Fig. 1

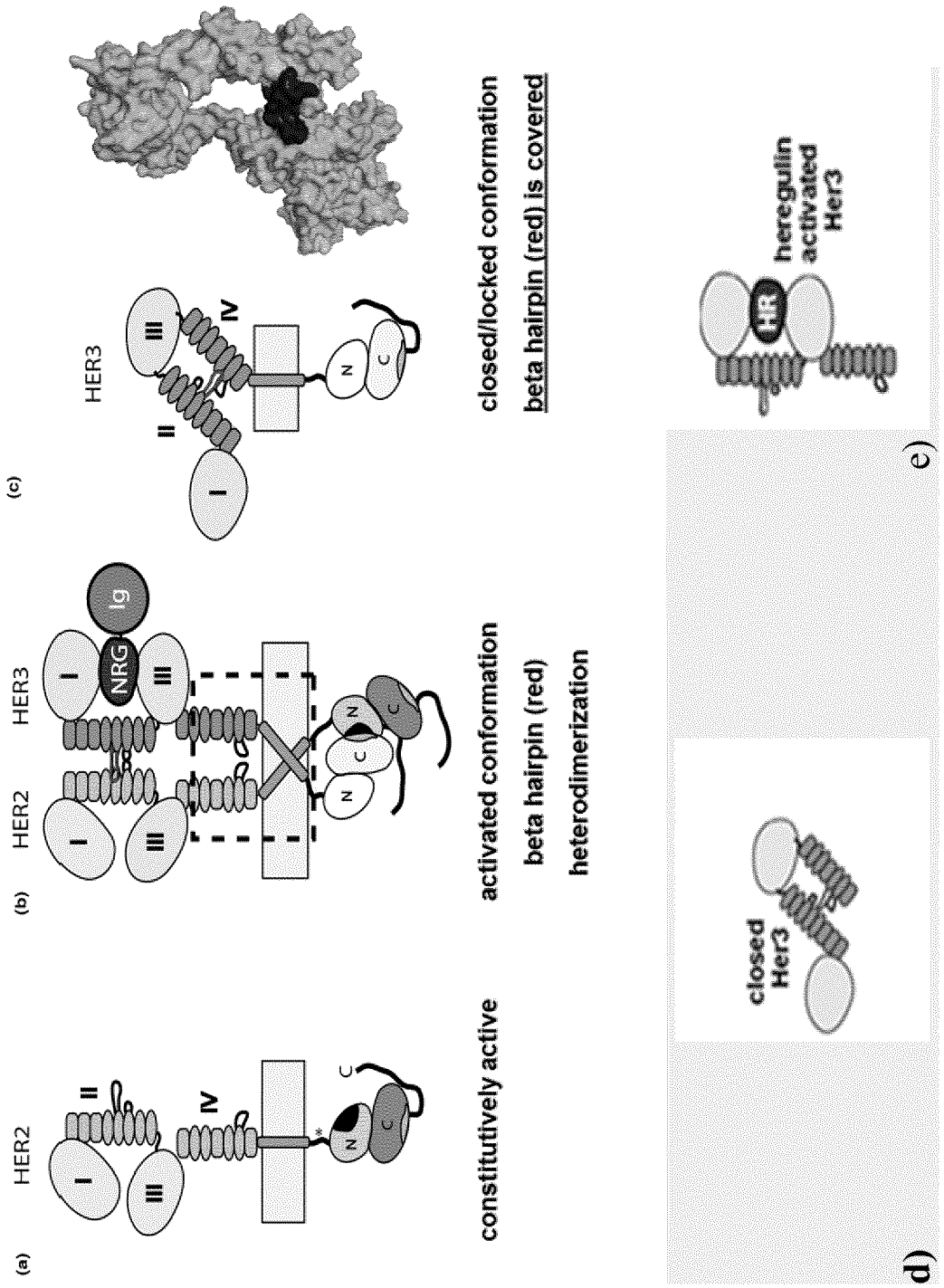

(a)
HER2
I
II
III
IV
C
N
C
constitutively active
(b)
HER2
HER3
I
III
NRG
Ig
N
C
C
N
activated conformation
beta hairpin (red)
heterodimerization
(c)
HER3
I
II
III
IV
N
C
closed/locked conformation
beta hairpin (red) is covered
d)
closed Her3
e)
HR
heregulin activated Her3

Fig. 2

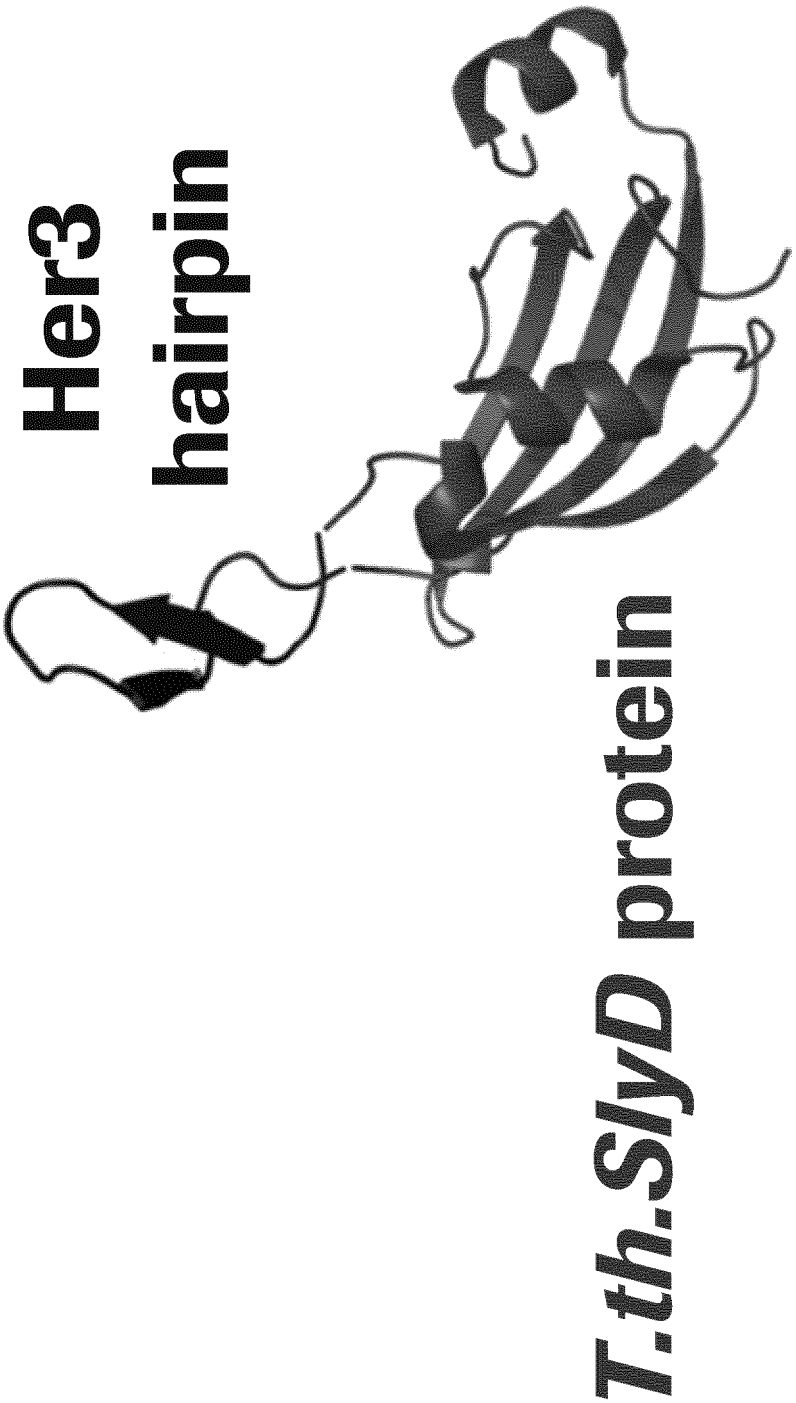


Fig. 3

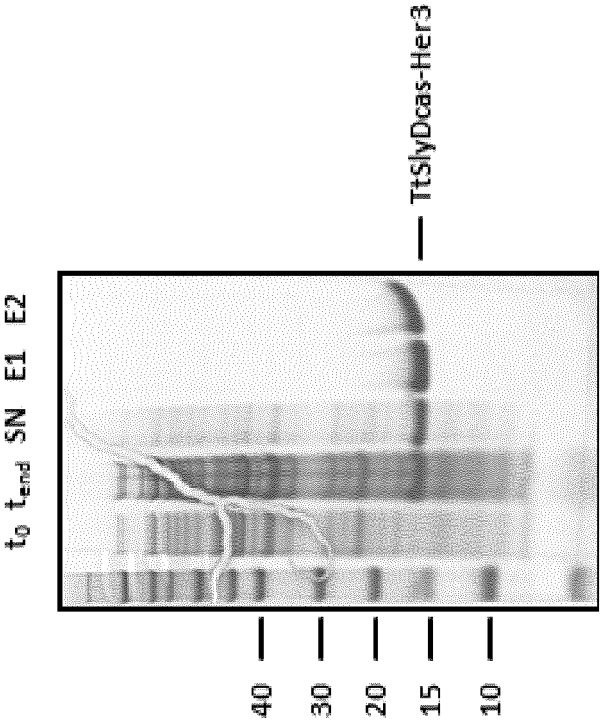


Fig. 4

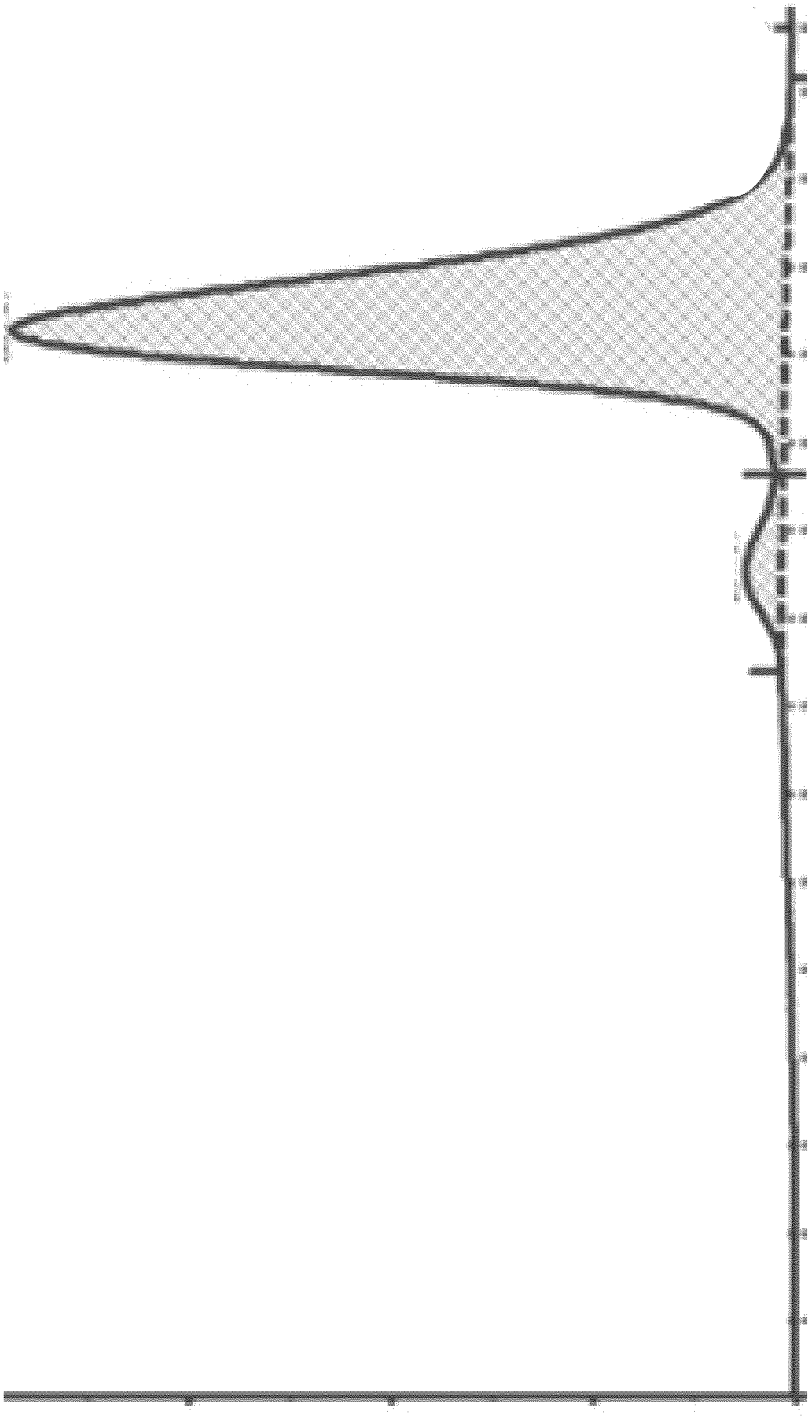


Fig. 5

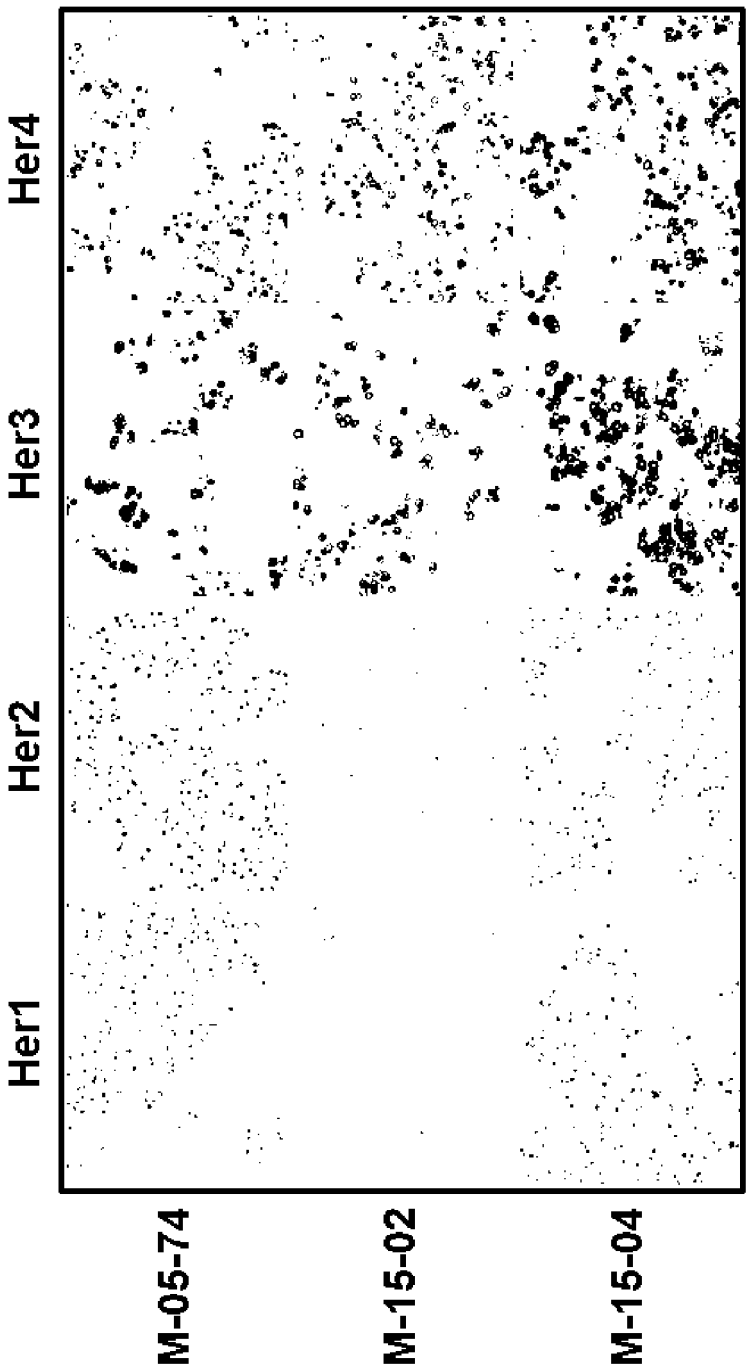


Fig. 6

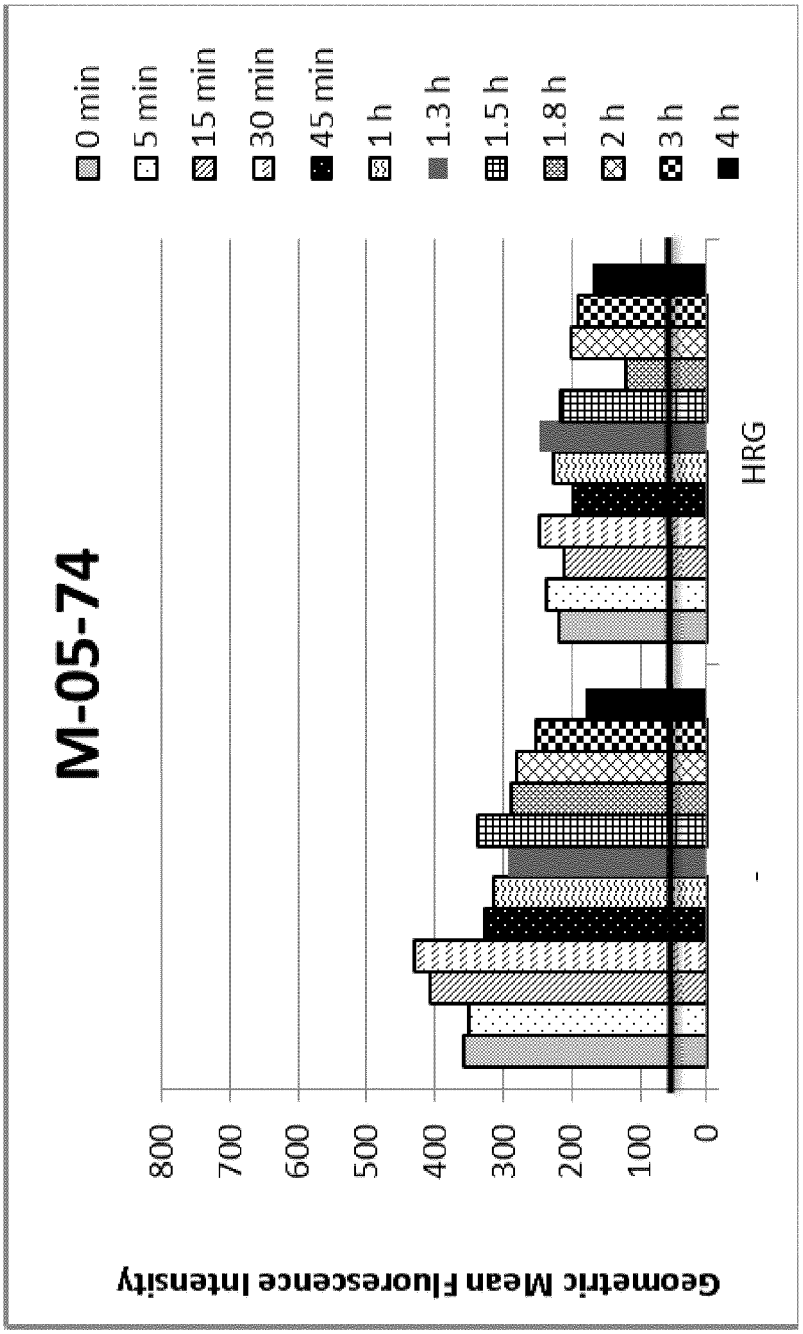

M-05-74
Geometric Mean Fluorescence Intensity
800
700
600
500
400
300
200
100
0
-
HRG
0 min
5 min
15 min
30 min
45 min
1 h
1.3 h
1.5 h
1.8 h
2 h
3 h
4 h

Fig. 7

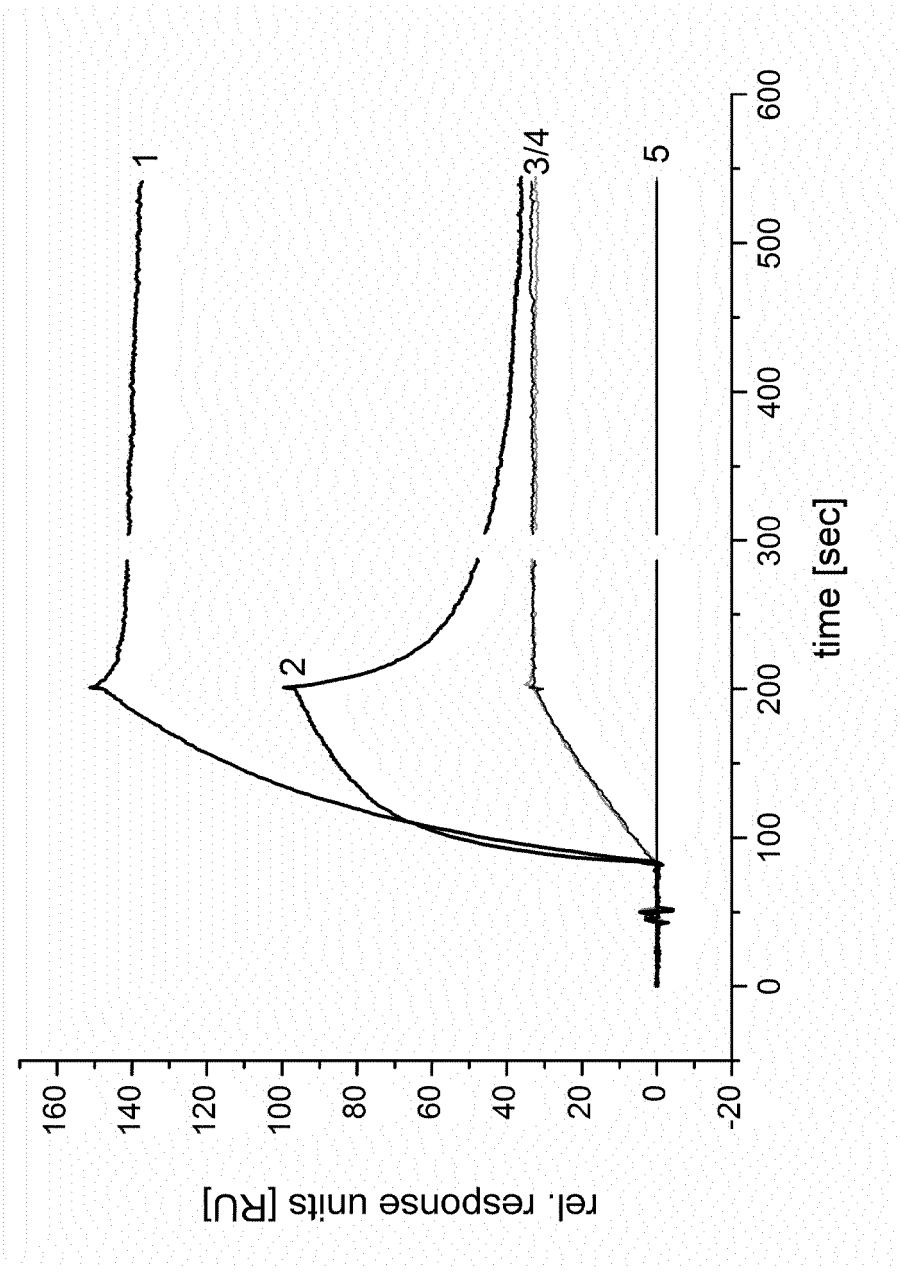

rel. response units [RU]
time [sec]
1
2
3/4
5
160
140
120
100
80
60
40
20
0
-20
0
100
200
300
400
500
600

Fig. 8

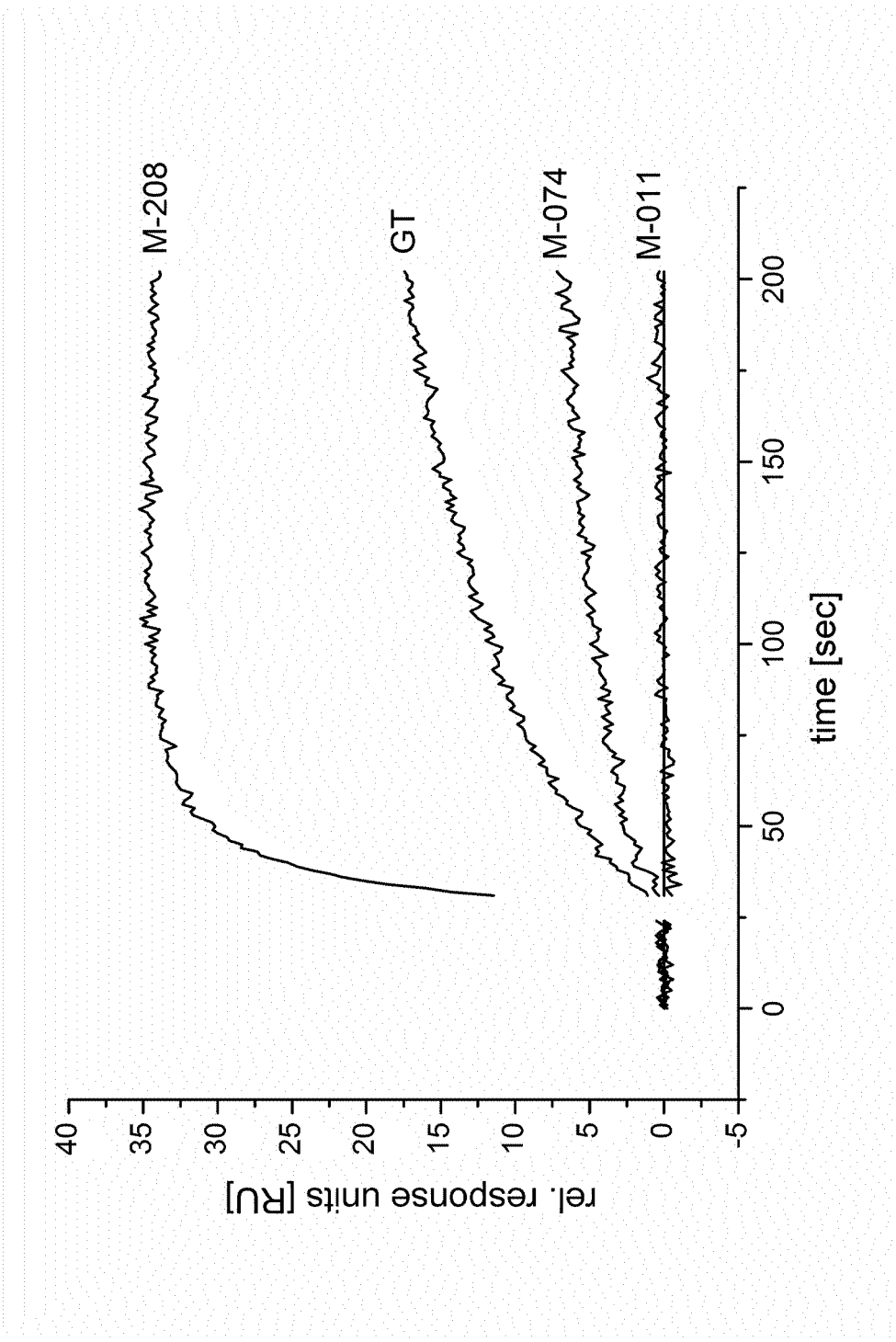

M-208
GT
M-074
M-011
rel. response units [RU]
time [sec]
40
35
30
25
20
15
10
5
0
-5
0
50
100
150
200

Fig. 9

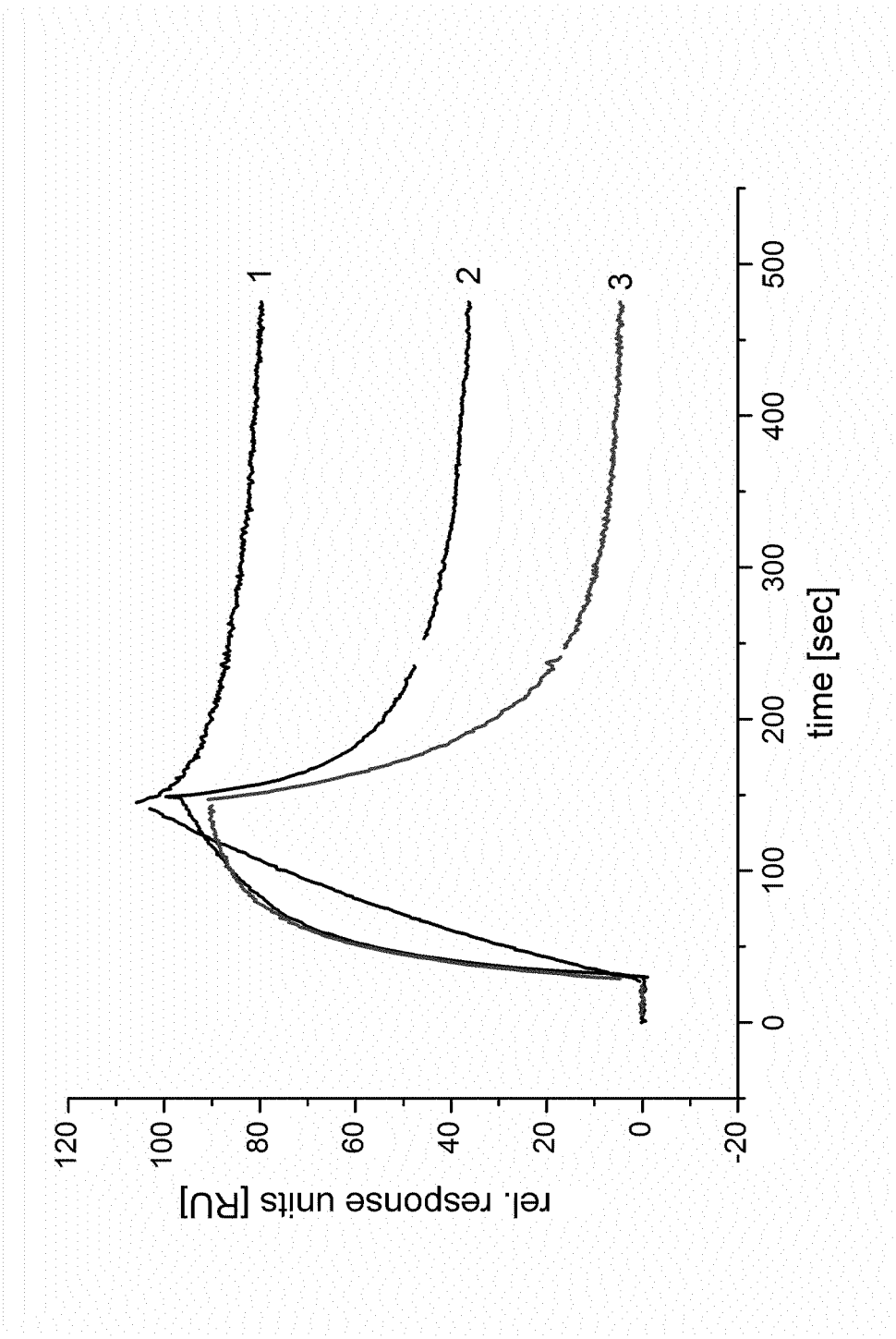

rel. response units [RU]
120
100
80
60
40
20
0
-20
0
100
200
300
400
500
time [sec]
1
2
3

Fig. 10

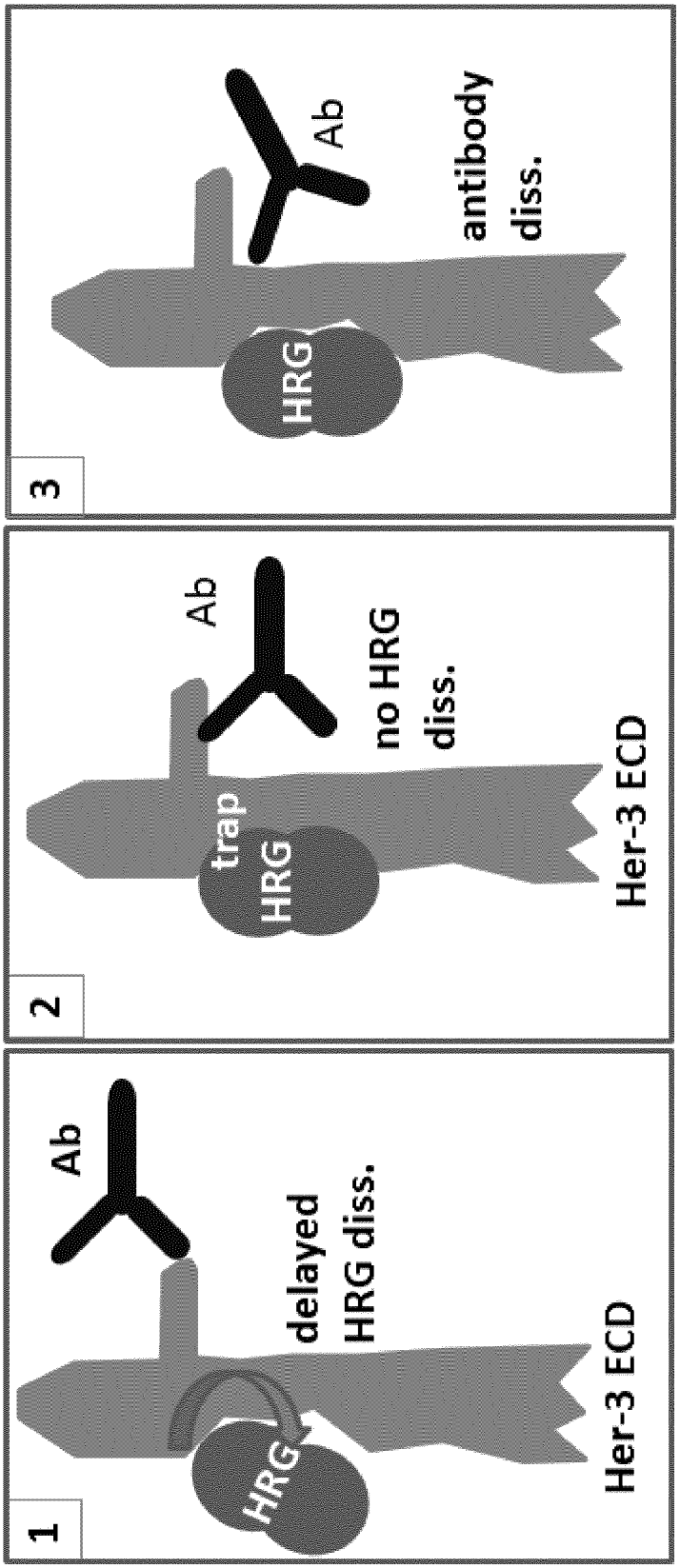

1
Ab
delayed
HRG diss.
HRG
Her-3 ECD
2
Ab
trap
HRG
no HRG
diss.
Her-3 ECD
3
Ab
antibody
diss.
HRG

Fig. 11

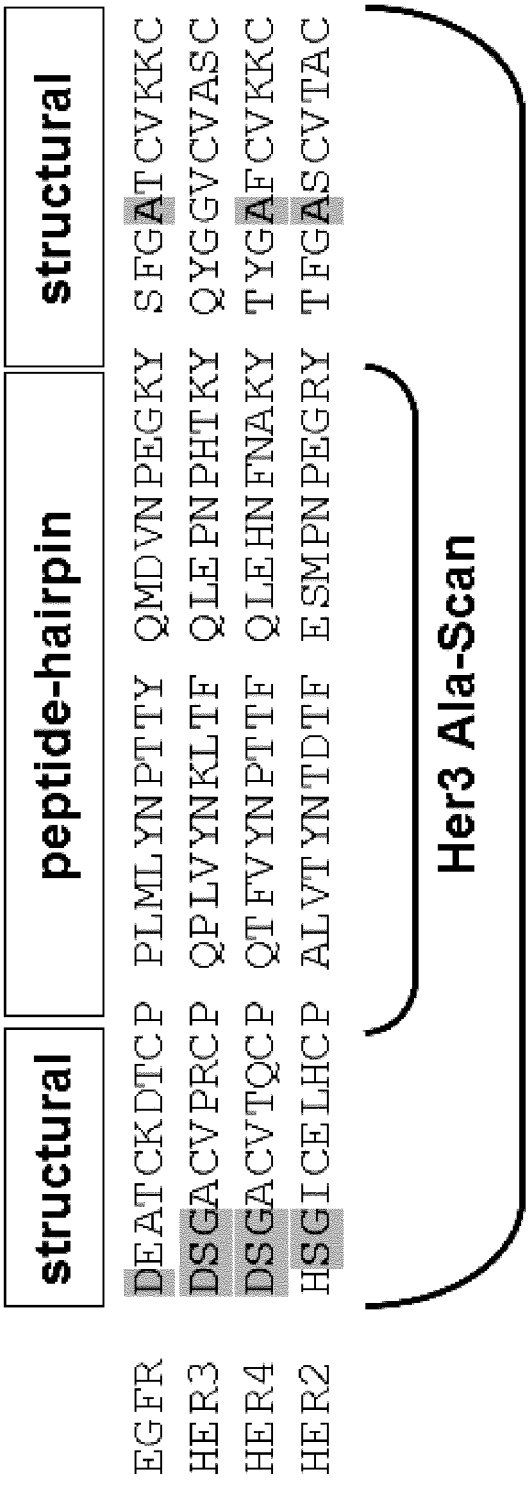

structural
peptide-hairpin
structural
EGFR DEATCKDTCP PLMLYNPTTY QMDVNPEGKY SFGATCVKKC
HER3 DSGACVPRCP QPLVYNKLTF QLEPNPHTKY QYGGVCVASC
HER4 DSGACVTQCP QTFVYNPTTF QLEHNFNAKY TYGAFCVKKC
HER2 HSGICELHCP ALVTYNTDTF ESMPNPEGRY TFGASCVTAC
Her3 Ala-Scan
Epitope Mapping
*Cys were exchanged to Ser

Fig. 12

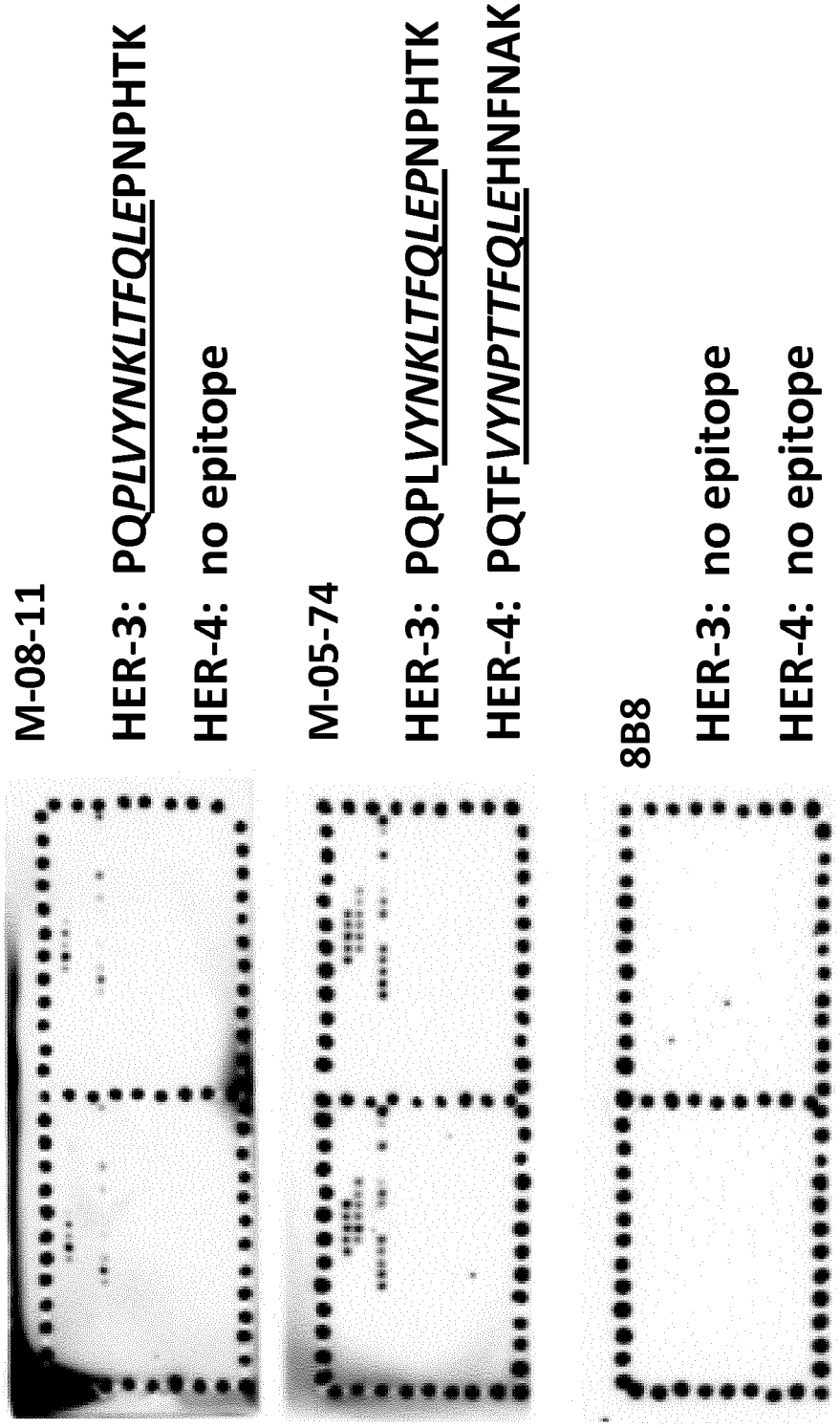

M-08-11
HER-3: PQPLVYNKLTFQLEPNPHTK
HER-4: no epitope
M-05-74
HER-3: PQPLVYNKLTFQLEPNPHTK
HER-4: PQTFVYNPTTFQLEHNFNAK
8B8
HER-3: no epitope
HER-4: no epitope

Fig. 13

M-074 HER3: PQPLVYNKLTFQLEPNPHTK
M-011 HER3: PQPLVYNKLTFQLEPNPHTK

Fig. 14

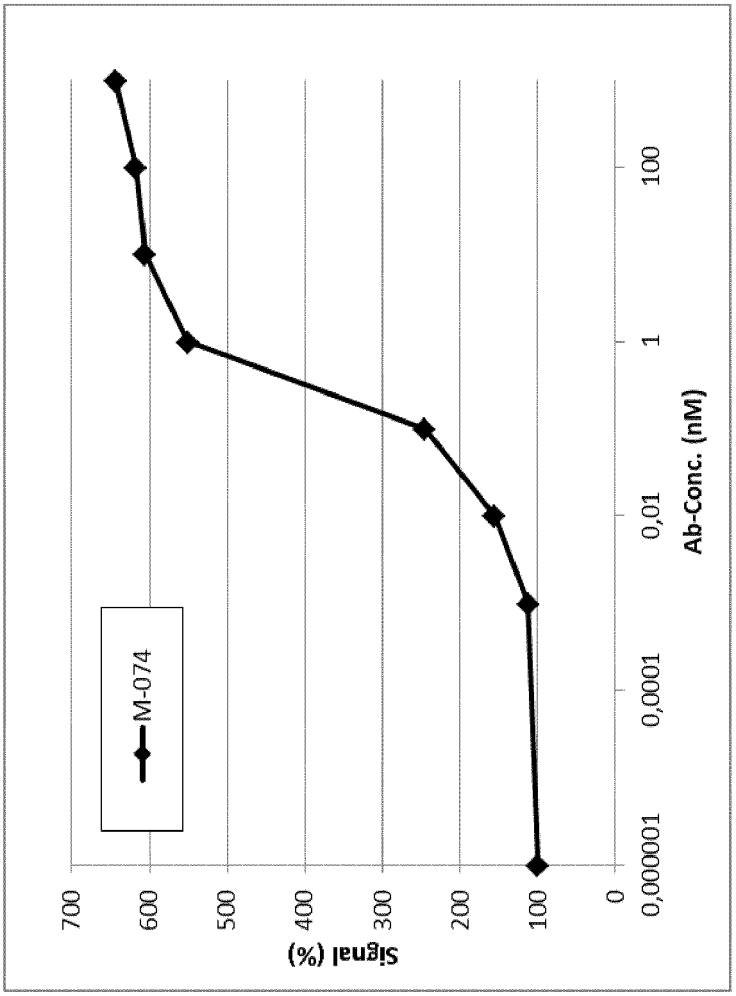


Fig. 15

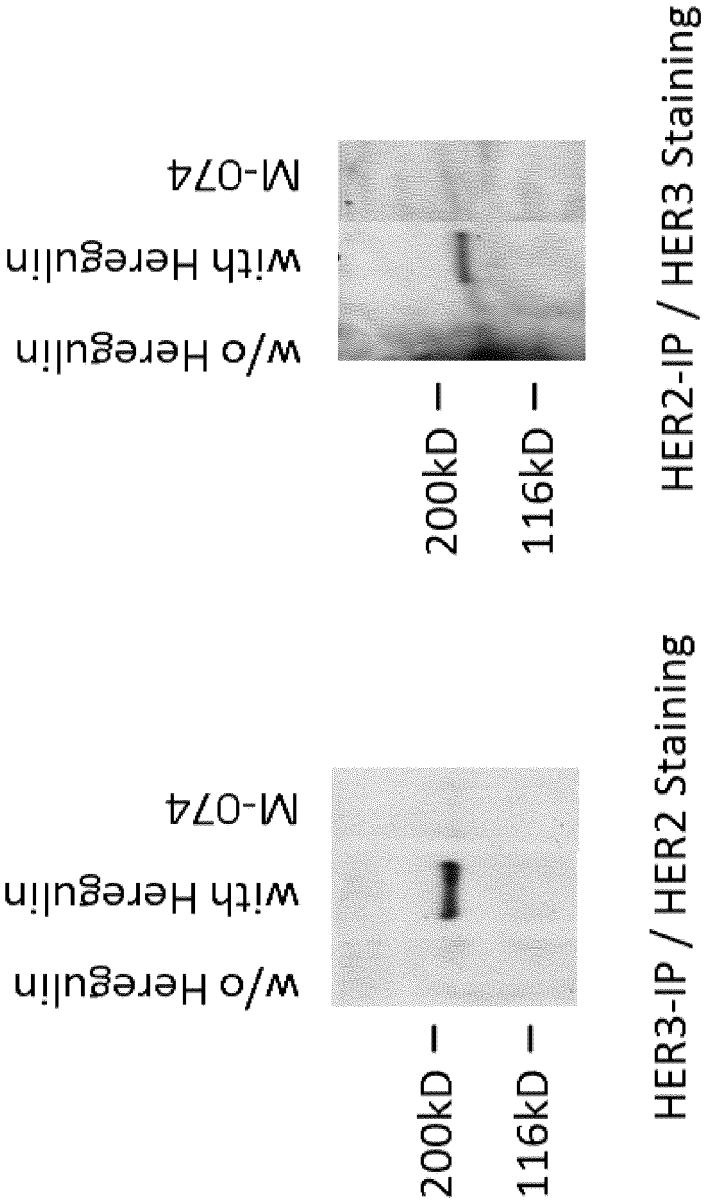

HER3-IP / HER2 Staining
HER2-IP / HER3 Staining
200kD
116kD
w/o Heregulin
with Heregulin
M-074

Fig. 16

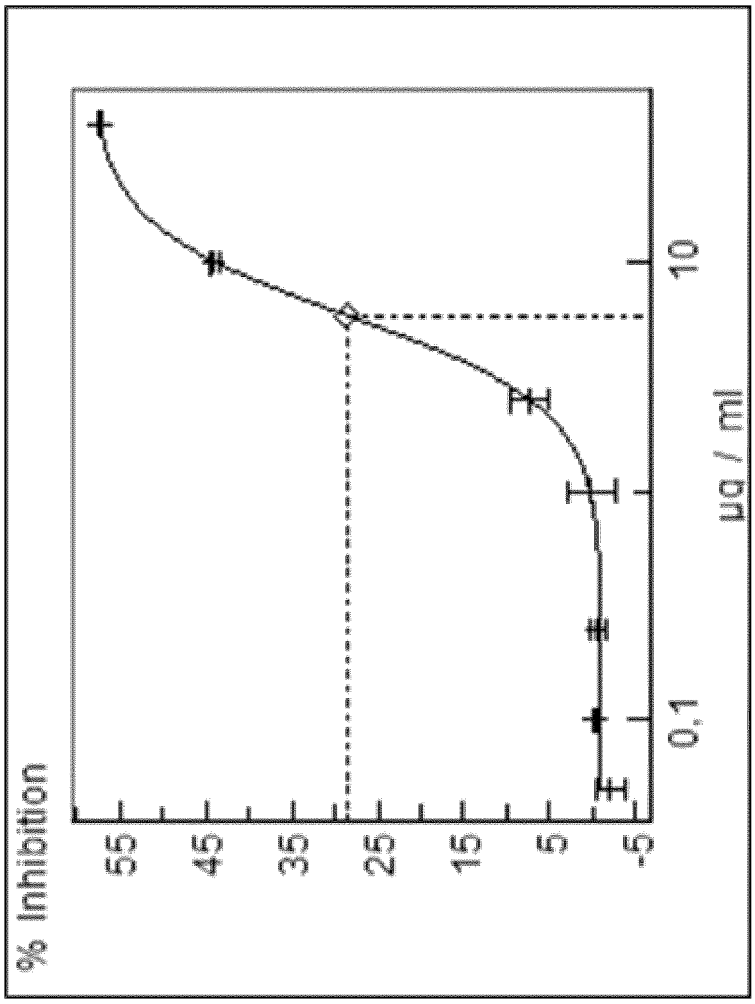


Fig. 17

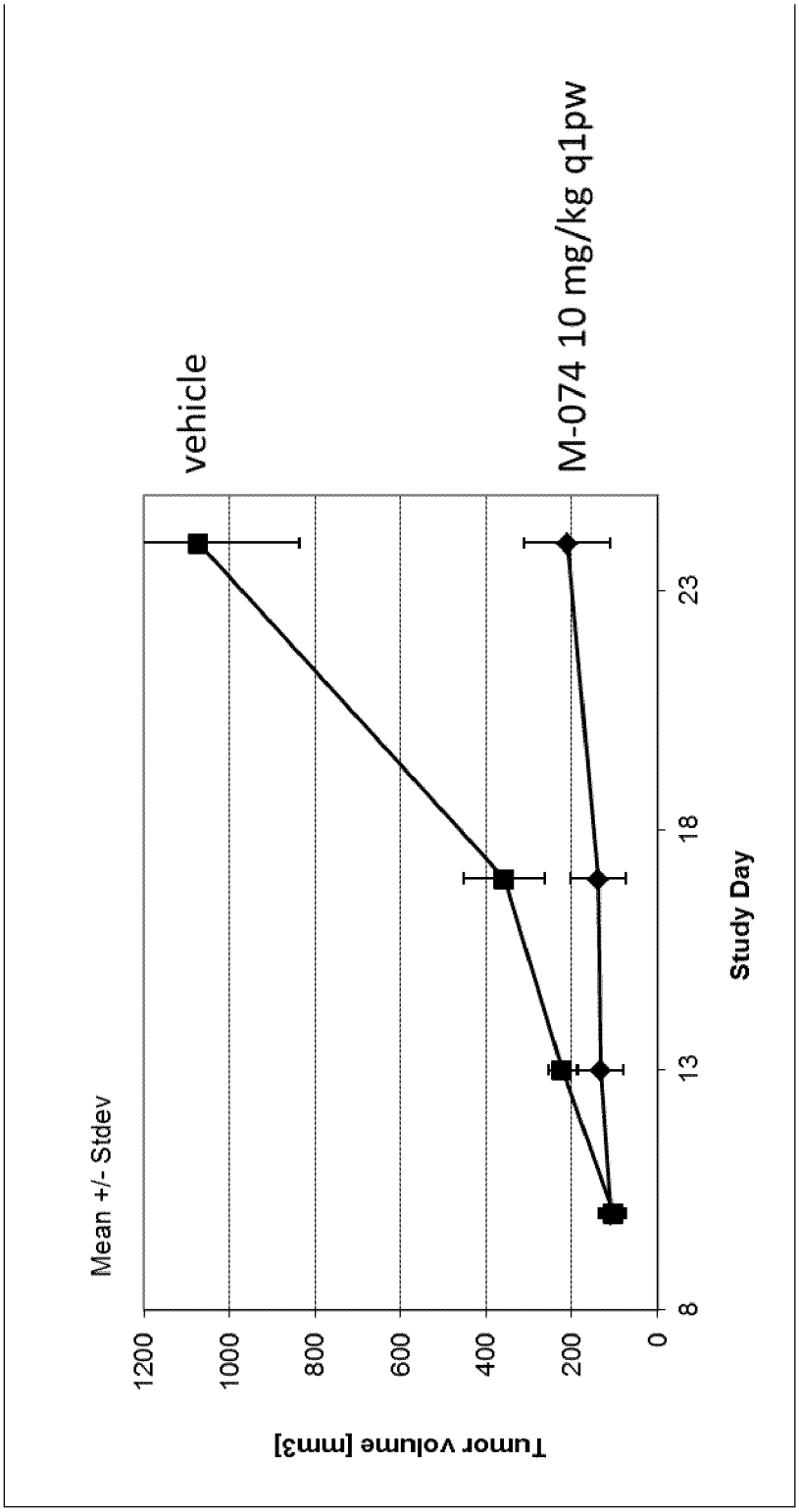

vehicle
M-074 10 mg/kg q1pw
Mean +/- Stdev
Tumor volume [mm3]
1200
1000
800
600
400
200
0
8
13
18
23
Study Day

Fig. 18

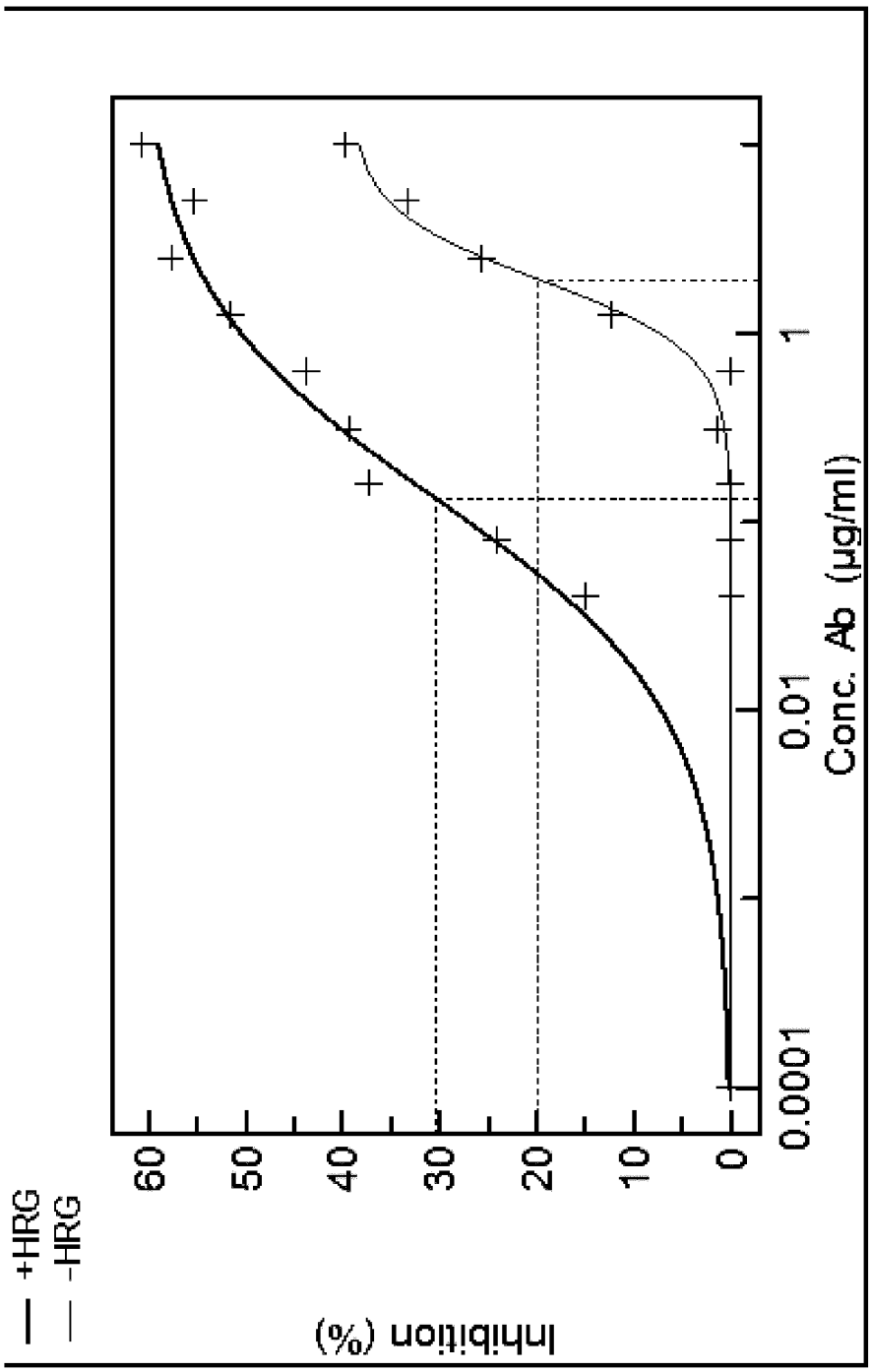


Fig. 19

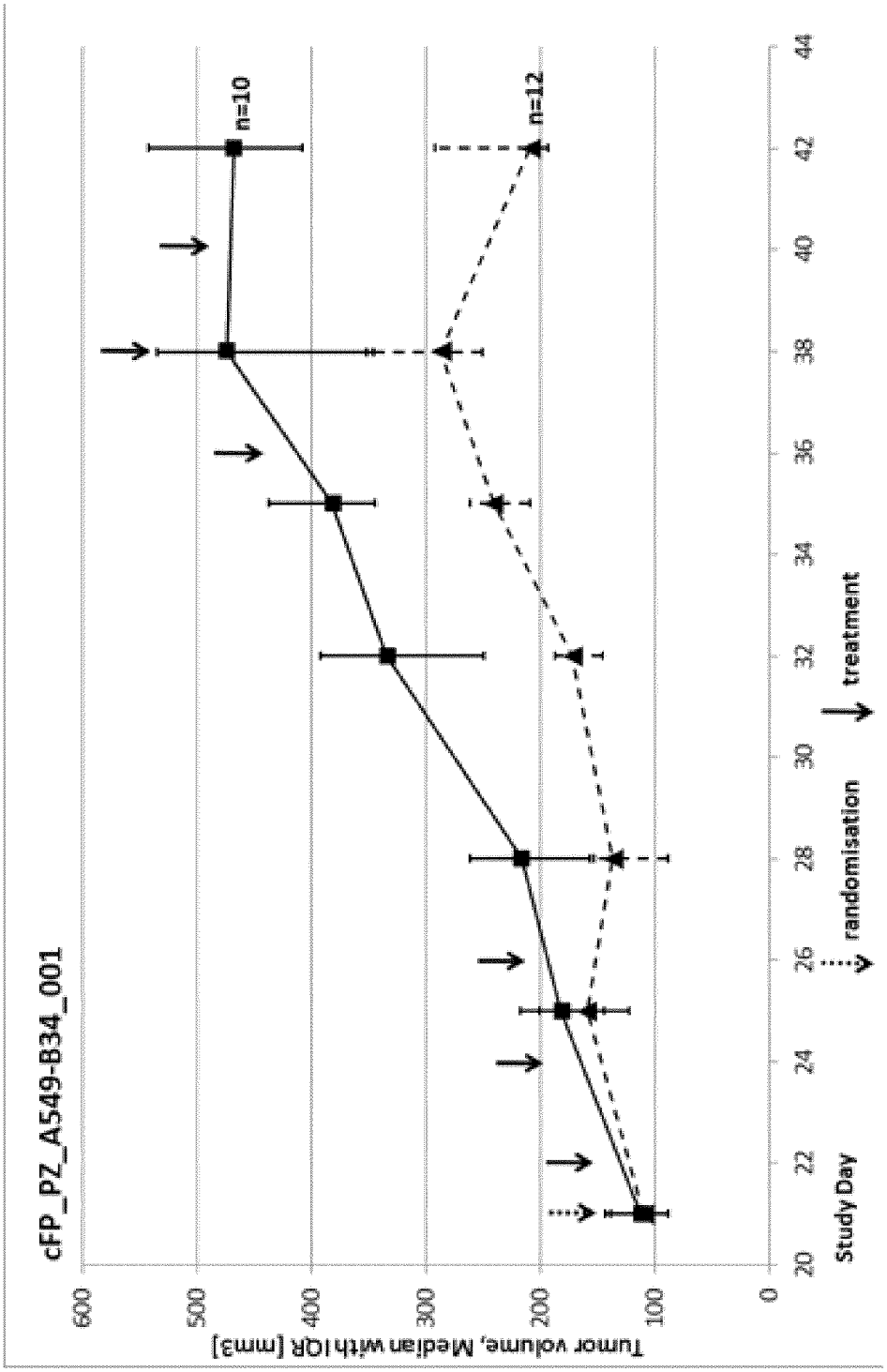

cFP_PZ_A549-B34_001
Tumor volume, Median with IQR [mm3]
600
500
400
300
200
100
0
20
22
24
26
28
30
32
34
36
38
40
42
44
Study Day
randomisation
treatment
n=10
n=12

Fig. 20

