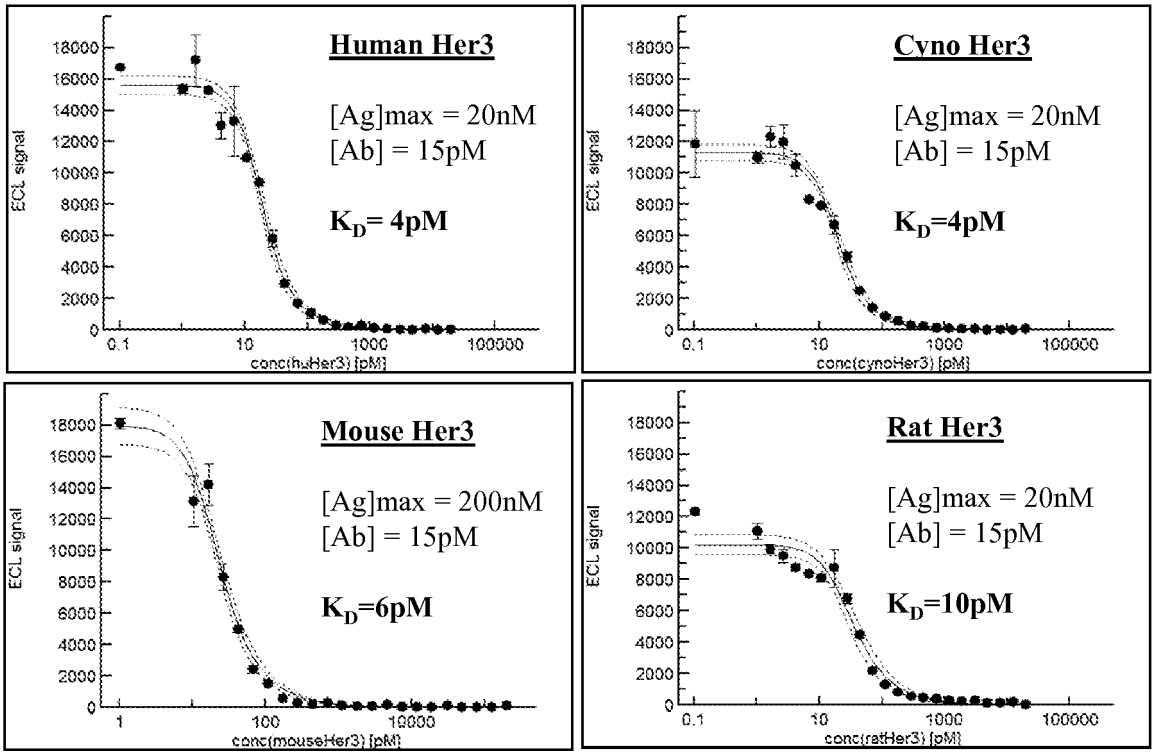

Human Her3
[Ag]max = 20nM
[Ab] = 15pM
K_D= 4pM
Cyno Her3
[Ag]max = 20nM
[Ab] = 15pM
K_D=4pM
Mouse Her3
[Ag]max = 200nM
[Ab] = 15pM
K_D=6pM
Rat Her3
[Ag]max = 20nM
[Ab] = 15pM
K_D=10pM
ECL signal
conc(huHer3) [pM]
conc(cynoHer3) [pM]
conc(mouseHer3) [pM]
conc(ratHer3) [pM]

Fig. 1

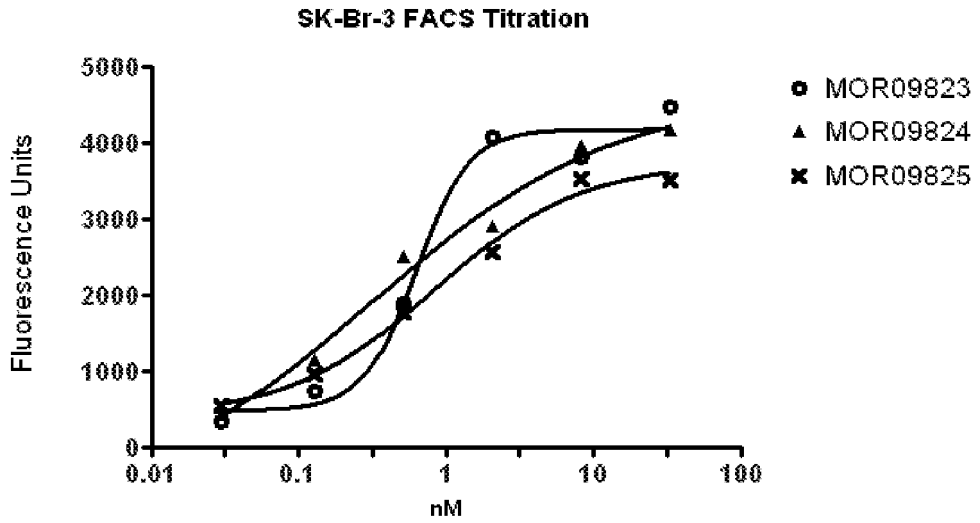

SK-Br-3 FACS Titration
Fluorescence Units
5000
4000
3000
2000
1000
0
0.01
0.1
1
10
100
nM
MOR09823
MOR09824
MOR09825

Fig. 2

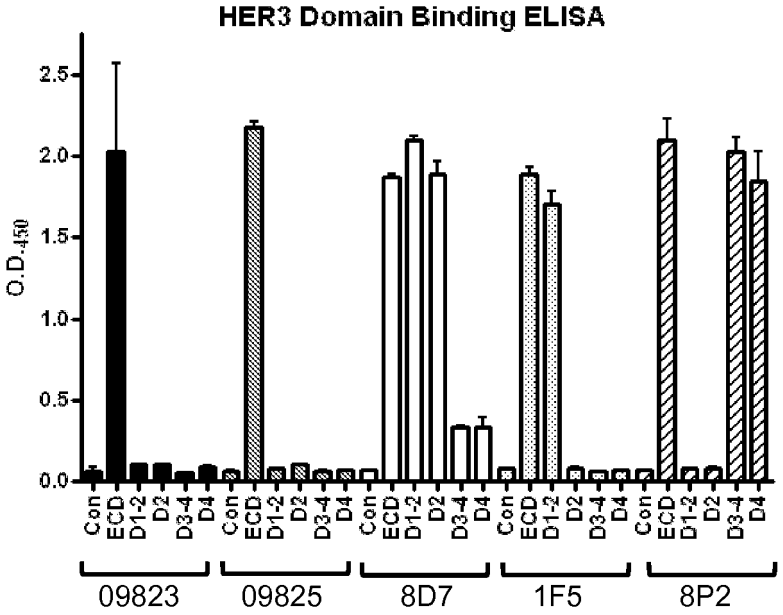

HER3 Domain Binding ELISA
O.D.450
2.5
2.0
1.5
1.0
0.5
0.0
Con
ECD
D1-2
D2
D3-4
D4
09823
09825
8D7
1F5
8P2

Fig. 3


20 SEVGNSQAVC PGTLNGLSVT GDAENQYQTL YKLYERCEVV MGNLEIVLTG HNADLSFLQW IREVTGYVLV AMNEFSTLPL
100 PNLRVVRGTQ VYDGKFAIFV MLNYNTNSSH ALRQLRLTQL TEILSGGVYI EKNDKLCHMD TIDWRDIVRD RDAEIVVKDN
180 GRSCPPCHEV CKGRCWGPGS EDCQTLTKTI CAPQCNGHCF GPNPNQCCHD ECAGGCSGPQ DTDCFACRHF NDSGACVPRC
260 PQPLVYNKLT FQLEPNPHTK YQYGGVCVAS CPHNFVVDQT SCVRACPPDK MEVDKNGLKM CEPCGGLCPK ACEGTGSGSR
340 FQTVDSSNID GFVNCTKILG NLDFLITGLN GDPWHKIPAL DPEKLNVFRT VREITGYLNI QSWPPHMHNF SVFSNLTTIG
420 GRSLYNRGFS LLIMKNINVT SLGFRSLKEI SAGRIYISAN RQLCYHHSLN WTKVLRGPTE ERLDIKHNRP RRDCVAEGKV
500 CDPLCSSGGC WGPGPGQCLS CRNYSRGGVC VTHCNFLNGE PREFAHEAEC FSCHPECQPM EGTATCNGSG SDTCAQCAHF
580 RDGPHCVSSC PHGVLGAKGP IYKYPDVQNE CRPCHENCTQ GCKGPELQDC LGQTLVLIGK TEFRHDS

Fig. 4A

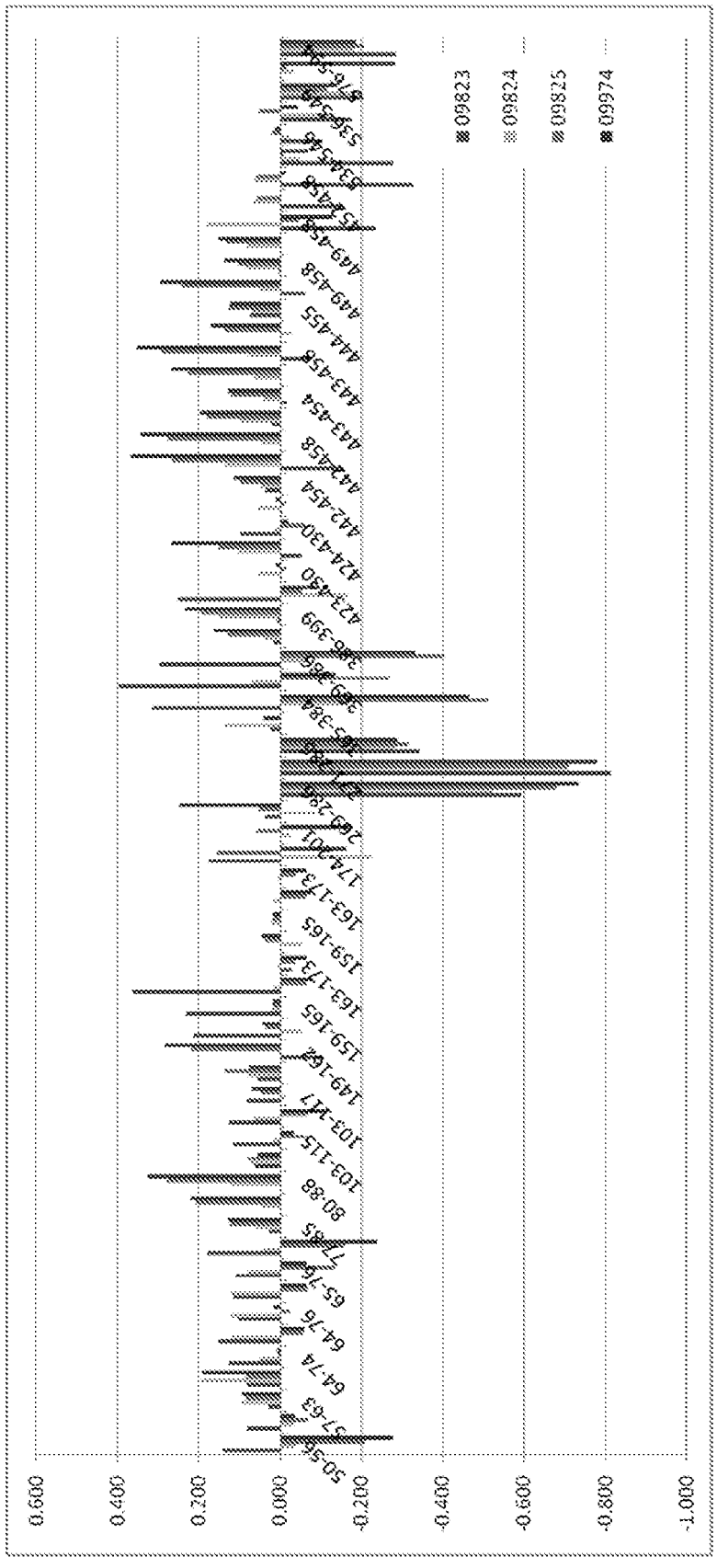

ΔD [HER3: Fab] vs HER3
ΔD
0.600
0.400
0.200
0.000
-0.200
-0.400
-0.600
-0.800
-1.000
09823
09824
09825
09974

Fig. 4B

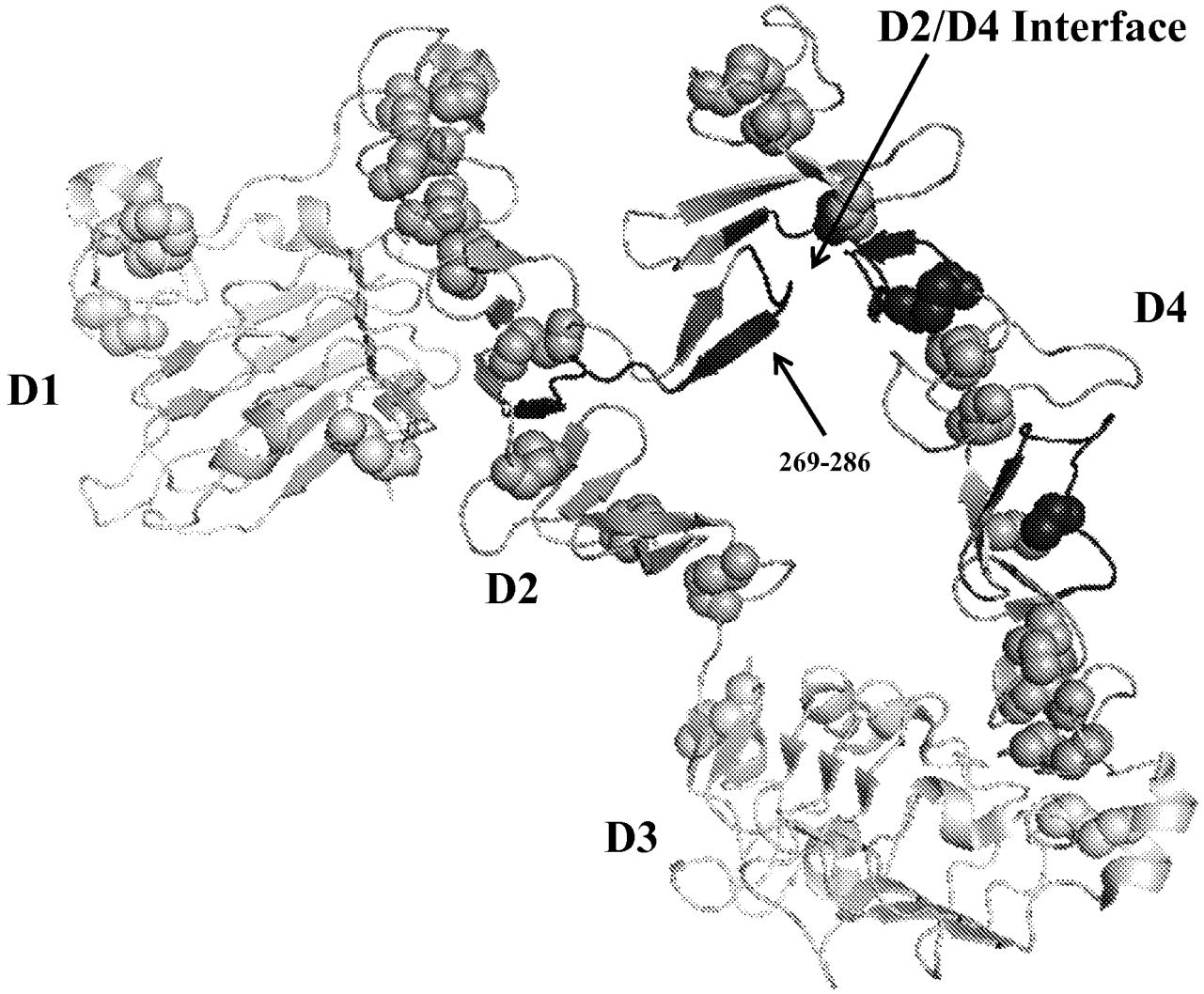


Fig. 4C

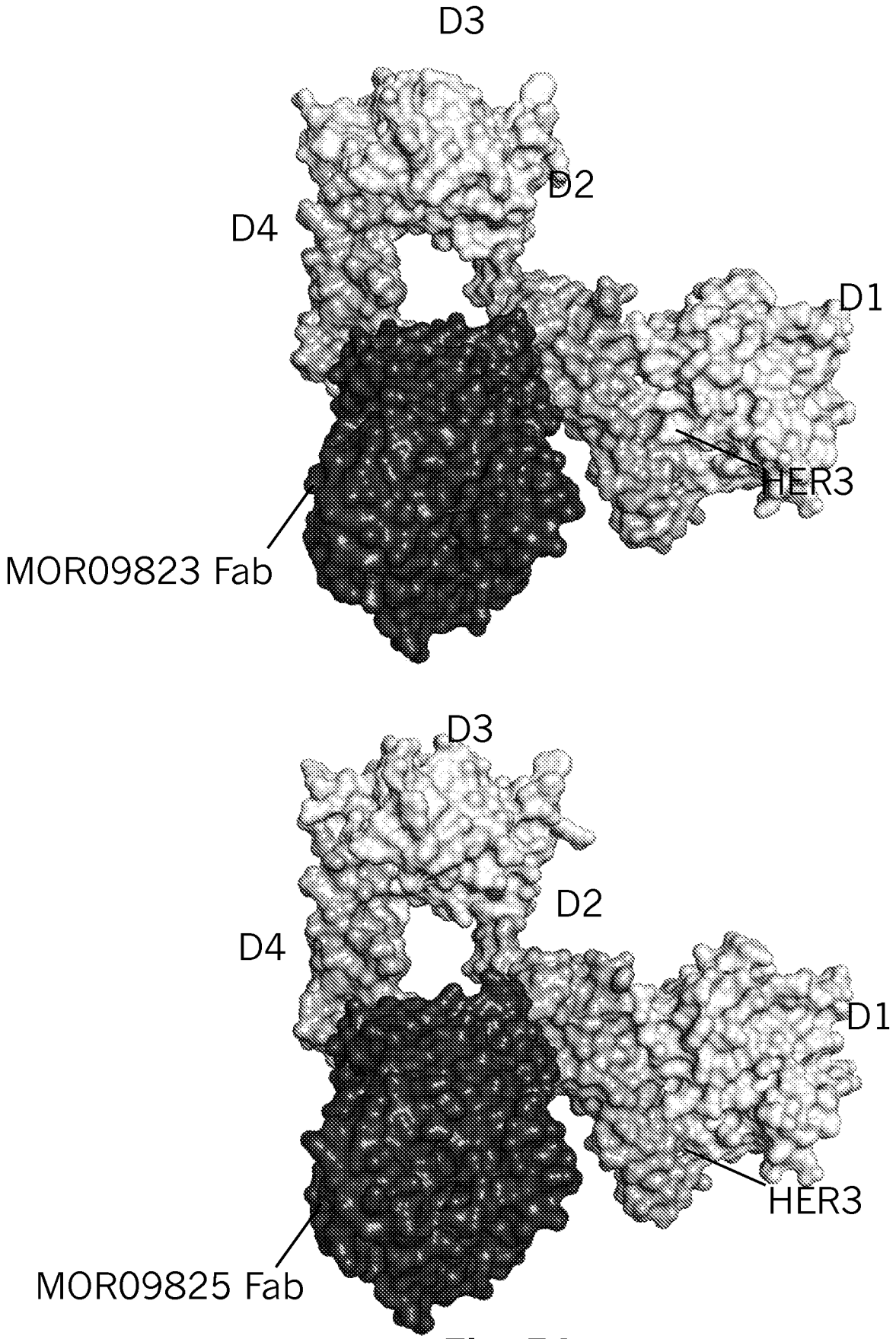


Fig. 5A

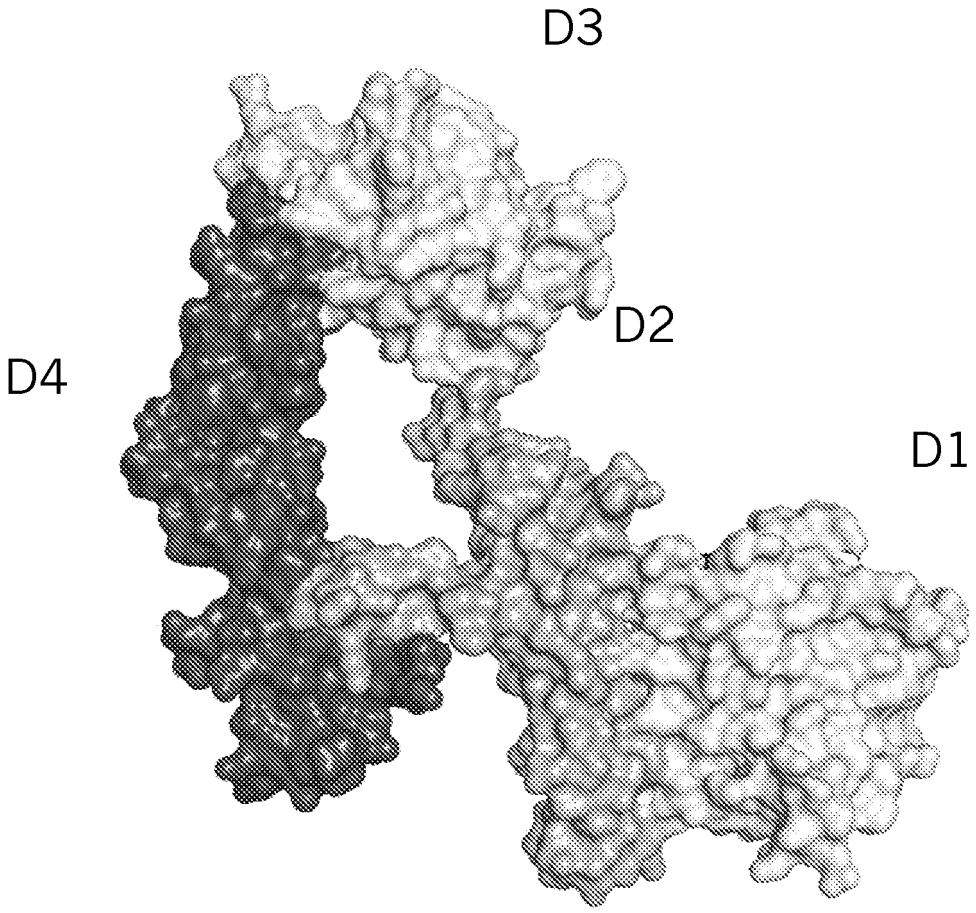


Fig. 5B

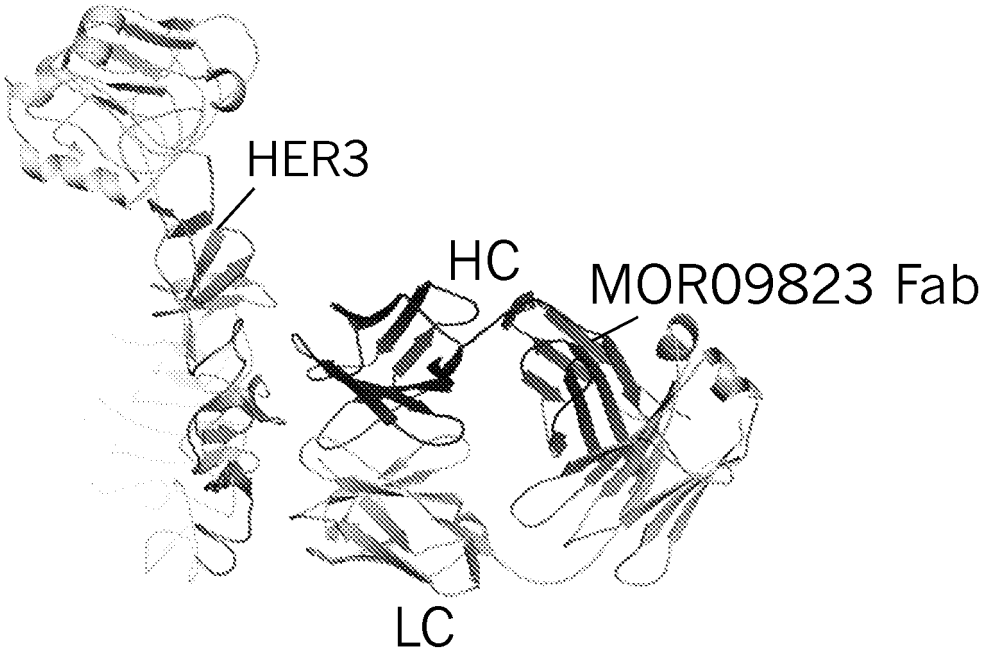

HER3
HC
MOR09823 Fab
LC

Fig. 5C

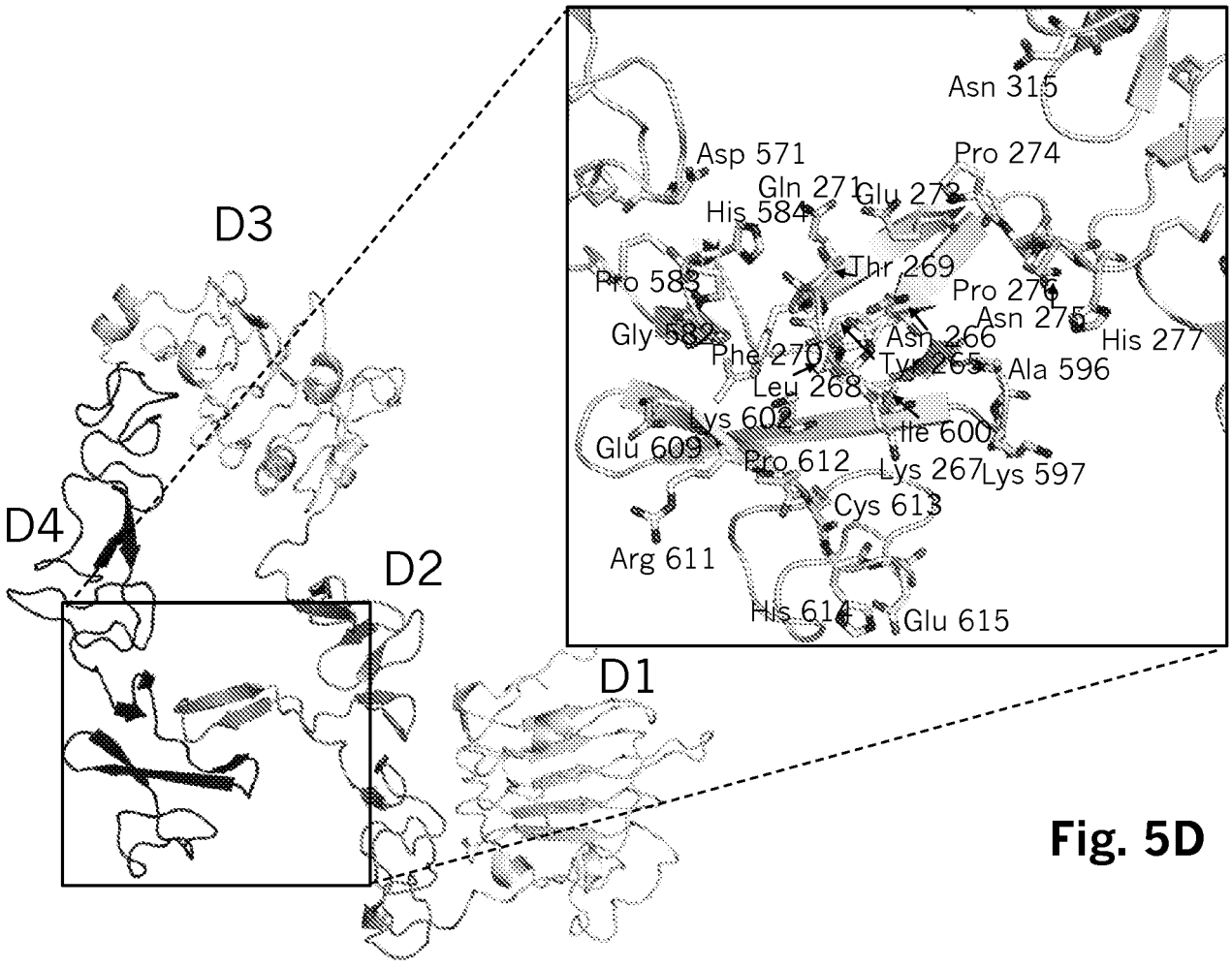

D3
D4
D2
D1
Asn 315
Asp 571
Pro 274
Gln 271
Glu 272
His 584
Thr 269
Pro 583
Pro 276
Asn 275
Gly 582
Asn 266
His 277
Phe 270
Tyr 265
Ala 596
Leu 268
Lys 602
Ile 600
Glu 609
Pro 612
Lys 267
Lys 597
Cys 613
Arg 611
His 614
Glu 615

Fig. 5D

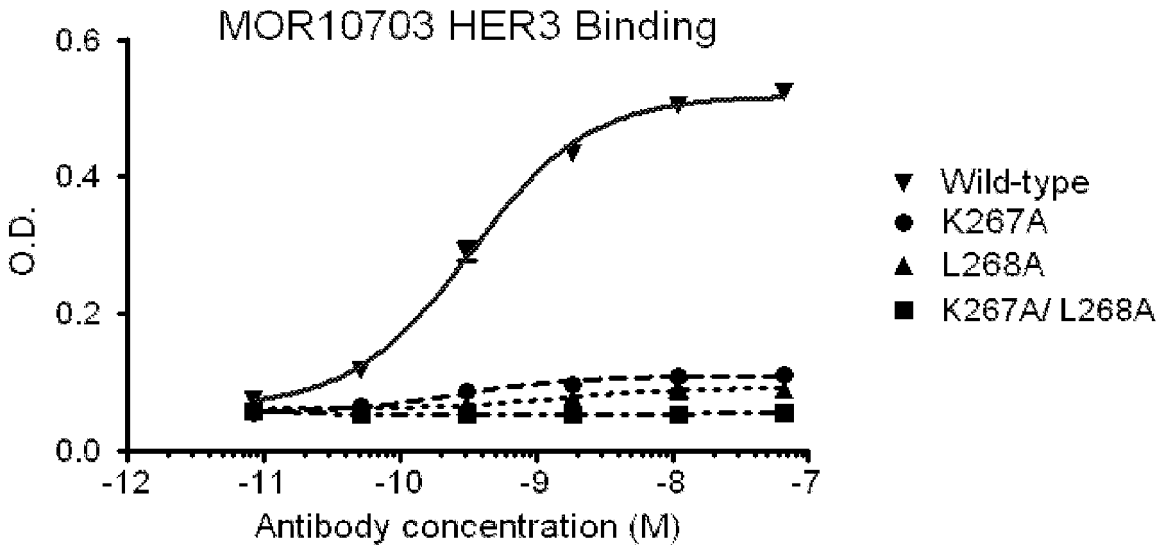

MOR10703 HER3 Binding
0.6
0.4
0.2
0.0
O.D.
-12
-11
-10
-9
-8
-7
Antibody concentration (M)
Wild-type
K267A
L268A
K267A/ L268A

Fig. 5E

Fig. 6A

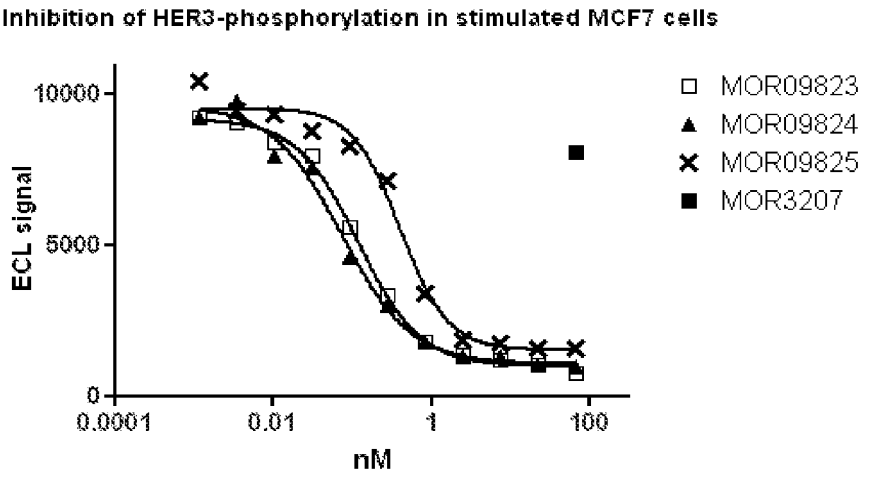

Inhibition of HER3-phosphorylation in stimulated MCF7 cells
ECL signal
10000
5000
0
0.0001
0.01
1
100
nM
MOR09823
MOR09824
MOR09825
MOR3207

Fig. 6B

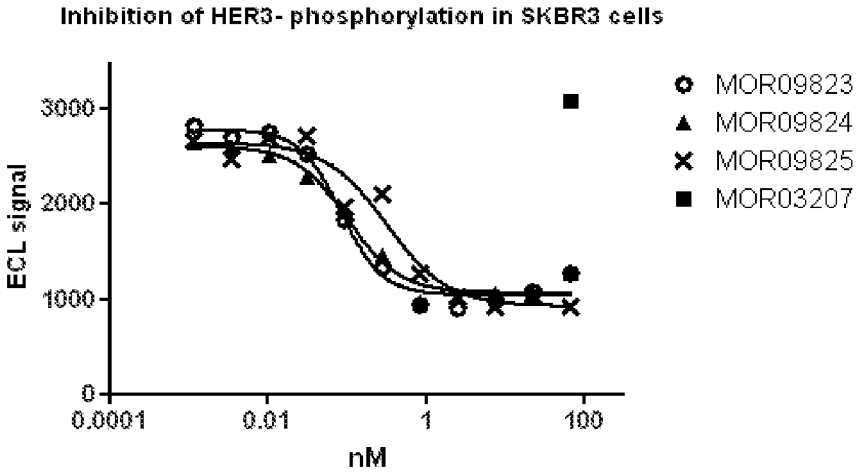

Inhibition of HER3- phosphorylation in SKBR3 cells
ECL signal
3000
2000
1000
0
0.0001
0.01
1
100
nM
MOR09823
MOR09824
MOR09825
MOR03207

Fig. 7A

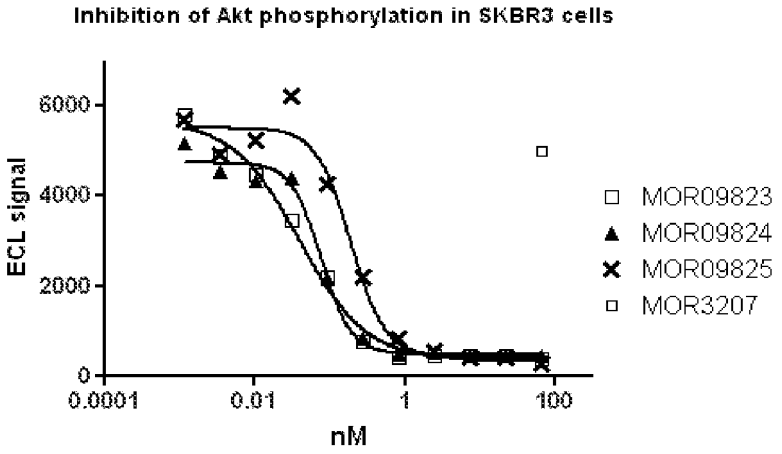

Inhibition of Akt phosphorylation in SKBR3 cells
ECL signal
6000
4000
2000
0
0.0001
0.01
1
100
nM
MOR09823
MOR09824
MOR09825
MOR3207

Fig. 7B

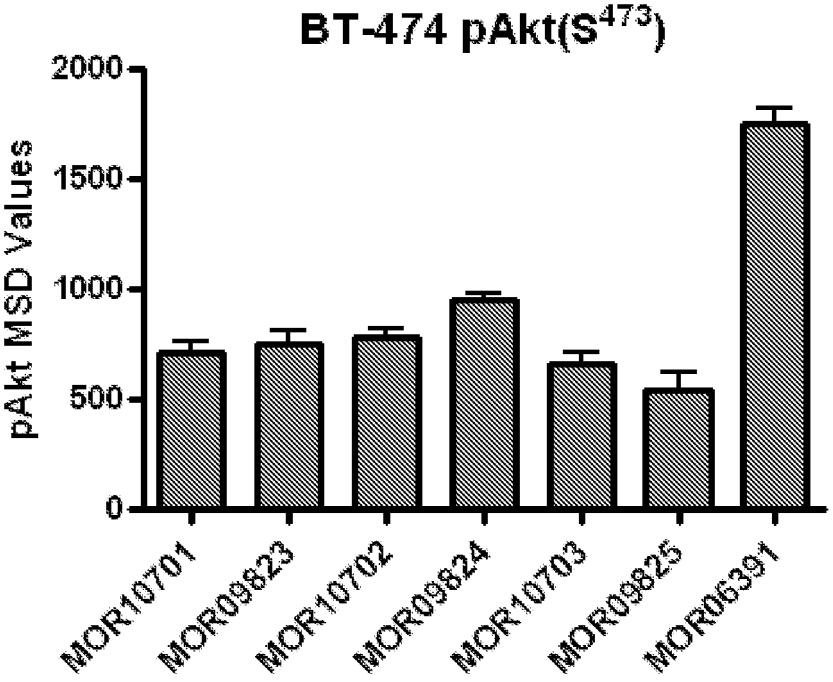

BT-474 pAkt(S473)
pAkt MSD Values
2000
1500
1000
500
0
MOR10701
MOR09823
MOR10702
MOR09824
MOR10703
MOR09825
MOR06391

Fig. 8A

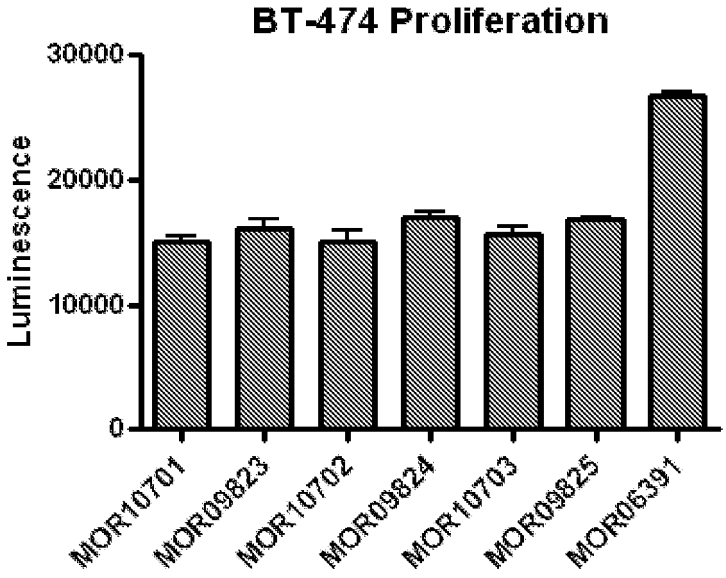
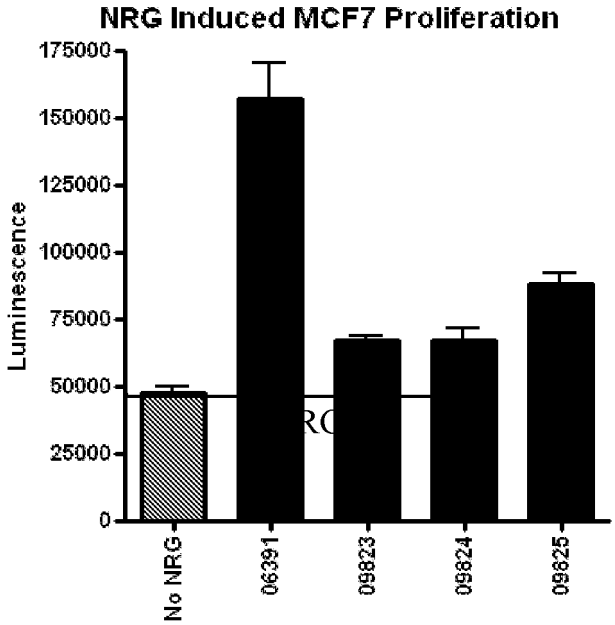

BT-474 Proliferation
Luminescence
30000
20000
10000
0
MOR10701
MOR09823
MOR10702
MOR09824
MOR10703
MOR09825
MOR06391

Fig. 8B


NRG Induced MCF7 Proliferation
Luminescence
175000
150000
125000
100000
75000
50000
25000
0
No NRG
06391
09823
09824
09825

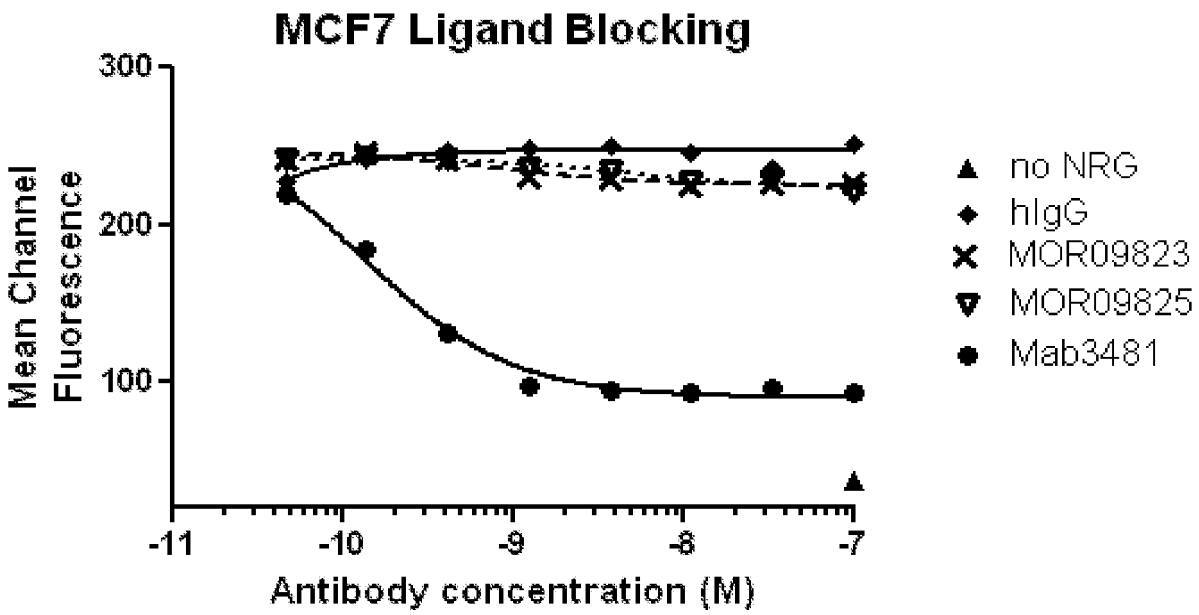

MCF7 Ligand Blocking
Mean Channel Fluorescence
300
200
100
-11
-10
-9
-8
-7
Antibody concentration (M)
no NRG
hIgG
MOR09823
MOR09825
Mab3481

Fig. 9

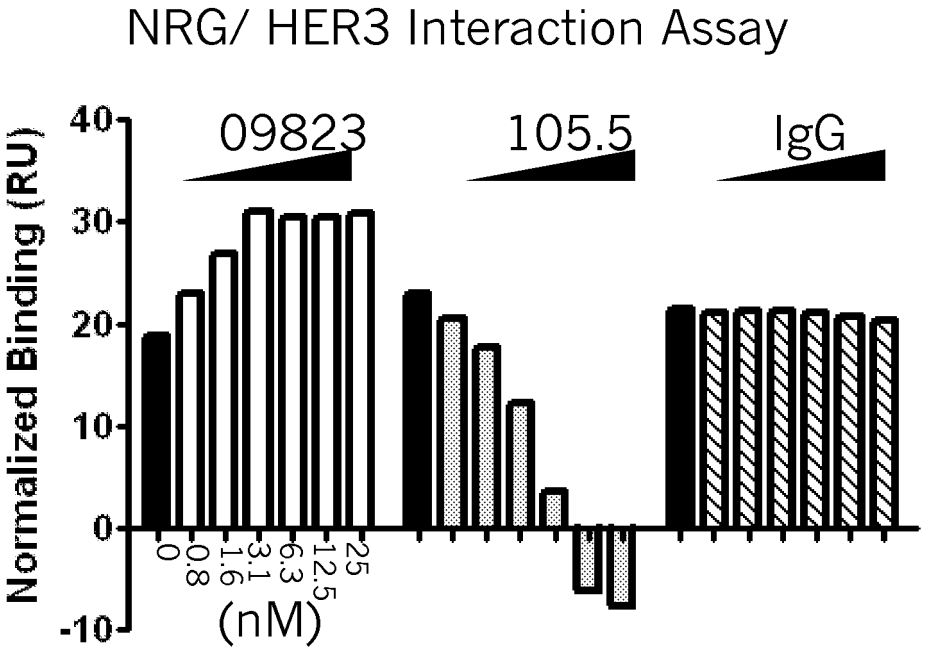
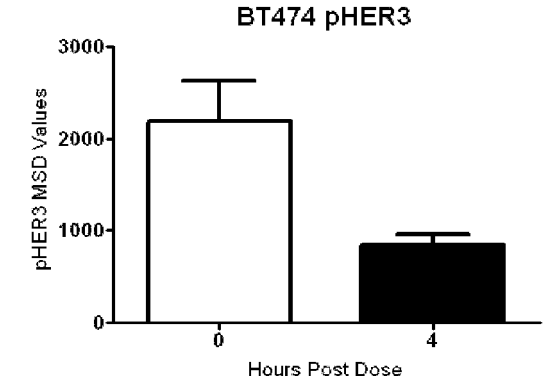

NRG/ HER3 Interaction Assay
Normalized Binding (RU)
40
30
20
10
0
-10
09823
105.5
IgG
0
0.8
1.6
3.1
6.3
12.5
25
(nM)

Fig. 10

Fig. 11A

MOR0923 treated BT474 xenografts



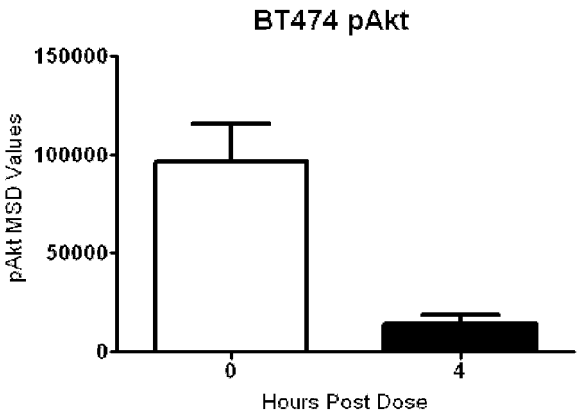
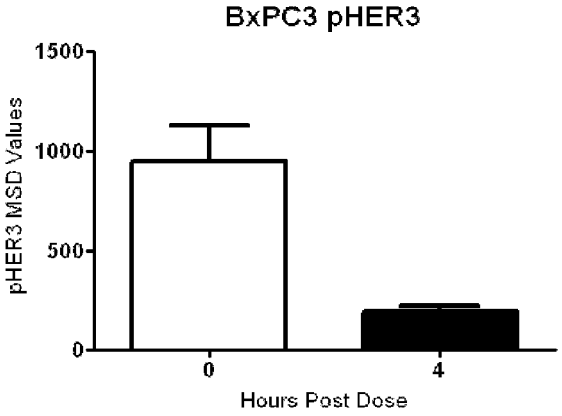


Fig. 11B

MOR09823 treated BxPC3 xenografts



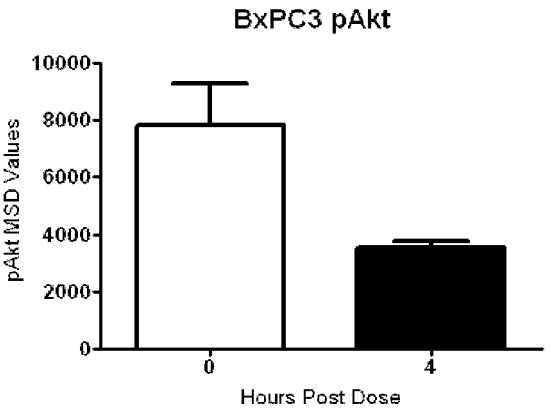


Fig. 12A

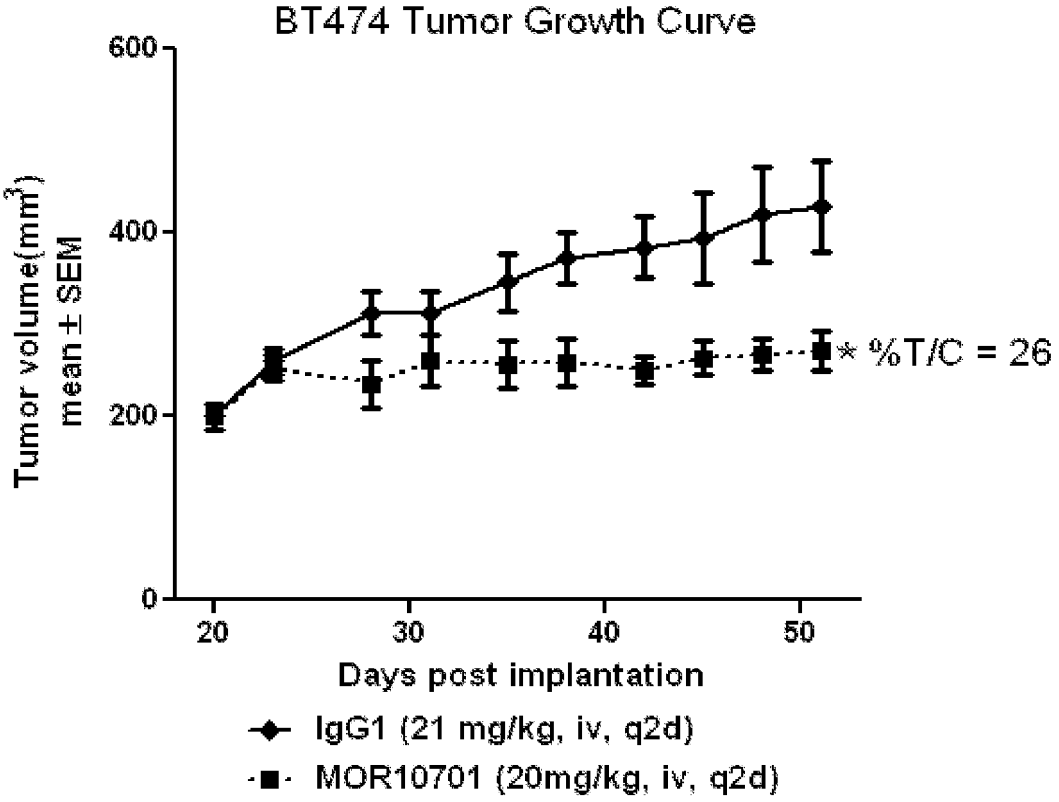
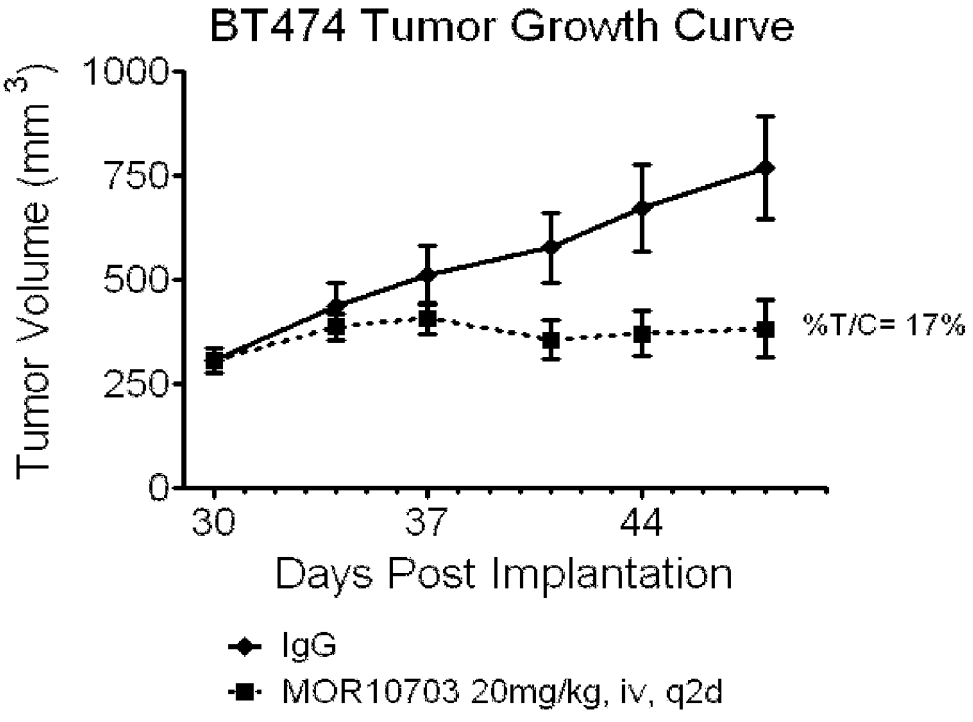


Fig. 12B



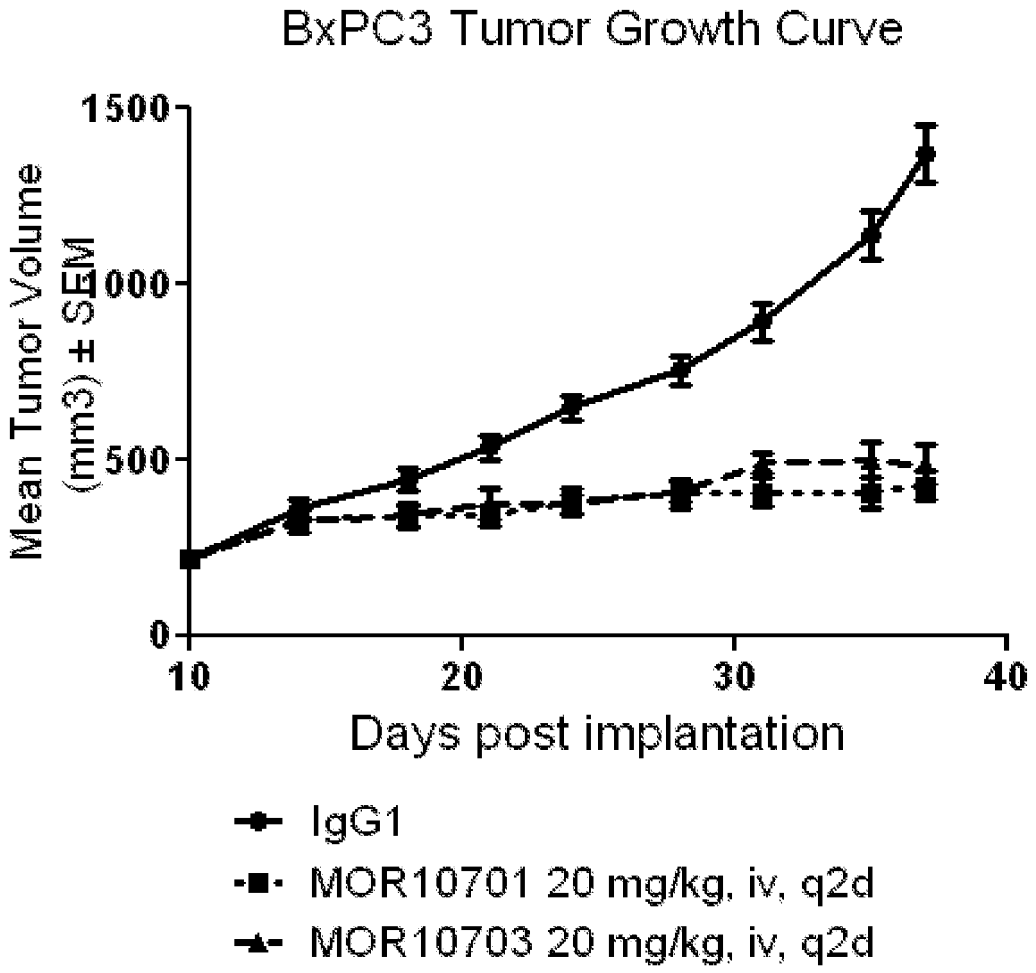

BxPC3 Tumor Growth Curve
Mean Tumor Volume (mm3) ± SEM
1500
1000
500
0
10
20
30
40
Days post implantation
IgG1
MOR10701 20 mg/kg, iv, q2d
MOR10703 20 mg/kg, iv, q2d

Fig. 13

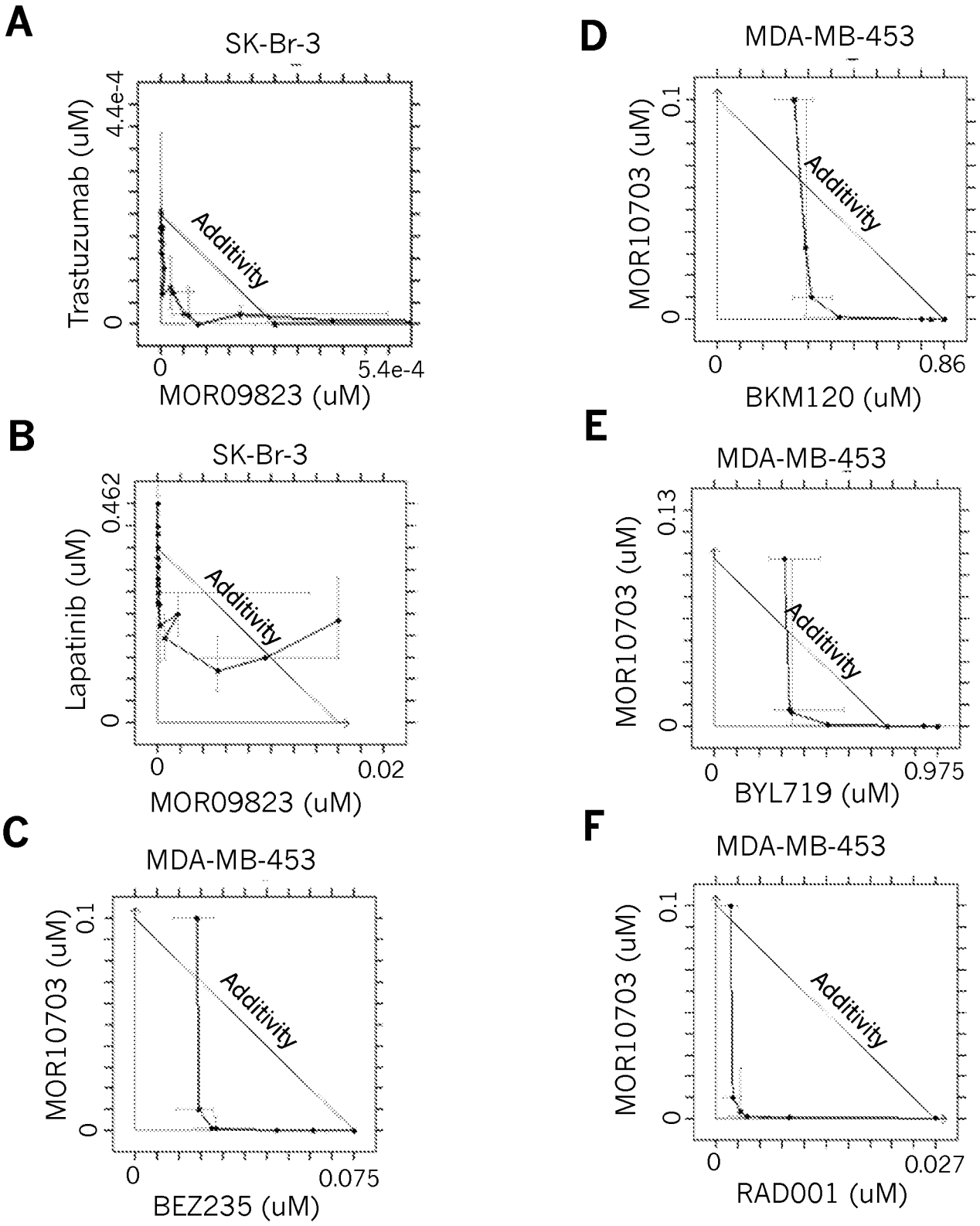
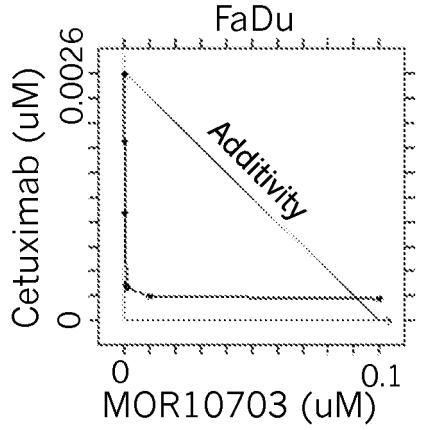

A
SK-Br-3
Trastuzumab (uM)
4.4e-4
0
0
5.4e-4
MOR09823 (uM)
Additivity
B
SK-Br-3
Lapatinib (uM)
0.462
0
0
0.02
MOR09823 (uM)
Additivity
C
MDA-MB-453
MOR10703 (uM)
0.1
0
0
0.075
BEZ235 (uM)
Additivity
D
MDA-MB-453
MOR10703 (uM)
0.1
0
0
0.86
BKM120 (uM)
Additivity
E
MDA-MB-453
MOR10703 (uM)
0.13
0
0
0.975
BYL719 (uM)
Additivity
F
MDA-MB-453
MOR10703 (uM)
0.1
0
0
0.027
RAD001 (uM)
Additivity

Fig. 14

G



H

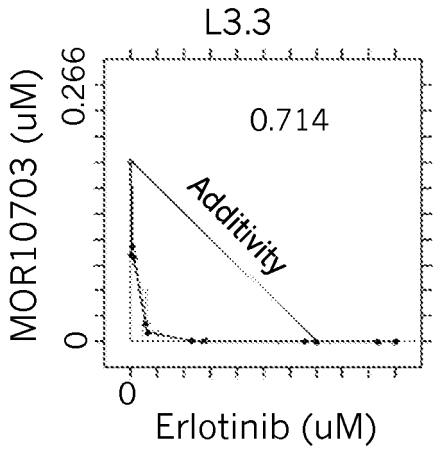
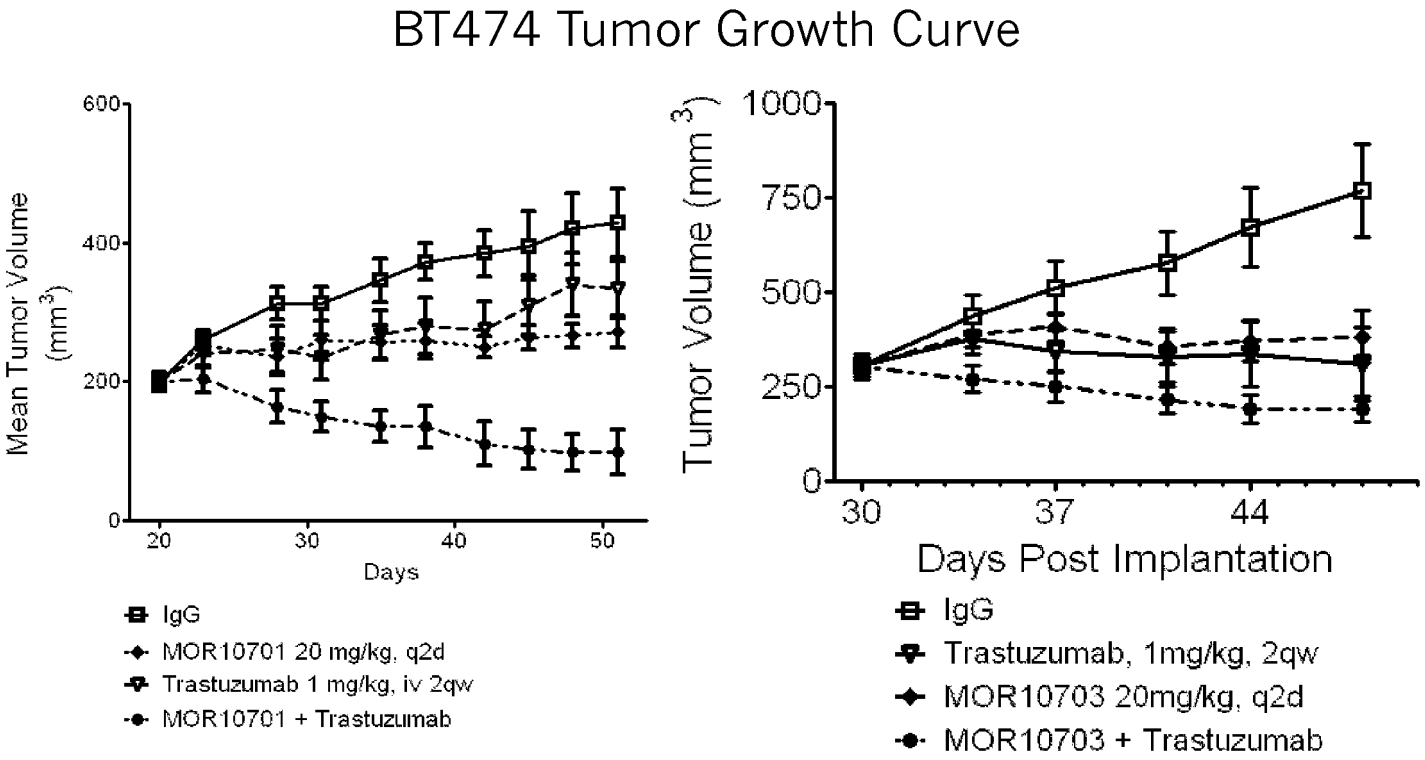


Fig. 14 (cont.)

Fig. 15A



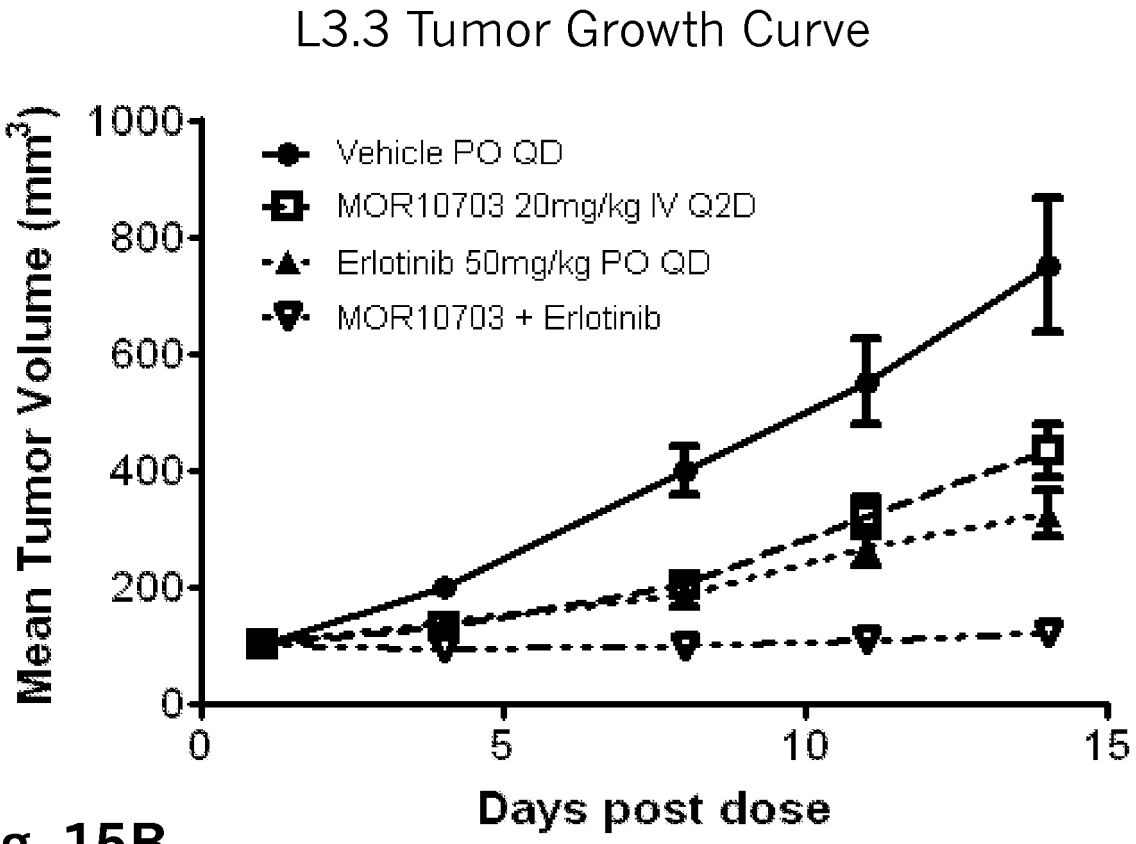


Fig. 15B

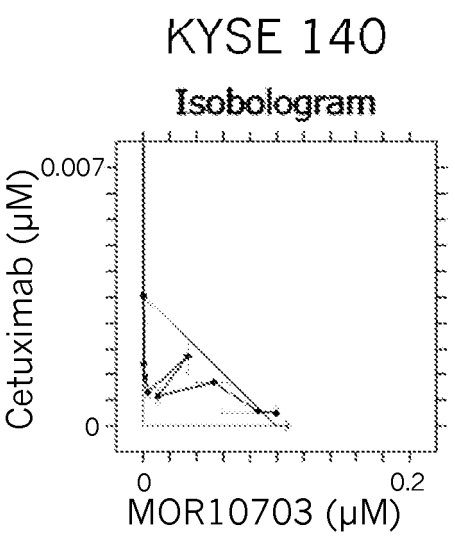

KYSE 140
Isobologram
Cetuximab (μM)
0.007
0
0
0.2
MOR10703 (μM)

Fig. 16

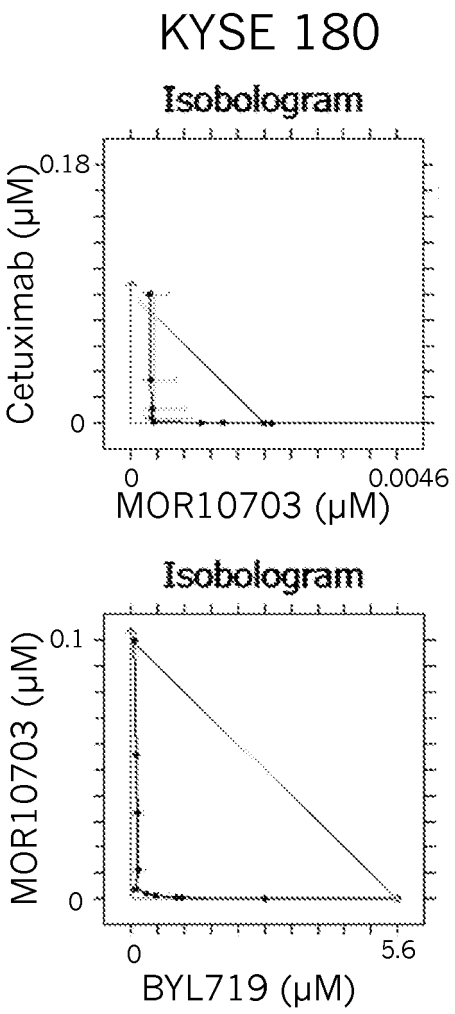

KYSE 180
Isobologram
Cetuximab (μM)
0.18
0
0
0.0046
MOR10703 (μM)
Isobologram
MOR10703 (μM)
0.1
0
0
5.6
BYL719 (μM)

Fig. 17

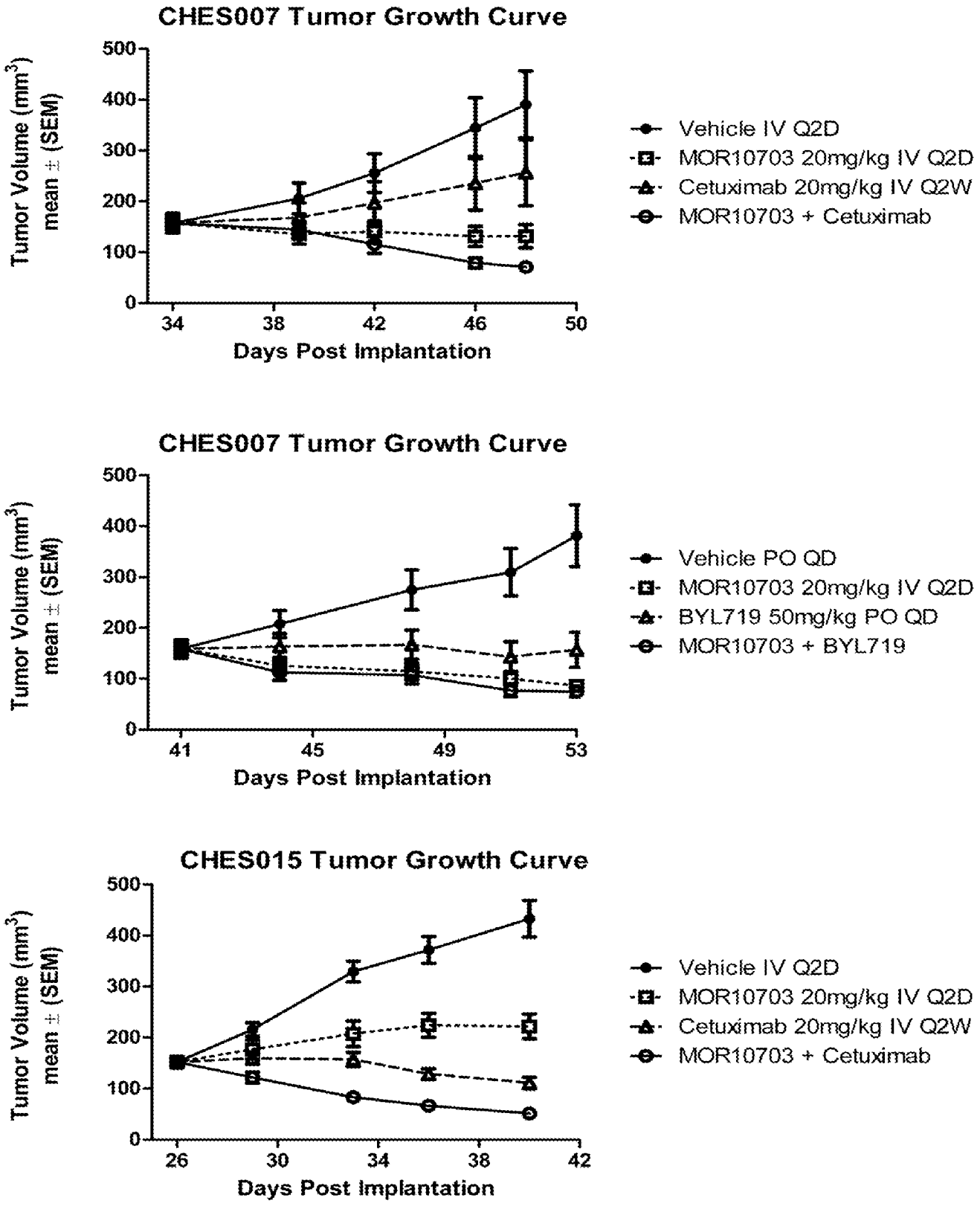

CHES007 Tumor Growth Curve
Tumor Volume (mm3) mean ± (SEM)
500
400
300
200
100
0
34
38
42
46
50
Days Post Implantation
Vehicle IV Q2D
MOR10703 20mg/kg IV Q2D
Cetuximab 20mg/kg IV Q2W
MOR10703 + Cetuximab
CHES007 Tumor Growth Curve
Tumor Volume (mm3) mean ± (SEM)
500
400
300
200
100
0
41
45
49
53
Days Post Implantation
Vehicle PO QD
MOR10703 20mg/kg IV Q2D
BYL719 50mg/kg PO QD
MOR10703 + BYL719
CHES015 Tumor Growth Curve
Tumor Volume (mm3) mean ± (SEM)
500
400
300
200
100
0
26
30
34
38
42
Days Post Implantation
Vehicle IV Q2D
MOR10703 20mg/kg IV Q2D
Cetuximab 20mg/kg IV Q2W
MOR10703 + Cetuximab

Fig. 18

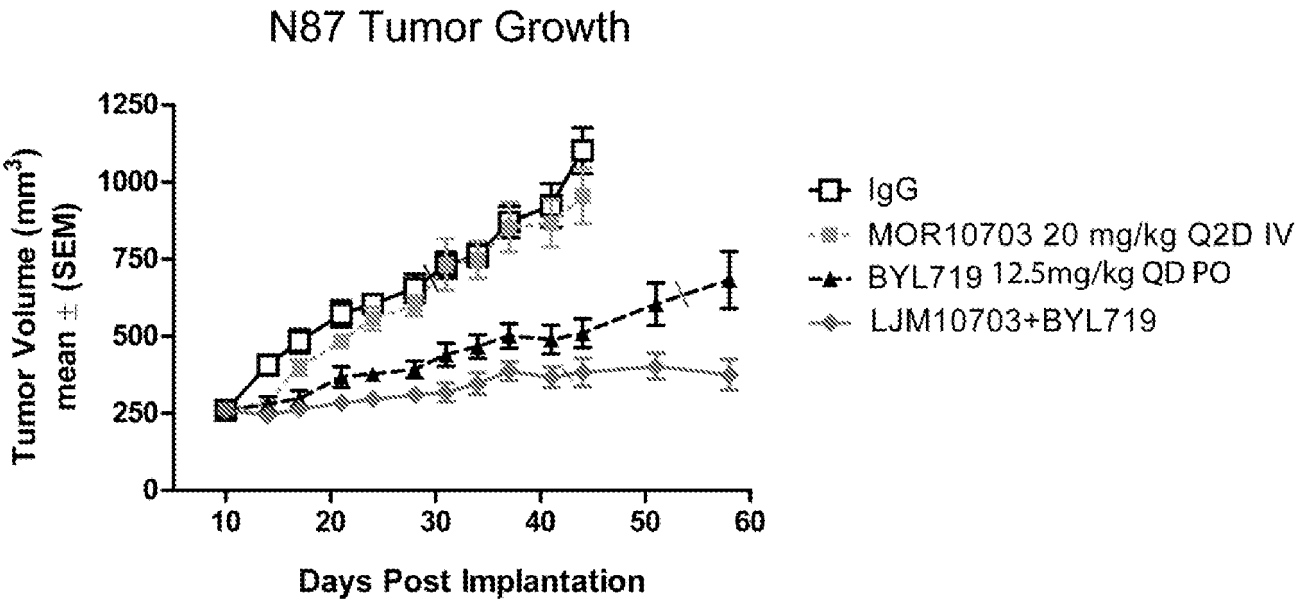

N87 Tumor Growth
Tumor Volume (mm3) mean ± (SEM)
1250
1000
750
500
250
0
10
20
30
40
50
60
Days Post Implantation
IgG
MOR10703 20 mg/kg Q2D IV
BYL719 12.5mg/kg QD PO
LJM10703+BYL719

Fig. 19

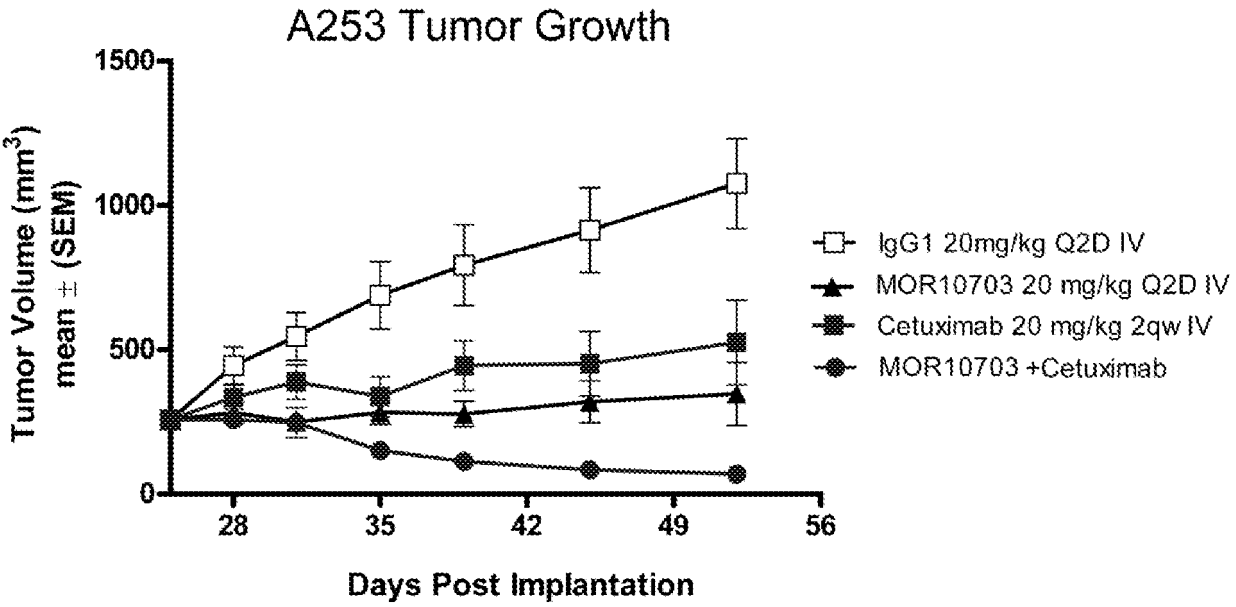

A253 Tumor Growth
Tumor Volume (mm3)
mean +/- (SEM)
1500
1000
500
0
28
35
42
49
56
Days Post Implantation
IgG1 20mg/kg Q2D IV
MOR10703 20 mg/kg Q2D IV
Cetuximab 20 mg/kg 2qw IV
MOR10703 +Cetuximab

Fig. 20