Figure 1A.


SEQ ID NO:
18 LPAPKNLVVSEVTEDSLRLSWADP-HGFYDSFLIQYQESEKVGEAINLTVPGSERSYDLTG (60)
19 LPAPKNLVVSEVTEDSLRLSWTYD-RDGYDSFLIQYQESEKVGEAINLTVPGSERSYDLTG
20 LPAPKNLVVSEVTEDSLRLSWGYN-GDHFDSFLIQYQESEKVGEAINLTVPGSERSYDLTG
21 LPAPKNLVVSEVTEDSLRLSWDDP-RGFYESFLIQYQESEKVGEAINLTVPGSERSYDLTG
22 LPAPKNLVVSEVTEDSLRLSWTWP-YADLDSFLIQYQESEKVGEAINLTVPGSERSYDLTG
23 LPAPKNLVVSEVTEDSLRLSWGYN-GDHFDSFLIQYQESEKVGEAINLTVPGSERSYDLTG
24 LPAPKNLVVSEVTEDSLRLSWDYDLGDHFDSFLIQYQESEKVGEAINLTVPGSERSYDLTG
25 LPAPKNLVVSEVTEDSLRLSWDDP-WAFYESFLIQYQESEKVGEAINLTVPGSERSYDLTG
27 LPAPKNLVVSEVTEDSARLSWDDP-WAFYESFLIQYQESEKVGEAIVLTVPGSERSYDLTG
29 LPAPKNLVVSEVTEDSLRLSWTWP-YADLDSFLIQYQESEKVGEAINLTVPGSERSYDLTG
107 LPAPKNLVVSEVTEDSARLSWADP-HGFYDSFLIQYQESEKVGEAIVLTVPGSERSYDLTG
108 LPAPKNLVVSEVTEDSARLSWDDP-WAFYESFLIQYQESEKVGEAIVLTVPGSERSYDLTG
109 LPAPKNLVVSEVTEDSARLSWDDP-HAFYESFLIQYQESEKVGEAIVLTVPGSERSYDLTG
110 LPAPKNLVVSEVTEDSARLSWADP-HGFYDSFLIQYQESEKVGEAIVLTVPGSERSYDLTG
18 LKPGTEYTVSIYGVHNVYKDTNMRGLPLSAEFTT (94)
19 LKPGTEYTVSIYGVHNVYKDTNMRGLPLSAEFTT
20 LKPGTEYTVSIYGVHNVYKDTNMRGLPLSAEFTT
21 LKPGTEYTVSIYGVHNVYKDTNMRGLPLSAEFTT
22 LKPGTEYTVSIYGVHNVYKDTNMRGLPLSAEFTT
23 LKPGTEYTVSIYGVHNVYKDTNMRGLPLSAEFTT
24 LKPGTEYTVSIYGVHNVYKDTNMRGLPLSAEFTT
25 LKPGTEYTVSIYGVHNVYKDTNMRGLPLSAEFTT
27 LKPGTEYTVSIYGVHNVYKDTNMRGLPLSAIFTT
29 LKPGTEYTVSIYGVHNVYKDTNMRGLPLSAEFTT
107 LKPGTEYTVSIYGVHNVYKDTNMRGLPLSAIFTT
108 LKPGTEYTVSIYGVHNVYKDTNIRGLPLSAIFTT
109 LKPGTEYTVSIYGVHNVYKDTNIRGLPLSAIFTT
110 LKPGTEYTVSIYGVHNVYKDTNIRGLPLSAIFTT

Figure 1B

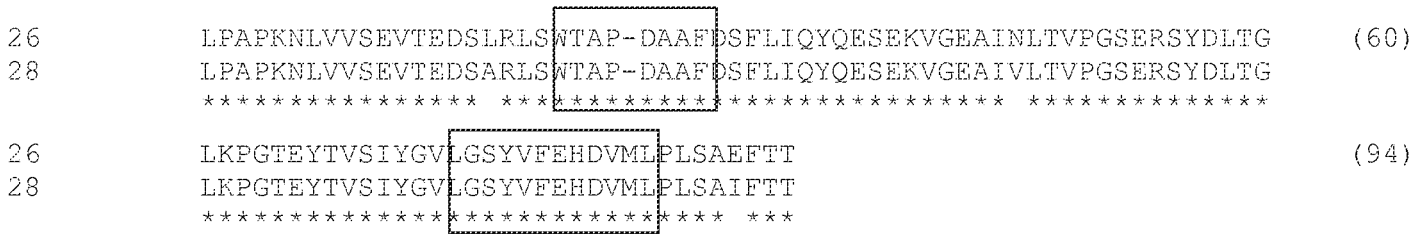

SEQ ID
NO:
26 LPAPKNLVVSEVTEDSLRLSWTAP-DAAFDSFLIQYQESEKVGEAINLTVPGSERSYDLTG (60)
28 LPAPKNLVVSEVTEDSARLSWTAP-DAAFDSFLIQYQESEKVGEAIVLTVPGSERSYDLTG
26 LKPGTEYTVSIYGVLGSYVFEHDVMLPLSAEFTT (94)
28 LKPGTEYTVSIYGVLGSYVFEHDVMLPLSAIFTT

Figure 2.

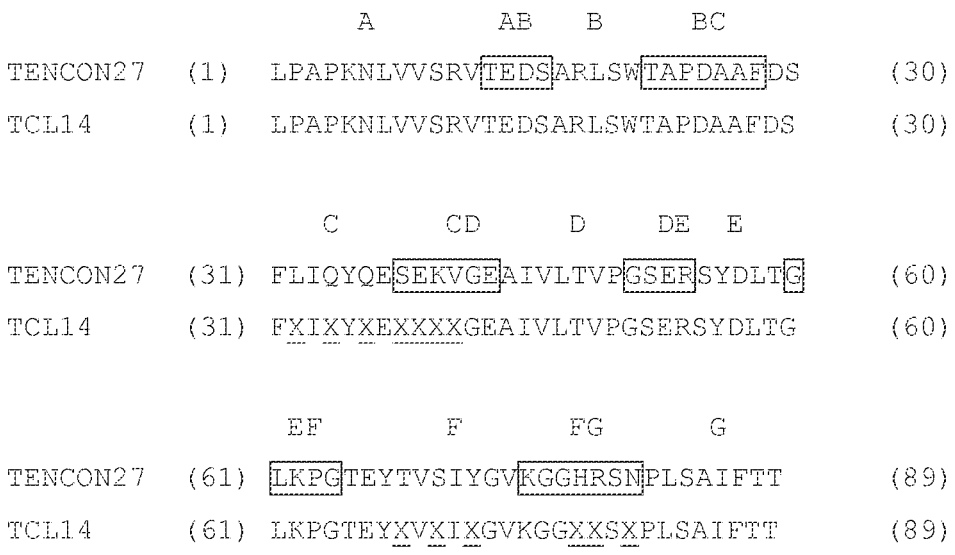

A AB B BC
TENCON27 (1) LPAPKNLVVSRVTEDSARLSWTAPDAAFDS (30)
TCL14 (1) LPAPKNLVVSRVTEDSARLSWTAPDAAFDS (30)
C CD D DE E
TENCON27 (31) FLIQYQESEKVGEAIVLTVPGSERSYDLTG (60)
TCL14 (31) FXIXYXEXXXXGEAIVLTVPGSERSYDLTG (60)
EF F FG G
TENCON27 (61) LKPGTEYTVSIYGVKGGHRSNPLSAIFTT (89)
TCL14 (61) LKPGTEYXVXIXGVKGGXXSXPLSAIFTT (89)

Figure 3.


SEQ ID
NO:
32 LPAPKNLVVSRVTEDSARLSWTAPDAAEDSFWIRYDEVVVGGEAIVLTVPGSERSYDLTG (60)
33 LPAPKNLVVSRVTEDSARLSWTAPDAAEDSFFIRYDEFLRSGEAIVLTVPGSERSYDLTG
34 LPAPKNLVVSRVTEDSARLSWTAPDAAEDSFWIRYFEFLGSGEAIVLTVPGSERSYDLTG
35 LPAPKNLVVSRVTEDSARLSWTAPDAAEDSFWIRYFEFLGSGEAIVLTVPGSERSYDLTG
36 LPAPKNLVVSRVTEDSARLSWTAPDAAEDSFVIRYFEFLGSGEAIVLTVPGSERSYDLTG
37 LPAPKNLVVSRVTEDSARLSWTAPDAAEDSFWIRYLEFLLGGEAIVLTVPGSERSYDLTG
38 LPAPKNLVVSRVTEDSARLSWTAPDAAEDSFWIRYFEFLGSGEAIVLTVPGSERSYDLTG
39 LPAPKNLVVSRVTEDSARLSWTAPDAAEDSFWIRYFEFLGSGEAIVLTVPGSERSYDLTD
40 LPAPKNLVVSRVTEDSARLSWTAPDAAEDSFWIRYFEFLGSGEAIVLTVPGSERSYDLTG
41 LPAPKNLVVSRVTEDSARLSWTAPDAAEDSFWIRYFEFLGSGEAIVLTVPGSERSYDLTG
42 LPAPKNLVVSRVTEDSARLSWTAPDAAEDSFWIRYFEFLGSGEAIVLTVPGSERSYDLTG
43 LPAPKNLVVSRVTEDSARLSWTAPDAAEDSFWIRYFEFLGSGEAIVLTVPGSERSYDLTG
44 LPAPKNLVVSRVTEDSARLSWTAPDAAEDSFWIRYFEFLGSGEAIVLTVPGSERSYDLTG
45 LPAPKNLVVSRVTEDSARLSWTAPDAAEDSFWIRYFEFLGSGEAIVLTVPGSERSYDLTG
46 LPAPKNLVVSRVTEDSARLSWTAPDAAEDSFWIRYFEFLGSGEAIVLTVPGSERSYDLTG
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49 LPAPKNLVVSRVTEDSARLSWTAPDAAEDSFWIRYFEFVSKGEAIVLTVPGSERSYDLTG
111 LPAPKNLVVSRVTEDSARLSWTAPDAAEDSFWIRYFEFLGSGEAIVLTVPGSERSYDLTG
112 LPAPKNLVVSRVTEDSARLSWTAPDAAEDSFWIRYFEFVGSGEAIVLTVPGSERSYDLTG
113 LPAPKNLVVSRVTEDSARLSWTAPDAAEDSFWIRYFEFVSKGDAIVLTVPGSERSYDLTG
114 LPAPKNLVVSRVTEDSARLSWTAPDAAEDSFWIRYFEFLGSGEAIVLTVPGSERSYDLTG

Figure 3 (continued)

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SEQ ID
NO:

32                LKPGTEYYVNILGVKGGSISVPLSAIFTT              (89)
33                LKPGTEYWVTILGVKGGLVSTPLSAIFTT
34                LKPGTEYIVNIMGVKGGSISHPLSAIFTT
35                LKPGTEYVVNILGVKGGGLSVPLSAIFTT
36                LKPGTEYVVQILGVKGGYISIPLSAIFTT
37                LKPGTEYVVQIMGVKGGTVSPPLSAIFTT
38                LKPGTEYVVGINGVKGGYISYPLSAIFTT
39                LKPGTEYGVTINGVKGGRVSTPLSAIFTT
40                LKPGTEYVVQIIGVKGGHISLPLSAIFTT
41                LKPGTEYVVNIMGVKGGKISPPLSAIFTT
42                LKPGTEYAVNIMGVKGGRVSVPLSAIFTT
43                LKPGTEYVVQILGVKGGSISVPLSAIFTT
44                LKPGTEYVVNIMGVKGGSISYPLSAIFTT
45                LKPGTEYVVQILGVKGGYISIPLSAIFTT
46                LKPGTEYVVQIMGVKGGTVSPPLSAIFTT
47                LKPGTEYVVNIMGVKGGSISPPLSAIFTT
48                LKPGTEYVVNIMGVKGGSISPPLSAIFTT
49                LKPGTEYVVNIMGVKGGSISPPLSAIFTT
111               LKPGTEYVVNILGVKGGKISPPLSAIFTT
112               LKPGTEYVVNILGVKGGSISPPLSAIFTT
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114               LKPGTEYVVNILSVKGGSISPPLSAIFTT
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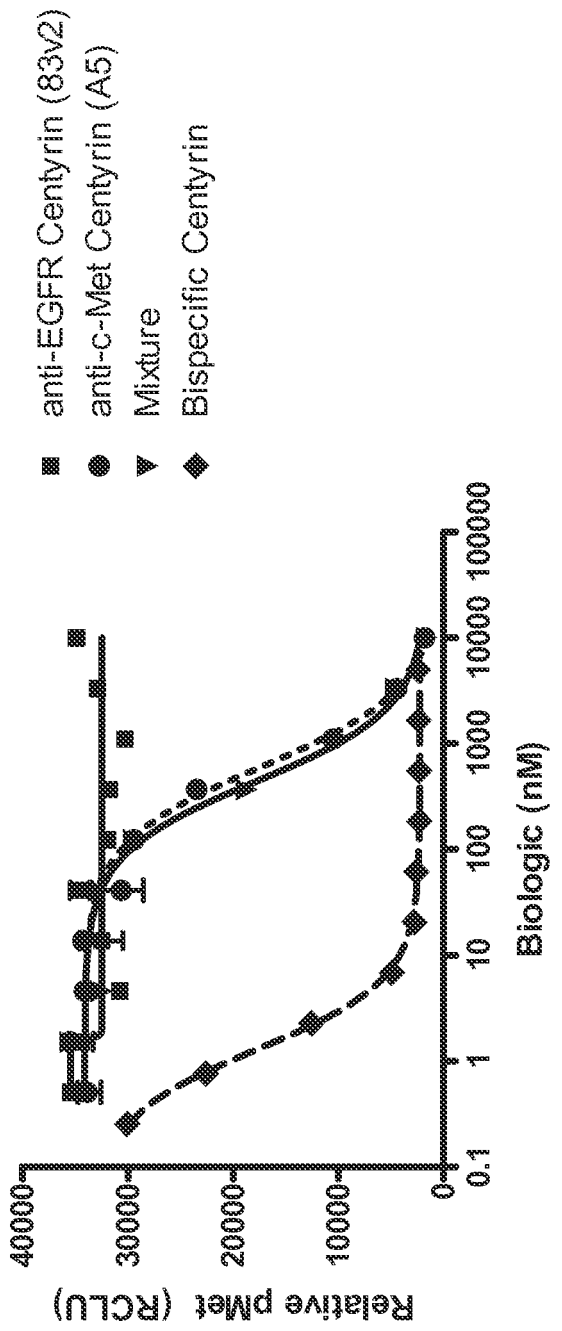
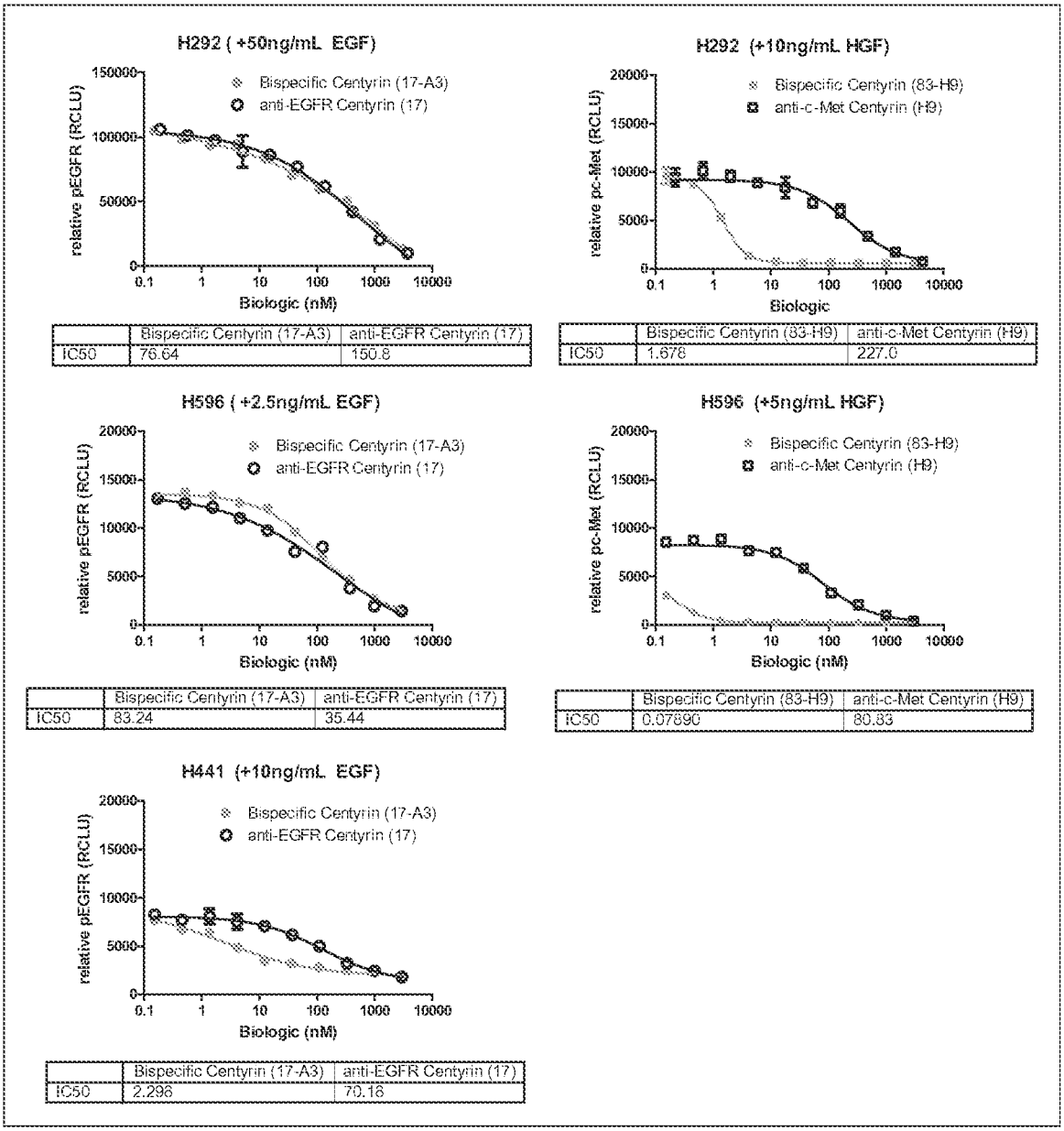

anti-EGFR Centyrin (83v2)
anti-c-Met Centyrin (A5)
Mixture
Bispecific Centyrin
Relative pMet (RCLU)
40000
30000
20000
10000
0
0.1
1
10
100
1000
10000
100000
Biologic (nM)

Figure 4.

Figure 5.



	Bispecific Centyrin (17-A3)	anti-EGFR Centyrin (17)
IC50	76.64	150.8

	Bispecific Centyrin (83-H9)	anti-c-Met Centyrin (H9)
IC50	1.676	227.0

	Bispecific Centyrin (17-A3)	anti-EGFR Centyrin (17)
IC50	83.24	35.44

	Bispecific Centyrin (83-H9)	anti-c-Met Centyrin (H9)
IC50	0.07890	80.83

	Bispecific Centyrin (17-A3)	anti-EGFR Centyrin (17)
IC50	2.296	70.16

Figure 6.

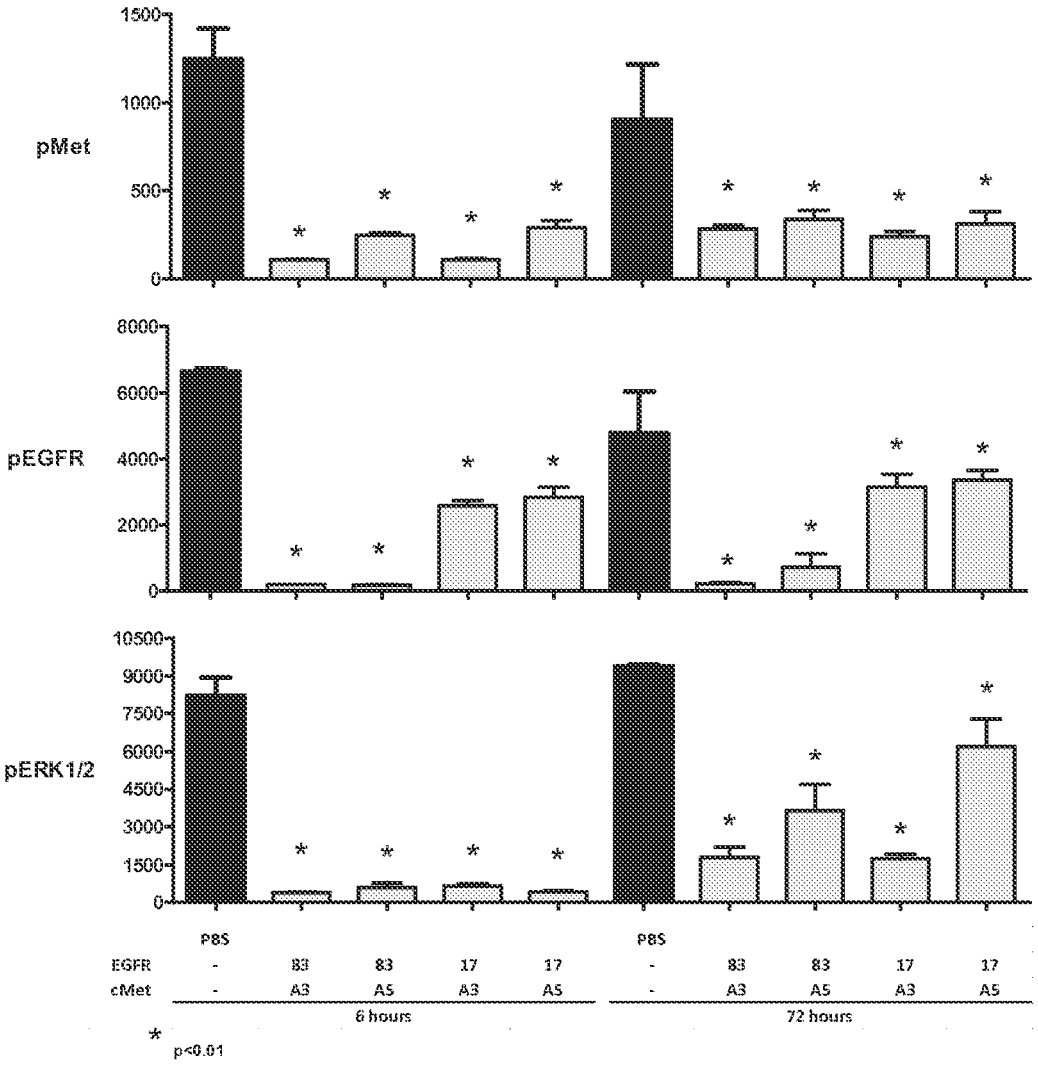


Figure 7.

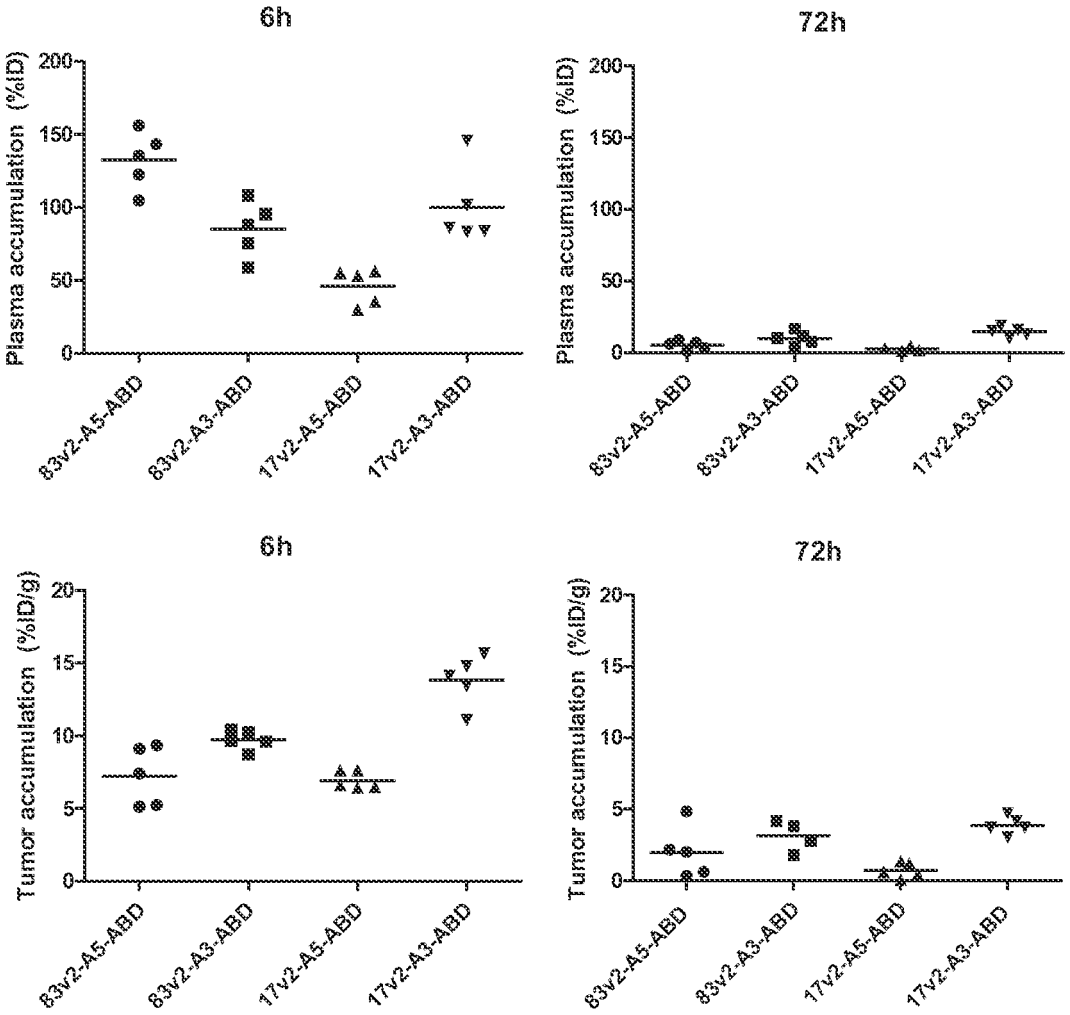

6h
72h
Plasma accumulation (%ID)
Tumor accumulation (%ID/g)
0
50
100
150
200
5
10
15
20
83v2-A5-ABD
83v2-A3-ABD
17v2-A5-ABD
17v2-A3-ABD

Figure 8.

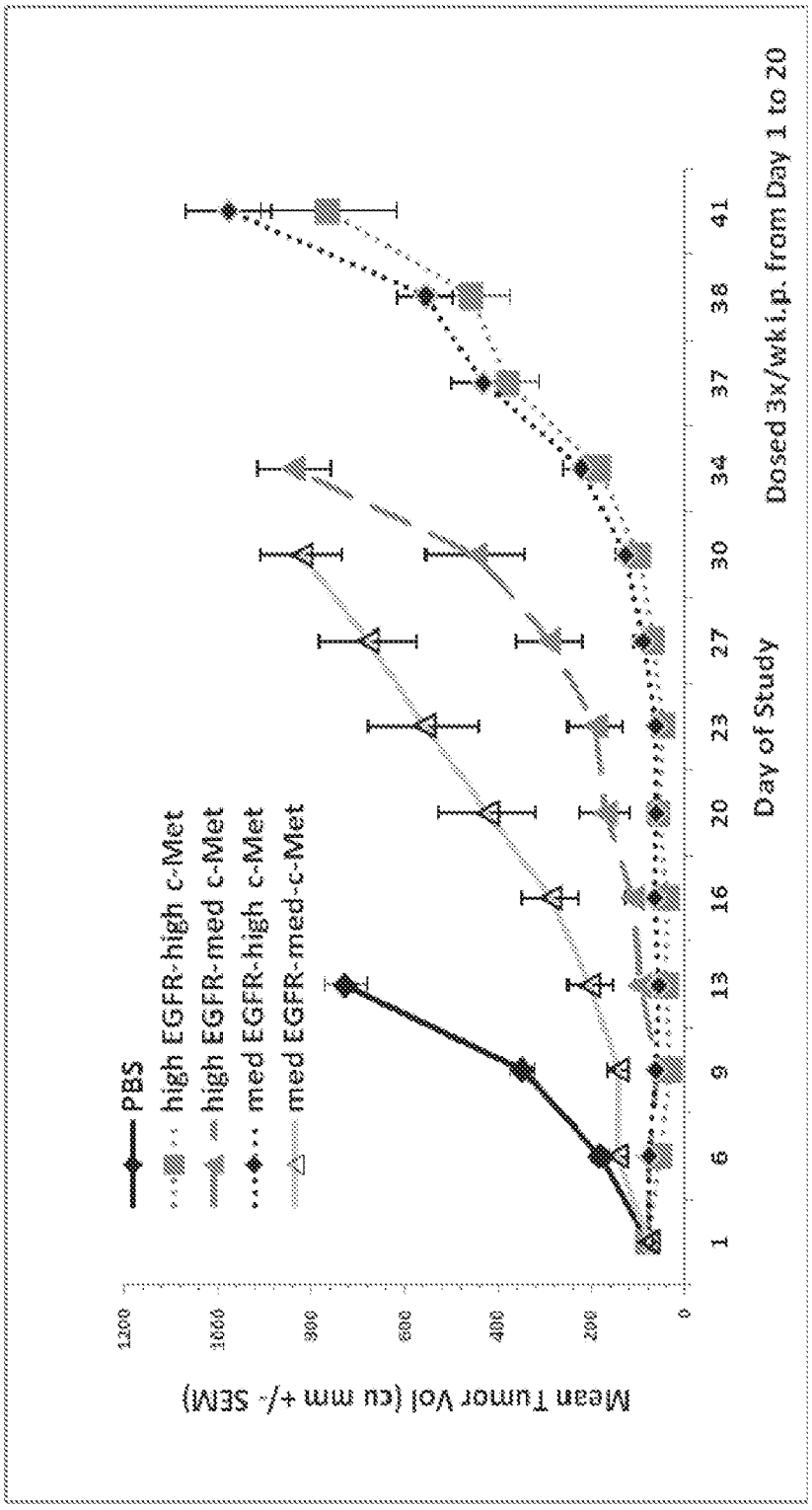
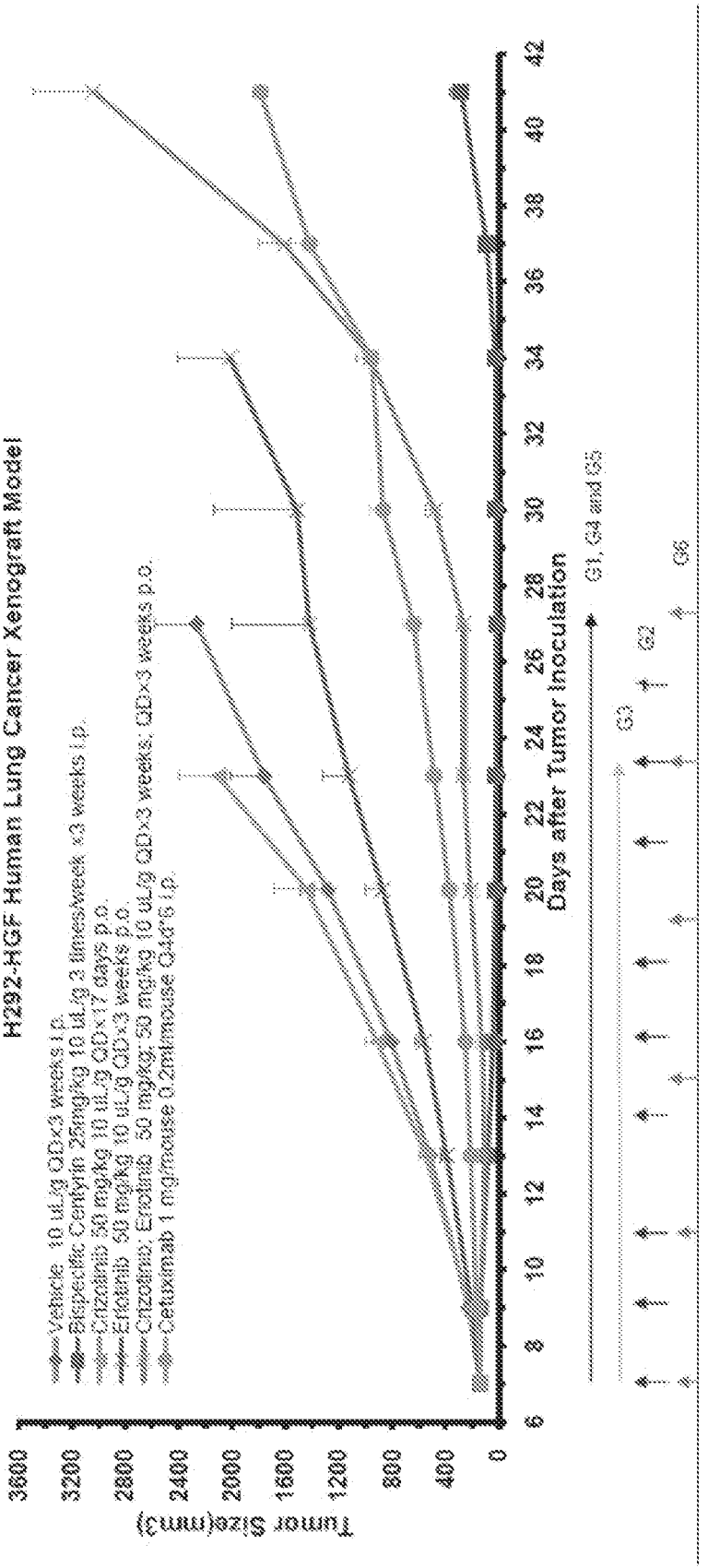

Mean Tumor Vol (cu mm +/- SEM)
1200
1000
800
600
400
200
0
1
6
9
13
16
20
23
27
30
34
37
38
41
Day of Study
Dosed 3x/wk i.p. from Day 1 to 20
PBS
high EGFR-high c-Met
high EGFR-med c-Met
med EGFR-high c-Met
med EGFR-med-c-Met

Figure 9.


H292-HGF Human Lung Cancer Xenograft Model
Vehicle 10 uL/g QDx3 weeks i.p.
Bispecific Centyrin 25mg/kg 10 uL/g 3 times/week x3 weeks i.p.
Crizotinib 50 mg/kg 10 uL/g QDx17 days p.o.
Erlotinib 50 mg/kg 10 uL/g QDx3 weeks p.o.
Crizotinib; Erlotinib 50 mg/kg; 50 mg/kg 10 uL/g QDx3 weeks, QDx3 weeks p.o.
Cetuximab 1 mg/mouse 0.2ml/mouse Q4d*6 i.p.
Tumor Size(mm3)
3600
3200
2800
2400
2000
1600
1200
800
400
0
6
8
10
12
14
16
18
20
22
24
26
28
30
32
34
36
38
40
42
Days after Tumor Inoculation
G1, G4 and G5
G3
G2
G6