D12.2 VH	D	T	A	V	Y	Y	C	A	R	V	G	L	G	D	A	F	D	I	W	G	Q	G	T	M	V	T	V	S	S

CDR3

Fig. 2B part II

Kabat #	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	27a	27b
CL16 (original)	Q	Y	E	L	T	Q	P	P	S	-	A	S	G	T	P	G	Q	S	V	T	M	S	C	S	G	S	S	S	N
CL16 (GL)	Q	S	V	L	T	Q	P	P	S	-	A	S	G	T	P	G	Q	R	V	T	I	S	C	S	G	S	S	S	N
1A4	Q	S	V	L	T	Q	P	P	S	-	A	S	G	T	P	G	Q	R	V	T	I	S	C	S	G	S	S	S	N
2C2	Q	S	V	L	T	Q	P	P	S	-	A	S	G	T	P	G	Q	R	V	T	I	S	C	S	G	S	L	S	N
3E.1	Q	S	V	L	T	Q	P	P	S	-	A	S	G	T	P	G	Q	R	V	T	I	S	C	R	G	S	S	S	N
2F10	Q	S	V	L	T	Q	P	P	S	-	A	S	G	T	P	G	Q	R	V	T	I	S	C	S	G	S	S	S	N
2B11	Q	S	V	L	T	Q	P	P	S	-	A	S	G	T	P	G	Q	R	V	T	I	S	C	S	G	S	S	S	N
																								CDR1					

Kabat #	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56
CL16 (original)	I	G	L	N	Y	V	S	W	Y	Q	H	L	P	G	T	A	P	K	L	L	I	S	R	N	N	Q	R	P	S
CL16 (GL)	I	G	L	N	Y	V	S	W	Y	Q	Q	L	P	G	T	A	P	K	L	L	I	S	R	N	N	Q	R	P	S
1A4	I	G	L	N	Y	V	S	W	Y	Q	Q	L	P	G	T	A	P	K	L	L	I	S	R	N	N	Q	R	P	S
2C2	I	G	L	N	Y	V	S	W	Y	Q	Q	L	P	G	T	A	P	K	L	L	I	S	R	N	N	Q	R	P	S
3E.1	I	G	L	N	Y	V	S	W	Y	Q	Q	L	P	G	T	A	P	K	L	L	I	S	R	N	N	Q	R	P	S
2F10	I	G	L	N	Y	V	S	W	Y	Q	Q	L	P	G	T	A	P	K	L	L	I	S	R	N	N	Q	R	P	S
2B11	I	G	L	N	Y	V	S	W	Y	Q	Q	L	P	G	T	A	P	K	L	L	I	S	R	N	N	Q	R	P	S
																										CDR2			

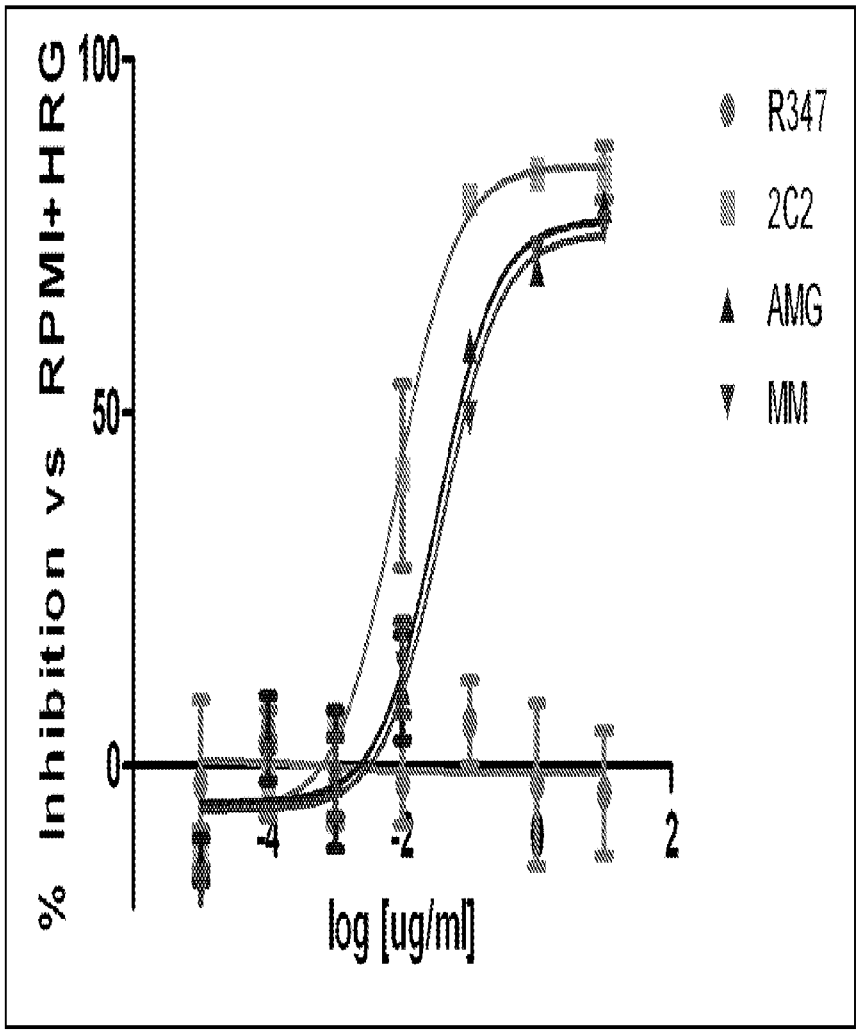
Fig. 2C part I

Kabat #	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85
CL16 (original)	G	V	P	D	R	F	S	G	S	K	S	G	T	S	A	S	L	A	I	S	G	L	R	S	E	D	E	A	D
CL16 (GL)	G	V	P	D	R	F	S	G	S	K	S	G	T	S	A	S	L	A	I	S	G	L	R	S	E	D	E	A	D
1A4	G	V	P	D	R	F	S	G	S	K	S	G	T	S	A	S	L	A	I	S	G	L	R	S	E	D	E	A	D
2C2	G	V	P	D	R	F	S	G	S	K	S	G	T	S	A	S	L	A	I	S	G	L	R	S	E	D	E	A	D
3E.1	G	V	P	D	R	F	S	G	S	K	S	G	T	S	A	S	L	A	I	S	G	L	R	S	E	D	E	A	D
2F10	G	V	P	D	R	F	S	G	S	K	S	G	T	S	A	S	L	A	I	S	G	L	R	S	E	D	E	A	D
2B11	G	V	P	D	R	F	S	G	S	K	S	G	T	S	A	S	L	A	I	S	G	L	R	S	E	D	E	A	D

Kabat #	86	87	88	89	90	91	92	93	94	95	95a	95b	96	97	98	99	100	101	102	103	104	105	106	107
CL16 (original)	Y	Y	C	A	A	W	D	D	S	L	S		G	E	V	F	G	G	G	T	K	L	T	V	L
CL16 (GL)	Y	Y	C	A	A	W	D	D	S	L	S		G	E	V	F	G	G	G	T	K	L	T	V	L
1A4	Y	Y	C	A	A	W	D	D	S	P	P		G	E	A	F	G	G	G	T	K	L	T	V	L
2C2	Y	Y	C	A	A	W	D	D	S	P	P		G	E	A	F	G	G	G	T	K	L	T	V	L
3E.1	Y	Y	C	A	A	W	D	D	S	P	P		G	E	A	F	G	G	G	T	K	L	T	V	L
2F10	Y	Y	C	A	A	W	D	D	S	P	S		G	E	A	F	G	G	G	T	K	L	T	V	L
2B11	Y	Y	C	A	A	W	D	D	S	L	P		G	E	V	F	G	G	G	T	K	L	T	V	L

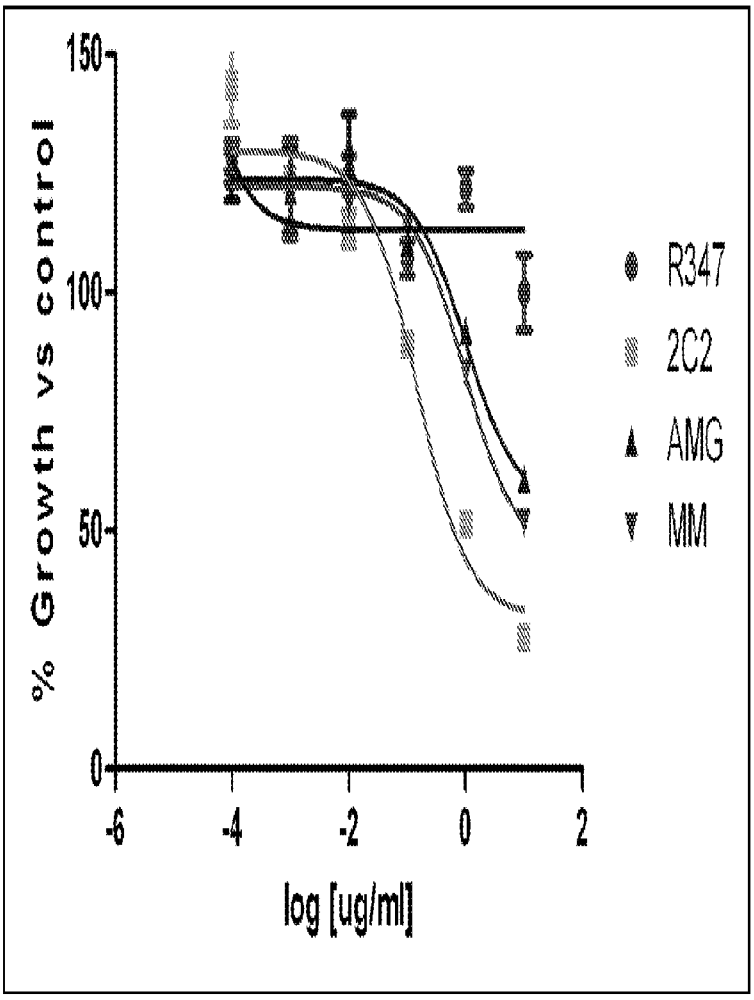
CDR3

Fig. 2C part II



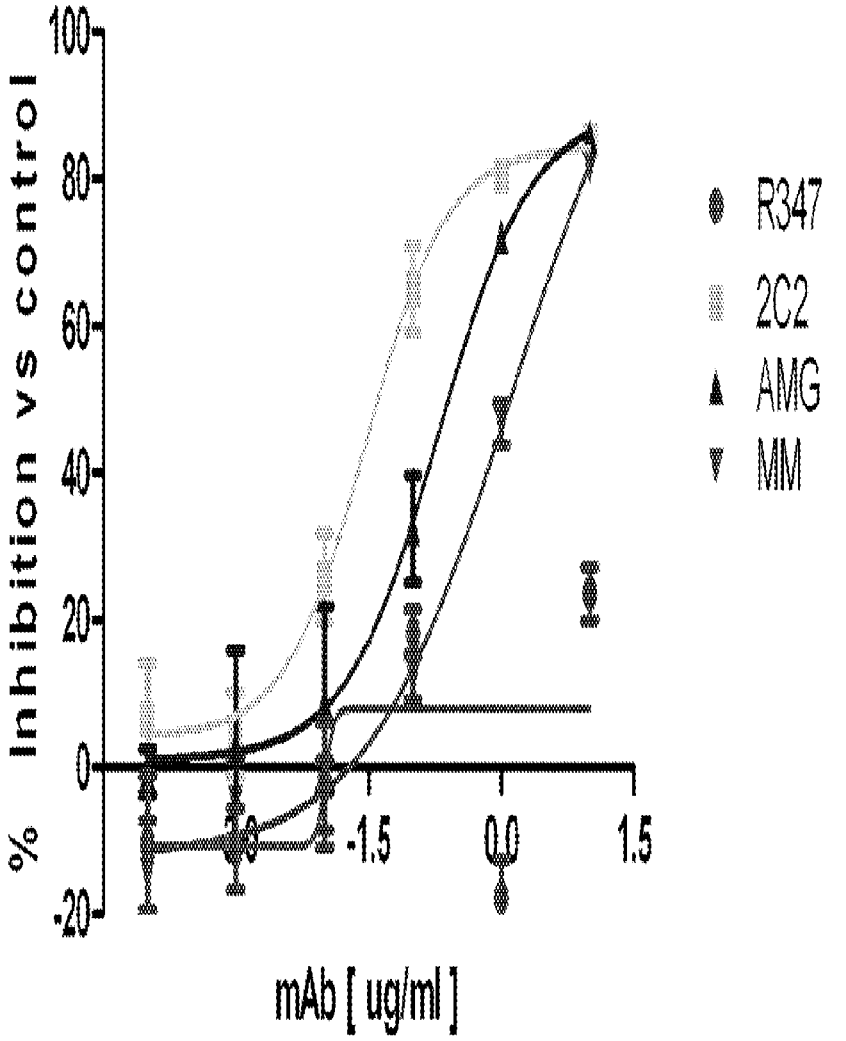
	2C2	AMG	MM
Maximum inhibition %	85	77	75
IC50 (ng/ml)	8.4	33	39

Fig. 3



	2C2	AMG	MM
Maximum inhibition %	72	39	49
IC50 (ug/ml)	0.14	0.99	0.95

Fig. 4



	2C2	AMG	MM
IC50 (ug/ml)	0.027 ug/ml	1.729 ug/ml	0.209 ug/ml

Fig. 5

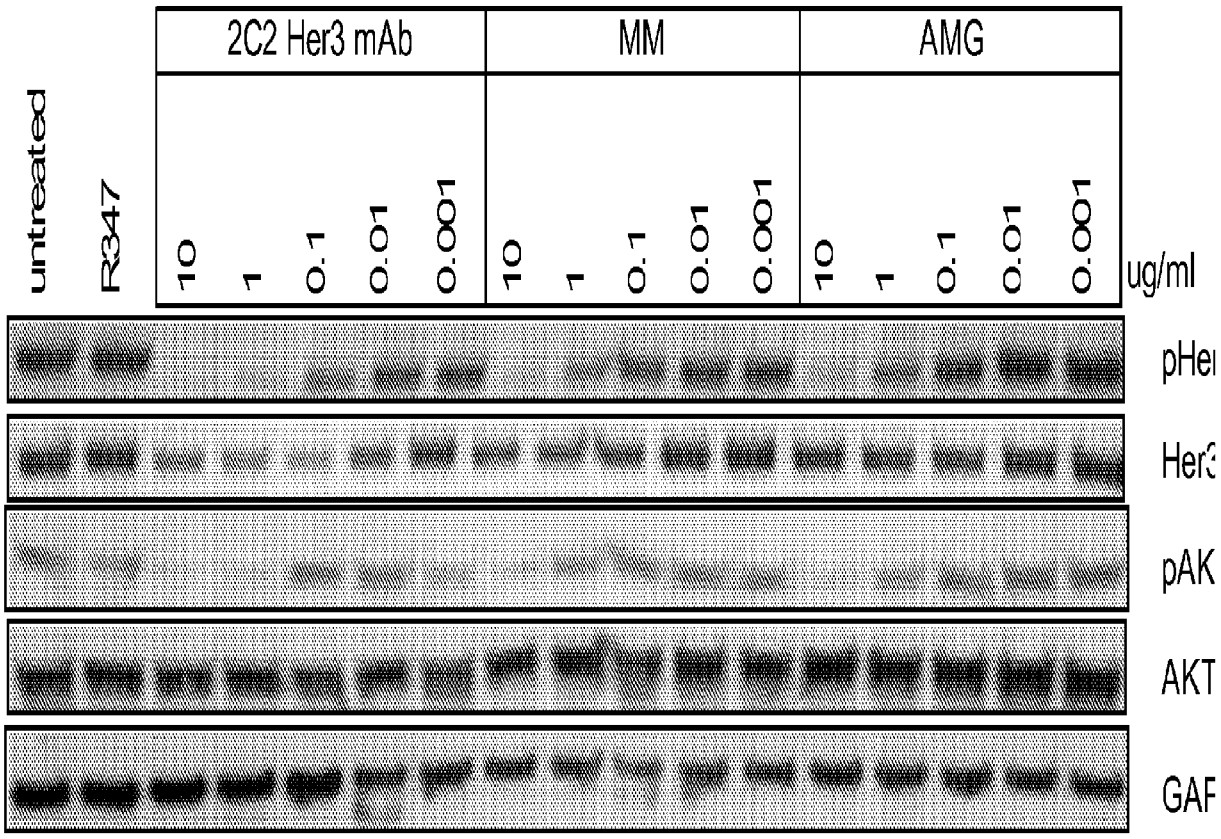

2C2 Her3 mAb
MM
AMG
untreated
R347
10
1
0.1
0.01
0.001
ug/ml
pHer
Her3
pAK
AKT
GAF

Fig. 6

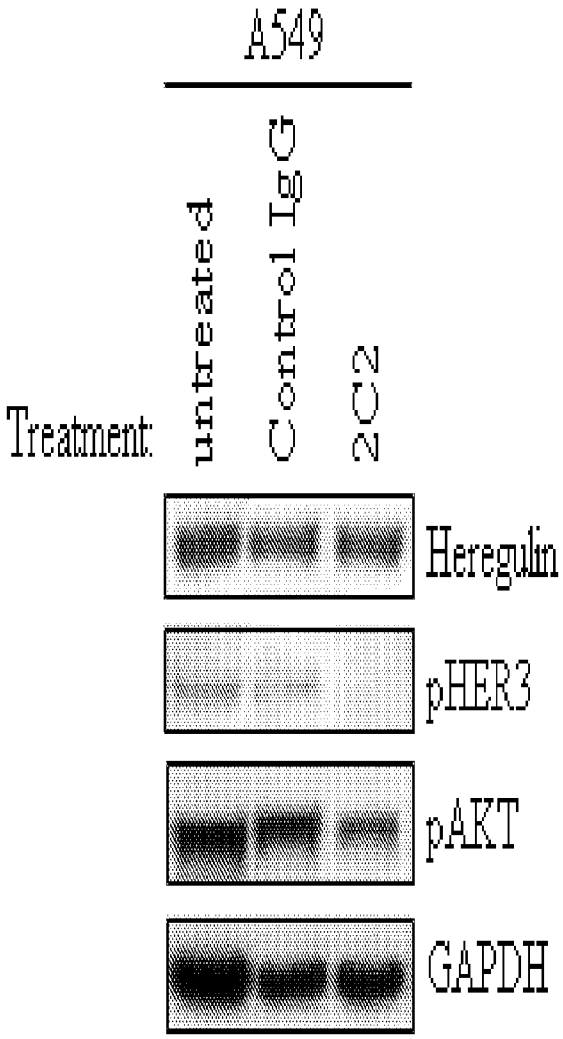
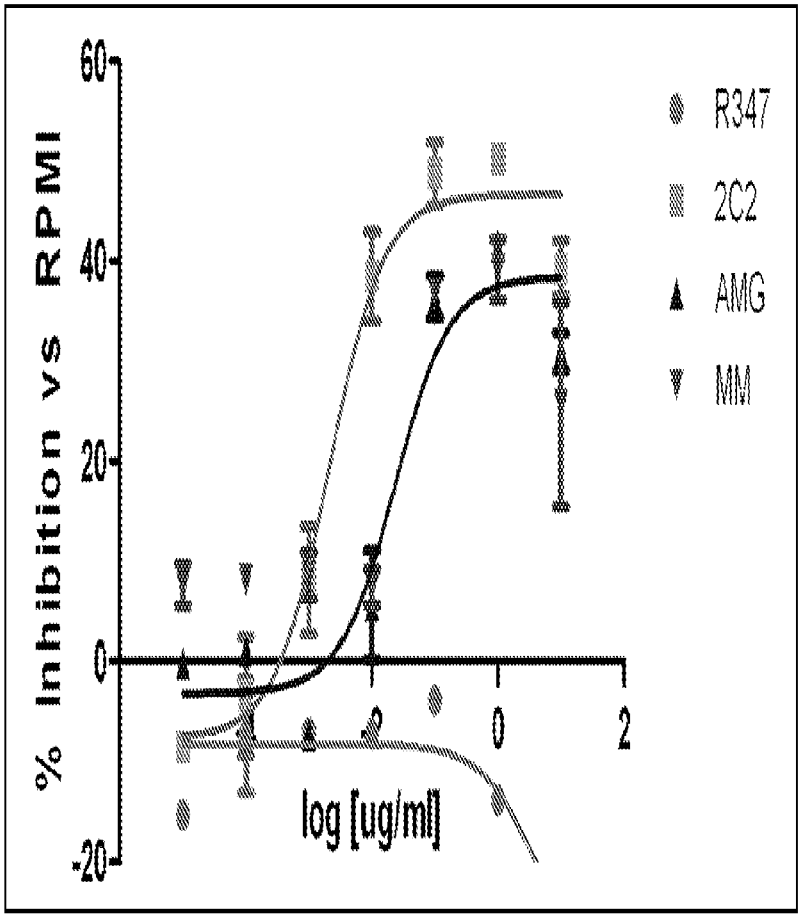
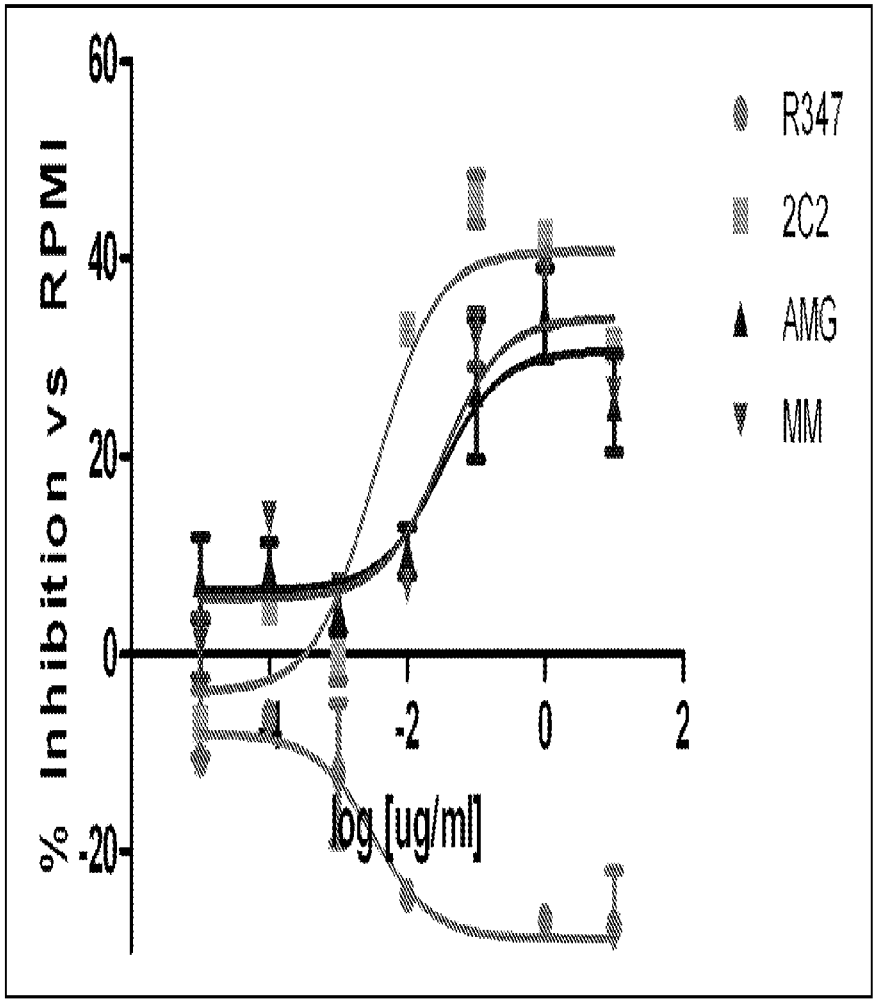

A549
Treatment:
untreated
Control IgG
2C2
Heregulin
pHER3
pAKT
GAPDH

Fig. 7



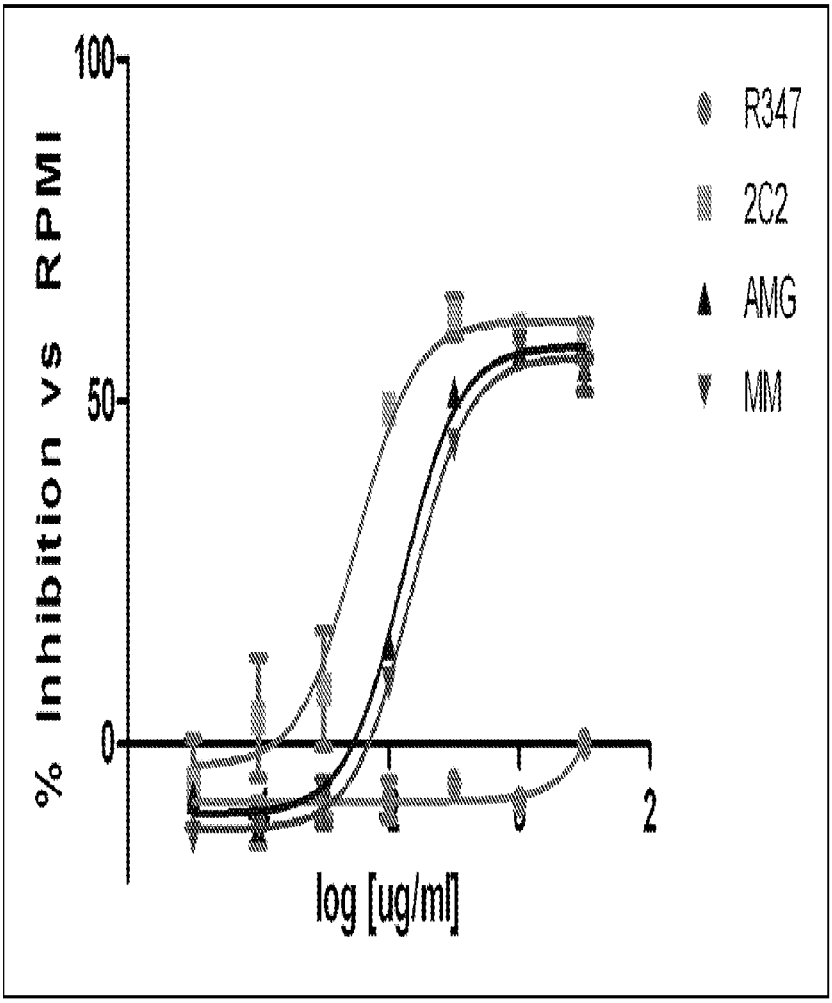
	2C2	AMG	MM
Maximum inhibition %	54	41	
IC50 (ng/ml)	2	23	

Fig. 8A



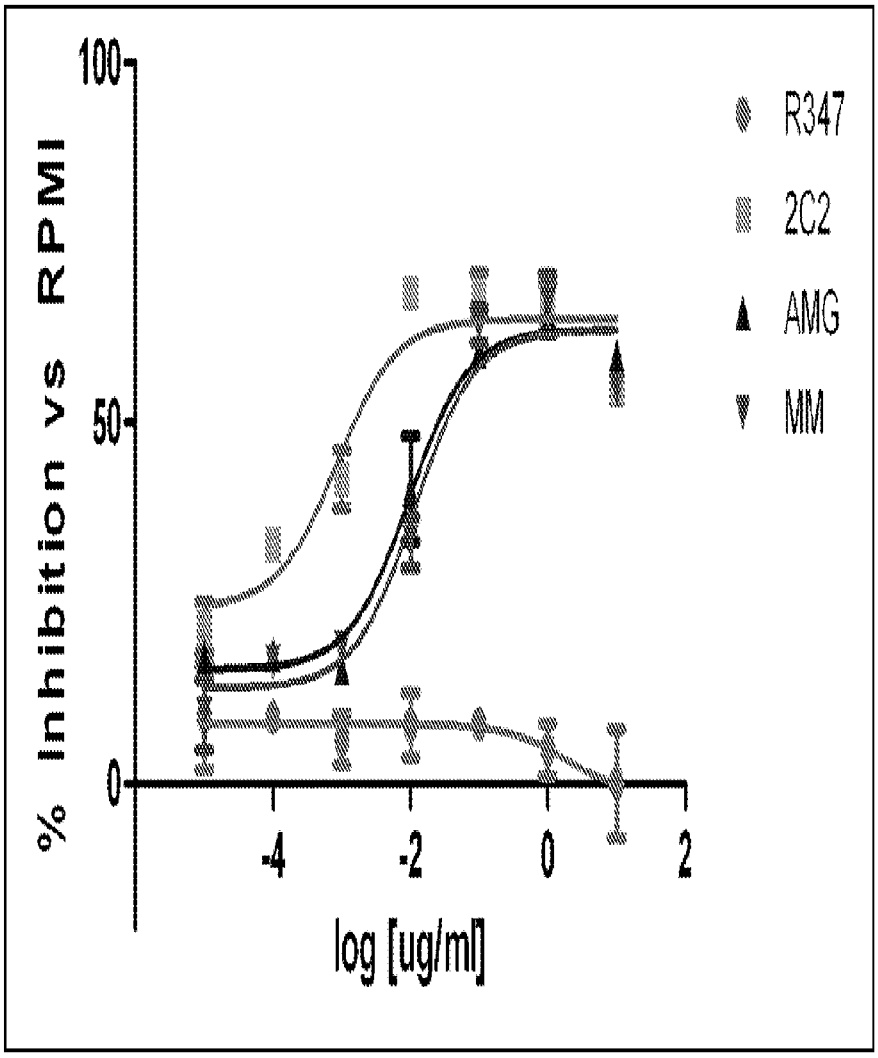
	2C2	AMG	MM
Maximum inhibition %	45	24	28
IC50 (ng/ml)	3.5	31	32

Fig. 8B



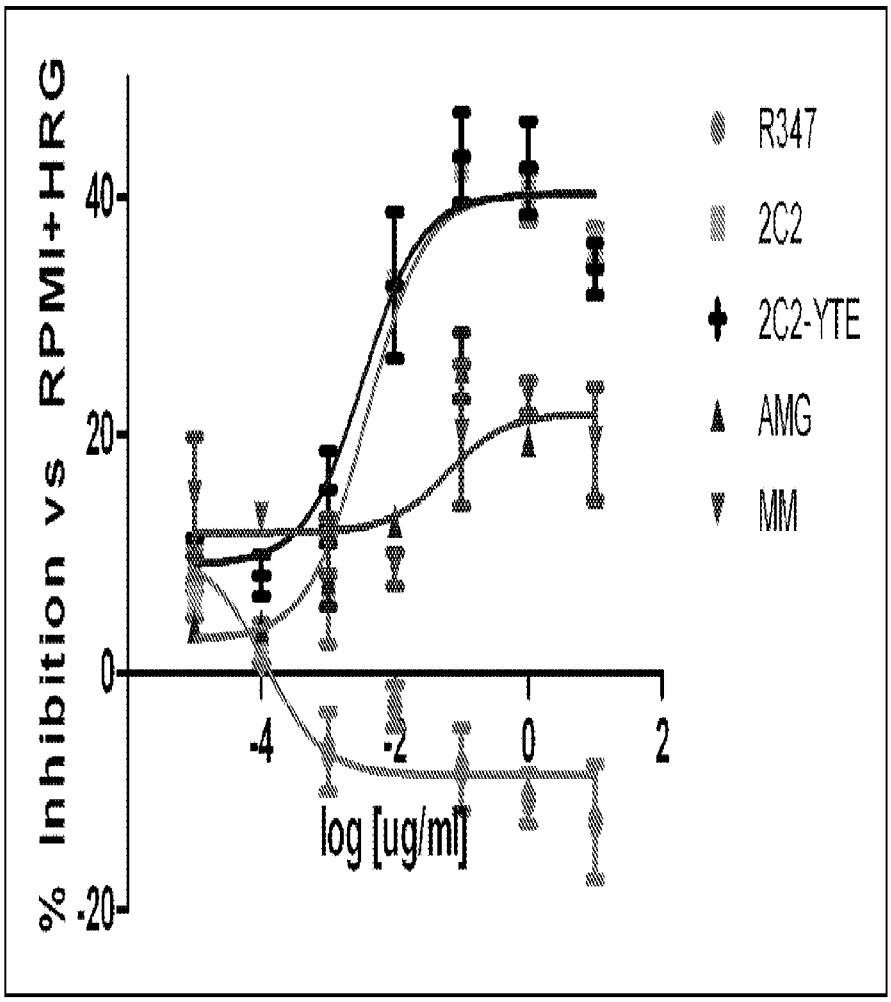
	2C2	AMG	MM
Maximum inhibition %	62	58	57
IC50 (ng/ml)	3.2	16.1	22.1

Fig. 8C



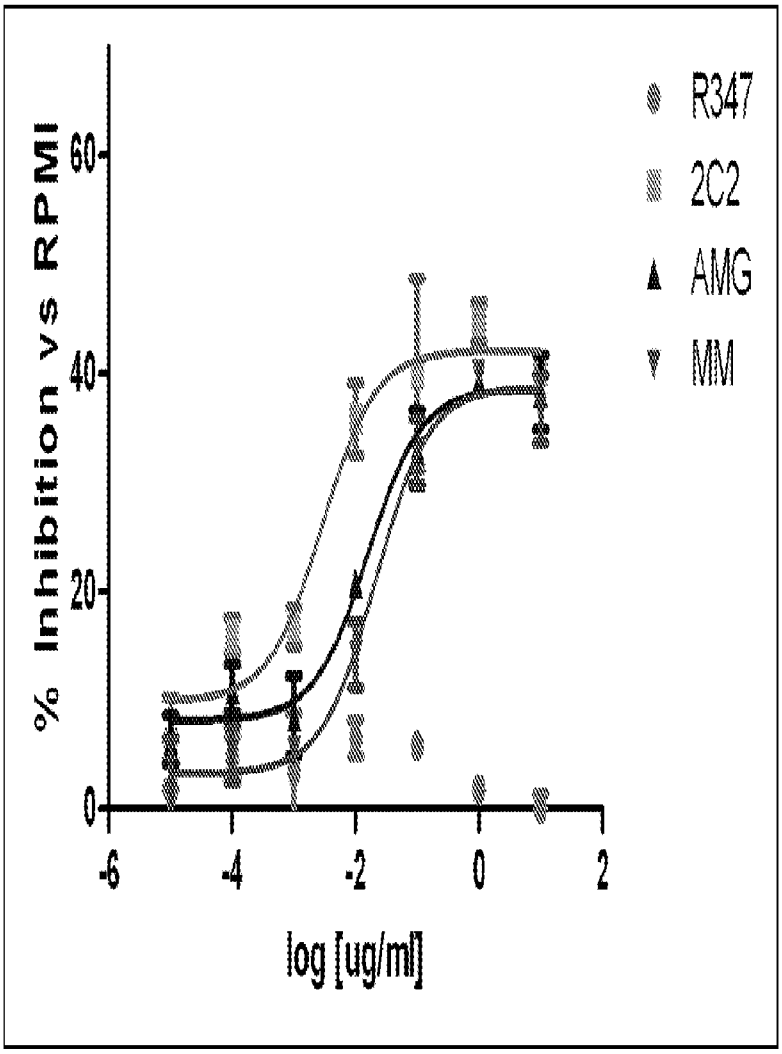
	2C2	AMG	MM
Maximum inhibition %	64	62	62
IC50 (ng/ml)	0.8	9.6	12.6

Fig. 8D



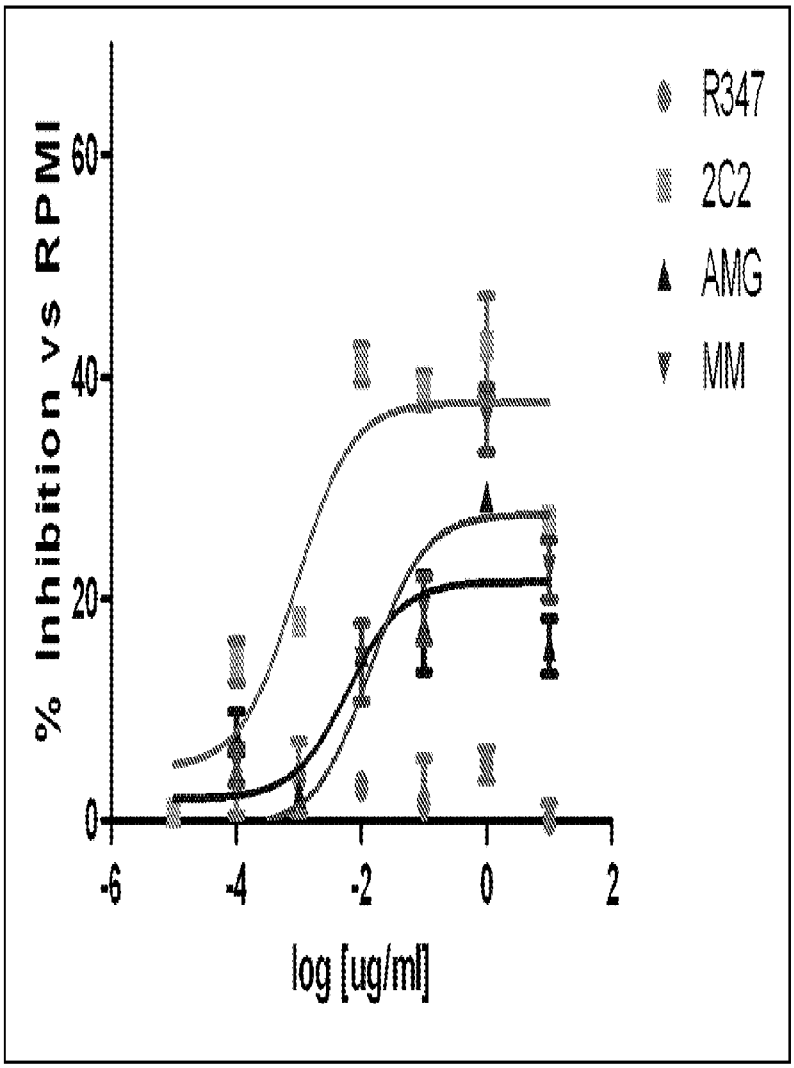
	2C2	AMG	MM
IC50 (ug/ml)	0.004	>10	>10
Max inhibition%	41		

Fig. 8E



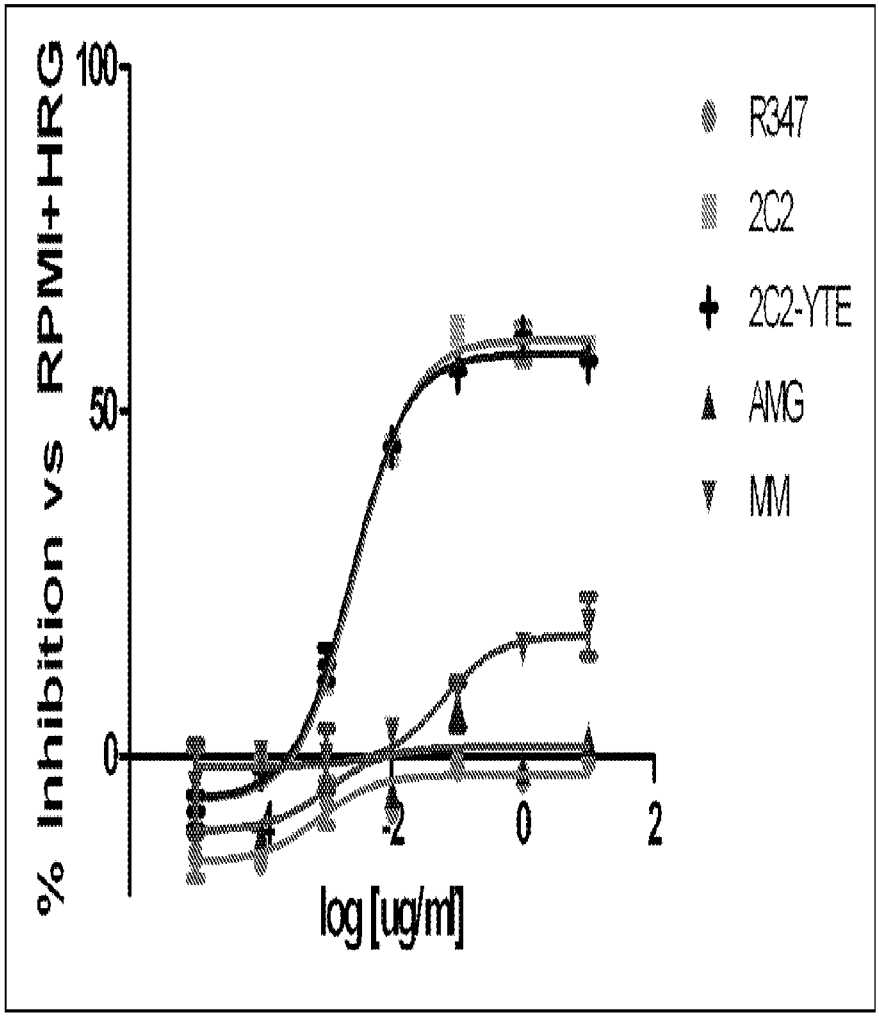
	2C2	AMG	MM
Maximum inhibition %	42	38	38
IC50 (ng/ml)	2.9	15.8	21.2

Fig. 9A



	2C2	AMG	MM
Maximum inhibition %	38	22	28
IC50 (ng/ml)	0.9	6.2	13.6

Fig. 9B



	2C2	AMG	MM
IC50 (ug/ml)	0.003	>10	>10
Max inhibition%	60	1	17

Fig. 9C

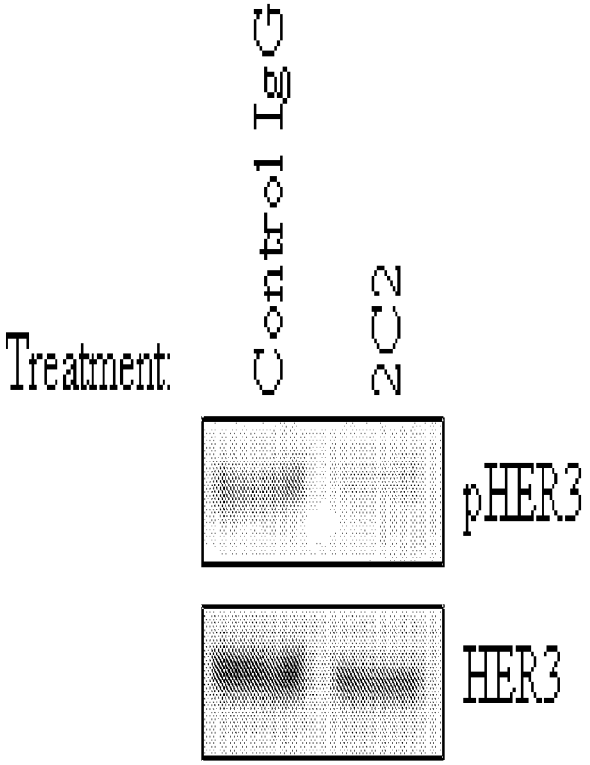


Fig. 10A

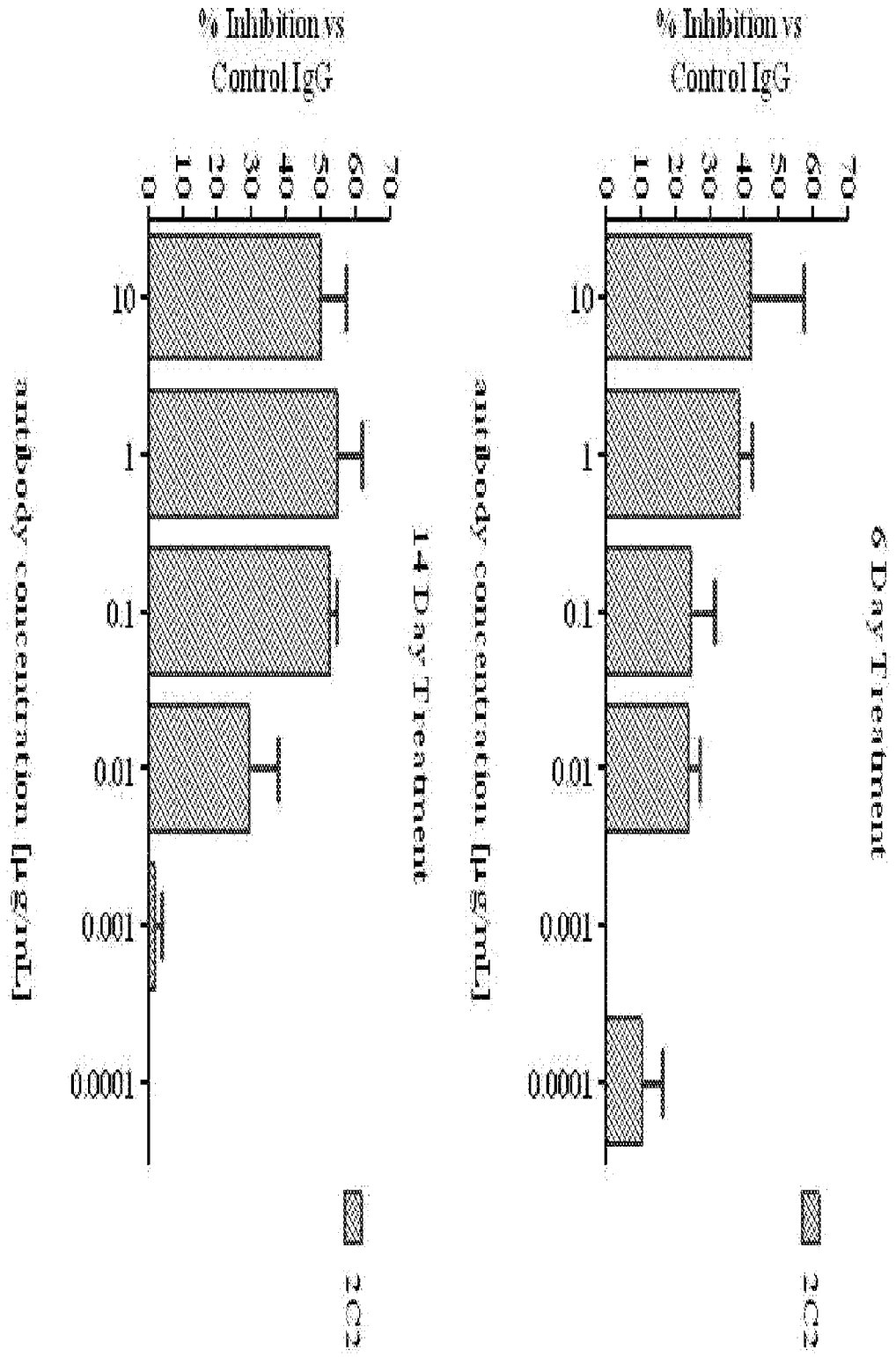

% Inhibition vs Control IgG
0
10
20
30
40
50
60
70
10
1
0.1
0.01
0.001
0.0001
antibody concentration [µg/mL]
14 Day Treatment
EC2
% Inhibition vs Control IgG
0
10
20
30
40
50
60
70
10
1
0.1
0.01
0.001
0.0001
antibody concentration [µg/mL]
9 Day Treatment
EC2

Fig. 10B

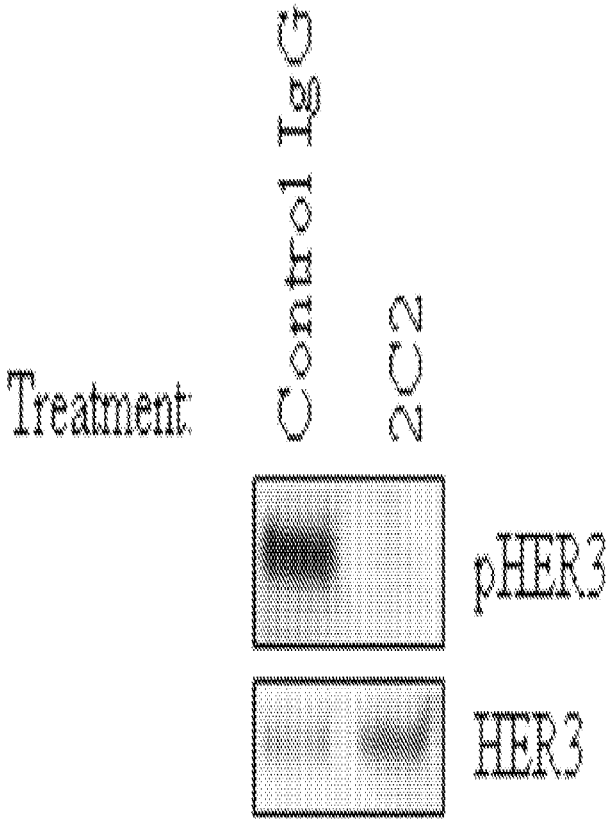


Fig. 11

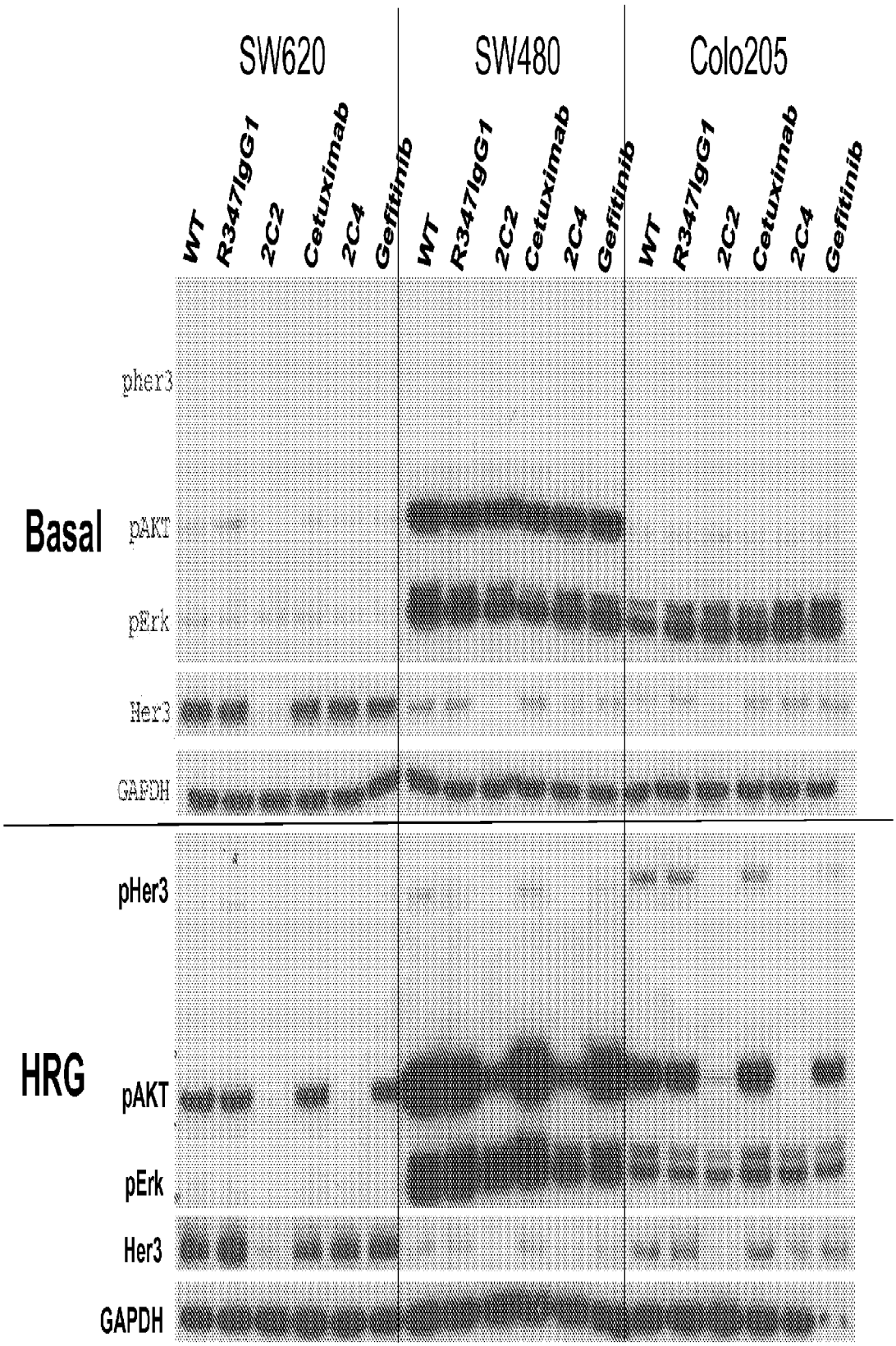

SW620
SW480
Colo205
WT
R347IgG1
2C2
Cetuximab
2C4
Gefitinib
pher3
Basal
pAKT
pErk
Her3
GAPDH
pHer3
HRG
pAKT
pErk
Her3
GAPDH

Fig. 12A

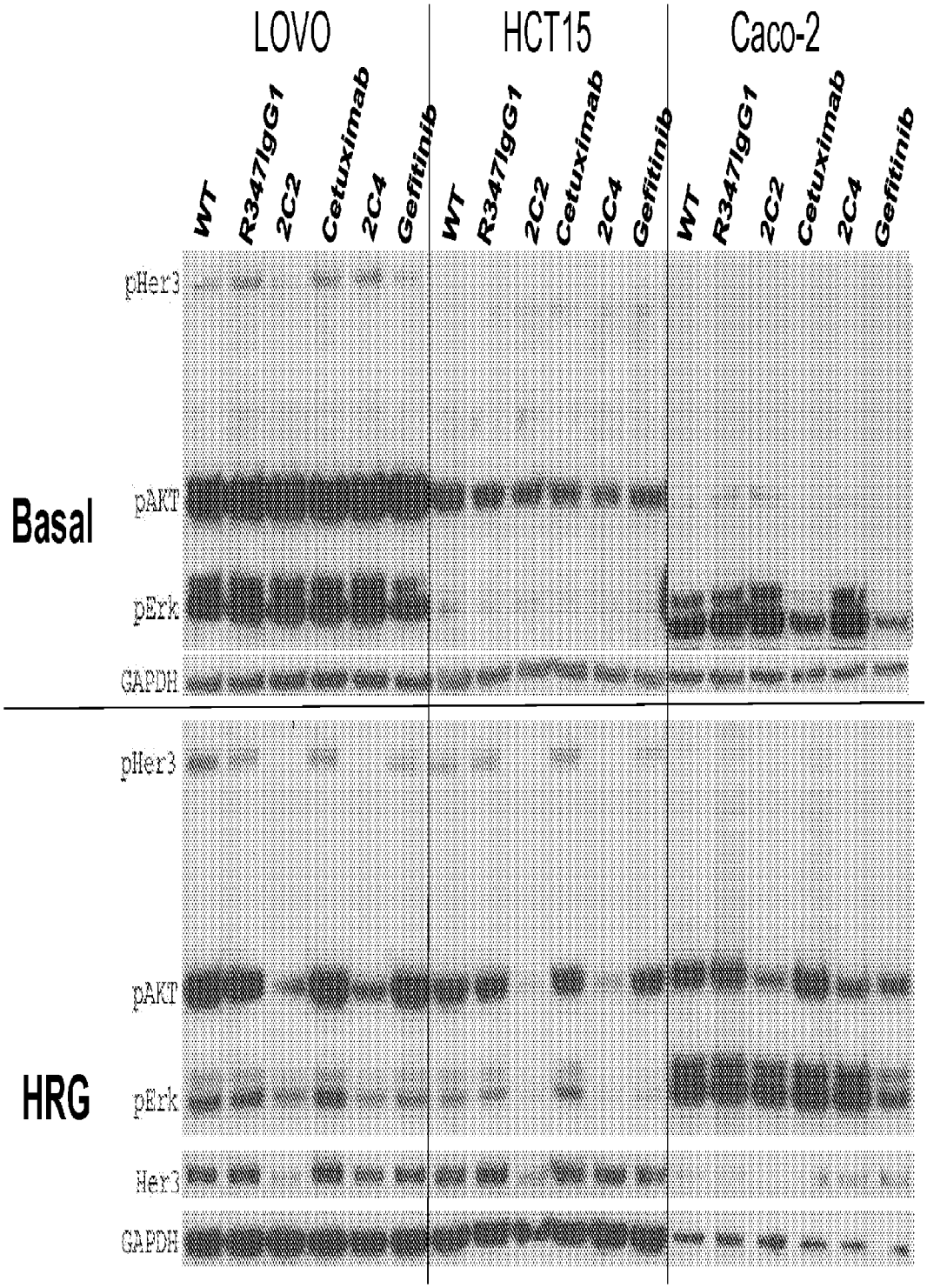

LOVO
HCT15
Caco-2
WT
R347IgG1
2C2
Cetuximab
2C4
Gefitinib
Basal
HRG
pHer3
pAKT
pErk
Her3
GAPDH

Fig. 12B

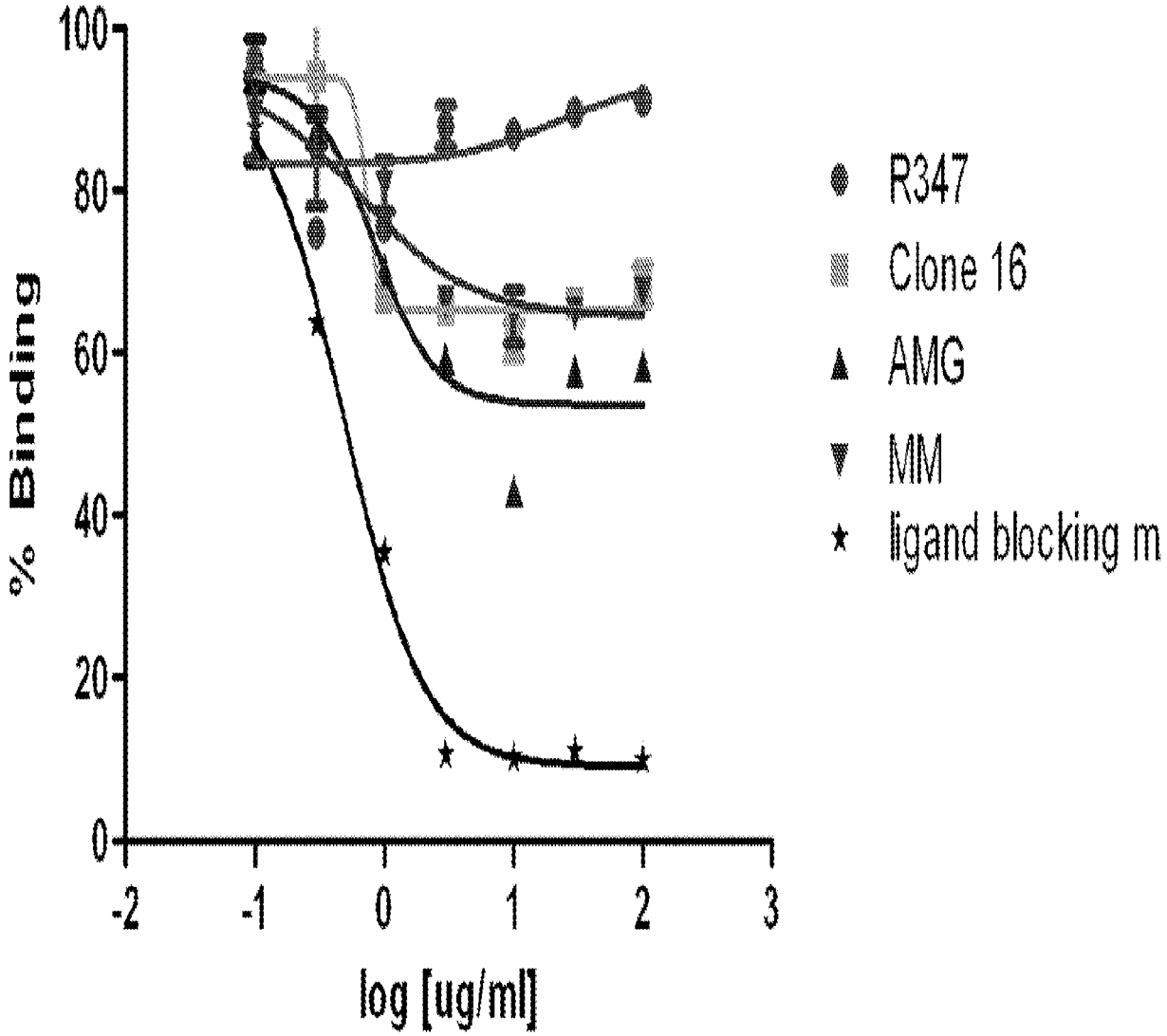

100
80
60
40
20
0
% Binding
-2
-1
0
1
2
3
log [ug/ml]
R347
Clone 16
AMG
MM
ligand blocking m

Fig. 13

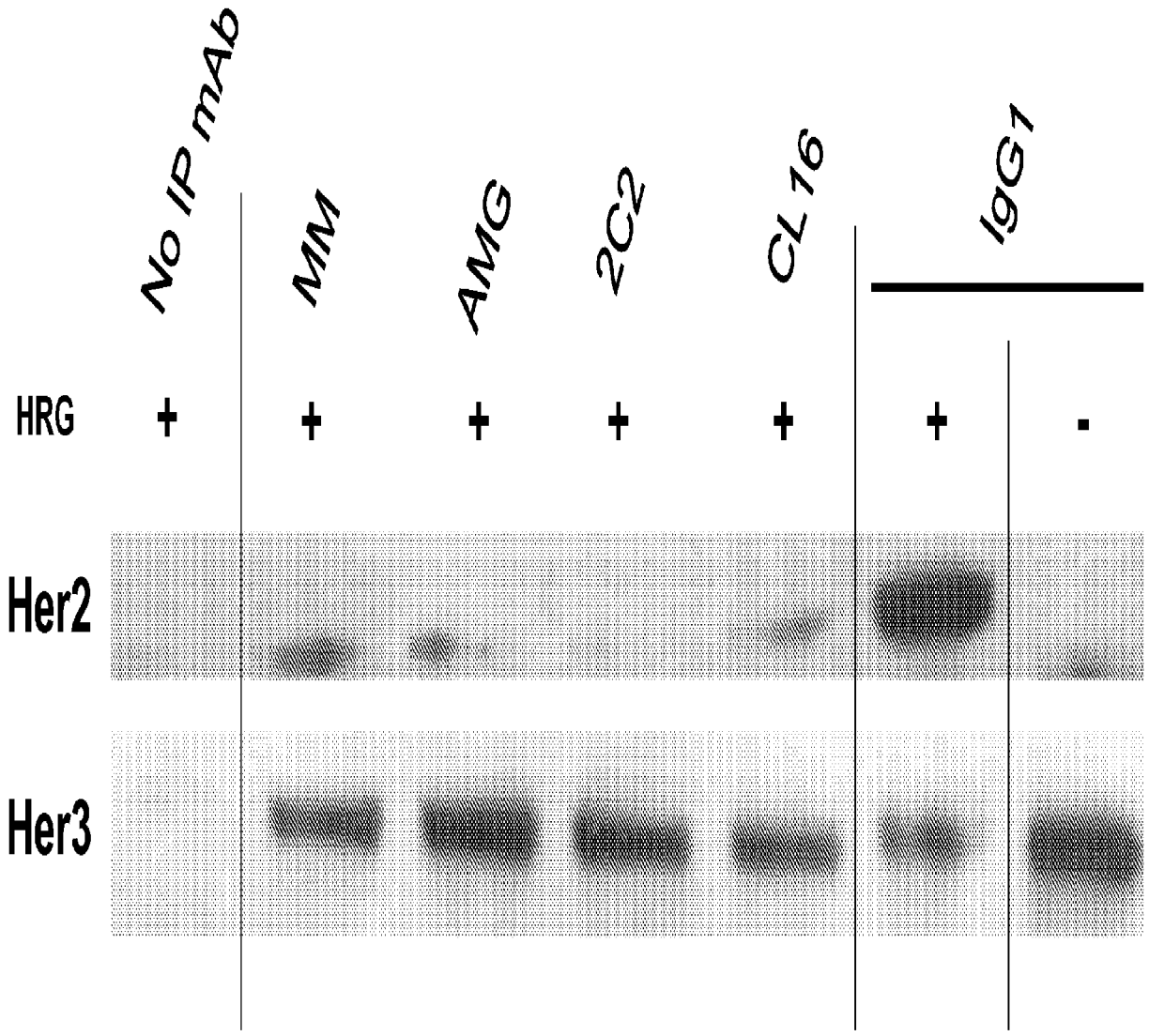


Fig. 14A

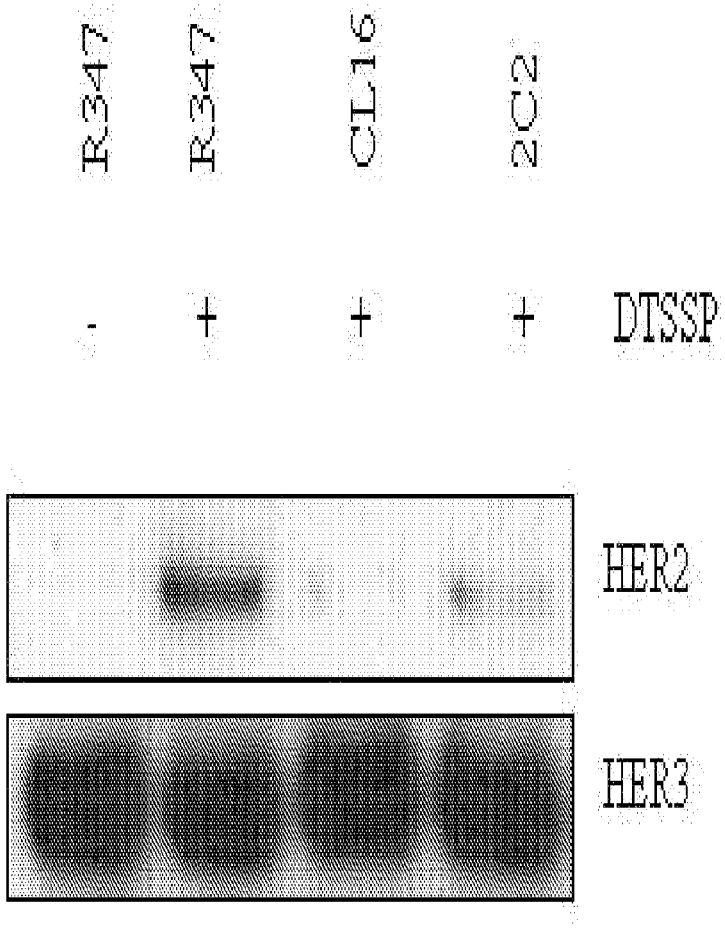


Fig. 14B

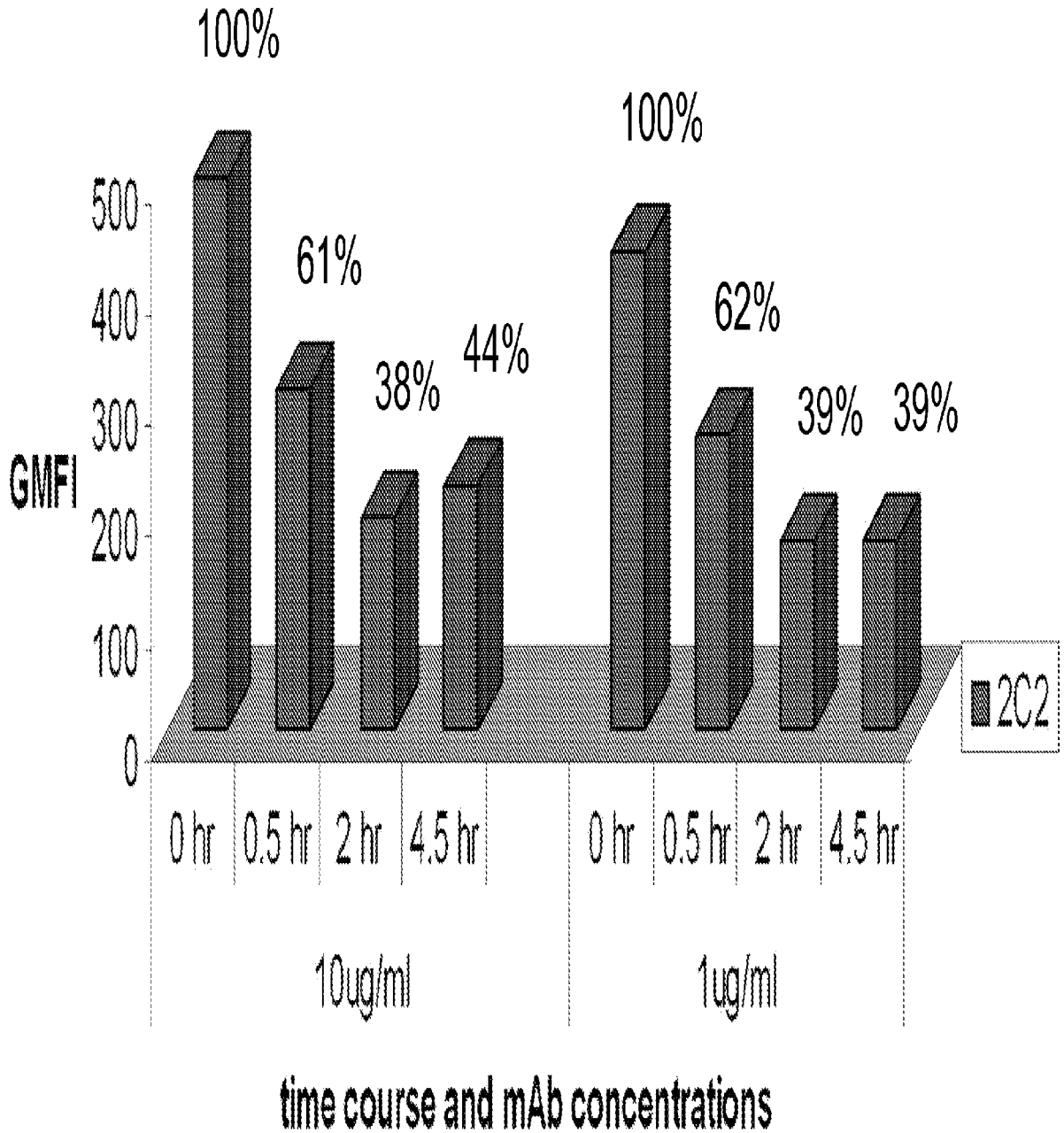

100%
61%
38%
44%
100%
62%
39%
39%
GMFI
500
400
300
200
100
0
2C2
0 hr
0.5 hr
2 hr
4.5 hr
0 hr
0.5 hr
2 hr
4.5 hr
10ug/ml
1ug/ml
time course and mAb concentrations

Fig. 15A

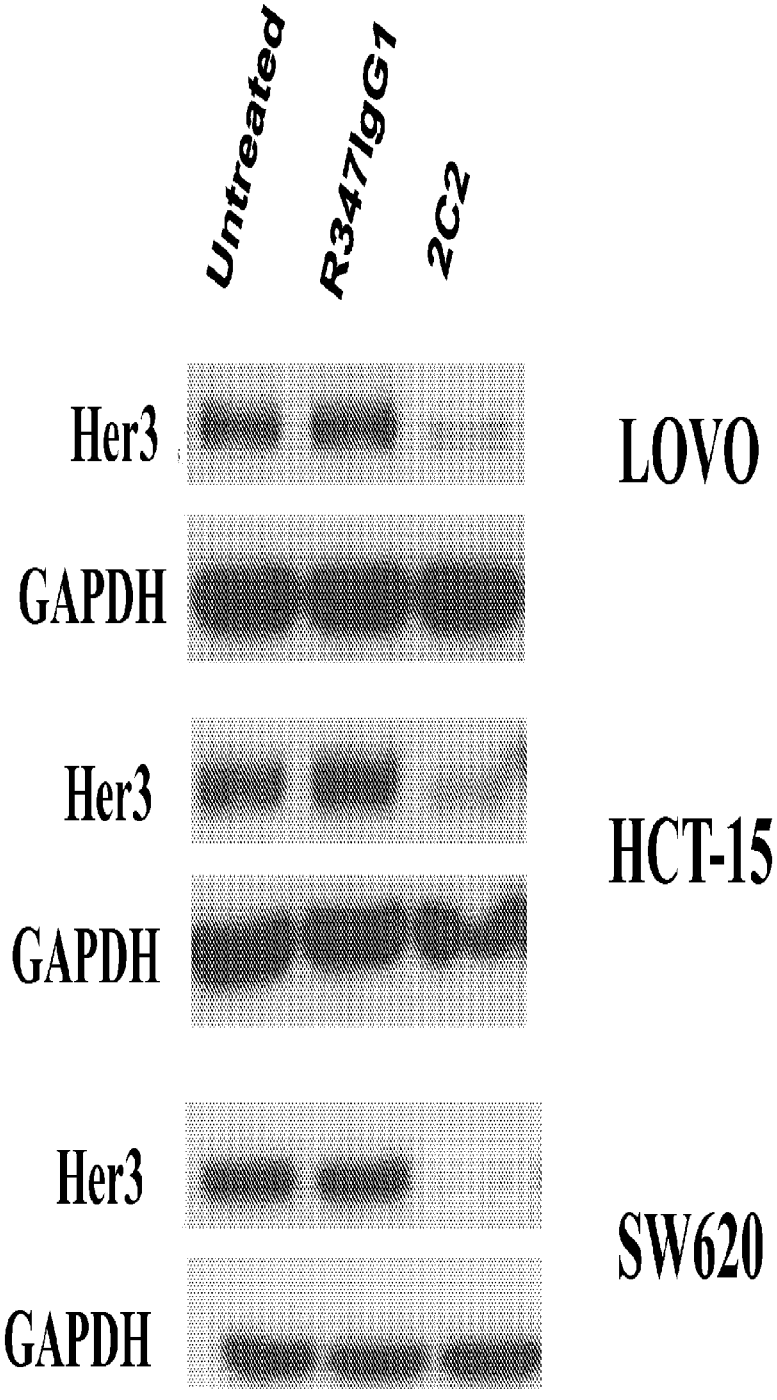

Untreated
R347IgG1
2C2
Her3
GAPDH
LOVO
Her3
GAPDH
HCT-15
Her3
GAPDH
SW620

Fig. 15B

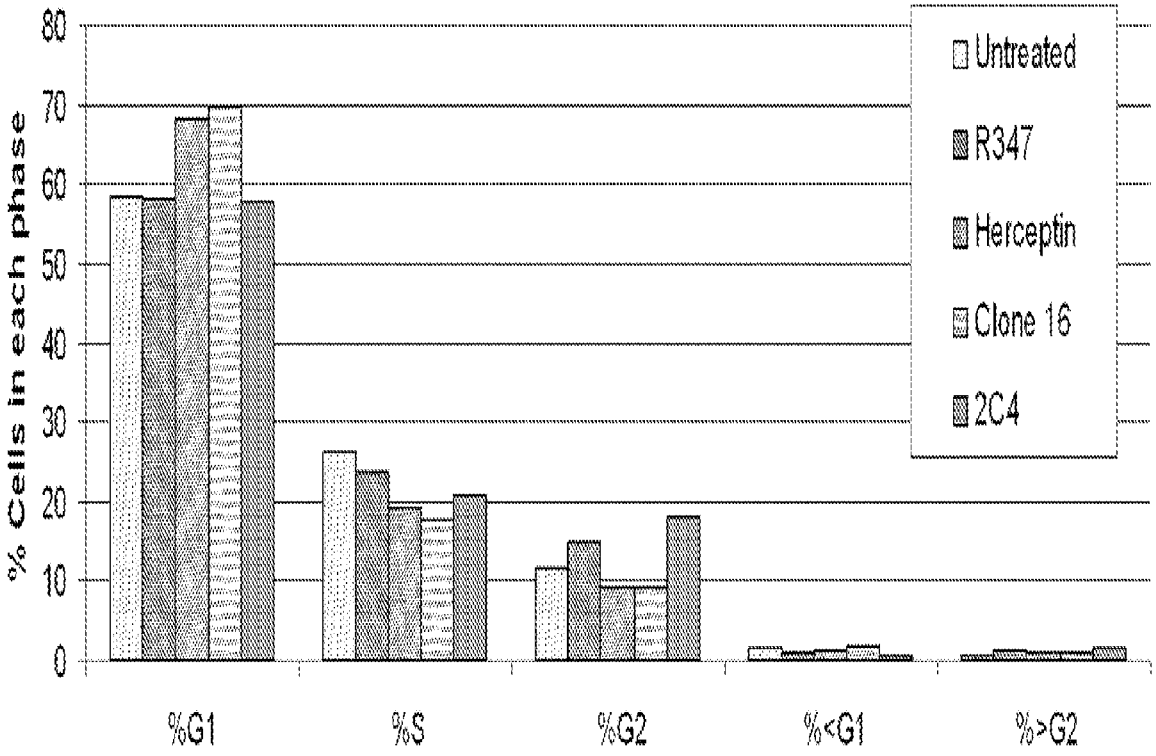

% Cells in each phase
80
70
60
50
40
30
20
10
0
%G1
%S
%G2
%<G1
%>G2
Untreated
R347
Herceptin
Clone 16
2C4

Fig. 16

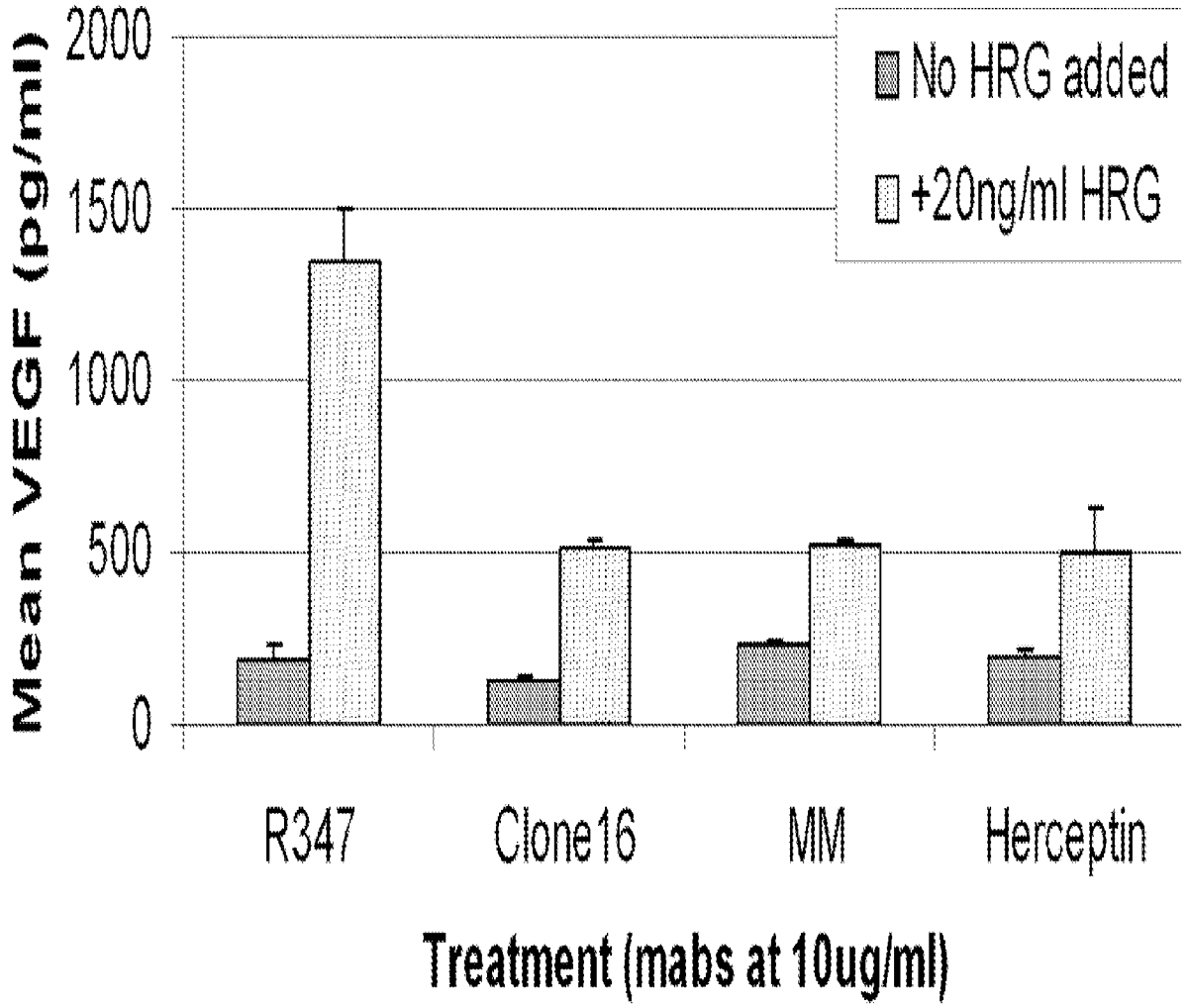

Mean VEGF (pg/ml)
2000
1500
1000
500
0
No HRG added
+20ng/ml HRG
R347
Clone16
MM
Herceptin
Treatment (mabs at 10ug/ml)

Fig. 17A

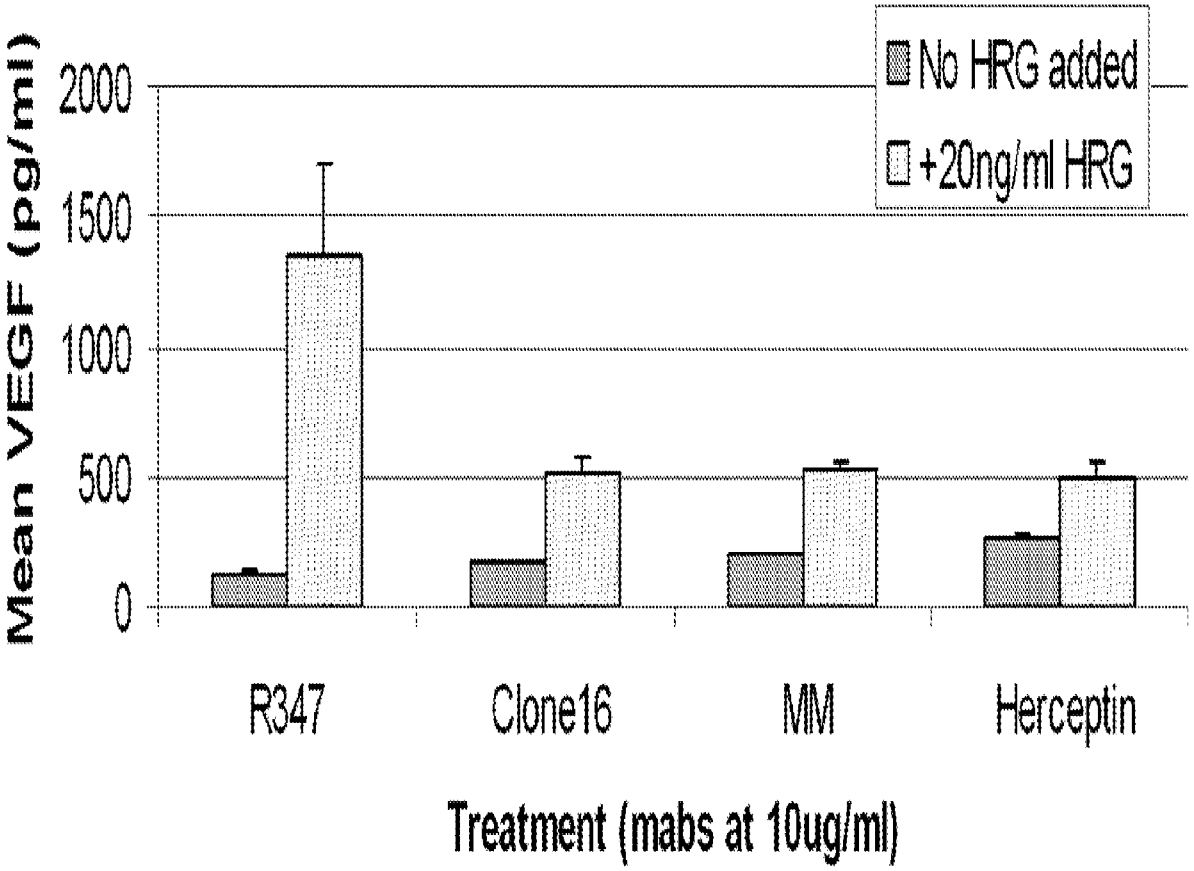

No HRG added
+20ng/ml HRG
Mean VEGF (pg/ml)
2000
1500
1000
500
0
R347
Clone16
MM
Herceptin
Treatment (mabs at 10ug/ml)

Fig. 17B

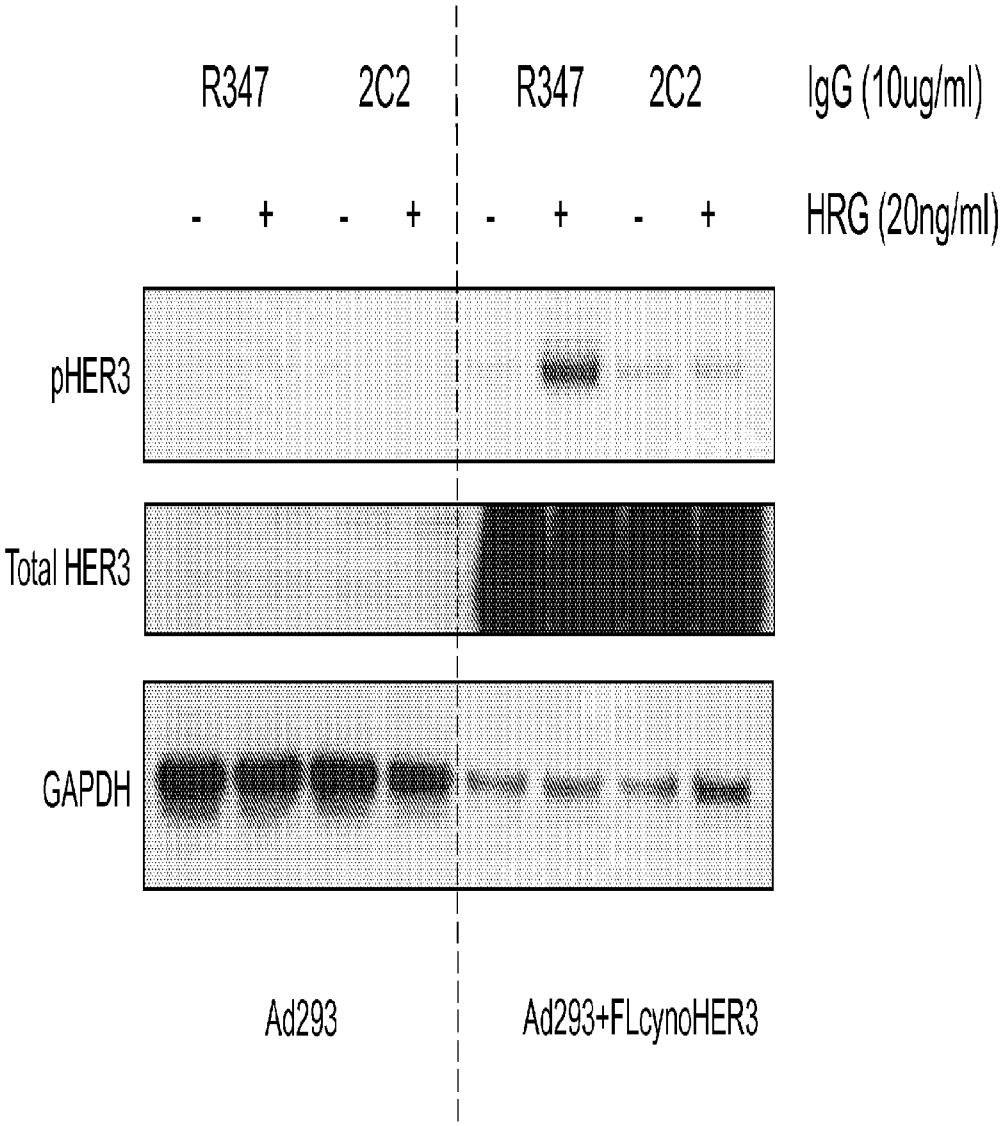

R347
2C2
R347
2C2
IgG (10ug/ml)
- + - + - + - +
HRG (20ng/ml)
pHER3
Total HER3
GAPDH
Ad293
Ad293+FLcynoHER3

Fig. 18A

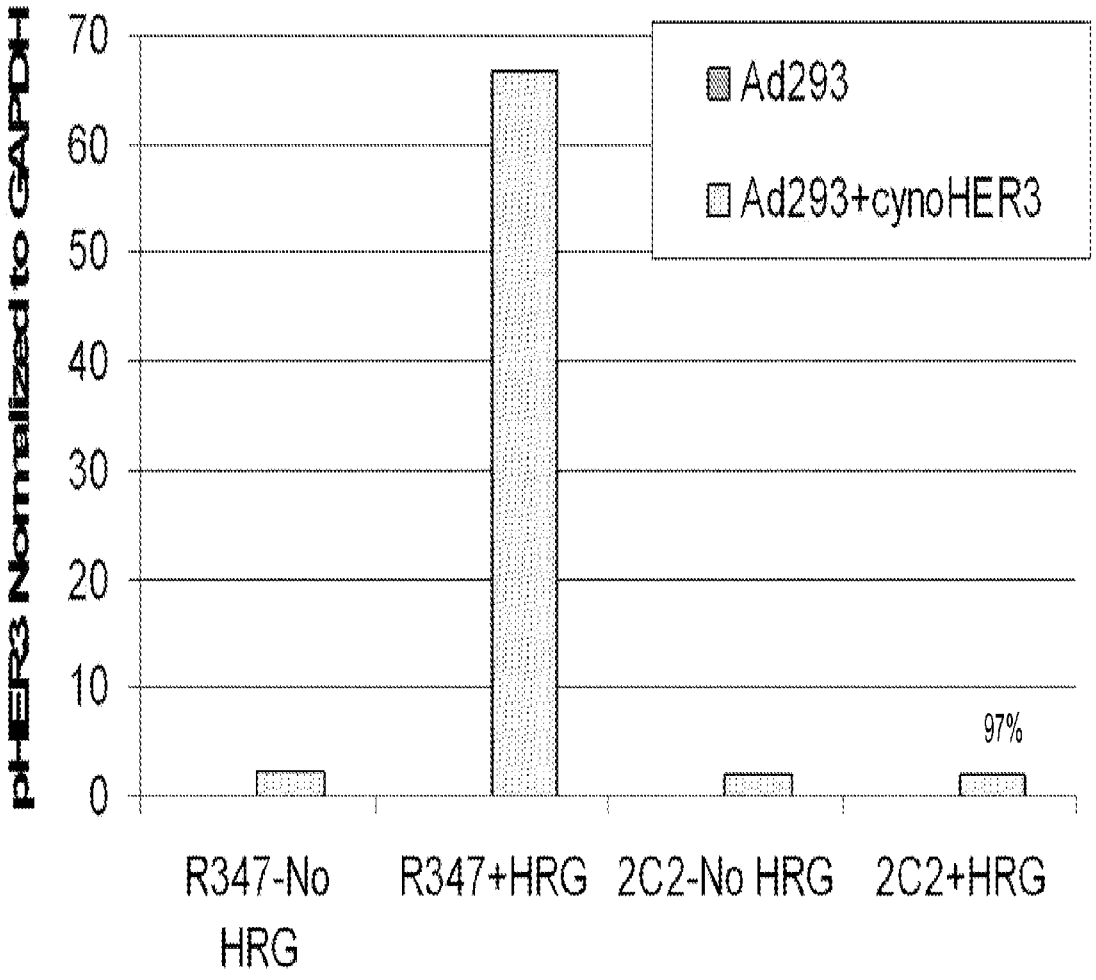

pHER3 Normalized to GAPDH
70
60
50
40
30
20
10
0
Ad293
Ad293+cynoHER3
97%
R347-No HRG
R347+HRG
2C2-No HRG
2C2+HRG

Fig. 18B

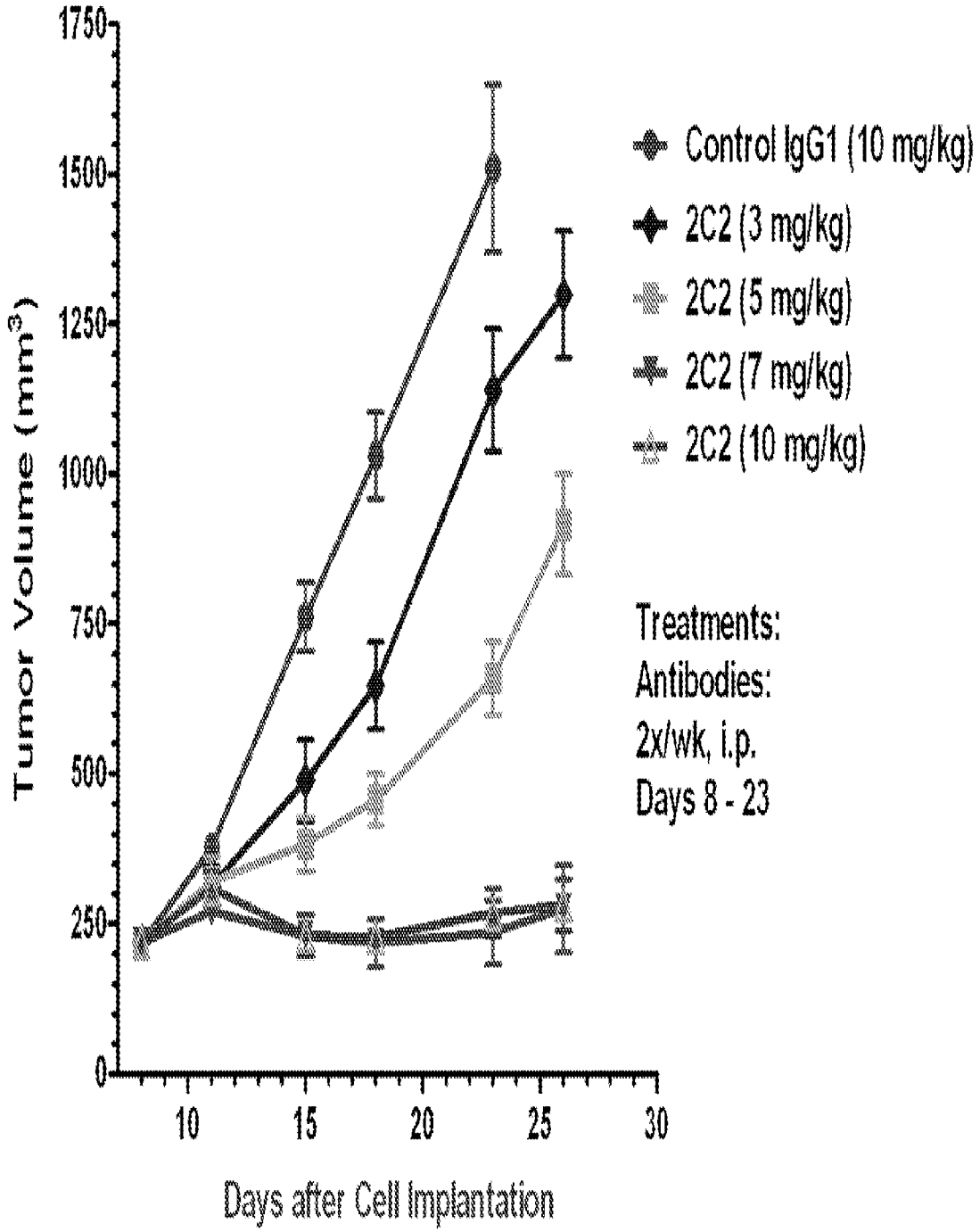

Tumor Volume (mm3)
1750
1500
1250
1000
750
500
250
0
10
15
20
25
30
Days after Cell Implantation
Control IgG1 (10 mg/kg)
2C2 (3 mg/kg)
2C2 (5 mg/kg)
2C2 (7 mg/kg)
2C2 (10 mg/kg)
Treatments:
Antibodies:
2x/wk, i.p.
Days 8 - 23

Fig. 19A

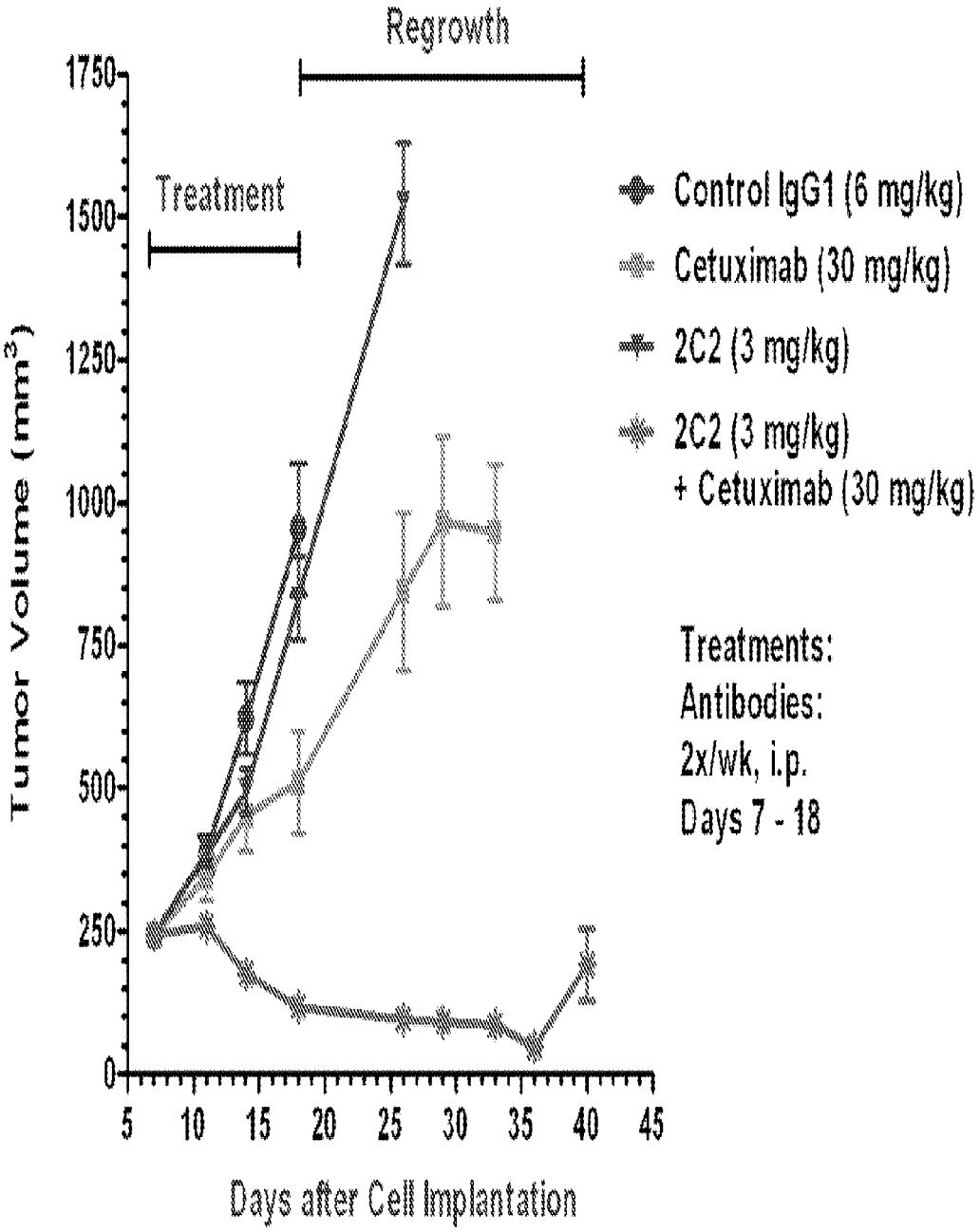

Regrowth
Treatment
Tumor Volume (mm³)
1750
1500
1250
1000
750
500
250
0
5
10
15
20
25
30
35
40
45
Days after Cell Implantation
Control IgG1 (6 mg/kg)
Cetuximab (30 mg/kg)
2C2 (3 mg/kg)
2C2 (3 mg/kg)
+ Cetuximab (30 mg/kg)
Treatments:
Antibodies:
2x/wk, i.p.
Days 7 - 18

Fig. 19B

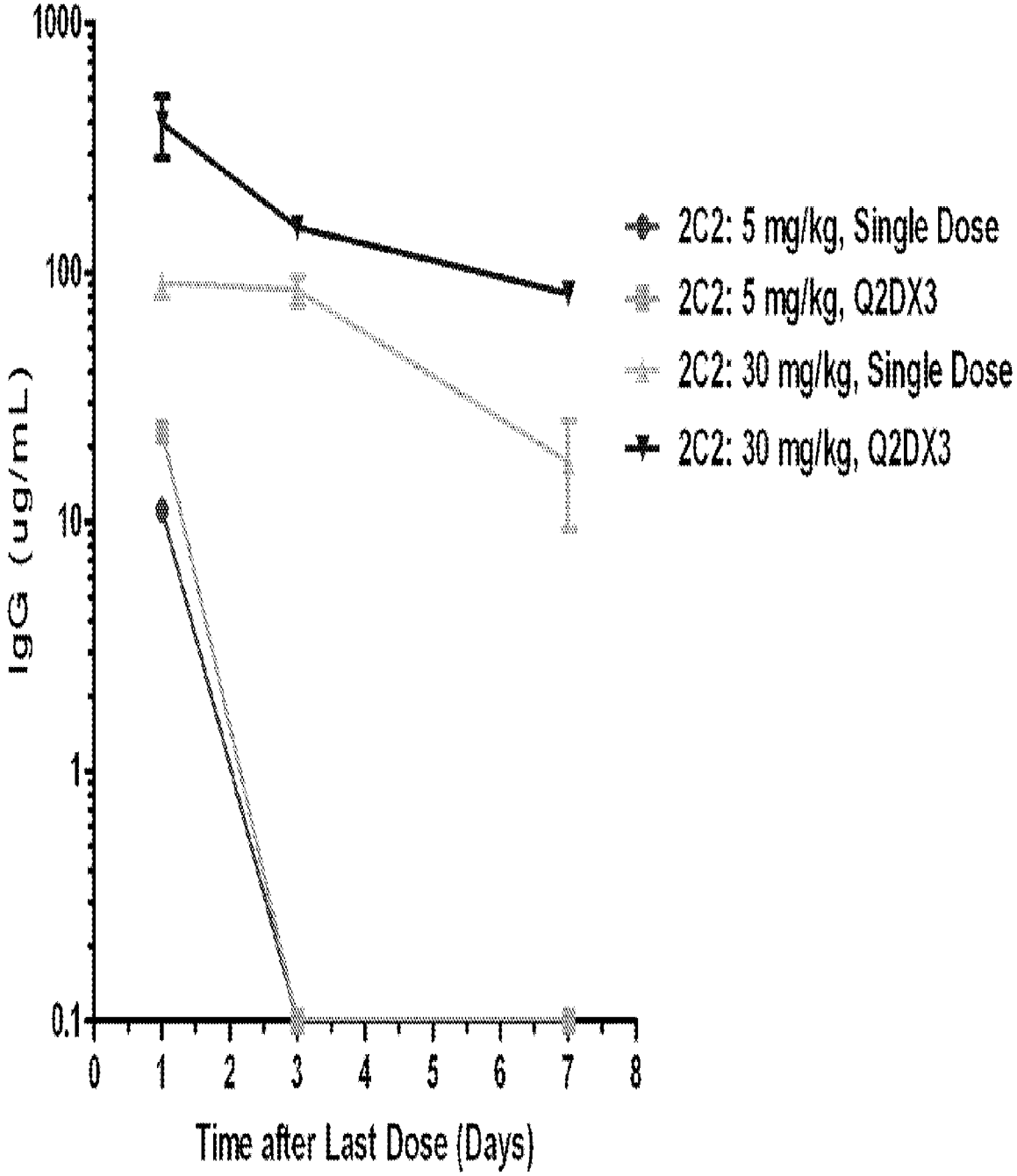

1000
100
10
1
0.1
IgG (ug/mL)
0
1
2
3
4
5
6
7
8
Time after Last Dose (Days)
2C2: 5 mg/kg, Single Dose
2C2: 5 mg/kg, Q2DX3
2C2: 30 mg/kg, Single Dose
2C2: 30 mg/kg, Q2DX3

Fig. 20

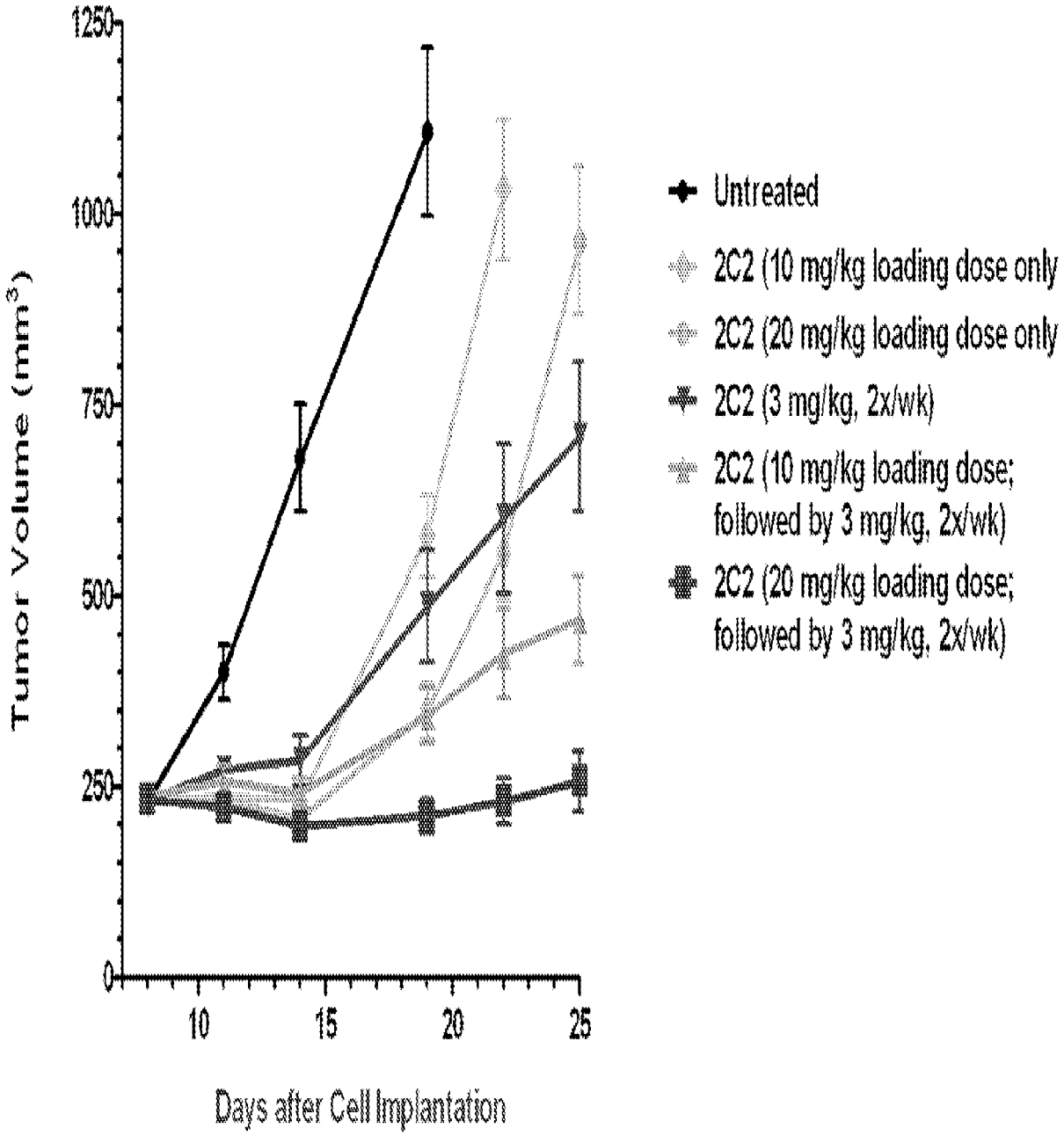

1250
1000
750
500
250
0
Tumor Volume (mm3)
10
15
20
25
Days after Cell Implantation
Untreated
2C2 (10 mg/kg loading dose only
2C2 (20 mg/kg loading dose only
2C2 (3 mg/kg, 2x/wk)
2C2 (10 mg/kg loading dose; followed by 3 mg/kg, 2x/wk)
2C2 (20 mg/kg loading dose; followed by 3 mg/kg, 2x/wk)

Fig. 21

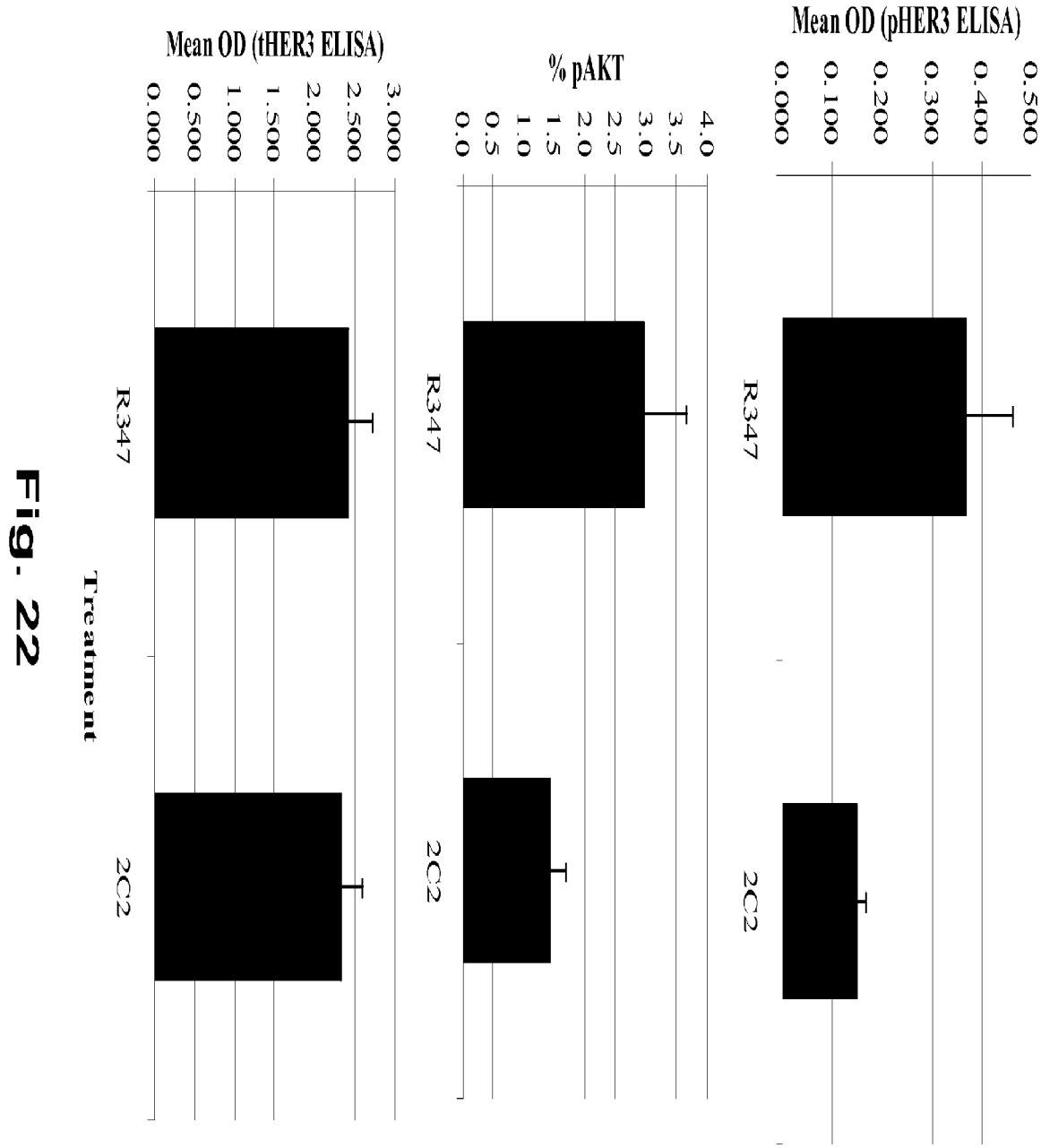

Mean OD (tHER3 ELISA)
0.000
0.500
1.000
1.500
2.000
2.500
3.000
% pAKT
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
Mean OD (pHER3 ELISA)
0.000
0.100
0.200
0.300
0.400
0.500
R347
2C2
Treatment

Fig. 22

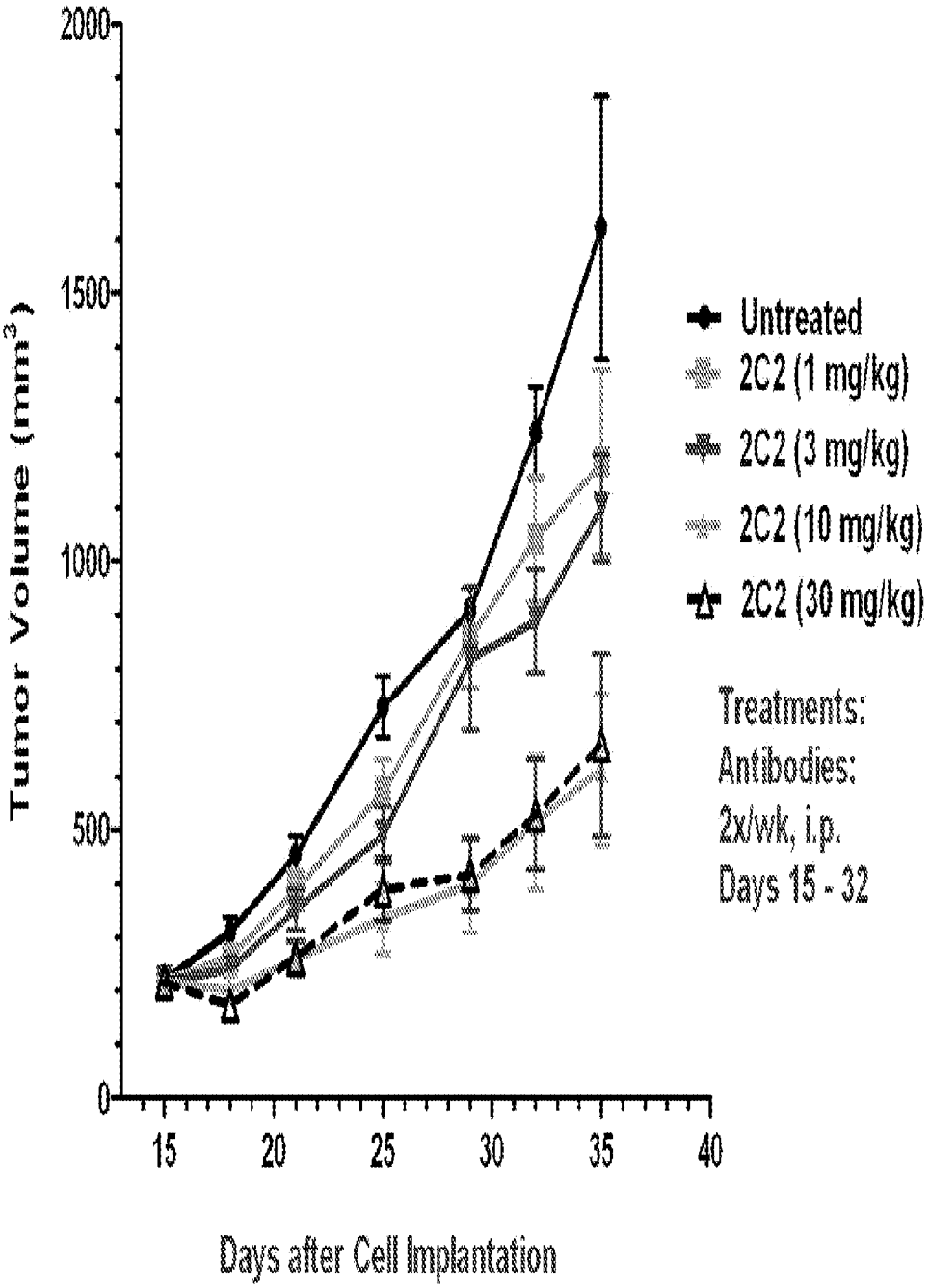

2000
1500
1000
500
0
Tumor Volume (mm3)
15
20
25
30
35
40
Days after Cell Implantation
Untreated
2C2 (1 mg/kg)
2C2 (3 mg/kg)
2C2 (10 mg/kg)
2C2 (30 mg/kg)
Treatments:
Antibodies:
2x/wk, i.p.
Days 15 - 32

Fig. 23A

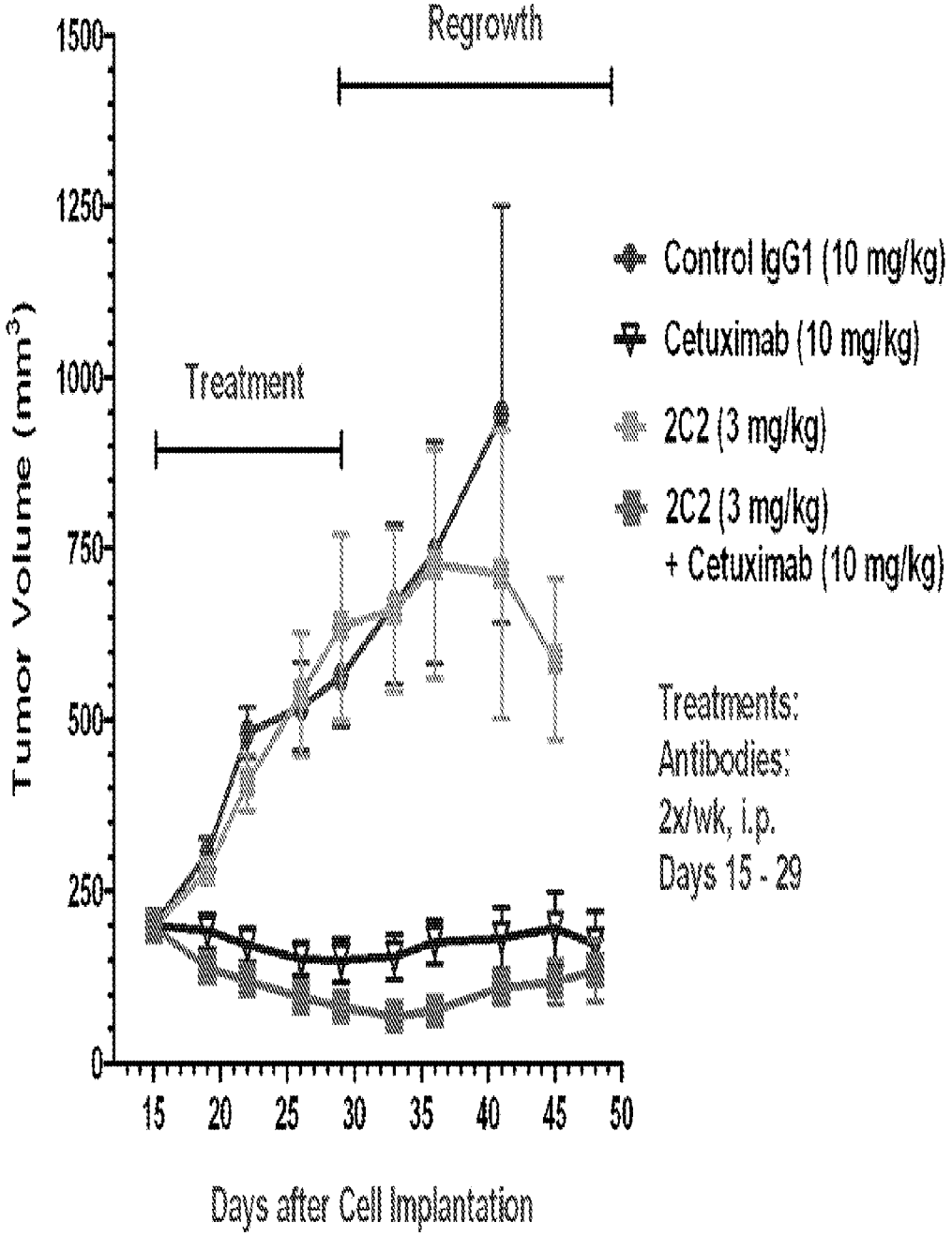

Regrowth
Treatment
Tumor Volume (mm3)
1500
1250
1000
750
500
250
0
15
20
25
30
35
40
45
50
Days after Cell Implantation
Control IgG1 (10 mg/kg)
Cetuximab (10 mg/kg)
2C2 (3 mg/kg)
2C2 (3 mg/kg)
+ Cetuximab (10 mg/kg)
Treatments:
Antibodies:
2x/wk, i.p.
Days 15 - 29

Fig. 23B

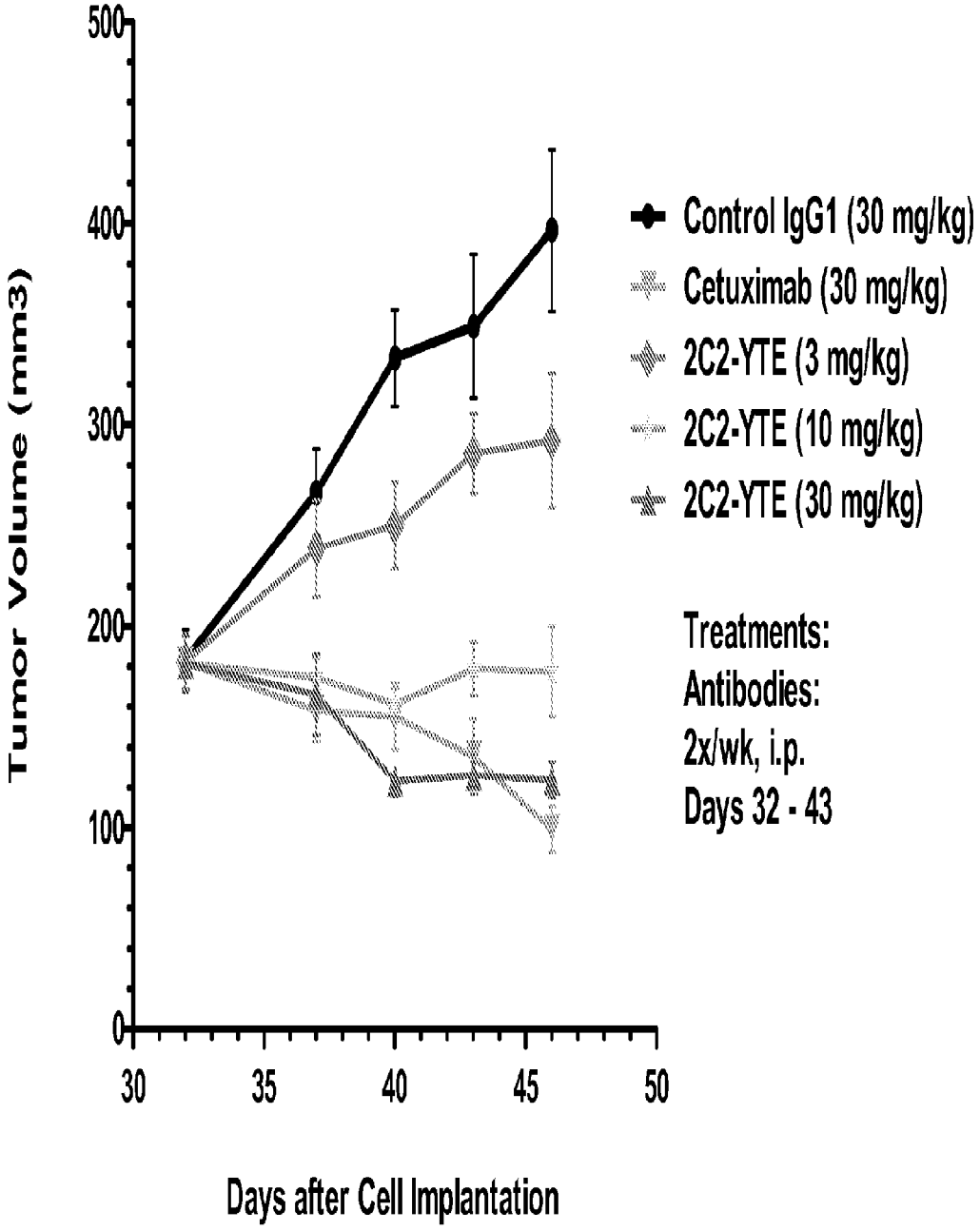

Tumor Volume (mm3)
500
400
300
200
100
0
30
35
40
45
50
Days after Cell Implantation
Control IgG1 (30 mg/kg)
Cetuximab (30 mg/kg)
2C2-YTE (3 mg/kg)
2C2-YTE (10 mg/kg)
2C2-YTE (30 mg/kg)
Treatments:
Antibodies:
2x/wk, i.p.
Days 32 - 43

Fig. 24

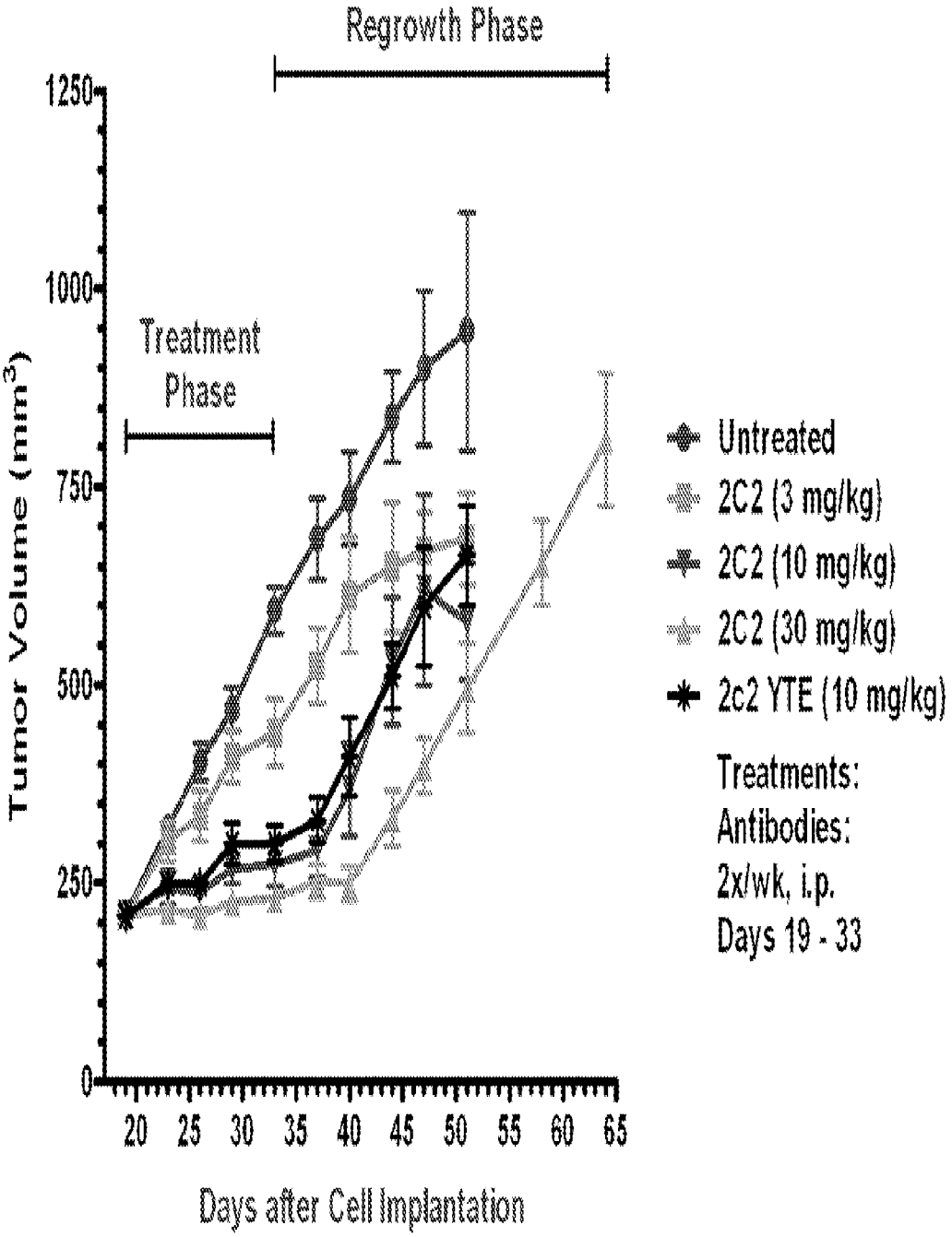

Regrowth Phase
Treatment Phase
Tumor Volume (mm3)
1250
1000
750
500
250
0
20 25 30 35 40 45 50 55 60 65
Days after Cell Implantation
Untreated
2C2 (3 mg/kg)
2C2 (10 mg/kg)
2C2 (30 mg/kg)
2c2 YTE (10 mg/kg)
Treatments:
Antibodies:
2x/wk, i.p.
Days 19 - 33

Fig. 25A

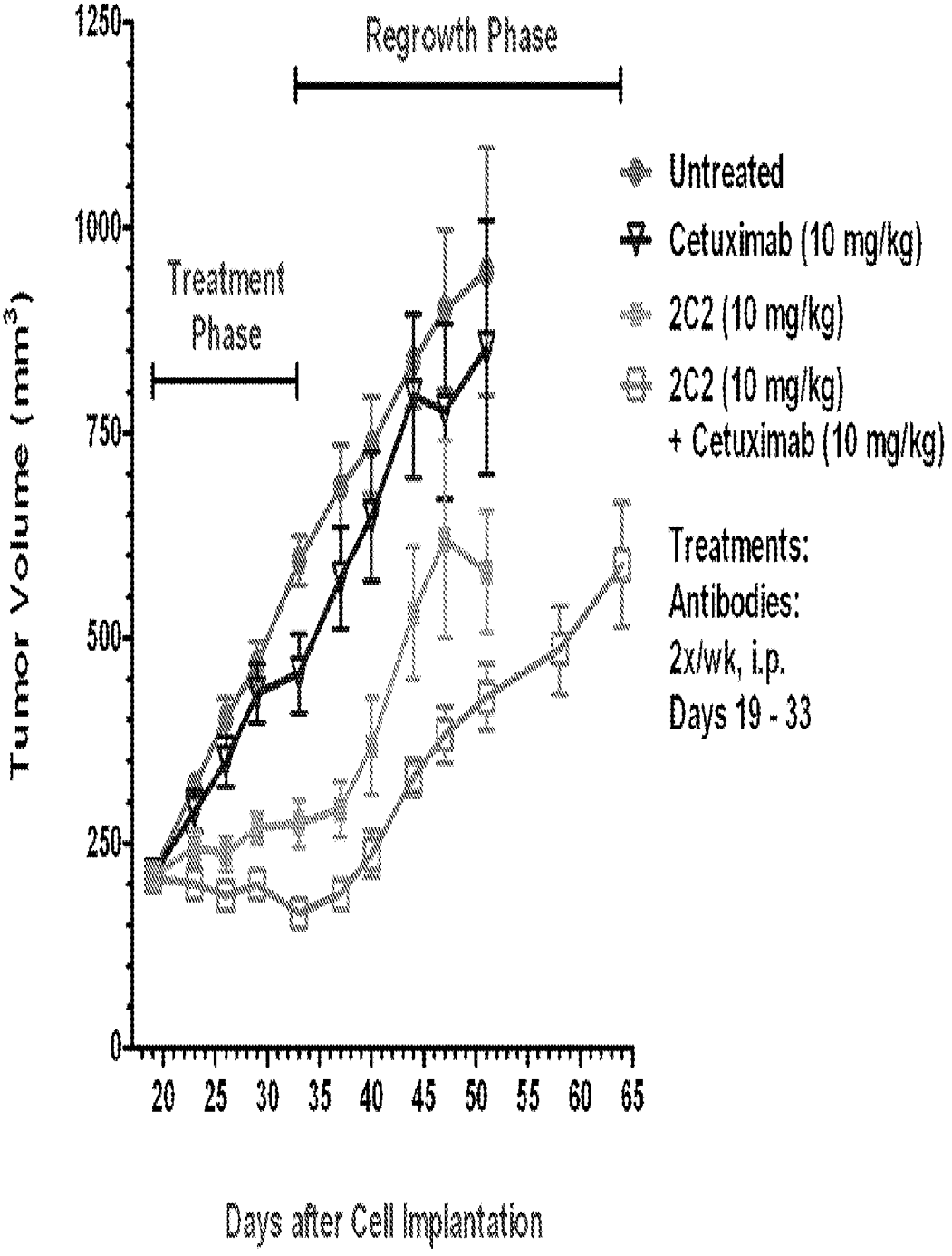

Regrowth Phase
Treatment Phase
Tumor Volume (mm3)
1250
1000
750
500
250
0
20 25 30 35 40 45 50 55 60 65
Days after Cell Implantation
Untreated
Cetuximab (10 mg/kg)
2C2 (10 mg/kg)
2C2 (10 mg/kg) + Cetuximab (10 mg/kg)
Treatments:
Antibodies:
2x/wk, i.p.
Days 19 - 33

Fig. 25B

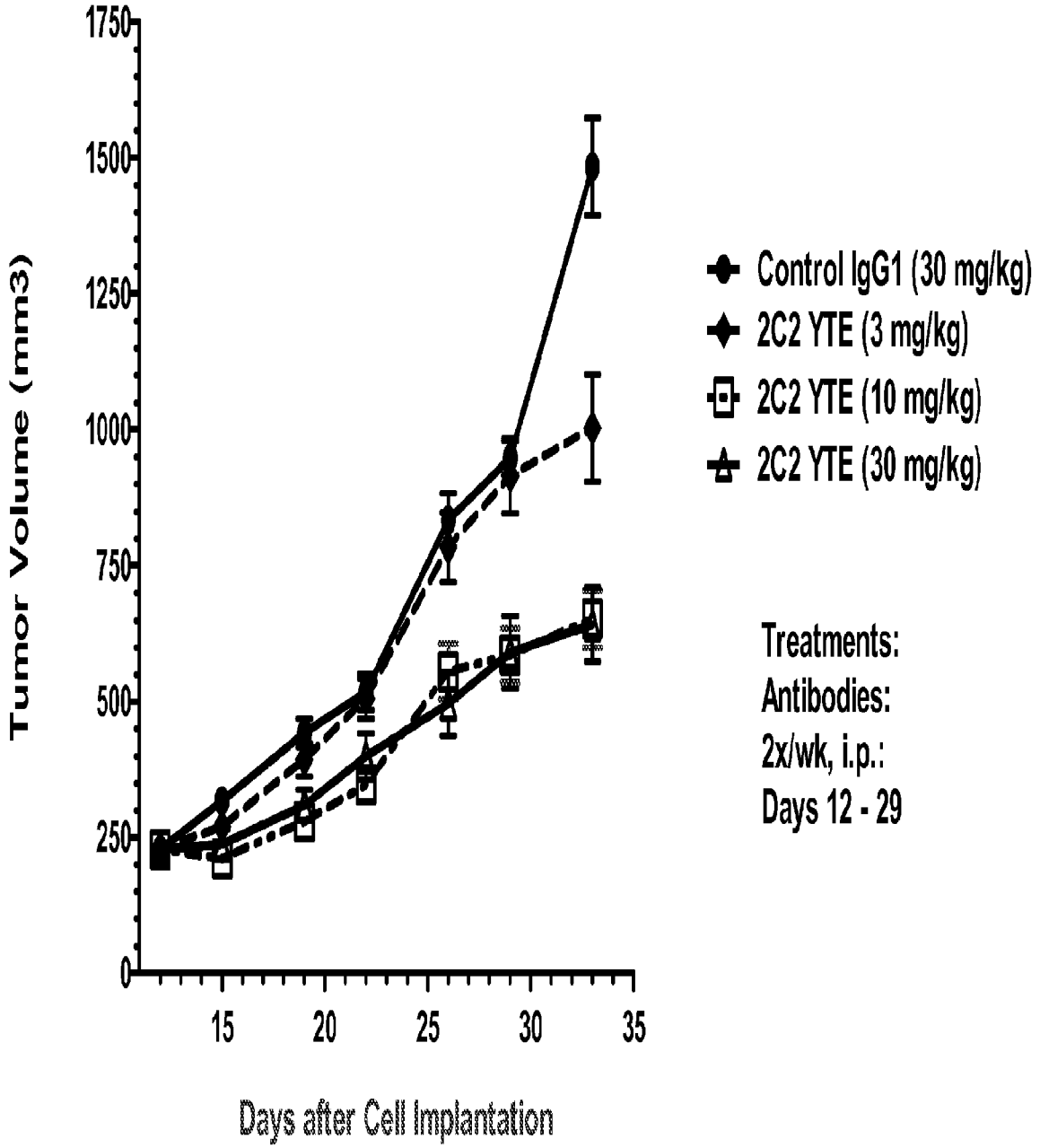

Tumor Volume (mm3)
1750
1500
1250
1000
750
500
250
0
15
20
25
30
35
Days after Cell Implantation
Control IgG1 (30 mg/kg)
2C2 YTE (3 mg/kg)
2C2 YTE (10 mg/kg)
2C2 YTE (30 mg/kg)
Treatments:
Antibodies:
2x/wk, i.p.:
Days 12 - 29

Fig. 26

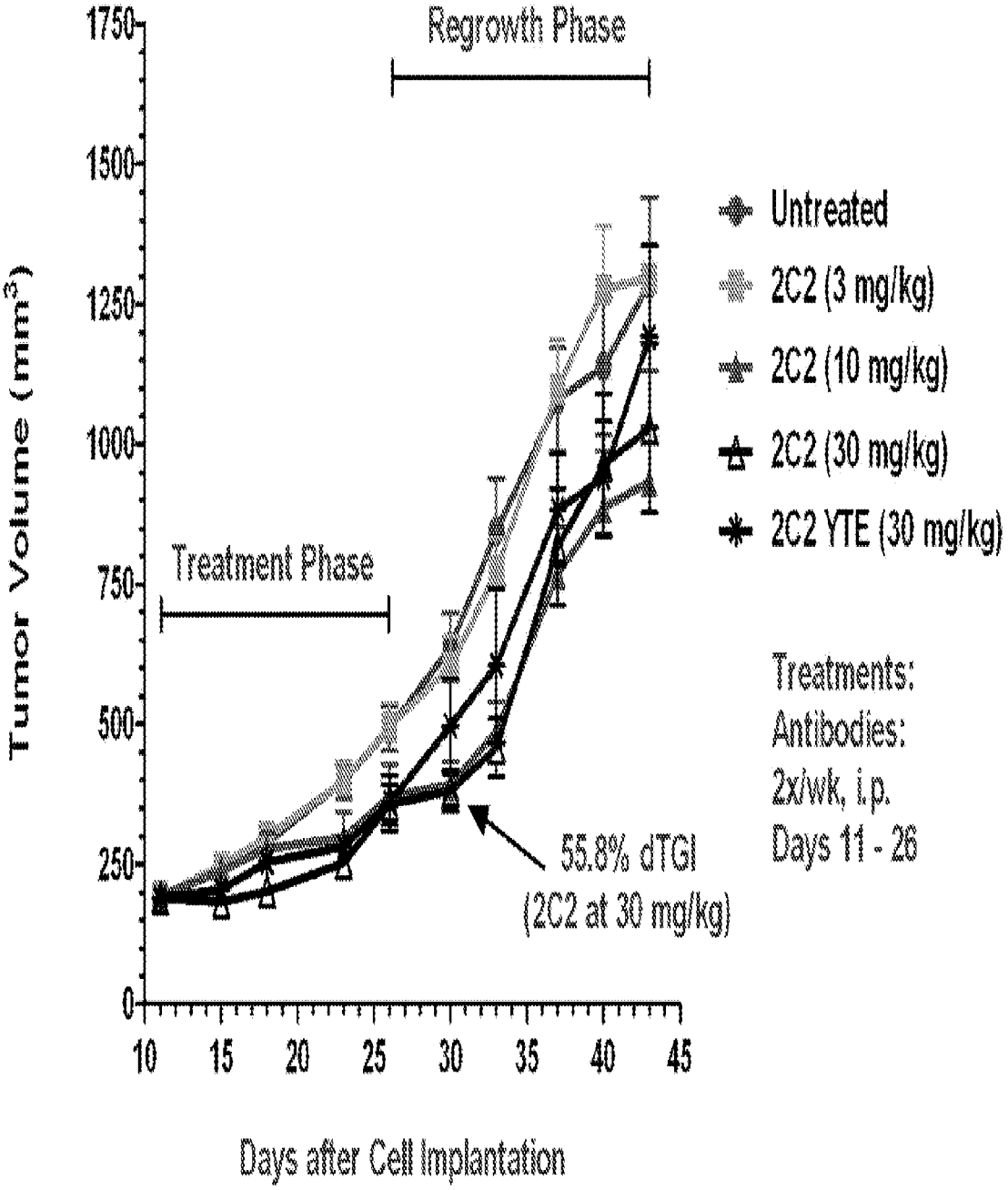

Regrowth Phase
Treatment Phase
Tumor Volume (mm3)
1750
1500
1250
1000
750
500
250
0
10
15
20
25
30
35
40
45
Days after Cell Implantation
Untreated
2C2 (3 mg/kg)
2C2 (10 mg/kg)
2C2 (30 mg/kg)
2C2 YTE (30 mg/kg)
Treatments:
Antibodies:
2x/wk, i.p.
Days 11 - 26
55.8% dTGI
(2C2 at 30 mg/kg)

Fig. 27

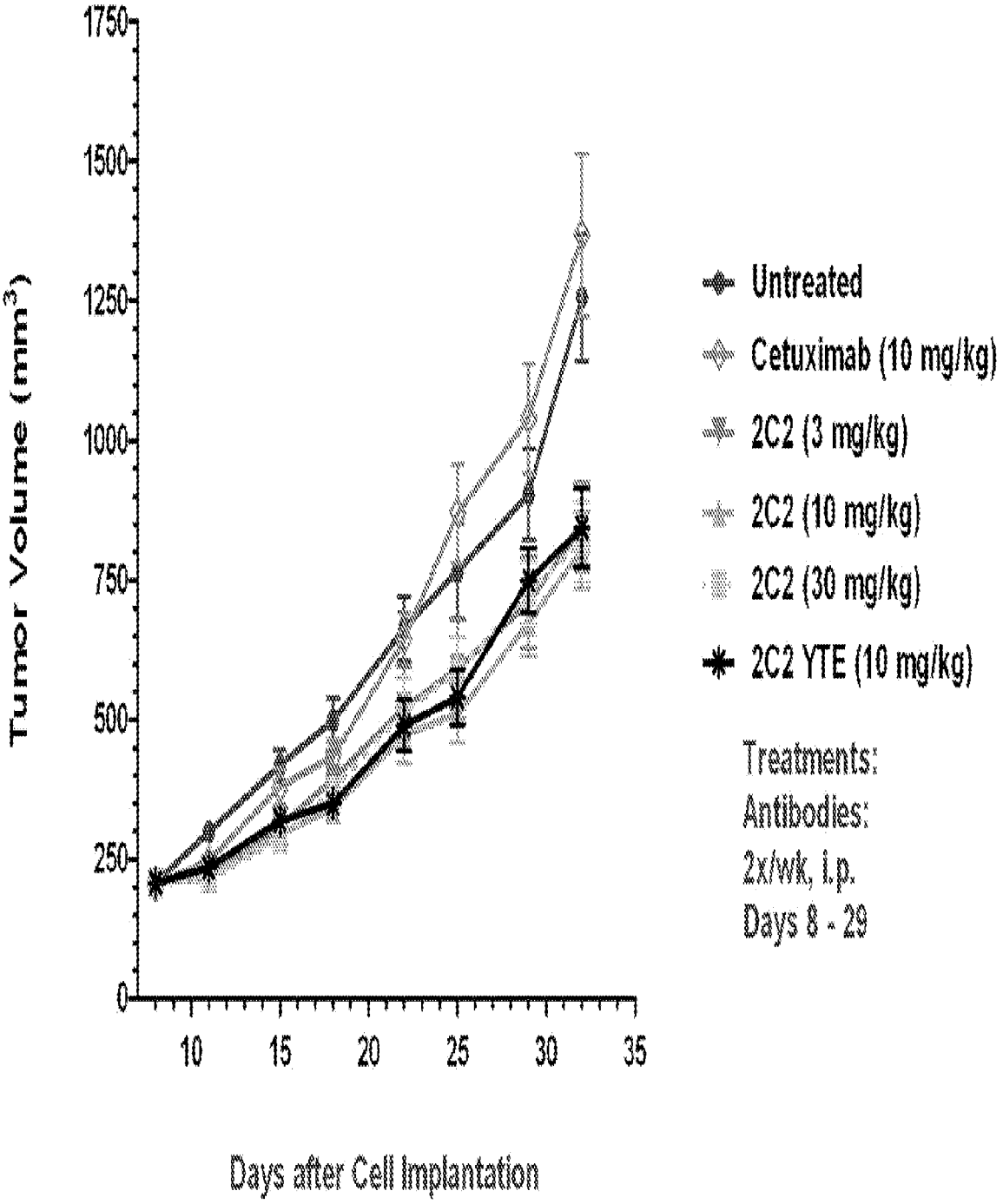

Tumor Volume (mm3)
1750
1500
1250
1000
750
500
250
0
10
15
20
25
30
35
Days after Cell Implantation
Untreated
Cetuximab (10 mg/kg)
2C2 (3 mg/kg)
2C2 (10 mg/kg)
2C2 (30 mg/kg)
2C2 YTE (10 mg/kg)
Treatments:
Antibodies:
2x/wk, i.p.
Days 8 - 29

Fig. 28

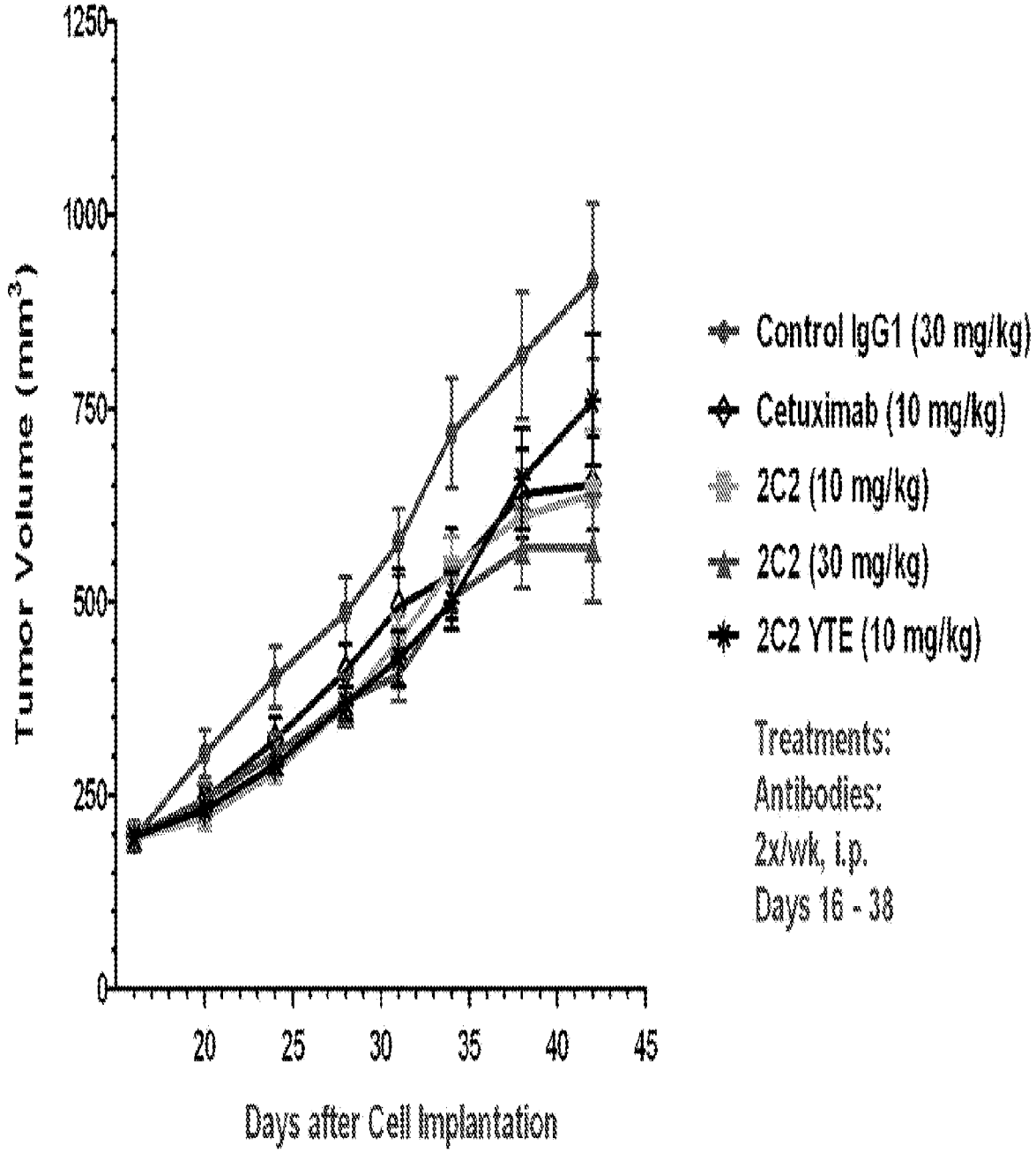

Tumor Volume (mm3)
1250
1000
750
500
250
0
20
25
30
35
40
45
Days after Cell Implantation
Control IgG1 (30 mg/kg)
Cetuximab (10 mg/kg)
2C2 (10 mg/kg)
2C2 (30 mg/kg)
2C2 YTE (10 mg/kg)
Treatments:
Antibodies:
2x/wk, i.p.
Days 16 - 38

Fig. 29

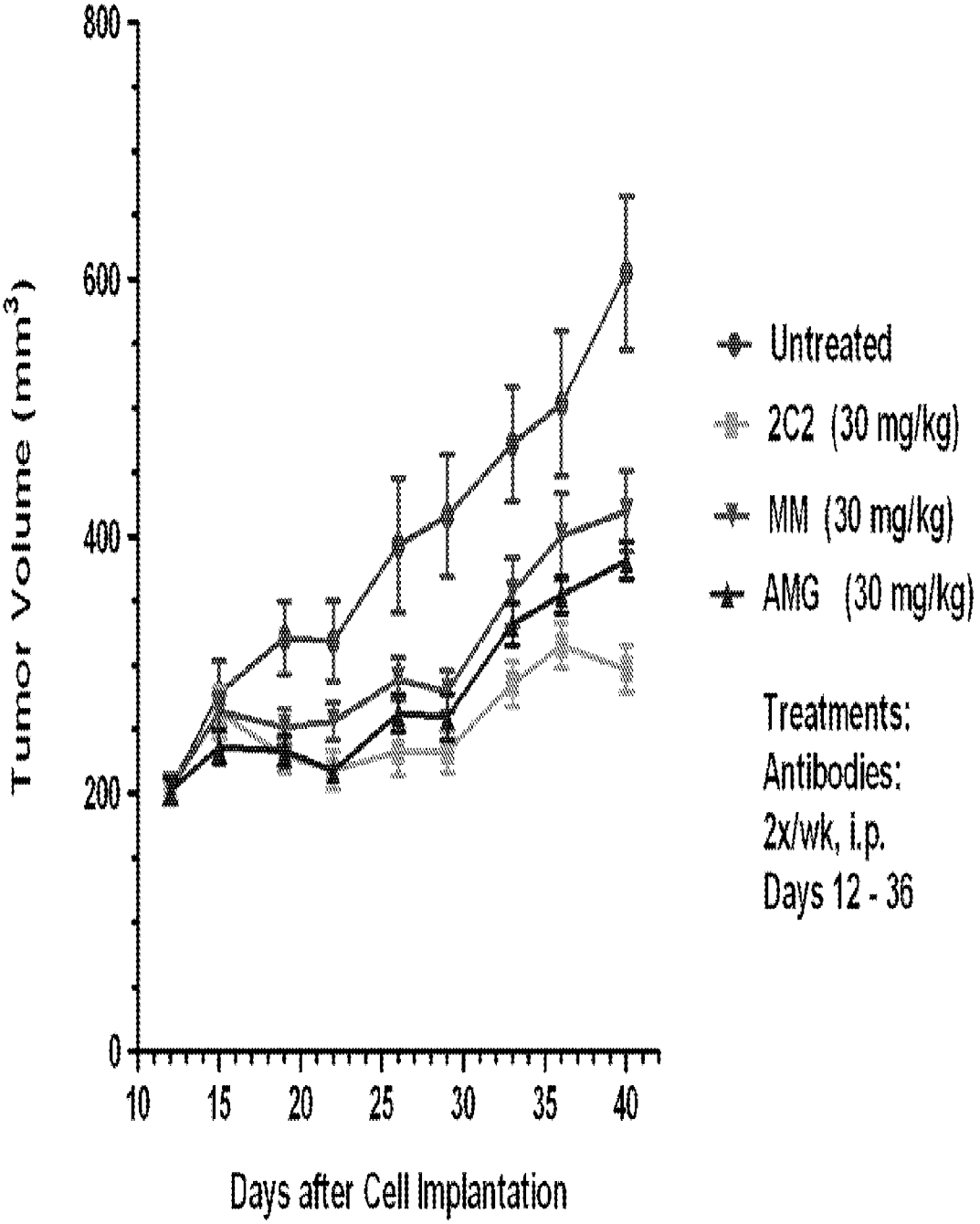

Tumor Volume (mm3)
800
600
400
200
0
10
15
20
25
30
35
40
Days after Cell Implantation
Untreated
2C2 (30 mg/kg)
MM (30 mg/kg)
AMG (30 mg/kg)
Treatments:
Antibodies:
2x/wk, i.p.
Days 12 - 36

Fig. 30

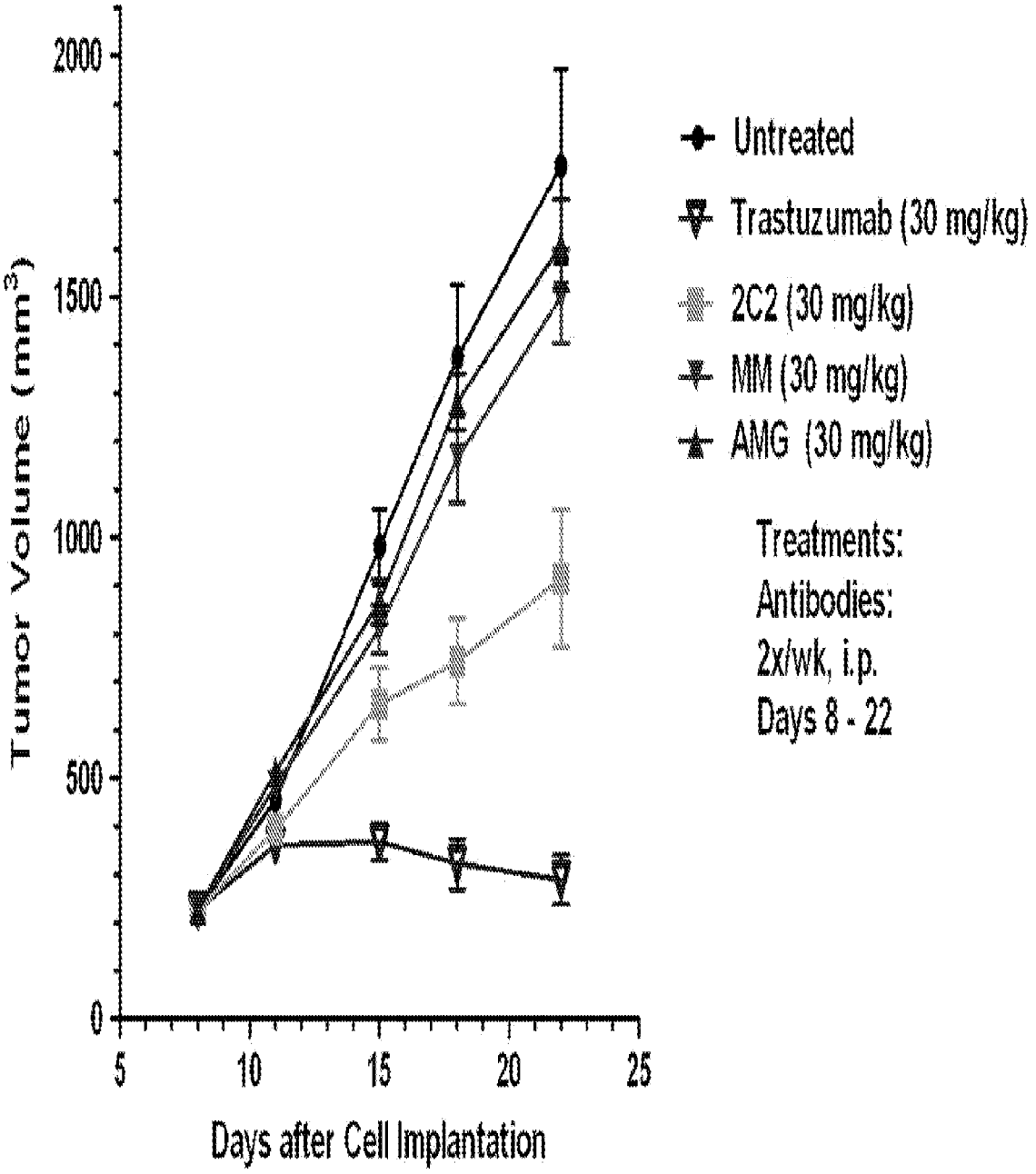

Tumor Volume (mm3)
2000
1500
1000
500
0
5
10
15
20
25
Days after Cell Implantation
Untreated
Trastuzumab (30 mg/kg)
2C2 (30 mg/kg)
MM (30 mg/kg)
AMG (30 mg/kg)
Treatments:
Antibodies:
2x/wk, i.p.
Days 8 - 22

Fig. 31A

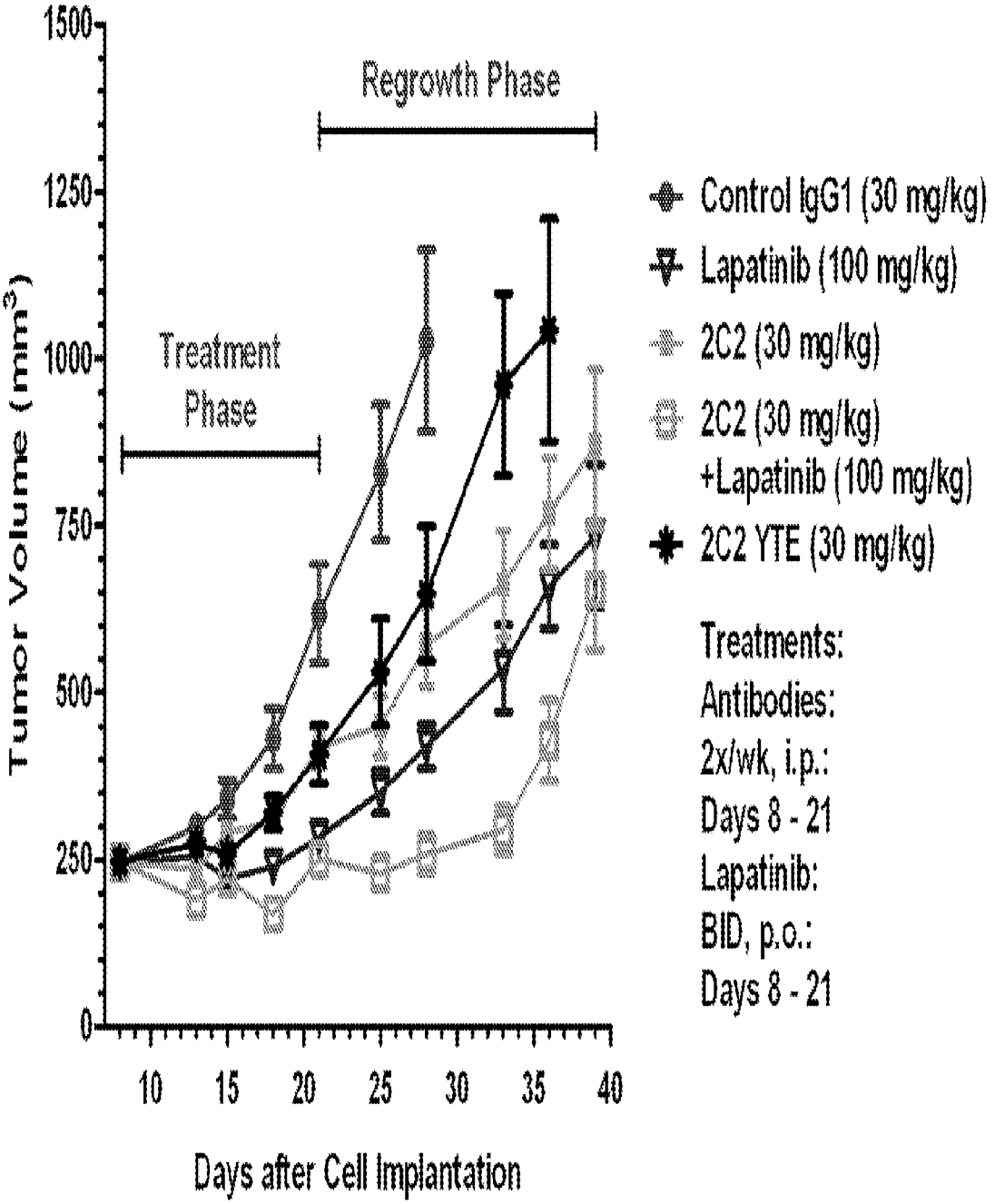

Regrowth Phase
Treatment Phase
Tumor Volume (mm3)
1500
1250
1000
750
500
250
0
10
15
20
25
30
35
40
Days after Cell Implantation
Control IgG1 (30 mg/kg)
Lapatinib (100 mg/kg)
2C2 (30 mg/kg)
2C2 (30 mg/kg) +Lapatinib (100 mg/kg)
2C2 YTE (30 mg/kg)
Treatments:
Antibodies:
2x/wk, i.p.:
Days 8 - 21
Lapatinib:
BID, p.o.:
Days 8 - 21

Fig. 31B

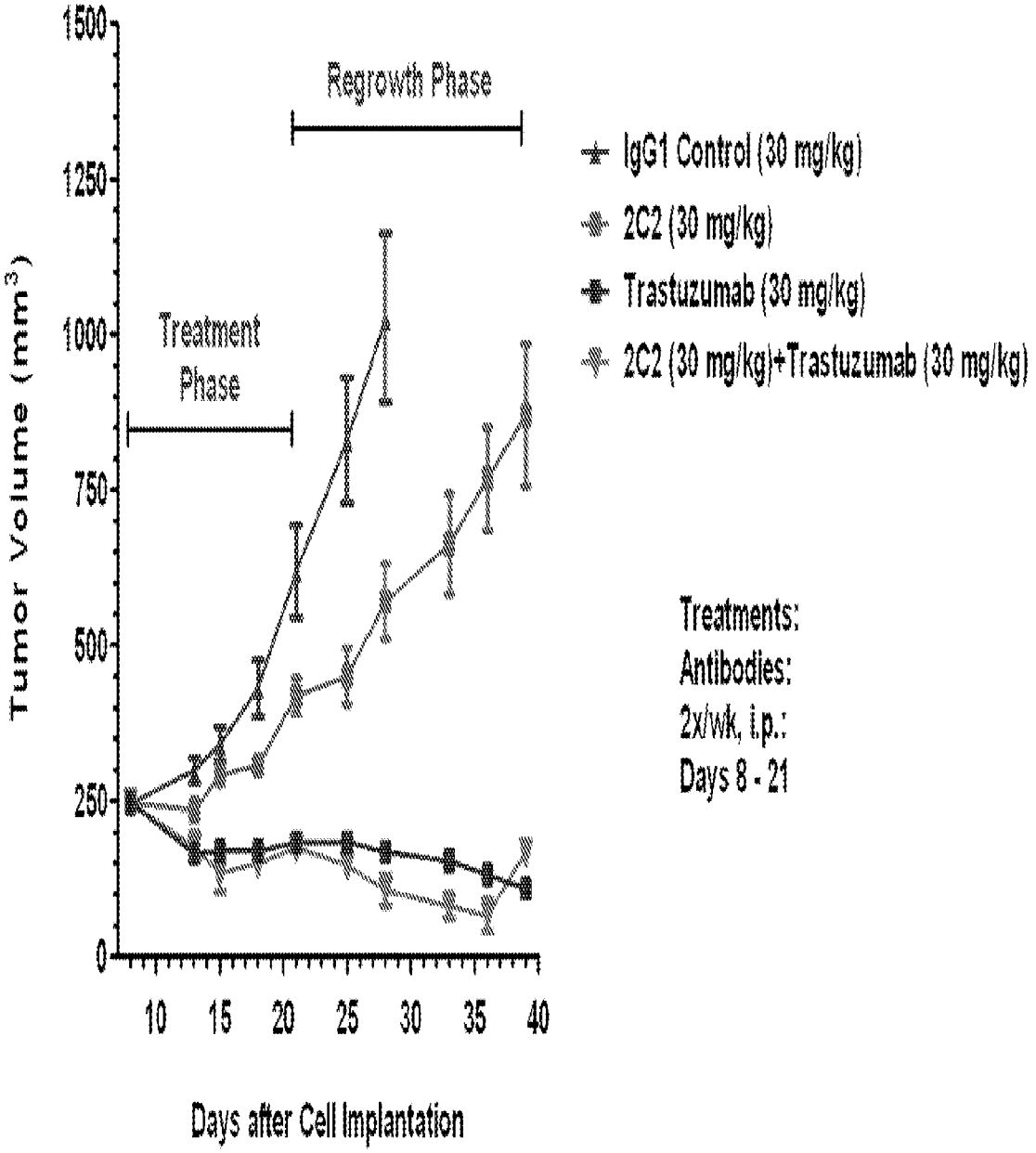

Regrowth Phase
Treatment Phase
IgG1 Control (30 mg/kg)
2C2 (30 mg/kg)
Trastuzumab (30 mg/kg)
2C2 (30 mg/kg)+Trastuzumab (30 mg/kg)
Treatments:
Antibodies:
2x/wk, i.p.:
Days 8 - 21
Tumor Volume (mm3)
Days after Cell Implantation
0
250
500
750
1000
1250
1500
10
15
20
25
30
35
40

Fig. 31C

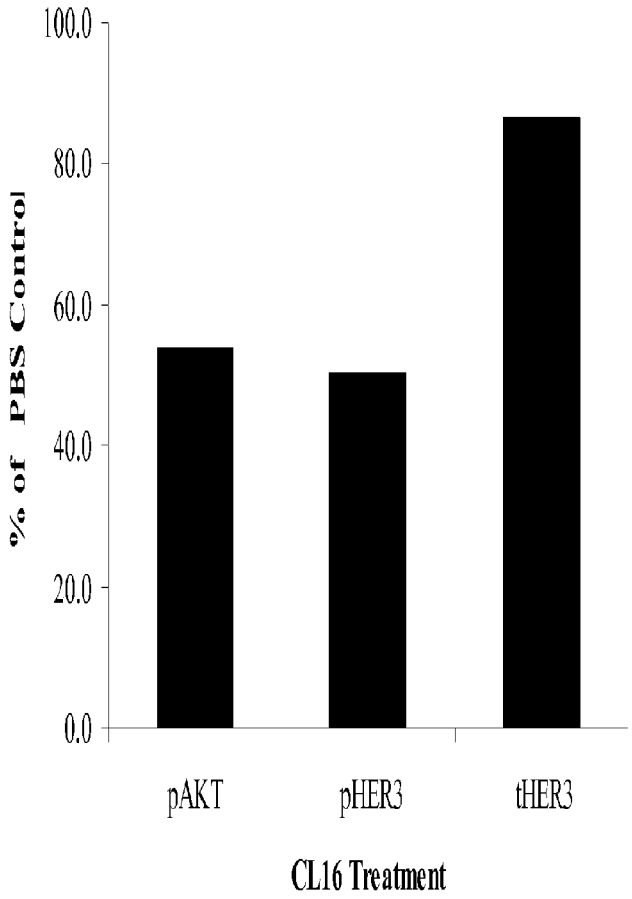

100.0
80.0
60.0
40.0
20.0
0.0
% of PBS Control
pAKT
pHER3
tHER3
CL16 Treatment

Fig. 32

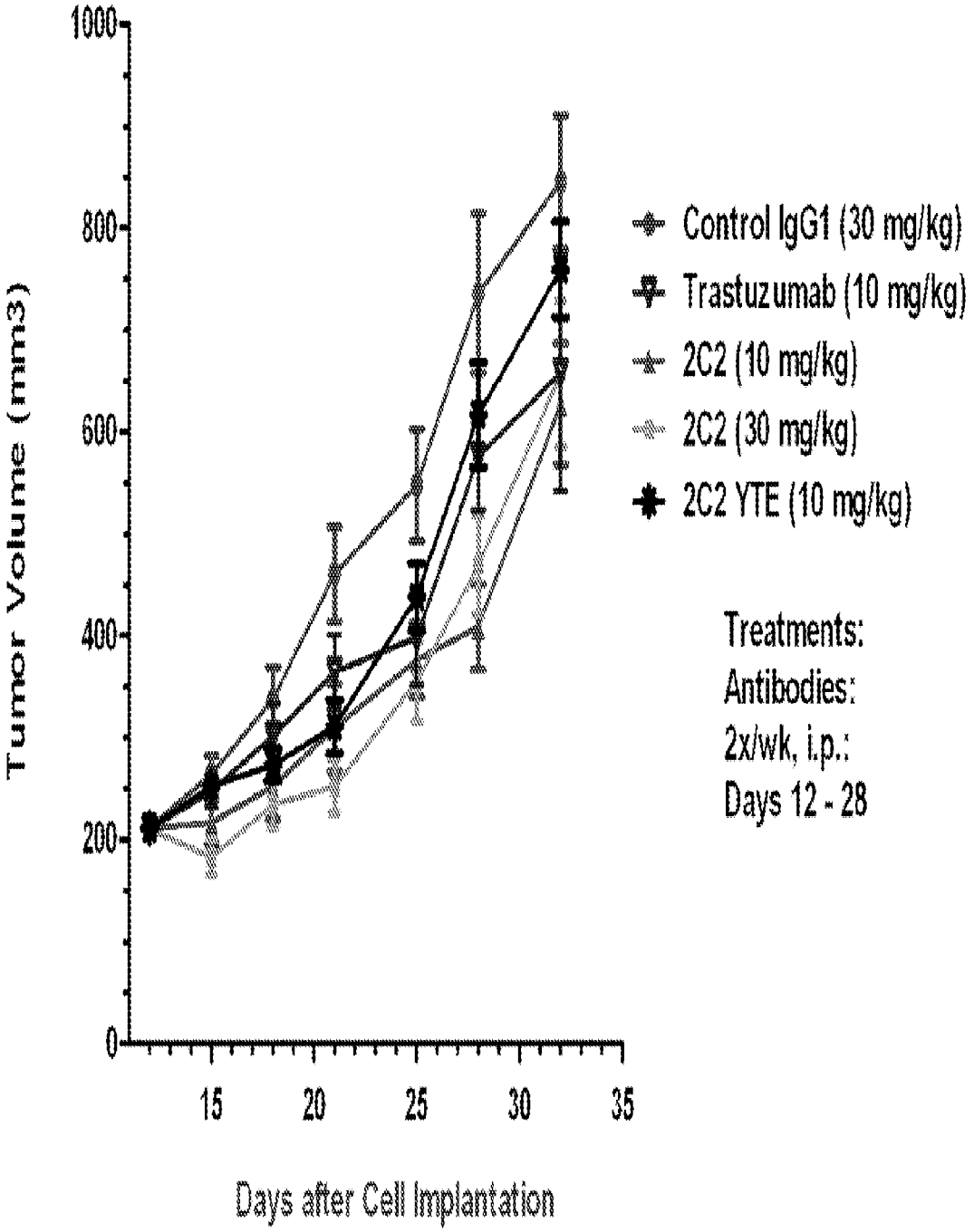

Tumor Volume (mm3)
1000
800
600
400
200
0
15
20
25
30
35
Days after Cell Implantation
Control IgG1 (30 mg/kg)
Trastuzumab (10 mg/kg)
2C2 (10 mg/kg)
2C2 (30 mg/kg)
2C2 YTE (10 mg/kg)
Treatments:
Antibodies:
2x/wk, i.p.:
Days 12 - 28

Fig. 33A

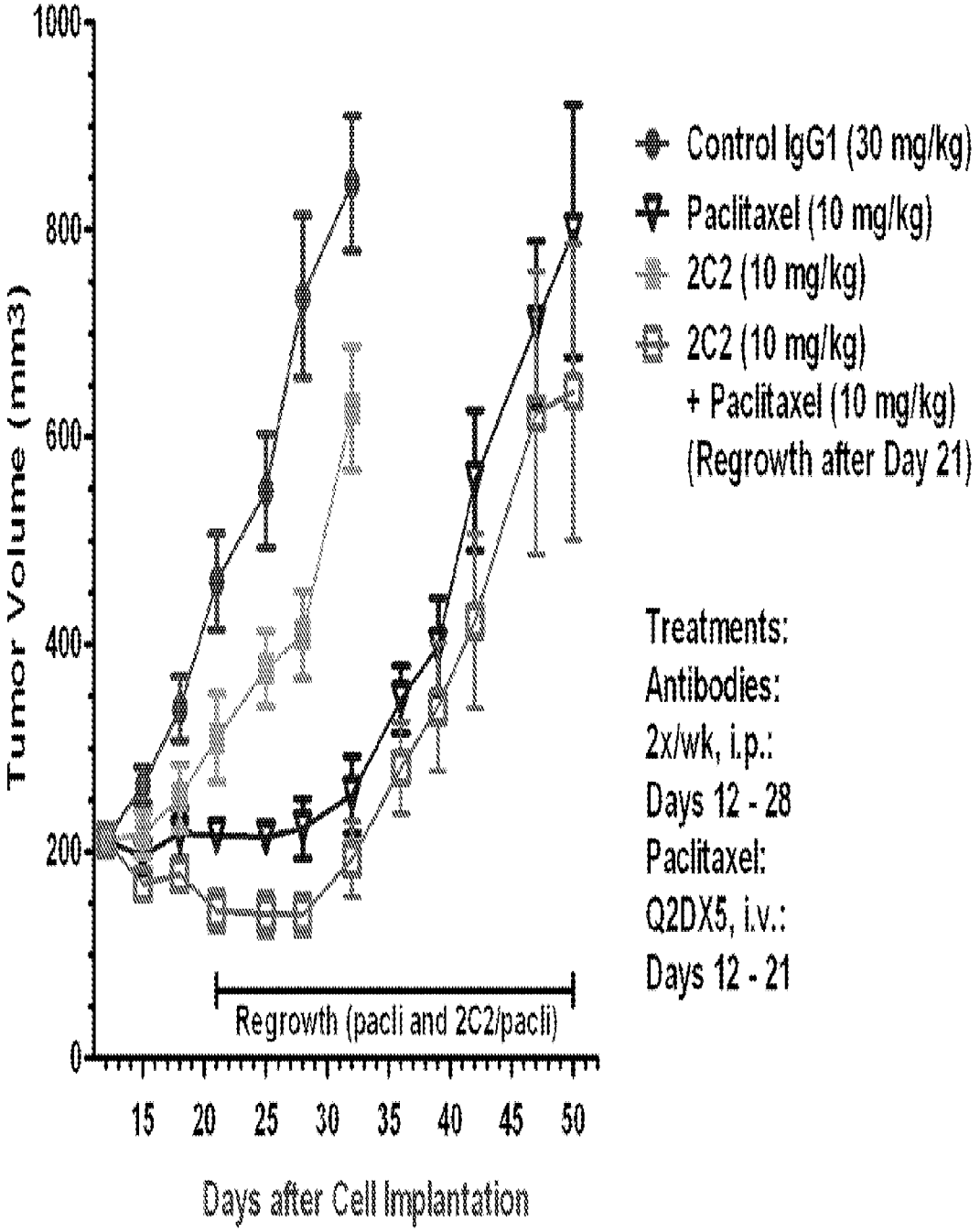

Tumor Volume (mm3)
1000
800
600
400
200
0
15
20
25
30
35
40
45
50
Days after Cell Implantation
Regrowth (pacli and 2C2/pacli)
Control IgG1 (30 mg/kg)
Paclitaxel (10 mg/kg)
2C2 (10 mg/kg)
2C2 (10 mg/kg)
+ Paclitaxel (10 mg/kg)
(Regrowth after Day 21)
Treatments:
Antibodies:
2x/wk, i.p.:
Days 12 - 28
Paclitaxel:
Q2DX5, i.v.:
Days 12 - 21

Fig. 33B

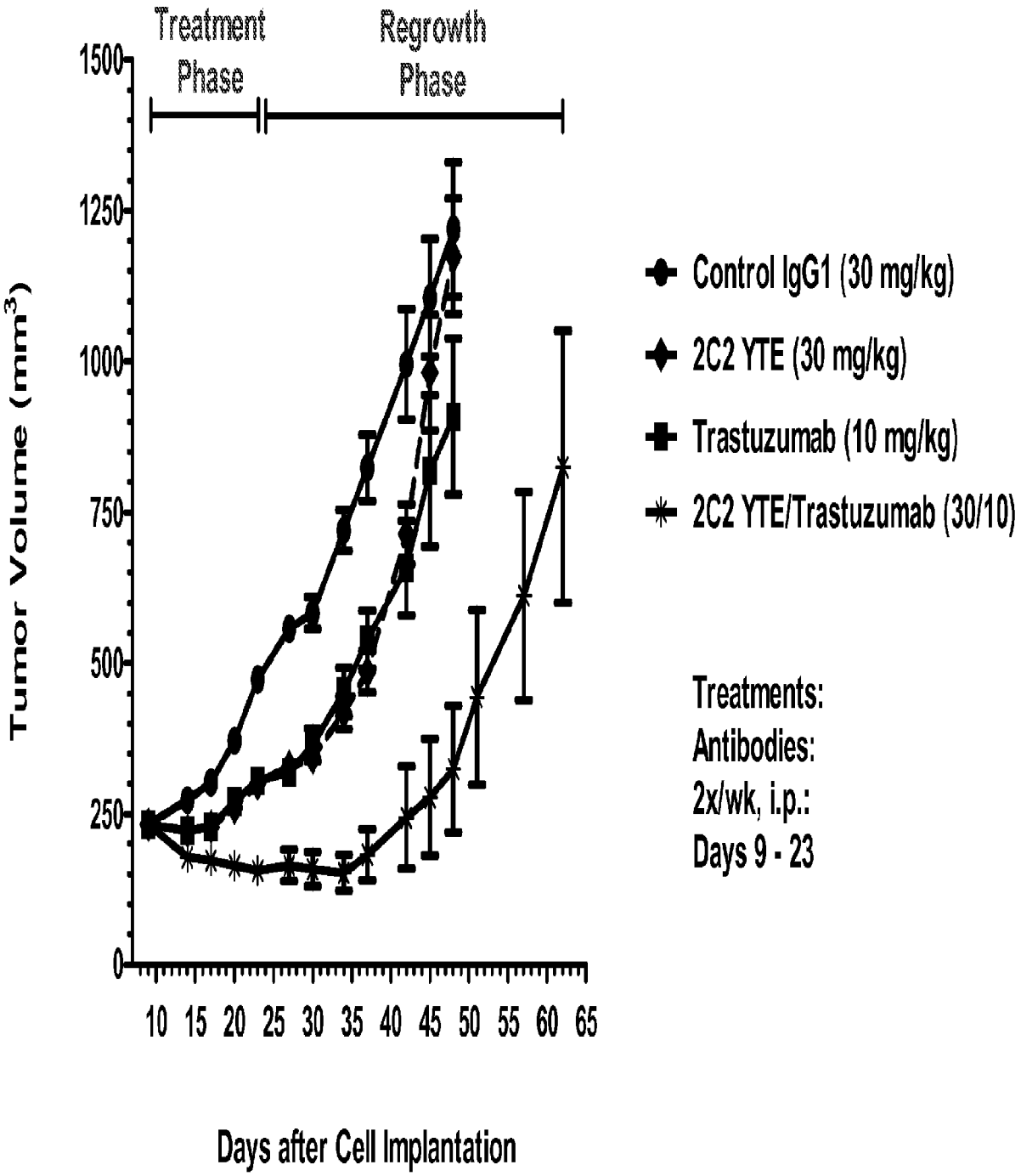

Treatment Phase
Regrowth Phase
Tumor Volume (mm3)
1500
1250
1000
750
500
250
0
10 15 20 25 30 35 40 45 50 55 60 65
Days after Cell Implantation
Control IgG1 (30 mg/kg)
2C2 YTE (30 mg/kg)
Trastuzumab (10 mg/kg)
2C2 YTE/Trastuzumab (30/10)
Treatments:
Antibodies:
2x/wk, i.p.:
Days 9 - 23

Fig. 34A

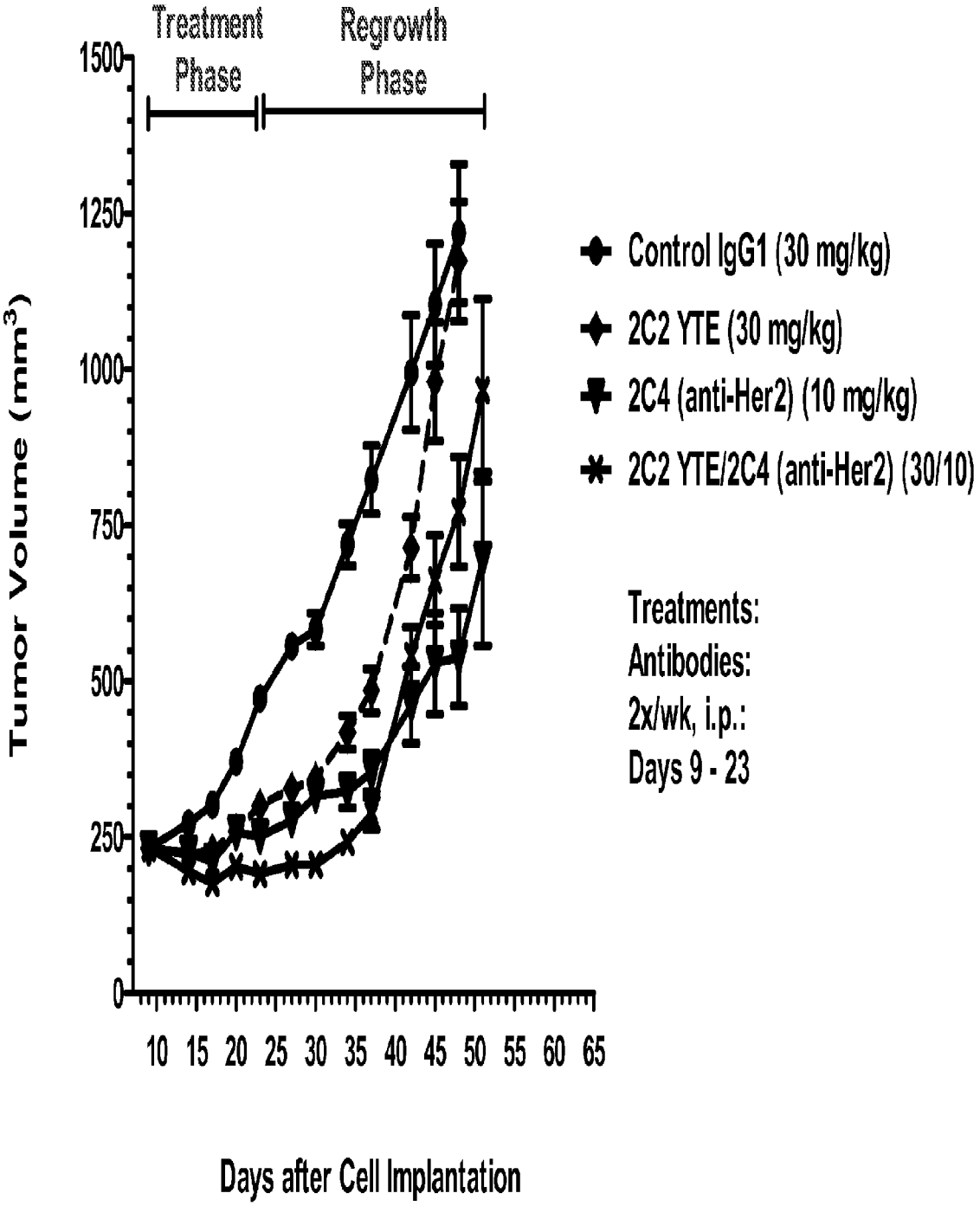

Treatment Phase
Regrowth Phase
Tumor Volume (mm3)
1500
1250
1000
750
500
250
0
10 15 20 25 30 35 40 45 50 55 60 65
Days after Cell Implantation
Control IgG1 (30 mg/kg)
2C2 YTE (30 mg/kg)
2C4 (anti-Her2) (10 mg/kg)
2C2 YTE/2C4 (anti-Her2) (30/10)
Treatments:
Antibodies:
2x/wk, i.p.:
Days 9 - 23

Fig. 34B

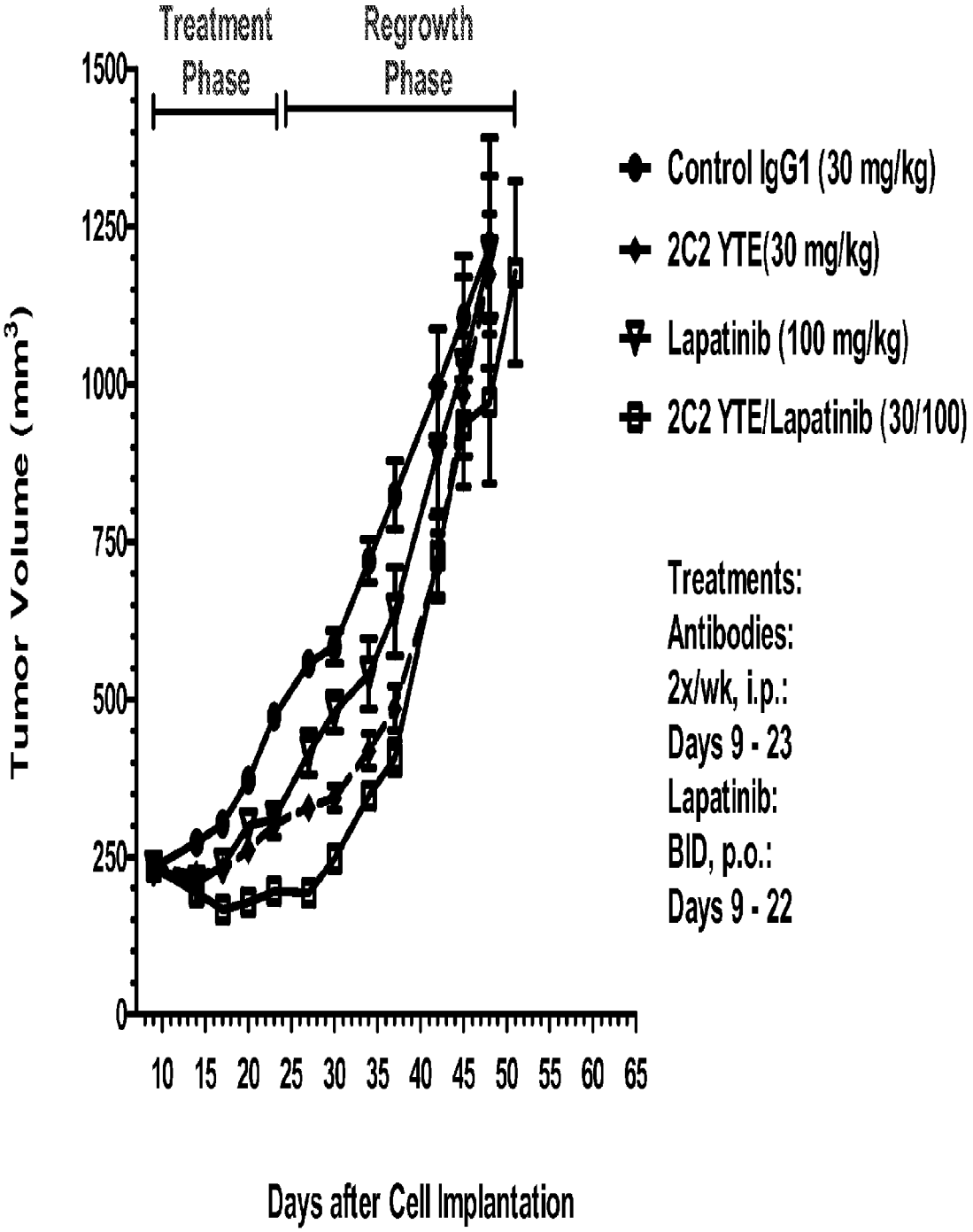

Treatment Phase
Regrowth Phase
Tumor Volume (mm3)
1500
1250
1000
750
500
250
0
10 15 20 25 30 35 40 45 50 55 60 65
Days after Cell Implantation
Control IgG1 (30 mg/kg)
2C2 YTE(30 mg/kg)
Lapatinib (100 mg/kg)
2C2 YTE/Lapatinib (30/100)
Treatments:
Antibodies:
2x/wk, i.p.:
Days 9 - 23
Lapatinib:
BID, p.o.:
Days 9 - 22

Fig. 34C

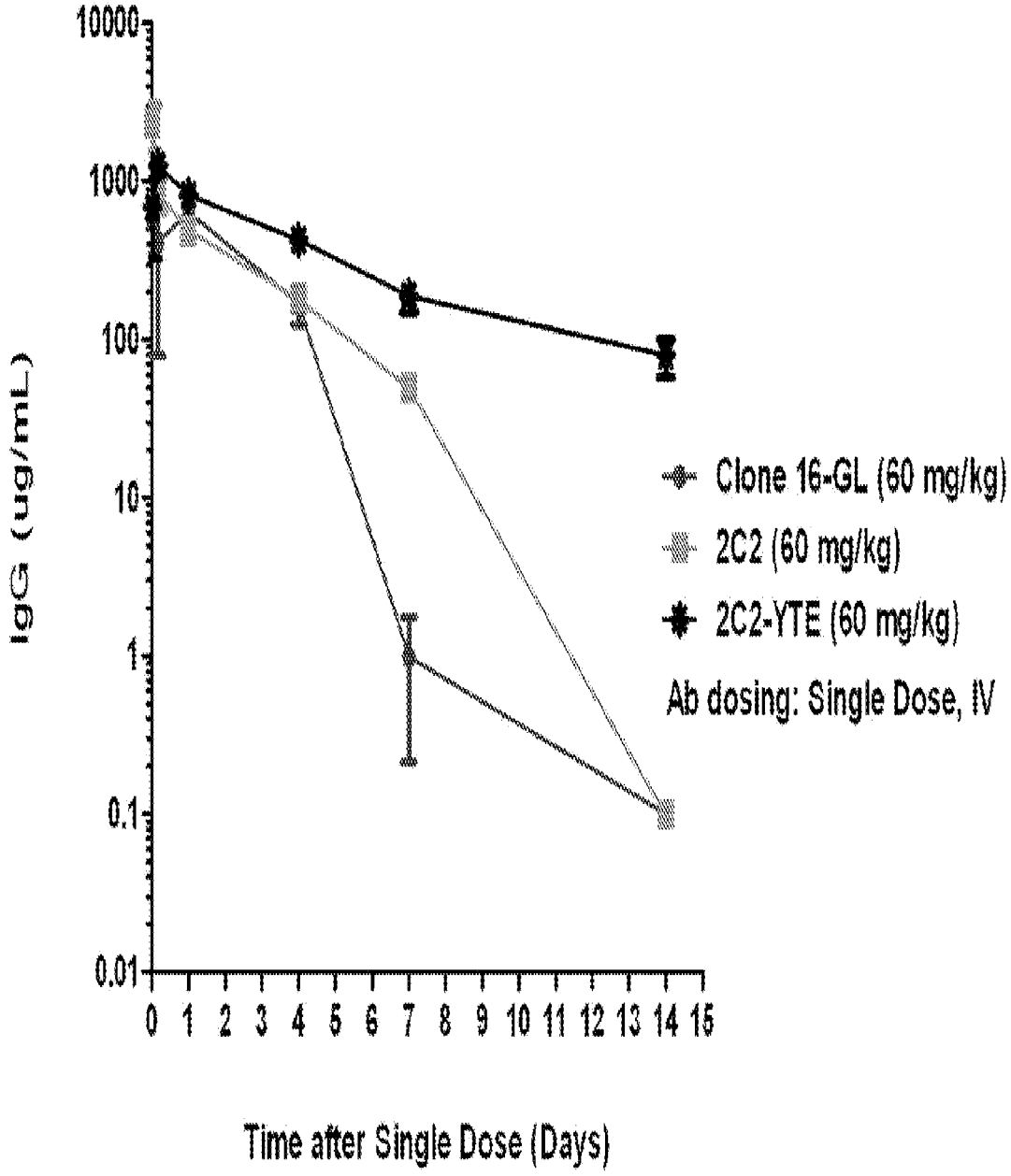

10000
1000
100
10
1
0.1
0.01
IgG (ug/mL)
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Time after Single Dose (Days)
Clone 16-GL (60 mg/kg)
2C2 (60 mg/kg)
2C2-YTE (60 mg/kg)
Ab dosing: Single Dose, IV

Fig. 35

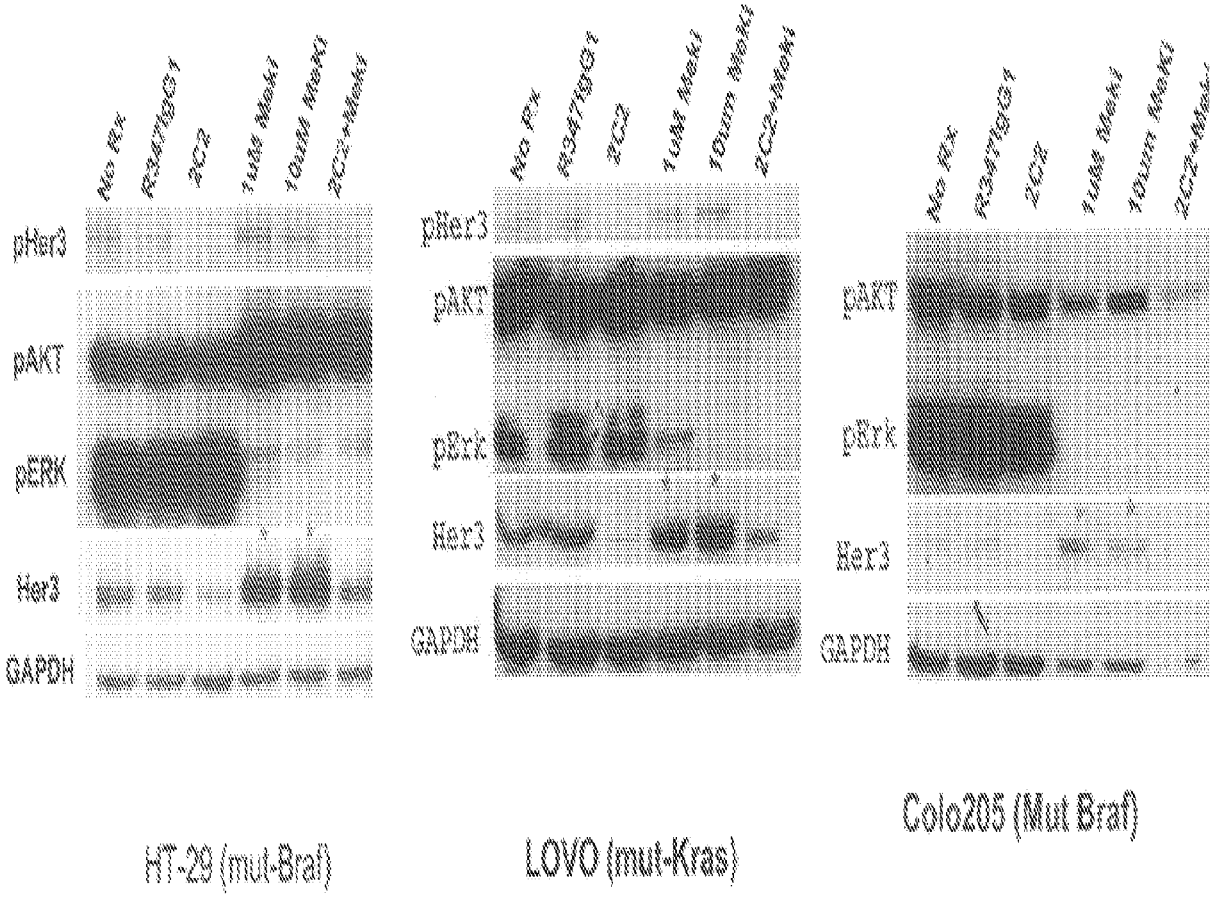

No Rx
R3477IgG1
2C2
1uM MekI
10um MekI
2C2+MekI
pHer3
pAKT
pERK
Her3
GAPDH
pHer3
pAKT
pErk
Her3
GAPDH
pAKT
pErk
Her3
GAPDH
HT-29 (mut-Braf)
LOVO (mut-Kras)
Colo205 (Mut Braf)

Fig. 36

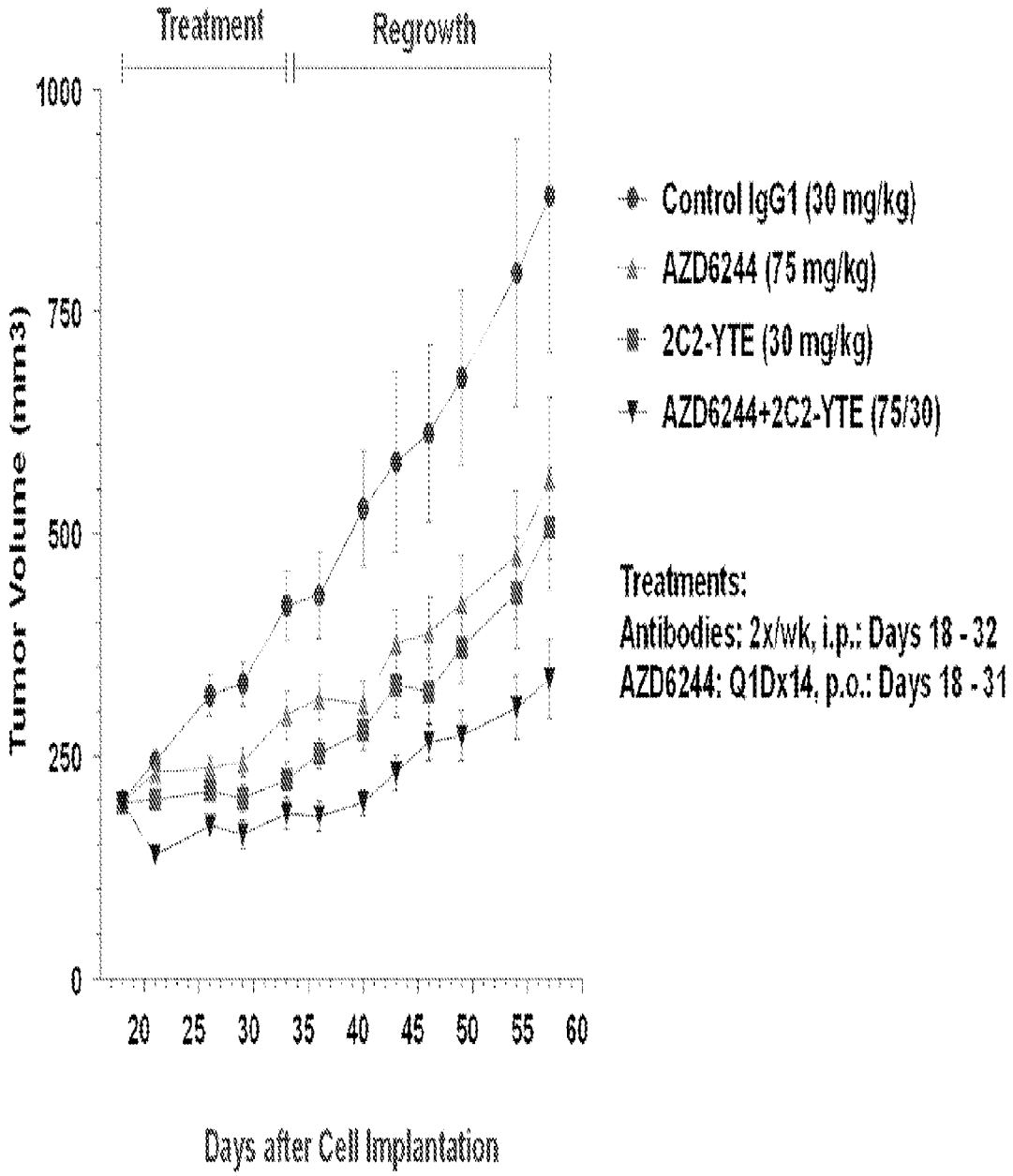


Fig. 37A part I

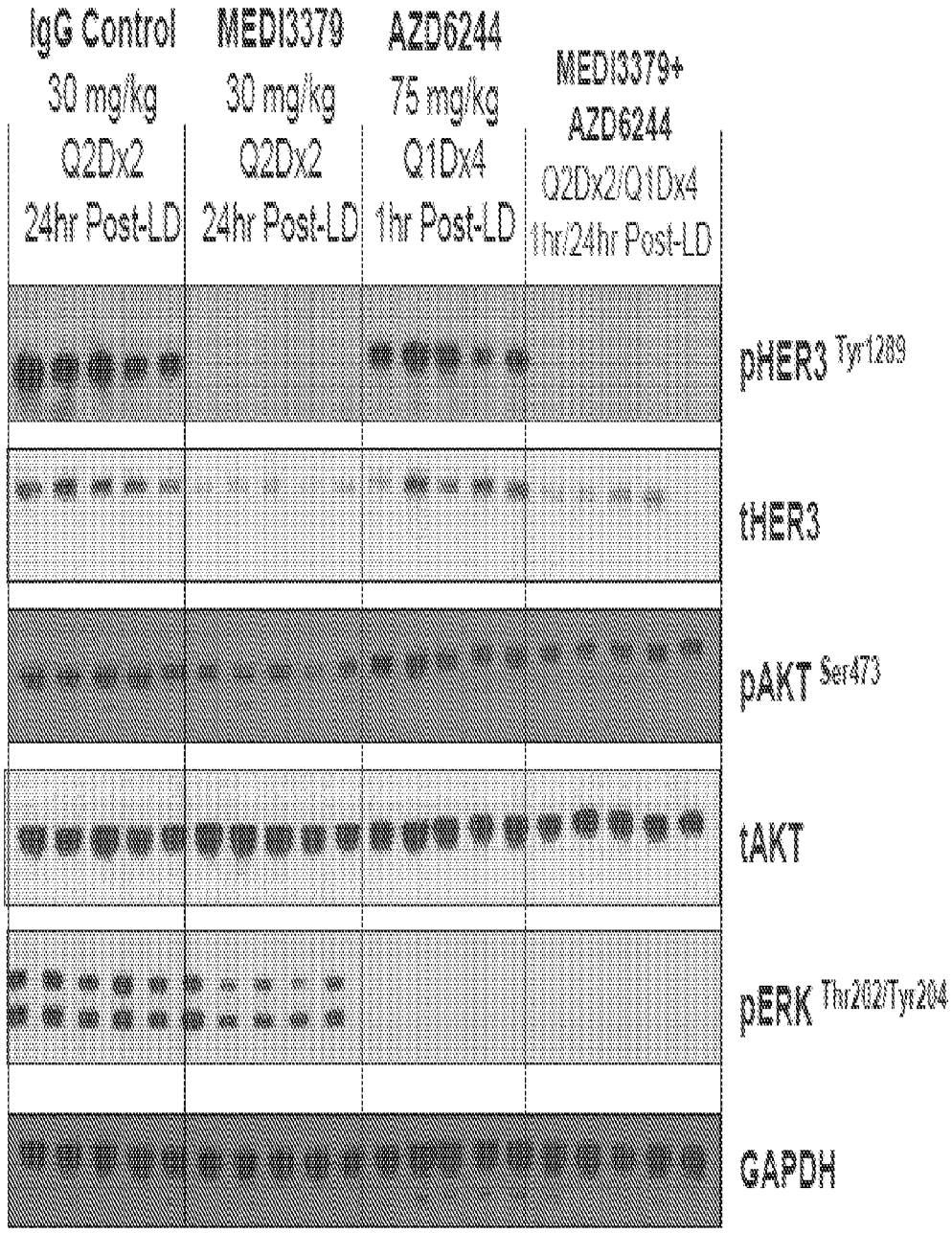


Fig. 37A part II

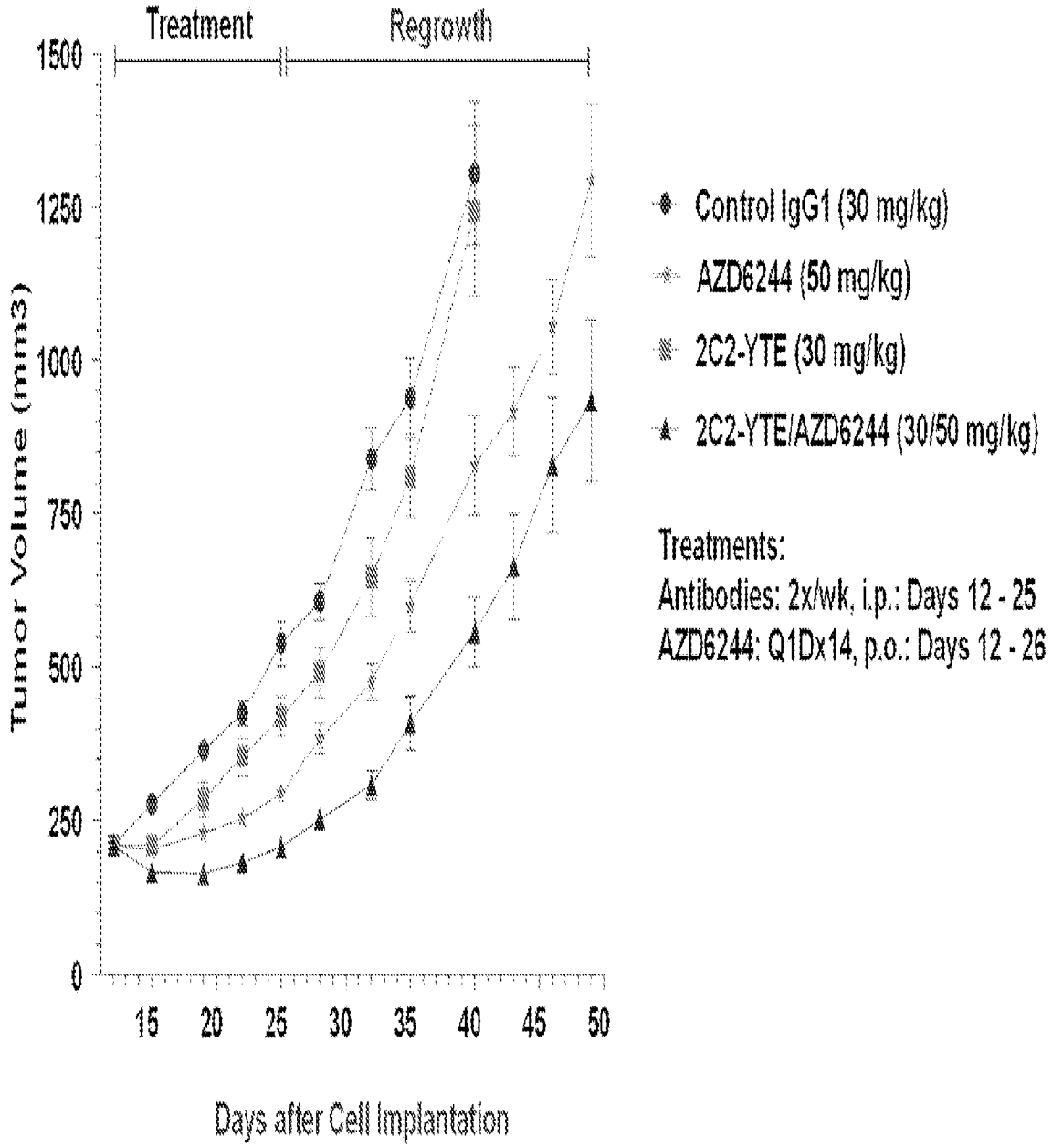


Fig. 37B part I

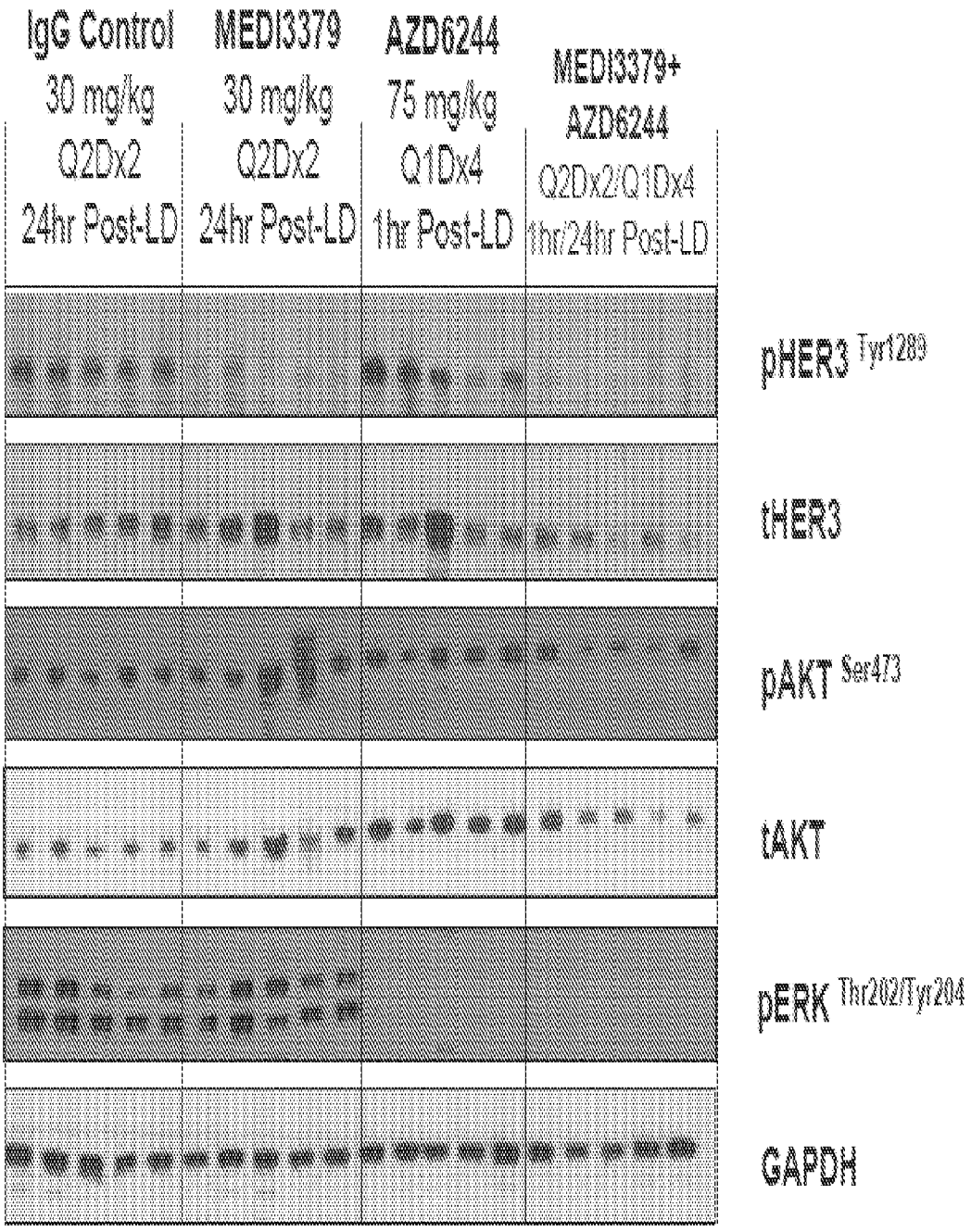


Fig. 37B part II

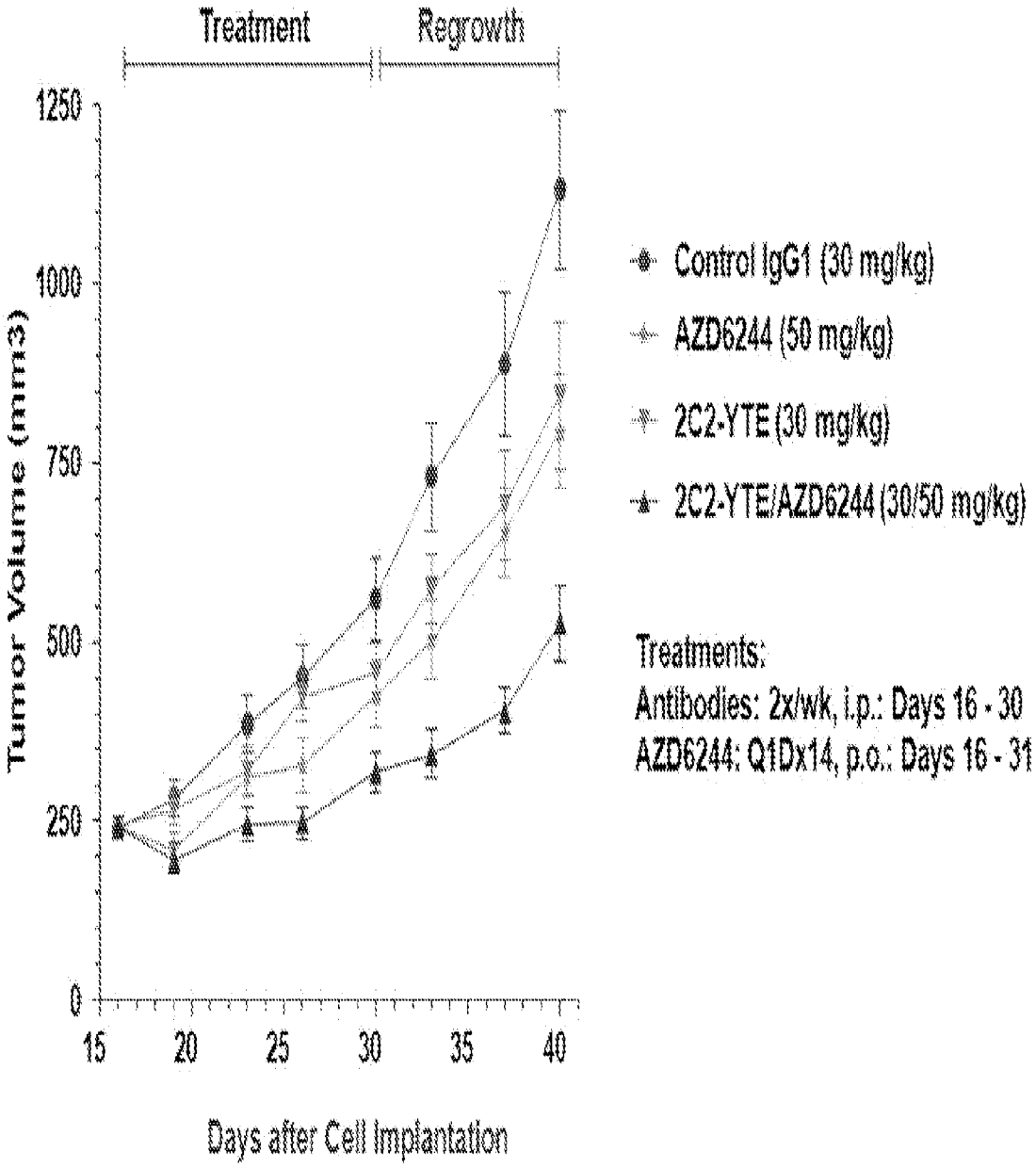


Fig. 37C part I

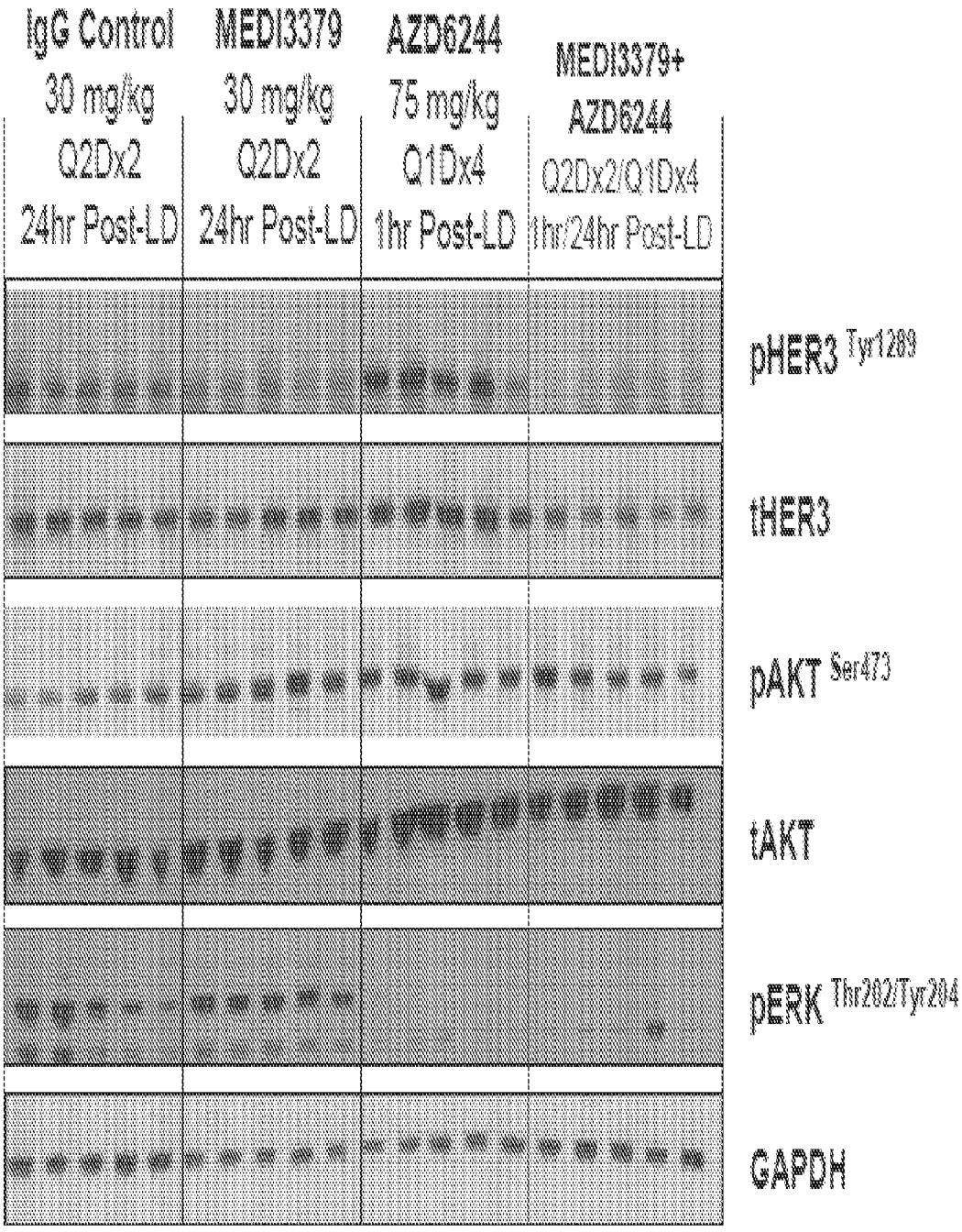


Fig. 37C part II