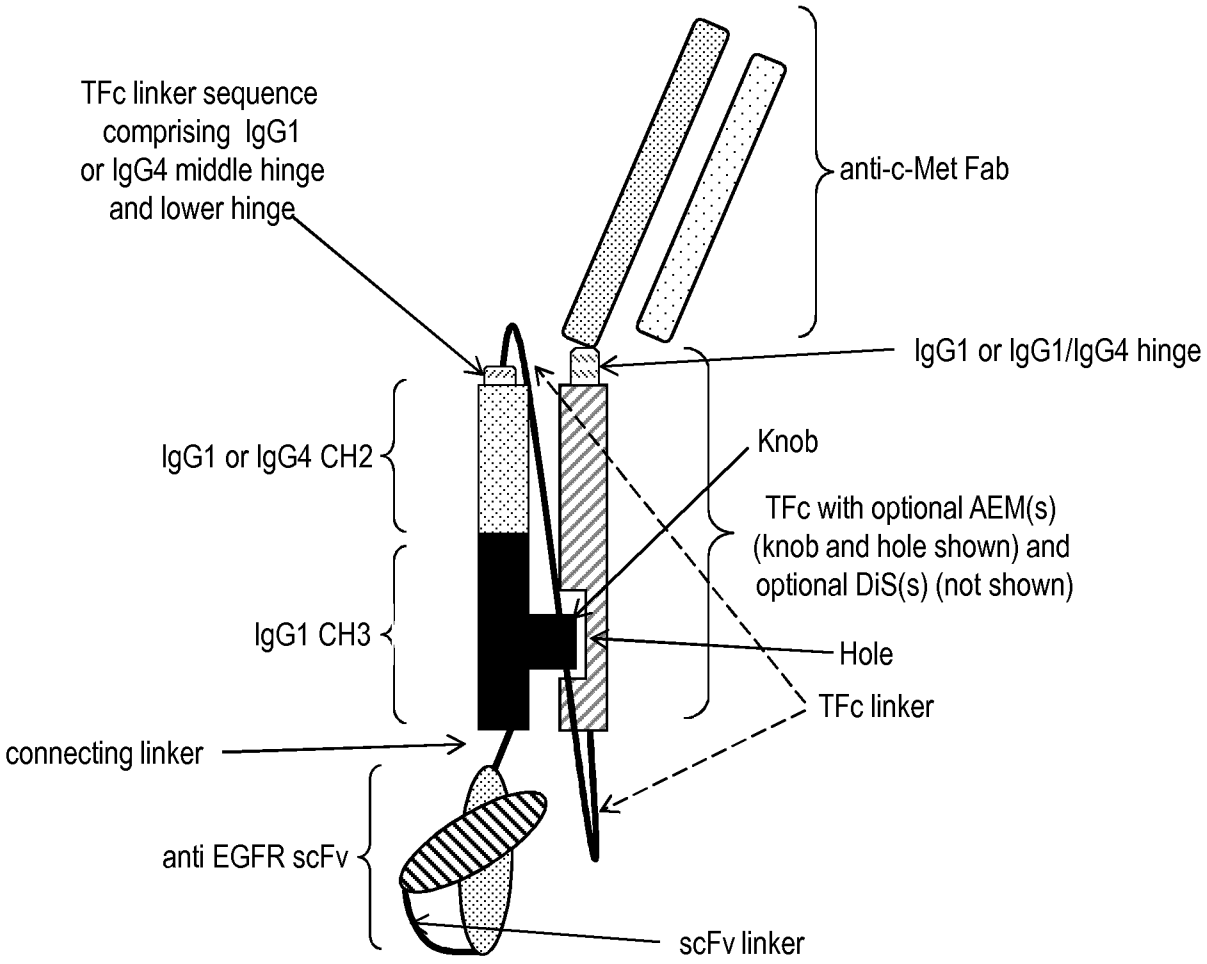

TFc linker sequence
comprising IgG1
or IgG4 middle hinge
and lower hinge
anti-c-Met Fab
IgG1 or IgG1/IgG4 hinge
IgG1 or IgG4 CH2
Knob
TFc with optional AEM(s)
(knob and hole shown) and
optional DiS(s) (not shown)
IgG1 CH3
Hole
TFc linker
connecting linker
anti EGFR scFv
scFv linker

Fig. 1A

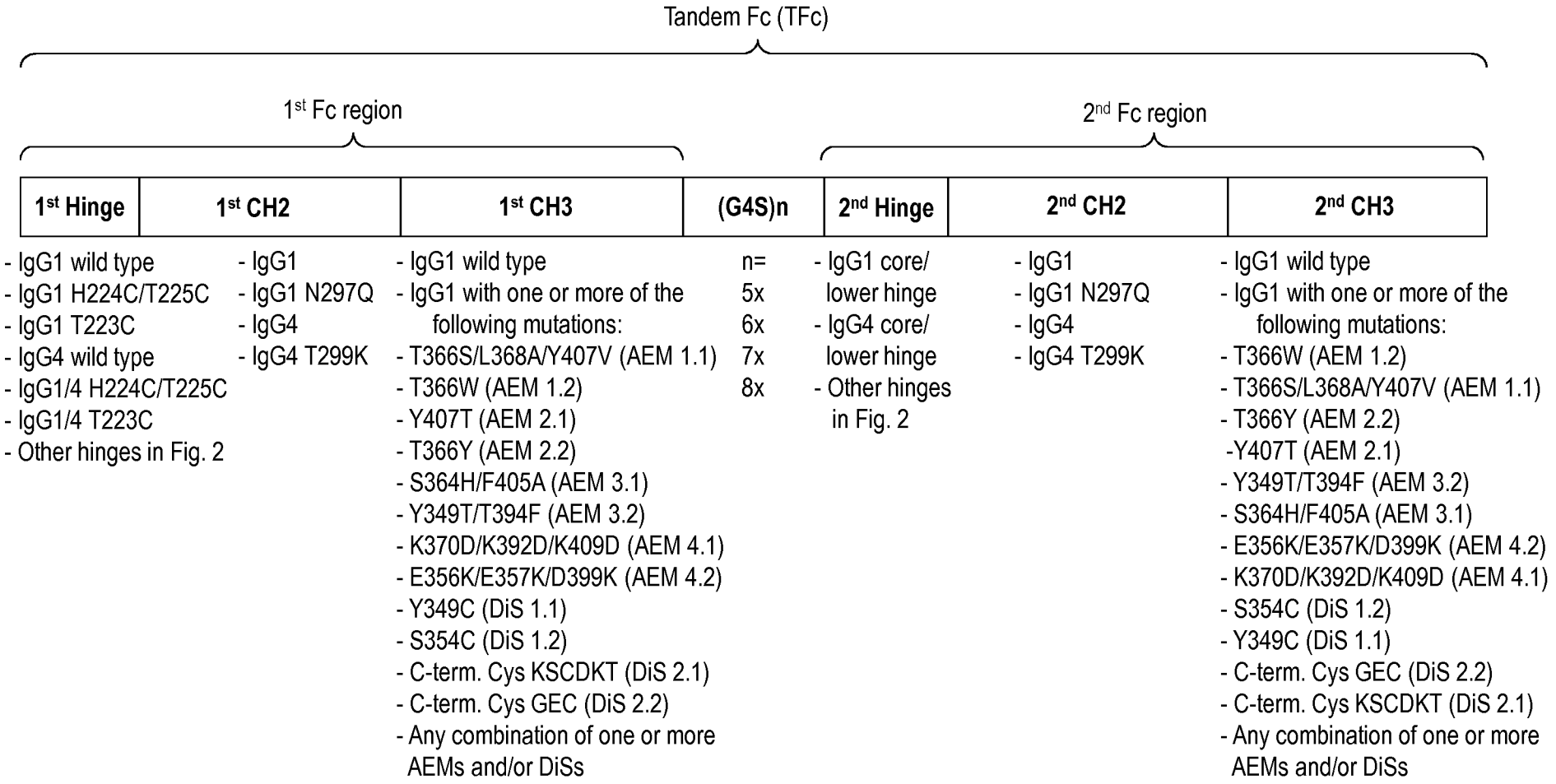

Tandem Fc (TFc)
1st Fc region
2nd Fc region
1st Hinge
1st CH2
1st CH3
(G4S)n
2nd Hinge
2nd CH2
2nd CH3
- IgG1 wild type
- IgG1 H224C/T225C
- IgG1 T223C
- IgG4 wild type
- IgG1/4 H224C/T225C
- IgG1/4 T223C
- Other hinges in Fig. 2
- IgG1
- IgG1 N297Q
- IgG4
- IgG4 T299K
- IgG1 wild type
- IgG1 with one or more of the following mutations:
- T366S/L368A/Y407V (AEM 1.1)
- T366W (AEM 1.2)
- Y407T (AEM 2.1)
- T366Y (AEM 2.2)
- S364H/F405A (AEM 3.1)
- Y349T/T394F (AEM 3.2)
- K370D/K392D/K409D (AEM 4.1)
- E356K/E357K/D399K (AEM 4.2)
- Y349C (DiS 1.1)
- S354C (DiS 1.2)
- C-term. Cys KSCDKT (DiS 2.1)
- C-term. Cys GEC (DiS 2.2)
- Any combination of one or more AEMs and/or DiSs
n=
5x
6x
7x
8x
- IgG1 core/ lower hinge
- IgG4 core/ lower hinge
- Other hinges in Fig. 2
- IgG1
- IgG1 N297Q
- IgG4
- IgG4 T299K
- IgG1 wild type
- IgG1 with one or more of the following mutations:
- T366W (AEM 1.2)
- T366S/L368A/Y407V (AEM 1.1)
- T366Y (AEM 2.2)
-Y407T (AEM 2.1)
- Y349T/T394F (AEM 3.2)
- S364H/F405A (AEM 3.1)
- E356K/E357K/D399K (AEM 4.2)
- K370D/K392D/K409D (AEM 4.1)
- S354C (DiS 1.2)
- Y349C (DiS 1.1)
- C-term. Cys GEC (DiS 2.2)
- C-term. Cys KSCDKT (DiS 2.1)
- Any combination of one or more AEMs and/or DiSs

Fig. 1B

A hIgG1 hinges:

	220 230	
Wild type	EPKSCDKTHTCPPCPAPELLG	SEQ ID NO:4
	----------	SEQ ID NO:1
	-----	SEQ ID NO:2
	------	SEQ ID NO:3
H224C/T225C	--------CC	SEQ ID NO:16
T223C	-------C--	SEQ ID NO:17
H224C/T225C	--------CC----------	SEQ ID NO:18
T223C	-------C----------	SEQ ID NO:19
	----------	SEQ ID NO:23
Extra Ps v1	PPPP----------	SEQ ID NO:263
Extra Ps v2	-----PPP -----	SEQ ID NO:264
Double core	---- -----C-PCP	SEQ ID NO:265

B hIgG1/IgG4 hvbrid hinges:

	220 230	
Wild type	EPKSCDKTHTcpscpapeflg	SEQ ID NO:20
	----------	SEQ ID NO:1
	-----	SEQ ID NO:13
	------	SEQ ID NO:14
H224C/T225C	--------CC----------	SEQ ID NO:21
T223C	-------C----------	SEQ ID NO:22
T223C	----------	SEQ ID NO:24

Fig. 2

(sheet 1 of 2)

C mIgG1 hinges:

```
220
|
Wild type      VPRDCGCKPCICT            SEQ ID NO:266
mIgG1/mIgG2A   -----TI---PPCP           SEQ ID NO:267
```

D hIgG2 hinges:

```
               230       240
                |         |
Wild type      ERKCCVECPPCPAPPVAGP       SEQ ID NO:7
C232P          ---P--------             SEQ ID NO:268
C233P          ----P-------             SEQ ID NO:269
```

E hIgA2 hinges:

```
Wild type      VPPPPP                   SEQ ID NO:270
Modified v1    EPKSCPC-----CCP          SEQ ID NO:271
Modified v2    EPKSCPC----CCP           SEQ ID NO:272
Modified v3    EPKSCP------CCP          SEQ ID NO:273
```

Fig. 2
(sheet 2 of 2)

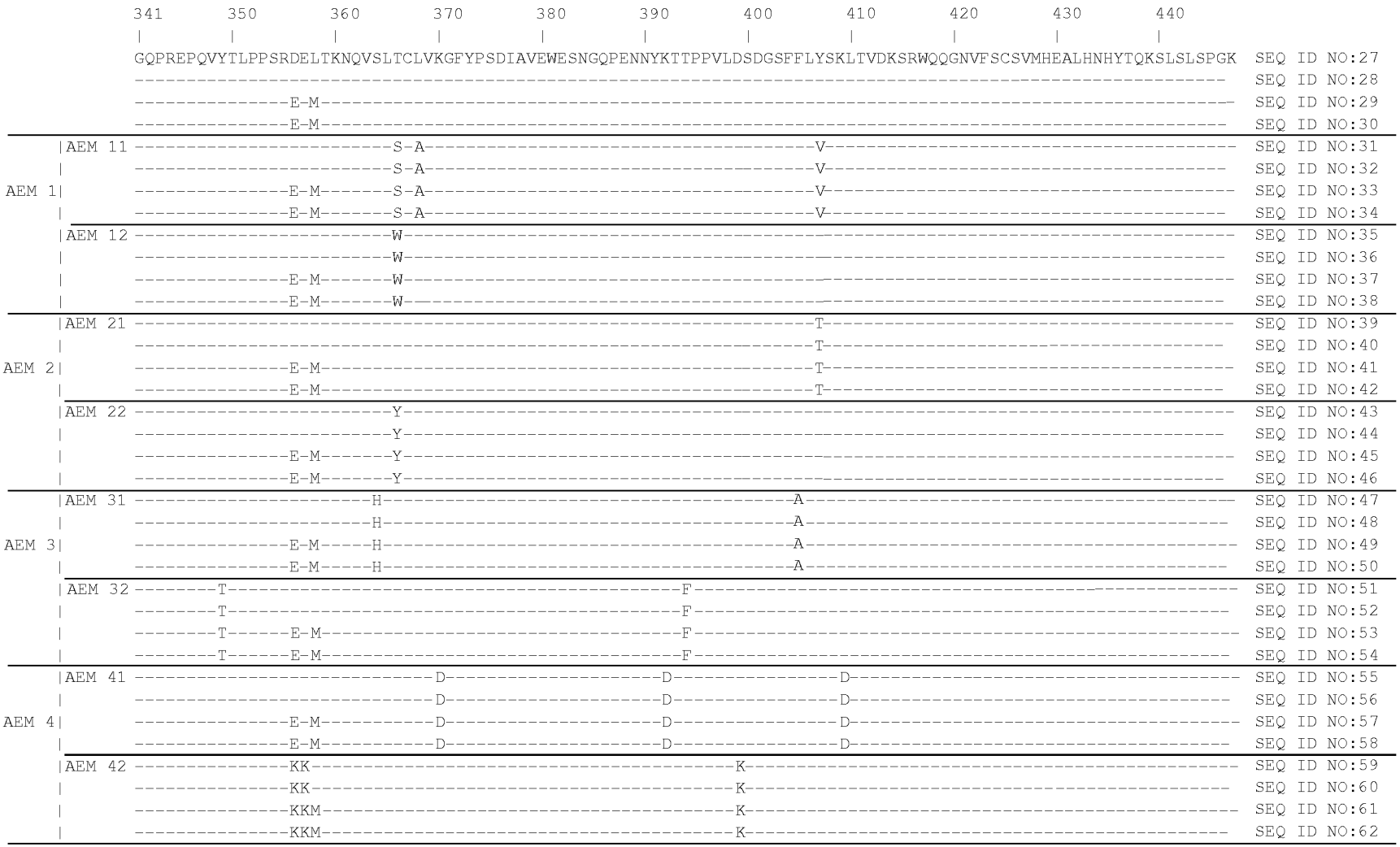


Fig. 3
(sheet 1 of 3)

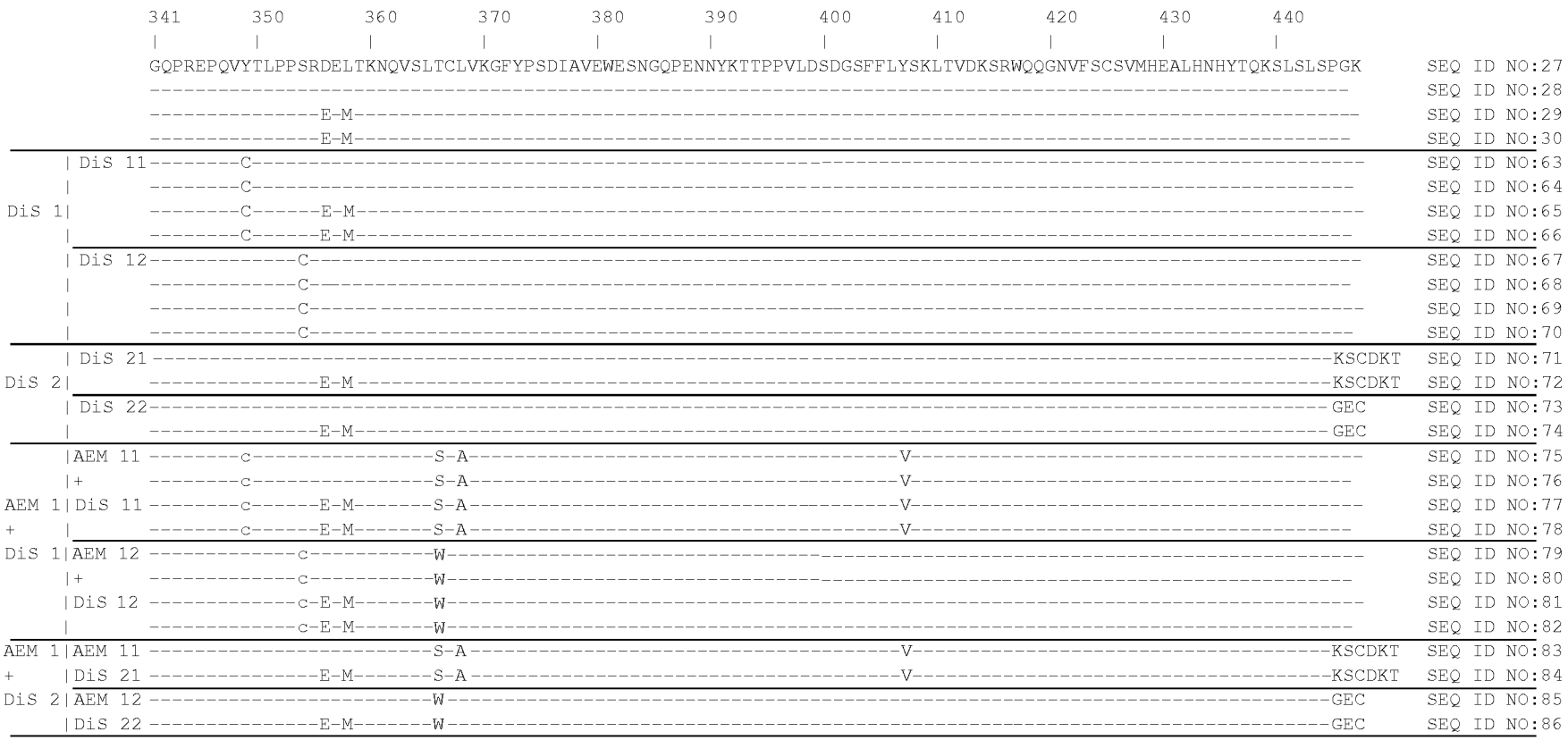


Fig. 3
(sheet 2 of 3)

```
                341       350       360       370       380       390       400       410       420       430       440
                 |         |         |         |         |         |         |         |         |         |         |
                GQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK  SEQ ID NO:27
                ------------------------------------------------------------------------------------------------------------  SEQ ID NO:28
                ----------E-M-------------------------------------------------------------------------------------------  SEQ ID NO:29
                ----------E-M-------------------------------------------------------------------------------------------  SEQ ID NO:30
AEM 1  |AEM 11--------------------S-A-------------------------------V-----------------------------------GEC  SEQ ID NO:87
+      |DiS 22----------E-M-------S-A-------------------------------V-----------------------------------GEC  SEQ ID NO:88
DiS 2I |AEM 12----------------------W-------------------------------------------------------------KSCDKT  SEQ ID NO:89
       |DiS 21----------E-M-------W---------------------------------------------------------------KSCDKT  SEQ ID NO:90
AEM 3  |AEM 31----------------------H-------------------------------A-----------------------------KSCDKT  SEQ ID NO:91
+      |DiS 21----------E-M-------H---------------------------------A-----------------------------KSCDKT  SEQ ID NO:92
DiS 2  |AEM 32----------T-------------------------------F-----------------------------------GEC  SEQ ID NO:93
       |DiS 22----------T-------E-M-----------------------------F-----------------------------GEC  SEQ ID NO:94
AEM 4  |AEM 41----------------------D-------------------------------D-----------------------------KSCDKT  SEQ ID NO:95
+      |DiS 21----------E-M-------D---------------------------------D-----------------------------KSCDKT  SEQ ID NO:96
DiS 2  |AEM 42----------KK------------------------------K-----------------------------------GEC  SEQ ID NO:97
       |DiS 22----------KKM-----------------------------K-----------------------------------GEC  SEQ ID NO:98
```

Fig. 3
(sheet 3 of 3)

220 230 240 250 260 270 280 290 300 310 320 330

EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI SEQ ID NO:99

SEQ ID NO:100

SEQ ID NO:101

SEQ ID NO:102

SEQ ID NO:103

SEQ ID NO:104

SEQ ID NO:105

SEQ ID NO:106

SEQ ID NO:107

SEQ ID NO:108

SEQ ID NO:109

SEQ ID NO:110

SEQ ID NO:111

SEQ ID NO:112

SEQ ID NO:113

SEQ ID NO:114

SEQ ID NO:115

SEQ ID NO:116

SEQ ID NO:117

SEQ ID NO:118

SEQ ID NO:119

SEQ ID NO:120

SEQ ID NO:121

SEQ ID NO:122

SEQ ID NO:123

SEQ ID NO:124

SEQ ID NO:125

SEQ ID NO:126

SEQ ID NO:127

SEQ ID NO:128

SEQ ID NO:129

SEQ ID NO:130

SEQ ID NO:131

SEQ ID NO:132

Fig. 4
(sheet 1 of 2)

```
       340       350       360       370       380       390       400       410       420       430       440
         |         |         |         |         |         |         |         |         |         |         |
EKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK        SEQ ID NO:99
-------------------------------------------------------------------------------------------------------------------        SEQ ID NO:100
---------------------------------S-A--------------------------------------V----------------------------------------        SEQ ID NO:101
---------------------------------W---------------------------------------------------------------------------------        SEQ ID NO:102
---------------------------------W---------------------------------------------------------------------------------        SEQ ID NO:103
---------------------------------S-A--------------------------------------V----------------------------------------        SEQ ID NO:104
----------------C----------------S-A--------------------------------------V----------------------------------------        SEQ ID NO:105
---------------------C-----------W---------------------------------------------------------------------------------        SEQ ID NO:106
---------------------C-----------W---------------------------------------------------------------------------------        SEQ ID NO:107
----------------C----------------S-A--------------------------------------V----------------------------------------        SEQ ID NO:108
--------------------------------------------------------------------------T----------------------------------------        SEQ ID NO:109
---------------------------------Y---------------------------------------------------------------------------------        SEQ ID NO:110
---------------------------------Y---------------------------------------------------------------------------------        SEQ ID NO:111
--------------------------------------------------------------------------T----------------------------------------        SEQ ID NO:112
---------------------------------S-A--------------------------------------V----------------------------------------        SEQ ID NO:113
---------------------------------W---------------------------------------------------------------------------------        SEQ ID NO:114
---------------------------------S-A--------------------------------------V----------------------------------------        SEQ ID NO:115
---------------------------------W---------------------------------------------------------------------------------        SEQ ID NO:116
---------------------------------S-A--------------------------------------V-------------------------------------KSCDKT     SEQ ID NO:117
---------------------------------W------------------------------------------------------------------------------GEC        SEQ ID NO:118
---------------------------------W------------------------------------------------------------------------------GEC        SEQ ID NO:119
---------------------------------S-A--------------------------------------V-------------------------------------KSCDKT     SEQ ID NO:120
---------------------------------S-A--------------------------------------V-------------------------------------GEC        SEQ ID NO:121
---------------------------------W------------------------------------------------------------------------------KSCDKT     SEQ ID NO:122
---------------------------------W------------------------------------------------------------------------------KSCDKT     SEQ ID NO:123
---------------------------------S-A--------------------------------------V-------------------------------------GEC        SEQ ID NO:124
-------------------------------H----------------------------------------A---------------------------------------KSCDKT     SEQ ID NO:125
----------------T--------------------------------------------F--------------------------------------------------GEC        SEQ ID NO:126
----------------T--------------------------------------------F--------------------------------------------------GEC        SEQ ID NO:127
-------------------------------H----------------------------------------A---------------------------------------KSCDKT     SEQ ID NO:128
-------------------------------------D---------------------D----------------D-----------------------------------KSCDKT     SEQ ID NO:129
-----------------------KK-----------------------------------------K---------------------------------------------GEC        SEQ ID NO:130
-----------------------KK-----------------------------------------K---------------------------------------------GEC        SEQ ID NO:131
-------------------------------------D---------------------D----------------D-----------------------------------KSCDKT     SEQ ID NO:132
```

Fig. 4
(sheet 2 of 2)

```
     220       230       240       250       260       270       280       290       300       310       320       330
       |         |         |         |         |         |         |         |         |         |         |         |
EPKSCDKTHTcpscpapeflggpsvflfppkpkdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfNsKyrvvsvltvlhqdwlngkeykckvsnkglpssi SEQ ID NO:133
          ----------------------------------------------------------------------------------------------------------- SEQ ID NO:134
--------------------------------------------------------------------------------------------------------------------- SEQ ID NO:135
          ----------------------------------------------------------------------------------------------------------- SEQ ID NO:136
--------------------------------------------------------------------------------------------------------------------- SEQ ID NO:137
          ----------------------------------------------------------------------------------------------------------- SEQ ID NO:138
--------------------------------------------------------------------------------------------------------------------- SEQ ID NO:139
          ----------------------------------------------------------------------------------------------------------- SEQ ID NO:140
--------------------------------------------------------------------------------------------------------------------- SEQ ID NO:141
          ----------------------------------------------------------------------------------------------------------- SEQ ID NO:142
--------------------------------------------------------------------------------------------------------------------- SEQ ID NO:143
          ----------------------------------------------------------------------------------------------------------- SEQ ID NO:144
--------------------------------------------------------------------------------------------------------------------- SEQ ID NO:145
          ----------------------------------------------------------------------------------------------------------- SEQ ID NO:146
--------CC----------------------------------------------------------------------------------------------------------- SEQ ID NO:147
          ----------------------------------------------------------------------------------------------------------- SEQ ID NO:148
-------C------------------------------------------------------------------------------------------------------------- SEQ ID NO:149
          ----------------------------------------------------------------------------------------------------------- SEQ ID NO:150
--------------------------------------------------------------------------------------------------------------------- SEQ ID NO:151
          ----------------------------------------------------------------------------------------------------------- SEQ ID NO:152
--------------------------------------------------------------------------------------------------------------------- SEQ ID NO:153
          ----------------------------------------------------------------------------------------------------------- SEQ ID NO:154
--------------------------------------------------------------------------------------------------------------------- SEQ ID NO:155
          ----------------------------------------------------------------------------------------------------------- SEQ ID NO:156
--------------------------------------------------------------------------------------------------------------------- SEQ ID NO:157
          ----------------------------------------------------------------------------------------------------------- SEQ ID NO:158
--------------------------------------------------------------------------------------------------------------------- SEQ ID NO:159
          ----------------------------------------------------------------------------------------------------------- SEQ ID NO:160
--------------------------------------------------------------------------------------------------------------------- SEQ ID NO:161
          ----------------------------------------------------------------------------------------------------------- SEQ ID NO:162
--------------------------------------------------------------------------------------------------------------------- SEQ ID NO:163
          ----------------------------------------------------------------------------------------------------------- SEQ ID NO:164
--------------------------------------------------------------------------------------------------------------------- SEQ ID NO:165
          ----------------------------------------------------------------------------------------------------------- SEQ ID NO:166
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Fig. 5

(sheet 1 of 2)

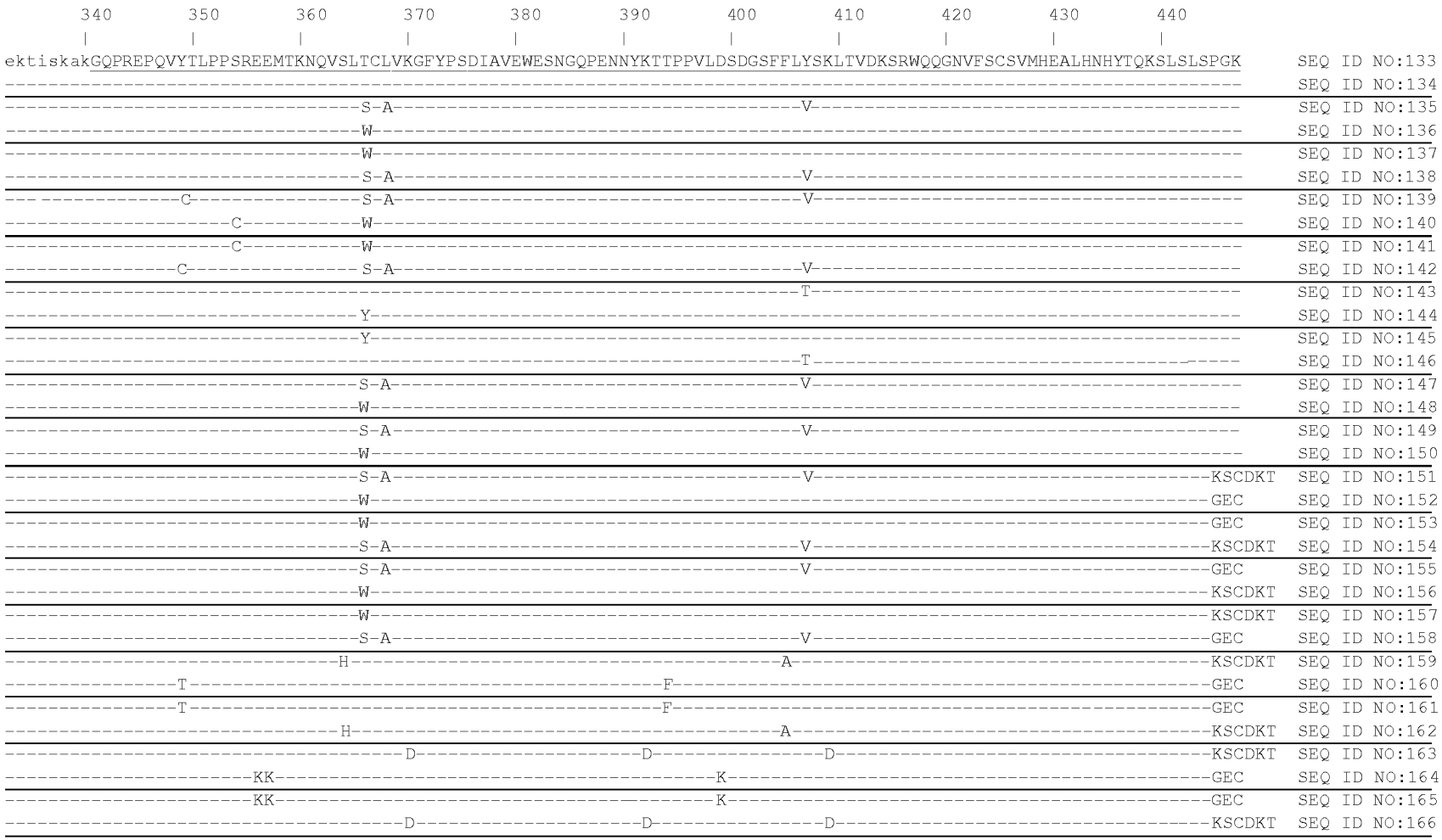


Fig. 5
(sheet 2 of 2)

23: T366S/L368A/Y407V::T366W

EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL**S**C**A**VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL**V**SKLT
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGS*CPPCPAPELLGGPSVFLFPPKP
KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPRE
PQVYTLPPSREEMTKNQVSL**W**CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSL
SPGK
(SEQ ID NO:171)

23A: Y349C/T366S/L368A/Y407V::S354C/T366W

EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQV**C**TLPPSREEMTKNQVSL**S**C**A**VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL**V**SKLT
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGS*CPPCPAPELLGGPSVFLFPPKP
KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPRE
PQVYTLPP**C**REEMTKNQVSL**W**CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSL
SPGK
(SEQ ID NO:173)

23B: Y407T::T366Y

EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL**T**SKLT
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGS*CPPCPAPELLGGPSVFLFPPKP
KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPRE
PQVYTLPPSREEMTKNQVSL**Y**CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSL
SPGK
(SEQ ID NO:175)

Fig. 6
(sheet 1 of 5)

23C: H224C/T225C/T366S/L368A/Y407V::T366W

EPKSCDKT**CC**CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL**S**C**A**VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL**V**SKLT
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGS*CPPCPAPELLGGPSVFLFPPKP
KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPRE
PQVYTLPPSREEMTKNQVSL**W**CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSL
SPGK
(SEQ ID NO:177)

23D: T223C/T366S/L368A/Y407V::T366W

EPKSCDK**C**HTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL**S**C**A**VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL**V**SKLT
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGS*CPPCPAPELLGGPSVFLFPPKP
KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPRE
PQVYTLPPSREEMTKNQVSL**W**CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSL
SPGK
(SEQ ID NO:179)

23E: T366S/L368A/Y407V/CH3 C-terminal Cysteine KSCDKT::T366W/CH3 C-terminal Cysteine GEC

EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL**S**C**A**VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL**V**SKLT
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS**KSCDKT***GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGS*CPPCPAPELLGGPSVFLFP
PKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQ
PREPQVYTLPPSREEMTKNQVSL**W**CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS
LSLS**GEC**
(SEQ ID NO:181)

Fig. 6
(sheet 2 of 5)

23F: T366S/L368A/Y407V::T366W and (G4S)4

EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL**S**C**A**VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL**V**SKLT
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK***GGGGSGGGGSGGGGSGGGGS***CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS
HEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL
WCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
(SEQ ID NO:183)

23E (35L): T366S/L368A/Y407V/CH3 C-terminal Cysteine KSCDKT::T366W/CH3 C-terminal Cysteine GEC and (G4S)7

EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL**S**C**A**VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL**V**SKLT
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS**KSCDKT*GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGS***CPPCPAPELLGGPSVFLFPPKPKD
TLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ
VYTLPPSREEMTKNQVSL**W**CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS**G
EC**
(SEQ ID NO:185)

23E (35L) Inverted: T366S/L368A/Y407V/CH3 C-terminal Cysteine GEC::T366W/CH3 C-terminal Cysteine KSCDKT and (G4S)7

EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL**S**C**A**VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL**V**SKLT
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS**GEC*GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGS***CPPCPAPELLGGPSVFLFPPKPKDTLM
ISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYT
LPPSREEMTKNQVSL**W**CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS**KSCD
KT**
(SEQ ID NO:187)

Fig. 6
(sheet 3 of 5)

23E (30L): T366S/L368A/Y407V/CH3 C-terminal Cysteine KSCDKT::T366W/CH3 C-terminal Cysteine GEC and (G4S)6

EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL**S**C**A**VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL**V**SKLT
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS**KSCDKT*GGGGSGGGGSGGGGSGGGGSGGGGSGGGGS***CPPCPAPELLGGPSVFLFPPKPKDTLMIS
RTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLP
PSREEMTKNQVSL**W**CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS**GEC**
(SEQ ID NO:189)

23E (25L): T366S/L368A/Y407V/CH3 C-terminal Cysteine KSCDKT:: T366W/CH3 C-terminal Cysteine GEC and (G4S)5

EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL**S**C**A**VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL**V**SKLT
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS**KSCDKT*GGGGSGGGGSGGGGSGGGGSGGGGS***CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEV
TCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREE
MTKNQVSL**W**CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS**GEC**
(SEQ ID NO:191)

23I: S364H/F405A::Y349T/T394F with CH3 terminal disulfide
EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQV**H**LTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF**A**LYSKLT
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS**KSCDKT***GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGS*CPPCPAPELLGGPSVFLFP
PKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQ
PREPQV**T**TLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKT**F**PPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS
LSLS**GEC**
(SEQ ID NO:193)

Fig. 6
(sheet 4 of 5)

23J: K370D/K392D/K409D::D356K/E357K/D399K with CH3 terminal disulfide

EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLV**D**GFYPSDIAVEWESNGQPENNY**D**TTPPVLDSDGSFFLYS**D**LT
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS**KSCDKT***GGGGSGGGGSGGGGSGGGGSGGGGSGGGGS*CPPCPAPELLGGPSVFLFP
PKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQ
PREPQVYTLPPSR**KK**MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVL**K**SDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS
LSLS**GEC**

(SEQ ID NO:195)

Fig. 6

(sheet 5 of 5)

39: T366S/L368A/Y407V::T366W

EPKSCDKTHTcpscpapeflggpsvflfppkpkdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltvlhqdw
lngkeykckvsnkglpssiektiskakGQPREPQVYTLPPSREEMTKNQVSL**S**C**A**VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL**V**SKLT
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGS*cpscpapeflggpsvflfppkp
kdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltvlhqdwlngkeykckvsnkglpssiektiskakGQPRE
PQVYTLPPSREEMTKNQVSL**W**CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSL
SPGK
(SEQ ID NO:197)

39A: Y349C/T366S/L368A/Y407V::S354C/T366W

EPKSCDKTHTcpscpapeflggpsvflfppkpkdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltvlhqdw
lngkeykckvsnkglpssiektiskakGQPREPQV**C**TLPPSREEMTKNQVSL**S**C**A**VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL**V**SKLT
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGS*cpscpapeflggpsvflfppkp
kdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltvlhqdwlngkeykckvsnkglpssiektiskakGQPRE
PQVYTLPP**C**REEMTKNQVSL**W**CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSL
SPGK
(SEQ ID NO:199)

39B: Y407T::T366Y

EPKSCDKTHTcpscpapeflggpsvflfppkpkdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltvlhqdw
lngkeykckvsnkglpssiektiskakGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL**T**SKLT
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGS*cpscpapeflggpsvflfppkp
kdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltvlhqdwlngkeykckvsnkglpssiektiskakGQPRE
PQVYTLPPSREEMTKNQVSL**Y**CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSL
SPGK
(SEQ ID NO:201)

Fig. 7
(sheet 1 of 5)

39C: H224C/T225C/T366S/L368A/Y407V::T366W

EPKSCDKT**CC**cpscpapeflggpsvflfppkpkdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltvlhqdw
lngkeykckvsnkglpssiektiskakGQPREPQVYTLPPSREEMTKNQVSL**S**C**A**VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL**V**SKLT
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGS*cpscpapeflggpsvflfppkp
kdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltvlhqdwlngkeykckvsnkglpssiektiskakGQPRE
PQVYTLPPSREEMTKNQVSL**W**CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSL
SPGK
(SEQ ID NO:203)

39D: T223C/T366S/L368A/Y407V::T366W

EPKSCDK**C**HTcpscpapeflggpsvflfppkpkdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltvlhqdw
lngkeykckvsnkglpssiektiskakGQPREPQVYTLPPSREEMTKNQVSL**S**C**A**VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL**V**SKLT
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGS*cpscpapeflggpsvflfppkp
kdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltvlhqdwlngkeykckvsnkglpssiektiskakGQPRE
PQVYTLPPSREEMTKNQVSL**W**CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSL
SPGK
(SEQ ID NO:205)

39E: T366S/L368A/Y407V/CH3 C-terminal Cysteine KSCDKT::T366W/CH3 C-terminal Cysteine GECG

EPKSCDKTHTcpscpapeflggpsvflfppkpkdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltvlhqdw
lngkeykckvsnkglpssiektiskakGQPREPQVYTLPPSREEMTKNQVSL**S**C**A**VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL**V**SKLT
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS**KSCDKT***GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGS*cpscpapeflggpsvflfp
pkpkdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltvlhqdwlngkeykckvsnkglpssiektiskakGQ
PREPQVYTLPPSREEMTKNQVSL**W**CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS
LSLS**GEC**
(SEQ ID NO:207)

Fig. 7
(sheet 2 of 5)

39F: T366S/L368A/Y407V::T366W and (G4S)4

EPKSCDKTHTcpscpapeflggpsvflfppkpkdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltvlhqdw
lngkeykckvsnkglpssiektiskakGQPREPQVYTLPPSREEMTKNQVSL**S**C**A**VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL**V**SKLT
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK***GGGGSGGGGSGGGGSGGGGS***cpscpapeflggpsvflfppkpkdtlmisrtpevtcvvvdvs
qedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltvlhqdwlngkeykckvsnkglpssiektiskakGQPREPQVYTLPPSREEMTKNQVSL
WCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
(SEQ ID NO:209)

39E (35L): T366S/L368A/Y407V/CH3 C-terminal Cysteine KSCDKT::T366W/CH3 C-terminal Cysteine GEC and (G4S)7

EPKSCDKTHTcpscpapeflggpsvflfppkpkdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltvlhqdw
lngkeykckvsnkglpssiektiskakgQPREPQVYTLPPSREEMTKNQVSL**S**C**A**VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL**V**SKLT
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS**KSCDKT*GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGS***cpscpapeflggpsvflfppkpkd
tlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltvlhqdwlngkeykckvsnkglpssiektiskakGQPREPQ
VYTLPPSREEMTKNQVSL**W**CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS**G
EC**
(SEQ ID NO:211)

39E (35L) Inverted: T366S/L368A/Y407V/CH3 C-terminal Cysteine GEC::T366W/CH3 C-terminal Cysteine KSCDKT and (G4S)7

EPKSCDKTHTcpscpapeflggpsvflfppkpkdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltvlhqdw
lngkeykckvsnkglpssiektiskakGQPREPQVYTLPPSREEMTKNQVSL**S**C**A**VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL**V**SKLT
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS**GEC*GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGS***cpscpapeflggpsvflfppkpkdtlm
isrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltvlhqdwlngkeykckvsnkglpssiektiskakGQPREPQVYT
LPPSREEMTKNQVSL**W**CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS**KSCD
KT**
(SEQ ID NO:213)

Fig. 7
(sheet 3 of 5)

39E (30L): T366S/L368A/Y407V/CH3 C-terminal Cysteine KSCDKT::T366W/CH3 C-terminal Cysteine GEC and (G4S)6

EPKSCDKTHTcpscpapeflggpsvflfppkpkdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltvlhqdw
lngkeykckvsnkglpssiektiskakGQPREPQVYTLPPSREEMTKNQVSL**S**C**A**VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL**V**SKLT
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS**KSCDKT*GGGGSGGGGSGGGGSGGGGSGGGGSGGGGS***cpscpapeflggpsvflfppkpkdtlmis
rtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltvlhqdwlngkeykckvsnkglpssiektiskakGQPREPQVYTLP
PSREEMTKNQVSL**W**CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS**GEC**
(SEQ ID NO:215)

39E (25L): T366S/L368A/Y407V/CH3 C-terminal Cysteine KSCDKT::T366W/CH3 C-terminal Cysteine GEC and (G4S)5

EPKSCDKTHTcpscpapeflggpsvflfppkpkdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltvlhqdw
lngkeykckvsnkglpssiektiskakGQPREPQVYTLPPSREEMTKNQVSL**S**C**A**VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL**V**SKLT
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS**KSCDKT*GGGGSGGGGSGGGGSGGGGSGGGGS***cpscpapeflggpsvflfppkpkdtlmisrtpev
tcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltvlhqdwlngkeykckvsnkglpssiektiskakGQPREPQVYTLPPSREE
MTKNQVSL**W**CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS**GEC**
(SEQ ID NO:217)

39I – S364H/F405A::Y349T/T394F with CH3 C-terminal disulfide
EPKSCDKTHTcpscpapeflggpsvflfppkpkdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltvlhqdw
lngkeykckvsnkglpssiektiskakGQPREPQVYTLPPSREEMTKNQV**H**LTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF**A**LYSKLT
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS**KSCDKT***GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGS*cpscpapeflggpsvflfp
pkpkdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltvlhqdwlngkeykckvsnkglpssiektiskakGQ
PREPQV**T**TLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKT**F**PPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS
LSLS**GEC**
(SEQ ID NO:219)

Fig. 7
(sheet 4 of 5)

39J - K370D/K392D/K409D::E356K/E357K/D399K with CH3 C-terminal disulfide

EPKSCDKTHTcpscpapeflggpsvflfppkpkdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltvlhqdw
lngkeykckvsnkglpssiektiskakGQPREPQVYTLPPSREEMTKNQVSLTCLV**D**GFYPSDIAVEWESNGQPENNY**D**TTPPVLDSDGSFFLYS**D**LT
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS**KSCDKT***GGGGSGGGGSGGGGSGGGGSGGGGSGGGGS*cpscpapeflggpsvflfp
pkpkdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltvlhqdwlngkeykckvsnkglpssiektiskakGQ
PREPQVYTLPPSR**KK**MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVL**K**SDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS
LSLS**GE**C
(SEQ ID NO:221)

Fig. 7
(sheet 5 of 5)

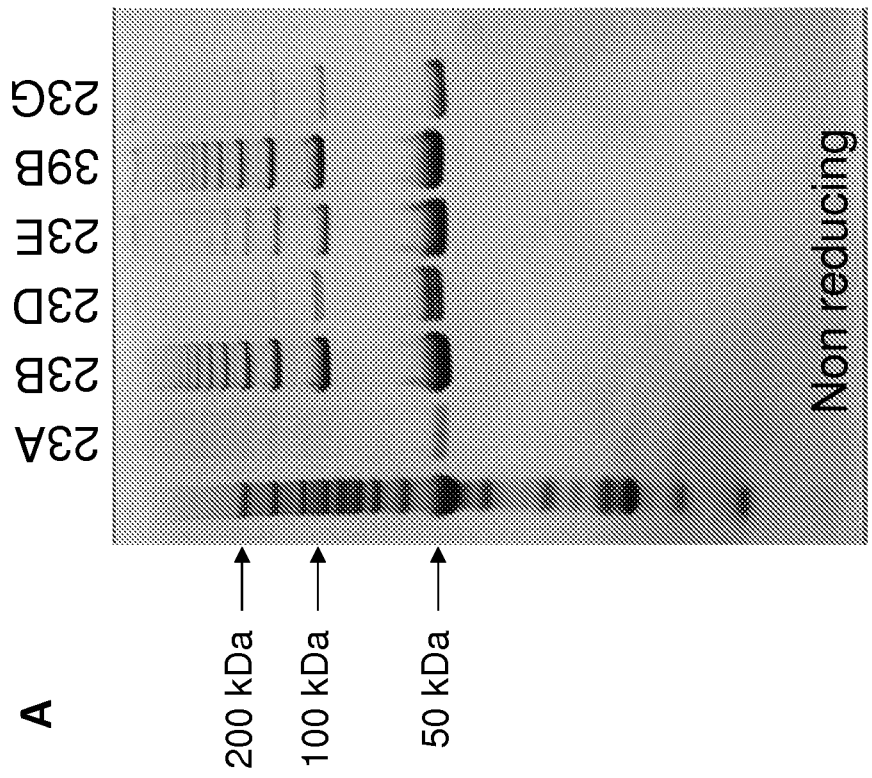

A
200 kDa
100 kDa
50 kDa
23A
23B
23D
23E
39B
23G
Non reducing
B
23A
23B
23D
23E
39B
23G
Reducing

Fig. 8

HEAVY CHAINS:

A) Anti-c-Met/anti-EGFR TFcBA with humanized 5D5 anti-c-Met and anti-EGFR paninumumab scFv with IgG1 TFc (with AEM 1 and DiS 2):

EVQLVESGGGLVQPGGSLRLSCAASGYTFTSYWLHWVRQAPGKGLEWVGMIDPSNSDTRFNPNFKDRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR
YGSYVSPLDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLG
TQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPR
EEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL**S**C**A**VKGFYPSDIAVEWESNGQPENN
YKTTPPVLDSDGSFFL**V**SKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS**KSCDKT***GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGG*
*GS*CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKC
KVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL**W**CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ
GNVFSCSVMHEALHNHYTQKSLSLS**GEC***GGGGSGGGGS*QVQLQESGPGLVKPSETLSLTCTVSGGSVSSGDYYWTWIRQSPGKGLEWIGHIYYSGNTN
YNPSLKSRLTISIDTSKTQFSLKLSSVTAADTAIYYCVRDRVTGAFDIWGQGTMVTSS*ASTGGGGSGGGGSGGGGSGGGGS*DIQMTQSPSSLSASVGD
RVTITCQASQDISNYLNWYQQKPGKAPKLLIYDASNLETGVPSRFSGSGSGTDFTFTISSLQPEDEATYFCQHFDHLPLAFGGGTKVEIKRT
(SEQ ID NO:235)

B) Anti-c-Met/anti-EGFR TFcBA with humanized 5D5 anti-c-Met and anti-EGFR paninumumab scFv with IgG1 TFc (with AEM 1 and DiS 2 Inverted):

EVQLVESGGGLVQPGGSLRLSCAASGYTFTSYWLHWVRQAPGKGLEWVGMIDPSNSDTRFNPNFKDRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR
YGSYVSPLDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLG
TQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPR
EEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL**S**C**A**VKGFYPSDIAVEWESNGQPENN
YKTTPPVLDSDGSFFL**V**SKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS**GEC***GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGS*CPPCPA
PELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALP
APIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL**W**CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLS**KSCDKT***GGGGSGGGGS*QVQLQESGPGLVKPSETLSLTCTVSGGSVSSGDYYWTWIRQSPGKGLEWIGHIYYSGNTNYNPSL
KSRLTISIDTSKTQFSLKLSSVTAADTAIYYCVRDRVTGAFDIWGQGTMVTSS*ASTGGGGSGGGGSGGGGSGGGGS*DIQMTQSPSSLSASVGDRVTIT
CQASQDISNYLNWYQQKPGKAPKLLIYDASNLETGVPSRFSGSGSGTDFTFTISSLQPEDEATYFCQHFDHLPLAFGGGTKVEIKRT
(SEQ ID NO: 343)

Fig. 9
(sheet 1 of 7)

C) Anti-c-Met/anti-EGFR TFcBA with humanized 5D5 anti-c-Met and anti-EGFR paninumumab scFv with IgG1 TFc (with AEM 1):

EVQLVESGGGLVQPGGSLRLSCAASGYTFTSYWLHWVRQAPGKGLEWVGMIDPSNSDTRFNPNFKDRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR
YGSYVSPLDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLG
TQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPR
EEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL**S**C**A**VKGFYPSDIAVEWESNGQPENN
YKTTPPVLDSDGSFFL**V**SKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGS*C
PPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVS
NKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL**W**CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV
FSCSVMHEALHNHYTQKSLSLSPGK*GGGGSGGGGS*QVQLQESGPGLVKPSETLSLTCTVSGGSVSSGDYYWTWIRQSPGKGLEWIGHIYYSGNTNYNP
SLKSRLTISIDTSKTQFSLKLSSVTAADTAIYYCVRDRVTGAFDIWGQGTMVTSS*ASTGGGGSGGGGSGGGGSGGGGS*DIQMTQSPSSLSASVGDRVT
ITCQASQDISNYLNWYQQKPGKAPKLLIYDASNLETGVPSRFSGSGSGTDFTFTISSLQPEDEATYFCQHFDHLPLAFGGGTKVEIKRT
(SEQ ID NO: 225)

D) Anti-c-Met/anti-EGFR TFcBA with humanized 5D5 anti-c-Met and anti-EGFR paninumumab scFv with IgG1/IgG4 hybrid TFc (with AEM 1):

EVQLVESGGGLVQPGGSLRLSCAASGYTFTSYWLHWVRQAPGKGLEWVGMIDPSNSDTRFNPNFKDRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR
YGSYVSPLDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLG
TQTYICNVNHKPSNTKVDKKVEPKSCDKTHTcpscpapeflggpsvflfppkpkdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpr
eeqfnskyrvvsvltvlhqdwlngkeykckvsnkglpssiektiskakGQPREPQVYTLPPSREEMTKNQVSL**S**C**A**VKGFYPSDIAVEWESNGQPENN
YKTTPPVLDSDGSFFL**V**SKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGS*c
pscpapeflggpsvflfppkpkdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltvlhqdwlngkeykckvs
nkglpssiektiskakGQPREPQVYTLPPSREEMTKNQVSL**W**CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV
FSCSVMHEALHNHYTQKSLSLSPGK*GGGGSGGGGS*QVQLQESGPGLVKPSETLSLTCTVSGGSVSSGDYYWTWIRQSPGKGLEWIGHIYYSGNTNYNP
SLKSRLTISIDTSKTQFSLKLSSVTAADTAIYYCVRDRVTGAFDIWGQGTMVTSS*ASTGGGGSGGGGSGGGGSGGGGS*DIQMTQSPSSLSASVGDRVT
ITCQASQDISNYLNWYQQKPGKAPKLLIYDASNLETGVPSRFSGSGSGTDFTFTISSLQPEDEATYFCQHFDHLPLAFGGGTKVEIKRT
(SEQ ID NO: 227)

Fig. 9
(sheet 2 of 7)

E) Anti-c-Met/anti-EGFR TFcBA with humanized 5D5 anti-c-Met and anti-EGFR paninumumab scFv with IgG1/IgG4 hybrid TFc (with AEM 1):

EVQLVESGGGLVQPGGSLRLSCAASGYTFTSYWLHWVRQAPGKGLEWVGMIDPSNSDTRFNPNFKDRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR
YGSYVSPLDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLG
TQTYICNVNHKPSNTKVDKKVEPKSCDKTHTcpscpapeflggpsvflfppkpkdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpr
eeqfNsKyrvvsvltvlhqdwlngkeykckvsnkglpssiektiskakGQPREPQVYTLPPSREEMTKNQVSL**S**C**A**VKGFYPSDIAVEWESNGQPENN
YKTTPPVLDSDGSFFL**V**SKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGS*c
pscpapeflggpsvflfppkpkdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltvlhqdwlngkeykckvs
nkglpssiektiskakGQPREPQVYTLPPSREEMTKNQVSL**W**CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV
FSCSVMHEALHNHYTQKSLSLSPGK*GGGGSGGGGS*QVQLQESGPGLVKPSETLSLTCTVSGGSVSSGDYYWTWIRQSPGKGLEWIGHIYYSGNTNYNP
SLKSRLTISIDTSKTQFSLKLSSVTAADTAIYYCVRDRVTGAFDIWGQGTMVTSS*ASTGGGGSGGGGSGGGGSGGGGS*DIQMTQSPSSLSASVGDRVT
ITCQASQDISNYLNWYQQKPGKAPKLLIYDASNLETGVPSRFSGSGSGTDFTFTISSLQPEDEATYFCQHFDHLPLAFGGGTKVEIKRT
(SEQ ID NO: 229)

F) Anti-c-Met/anti-EGFR TFcBA with humanized 5D5 anti-c-Met and anti-EGFR scFv 2224 with IgG1 TFc (with AEM 1 and DiS 2):

EVQLVESGGGLVQPGGSLRLSCAASGYTFTSYWLHWVRQAPGKGLEWVGMIDPSNSDTRFNPNFKDRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR
YGSYVSPLDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLG
TQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPR
EEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL**S**C**A**VKGFYPSDIAVEWESNGQPENN
YKTTPPVLDSDGSFFL**V**SKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS**KSCDKT***GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGG*
*GS*CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKC
KVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL**W**CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ
GNVFSCSVMHEALHNHYTQKSLSLS**GEC***GGGGSGGGGS*EVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAIGWVRQAPGQGLEWMGGIIPIFGIANY
AQKFQGRVTITADESTSSAYMELSSLRSEDTAVYYCAREEGPYCSSTSCYAAFDIWGQGTLVTVSS*ASTGGGGSGGGGSGGGGSGGGGS*QSVLTQDPA
VSVALGQTVKITCQGDSLRSYFASWYQQKPGQAPTLVMYARNDRPAGVPDRFSGSKSGTSASLAISGLQPEDEADYYCAAWDDSLNGYLFGAGTKLTV
L
(SEQ ID NO:239)

Fig. 9
(sheet 3 of 7)

G) Anti-c-Met/anti-EGFR TFcBA with humanized 5D5 anti-c-Met and humanized anti-EGFR cetuximab scFv H1 L1 with IgG1 TFc (with AEM 1 and DiS 2):

EVQLVESGGGLVQPGGSLRLSCAASGYTFTSYWLHWVRQAPGKGLEWVGMIDPSNSDTRFNPNFKDRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR
YGSYVSPLDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLG
TQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPR
EEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL**S**C**A**VKGFYPSDIAVEWESNGQPENN
YKTTPPVLDSDGSFFL**V**SKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS**KSCDKT***GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGG*
*GS*CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKC
KVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL**W**CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ
GNVFSCSVMHEALHNHYTQKSLSLS**GEC***GGGGSGGGGS*QVQLVESGGGVVQPGESLRLSCAvSGFSLTNYGVHWVRQAPGKGLEWVgVIWSGGNTDYN
TPFTSRFTISkDNSKNTvYLQMNSLRAEDTAVYYCARALTYYDYEFAYWGQGTLVTVSS*ASTGGGGSGGGGSGGGGSGGGGS*dIVLTQSPDFQSVTPG
EKVTITCRASQSIGTNIHWYQQKPDQSPKLLIKYASESISGVPSRFSGSGSGTDFTLTINSLEAEDEATYYCQQNNNWPTTFGQGTKVEIKRT
(SEQ ID NO:260)

H) Anti-c-Met/anti-IGFR TFcBA with humanized 5D5 anti-c-Met and humanized anti-EGFR cetuximab scFv H1 L2 with IgG1 TFc (with AEM 1 and DiS 2):

EVQLVESGGGLVQPGGSLRLSCAASGYTFTSYWLHWVRQAPGKGLEWVGMIDPSNSDTRFNPNFKDRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR
YGSYVSPLDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLG
TQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPR
EEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL**S**C**A**VKGFYPSDIAVEWESNGQPENN
YKTTPPVLDSDGSFFL**V**SKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS**KSCDKT***GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGG*
*GS*CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKC
KVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL**W**CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ
GNVFSCSVMHEALHNHYTQKSLSLS**GEC***GGGGSGGGGS*QVQLVESGGGVVQPGESLRLSCAvSGFSLTNYGVHWVRQAPGKGLEWVgVIWSGGNTDYN
TPFTSRFTISkDNSKNTvYLQMNSLRAEDTAVYYCARALTYYDYEFAYWGQGTLVTVSS*ASTGGGGSGGGGSGGGGSGGGGS*dIVLTQSPsslSVTPG
EKVTfTCRASQSIGTNIHWYQQKPgQSPKLLIKYASESISGVPSRFSGSGSGTDFTLTINSvEAEDEATYYCQQNNNWPTTFGQGTKlEIKRT
(SEQ ID NO:281)

Fig. 9
(sheet 4 of 7)

I) Anti-c-Met/anti-EGFR TFcBA with humanized 5D5 anti-c-Met and humanized anti-EGFR cetuximab scFv H2 L1 with IgG1 TFc (with AEM 1 and DiS 2):

EVQLVESGGGLVQPGGSLRLSCAASGYTFTSYWLHWVRQAPGKGLEWVGMIDPSNSDTRFNPNFKDRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR
YGSYVSPLDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLG
TQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPR
EEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL**S**C**A**VKGFYPSDIAVEWESNGQPENN
YKTTPPVLDSDGSFFL**V**SKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS**KSCDKT***GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGG*
*GS*CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKC
KVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL**W**CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ
GNVFSCSVMHEALHNHYTQKSLSLS**GEC***GGGGSGGGGS*QVQLVESGGGVVQPGESLRiSCAvSGFSLTNYGVHWVRQAPGKGLEWlgVIWSGGNTDYN
TPFTSRlTISkDNSKsTvYfQMNSLRAEDTAVYYCARALTYYDYEFAYWGQGTLVTVSS*ASTGGGGSGGGGSGGGGSGGGGS*dIVLTQSPDFQSVTPG
EKVTITCRASQSIGTNIHWYQQKPDQSPKLLIKYASESISGVPSRFSGSGSGTDFTLTINSLEAEDEATYYCQQNNNWPTTFGQGTKVEIKRT
(SEQ ID NO:283)

J) Anti-c-Met/anti-EGFR TFcBA with humanized 5D5 anti-c-Met and humanized anti-EGFR cetuximab scFv H2 L2 with IgG1 TFc (with AEM 1 and DiS 2):

EVQLVESGGGLVQPGGSLRLSCAASGYTFTSYWLHWVRQAPGKGLEWVGMIDPSNSDTRFNPNFKDRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR
YGSYVSPLDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLG
TQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPR
EEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL**S**C**A**VKGFYPSDIAVEWESNGQPENN
YKTTPPVLDSDGSFFL**V**SKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS**KSCDKT***GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGG*
*GS*CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKC
KVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL**W**CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ
GNVFSCSVMHEALHNHYTQKSLSLS**GEC***GGGGSGGGGS*QVQLVESGGGVVQPGESLRiSCAvSGFSLTNYGVHWVRQAPGKGLEWlgVIWSGGNTDYN
TPFTSRlTISkDNSKsTvYfQMNSLRAEDTAVYYCARALTYYDYEFAYWGQGTLVTVSS*ASTGGGGSGGGGSGGGGSGGGGS*dIVLTQSPsslSVTPG
EKVTfTCRASQSIGTNIHWYQQKPgQSPKLLIKYASESISGVPSRFSGSGSGTDFTLTINSvEAEDEATYYCQQNNNWPTTFGQGTKlEIKRT
(SEQ ID NO:285)

Fig. 9
(sheet 5 of 7)

K) Anti-c-Met/anti-EGFR TFcBA with anti-c-Met VH domain from anti-c-Met binding site 2 and humanized anti-EGFR cetuximab scFv H1 L1 with IgG1 TFc (with AEM 1 and DiS 2):

QVQLVQSGAEVKKPGASVKVSCKASGYIFTAYTMHWVRQAPGQGLEWMGWIKPNNGLANYAQKFQGRVTMTRDTSISTAYMELSRLRSDDTAVYYCAR
SEITTEFDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT
QTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNY
KTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSKSCDKTGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGG
SCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCK
VSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG
NVFSCSVMHEALHNHYTQKSLSLSGECGGGGSGGGGSQVQLVESGGGVVQPGESLRLSCAvSGFSLTNYGVHWVRQAPGKGLEWVgVIWSGGNTDYNT
PFTSRFTISkDNSKNTvYLQMNSLRAEDTAVYYCARALTYYDYEFAYWGQGTLVTVSSASTGGGGSGGGGSGGGGSGGGGSdIVLTQSPDFQSVTPGE
KVTITCRASQSIGTNIHWYQQKPDQSPKLLIKYASESISGVPSRFSGSGSGTDFTLTINSLEAEDEATYYCQQNNNWPTTFGQGTKVEIKRT
(SEQ ID NO:291)

L) Anti-c-Met/anti-EGFR TFcBA with humanized 5D5 anti-c-Met and anti-EGFR paninumumab scFv with IgG1 TFc (with AEM 1 and- 40 aa TFc linker):

EVQLVESGGGLVQPGGSLRLSCAASGYTFTSYWLHWVRQAPGKGLEWVGMIDPSNSDTRFNPNFKDRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR
YGSYVSPLDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLG
TQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPR
EEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENN
YKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKTRPAPPSTATTAGSTPQPESASPSGKEPAASSPSSTNTGSC
PPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVS
NKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV
FSCSVMHEALHNHYTQKSLSLSPGKGGGGSGGGGSQVQLQESGPGLVKPSETLSLTCTVSGGSVSSGDYYWTWIRQSPGKGLEWIGHIYYSGNTNYNP
SLKSRLTISIDTSKTQFSLKLSSVTAADTAIYYCVRDRVTGAFDIWGQGTMVTSSASTGGGGSGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVT
ITCQASQDISNYLNWYQQKPGKAPKLLIYDASNLETGVPSRFSGSGSGTDFTFTISSLQPEDEATYFCQHFDHLPLAFGGGTKVEIKRT
(SEQ ID NO:347)

Fig. 9
(sheet 6 of 7)

M) Anti-c-Met/anti-EGFR TFcBA with humanized 5D5 anti-c-Met and anti-EGFR paninumumab scFv with IgG1/IgG4 hybrid TFc (with AEM 1 and 40 aa TFc linker):

EVQLVESGGGLVQPGGSLRLSCAASGYTFTSYWLHWVRQAPGKGLEWVGMIDPSNSDTRFNPNFKDRFTISADTSKNTAYLQMNSLRAEDTAVYYCAR
YGSYVSPLDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLG
TQTYICNVNHKPSNTKVDKKVEPKSCDKTHTcpscpapeflggpsvflfppkpkdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpr
eeqfNsKyrvvsvltvlhqdwlngkeykckvsnkglpssiektiskakGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENN
YKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKTRPAPPSTATTAGSTPQPESASPSGKEPAASSPSSTNTGSc
pscpapeflggpsvflfppkpkdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltvlhqdwlngkeykckvs
nkglpssiektiskakGQPREPQVYTLPPSREEMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV
FSCSVMHEALHNHYTQKSLSLSPGKGGGSGGGGSGGGSQVQLQESGPGLVKPSETLSLTCTVSGGSVSSGDYYWTWIRQSPGKGLEWIGHIYYSGNTNYNP
SLKSRLTISIDTSKTQFSLKLSSVTAADTAIYYCVRDRVTGAFDIWGQGTMVTSSASTGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVT
ITCQASQDISNYLNWYQQKPGKAPKLLIYDASNLETGVPSRFSGSGSGTDFTFTISSLQPEDEATYFCQHFDHLPLAFGGGTKVEIKRT
(SEQ ID NO:349)

Fig. 9
(sheet 7 of 7)

Nucleotide sequences encoding the polypeptides of Figure 6:

SEQ ID NO:170 (encodes SEQ ID NO:171):
gaaccgaaatcatgcgataagacccacacatgccctccctgtccagcacccgagctgctcgggggaccctcggtgttcttgtttcctcccaaacccaa
agataccccttatgattagccggacaccagaggtgacgtgcgtggtagtagacgtgtcccatgaggacccggaggtcaagttcaactggtacgtggacg
gagtggaggtgcacaatgcaaagaccaagccgagggaagagcaataccagtccacatatagagtcgtgtcggtcctacggtcttgcatcaggactgg
ctgaatggcaaagaatacaaatgtaaagtctccaacaaagctctcccagcgcccattgagaaaacaatctcaaaagcgaaaggccaaccgagagaacc
tcaagtctatactcttcccccgtcgagagaggaaatgaccaaaaaccaggtatccctgtcatgcgcggtcaaggggttttacccaagcgacatcgccg
tggagtgggagtcgaacggacagccagagaataactataagacgacccctcccgtgctggattcggatggatcgttctttcttgtcagcaaactcaca
gtcgacaaatcaaggtggcagcaagggaacgtgttcagctgttcggtaatgcatgaagccctccacaatcactacacgcagaaatccctgtcgctctc
accagggaagggtgggggtggctcaggggtgggggatcaggtggtggtggtagcggaggtggagggagcggaggcggaggctccggtggaggaggtt
ccggaggtggcgggtcaggggaggagggtcatgtccgccgtgccctgcccccgaattgctgggaggtccgtccgtatttctgtttcccccgaagcct
aaagatactcttatgatctcgcgaacgccggaagtaacttgtgtcgtggtagatgtctcacacgaagatcccgaagtgaaattcaattggtatgtcga
cggcgtggaggtacataacgccaagacgaagcctagagaggaacagtaccagtcaacgtatcgggtcgtatccgtgctcaccgtgctccaccaggatt
ggctgaacggaaaggagtacaagtgcaaagtctcgaacaaggcgttgcctgcgccaatcgaaaagacgatctccaaagctaagggacaaccaagggaa
ccacaagtgtatactctcccgccctcgcgcgaagagatgacaaagaatcaggtgtcactttggtgcttggtgaaggggttctatccctcggatattgc
ggtcgagtgggagagcaatggtcaaccggagaacaattacaagacgacaccgcccgtattggactccgacgggtccttctttctctactcgaagctca
ctgtagataagtcgcgatggcagcaggggaacgtctttagctgttccgtgatgcacgaggcacttcataaccactatacccagaagtcgttgtcgctt
tcccccggaaaa

SEQ ID NO:172 (encodes SEQ ID NO:173):
gaaccgaaatcatgcgataaaactcacacgtgccctccatgccctgctccggaacttctcgggggaccgtccgtattcctctttcctcctaagcctaa
ggacaccctcatgatcagcaggacccccgaggtgacgtgtgtagtcgtggatgtgtcccacgaggacccggaagtcaagttcaactggtatgtagatg
gagtggaggtccataatgccaagaccaagccaagagaggagcagtatcagtcgacttatcgggtggtcagcgtcctcacggtacttcatcaggattgg
ctgaatggaaaggagtacaaatgtaaggtatccaacaaagcgttgccagcgcccatcgaaaagacaatctcgaaggcgaagggacaaccccgggaacc
gcaagtgtgtaccctgccaccttcccgggaggagatgacgaaaaaccaggtatccctgtcgtgcgccgtgaaagggttttacccatcggatatcgcag
tggagtgggaaagcaatgggcagccggaaaacaactataagaccacgcccctgtactcgactcggatgggtccttttttcctcgtcagcaaacttacg
gtagacaaaagcaggtggcaacaggggaatgtgttcagctgctcagtcatgcacgaggcactccataaccattacactcagaaatcactgtcgctgtc
gcccggtaaaggggaggtgggtcgggcggtgggggaagcggtggtgggggatcaggtgggggaggttcgggaggtggtgggagcggtggaggcggtt
ccggaggaggcgggtcgggtggaggtggatcgtgcccaccgtgccccgcaccggaactccttgggggaccatccgtgtttctgtttccaccgaagcca
aaggacactctcatgatctcgcgcacaccagaggtgacatgtgtcgtcgtcgatgtgtcacacgaagatccagaggtcaagtttaactggtacgtgga
cggagtcgaggtccacaatgcgaaaacgaaacccagagaagagcagtaccagtcaacataccgggtggtgagcgtattgaccgtgcttcaccaggact
ggcttaacgggaaagagtacaagtgtaaggtcagcaataaggcgctcccagcgcctattgagaaaactatctcgaaagcaaaggggcagccacgagag
ccccaagtgtgtacgctgccaccctgtcgggaggaaatgaccaagaatcaagtctcgctttggtgccttgtgaagggattctatcccagcgacattgc
tgtagagtgggagtcgaacgggcaacccgagaataactacaagactactccgccggtgttggactcggacgggtcgttcttcctttatagcaaactca
cagtcgacaagtccagatggcagcagggaaatgtcttttcctgctcggtaatgcacgaagcgttgcataaccactatacacagaagtcgctttcgttg
tcacccgggaaa

Fig. 10 (sheet 1 of 31)

SEQ ID NO:174 (encodes SEQ ID NO:175):
gaaccgaaatcatgcgacaaaacgcacacttgtccgccgtgccctgccccagagttgcttggaggaccatcagtatttctcttccctcctaagccgaa
agacacactcatgatctcacgcacaccggaagtaacttgcgtggtggtggatgtgtcgcatgaagatcccgaggtcaaattcaactggtacgtcgacg
gtgtggaggtgcacaacgccaagacgaaacccagagaagagcagtatcagtcgacctaccgagtggtatccgtgcttacggtgctgcatcaggattgg
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gtcgataaaagcaggtggcagcaagggaatgtgttttcgtgctcggtcatgcacgaagcacttcataaccactacacccagaaatccttgagcctgtc
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cgggaggggaggaagcggaggggtggatcgtgtcctccgtgcccagcccccgaactcctcgggggaccctcggtattccttttccgccgaaaccc
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tcacccgggaag

SEQ ID NO:176 (encodes SEQ ID NO:177):
gaaccgaaatcatgcgataagacttgctgctgtcctccctgtccagcacccgagctgctcgggggaccctcggtgttcttgtttcctcccaaacccaa
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ccggaggtggcgggtcaggggggaggagggtcatgtccgccgtgccctgcccccgaattgctgggaggtccgtccgtatttctgtttcccccgaagcct
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ggtcgagtgggagagcaatggtcaaccggagaacaattacaagacgacaccgcccgtattggactccgacgggtccttctttctctactcgaagctca
ctgtagataagtcgcgatggcagcaggggaacgtctttagctgttccgtgatgcacgaggcacttcataaccactatacccagaagtcgttgtcgctt
tcccccggaaaa

Fig. 10 *(sheet 2 of 31)*

SEQ ID NO:178 (encodes SEQ ID NO:179):

gaaccgaaatcatgcgataagtgccacacatgccctccctgtccagcacccgagctgctcgggggacgctcggtgttcttgtttcctcccaaacccaa
agataccccttatgattagccggacaccagaggtgacgtgcgtggtagtagacgtgtcccatgaggacccggaggtcaagttcaactggtacgtggacg
gagtggaggtgcacaatgcaaagaccaagccgagggaagagcaataccagtccacatatagagtcgtgtcggtccttacggtcttgcatcaggactgg
ctgaatggcaaagaatacaaatgtaaagtctccaacaaagctctcccagcgcccattgagaaaacaatctcaaaagcgaaaggccaaccgagagaacc
tcaagtctatactcttcccccgtcgagagaggaaatgaccaaaaaccaggtatccctgtcatgcgcggtcaaggggttttacccaagcgacatcgccg
tggagtgggagtcgaacggacagccagagaataactataagacgacccctcccgtgctggattcggatggatcgttctttcttgtcagcaaactcaca
gtcgacaaatcaaggtggcagcaagggaacgtgttcagctgttcggtaatgcatgaagccctccacaatcactacacgcagaaatccctgtcgctctc
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aaagatactcttatgatctcgcgaacgccggaagtaacttgtgtcgtggtagatgtctcacacgaagatcccgaagtgaaattcaattggtatgtcga
cggcgtggaggtacataacgccaagacgaagcctagagaggaacagtaccagtcaacgtatcgggtcgtatccgtgctcaccgtgctccaccaggatt
ggctgaacggaaaggagtacaagtgcaaagtctcgaacaaggcgttgcctgcgccaatcgaaaagacgatctccaaagctaagggacaaccaagggaa
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ggtcgagtgggagagcaatggtcaaccggagaacaattacaagacgacaccgcccgtattggactccgacgggctccttctttctctactcgaagctca
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tccccccggaaaa

SEQ ID NO:180 (encodes SEQ ID NO:181):

gaaccgaaatcatgcgataaaacacacacatgcccaccatgcccagcgcctgaacttttgggaggtccctcggtgttttttgtttcctcctaagcctaa
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gtgtggaggtgcataatgcaaaaactaagcctcgggaggaacaatatcaaagcacataccgggtcgtgtccgtgctcacggtacttcatcaggattgg
ctcaacgggaaagaatacaaatgtaaggtgtccaacaaggctctcccggcaccgattgagaaaacgatcagcaaggccaaggggcagccccgagaacc
ccaagtatacacacttcccccgtccagggaggagatgaccaagaaccaggtgtcgctgtcgtgtgcggtcaaggggttttatcccagcgacatcgcgg
tagagtgggagtcgaacggccagcccgagaacaactacaagacaacaccgcctgtattggactcggacgggtcgtttttcctggtcagcaagctcaca
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caaagcttactgtcgataagtcgcggtggcagcaaggcaatgtgtttagctgttcggtaatgcatgaggcgctccacaatcactatacacagaagagc
ttgtccctcagcggggagtgc

Fig. 10 *(sheet 3 of 31)*

SEQ ID NO:182 (encodes SEQ ID NO:183):
gaaccgaaatcatgcgacaagacccacacctgcccaccgtgtccagcgcccgagctcctcggagggccgtcggtgttcctctttccccccaaagcctaa
agacactctgatgatcagccgcactccagaagtgacatgtgtggtggtggatgtctcgcatgaggacccggaagtcaaattcaattggtacgtggatg
gtgtcgaagtgcacaacgccaagacaaaaccgcgcgaggagcagtaccagagcacctaccgggtggtatcagtgcttacagtactgcatcaggattgg
ctgaacggaaaggagtacaagtgtaaagtcagcaacaaagcgctcccggctccgatcgagaaaacgatctcaaaggccaagggccagccgcgagaacc
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tcgggtcgtgtcggtcctgaccgtacttcaccaggactggctcaatgggaaagagtacaaatgcaaggtgtccaataaggcgctgcctgcgccaattg
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tgactccgatggctcatttttcctctattcgaagctcactgtcgacaagtcgcgctggcagcagggtaacgtctttagctgctccgtgatgcacgagg
ccctccacaatcattatacacagaaatcgctgtcactttcgcccggaaaa

SEQ ID NO:184 (encodes SEQ ID NO:185):
gaaccgaaatcatgcgacaaaacgcacacctgtccgccctgtcctgccccggaacttctcggagggccttccgtgtttctcttccctccgaagcccaa
ggacacgctgatgatctcccggaccccggaggtcacgtgtgtggtagtagacgtgtcacacgaagatccggaggtgaagttcaactggtacgtagatg
gcgtggaggtgcacaacgccaaaacgaagccccgagaggaacagtaccagtcaacgtaccgcgtcgtgtcggtattgactgtattgcatcaagactgg
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ataagtcgcgatggcaacagggcaatgtgttttcgtgcagcgtgatgcatgaggcgctgcacaaccactatactcagaaatcgttaagcttatcggga
gagtgt

Fig. 10 *(sheet 4 of 31)*

SEQ ID NO:186 (encodes SEQ ID NO:187):

gaaccgaaatcatgcgacaaaacgcacacctgtccgccctgtcctgccccggaacttctcggagggccttccgtgtttctcttccctccgaagcccaa
ggacacgctgatgatctcccggaccccgaggtcacgtgtgtagtagacgtgtcacacgaagatccggaggtgaagttcaactggtacgtagatg
gcgtggaggtgcacaacgccaaaacgaagccccgagaggaacagtaccagtcaacgtaccgcgtcgtgtcggtattgactgtattgcatcaagactgg
ttgaacgggaaggagtataagtgtaaagtcagcaacaaggctcttcccgcacccattgaaaagacaatttcgaaagccaaggcccagcccagggagcc
ccaagtgtacaccctgccacccagccgggaagagatgacaaagaatcaagtctcgcttagctgcgctgtcaagggcttctatccatcggacattgcag
tggaatgggaatcaaacggacagccggagaataactataagacgacacccccctgtcctcgacagcgacgggtcgttcttccttgtgagcaagctcacg
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gatggcaacagggcaatgtgtttcgtgcagcgtgatgcatgaggcgctgcacaaccactatactcagaaatcgttaagcttatcgaagtcatcgcgac
aagact

SEQ ID NO:188 (encodes SEQ ID NO:189):

gaaccgaaatcatgcgacaaaacgcacacctgtccgccctgtcctgccccggaacttctcggagggccttccgtgtttctcttccctccgaagcccaa
ggacacgctgatgatctcccggaccccgaggtcacgtgtgtagtagacgtgtcacacgaagatccggaggtgaagttcaactggtacgtagatg
gcgtggaggtgcacaacgccaaaacgaagccccgagaggaacagtaccagtcaacgtaccgcgtcgtgtcggtattgactgtattgcatcaagactgg
ttgaacgggaaggagtataagtgtaaagtcagcaacaaggctcttcccgcacccattgaaaagacaatttcgaaagccaaggcccagcccagggagcc
ccaagtgtacaccctgccacccagccgggaagagatgacaaagaatcaagtctcgcttagctgcgctgtcaagggcttctatccatcggacattgcag
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cgcacgccggaggtaacatgcgtggtggatgtgtcacatgaggaccccgagtcaagttcaattggtacgtcgatggaagtgcacaatgc
gaaaacaaaacccgggaggagcagtatcagagcacgtacagggtagtctccgtcctgactgtactcaccaagactggcttaacggaaaagagtata
agtgcaaggtcagcaacaaggcgcttcctgccctatcgagaaaaccatctcgaaggccaagggacagccgagggagcctcaagtatacacgctgccg
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acagcctgagaacaactataagactacgcccccctgtgttggacagcgatgggtcattctttctgtattcgaaactcacggtggataagtcgcgatggc
aacagggcaatgtgtttcgtgcagcgtgatgcatgaggcgctgcacaaccactatactcagaaatcgttaagcttatcgggagagtgt

Fig. 10 *(sheet 5 of 31)*

SEQ ID NO:190 (encodes SEQ ID NO:191):

gaaccgaaatcatgcgacaaaacgcacacctgtccgccctgtcctgccccggaacttctcggagggcctccgtgtttctcttcctccgaagcccaa
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gcgtggaggtgcacaacgccaaaacgaagcccccgagaggaacagtaccagtcaacgtaccgcgtcgtgtcggtattgactgtattgcatcaagactgg
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gtcgacaaaagccgctggcagcagggaaacgtattctcatgttcggtgatgcacgaagcattgcataaccactacacgcagaagagacttgtcgttgag
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cgccgtgcccgggcacccgaactgctcggaggtccctcggtgttcctgttcccgccaaagcctaaggatacgttgatgatttcgcgcacgccgcggaggta
acatgcgtggtggtggatgtgtcacatgaggacccgaggttcaagttcaattggtacgtcgatggagtggcacaatgcgaaaacaaaacacccg
ggaggagcagtatcagagcacgtacagggtagtctccgtcctgactgtacttcaccaagactggcttaacggaaaagagtataagtgcaaggtcagca
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ctataagactacgccccctgtgttggacagcgatgggtcattctttctgtattcgaaactcacggtggataagtcgcgatggcaacagggcaatgtgt
ttcgtgcagcgtgatgcatgaggcgctgcacaaccactatactcagaaatcgttaagcttatcgggagagtgt

SEQ ID NO:192 (encodes SEQ ID NO:193):

gaaccgaaatcatgcgacaaaacgcacacttgtccgccctgccctgcccgaactgcttggaggccctcggtgtttttgtttccgcccaagcctaa
ggacaccttgatgatcagccggacaccggaggtcacatgtgtcgtggatgtctcgcacgaggatcccgaggtcaagtttaactggtatgtggatg
gagtggaggtccacaacgccaaaacccaagcccaggggagagcaatacccatcgggtagtctcggtgctgacgaccaggactgg
ttgaatggaaaaagagtacaaatgcaaggtatcaaaacaaggccctcccgctcccatcgaaaaagacgatcagcaaagcgaaaagggcaacccagagagcc
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gtcgacaagtcccgctggcagcagggtaacgtgtttttcgtgttcagtgatgcacgaggctctgcataatcactacacacagaagtccctctccttgag
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gtacgtggacgggagtcgaagtccataacgctaaaacgaaaccgagagaggaacagtatcagagcacccgattgagaaaacaatctcaaaagcgaagggacag
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ctttcgctctccggtgaatgc

Fig. 10 *(sheet 6 of 31)*

SEQ ID NO:194 (encodes SEQ ID NO:195):
gaaccgaaatcatgcgacaaaacgcacacttgtccgccgtgcccagcgcccgagttgcttggcggacccagcgtgtttttgtttcccccgaaaccgaa
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acaagtctacactctcccaccctcccgcgaagaaatgacgaaaaaccaagtgtcactgacgtgtcttgtagatggtttctacccctcggacatcgcgg
tcgaatgggagtcgaatggacagccggagaacaattacgataccacœtcctgtcttggattcggacggctcattcttcctttacagcgatctcact
gtcgacaagtcgcgctggcagcagggaaacgtcttttcctgttcggtaatgcacgaagctctgcacaatcactacacgcagaagtcgctttcactttc
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gaggagggtccgggggaggggttccggaggggtgggtcctgtccccttgtccagcgccggagctgttgggcggaccttcggtattcttgtttcct
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cgaagctcacggtagataagtcgaggtggcaacaaggaaatgtgttttcatgttcggtgatgcatgaagcgctccataaccactatacgcagaaatcg
ctttcgctctccggtgaatgc

Nucleotide sequences encoding the polypeptides of Figure 7:

SEQ ID NO:196 (encodes SEQ ID NO:197):
gaaccgaaatcatgcgacaagacccatacatgcccaagctgtcccgctccggagtttctcggtggaccgtcggtgtttctgttccctccgaagccaaa
agataccttgatgatttcgcgaactcccgaagtcacgtgtgtcgtcgtggacgtaagccaggaggacccggaggtccagttcaattggtatgtagacg
gcgtagaggtacataatgcgaaaacgaagcccagagaggaacagttcaatagcaaataccgcgtagtatcggtgctgacagtgttgcaccaggactgg
ctgaatggaaaagaatacaagtgtaaagtgtccaacaagggccttccatcgtcgattgaaaagacaatctccaaggcaaaggggcagcctagggagcc
ccaagtctacaccctgccccttcgcgggaggagatgacgaagaaccaggtatcactgtcatgcgcggtcaaaggatttaœccgagcgacatcgccg
tagaatgggagtccaacggacagccagaaaacaattacaagaccactcctccagtgctcgatagcgatggctccttctttcttgtcagcaaattgaca
gtcgataagtcaagatggcagcagggtaatgtgttctcatgtagcgtcatgcacgaagcactccacaatcattatacacagaagagcctctcgttgtc
gcccggaaaaggcggaggtgggtcgggcggaggggaagcggtggaggagggtcaggaggtggaggttccgggggaggcggttcgggaggagggggtt
cgggtggtggaggatcgggtggcggaggaagctgcccttcatgtccagcccccgagttcctcggaggcccgtcggtctttcttttcccccctaagcct
aaagataccctgatgatcagccggacgcctgaggtgacttgtgtggtagtcgacgtgtcccaagaagatccggaagtccagtttaactggtatgtgga
tggagtggaggtccataatgccaagacaaagccaagggaggagcaattcaactcgaagtaccgcgtcgtgtccgtgctcacagtgcttcatcaagact
ggttgaacggaaaggagtacaaatgtaaggtatcaaacaagggtttgccctcgtccatcgagaaaaccatctcgaaagcgaaagggcaaccccgcgag
ccccaggtatatacgctcccgccttcaagagaagaaatgacgaaaaaccaagtgagcttgtggtgœctggtcaaggggttctatccctccgatatcgc
ggtagagtgggaaagcaatgggcagccggagaacaactataagacaacgcctcccgtgttggactcagatggatcgttcttcttgtactcaaagctta

Fig. 10 (sheet 7 of 31)

SEQ ID NO:198 (encodes SEQ ID NO:199):

gaaccgaaatcatgcgataagacacacacgtgcccctcgtgccccgcaccggagttccttggggtccgtcggtctttttgtttcccctaaacccaa
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gcgtggaggtgcacaatgccaagacgaaaccaagaggaacagttcaactcaaagtaccgggtagtatcggtgctgacggtgctccatcaggattggg
cttaacggtaaagagtacaagtgtaaagtcagcaataagggtctgcccagctccatcgaaaagactatctccaaggccaagggcagcctcgcgaacc
gcaagtgtgtacgttgcccccgtcccgggaggagatgacgaaaaatcaggtcagcctctcgtgtgcggtgaagggtttacccatccgacattgcgg
tggaatgggagagcaacggacaggcccgaaaacaattacaagactacccgccagtactcgatagcgacgggtcgttcttcttgtgtcgaaactgaca
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cggtcgacaaatcacgctggcagcagggcaacgtgtttcctgctcggtaatgcatgaggcgcttcacaaccactatacccagaagtcactgtcgctt
agcccagggaaa

SEQ ID NO:200 (encodes SEQ ID NO:201):

gaaccgaaatcatgcgacaagacccatacgtgcccatcgtgcccgcaccggagttcctcggaggcccgtcagtatttcctttttcctccgaagcccaa
agatacattgatgatcagcaggacgcctgaagtgacatgtgtagtggtagacgtgtcgcaagaagatccagaggtacagtttaactggtatgtcgacg
gggtggaagtccatacgccaagactaaacccgcgaagagcagttcaactcaaagtatagagtagtctccgtcctgacagtcctccatcaggactgg
ctgaacgggaaagaatacaagtgcaaagtctcgaacaaagggcttccgtcatcgatcgagaaaacgatttcaaaagccaagggacagcctagggagcc
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tggagtgggaatcgaatgggcaaccagagaacaactacaagaccactccccggtgctggactcggacgggctcctttttcttgacatcaaagctcaca
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cccggaaagggagtggaggtccggtgggggtggagcggcagcggtggcggaggtcaggtggaggcggatcaggtgggggaggttcaggcggctgctcg
aaggacacgctgatgatttcgcggacacccgaagtgacttgtgtcgtggtcgacgtaagccaggaggaccccgaggtgcaattcaactggtacgtcga
cggagtcgaggtccacaatgcgaaaacaaaacccagagaagaacagttcaattcgagtggtatcagtcctgaccgtgcttcatcaggatt
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ggtggaatgggagtcgaatggacagccggagaataactacaaaacgactccgcctgtcctcgacagcgatgggtccttcttcctttactcaaaattga
cagtagataagtcgcgctggcagcagggaaatgtattcctgttccgtcatgcatgaggcgcttcacaatcactacactcagaagtccttgtcgttg
tcaccaggaaaa

Fig. 10 *(sheet 8 of 31)*

SEQ ID NO:202 (encodes SEQ ID NO:203):
gaaccgaaatcatgcgacaagacatgctgttgcccaagctgtcccgctccggagtttctcggtggaccgtcggtgtttctgttccctccgaagccaaa
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gcgtagaggtacataatgcgaaaacgaagcccagagaggaacagttcaatagcaaatacgcgtagtatcggtgctgacagtgttgcaccaggactgg
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ccaagtctacacccctgcccccttcgcgggaggagatgacgaagaaccaggtatcactgtcatgcgcggtcaaaggatttaccgagcgacatcgccg
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tcaccaggaaaa

SEQ ID NO:204 (encodes SEQ ID NO:205):
gaaccgaaatcatgcgacaagtgccatacatgcccaagctgtcccgctccggagtttctcggtggaccgtcggtgtttctgttccctccgaagccaaa
agatacctttgatgatttcgcgaactcccgaagtcacgtgtgtcgtggacgtaagccaggaggacccggaggtccagttcaattggtatgtagacg
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cggtggacaagtcacgctggcagcaagggaacgtgtttcgtgctcggtgatgcacgaggcgcttcacaatcactacactcagaaatcgcttagcttg
tcaccaggaaaa

Fig. 10 *(sheet 9 of 31)*

SEQ ID NO:206 (encodes SEQ ID NO:207):

gaaccgaaatcatgcgataaaacgcacacgtgccctcgtgtccggcaccgagtttcttggaggtccctcggtgttcctgttcctcccaagccgaa
ggacacgttgatgatttcgaggacgccggaggtgacgtgtgtggtcgtagacgtgagccaggaggacccggaagtgcagtttaactggtacgtcgatg
gagtagaagtacataatgccaagacgaagcccaggggaggaacaattcgaagtatcgcgtcgtatccgtgctgactgtgctcœaccaggactgg
cttaacggaaaagaatacaagtgcaaggtatcaaataagggactcccctcgtcgatcgagaaaacaatcagcaaagcgaaaggacagccgagggaacc
gcaagtgtacacattgccgccgtcgcgagaagaaatgaccaagaaccaggtatcactctcgtgcgccgtgaagggctttacccatcggacattgctg
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cgatatcgcggtagagtgggaatcaaacgggccœagccggagaacaattacaaagaccaccgccccctgtattggattcggacggatcgttcttcttgtatt
cgaaactcacggtggacaagtcgcggtggcagcagggtaatgtgtttttcatgctcagtcatgcacgaggcgctcccataaccattatactcagaagtcg
ctgtccttgtccggggagtgc

SEQ ID NO:208 (encodes SEQ ID NO:209):

gaaccgaaatcatgcgacaagacccatacatgcccaagctgtcccgctccggagtttctcggtggaccgtcggtgtttctgttccctccgaagccaaa
agataccttgatgatttcgcgaactcccgaagtcacgtgtgtcgtcgtggacgtaagccaggaggacccggaggttccagttcaattggtatgtagacg
gcgtagaggtacataatgcgaaaacgaagcccagagaggaacagttcaatagcaaatacccgcgtagatcggtgctgacagtgttgcacœaggactgg
ctgaatggaaaagaatacaagtgtaaagtgtccaacaaggcctccatcgtcgattgaaaagacaatctccaaggcaaagggcagcctagggagcc
ccaagtctacaccctgcccccttcgcgggaggagatgacgaagaaccaggtatcactgtcatgcgcggtcaaaggatttttacccgagcgacatcgccg
tagaatgggagtccaacggacagccagaaaaacaattacaagaccactcctccœagtgctcgatagcgatggctccttcttcttgtcagcaaattgaca
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caagaagatccggaagtccagtttaactggtatgtggagtggaggtccataatgccaagacaaagccaagggaggagcaattcaactcgaagta
ccgcgtcgtgtccgtgctcacagtgcttcatcaagaggaaaggagtacaaatgtaaggtatcaæacaagggtttgccctcgtccatcg
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Fig. 10 (sheet 10 of 31)

SEQ ID NO:210 (encodes SEQ ID NO:211):
gaaccgaaatcatgcgacaaaacgcacacctgtccgtcatgtcctgccccggaattccttggagggccttccgtgtttctcttccctccgaagcccaa
ggacacgctgatgatctcccggaccccggaggtcacgtgtgtggtagtagacgtgtcacaagaagatccggaggtgcagttcaactggtacgtagatg
gcgtggaggtgcacaacgccaaaacgaagccccgagaggaacagttcaattcgaagtaccgcgtcgtgtcggtattgactgtattgcatcaagactgg
ttgaacgggaaggagtataagtgtaaagtcagcaacaagggacttccctcgtcaattgaaaagacaatttcgaaagccaaaggccagcccagggagcc
ccaagtgtacaccctgccacccagccgggaagagatgacaaagaatcaagtctcgcttagctgcgctgtcaagggcttctatccatcggacattgcag
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gaaaagctgcgacaagacgggaggggggagggtccgggggtggtgggagcggcggaggaggtagcggcggaggtggctcgggaggaggtgggtcgggtg
gtgggggaagcggaggcggagggtcatgtccgagctgcccggcacccgaatttctcggaggtccctcggtgttcctgttcccgccaaagcctaaggat
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ggaagtgcacaatgcgaaaacaaaaccccgggaggagcagttcaatagcaagtacagggtagtctccgtcctgactgtacttcaccaagactggctta
acggaaaagagtataagtgcaaggtcagcaacaaggggcttccttcatccatcgagaaaaccatctcgaaggccaagggacagccgagggagcctcaa
gtatacacgctgccgccatcgagagaagaaatgaccaaaaaccaggtgtccctttggtgtttggtgaagggtttctatccctccgatatcgccgtaga
gtgggagtcaaatggacagcctgagaacaactataagactacgccccctgtgttggacagcgatgggtcattctttctgtattcgaaactcacggtgg
ataagtcgcgatggcaacagggcaatgtgttttcgtgcagcgtgatgcatgaggcgctgcacaaccactatactcagaaatcgttaagcttatcggga
gagtgt

SEQ ID NO:212 (encodes SEQ ID NO:213):
gaaccgaaatcatgcgacaaaacgcacacctgtccgtcatgtcctgccccggaattccttggagggccttccgtgtttctcttccctccgaagcccaa
ggacacgctgatgatctcccggaccccggaggtcacgtgtgtggtagtagacgtgtcacaagaagatccggaggtgcagttcaactggtacgtagatg
gcgtggaggtgcacaacgccaaaacgaagccccgagaggaacagttcaattcgaagtaccgcgtcgtgtcggtattgactgtattgcatcaagactgg
ttgaacgggaaggagtataagtgtaaagtcagcaacaagggacttccctcgtcaattgaaaagacaatttcgaaagccaaaggccagcccagggagcc
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gatggcaacagggcaatgtgttttcgtgcagcgtgatgcatgaggcgctgcacaaccactatactcagaaatcgttaagcttatcgaagtcatgcgac
aagact

Fig. 10 (sheet 11 of 31)

SEQ ID NO:214 (encodes SEQ ID NO:215):
gaaccgaaatcatgcgacaaaacgcacacctgtccgtcatgtcctgccccggaattccttggagggccttccgtgtttctcttccctccgaagcccaa
ggacacgctgatgatctcccggaccccggaggtcacgtgtgtggtagtagacgtgtcacaagaagatccggaggtgcagttcaactggtacgtagatg
gcgtggaggtgcacaacgccaaaacgaagccccgagaggaacagttcaattcgaagtaccgcgtcgtgtcggtattgactgtattgcatcaagactgg
ttgaacgggaaggagtataagtgtaaagtcagcaacaagggacttccctcgtcaattgaaaagacaatttcgaaagccaaaggccagcccagggagcc
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cgcacgccggaggtaacatgcgtggtggtggatgtgtcacaagaggaccccgaggtccagttcaattggtacgtcgatggagtggaagtgcacaatgc
gaaaacaaaaccccgggaggagcagttcaatagcaagtacagggtagtctccgtcctgactgtacttcaccaagactggcttaacggaaaagagtata
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aacagggcaatgtgttttcgtgcagcgtgatgcatgaggcgctgcacaaccactatactcagaaatcgttaagcttatcgggagagtgt

SEQ ID NO:216 (encodes SEQ ID NO:217):
gaaccgaaatcatgcgacaaaacgcacacctgtccgtcatgtcctgccccggaattccttggagggcctccgtgtttctcttccctccgaagcccaa
ggacacgctgatgatctcccggaccccggaggtcacgtgtgtggtagtagacgtgtcacaagaagatccggaggtgcagttcaactggtacgtagatg
gcgtggaggtgcacaacgccaaaacgaagccccgagaggaacagttcaattcgaagtaccgcgtcgtgtcggtattgactgtattgcatcaagactgg
ttgaacgggaaggagtataagtgtaaagtcagcaacaagggacttccctcgtcaattgaaaagacaatttcgaaagccaaaggccagcccagggagcc
ccaagtgtacaccctgccacccagccgggaagagatgacaaagaatcaagtctcgcttagctgcgctgtcaagggcttctatccatcggacattgcag
tggaatgggaatcaaacggacagccggagaataactataagacgacacccccctgtcctcgacagcgacgggtcgttcttccttgtgagcagctcacg
gtcgacaaaagccgctggcagcagggaaacgtattctcatgttcggtgatgcacgaagcattgcataaccactacacgcagaagagcttgtcgttgtc
gaaaagctgcgacaagacgggaggggggagggtccgggggtggtgggagcggcggaggaggtagcggcggaggtggctcgggaggaggtgggtcatgtc
cgagctgcccggcacccgaatttctcggaggtccctcggtgttcctgttcccgccaaagcctaaggatacgttgatgatttcgcgcacgccggaggta
acatgcgtggtggtggatgtgtcacaagaggaccccgaggtccagttcaattggtacgtcgatggagtggaagtgcacaatgcgaaaacaaaaccccg
ggaggagcagttcaatagcaagtacagggtagtctccgtcctgactgtacttcaccaagactggcttaacggaaaagagtataagtgcaaggtcagca
acaaggggcttccttcatccatcgagaaaaccatctcgaaggccaagggacagccgagggagcctcaagtatacacgctgccgccatcgagagaagaa
atgaccaaaaaccaggtgtccctttggtgtttggtgaagggtttctatccctccgatatcgccgtagagtgggagtcaaatggacagcctgagaacaa
ctataagactacgcccccctgtgttggacagcgatgggtcattctttctgtattcgaaactcacggtggataagtcgcgatggcaacagggcaatgtgt
tttcgtgcagcgtgatgcatgaggcgctgcacaaccactatactcagaaatcgttaagcttatcgggagagtgt

Fig. 10 *(sheet 12 of 31)*

SEQ ID NO:218 (encodes SEQ ID NO:219):
gaaccgaaatcatgcgacaaaacgcacacttgtcctcctgccccggagttccttggcggaccctcggtctttttgtttccgccgaaaccgaa
agacaccttatgattagcaggacacccgaagtcacgtgtgtcgtcgtggacgtgtcgcaagaggatcccgaggtgcagttcaactggtacgtggacg
gggtagaagtccacaatgccaagacaaaaccccgggaagaacagtttaactcgaagtaccgcgtagtgtcagtcttgacagtcctccatcaggactgg
cttaacgggaaggagtacaaatgtaaagtgtcaacaacaagggtctgccttccagcattgagaaaaacgatctccaaggctæaagggcagccccgagaacc
acaagtctatacgcttccaccatcgcgggaggagatgaccaagaaccaggtccacttgacctgtctcgtgaagggttctacccgtcagatatcgcgg
tagagtgggaatcgaacggccagcccgagaatactacaagacgactcctccggtcctcgattcgagatgggtcgttcgcactctactcaaaacttacg
gtggacaagtcgagatggcagcagggcaacgtgtttagctgctcagtcatgcacgaggcgctgcataatcactatacacagaagtcgctgtcattgtc
aaaaagctgcgacacaagacagggggtggaggttcaggcggtgtgggtcgggagggggagggtcaggtggagggcggcagcgggggtgggggatcgggag
gaggagggtccgggggagggggttccggagggggtgggtcctgtccgtcgtgccctgcaccggaattcttgggcggtccgtcagtgttcctgtttccc
ccgaaacccaaagatacgctcatgatttcccgcatcccttcccgagaggaatcaagtgtcactcacatgtcttgtgaaggattctatcccag
cgacatcgccgtcgagtgggagtccaatgggcagccggaaaacaattacaaaacgtttccacccgtccttgactcagatggatcgttctttctctatt
cgaagctcacggtagataagtcgaggtggcaacaaggaaatgtgtttcatgttcggtgatgcatgaagcgctcccataaccactatacgcagaaatcg
ctttcgctctccggtgaatgc

SEQ ID NO:220 (encodes SEQ ID NO:221):
gaaccgaaatcatgcgacaaaacgcacacttgtccttcctgccccggagttccttggcggaccctcggtctttttgtttccgccgaaaccgaa
agacaccttatgattagcaggacacccgaagtcacgtgtgtcgtcgtggacgtgtcgcaagaggatcccgaggtgcagttcaactggtacgtggacg
gggtagaagtccacaatgccaagacaaaaccccgggaagaacagtttaactcgaagtaccgcgtagtgtcagtcttgacagtcctccatcaggactgg
cttaacgggaaggagtacaaatgtaaagtgtcaacaacaagggtctgccttccagcattgagaaaaacgatctccaaggctaaagggcagccccgagaacc
tcaagtctatacattgccccgagccgggaggaaatgaccaaaaaacccaggtatcgcttgctggacgggtttttaccccttcagacatcgcag
tggagtgggaatccaacgggcagccagagaacaattacgataccactccacccgtgcttgacagcgatggctcattctcctctattccgacttgacc
gtcgataagtcacgatggcagcagggggaatgtgtttagctgttcgtcatgcacgaagcgctgcacaaccactacacgcagaagtcgctctcattgtc
caaaagctgcgacaagacagggggtggaggttcaggcggtggtgggtcgggaggggaggggtcaggtggaggcggcagcgggggtgggggatcgggag
gaggagggtccgggggagggggttccggagggggtgggtcctgtccgtcgtgccctgcaccggaattcttgggcggtccgtcagtgttcctgtttccc
ccgaaacccaaagatacgctcatgatttcccgcatcccttcccgagaggaatcaagtgtcactcacatgtcttgtgaaggattctatcccgtc
gtacgtagatggtgtagaagtacacaacgctaaaactaagcctcgcgaagagcagttcaattcgaagtatcgggtagtaagcgtgctgactgtgctcc
atcaagactgtgctgaatggaaaagagtataagtgcaaagtctcgaataagggattgcccagctccattaaccactatacgcagaaatcg
cccagagaacccaagtgtatacgcttcccctcaagaaagagatgactaagaatcaggtgtcactcacgtgcctcgtgaagggattctatccgtc
ggacatcgcggtcgaatgggagtcgaatggacagccggagaacaactacaagacaacacctccagtgctgaaatcgggagcttctttctgtatt
cgaagctcacggtagataagtcgaggtggcaacaaggaaatgtgtttcatgttcggtgatgcatgaagcgctcccataaccactatacgcagaaatcg
cttcgctctccggtgaatgc

Fig. 10 *(sheet 13 of 31)*

Nucleotide sequences encoding the proteins provided in Example 3:

SEQ ID NO:230 (encodes SEQ ID NO:231):
gacattcagatgacacagtcgccgtcgtcgcttagcgcgtcagtgggagatagggtgacgattacgtgcaagtcatcccagtcgctgttgtatacatc
gagccagaagaactacctcgcgtggtaccaacagaagccggggaaagcgcccaaactcctgatctattgggcctcgaccagagagtccggagtaccat
cgcgcttctcaggcagcgggagcgggacggacttcacactgacgatctcctccttgcaaccgaagattttgctacgtattactgtcaacaatactat
gcctaccccctggacctttggccagggtactaaggtcgagatcaaacgtacggtggccgctccctccgtctttatctttcctccaagcgacgagcagct
gaagtctggcaccgcaagtgtggtgtgtctgctgaacaatttctaccccagggaagccaaagtgcaatggaaagtggataacgctctgcagtcaggaa
attcccaggagagcgtcacagaacaagactctaaagatagtacttattcactgtccagcaccctgacactgtctaaggccgattatgagaaacacaag
gtgtatgcctgtgaagtcactcatcaggggctgagttcacctgtgaccaaatcctttaacagaggtgagtgc

SEQ ID NO:246 (encodes SEQ ID NO:247):
atgggcacccccgcacagctcttgttcttgctgcttctttggctccctgacacaactggtgacattcagatgacacagtcgccgtcgtcgcttagcgc
gtcagtgggagatagggtgacgattacgtgcaagtcatcccagtcgctgttgtatacatcgagccagaagaactacctcgcgtggtaccaacagaagc
cggggaaagcgcccaaactcctgatctattgggcctcgaccagagagtccggagtaccatcgcgcttctcaggcagcgggagcgggacggacttcaca
ctgacgatctcctccttgcaacccgaagattttgctacgtattactgtcaacaatactatgcctacccctggacctttggccagggtactaaggtcga
gatcaaacgtacggtggccgctccctccgtctttatctttcctccaagcgacgagcagctgaagtctggcaccgcaagtgtggtgtgtctgctgaaca
atttctaccccagggaagccaaagtgcaatggaaagtggataacgctctgcagtcaggaaattcccaggagagcgtcacagaacaagactctaaagat
agtacttattcactgtccagcaccctgacactgtctaaggccgattatgagaaacacaaggtgtatgcctgtgaagtcactcatcaggggctgagttc
acctgtgaccaaatcctttaacagaggtgagtgc

SEQ ID NO:222 (encodes SEQ ID NO:223):
gaggtgcaactggtagaaagcggaggtggtcttgtacagcccggtggttcactcagactgtcgtgcgcagcttcagggtatacgttcacctcctactg
gctccattgggtgcgacaggctccggggaaaggactggaatgggtcgggatgattgatccgtcgaattcggatactaggttcaatcccaacttcaagg
accggtttaccattagcgcggatacctcgaaaaacaccgcatatctccaaatgaactcgttgagagccgaggacacggcggtgtattactgcgcaaga
tacgggtcgtatgtgtcaccgttggactactggggccaggggacactggtaacggtcagctcagctagcacgaagggacctagcgtgttcccattggc
gcccagctcgaaatccacatcgggcggaacggcagcccttgggtgcctcgtgaaagactactttcccgaaccggtgactgtgtcgtggaattcagggg
cattgacttccggtgtccacacatttccagccgtgctgcagtccagcgggttgtattcgctctcgtcagtggtcacagtcccatcctcctcgctcgga
acacaaacctatatctgtaatgtcaaccataaaccttcaaatacaaaagtggacaaaaaggta

Fig. 10 (sheet 14 of 31)

SEQ ID NO:244 (encodes SEQ ID NO:245):
atgggctttggactttcgtggctttttctcgtagcgattttgaagggcgtgcagtgcgaggtgcaactggtagaaagcggaggtggtcttgtacagcc
cggtggttcactcagactgtcgtgcgcagcttcagggtatacgttcacctcctactggctccattgggtgcgacaggctccggggaaaggactggaat
gggtcgggatgattgatccgtcgaattcggatactaggttcaatcccaacttcaaggaccggtttaccattagcgcggatacctcgaaaaacaccgca
tatctccaaatgaactcgttgagagccgaggacacggcggtgtattactgcgcaagatacgggtcgtatgtgtcaccgttggactactggggccaggg
gacactggtaacggtcagctcagctagcacgaagggacctagcgtgttcccattggcgcccagctcgaaatccacatcgggcggaacggcagcccttg
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tccagcgggttgtattcgctctcgtcagtggtcacagtcccatcctcctcgctcggaacacaaacctatatctgtaatgtcaaccataaaccttcaaa
tacaaaagtggacaaaaaggta

SEQ ID NO:286 (encodes SEQ ID NO:287):
caggtacaacttgtgcagtcaggagcggaggtgaagaagcctggtgcatcggtcaaagtgtcatgcaaagcctcggggtacatctttactgcgtacac
aatgcactgggtcagacaggctccgggacaaggtctggaatggatggggtggatcaagcccaataacgggctcgcgaattacgcccagaaattccagg
ggagagtgactatgacaagggatacgagcatttcgacggcgtatatggagctctcgcgcctgcggtcagatgacacagccgtatactattgcgcgcga
tcggaaatcaccaccgaattcgactattggggtcagggaactcttgtcacggtatccagcgctagcaccaagggcccgtcagtattcccgcttgcacc
ctcgtcgaaatcaacatcgggcggaacagcagcccttggctgcttggtaaaagactacttcccagagccagtaacggtatcgtggaattccggagctc
ttacgtcgggggtccatacatttcccgcggtactccaatcgtcgggactgtactcattgtcgtcagtcgtgaccgtgccatccagctccttgggaacc
cagacttacatctgcaacgtcaaccacaagccctcgaacactaaagtggacaagaaagtg

SEQ ID NO:255 (encodes SEQ ID NO:256):
atgggattcggactctcctggttgtttttggtggcaattctcaagggcgtccaatgtcaggtacaacttgtgcagtcaggagcggaggtgaagaagcc
tggtgcatcggtcaaagtgtcatgcaaagcctcggggtacatctttactgcgtacacaatgcactgggtcagacaggctccgggacaaggtctggaat
ggatggggtggatcaagcccaataacgggctcgcgaattacgcccagaaattccaggggagagtgactatgacaagggatacgagcatttcgacggcg
tatatggagctctcgcgcctgcggtcagatgacacagccgtatactattgcgcgcgatcggaaatcaccaccgaattcgactattggggtcagggaac
tcttgtcacggtatccagcgctagcaccaagggcccgtcagtattcccgcttgcaccctcgtcgaaatcaacatcgggcggaacagcagcccttggct
gcttggtaaaagactacttcccagagccagtaacggtatcgtggaattccggagctcttacgtcgggggtccatacatttcccgcggtactccaatcg
tcgggactgtactcattgtcgtcagtcgtgaccgtgccatccagctccttgggaacccagacttacatctgcaacgtcaaccacaagccctcgaacac
taaagtggacaagaaagtg

Fig. 10 *(sheet 15 of 31)*

SEQ ID NO:288 (encodes SEQ ID NO:289):
gacatcgtgctgacccagtcaccggattcgcttgcagtctcactgggagagagagccacgatcaattgcaagtcctcggaatcagtggacagctacgc
taactcattcatgcactggtatcagcagaagcctggccagccgcccaagttgctgatctaccgcgcaagcacacgggagtcgggggtgccagataggt
tttccggatcgggttcccgaacggacttcacactcacgatttcatccttgcaagccgaagatgtggcggtctattactgtcaacagtcgaaagaggat
ccccttacttttggtgggggtactaaagtagagattaagcgtacggtggcagcgccgtcagtctttatcttccctccttcggatgagcagcttaagag
cgggacagcctcagtagtctgccttctcaacaacttttacccgagagaggccaaggtgcagtggaaggtggataatgccttgcagtcagggaactcac
aagaatcggtcacagaacaggactccaaagatagcacttattccctgtcaagcacgctcactttgtccaaagcggactacgagaagcacaaagtgtac
gcttgcgaggtgactcatcaaggattgtcgagccccgtaacgaagagcttcaatcggggcgagtgt

SEQ ID NO:343 (encodes SEQ ID NO:344):
atggggacccctgcgcagttgcttttcctcctccttctctggttgcccgacacgacaggagacatcgtgctgacccagtcaccggattcgcttgcagt
ctcactgggagagagagccacgatcaattgcaagtcctcggaatcagtggacagctacgctaactcattcatgcactggtatcagcagaagcctggcc
agccgcccaagttgctgatctaccgcgcaagcacacgggagtcgggggtgccagataggttttccggatcgggttcccgæcggacttcacactcacg
atttcatccttgcaagccgaagatgtggcggtctattactgtcaacagtcgaaagaggatcccccttacttttggtgggggtactaaagtagagattaa
gcgtacggtggcagcgccgtcagtctttatcttccctccttcggatgagcagcttaagagcgggacagcctcagtagtctgccttctcaacaacttttt
acccgagagaggccaaggtgcagtggaaggtggataatgccttgcagtcagggaactcacaagaatcggtcacagaacaggactccaaagatagcact
tattccctgtcaagcacgctcactttgtccaaagcggactacgagaagcacaaagtgtacgcttgcgaggtgactcatcaaggattgtcgagccccgt
aacgaagagcttcaatcggggcgagtgt

SEQ ID NO:232 (encodes SEQ ID NO:233):
caagtccagttgcaagaaagcgggccaggactcgtgaaaccctcggaaaccctgtcactgacgtgcacggtgagcggagggtccgtgtcgagcggaga
ttactattggacttggattagacagtcgcccggaaaaggtctggagtggatcggacacatctactactcggggaatacgaattacaacccgtcgttga
aatcacggctcacgattagcatcgatacctccaagacgcagttctcgctcaaacttagctccgtaactgcggccgacaccgcaatctactattgtgta
cgcgaccgcgtcacaggggcttttgacatttggggtcagggcactatggtgacctcgtcagcgtcgacaggtggtgggggatcaggaggaggtggctc
cgggggaggcggaagcggcggtgggggctccgacatccagatgacgcagtcgccctcatcattgtcagcatcagtcggggacagggtcactattactt
gtcaggccagccaagatatctcgaactatctgaactggtatcagcagaagcctggaaaagcgcctaagctccttatctatgatgcgtccaatcttgag
acaggggtgccgtcgcggttttccggttcagggtcgggaacggacttcacgtttacaatctccagcctgcagccggaggacgaagccacctacttctg
ccaacacttcgaccatttgcctcttgcgttcggaggtgggacaaaggtggagatcaagcgaact

Fig. 10 (sheet 16 of 31)

SEQ ID NO:236 (encodes SEQ ID NO:237):
gaggtgcaactggtccagtcaggggcggaggtcaagaagcccggaagctccgtaaaggtatcatgcaaggcctcgggtggaaccttctcctcgtacgc
catcggttgggtgagacaagctcccgggcagggcctcgaatggatgggcggaatcattcccatctttggaatcgcgaactatgcgcagaaatttcagg
gtagagtaacgattacagcggatgaatcgacttcgtccgcatacatggagctttcgtcactcggtcagaggacactgccgtgtattactgtgcgcgg
gaggaaggcccgtattgtagctcgacctcgtgctacgctgcctttgacatttgggggcagggaacacttgtcacagtatcgagcgcgtccacgggcgg
aggggaagcggaggtgggggatcgggaggggggaggatcaggggagggggctcccagagcgtgttgacccaagatccagctgtgtccgtcgcactgg
gacagacggtcaaaatcacgtgccagggtgactcgcttcgctcgtacttcgcgtcatggtatcagcaaaaacctggtcaggcaccgacgttggtgatg
tacgcaaggaatgatcgacctgccggggtcccggacaggttctcggggagcaagagcgggacatccgcgtcgttggcgatctccggcctccagcccga
agatgaggccgattactattgtgcagcgtgggacgactcactgaacgggtatctcttcggggcaggcactaaactcacggtgctg

SEQ ID NO:257 (encodes SEQ ID NO:258):
caggtgcagctggtggagagcggcggcggcgtggtgcagcccggcgagagcctgagactgagctgcgccgtgagcggcttcagcctgaccaactacgg
cgtgcactgggtgagacaggcccccggcaagggcctggagtgggtgggcgtgatctggagcggcggcaacaccgactacaacacccccttcaccagca
gattcaccatcagcaaggacaacagcaagaacaccgtgtacctgcagatgaacagcctgagagccgaggacaccgccgtgtactactgcgccagagcc
ctgacctactacgactacgagttcgcctactggggccagggcaccctggtgaccgtgagcagcgccagcaccggcggcggcggcagcggcggcggcgg
cagcggcggcggcggcagcggcggcggcggcagcgacatcgtgctgacccagagccccgacttccagagcgtgaccccggcgagaaggtgaccatca
cctgcagagccagccagagcatcggcaccaacatccactggtaccagcagaagcccgaccagagccccaagctgctgatcaagtacgccagcgagagc
atcagcggcgtgcccagcagattcagcggcagcggcagcggcaccgacttcaccctgaccatcaacagcctggaggccgaggacgaggccacctacta
ctgccagcagaacaacaactggcccaccaccttcggccagggcaccaaggtggagatcaagagaacc

SEQ ID NO:274 (encodes SEQ ID NO:275):
caggtgcagctggtggagagcggcggcggcgtggtgcagcccggcgagagcctgagactgagctgcgccgtgagcggcttcagcctgaccaactacgg
cgtgcactgggtgagacaggcccccggcaagggcctggagtgggtgggcgtgatctggagcggcggcaacaccgactacaacacccccttcaccagca
gattcaccatcagcaaggacaacagcaagaacaccgtgtacctgcagatgaacagcctgagagccgaggacaccgccgtgtactactgcgccagagcc
ctgacctactacgactacgagttcgcctactggggccagggcaccctggtgaccgtgagcagcgccagcaccggcggcggcggcagcggcggcggcgg
cagcggcggcggcggcagcggcggcggcggcagcgacatcgtgctgacccagagccccagcagcctgagcgtgacccccggcgagaaggtgaccttca
cctgcagagccagccagagcatcggcaccaacatccactggtaccagcagaagcccggccagagccccaagctgctgatcaagtacgccagcgagagc
atcagcggcgtgcccagcagattcagcggcagcggcagcggcaccgacttcaccctgaccatcaacagcgtggaggccgaggacgaggccacctacta
ctgccagcagaacaacaactggcccaccaccttcggccagggcaccaagctggagatcaagagaacc

Fig. 10 (sheet 17 of 31)

SEQ ID NO:276 (encodes SEQ ID NO:277):

caggtgcagctggtggagagcggcggcgcggtggtgcagcccggcgagagcctgagaatcagctgcgccgtgagcggcttcagcctgaccaactacgg
cgtgcactgggtgagacaggcccccggcaagggcctggagtgggctgggcgtgatctggagcggcggcaacaccgactacaacacccccttcaccagca
gactgaccatcagcaaggacaacagcaagagcacccgtgtacttccagatgaacagcctgagagccgaggacaccgccgtgtactactgcgccagagcc
ctgacctactacgactacgagttcgcctactgggccagggcacccttggtgaccgtgagcagccaccggcggcagcggcggcgcggcgg
cagcggcggcggcggcagcggcggcggcagcgacatcgtgctgacccagagccccgacttccagagcgtgaccccgcgagaaggtgaccatca
cctgcagagccagccagagcatcggcaccaacatccactggtaccagcagaagccccgaccagagccccaagctgctgatcaagtacgccagcgagagc
atcagcggcgtgcccagcagattcagcggcagcggcagcggcaccgacttcaccctgaccatcaacagcctggaggccgaggacgtggcggcgaggc
ctgccagcagaacaacaactggcccaccacccttcggccagggcaccaaggtggagatcaagagaacc

SEQ ID NO:278 (encodes SEQ ID NO:279):

caggtgcagctggtggagagcggcggcgcggtggtgcagcccggcgagagcctgagaatcagctgcgccgtgagcggcttcagcctgaccaactacgg
cgtgcactgggtgagacaggcccccggcaagggcctggagtgggctgggcggcgcaacaccgactacaacacccccttcaccagca
gactgaccatcagcaaggacaacagcaagagcacccgtgtacttccagatgaacagcctgagagccgaggacaccgccgtgtactactgcgccagagcc
ctgacctactacgactacgagttcgcctactgggccagggcacccttggtgaccgtgagcagccaccggcggcagcggcggcgcggcgg
cagcggcggcggcggcagcggcggcggcagcgacatcgtgctgacccagagccccgacttccagagcgtgaccccgcgagaaggtgaccttca
cctgcagagccagccagagcatcggcaccaacatccactggtaccagcagaagccccgaccagagccccaagctgctgatcaagtacgccagcgagagc
atcagcggcgtgcccagcagattcagcggcagcggcaccgacttcaccctgaccatcaacagcgtggaggccgaggacgtggcggcgaggc
ctgccagcagaacaacaactggcccaccacccttcggccagggcaccaagctggagatcaagagaacc

Fig. 10 (sheet 18 of 31)

SEQ ID NO:234 (encodes SEQ ID NO:235) (SEQ ID NO:222 (5D5) + SEQ ID NO:180 (AEM1 DiS2)+ G4S connecting linker + SEQ ID NO:232 (panitumumab)):

gaggtgcaactggtagaaagcggaggtggttcttgtacagcccggtgttcactcagactgtcgtgcgcagcttcagggtatacgttcacctcctactg
gctccattgggtgcgacaggctccgggaaaggactggaatgggtcgggatgattgatccgtcgaattcggatactagggttcaatcccaacttcaagg
accggtttaccattagcgcggatacctcgaaaaacaccgcatatctccaaatgaactcgttgagaggccgaggacacgggcggtgtattactgcgcaaga
tacgggtcgtatgtgtcaccgttggactactgggggccaggggacactggtaacggtcagctcagctagcacgaagggacctagcgtgttcccattggc
gcccagctcgaaatccacatcgggcggaacgggcagcccttgggtgcctcgtgaaagactacttcccgaaccggtgactgtgtcgtggaattcagggg
cattgacttccggtgtccacacatttccagccgtgctgcagtccagcgggttgtattcgctctcgtcagtggtcacagtcccatcctcctcgctcgga
acacaaacctatatctgtaatgtcaaccataaacctcaaatacaaaaaggtagaaccgaaatcatgcgataaaacacacacatgccc
accatgcccagcgcctgaacttttgggaggtccctcggtgtttttgtttcctaagcctaaggacaccctgatgatctcccgcacccggaagtga
cgtgtgtcgtagtcgacgtcagccatgaggaccctgaggtgaaattcaactggtacgtagatggtgtggaggtgcataatgcaaaaactaagcctcgg
gaggaacaatatcaaagcacataccgggtcgtgtccgtgctcacggtacttcatcaggattggctcaacgggaaagaatacaaatgtaaggtgtccaa
caaggctctcccggcaccgattgagaaaacgatcagcaagggcagcccgagaacccaagtatacacacttccccgtccagggaggaga
tgaccaagaaccaggtgtcgctgtcgtgtcggtcaaggggttttatcccagcgacatcgcggtagagtgggagtcgaacggccagcccgagaacaac
tacaagacaacaccgccttgtattggactcggacgggtcgtttttcctggtcagcaagctcacagtggataaaagccgctggcagcagggaatgtatt
ctcctgctccgtcatgcacgaggcgcttcacaaccattacacgcaaaaatccctgtccttgtccaagtcatgcgacaagacgggaggaggaggtcag
gcggaggaggaagcgggggtggagggtccggtggtgggagcggatggtggaggtggtagcgggggaggtggatcgggaggggt
gggagctgtccgccatgtccagcccccggaacttctcgggggaccgtcagtctttctttttccgccgaagccaaggacaccttgatgattagccgcac
gccggaggtcacgtgcgtagtagtggatgtatcccacgaggacccgaggtcaaattcaattggtatgtcgacggagtggaagtacacaacgcaaaga
caaagccgagagaagagcagtaccaatccacttatagggtagtctcggtcttgacagtactgcaccaggactggcttaatggaaaggaatacaagtgc
aaagtctcaaacaaagcccctcccgcacccatcgaaaagacaatctcgaaaggcgaaaggagcctcaagtgtataccctgccccgtc
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ggcaatgtgtttagctgttcggtaatgcatgaggcgctccacaatcactatacacagaagagcttgtccctcagcgggggagtgcggaggtggaggggag
cggtggtgggggatcccaagtccagttgcaagaaagcgggccaggactcgtgaaaccctcggaaaccctgtcactgacgtgcacggtgagcggaggggt
ccgtgtcgagcggagattactattggacttggattagacagtcgcccggaaaaggctctggagtggatcggacacatctactactcgggggaatacgaat
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aatctactattgtgtacgcgaccgcgtcacagggcttttgacatttgggtcagggcactatggtgacctcgtcagcgtcgacaggtggtgggggat
caggaggaggtggctccgggggaggcggaagcggcggtgggggctccgacatccagatgacgcagtcgcccctcatcattgtcagcatcagtcgggggac
agggtcactattacttgtcaggccagccaagatatctcgaactatctggtatcagcagaagcctggaaaagcgcctaagctccttatctatga
tgcgtccaatcttgagacagggtgccgtcgcggttttccggttcagggtcgggaacggacttcacgtttacaatctccagccctgcagccggaggacg
aagccacctacttctgccaacacttcgaccattgcctcttgcgttcggaggtgggacaaaggtggagatcaagcgaact

Fig. 10 *(sheet 19 of 31)*

SEQ ID NO:342 (encodes SEQ ID NO:343) (SEQ ID NO:222 (5D5) + SEQ ID NO:186 (AEM1 + DiS2 inverted) + G4S connecting linker + SEQ ID NO:232 (panitumumab)):

Gaggtgcaactggtagaaagcggaggtggtcttgtacagcccggtggttcactcagactgtcgtgcgcagcttcagggtatacgttcacctcctactg
gctccattgggtgcgacaggctccgggaaaggactggatgggtcgggatgattgatccgtcgaattcggatactaggttcaatcccaacttcaaggg
accgtttaccattagcgcggatacctcgaaaaacaccgcatatctccaaatgaactcgttgagagccgaggacacgcggcgtgtattactgcgcaaga
tacgggtcgtatgtgtcaccgttggactactgggccagggacactggtaacggtcagctcagctagcacgcgaaggacctagcgtgttcccattggc
gcccagctcgaaatccacatcgggcggaacggcagccctgggtgcctcgtgaaagactacttttcccgaaccggtgactgtgtcgtggaattcagggg
cattgacttccggtgtccacacattttccagccgtgctgcagtccagcgggttgtattcgctctcgtcagtggtcacagtcccatcctcctcgctcgga
acacaaacctatatctgtaatgtcaaccataaaccttcaaatacaaaaaggtagaaccgaaatcatgcgacaaaacgcacacctgtcc
gccctgtcctgcccggaacttctcggagggccttccgtgtttctcttccctccgaagcccaaggacacgctgatgatcttccggaccccggaggtca
cgtgtgtggtagtagacgtgtcacacgaagatccggaggtgaagttcaactggtacgtagatggcgtggaggtgcacaacgccaaaacgaagccccga
gaggaacagtaccagtcaacgtaccgcgtcgtgtattgactgtatattgcatcaagactggttgaacgggaaggagtataagtgtaaagtcagcaa
caaggctcttcccgcacccattgaaaagacaatttcgaaagccaaggccagcccagggagccccaagtgtacaccctgccacccagccgggaagaga
tgacaaagaatcaagtctcgcttagctgcgctgtcaagggcttctatccatcggacattgcagtggaatgggaatcaaacggacagccggagaataac
tataagacgacgacacccccctgtcctcgacagcgacgggtcgttcttccttgtgagcaagctcacggtcgacaaaagccgctggcagcagggaaacgtatt
ctcatgttcggtgatgcacgaagcattgcataaccactacacgcagaagagcttgtcgttgagcgggaatgcggaggggagggtccggggtggtg
ggagcggcggaggaggtagcggcggaggtggctcgggaggaggtgggtcgggtggtggaggcggaggaggtcatgtccgccgtgcccggca
cccgaactgctcggaggtcccctcggtgttcctgttcccgccaaagcctaaggatacgttgatgattcgcgcacgccggaggtaacatgcgtggtggt
ggatgtgtcacatgaggacccgaggtcaagttcaattggtacgtcgatggagtgcacaatgcgaaacaaaacccgggaggagcagtatc
agagcacgtacagggtagtctccgtcctgactgtacttcaccaagactggcttaacggaaaagagtataaggtcaaggtcagcaacaaggcgcttcct
gcccctatcgagaaaaccatctcgaaggccaagggacagccgagggagcctcaagtatacacgctgccgccatcgagaagaaatgaccaaaaacca
ggtgtccctttggtgtttggtgaagggtttctatccctccgatatcgccgtagagtgggagtcaaatggacagcctgagaacactatagactacgc
ccctgtgttggacagcgatgggtcattcttctgtattcgaaactccacggtggataagtcgcgatggcaacagggcaatgtgtttttcgtgcagcgtg
atgcatgaggcgctgcacaaccactatactcagaaatcgttaagcttatcgaagtcggagtggagggagcggtggtgtgggggatc
ccaagtccagttgcaagaaagcgggccaggactcgtgaaaaccctcggaaaccctgtcactgacgtgcacggtgagcgggtccgtgtcgagcggag
attactattggacttggattagacagtcgcccggaaaaggtctggagtggatcggacacatctactactcgggaatacgaattacaaccccgtcgttg
aaatcacggctcacgattagcatcgatacctccaagacgcagttctcgctcaaacttagctccgtaactgcggccgacaccgcaatctactattgtgt
acgcgaccgcgtcacagggggctttgacattgggtcagggcactatggtgacctcgtcagcgtcgacaggtggtgggggatcaggaggaggtggct
ccgggggaggcggaagcggcggtgggggctccgacatccagatgacgcagtcgccctcatcattgtcagcatcagtcgggacagggtcactattact
tgtcaggccagccaagatatctcgaactatctgaactggtatcagcagaagcctggaaaagcgcctaagctccttatctatgatgcgtccaatcttga
gacaggggtgccgtcgcggtttccggttcagggtcgggaacggacttcacgtttacaatctccagcctgcgagccgggaggacgaagccacctacttct
gccaacacttcgaccatttgcctcttgcgttcggaggtgggacaaaggtggagatcaagcgaact

Fig. 10 (sheet 20 of 31)

SEQ ID NO:224 (encodes SEQ ID NO:225) (SEQ ID NO:222 (5D5) + SEQ ID NO:171 (AEM-1)+ G4S connecting linker + SEQ ID NO:232 (panitumumab)):

Gaggtgcaactggtagaaagcggaggtggtcttgtacagcccggtggttcactcagactgtcgtgcgcagcttcaggtatacgttcacctcctactg
gctccattgggtgcgacaggctccggggaaaggactgggatgggtcgggatgattgatccgtcgaattcggattactaggttcaatcccaacttcaagg
accggtttaccattagcgcggataccttcgaaaaacaccgcatatctccaaatgaactcgttgagagccgagacacggcggtgtattactgcgcaaga
tacgggtcgtatgtgtcaccgttggactactgggccagggacactggtaacggtcagctcagctagcacgaagggacctagcgtgttcccattggc
gcccagctcgaaatccacatcgggcggaacggcagcccttgggtgcctcgtgaaagactactttcccgaaccggtgactgtgtcgtggaattcagggg
cattgacttccggtgtcccacacatttccagccgtgctgcagtccagcgggttgtattcgctctcgtcagtggtcacagtcccatcctcctcgctcgga
acacaaacctatatctgtaatgtcaaccataaaccttcaaatacaaaaagtggacaaaaagtagaaccgaaatcatgcgataaagacccacacatgccc
tccctgtccagcacccgagctgctcgggggaccctcggtgttcttgtttcctcccaaacccaaagatacccttatgattagccggacaccagaggtga
cgtgcgtggtagtagacgtgtcccatgaggacccggagtcaagttcaactggtacgtggacggagtggaggtgcacaatgcaaagaccaagccgagg
gaagagcaataccagtccacatatagagtcgtgtcggtccttacggtcttgcatcaggactggctggaatggcaaagaatacaaatgtaaagtctccaa
caaagctctcccagcgcccattgagaaaacaatctcaaaagcgaaaggccaaccgagagaacctcaagtctatactcttcccccgtcgagagaggaaa
tgaccaaaaaccaggtatcccttgtcatgcgcggtcaaggggttttacccaagcgacatcgccgtggagtgggagtcgaacggacagccagagaaataac
tataagacgacccctcccgtgctggattcggatggatcgttctttcttgtcagcaaactcacagtcgacaaatcaaggtggcagcaagggaacgtgtt
cagctgttcggtaatgcatgaagccctccacaatcactacacgcagaaatccctgtcgctctcaccagggaagggtgggctcagggggtgtgggg
gatcaggtggtggtggtagcggaggtggagggagcggaggctccggtggaggaggttccggaggtggcgggtcagggggaggagggtcatgt
ccgccgtgccctgcccccgaattgctgggaggtccgtcccgtatttctgtttcccccgaagcctaaagatactcttatgatctcgcgaacgccgggaagt
aacttgtgtcgtggtagatgtctcacacgaagatcccgaagtgaaattcaattggtatgtcgacggcgtggaggtacataacgccaagacgaagccta
gagaggaacagtaccagtcaacgtatcgggtcgtatccgtgctcaccgtgctccaccaggattggctgaacggaaaggagtacaagtgcaaagtctcg
aacaaggcgttgcctgcgccaatcgaaaagacgatctccaaagctaagggacaaccacaagggaaccacaagtgtatactctcccgccctcgcgcgaaga
gatgacaaagaatcaggtgtcacttggtgcttctatccctcggatattgcggtcgagtgggagagcaatggtcaacggagaaaca
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tcttgagacaggggtgccgtcgcggtttccggttcagggtcgggaacggacttcacgtttacaatctccagcctgcagccggaggacgaagccgact
acttctgccaacacttcgaccatttgccttgcgttcggaggtgggacaaaggtggagatcaagcgaact

Fig. 10 (sheet 21 of 31)

SEQ ID NO:226 (encodes SEQ ID NO:227) (SEQ ID NO:222 (5D5) + SEQ ID NO:196 (IgG1/IgG4 AEM1) + G4S connecting linker + SEQ ID NO:232 (panitumumab)):

Gaggtgcaactggtagaaagcggaggtggttcttgtacagcccggtggttcactcagactgtcgtgcgcagcttcagggtatacgttcacctcctactg
gctccattgggtgcgacaggctccgggaaaggactggaatgggtcgggatgattgatccgttcgaattcgaattcgatactaggttcaatcccaacttcaagg
accggtttaccattagcgcggatacctcgaaaaacaccgcatatctccaaatgaactcgttgagagccgaggacacgacggcgtgtattactgcgcaaga
tacgggtcgtatgtgtcaccgttggactactgggccaggggacactggtaacggtcagctcagctagcacgaagggacctagcgtgttcccattggc
gcccagctcgaaatccacatcgggcggaacggcagccctgggtgcctcgtgaaagactactttcccgaaccggtgactgtgtcgtggaattcagggg
cattgacttccggtgtcccacacatttccagccgtgctgcagtccagcgggttgtattcgctctcgtcagtggtcacagtcccatcctcctcgctcggga
acacaaacctatatctgtaatgtcaaccataaaccttcaaatacaaaagtggacaaaaaggtagaaccgaaatcatgcgacaagacccatacatgccc
aagctgtcccgctccggagtttctcggtggaccgtcggtgtttctgttccctccgaagccaaaagatacctgatgatttcgcgaactcccgaagtca
cgtgtgtcgtcgtggacgtaagccaggaggacccggaggtccagttcaattggtatgtagacggcgtagaggtacataaatgcgaaaacgaagcccaga
gaggaacagttcaatagcaaataccgcgtagtatcggtgctgacagtgttgcaccaggactggctgaatggaaaagaatacaagtgtaaagtgtccaa
caagggccttccatcgtcgattgaaaagacaatctccaaggcaaaggggcagcctagggagccccaagtctacaccctgccccttcgcgggaggaga
tgacgaagaaccaggtatcactgtcatgcgcggtcaaaggatttttacccgagcgacatcgccgtagaatgggagtccaacggacagccagaaaaacaat
tacaagaccactcctccagtgctcgatagcgatggctcctcttctttctgtcagcaaattgacagtcgatgtaagtcaaggatggcagcagcgataatgtgtt
ctcatgtagcgtcatgcacgaagcactccacaatcattatacacagaagagcctctcgttgtcgcccggaaaaggcggagtggtcgggcggaggggg
gaagcggtggaggagggtcaggaggtggaggttccgggggaggaggggttcgggtggtggcggaggaagctgc
ccttcatgtccagcccccgagttcctcggaggcccgtcggtctttctttttcccctaagcctaaagatacccgtgatcagccggacgcctgaggt
gacttgtgtggtagtcgacgtgtcccaagaagatccggaagtccagttaactggatggagtggaggtccataatgccaagacaaagccaa
gggaggagcaattcaactcgaagtaccgcgtcgtgctcacagtgcttcatcaagactggttgaacggaaaggagtacaaatgtaaggtatca
aacaagggtttgccctcgtccatcgagaaaaccatctcgaaagcgaaagggcaacccccggaggccccaggtatatacgctcccgccttcaagagaaaga
aatgacgaaaaaccaagtgagcttgtggtgcctggtcaagggttctatcccctccgatatcgcggtagagtgggaaagcaatgggcagccggagaaca
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tttcgtgctcggtgatgcacgaggcgcttcacaatcactacactcagaaatcgcttagcttgtcaccaggaaaaggaggtggagggagcggtggtgg
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gcggagattactattggacttggattagacagtcgcccggaaaaggtctggagtggatcggacacatctactactcggggaatacgaattacaacccg
tcgttgaaatcacggctcacgattagcatcgatacctccaagacgcagttctcgctcaaacttagctccgtaactgcggccgacaccgcaatctacta
ttgtgtacgcgaccgcgtcacagggcttttgacattgggtcagggcactatggtgacctcgtcagcgtcgacaggtggtgggggatcaggaggag
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attacttgtcaggccagccaagatatctcgaactatctgaactggtatcagcagaagcctggaaaagcgcctaagctccttatctatgatgcgtccaa
tcttgagacagggggtgccgtcgcggtttccggttcagggtcgggaacggacttcacgtttacaatctccagcctgcagccgggaggacgaagccacct
acttctgccaacacttcgaccatttgcctcttgcgttcggaggtgggacaaaggtggagatcaagcgaact

Fig. 10 *(sheet 22 of 31)*

SEQ ID NO:228 (encodes SEQ ID NO:229)(SEQ ID NO:222 (5D5) + SEQ ID NO:196 (IgG1/IgG4 AEM1)+ G4S connecting linker + SEQ ID NO:232 (panitumumab)):

Gaggtgcaactggtagaaagcggaggtggttcttgtacagcccggtggttcactcagactgtcgtgcgcagcttcagggtatacgttcacctcctactg
gctccattgggtgcgacaggctccgggggaaaggactggtcgggatgattgatccgtcgaattcgatactaggttcaatcccaacttcaaggg
accggtttaccattagcgcggataccttcgaaaaacaccgcatatcctccaaatgaactcgttgagagccgagacacggcggtgtattactgcgcaaga
tacgggtcgtatgtgtcaccgttggactactgggccagggacactggtaacggtcagctcagctagcacgaagggacctagcgtgttcccattggc
gcccagctcgaaatccacatcgggcggaacggcagcccttgggtgcctcgtgaaagactactttcccgaaccggtgactgtgtcgtggaattcagggg
cattgacttccggtgtcccacacatttccagccgtgctgcagtccagcgggttgtattcgctctcgtcagtggtcacagtcccatcctcctcgctcgga
acacaaacctatatctgtaatgtcaacctaaacctcaaatacaaaagtggacaaaaaggtagaaccgaaatcatgcgacaagacccatacatgccc
aagctgtcccgctccggagtttctcggtggaccgtcggtgtttctgttccctccgaagccaaaagatacctgatttcgcgaactcccgaagtca
cgtgtgtcgtcgtggacgtaagccaggaggacccggaggtccagttcaattggtatgtagacggcgtagaggtacataatgcgaaaacgaagcccaga
gaggaacagttcaatagcaaatacccgcgtagtatcggtgctgacacagtgttgcaccaggactggctgaatggaaagaatacaagtgtaaagtgtccaa
caagggccttccatcgtcgattgaaaagacaatctccaaggcaaaggggcagcctagggagccccaagtctcacaccctgccccttcgcgggaggaga
tgacgaagaaccaggtatcactgtcatgcgcggtcaaaggatttttacccgagcgacatcgccgtagaatgggagtccaacggacagccagaaaaacaat
tacaagaccactcctccagtgctcgatagcgatggctccttcttcttctgtcagcaaattgacagtcgataagtcaagatggcagcagggtaatgtgtt
ctcatgtagcgtcatgcacgaagcactccacaatcattatacacagaagagcctcttcgttgtcgcccggaaaaggcggagtgggtcgggcggagggg
gaagcggtggaggagggtcaggaggtggaggttccgggggaggcggttcgggtggtggcggaggatcgggtggcggaggaagctgc
ccttcatgtccagccccgagttcctcggaggcccgtcggtctttctttttcccctaagcctaaagatacccgatgatcagccggacgcctgaggt
gacttgtgtggtagtcgacgtgtcccaagaagatccggaagtccagtttaactggtatgtggatggagtccataatgccaagacaaagccaa
gggaggagcaattcaactcgaagtaccgcgtcgtgctcacagtgcttcatcaagactggttgaacggaaaggagtacaaatgtaaggtatca
aacaagggtttgcccctcgtccatcgagaaaaccatctcgaaagcgaaagggcaacccccgcgagccccaggtatatacgctcccgccttcaagagaaga
aatgacgaaaaaccaagtgagcttgtggtgcctggtcaagggggttctatccctccgatatcgcggtagagtgggaaagcaatgggcagccggagaacca
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gggatcccaagtccagttgcaagaaagcgggccaggactcgtgaaaccctcggaaaccctgtcactgacgtgcacggtgagcggagggtccgtgtcga
gcggagattactattggacttggattagacagtcgcccggaaaaggtctggagtggatcggagacacatctactactcgggaatacgaattacaacccg
tcgttgaaatcacggctcacgattagcatcgatacctccaagacgcagttctcgctcaaacttagctccgtaactgcggccgacaccgcaatctacta
ttgtgtacgcgaccgctcacaggggcttttgacattggggtcagggcactatggtgacctcgtcagcgtcgacaggtggtgggggatcaggaggag
gtggctccgggggaggcggcggtgggggctccgacatccagatgacgcagtcgccctcatcattgtcagcatcagtcgggacagggtcact
attacttgtcaggccagccaagatatctcgaactatctgaactgtggtatcagcagaagcctggaaaagcgcctaagctccttatctatgatgcgtccaa
tcttgagacagggggtgccgtcgcggtttccggttcagggtcgggaacggacttcacgtttacaatctccagcctgcagccggaggacgaaggccacct
acttctgccaacacttcgaccatttgccttcttgcgttccgaggtgggacaaaggtggagatcaagcgaact

Fig. 10 *(sheet 23 of 31)*

SEQ ID NO:238 (encodes SEQ ID NO:239) (SEQ ID NO:222 (5D5)+ SEQ ID NO:180 + G4S connecting linker + SEQ ID NO:237 (2224)):

gaggtgcaactggtagaaagcggaggtggtcttgtacagcccggtggttcactcagactgtcgtgcgcagcttcagggtatacgttcacctcctactg
gctccattgggtgcgacaggctccggggaaaggactggaatgggtcgggatgattgatccgtcgaattcggatactaggttcaatcccaacttcaagg
accggtttaccattagcgcggatacctcgaaaaacaccgcatatctccaaatgaactcgttgagagccgaggacacggcggtgtattactgcgcaaga
tacgggtcgtatgtgtcaccgttggactactggggccaggggacactggtaacggtcagctcagctagcacgaagggacctagcgtgttcccattggc
gcccagctcgaaatccacatcgggcggaacggcagcccttgggtgcctcgtgaaagactactttcccgaaccggtgactgtgtcgtggaattcagggg
cattgacttccggtgtccacacatttccagccgtgctgcagtccagcgggttgtattcgctctcgtcagtggtcacagtcccatcctcctcgctcgga
acacaaacctatatctgtaatgtcaaccataaaccttcaaatacaaaagtggacaaaaaggtagaaccgaaatcatgcgataaaacacacacatgccc
accatgcccagcgcctgaacttttgggaggtccctcggtgtttttgtttcctcctaagcctaaggacaccctgatgatctcccgcactccggaagtga
cgtgtgtcgtagtcgacgtcagccatgaggaccctgaggtgaaattcaactggtacgtagatggtgtggaggtgcataatgcaaaaactaagcctcgg
gaggaacaatatcaaagcacataccgggtcgtgtccgtgctcacggtacttcatcaggattggctcaacgggaaagaatacaaatgtaaggtgtccaa
caaggctctcccggcaccgattgagaaaacgatcagcaaggccaaggggcagccccgagaaccccaagtatacacacttcccccgtccagggaggaga
tgaccaagaaccaggtgtcgctgtcgtgtgcggtcaaggggttttatcccagcgacatcgcggtagagtgggagtcgaacggccagcccgagaacaac
tacaagacaacaccgcctgtattggactcggacgggtcgtttttcctggtcagcaagctcacagtggataaaagccgctggcagcaggggaatgtatt
ctcctgctccgtcatgcacgaggcgcttcacaaccattacacgcaaaaatccctgtccttgtccaagtcatgcgacaagacgggaggaggagggtcag
gcggaggaggaagcgggggtggagggtccggtggtggtgggagcggaggtggagggagcggtggaggtggtagcgggggaggtggatcgggaggggt
gggagctgtccgccatgtccagccccggaacttctcgggggaccgtcagtctttcttttttccgccgaagcccaaggacaccttgatgattagccgcac
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ggcaatgtgtttagctgttcggtaatgcatgaggcgctccacaatcactatacacagaagagcttgtccctcagcggggagtgcggaggtggagggag
cggtggtgggggatccgaggtgcaactggtccagtcaggggcggaggtcaagaagcccggaagctccgtaaaggtatcatgcaaggcctcgggtggaa
ccttctcctcgtacgccatcggttgggtgagacaagctcccgggcagggcctcgaatggatgggcggaatcattcccatctttggaatcgcgaactat
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gcgcgtccacgggcggaggggggaagcggaggtgggggatcgggaggggggaggatcaggggggaggggctcccagagcgtgttgacccaagatccagct
gtgtccgtcgcactgggacagacggtcaaaatcacgtgccagggtgactcgcttcgctcgtacttcgcgtcatggtatcagcaaaaacctggtcaggc
accgacgttggtgatgtacgcaaggaatgatcgacctgccggggtcccggacaggttctcggggagcaagagcgggacatccgcgtcgttggcgatct
ccggcctccagcccgaagatgaggccgattactattgtgcagcgtgggacgactcactgaacgggtatctcttcggggcaggcactaaactcacggtg
ttg

Fig. 10 (sheet 24 of 31)

SEQ ID NO:259 (encodes SEQ ID NO:260) (SEQ ID NO:222 (5D5) + SEQ ID NO:180 + G4S connecting linker + SEQ ID NO:257 (cetuximab H1L1)):

gaggtgcaactggtagaaagcggaggtggtcttgtacagcccggtggttcactcagactgtcgtgcgcagcttcagggtatacgttcacctcctactg
gctccattgggtgcgacaggctccgggaaaggactggaatgggtcgggatgattgatccgtcgaattcgaattactaggttcaatcccaacttcaagg
accggtttaccattagcgcggatacctcgaaaaacaccgcatatctccaaatgaactcgttgagagccgaggacacggcggtgtattactgcgcaaga
tacgggtcgtatgtgtcaccgttggactactgggccagggacactggtaacggtcagctagcacgaagggacctagcgtgttcccattggc
gcccagctcgaaatccacatcgggcggaacggcagccgcttgggtgcctcgtgaaagactacttcccgaaccggtgactgtgtcgtggaattcagggg
cattgacttccggtgtccacacatttccagccgtgctgcagtccagcgggttgtattcgctctcgtcgtcagtggtcacagtcccatcctcctcgctcgga
acacaaacctatatctgtaatgtcaaccataaaccttcaaatacaaaagtggacaaaaagtagaaccgaaatcatgcgataaaacacacacatgccc
accatgcccagcgccctgaactttgggaggtcccttcggtgtttttgtttcctaagcctaaggacaccctgatgatctcccgcactccggaagtga
cgtgtgtcgtagtcgacgtcagccatgaggacccctgaggtgtacgtagatggtgtggaggtgcataatgcaaaaactaagcctcgg
gaggaacaatatcaaagcacatacccggtcgtgtccgtgctcacgtcaggattggctcaacgggaaagaatacaaatgtaaggtgtccaa
caaggctctcccggcaccgattgagaaaacgatcagcaaggccaagggcagcccccgagaaccccaagtatacacacttcccccgtccctccaggaggaga
tgaccaagaaccaggtgtcgctgtcgtgtcggtcaagggtttttatcccagcgacatcgcggtagatgggagtcgaacggcccagcccgagaacaac
tacaagacaacaccgcctgtattggactcggacgggtcgtttttcctggtcagcaagctcacagtggataaaagccgctggcagcaggggaatgtatt
ctcctgctccgtcatgcacgaggcgcttcacaaccattacacgcaaaaatacctgtccttgtccaagtcatgcgacaagacgggaggaggaggtcag
gcggaggaggaagcgggggtggagggtccggtggtggtgggagcggaggtggagcggtggtagcgggggaggtggatcgggaggggggt
gggagctgtccgccatgtccagcccccggaacttcctcgggggaccgtcagtctttctttttccgccgaagcccaaggacacccttgatgattagccgcac
gccggaggtcacgtgcgtagtagtggatgtatcccacgaggaccccgaggtcaaattcaattggtatgtcgacggagtggaagtacacaacgcaaaga
caaagccgagagaagagcagtaccaatccacttatagggtagtctcggtcttgacagtactgcaccaggactggcttaatggaaaggaatacaagtgc
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agagaagaagatgacgaagaaccaagtgtcccctctggtgtctcgtgaaaggttttttacccagcgatattgccgtcgtcgaatgggaaagcaatggtcagc
ccgaaaacaattacaagactacgcctcccgtattggattcggatggttcgttcttcttgtactcaaagcttactgtcgataagtcgcggtggcagcaa
ggcaatgtgtttagctgttcggtaatgcatgaggcgctccacaatcactatacacagaagagcttgtccctcagcgggggagtgcggaggtggagggag
cggtggtgggggatcccaggtgcagctggtggagagcggcggcgtggtgcagcccggcgagagcctgagactgagctgcgccgtgagcggcttca
gcctgaccaactacggcgtgcactgggtgagacaggccccccggcaaggggcctgggagtgggtgggcgtgatctggagcggcgcggcaacaccgactacaac
acccccttcaccagcagattcaccatcagcaaggacaacagcaagaacaccgtgtacctgcagatgaacagcctgagagccgaggacaccgccgtgta
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gcagcggcggcggcggcagcggcggcggcggcagcgacatcgtgctgacccagagccccgacttccagagcgtgacccccggc
gagaaggtgaccatcacctgcagagccagcgagagcatcggcaccaacatccactggtaccagcagaagcccgaccagagcccccaagctgctgatcaa
gtacgccagcgagagcatcagcggcgtgcccagcagattcagcggcagcggcaccgacttcaccctgaccatcaacagcctggaggccgaggacgtcgcc
acgaggccacctactactgccagcagaacaacaactggcccaccacccttcggccagggcaccaaggtggagatcaagagaacc

Fig. 10 (sheet 25 of 31)

SEQ ID NO:280 (encodes SEQ ID NO:281)(SEQ ID NO:222 (5D5) + SEQ ID NO:180 + G4S connecting linker + SEQ ID NO:274 (cetuximab H1L2)):

gaggtgcaactggtagaaagcggaggtggtcttgtacagcccggtgttcactcagactgtcgtgcgcagcttcaggtatacgttcacctcctactg
gctccattgggtgcgacaggctccgggaaaggactgggaatgggtcgggatgattgatccgtcgaattcgatactaggttcaatcccaacttcaagg
accgtttaccattagcgcggatacctcgaaaaacaccgcatatctccaaatgaactcgttgagagccgagacacggcggtgtattactgcgcaaga
tacgggtcgtatgtgtcaccgttggactactgggccagggacactggtaacggtcagctcagctagcacgaagggacctagcgtgttcccattggc
gcccagctcgaaatccacatcgggcggaacggcagccctgggtgcctcgtgaaagactactttcccgaaccggtgactgtgtcgtggaattcagggg
cattgacttccggtgtcccacacatttccagccgtgctgcagtccagcgggttgtattcgctctcgtcagtggtcacagctcccatcctcctcgctcgga
acacaaacctatatctgtaatgtcaaccataaacctcaaatacaaaaaggtagaaccgaaatcatgcgataaaacacacacatgcccc
accatgcccagcgcctgaactttgggaggtcccgtgtttttgtttcctcctaagcctaaggacaccctgatgatctcccgcactccggaagtga
cgtgtgtcgtagtcgacgtcagccatgaggaccctgaggtgaaattcaactggtacgtagatggtgtggaggtgcataatgcaaaaactaagcctcgg
gaggaacaatatcaaagcacatacggtcgtgtccgtgctcacggtacttcatcaggattggctcaacgggaaagaatacaaatgtaaggtgtccaa
caaggctctcccggcaccgattgagaaaacgatcagcaagggccaagggcagcccccgagaacccaagtatacacacttccccgtccagggaggaga
tgaccaagaaccaggtgtcgctgtcgtgtcgagtcaagggttttatcccagcgacatcgcggtagagtgggagtcgaacggccagcccgagaacaac
tacaagacaacaccgcctgtattggactcggacgggtcgtttttcctggtcagcaagctcacagtggataaaagccgctggcagcagggaatgtatt
ctcctgctccgtcatgcacgaggcgcttcacaaccattacacgcaaaaatccctgtccttgtccaagtcatgcgacaagacgggaggaggaggtcag
gcggaggaggaagcgggggtggagggtccggtgtggtgggagcggagtggagggtggtagcgggggaggtggatcgggagggggt
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gccggaggtcacgtgcgtagtagtggatgtatcccacgaggaccccgaggtcaaattcaattggtatgtcgacggagtggaagtacacaacgcaaaga
caaagccgagagaagagcagtaccaatccacttatagggtagtctcggtcttgacagtactgcaccaggactggcttaatggaaaggaatacaagtgc
aaagtctcaaacaaagccctcccgcacccatcgaaaagcgaaaggacagcccagagagcctcaagtgtatacccctgccccgtc
aagagaagagatgacgaagaaccaagtgtccctctggtgtctcgtgaaaggttttaccccagcgatattgccgtcgaatgggaaagcaatggtcagc
ccgaaaacaattacaagactacgcctcccgtatttggattcggatggttcgttcttcttgtactcaaagcttactgtcgcggtggcagcaa
ggcaatgtgtttagctgttcggtaatgcatgaggcgctccacaatcactatacacagaaagagctttgtccctcagcgggagtgcggaggtggagggag
cggtggtgggggatcccaggtgcagctggtggagagcggcgcggcgtggtgcagcccggcgagagcctgagactgagctgcgccgtgagcggcttca
gcctgaccaactacgggcgtgcactgggtgagacaggccccccggcaagggcctggagtgggtgggcgtgatctggagcggcggcaacaccgactacaac
acccccttcaccagcagattcaccatcagcaaggacaacagcaagaacaccgtgtacctgcagatgaacagcctgagagccgaggacaccgccgtgta
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gtacgccagcgagagcatcagcggcgtgcccagcagattcagcggcagcggcaccgacttcaccctgaccatcaacagcgtggaggccgaggacgc
acgaggccacctactactgccagcagaacaactggcccaccaccttcggccagggcaccaagctggagatcaagagaacc

Fig. 10 *(sheet 26 of 31)*

SEQ ID NO:282 (encodes SEQ ID NO:283)(SEQ ID NO:222 (5D5) + SEQ ID NO:180 + G4S connecting linker + SEQ ID NO:276 (cetuximab H2L1)):

gaggtgcaactggtagaaagcggaggtggtcttgtacagcccggtggttcactcagactgtcgtgcgcagcttcagggtatacgttcacctcctactg
gctccattgggtgcgacaggctccggggaaaggactggaatgggtcgggatgattgatccgtcgaattcggatactaggttcaatcccaacttcaagg
accggtttaccattagcgcggatacctcgaaaaacaccgcatatctccaaatgaactcgttgagagccgaggacacggcggtgtattactgcgcaaga
tacgggtcgtatgtgtcaccgttggactactggggccaggggacactggtaacggtcagctcagctagcacgaagggacctagcgtgttcccattggc
gcccagctcgaaatccacatcgggcggaacggcagcccttgggtgcctcgtgaaagactactttcccgaaccggtgactgtgtcgtggaattcagggg
cattgacttccggtgtccacacatttccagccgtgctgcagtccagcgggttgtattcgctctcgtcagtggtcacagtcccatcctcdcgctcgga
acacaaacctatatctgtaatgtcaaccataaaccttcaaatacaaaagtggacaaaaaggtagaaccgaaatcatgcgataaaacacacacatgccc
accatgcccagcgcctgaacttttgggaggtccctcggtgtttttgtttcctcctaagcctaaggacaccctgatgatctcccgcactccggaagtga
cgtgtgtcgtagtcgacgtcagccatgaggaccctgaggtgaaattcaactggtacgtagatggtgtggaggtgcataatgcaaaaactaagcctcgg
gaggaacaatatcaaagcacataccgggtcgtgtccgtgctcacggtacttcatcaggattggctcaacgggaaagaatacaaatgtaaggtgtccaa
caaggctctcccggcaccgattgagaaaacgatcagcaaggccaaggggcagccccgagaaccccaagtatacacacttcccccgtccagggaggaga
tgaccaagaaccaggtgtcgctgtcgtgtgcggtcaaggggttttatcccagcgacatcgcggtagagtgggagtcgaacggccagcccgagaacaac
tacaagacaacaccgcctgtattggactcggacgggtcgtttttcctggtcagcaagctcacagtggataaaagccgctggcagcaggggaatgtatt
ctcctgctccgtcatgcacgaggcgcttcacaaccattacacgcaaaaatccctgtccttgtccaagtcatgcgacaagacgggaggaggagggtcag
gcggaggaggaagcgggggtggagggtccggtggtggtgggagcggaggtggagggagcggtggaggtggtagcgggggaggtggatcgggaggggt
gggagctgtccgccatgtccagccccggaacttctcggggaccgtcagtctttcttttccgccgaagcccaaggacaccttgatgattagccgcac
gccggaggtcacgtgcgtagtagtggatgtatcccacgaggaccccgaggtcaaattcaattggtatgtcgacggagtggaagtacacaacgcaaaga
caaagccgagagaagagcagtaccaatccacttatagggtagtctcggtcttgacagtactgcaccaggactggcttaatggaaaggaatacaagtgc
aaagtctcaaacaaagccctccccgcacccatcgaaaagacaatctcgaaagcgaaaggacagcccagagagcctcaagtgtataccctgccccgtc
aagagaagagatgacgaagaaccaagtgtccctctggtgtctcgtgaaaggtttttaccccagcgatattgccgtcgaatgggaaagcaatggtcagc
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ggcaatgtgtttagctgttcggtaatgcatgaggcgctccacaatcactatacacagaagagcttgtccctcagcggggagtgcggaggtggagggag
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acccccttcaccagcagactgaccatcagcaaggacaacagcaagagcaccgtgtacttccagatgaacagcctgagagccgaggacaccgccgtgta
ctactgcgccagagccctgacctactacgactacgagttcgcctactggggccagggcaccctggtgaccgtgagcagcgccagcaccggcggcggcg
gcagcggcggcggcggcagcggcggcggcggcagcggcggcggcggcagcgacatcgtgctgacccagagccccgacttccagagcgtgacccccggc
gagaaggtgaccatcacctgcagagccagccagagcatcggcaccaacatccactggtaccagcagaagcccgaccagagccccaagctgctgatcaa
gtacgccagcgagagcatcagcggcgtgcccagcagattcagcggcagcggcagcggcaccgacttcaccctgaccatcaacagcctggaggccgagg
acgaggccacctactactgccagcagaacaacaactggcccaccaccttcggccagggcaccaaggtggagatcaagagaacc

Fig. 10 *(sheet 27 of 31)*

SEQ ID NO:284 (encodes SEQ ID NO:285)(SEQ ID NO:222 (5D5) + SEQ ID NO:180 + G4S connecting linker + SEQ ID NO:278 (cetuximab H2L2)):

gaggtgcaactggtagaaagcggaggtggtcttgtacagcccggtggttcactcagactgtcgtgcgcagcttcagggtatacgttcacctcctactg
gctccattgggtgcgacaggctccggggaaaggactggaatgggtcgggatgattccgtcgaattcgggatactaggttcaatcccaacttcaagg
accggtttaccattagcgcggatacctcgaaaaacaccgcatatcttccaaatgaactcgttgagagccgaggacacggcggtgtattactgcgcaaga
tacgggtcgtatgtgtcaccgttggactactgggggccagggggacactggtcagctcagctagcacgaagggacctagcgtgttcccattggc
gcccagctcgaaatccacatcgggcggaacggcagccctttgggtgcctcgtgaaagactactttcccgaaccggtgactgtgtcgtggaattcagggg
cattgacttccggtgtccacacatttccagccgtgctgcagtccagcgggttgtattcgctctcgtcagtggtcacagtcccatcctctcgctcggga
acacaaacctatatctgtaatgtcaaccataaacctttcaaatacaaaaaggtagaaccgaaatcatgcgataaaacacacacatgccc
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cgtgtgtcgtagtcgacgtcagccatgaggaccctgaggtgaaattcaactggtacgtagatggtgtggaggtgcataatgcaaaaactaagcctcgg
gaggaacaatatcaaagcacatacccggtcgtgtccgtgctcacggattggctcaacgggaaagaatacaaatgtaaggtgtccaa
caaggctctcccggcaccgattgagaaaacgatcagcaaggccaagggcagcccccgagaacccaagtatacacacttccccgtccagggagggaga
tgaccaagaaccaggtgtcgctgtcgtgtgcggtcaaggggtttatcccagcgacatcgcggtagagtgggagtcgaacggcccagcccgagaacaac
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gcggaggaggaagcgggggtggagggtccggtggtgggagcggaggtggagggagcggtggatcgggagggggt
gggagctgtccgccatgtccagcccccggaacttctcgggggaccgtcagtctttctttttccgccgaagcccaaggacacacttgatgattagccgcac
gccggaggtcacgtgcgtagtagtggatgtatcccacgaggacccggaggtcaaattcaattggtatgtcgacggagtggaagtacacaacgcaaaga
caaagccgagagaagagcagtaccaatccacttataggtagtctcggtcttgacagtactgcaccaggactggcttaatggaaaggaatacaagtgc
aaagtctcaaacaaagccctcccccgcacccatcgaaaagcgaaaggacagcccagagagcctcaagtgtataccctgccccccgtc
aagagaagagatgacgaagaaccaagtgtcccctcggtgtctcgtgaaaggtttttacccccagcgatattgccgtcgaatgggaaaagcaatggtcagc
ccgaaaacaattacaagactacgcctcccgtattggatttcgttcttcttgtactcaaagcttactgtcgcggtggcagcaa
ggcaatgtgtttagctgttcggtaatgcatgaggcgctccacaatcactatacacagaagagcttgtccctcagcggggagtgcggaggtggaggggag
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gcctgaccaactacggcgtgcactgggtgagacaggcccccggcaagggcctggagtggctgggcgtgatctggagcggcgcaacaccgactacaac
acccccttcaccagcagactgaccatcagcaaggacaacagcaagagcaccgtgtacttccagatgaacagcctgagagccgaggacaccgccgtgta
ctactgcgccagagccctgacctactacgactacgagttcgcctactgggccagggcaccctggtgaccgtgagcagcgccagcaccgcggcgcggcg
gcagcggcggcggcggcagcggcggcggcggcgcgacatcgtgctgacccagagcccccagcagcctgagcgtgagcccccggc
gagaaggtgaccttcacctgcagagccagcatcggcaccaacatccactggtaccagcagaagcccggccagagcccccaagctgctgatcaa
gtacgccagcgagagcatcagcggcgtgcccagcagattcagcggcagcggcaccgacttcaccctgaccatcaacagcgtggaggccgagg
acgaggccacctactactgccagcagaacaacaactggccccaccacctcggccagggcaccaagctggagatcaagagaacc

Fig. 10 *(sheet 28 of 31)*

SEQ ID NO:290 (encodes SEQ ID NO:291) (SEQ ID NO:284 (c-Met binding site 2) + SEQ ID NO:180 + G4S connecting linker + SEQ ID NO:257 (cetuximab H1L1)):

caggtacaacttgtgcagtcaggagcggaggtgaagaagcctggtgcatcggtcaaagtgtcatgcaaagcctcggggtacatctttactgcgtacac
aatgcactgggtcagacaggctccgggacaaggtctggaatggatggggtggatcaagcccaataacgggctcgcgaattacgcccagaaattccagg
ggagagtgactatgacaagggatacgagcatttcgacggcgtatatggagctctcgcgcctgcggtcagatgacacagccgtatactattgcgcgcga
tcggaaatcaccaccgaattcgactattggggtcagggaactcttgtcacggtatccagcgctagcaccaagggcccgtcagtattcccgcttgcacc
ctcgtcgaaatcaacatcgggcggaacagcagcccttggctgcttggtaaaagactacttcccagagccagtaacggtatcgtggaattccggagctc
ttacgtcgggggtccatacatttcccgcggtactccaatcgtcgggactgtactcattgtcgtcagtcgtgaccgtgccatccagctccttgggaacc
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Fig. 10 *(sheet 29 of 31)*

SEQ ID NO:346 (encodes SEQ ID NO:345):

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Fig. 10 (sheet 30 of 31)

SEQ ID NO:348 (encodes SEQ ID NO:349):

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Fig. 10 *(sheet 31 of 31)*

23: T366S/L368A/Y407V::T366W

MGFGLSWLFLVAILKGVQCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTV
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CVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLWC
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(SEQ ID NO:292)

Fig. 11
(sheet 1 of 25)

23A: Y349C/T366S/L368A/Y407V::Y349C/S354C/T366W

MGFGLSWLFLVAILKGVQCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTV
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RWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGGSGGGGSGGGGSGGGGSGGGGSCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVT
CVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVCTLPPCREEMTKNQVSLWC
LVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
(SEQ ID NO:295)

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(SEQ ID NO:294)

Fig. 11
(sheet 2 of 25)

23B: Y407T::T366Y

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RWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGS*CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVT
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(SEQ ID NO:297)

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Fig. 11
(sheet 3 of 25)

23C: H224C/T225C/T366S/L368A/Y407V::T366W

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(SEQ ID NO:299)

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ttgcatcaggactggctgaatggcaaagaatacaaatgtaaagtctccaacaaagctctcccagcgcccattgagaaaacaatctcaaaagcgaaaggccaaccgag
agaacctcaagtctatactcttcccccgtcgagagaggaaatgaccaaaaatcaggtatccctgtcatgcgcggtcaaggggttttacccaagcgacatcgccgtgg
agtgggagtcgaacggacagccagagaataactataagacgacccctcccgtgctggattcggatggatcgttctttcttgtcagcaaactcacagtcgacaaatca
aggtggcagcaagggaacgtgttcagctgttcggtaatgcatgaagccctccacaatcactacacgcagaaatccctgtcgctctcaccagggaagggtgggggtgg
ctcaggggtgggggatcaggtggtggtggtagcggaggtggagggagcggaggcggaggctccggtggaggaggttccggaggtggcgggtcaggggggaggagggt
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agtcgttgtcgctttcccccggaaaatgataa
(SEQ ID NO:298)

Fig. 11
(sheet 4 of 25)

23D: T223C/T366S/L368A/Y407V::T366W

MGFGLSWLFLVAILKGVQCDKCHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTV
LHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKS
RWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGS*CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVT
CVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLWC
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(SEQ ID NO:301)

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aggtggcagcaagggaacgtgttcagctgttcggtaatgcatgaagccctccacaatcactacacgcagaaatccctgtcgctctcaccagggaagggtgggggtgg
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ccagtcaacgtatcgggtcgtatccgtgctcaccgtgctccaccaggattggctgaacggaaaggagtacaagtgcaaagtctcgaacaaggcgttgcctgcgccaa
tcgaaaagacgatctccaaagctaagggacaaccaagggaaccacaagtgtatactctcccgccctcgcgcgaagagatgacaaagaatcaggtgtcactttggtgc
ttggtgaaggggttctatccctcggatattgcggtcgagtgggagagcaatggtcaaccggagaacaattacaagacgacaccgcccgtattggactccgacgggtc
cttctttctctactcgaagctcactgtagataagtcgcgatggcagcaggggaacgtctttagctgttccgtgatgcacgaggcacttcataaccactatacccaga
agtcgttgtcgctttcccccggaaaatgataa
(SEQ ID NO:300)

Fig. 11
(sheet 5 of 25)

23E: T366S/L368A/Y407V/CH3 C-terminal Cysteine KSCDKT::T366W/CH3 C-terminal Cysteine GEC

MGFGLSWLFLVAILKGVQCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTV
LHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKS
RWQQGNVFSCSVMHEALHNHYTQKSLSLSKSCDKT*GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGS*CPPCPAPELLGGPSVFLFPPKPKDTLMISRTP
EVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVS
LWCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSGEC
(SEQ ID NO:303)

atgggcttcggactgtcgtggctttttctggtggcgattcttaaggggtccagtgcgataaaacacacacatgcccaccatgcccagcgcctgaacttttgggagg
tccctcggtgtttttgtttcctcctaagcctaaggacaccctgatgatctcccgcactccggaagtgacgtgtgtcgtagtcgacgtcagccatgaggaccctgagg
tgaaattcaactggtacgtagatggtgtggaggtgcataatgcaaaaactaagcctcgggaggaacaatatcaaagcacataccgggtcgtgtccgtgctcacggta
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agaaccccaagtatacacacttcccccgtccagggaggagatgaccaagaaccaggtgtcgctgtcgtgtgcggtcaaggggttttatcccagcgacatcgcggtag
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gaggtcacgtgcgtagtagtggatgtatcccacgaggaccccgaggtcaaattcaattggtatgtcgacggagtggaagtacacaacgcaaagacaaagccgagaga
agagcagtaccaatccacttatagggtagtctcggtcttgacagtactgcaccaggactggcttaatggaaaggaatacaagtgcaaagtctcaaacaaagccctcc
ccgcacccatcgaaaagacaatctcgaaagcgaaaggacagcccagagagcctcaagtgtataccctgcccccgtcaagagaagagatgacgaagaaccaagtgtcc
ctctggtgtctcgtgaaaggtttttaccccagcgatattgccgtcgaatgggaaagcaatggtcagcccgaaaacaattacaagactacgcctcccgtattggattc
ggatggttcgttcttcttgtactcaaagcttactgtcgataagtcgcggtggcagcaaggcaatgtgtttagctgttcggtaatgcatgaggcgctccacaatcact
atacacagaagagcttgtccctcagcggggagtgctgataa
(SEQ ID NO:302)

Fig. 11
(sheet 6 of 25)

23G: T366S/L368A/Y407V::T366W and (G4S)4

MGFGLSWLFLVAILKGVQCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTV
LHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKS
RWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*GGGGSGGGGSGGGGSGGGGS*CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVD
GVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
(SEQ ID NO:305)

atgggcttcggactgtcgtggcttttctggtggcgattcttaaggggtccagtgcgacaagacccacacctgcccaccgtgtccagcgcccgagctcctcggagg
gccgtcggtgttcctctttcccccaaagcctaaagacactctgatgatcagccgcactccagaagtgacatgtgtggtggtggatgtctcgcatgaggacccggaag
tcaaattcaattggtacgtggatggtgtcgaagtgcacaacgccaagacaaaaccgcgcgaggagcagtaccagagcacctaccgggtggtatcagtgcttacagta
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cggtggcagcaaggtaacgtattttcgtgttcggtgatgcatgaagcgctgcataaccactatacgcagaagagcttgtccttgtcaccaggcaagggaggtggggg
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ccaagccgaaagacacgctgatgatctcgaggacgcccgaggtaacgtgcgtcgtcgtcgatgtatcccacgaagatcccgaggtcaagttcaactggtatgtagat
ggggtcgaagtccataacgctaagacaaagccgagagaggaacaatatcagtcaacttatcgggtcgtgtcggtcctgaccgtacttcaccaggactggctcaatgg
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caccctcgagagaagaaatgacgaagaatcaagtctccttgtggtgtttggtgaaggggttttacccttcagacatcgcagtggaatgggaatcgaacgggcagcca
gaaaacaattacaaaaccacacctcctgtccttgactccgatggctcatttttcctctattcgaagctcactgtcgacaagtcgcgctggcagcagggtaacgtctt
tagctgctccgtgatgcacgaggccctccacaatcattatacacagaaatcgctgtcactttcgcccggaaaatgataa
(SEQ ID NO:304)

Fig. 11
(sheet 7 of 25)

23E (35L): T366S/L368A/Y407V/CH3 C-terminal Cysteine KSCDKT::T366W/CH3 C-terminal Cysteine GEC and (G4S)7

MGFGLSWLFLVAILKGVQCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTV
LHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKS
RWQQGNVFSCSVMHEALHNHYTQKSLSLSKSCDKT*GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGS*CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCV
VVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLV
KGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSGEC
(SEQ ID NO:307)

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aatgggaatcaaacggacagccggagaataactataagacgacacccccctgtcctcgacagcgacgggtcgttcttccttgtgagcaagctcacggtcgacaaaagc
cgctggcagcagggaaacgtattctcatgttcggtgatgcacgaagcattgcataaccactacacgcagaagagcttgtcgttgagcaaatcatgcgacaagaccgg
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gtggtggatgtgtcacatgaggaccccgaggtcaagttcaattggtacgtcgatggagtggaagtgcacaatgcgaaaacaaaaccccgggaggagcagtatcagag
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aaaccatctcgaaggccaagggacagccgagggagcctcaagtatacacgctgccgccatcgagagaagaaatgaccaaaaaccaggtgtccctttggtgtttggtg
aagggtttctatccctccgatatcgccgtagagtgggagtcaaatggacagcctgagaacaactataagactacgccccctgtgttggacagcgatgggtcattctt
tctgtattcgaaactcacggtggataagtcgcgatggcaacagggcaatgtgttttcgtgcagcgtgatgcatgaggcgctgcacaaccactatactcagaaatcgt
taagcttatcgggagagtgttgataa
(SEQ ID NO:306)

Fig. 11
(sheet 8 of 25)

23E (35L) Inverted: T366S/L368A/Y407V/CH3 C-terminal Cysteine GEC::T366W/CH3 C-terminal Cysteine KSCDKT and (G4S)7

MGFGLSWLFLVAILKGVQCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTV
LHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKS
RWQQGNVFSCSVMHEALHNHYTQKSLSLSGEC*GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGS*CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVD
VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVKGF
YPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSKSCDKT
(SEQ ID NO:309)

atgggcttcggactgtcgtggctttttctggtggcgattcttaaggggtccagtgcgacaaaacgcacacctgtccgccctgtcctgccccggaacttctcggagg
gccttccgtgtttctcttccctccgaagcccaaggacacgctgatgatctcccggaccccggaggtcacgtgtgtggtagtagacgtgtcacacgaagatccggagg
tgaagttcaactggtacgtagatggcgtggaggtgcacaacgccaaaacgaagccccgagaggaacagtaccagtcaacgtaccgcgtcgtgtcggtattgactgta
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gtccgggggtggtgggagcggcggaggaggtagcggcggaggtggctcgggaggaggtgggtcgggtggtgggggaagcggaggcggagggtcatgtccgccgtgcc
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cgaaggccaagggacagccgagggagcctcaagtatacacgctgccgccatcgagagaagaaatgaccaaaaaccaggtgtccctttggtgtttggtgaagggtttc
tatccctccgatatcgccgtagagtgggagtcaaatggacagcctgagaacaactataagactacgccccctgtgttggacagcgatgggtcattctttctgtattc
gaaactcacggtggataagtcgcgatggcaacagggcaatgtgttttcgtgcagcgtgatgcatgaggcgctgcacaaccactatactcagaaatcgttaagcttat
cgaagtcatgcgacaagacttgataa
(SEQ ID NO:308)

Fig. 11
(sheet 9 of 25)

23E (30L): T366S/L368A/Y407V/CH3 C-terminal Cysteine KSCDKT::T366W/CH3 C-terminal Cysteine GEC and (G4S)6

MGFGLSWLFLVAILKGVQCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTV
LHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKS
RWQQGNVFSCSVMHEALHNHYTQKSLSLSKSCDKT*GGGGSGGGGSGGGGSGGGGSGGGGSGGGGS*CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS
HEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVKGFYP
SDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSGEC
(SEQ ID NO:311)

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cacggtggataagtcgcgatggcaacagggcaatgtgttttcgtgcagcgtgatgcatgaggcgctgcacaaccactatactcagaaatcgttaagcttatcgggag
agtgttgataa
(SEQ ID NO:310)

Fig. 11
(sheet 10 of 25)

23E (25L): T366S/L368A/Y407V/CH3 C-terminal Cysteine KSCDKT:: T366W/CH3 C-terminal Cysteine GEC and (G4S)5

MGFGLSWLFLVAILKGVQCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTV
LHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKS
RWQQGNVFSCSVMHEALHNHYTQKSLSLSKSCDKT*GGGGSGGGGSGGGGSGGGGSGGGGS*CPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPE
VKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVKGFYPSDIAV
EWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSGEC
(SEQ ID NO:313)

atgggcttcggactgtcgtggcttttctggtggcgattcttaaggggtccagtgcgacaaaacgcacacctgtccgccctgtcctgccccggaacttctcggagg
gccttccgtgtttctcttccctccgaagcccaaggacacgctgatgatctcccggaccccggaggtcacgtgtgtggtagtagacgtgtcacacgaagatccggagg
tgaagttcaactggtacgtagatggcgtggaggtgcacaacgccaaaacgaagccccgagaggaacagtaccagtcaacgtaccgcgtcgtgtcggtattgactgta
ttgcatcaagactggttgaacgggaaggagtataagtgtaaagtcagcaacaaggctcttcccgcacccattgaaaagacaatttcgaaagccaaaggccagcccag
ggagccccaagtgtacaccctgccacccagccgggaagagatgacaaagaatcaagtctcgcttagctgcgctgtcaagggcttctatccatcggacattgcagtgg
aatgggaatcaaacggacagccggagaataactataagacgacacccccctgtcctcgacagcgacgggtcgttcttccttgtgagcaagctcacggtcgacaaaagc
cgctggcagcagggaaacgtattctcatgttcggtgatgcacgaagcattgcataaccactacacgcagaagagcttgtcgttgagcaaatcatgcgacaagaccgg
gggtggtgggagcggcggaggaggtagcggcggaggtggctcgggaggaggtgggtcgggtggtgggggatcatgtccgccgtgcccggcacccgaactgctcggag
gtccctcggtgttcctgttcccgccaaagcctaaggatacgttgatgatttcgcgcacgccggaggtaacatgcgtggtggtggatgtgtcacatgaggaccccgag
gtcaagttcaattggtacgtcgatggagtggaagtgcacaatgcgaaaacaaaaccccgggaggagcagtatcagagcacgtacagggtagtctccgtcctgactgt
acttcaccaagactggcttaacggaaaagagtataagtgcaaggtcagcaacaaggcgcttcctgcccctatcgagaaaaccatctcgaaggccaagggacagccga
gggagcctcaagtatacacgctgccgccatcgagagaagaaatgaccaaaaaccaggtgtccctttggtgtttggtgaagggtttctatccctccgatatcgccgta
gagtgggagtcaaatggacagcctgagaacaactataagactacgccccctgtgttggacagcgatgggtcattctttctgtattcgaaactcacggtggataagtc
gcgatggcaacagggcaatgtgttttcgtgcagcgtgatgcatgaggcgctgcacaaccactatactcagaaatcgttaagcttatcgggagagtgttgataa
(SEQ ID NO:312)

Fig. 11
(sheet 11 of 25)

23I: S364H/F405A::Y349T/T394F with CH3 terminal disulfide

MGFGLSWLFLVAILKGVQCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTV
LHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVHLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFALYSKLTVDKS
RWQQGNVFSCSVMHEALHNHYTQKSLSLSKSCDKTGGGSGGGGSGGGGSGGGGSGGGGSGGGGSCPPCPAPELLGGPSVFLFPPKPKDTLMISRTP
EVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVTTLPPSREEMTKNQVS
LTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSLGEC
(SEQ ID NO:315)

atgggcttcggactgtcgtggctttttctggtggcgattcttaaggggtccagtgcgacaaaacgcacacttgtccgccctgccctgcgcccgaactgcttggagg
ccctcggtgtttttgtttccgcccaagcctaaggacaccttgatgatcagccggacaccggaggtcacatgtgtcgtcgtggatgtctcgcacgaggatcccgagg
tcaagtttaactggtatgtggatggagtggaggtccacacaacgccaaaaccaagcccacgcgaggagcaataccagtcaacctatcgggtagtctcggtgctgacggta
ctgcaccaggactggttgaatggaaaagagtacaaatgcaaggtatcaaacaaggccctcccgctcccatcgaaaagacgatcagcaaagcgaaagggcaacccag
agagcccaagtctatacgctgcctccctcccaagggaagaaatgacgaaaaaccaggtgcacttgacatgcctcgtgaaaggcttctacccgagcgacattgcggtgg
aatgggagtcaaatggtcagccggaaaacaactacaagacaactccaccggtcctttgattcagacgggtcgttcgccctctatagcaaactcacggtcgacaagtcc
cgctggcagcagggtaacgtgtttcgtgttcagtgatgcacgaggctctgcataatcactacacacagaagtccctcctcctgagcaaaagctgcgacaagacagg
gggtggaggttcaggcggtggtgggtcgggagggggaggtcaggtggagggcgcagcgggggtggggaggaggagtccgggggaggggttccggag
gggtgggtcctgtcccctttgtccagcgccggagctgttgggcggaccttcggtattcttgtttcctcctaagcccaaagatacgcttatgatctcccgcacccccg
gaggtaacttgcgtcgtagtggatgtatcacatgaggacccagaagtcaagttcaattggtacgtggacggagtcgaagtccataacgctaaacgaaaccgaaaccgagaga
ggaacagtatcagagcacctaccgggtagtgagcgtgctcacagtgttgcatcaggattgggctgaatgggaaggaatacaagtgtcgaataaggcattgc
cagcaccgattgagaaaacaatctcaaaagcgaagggacagcccgagagccctcaagtcactacactgccacccagccgcgaagagatgacaaagaatcaggtatcc
ctcacgtgtcttgtgaaggggttctatcgcctccgatatcgcagtagagtgggaatcgaacgggcagccggagaacaattacaagacttcccgccagtgcttgattc
ggacggtagcttctttttgtattcgaagctcacggtagataagtcgaggtggcaacaaggaaatgtgtttcatgttcggtgatgcatgaagcgctccataaccact
atacgcagaaatcgctttcgctctccggtgaatgctgata
(SEQ ID NO:314)

Fig. 11
(sheet 12 of 25)

23J: K370D/K392D/K409D::D356K/E357K/D399K with CH3 terminal disulfide
MGFGLSWLFLVAILKGVQCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTV
LHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVDGFYPSDIAVEWESNGQPENNYDTTPPVLDSDGSFFLYSDLTVDKS
RWQQGNVFSCSVMHEALHNHYTQKSLSLSKSCDKT*GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGS*CPPCPAPELLGGPSVFLFPPKPKDTLMISRTP
EVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRKKMTKNQVS
LTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLKSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSGEC
(SEQ ID NO:317)

atgggcttcggactgtcgtggcttttctggtggcgattcttaaggggtccagtgcgacaaaacgcacacttgtccgccgtgcccagcgcccgagttgcttggcgg
acccagcgtgtttttgtttccccccgaaaccgaaagatacattgatgattagcagaacgcccgaagtgacgtgtgtagtagtcgacgtgtcgcacgaagatccggagg
tgaagttcaactggtatgtcgatggggtagaggtgcacaacgcgaaaaccaagcccagggaggagcagtaccagtcgacatatcgggtcgtgtcagtgctgacagtg
ctccatcaggactggttgaacgggaaggagtataagtgtaaagtcagcaacaaagccctccccgcacccatcgagaaaaccatttccaaggcaaagggacaaccgag
ggaaccacaagtctacactctcccaccctcccgcgaagaaatgacgaaaaaccaagtgtcactgacgtgtcttgtagatggtttctacccctcggacatcgcggtcg
aatgggagtcgaatggacagccggagaacaattacgataccacacctcctgtcttggattcggacggctcattcttcctttacagcgatctcactgtcgacaagtcg
cgctggcagcagggaaacgtcttttcctgttcggtaatgcacgaagctctgcacaatcactacacgcagaagtcgctttcactttccaaaagctgcgacaagacagg
gggtggaggttcaggcggtggtgggtcgggaggggagggtcaggtggaggcggcagcgggggtgggggatcgggaggaggagggtccgggggaggggttccggag
ggggtgggtcctgtccccttgtccagcgccggagctgttgggcggaccttcggtattcttgtttcctcctaagcccaaagatacgcttatgatctcccgcaccccg
gaggtaacttgcgtcgtagtggatgtatcacatgaggacccagaagtcaagttcaattggtacgtggacggagtcgaagtccataacgctaaaacgaaaccgagaga
ggaacagtatcagagcacctaccgggtagtgagcgtgctcacagtgttgcatcaggattggctgaatgggaaggaatacaagtgcaaagtgtcgaataaggcattgc
cagcaccgattgagaaaacaatctcaaaagcgaagggacagccccgagagcctcaagtctatacactgccgccaagccggaagaagatgaccaaaaaccaggtgtcc
ctcacgtgcctcgtgaaagggttttacccgtcagatatcgccgtagaatgggagagcaatgggcagcccgagaataactataagactacgccccctgtactcaaatc
ggacgggtcattctttctgtattcgaagctcacggtagataagtcgaggtggcaacaaggaaatgtgttttcatgttcggtgatgcatgaagcgctccataaccact
atacgcagaaatcgctttcgctctccggtgaatgctgataa
(SEQ ID NO:316)

Fig. 11
(sheet 13 of 25)

39: T366S/L368A/Y407V::T366W

MGFGLSWLFLVAILKGVQCDKTHTcpscpapeflggpsvflfppkpkdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltv
lhqdwlngkeykckvsnkglpssiektiskakGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKS
RWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGS*cpscpapeflggpsvflfppkpkdtlmisrtpevt
cvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltvlhqdwlngkeykckvsnkglpssiektiskakGQPREPQVYTLPPSREEMTKNQVSLWC
LVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
(SEQ ID NO:319)

atgggcttcggactgtcgtggctttttctggtggcgattcttaaggggtccagtgcgacaagacccatacatgcccaagctgtcccgctccggagtttctcggtgg
accgtcggtgtttctgttccctccgaagccaaaagataccttgatgatttcgcgaactcccgaagtcacgtgtgtcgtcgtggacgtaagccaggaggacccggagg
tccagttcaattggtatgtagacggcgtagaggtacataatgcgaaaacgaagcccagagaggaacagttcaatagcaaataccgcgtagtatcggtgctgacagtg
ttgcaccaggactggctgaatggaaaagaatacaagtgtaaagtgtccaacaagggccttccatcgtcgattgaaaagacaatctccaaggcaaaggggcagcctag
ggagccccaagtctacaccctgccccctcgcgggaggagatgacgaagaaccaggtatcactgtcatgcgcggtcaaaggattttacccgagcgacatcgccgtag
aatgggagtccaacggacagccagaaaacaattacaagaccactcctccagtgctcgatagcgatggctccttctttcttgtcagcaaattgacagtcgataagtca
agatggcagcagggtaatgtgttctcatgtagcgtcatgcacgaagcactccacaatcattatacacagaagagcctctcgttgtcgcccggaaaaggcggaggtgg
gtcgggcggaggggggaagcggtggaggagggtcaggaggtggaggttccgggggaggcggttcgggaggaggggttcgggtggtggaggatcgggtggcggaggaa
gctgcccttcatgtccagccccgagttcctcggaggcccgtcggtctttcttttcccccctaagcctaaagataccctgatgatcagccggacgcctgaggtgact
tgtgtggtagtcgacgtgtcccaagaagatccggaagtccagtttaactggtatgtggatggagtggaggtccataatgccaagacaaagccaagggaggagcaatt
caactcgaagtaccgcgtcgtgtccgtgctcacagtgcttcatcaagactggttgaacggaaaggagtacaaatgtaaggtatcaaacaagggtttgccctcgtcca
tcgagaaaaccatctcgaaagcgaaagggcaaccccgcgagccccaggtatatacgctcccgccttcaagagaagaaatgacgaaaaaccaagtgagcttgtggtgc
ctggtcaaggggttctatccctccgatatcgcggtagagtgggaaagcaatgggcagccggagaacaactataagacaacgcctcccgtgttggactcagatggatc
gttcttcttgtactcaaagcttacggtggacaagtcacgctggcagcaagggaacgtgttttcgtgctcggtgatgcacgaggcgcttcacaatcactacactcaga
aatcgcttagcttgtcaccaggaaaatgataa
(SEQ ID NO:318)

Fig. 11
(sheet 14 of 25)

39A: Y349C/T366S/L368A/Y407V::Y349C/S354C/T366W

MGFGLSWLFLVAILKGVQCDKTHTcpscpapeflggpsvflfppkpkdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltv
lhqdwlngkeykckvsnkglpssiektiskakGQPREPQVCTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKS
RWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGS*cpscpapeflggpsvflfppkpkdtlmisrtpevt
cvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltvlhqdwlngkeykckvsnkglpssiektiskakGQPREPQVCTLPPCREEMTKNQVSLWC
LVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
(SEQ ID NO:321)

atgggcttcggactgtcgtggctttttctggtggcgattcttaaggggtccagtgcgataagacacacacgtgcccctcgtgccccgcaccggagttccttggggg
tccgtcggtctttttgtttccccctaaacccaaggacacgctcatgatctcccgcacaccggaagtcacgtgcgtagtcgtggatgtctcacaagaggacccggaag
tgcaattcaactggtacgtcgacggcgtggaggtgcacaatgccaagacgaaaccaagagaggaacagttcaactcaaagtaccgggtagtatcggtgttgacggtg
ctccatcaggattggcttaacggtaaagagtacaagtgtaaagtcagcaataagggtctgcccagctccatcgaaaagactatctccaaggccaaggggcagcctcg
cgaaccgcaagtgtgtacgttgcccccgtcccgggaggagatgacgaaaaatcaggtcagcctctcgtgtgcggtgaaggggttttacccatccgacattgcggtgg
aatgggagagcaacggacagcccgaaaacaattacaagactaccccgccagtactcgatagcgacgggtcgttctttcttgtgtcgaaactgacagtggacaagtca
agatggcagcaaggaaatgtgttctcgtgtagcgtgatgcacgaggcactccacaatcattacacacagaagagcttgtccctctcccctggtaaaggaggaggagg
gtcgggtgggggaggcagcgggggaggaggatcaggaggtgggggttcaggcggaggggttcgggtggtgggggatcgggaggtggaggttcgggaggaggggggct
cctgtccgagctgccccgctcccgagttcttgggaggtccctcagtgtttcttttcccgccgaagcctaaagatacactgatgatttcacgaacccccgaagtgaca
tgcgtagtagtagatgtgtcgcaagaagatccggaagtccagttcaattggtatgtggatggggtggaggtccataatgcgaaaacaaaaccgcgggaagagcaatt
caattcaaagtatagggtcgtcagcgtgctcacagtgctgcaccaggactggcttaatgggaaagaatacaagtgcaaggtatccaacaaggggttgccctcgtcga
tcgagaaaacgatttcaaaagccaagggacaaccgagggaaccacaagtatgcacgctgccgccgtgtagggaagaaatgacgaagaaccaagtgagcctctggtgc
ctggtgaagggcttttatccctccgacatcgcagtcgagtgggaatcgaatgggcagccggagaacaactataagactactccccagtgttggattcggatggatc
atttttcctctactcgaaacttacggtcgacaaatcacgctggcagcagggcaacgtgttttcctgctcggtaatgcatgaggcgcttcacaaccactatacccaga
agtcactgtcgcttagcccagggaaatgataa
(SEQ ID NO:320)

Fig. 11
(sheet 15 of 25)

39B: Y407T::T366Y

MGFGLSWLFLVAILKGVQCDKTHTcpscpapeflggpsvflfppkpkdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltv
lhqdwlngkeykckvsnkglpssiektiskakGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLTSKLTVDKS
RWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGS*cpscpapeflggpsvflfppkpkdtlmisrtpevt
cvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltvlhqdwlngkeykckvsnkglpssiektiskakGQPREPQVYTLPPSREEMTKNQVSLYC
LVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
(SEQ ID NO:323)

atgggcttcggactgtcgtggcttttctggtggcgattcttaaggggtccagtgcgacaagacccatacgtgcccatcgtgccccgcaccggagttcctcggagg
cccgtcagtattccttttcctccgaagcccaaagatacattgatgatcagcaggacgcctgaagtgacatgtgtagtggtagacgtgtcgcaagaagatccagagg
tacagtttaactggtatgtcgacggggtggaagtccataacgccaagactaaaccccgcgaagagcagttcaactcaaagtatagagtagtctccgtcctgacagtc
ctccatcaggactggctgaacgggaaagaatacaagtgcaaagtctcgaacaaagggcttccgtcatcgatcgagaaaacgatttcaaaagccaagggacagcctag
ggagccgcaagtgtatactctgccccgtcgcgcgaggagatgacgaaaaatcaggtgtccctcacgtgcctcgtcaaaggattttacccgtcggatatcgccgtgg
agtgggaatcgaatgggcaaccagagaacaactacaagaccactcccccggtgctggactcggacggctccttttttcttgacatcaaagctcacagtcgataagagc
cgctggcaacaagggaatgtgttcagctgctcggtgatgcacgaagcgctgcacaaccactatacccagaaatcattgtccctcagccccggaaagggaggtggagg
gtccggtgggggtggatcaggaggggtgggagcggaggaggcggcagcggtggcggagggtcaggtggaggcggatcaggtgggggaggttcaggcggtgggggct
cgtgccccagctgtcctgctcccgagtttctcgggggaccttcagtctttctcttccctccgaaacccaaggacacgctgatgatttcgcggacacccgaagtgact
tgtgtcgtggtcgacgtaagccaggaggaccccgaggtgcaattcaactggtacgtcgacggagtcgaggtccacaatgcgaaaacaaaacccagagaagaacagtt
caattcgaaatatcgagtggtatcagtcctgaccgtgcttcatcaggattggctcaatgggaaagagtacaaatgcaaggtatcaaacaagggactgccaagctcaa
tcgaaaagactatctcgaaagcaaagggtcagcctcgggagccccaagtgtacacgcttcccccatccagggaagaaatgacgaagaaccaggtgtcgctctactgt
ttggtgaaggggttttatccttcggacatcgcggtggaatgggagtcgaatggacagccggagaataactacaaaacgactccgcctgtcctcgacagcgatgggtc
cttcttcctttactcaaaattgacagtagataagtcgcgctggcagcagggaaatgtattctcctgttccgtcatgcatgaggcgcttcacaatcactacactcaga
agtccttgtcgttgtcaccaggaaaatgataa
(SEQ ID NO:322)

Fig. 11
(sheet 16 of 25)

39C: H224C/T225C/T366S/L368A/Y407V::T366W

MGFGLSWLFLVAILKGVQCDKTCCcpscpapeflggpsvflfppkpkdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltv
lhqdwlngkeykckvsnkglpssiektiskakGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKS
RWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGS*cpscpapeflggpsvflfppkpkdtlmisrtpevt
cvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltvlhqdwlngkeykckvsnkglpssiektiskakGQPREPQVYTLPPSREEMTKNQVSLWC
LVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
(SEQ ID NO:325)

atgggcttcggactgtcgtggctttttctggtggcgattcttaaggggtccagtgcgacaagacatgctgttgcccaagctgtcccgctccggagtttctcggtgg
accgtcggtgtttctgttccctccgaagccaaaagataccttgatgatttcgcgaactcccgaagtcacgtgtgtcgtcgtggacgtaagccaggaggacccggagg
tccagttcaattggtatgtagacggcgtagaggtacataatgcgaaaacgaagcccagagaggaacagttcaatagcaaataccgcgtagtatcggtgctgacagtg
ttgcaccaggactggctgaatggaaaagaatacaagtgtaaagtgtccaacaagggccttccatcgtcgattgaaaagacaatctccaaggcaaaggggcagcctag
ggagccccaagtctacaccctgccccctcgcgggaggagatgacgaagaaccaggtatcactgtcatgcgcggtcaaaggatttacccgagcgacatcgccgtag
aatgggagtccaacggacagccagaaaacaattacaagaccactcctccagtgctcgatagcgatggctccttctttcttgtcagcaaattgacagtcgataagtca
agatggcagcagggtaatgtgttctcatgtagcgtcatgcacgaagcactccacaatcattatacacagaagagcctctcgttgtcgcccggaaaaggcggaggtgg
gtcgggcggaggggggaagcggtggaggagggtcaggaggtggaggttccgggggaggcggttcgggaggaggggttcgggtggtggaggatcgggtggcggaggaa
gctgcccttcatgtccagcccccgagttcctcggaggcccgtcggtctttcttttcccccctaagcctaaagataccctgatgatcagccggacgcctgaggtgact
tgtgtggtagtcgacgtgtcccaagaagatccggaagtccagtttaactggtatgtggatggagtggaggtccataatgccaagacaaagccaagggaggagcaatt
caactcgaagtaccgcgtcgtgtccgtgctcacagtgcttcatcaagactggttgaacggaaaggagtacaaatgtaaggtatcaaacaagggtttgccctcgtcca
tcgagaaaaccatctcgaaagcgaaagggcaaccccgcgagccccaggtatatacgctcccgccttcaagagaagaaatgactaaaaaccaagtgagcttgtggtgc
ctggtcaaggggttctatccctccgatatcgcggtagagtgggaaagcaatgggcagccggagaacaactataagacaacgcctcccgtgttggactcagatggatc
gttcttcttgtactcaaagcttacggtggacaagtcacgctggcagcaagggaacgtgttttcgtgctcggtgatgcacgaggcgcttcacaatcactacactcaga
aatcgcttagcttgtcaccaggaaaatgataa
(SEQ ID NO:324)

Fig. 11
(sheet 17 of 25)

39D: T223C/T366S/L368A/Y407V::T366W

MGFGLSWLFLVAILKGVQCDKCHTcpscpapeflggpsvflfppkpkdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltv
lhqdwlngkeykckvsnkglpssiektiskakGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKS
RWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGS*cpscpapeflggpsvflfppkpkdtlmisrtpevt
cvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltvlhqdwlngkeykckvsnkglpssiektiskakGQPREPQVYTLPPSREEMTKNQVSLWC
LVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
(SEQ ID NO:327)

atgggcttcggactgtcgtggctttttctggtggcgattcttaaggggtccagtgcgacaagtgccatacatgcccaagctgtcccgctccggagtttctcggtgg
accgtcggtgtttctgttccctccgaagccaaaagataccttgatgatttcgcgaactcccgaagtcacgtgtgtcgtcgtggacgtaagccaggaggacccggagg
tccagttcaattggtatgtagacggcgtagaggtacataatgcgaaaacgaagcccagagaggaacagttcaatagcaaataccgcgtagtatcggtgctgacagtg
ttgcaccaggactggctgaatggaaaagaatacaagtgtaaagtgtccaacaagggccttccatcgtcgattgaaaagacaatctccaaggcaaaggggcagcctag
ggagccccaagtctacaccctgccccctcgcgggaggagatgacgaagaaccaggtatcactgtcatgcgcggtcaaaggattttacccgagcgacatcgccgtag
aatgggagtccaacggacagccagaaaacaattacaagaccactcctccagtgctcgatagcgatggctccttctttcttgtcagcaaattgacagtcgataagtca
agatggcagcagggtaatgtgttctcatgtagcgtcatgcacgaagcactccacaatcattatacacagaagagcctctcgttgtcgcccggaaaaggcggaggtgg
gtcgggcggaggggggaagcggtggaggagggtcaggaggtggaggttccgggggaggcggttcgggaggaggggttcgggtggtggaggatcgggtggcggaggaa
gctgcccttcatgtccagcccccgagttcctcggaggcccgtcggtctttcttttcccccctaagcctaaagataccctgatgatcagccggacgcctgaggtgact
tgtgtggtagtcgacgtgtcccaagaagatccggaagtccagtttaactggtatgtggatggagtggaggtccataatgccaagacaaagccaagggaggagcaatt
caactcgaagtaccgcgtcgtgtccgtgctcacagtgcttcatcaagactggttgaacggaaaggagtacaaatgtaaggtatcaaacaagggtttgccctcgtcca
tcgagaaaaccatctcgaaagcgaaagggcaaccccgcgagccccaggtatatacgctcccgccttcaagagaagaaatgacgaaaaaccaagtgagcttgtggtgc
ctggtcaaggggttctatccctccgatatcgcggtagagtgggaaagcaatgggcagccggagaacaactataagacaacgcctcccgtgttggactcagatggatc
gttcttcttgtactcaaagcttacggtggacaagtcacgctggcagcaagggaacgtgttttcgtgctcggtgatgcacgaggcgcttcacaatcactacactcaga
aatcgcttagcttgtcaccaggaaaatgataa
(SEQ ID NO:326)

Fig. 11
(sheet 18 of 25)

39E: T366S/L368A/Y407V/CH3 C-terminal Cysteine KSCDKT::T366W/CH3 C-terminal Cysteine GECG

MGFGLSWLFLVAILKGVQCDKTHTcpscpapeflggpsvflfppkpkdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltv
lhqdwlngkeykckvsnkglpssiektiskakGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKS
RWQQGNVFSCSVMHEALHNHYTQKSLSLSKSCDKT*GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGS*cpscpapeflggpsvflfppkpkdtlmisrtp
evtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltvlhqdwlngkeykckvsnkglpssiektiskakGQPREPQVYTLPPSREEMTKNQVS
LWCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSGEC
(SEQ ID NO:329)

atgggcttcggactgtcgtggcttttctggtggcgattcttaaggggtccagtgcgataaaacgcacacgtgcccctcgtgtccggcaccggagtttcttggagg
tccctcggtgttcctgttccctcccaagccgaaggacacgttgatgatttcgaggacgccggaggtgacgtgtgtggtcgtagacgtgagccaggaggacccggaag
tgcagtttaactggtacgtcgatggagtagaagtacataatgccaagacgaagcccagggaggaacaattcaattcgaagtatcgcgtcgtatccgtgctgactgtg
ctccaccaggactggcttaacggaaaagaatacaagtgcaaggtatcaaataagggactcccctcgtcgatcgagaaaacaatcagcaaagcgaaaggacagccgag
ggaaccgcaagtgtacacattgccgccgtcgcgagaagaaatgaccaagaaccaggtatcactctcgtgcgccgtgaagggcttttacccatcggacattgctgtgg
agtgggagagcaacggtcaacccgagaataactacaaaactacaccgcccgtgctggattccgacggctcattctttctcgtgtcaaaactgactgtggataagtcg
cgctggcaacaggggaatgtgttctcgtgcagcgtcatgcatgaagctcttcataatcactacacccaaaaatccctgtcactctcgaaaagctgtgataagaccgg
gggtgggggctccggaggaggcggttcgggtggcggtgggtcgggtggaggcggatcgggcggtgggggaagcggtggtggtggaagcggaggggggtggatcaggtg
gaggggcagctgtccatcctgccctgcaccagagtttttgggaggaccgtccgtatttctgtttccgcccaagcccaaagatactttgatgatcagcaggacgcct
gaggtaacatgtgtagtggtcgatgtctcgcaagaggaccctgaggtccagttcaattggtacgtggacggggtggaagtccacaacgcgaaaacgaaaccacgcga
agaacagttcaacagcaaatacagagtcgtgtcagtcttgacagtccttcaccaggattggttgaatggaaaggagtacaagtgtaaggtgtcaaacaaaggactgc
ccagctcgatcgaaaagacaatttcgaaggcaaaaggtcaaccgcgggagccacaagtgtatacgctgccgccctcgcgggaggagatgacaaagaatcaggtgtcg
ctgtggtgtctggtaaaaggattctatccatccgatatcgcggtagagtgggaatcaaacggccagccggagaacaattacaagaccacgccccctgtattggattc
ggacggatcgttcttcttgtattcgaaactcacggtggacaagtcgcggtggcagcagggtaatgtgttttcatgctcagtcatgcacgaggcgctccataaccatt
atactcagaagtcgctgtccttgtccggggagtgctgataa
(SEQ ID NO:328)

Fig. 11
(sheet 19 of 25)

39E (35L): T366S/L368A/Y407V/CH3 C-terminal Cysteine KSCDKT::T366W/CH3 C-terminal Cysteine GEC and (G4S)7

MGFGLSWLFLVAILKGVQCDKTHTcpscpapeflggpsvflfppkpkdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltv
lhqdwlngkeykckvsnkglpssiektiskakgQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKS
RWQQGNVFSCSVMHEALHNHYTQKSLSLSKSCDKT*GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGS*cpscpapeflggpsvflfppkpkdtlmisrtpevtcv
vvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltvlhqdwlngkeykckvsnkglpssiektiskakGQPREPQVYTLPPSREEMTKNQVSLWCLV
KGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSGEC
(SEQ ID NO:331)

atgggcttcggactgtcgtggctttttctggtggcgattcttaaggggtccagtgcgacaaaacgcacacctgtccgtcatgtcctgccccggaattccttggagg
gccttccgtgtttctcttccctccgaagcccaaggacacgctgatgatctcccggaccccggaggtcacgtgtgtggtagtagacgtgtcacaagaagatccggagg
tgcagttcaactggtacgtagatggcgtggaggtgcacaacgccaaaacgaagccccgagaggaacagttcaattcgaagtaccgcgtcgtgtcggtattgactgta
ttgcatcaagactggttgaacgggaaggagtataagtgtaaagtcagcaacaagggacttccctcgtcaattgaaaagacaatttcgaaagccaaaggccagcccag
ggagccccaagtgtacaccctgccacccagccgggaagagatgacaaagaatcaagtctcgcttagctgcgctgtcaagggcttctatccatcggacattgcagtgg
aatgggaatcaaacggacagccggagaataactataagacgacacccccctgtcctcgacagcgacgggtcgttcttccttgtgagcaagctcacggtcgacaaaagc
cgctggcagcagggaaacgtattctcatgttcggtgatgcacgaagcattgcataaccactacacgcagaagagcttgtcgttgtcgaaaagctgcgacaagacggg
aggggagggtccgggggtggtgggagcggcggaggaggtagcggcggaggtggctcgggaggaggtgggtcgggtggtgggggaagcggaggcggagggtcatgtc
cgagctgcccggcacccgaatttctcggaggtccctcggtgttcctgttcccgccaaagcctaaggatacgttgatgatttcgcgcacgccggaggtaacatgcgtg
gtggtggatgtgtcacaagaggaccccgaggtccagttcaattggtacgtcgatggagtggaagtgcacaatgcgaaaacaaaaccccgggaggagcagttcaatag
caagtacagggtagtctccgtcctgactgtacttcaccaagactggcttaacggaaaagagtataagtgcaaggtcagcaacaaggggcttccttcatccatcgaga
aaaccatctcgaaggccaagggacagccgagggagcctcaagtatacacgctgccgccatcgagagaagaaatgaccaaaaaccaggtgtccctttggtgtttggtg
aagggtttctatccctccgatatcgccgtagagtgggagtcaaatggacagcctgagaacaactataagactacgccccctgtgttggacagcgatgggtcattctt
tctgtattcgaaactcacggtggataagtcgcgatggcaacagggcaatgtgttttcgtgcagcgtgatgcatgaggcgctgcacaaccactatactcagaaatcgt
taagcttatcgggagagtgttgataa
(SEQ ID NO:330)

Fig. 11
(sheet 20 of 25)

39E (35L) Inverted: T366S/L368A/Y407V/CH3 C-terminal Cysteine GEC::T366W/CH3 C-terminal Cysteine KSCDKT and (G4S)7

MGFGLSWLFLVAILKGVQCDKTHTcpscpapeflggpsvflfppkpkdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltv
lhqdwlngkeykckvsnkglpssiektiskakGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKS
RWQQGNVFSCSVMHEALHNHYTQKSLSLSGEC*GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGS*cpscpapeflggpsvflfppkpkdtlmisrtpevtcvvvd
vsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltvlhqdwlngkeykckvsnkglpssiektiskakGQPREPQVYTLPPSREEMTKNQVSLWCLVKGF
YPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSKSCDKT
(SEQ ID NO:333)

atgggcttcggactgtcgtggctttttctggtggcgattcttaaggggtccagtgcgacaaaacgcacacctgtccgtcatgtcctgccccggaattccttggagg
gccttccgtgtttctcttccctccgaagcccaaggacacgctgatgatctcccggaccccggaggtcacgtgtgtggtagtagacgtgtcacaagaagatccggagg
tgcagttcaactggtacgtagatggcgtggaggtgcacaacgccaaaacgaagccccgagaggaacagttcaattcgaagtaccgcgtcgtgtcggtattgactgta
ttgcatcaagactggttgaacgggaaggagtataagtgtaaagtcagcaacaagggacttccctcgtcaattgaaaagacaatttcgaaagccaaaggccagcccag
ggagccccaagtgtacaccctgccacccagccgggaagagatgacaaagaatcaagtctcgcttagctgcgctgtcaagggcttctatccatcggacattgcagtgg
aatgggaatcaaacggacagccggagaataactataagacgacacccccctgtcctcgacagcgacgggtcgttcttccttgtgagcaagctcacggtcgacaaaagc
cgctggcagcagggaaacgtattctcatgttcggtgatgcacgaagcattgcataaccactacacgcagaagagcttgtcgttgtcgggggaatgcggaggggggagg
gtccggaggggagggtccgggggtggtgggagcggcggaggaggtagcggcggaggtggctcgggaggaggtgggtcgggtggtgggggatcatgtccgagctgcc
cggcacccgaatttctcggaggtccctcggtgttcctgttcccgccaaagcctaaggatacgttgatgatttcgcgcacgccggaggtaacatgcgtggtggtggat
gtgtcacaagaggaccccgaggtccagttcaattggtacgtcgatggagtggaagtgcacaatgcgaaaacaaaaccccgggaggagcagttcaatagcaagtacag
ggtagtctccgtcctgactgtacttcaccaagactggcttaacggaaaagagtataagtgcaaggtcagcaacaaggggcttccttcatccatcgagaaaaccatct
cgaaggccaagggacagccgagggagcctcaagtatacacgctgccgccatcgagagaagaaatgaccaaaaaccaggtgtccctttggtgtttggtgaagggtttc
tatccctccgatatcgccgtagagtgggagtcaaatggacagcctgagaacaactataagactacgccccctgtgttggacagcgatgggtcattctttctgtattc
gaaactcacggtggataagtcgcgatggcaacagggcaatgtgttttcgtgcagcgtgatgcatgaggcgctgcacaaccactatactcagaaatcgttaagcttat
cgaagtcatgcgacaagacttgataa
(SEQ ID NO:332)

Fig. 11
(sheet 21 of 25)

39E (30L): T366S/L368A/Y407V/CH3 C-terminal Cysteine KSCDKT::T366W/CH3 C-terminal Cysteine GEC and (G4S)6

MGFGLSWLFLVAILKGVQCDKTHTcpscpapeflggpsvflfppkpkdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltv
lhqdwlngkeykckvsnkglpssiektiskakGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKS
RWQQGNVFSCSVMHEALHNHYTQKSLSLSKSCDKT*GGGGSGGGGSGGGGSGGGGSGGGGSGGGGS*cpscpapeflggpsvflfppkpkdtlmisrtpevtcvvvdvs
qedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltvlhqdwlngkeykckvsnkglpssiektiskakGQPREPQVYTLPPSREEMTKNQVSLWCLVKGFYP
SDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSGEC
(SEQ ID NO:335)

atgggcttcggactgtcgtggctttttctggtggcgattcttaaggggtccagtgcgacaaaacgcacacctgtccgtcatgtcctgccccggaattccttggagg
gccttccgtgtttctcttccctccgaagcccaaggacacgctgatgatctcccggaccccggaggtcacgtgtgtggtagtagacgtgtcacaagaagatccggagg
tgcagttcaactggtacgtagatggcgtggaggtgcacaacgccaaaacgaagccccgagaggaacagttcaattcgaagtaccgcgtcgtgtcggtattgactgta
ttgcatcaagactggttgaacgggaaggagtataagtgtaaagtcagcaacaagggacttccctcgtcaattgaaaagacaatttcgaaagccaaaggccagcccag
ggagccccaagtgtacaccctgccacccagccgggaagagatgacaaagaatcaagtctcgcttagctgcgctgtcaagggcttctatccatcggacattgcagtgg
aatgggaatcaaacggacagccggagaataactataagacgacacccccctgtcctcgacagcgacgggtcgttcttccttgtgagcaagctcacggtcgacaaaagc
cgctggcagcagggaaacgtattctcatgttcggtgatgcacgaagcattgcataaccactacacgcagaagagcttgtcgttgtcgaaaagctgcgacaagacggg
aggggagggtccgggggtggtgggagcggcggaggaggtagcggcggaggtggctcgggaggaggtgggtcgggtggtgggggatcatgtccgagctgcccggcac
ccgaatttctcggaggtccctcggtgttcctgttcccgccaaagcctaaggatacgttgatgatttcgcgcacgccggaggtaacatgcgtggtggtggatgtgtca
caagaggaccccgaggtccagttcaattggtacgtcgatggagtggaagtgcacaatgcgaaaacaaaaccccgggaggagcagttcaatagcaagtacagggtagt
ctccgtcctgactgtacttcaccaagactggcttaacggaaaagagtataagtgcaaggtcagcaacaaggggcttccttcatccatcgagaaaaccatctcgaagg
ccaagggacagccgagggagcctcaagtatacacgctgccgccatcgagagaagaaatgaccaaaaaccaggtgtccctttggtgtttggtgaagggtttctatccc
tccgatatcgccgtagagtgggagtcaaatggacagcctgagaacaactataagactacgccccctgtgttggacagcgatgggtcattctttctgtattcgaaact
cacggtggataagtcgcgatggcaacagggcaatgtgttttcgtgcagcgtgatgcatgaggcgctgcacaaccactatactcagaaatcgttaagcttatcgggag
agtgttgataa
(SEQ ID NO:334)

Fig. 11
(sheet 22 of 25)

39E (25L): T366S/L368A/Y407V/CH3 C-terminal Cysteine KSCDKT::T366W/CH3 C-terminal Cysteine GEC and (G4S)5

MGFGLSWLFLVAILKGVQCDKTHTcpscpapeflggpsvflfppkpkdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltv
lhqdwlngkeykckvsnkglpssiektiskakGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKS
RWQQGNVFSCSVMHEALHNHYTQKSLSLSKSCDKT*GGGGSGGGGSGGGGSGGGGSGGGGS*cpscpapeflggpsvflfppkpkdtlmisrtpevtcvvvdvsqedpe
vqfnwyvdgvevhnaktkpreeqfnskyrvvsvltvlhqdwlngkeykckvsnkglpssiektiskakGQPREPQVYTLPPSREEMTKNQVSLWCLVKGFYPSDIAV
EWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSGEC
(SEQ ID NO:337)

atgggcttcggactgtcgtggctttttctggtggcgattcttaaggggtccagtgcgacaaaacgcacacctgtccgtcatgtcctgccccggaattccttggagg
gccttccgtgtttctcttccctccgaagcccaaggacacgctgatgatctcccggaccccggaggtcacgtgtgtggtagtagacgtgtcacaagaagatccggagg
tgcagttcaactggtacgtagatggcgtggaggtgcacaacgccaaaacgaagccccgagaggaacagttcaattcgaagtaccgcgtcgtgtcggtattgactgta
ttgcatcaagactggttgaacgggaaggagtataagtgtaaagtcagcaacaagggacttccctcgtcaattgaaaagacaatttcgaaagccaaaggccagcccag
ggagccccaagtgtacaccctgccacccagccgggaagagatgacaaagaatcaagtctcgcttagctgcgctgtcaagggcttctatccatcggacattgcagtgg
aatgggaatcaaacggacagccggagaataactataagacgacacccccctgtcctcgacagcgacgggtcgttcttccttgtgagcaagctcacggtcgacaaaagc
cgctggcagcagggaaacgtattctcatgttcggtgatgcacgaagcattgcataaccactacacgcagaagagcttgtcgttgtcgaaaagctgcgacaagacggg
aggggagggtccgggggtggtgggagcggcggaggaggtagcggcggaggtggctcgggaggaggtgggtcatgtccgagctgcccggcacccgaatttctcggag
gtccctcggtgttcctgttcccgccaaagcctaaggatacgttgatgatttcgcgcacgccggaggtaacatgcgtggtggtggatgtgtcacaagaggaccccgag
gtccagttcaattggtacgtcgatggagtggaagtgcacaatgcgaaaacaaaaccccgggaggagcagttcaatagcaagtacagggtagtctccgtcctgactgt
acttcaccaagactggcttaacggaaaagagtataagtgcaaggtcagcaacaaggggcttccttcatccatcgagaaaaccatctcgaaggccaagggacagccga
gggagcctcaagtatacacgctgccgccatcgagagaagaaatgaccaaaaaccaggtgtccctttggtgtttggtgaagggtttctatccctccgatatcgccgta
gagtgggagtcaaatggacagcctgagaacaactataagactacgccccctgtgttggacagcgatgggtcattctttctgtattcgaaactcacggtggataagtc
gcgatggcaacagggcaatgtgttttcgtgcagcgtgatgcatgaggcgctgcacaaccactatactcagaaatcgttaagcttatcgggagagtgttgataa
(SEQ ID NO:336)

Fig. 11
(sheet 23 of 25)

39I - S364H/F405A::Y349T/T394F with CH3 C-terminal disulfide

MGFGLSWLFLVAILKGVQCDKTHTcpscpapeflggpsvflfppkpkdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltv
lhqdwlngkeykckvsnkglpssiektiskakGQPREPQVYTLPPSREEMTKNQVHLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFALYSKLTVDKS
RWQQGNVFSCSVMHEALHNHYTQKSLSLSKSCDKT*GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGS*cpscpapeflggpsvflfppkpkdtlmisrtp
evtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltvlhqdwlngkeykckvsnkglpssiektiskakGQPREPQVTTLPPSREEMTKNQVS
LTCLVKGFYPSDIAVEWESNGQPENNYKTFPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSGEC
(SEQ ID NO:339)

atgggcttcggactgtcgtggcttttctggtggcgattcttaaggggtccagtgcgacaaaacgcacacttgtccttcctgccctgccccggagttccttggcgg
accctcggtctttttgtttccgccgaaaccgaaagacacccttatgattagcaggacacccgaagtcacgtgtgtcgtcgtggacgtgtcgcaagaggatcccgagg
tgcagttcaactggtacgtggacggggtagaagtccacaatgccaagacaaaaccccgggaagaacagtttaactcgaagtaccgcgtagtgtcagtcttgacagtc
ctccatcaggactggcttaacgggaaggagtacaaatgtaaagtgtcaaacaagggtctgccttccagcattgagaaaacgatctccaaggctaaagggcagccccg
agaaccacaagtctatacgcttccaccatcgcgggaggagatgaccaagaaccaggtccacttgacctgtctcgtgaaggggttctacccgtcagatatcgcggtag
agtgggaatcgaacggccagcccgagaataactacaagacgactcctccggtcctcgattcagatgggtcgttcgcactctactcaaaacttacggtggacaagtcg
agatggcagcagggcaacgtgtttagctgctcagtcatgcacgaggcgctgcataatcactatacacagaagtcgctgtcattgtcaaaaagctgcgacaagacagg
gggtggaggttcaggcggtggtgggtcgggaggggagggtcaggtggaggcggcagcgggggtgggggatcgggaggaggagggtccgggggaggggggttccggag
ggggtgggtcctgtccgtcgtgccctgcaccggaattcttgggcggtccgtcagtgttcctgtttcccccgaaacccaaagatacgctcatgatttcccgcacccct
gaggtcacttgcgtggtagtcgatgtcagccaggaagatcccgaagtacagttcaattggtacgtagatggtgtagaagtacacaacgctaaaactaagcctcgcga
agagcagttcaattcgaagtatcgggtagtaagcgtgctgactgtgctccatcaagactggctgaatggaaaagagtataagtgcaaagtctcgaataagggattgc
ccagctccatcgagaaaaccatctcgaaagcgaagggacagcccagagaaccccaagtgaccacattgccaccctcccgagaggaaatgactaagaatcaagtgtca
ctcacatgtcttgtgaagggattctatcccagcgacatcgccgtcgagtgggagtccaatgggcagccggaaaacaattacaaaacgtttccacccgtccttgactc
agatggatcgttctttctctattcgaagctcacggtagataagtcgaggtggcaacaaggaaatgtgttttcatgttcggtgatgcatgaagcgctccataaccact
atacgcagaaatcgctttcgctctccggtgaatgctgataa
(SEQ ID NO:338)

Fig. 11
(sheet 24 of 25)

39J - K370D/K392D/K409D::E356K/E357K/D399K with CH3 C-terminal disulfide

MGFGLSWLFLVAILKGVQCDKTHTcpscpapeflggpsvflfppkpkdtlmisrtpevtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltv
lhqdwlngkeykckvsnkglpssiektiskakGQPREPQVYTLPPSREEMTKNQVSLTCLVDGFYPSDIAVEWESNGQPENNYDTTPPVLDSDGSFFLYSDLTVDKS
RWQQGNVFSCSVMHEALHNHYTQKSLSLSKSCDKTGGGSGGGGSGGGGSGGGGSGGGGScpscpapeflggpsvflfppkpkdtlmisrtp
evtcvvvdvsqedpevqfnwyvdgvevhnaktkpreeqfnskyrvvsvltvlhqdwlngkeykckvsnkglpssiektiskakGQPREPQVYTLPPSRKKMTKNQVS
LTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLKSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSLGEC
(SEQ ID NO:341)

atgggcttcggactgtcgtggctttttctggtggcgattcttaaggggtccagtgcgacaaaacgcacacttgtccttcctgccccggagttccttggcgg
accctcggtctttttgtttccgccgaaaccgaaagacacccttatgattagcaggacacccgaagtcacgtgtgtcgtcgtggacgtgtcgcaagaggatcccgagg
tgcagttcaactggtacgtggacggggtagaagtccacaatgccaagacaaaacccgggaagaacagtttaactcgaagtaccgcgtagtgtcagtcttgacagtc
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ggatgggagcttctttctgtattcgaagctcacggtagataagtcgaggtggcaacaaggaaatgtgtttcatgttcggtgatgcatgaagcgctcccataaccact
atacgcagaaatcgctttcgctctccggtgaatgctgataa
(SEQ ID NO:340)

Fig. 11
(sheet 25 of 25)

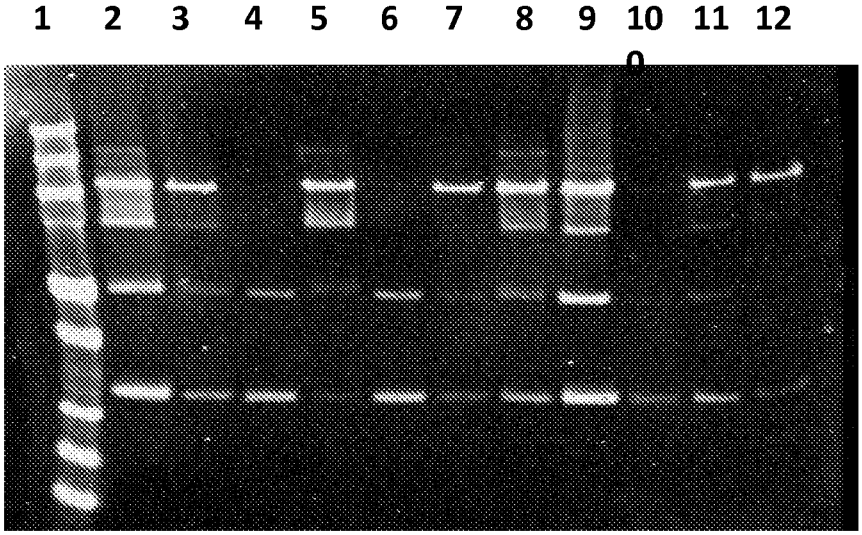


Fig. 12A

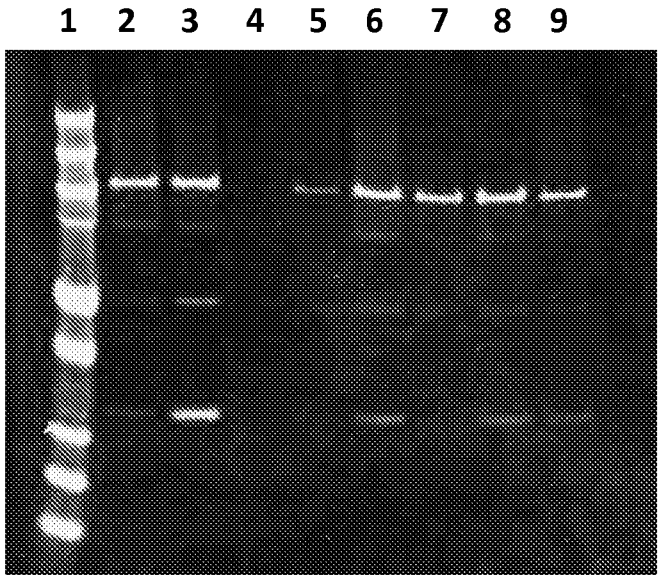


Fig. 12B

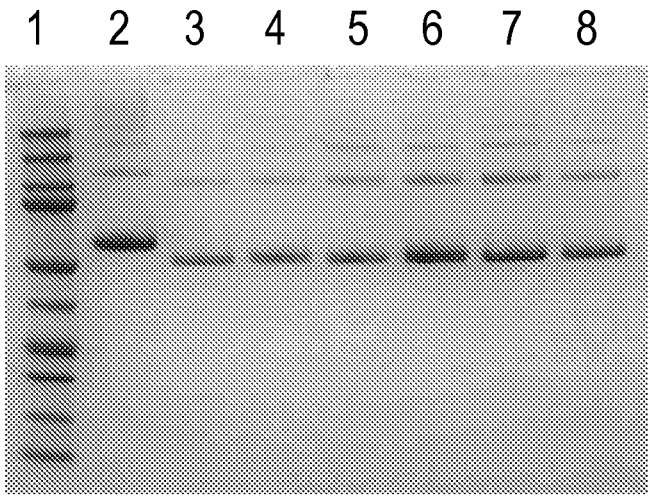


Fig. 13A

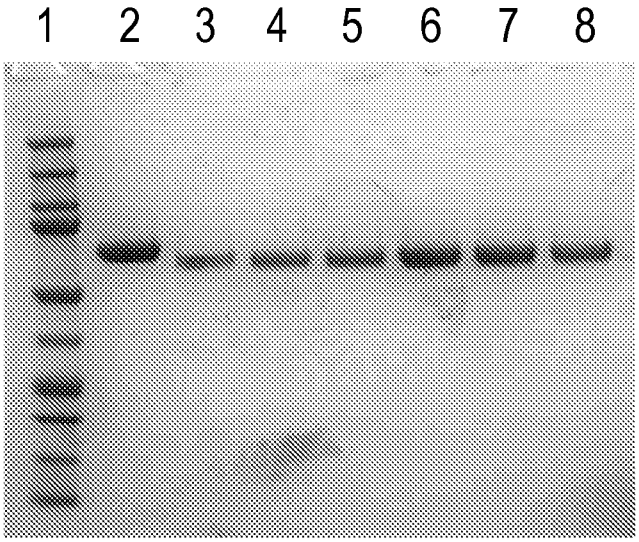


Fig. 13B

>Ron-23E-2224

EVQLLESGGGLVQPGGSLRLSCAASGFTFSDYQMEWVRQAPGKGLEWVSYIYSSGGKTVYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARLPRVGATII
NDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTK
VDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGK
EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFS
CSVMHEALHNHYTQKSLSLSKSCDKTGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDV
SHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVKGFY
PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSGECGGGGSGGGGSEVQLVQSGAEVKKPGSSVKVSCK
ASGGTFSSYAIGWVRQAPGQGLEWMGGIIPIFGIANYAQKFQGRVTITADESTSSAYMELSSLRSEDTAVYYCAREEGPYCSSTSCYAAFDIWGQGTLVTVSSASTG
GGGSGGGGSGGGGSGGGGSQSVLTQDPAVSVALGQTVKITCQGDSLRSYFASWYQQKPGQAPTLVMYARNDRPAGVPDRFSGSKSGTSASLAISGLQPEDEADYYCA
AWDDSLNGYLFGAGTKLTVL**
(SEQ ID NO:350)

>Ron-39Egy4-2224-HC

EVQLLESGGGLVQPGGSLRLSCAASGFTFSDYQMEWVRQAPGKGLEWVSYIYSSGGKTVYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARLPRVGATII
NDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTK
VDKKVEPKSCDKTHTCPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSKYRVVSVLTVLHQDWLNGK
EYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFS
CSVMHEALHNHYTQKSLSLSKSCDKTGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSCPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDV
SQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSDYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVKGFY
PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSGECGGGGSGGGGSEVQLVQSGAEVKKPGSSVKVSCK
ASGGTFSSYAIGWVRQAPGQGLEWMGGIIPIFGIANYAQKFQGRVTITADESTSSAYMELSSLRSEDTAVYYCAREEGPYCSSTSCYAAFDIWGQGTLVTVSSASTG
GGGSGGGGSGGGGSGGGGSQSVLTQDPAVSVALGQTVKITCQGDSLRSYFASWYQQKPGQAPTLVMYARNDRPAGVPDRFSGSKSGTSASLAISGLQPEDEADYYCA
AWDDSLNGYLFGAGTKLTVL**
(SEQ ID NO:351)

Fig. 14
(sheet 1 of 24)

>Ron-23E-sm3E
EVQLLESGGGLVQPGGSLRLSCAASGFTFSDYQMEWVRQAPGKGLEWVSYIYSSGGKTVYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARLPRVGATII
NDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTK
VDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGK
EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFS
CSVMHEALHNHYTQKSLSLSKSCDKTGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDV
SHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVKGFY
PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSGECGGGGSGGGGSQVKLEQSGAEVVKPGASVKLSCK
ASGFNIKDSYMHWLRQGPGQRLEWIGWIDPENGDTEYAPKFQGKATFTTDTSANTAYLGLSSLRPEDTAVYYCNEGTPTGPYYFDYWGQGTLVTVSSASTGGGGSGG
GGSGGGGSGGGGSENVLTQSPSSMSVSVGDRVTIACSASSSVPYMHWLQQKPGKSPKLLIYLTSNLASGVPSRFSGSGSGTDYSLTISSVQPEDAATYYCQQRSSYP
LTFGGGTKLEIK**
(SEQ ID NO:352)

>Ron-39Egy4-sm3E
EVQLLESGGGLVQPGGSLRLSCAASGFTFSDYQMEWVRQAPGKGLEWVSYIYSSGGKTVYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARLPRVGATII
NDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTK
VDKKVEPKSCDKTHTCPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSKYRVVSVLTVLHQDWLNGK
EYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFS
CSVMHEALHNHYTQKSLSLSKSCDKTGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSCPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDV
SQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSDYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVKGFY
PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSGECGGGGSGGGGSQVKLEQSGAEVVKPGASVKLSCK
ASGFNIKDSYMHWLRQGPGQRLEWIGWIDPENGDTEYAPKFQGKATFTTDTSANTAYLGLSSLRPEDTAVYYCNEGTPTGPYYFDYWGQGTLVTVSSASTGGGGSGG
GGSGGGGSGGGGSENVLTQSPSSMSVSVGDRVTIACSASSSVPYMHWLQQKPGKSPKLLIYLTSNLASGVPSRFSGSGSGTDYSLTISSVQPEDAATYYCQQRSSYP
LTFGGGTKLEIK**
(SEQ ID NO:353)

Fig. 14
(sheet 2 of 24)

>sm3E-23E-Onartuzumab
QVKLEQSGAEVVKPGASVKLSCKASGFNIKDSYMHWLRQGPGQRLEWIGWIDPENGDTEYAPKFQGKATFTTDTSANTAYLGLSSLRPEDTAVYYCNEGTPTGPYYF
DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV
DKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSC
SVMHEALHNHYTQKSLSLSKSCDKTGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS
HEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVKGFYP
SDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSGECGGGGSGGGGSEVQLVESGGGLVQPGGSLRLSCAA
SGYTFTSYWLHWVRQAPGKGLEWVGMIDPSNSDTRFNPNFKDRFTISADTSKNTAYLQMNSLRAEDTAVYYCATYRSYVTPLDYWGQGTLVTVSSASTGGGGSGGGG
SGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCKSSQSLLYTSSQKNYLAWYQQKPGKAPKLLIYWASTRESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQ
YYAYPWTFGQGTKVEIK**
(SEQ ID NO:354)

>sm3E-23E-Ron
QVKLEQSGAEVVKPGASVKLSCKASGFNIKDSYMHWLRQGPGQRLEWIGWIDPENGDTEYAPKFQGKATFTTDTSANTAYLGLSSLRPEDTAVYYCNEGTPTGPYYF
DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV
DKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSC
SVMHEALHNHYTQKSLSLSKSCDKTGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS
HEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVKGFYP
SDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSGECGGGGSGGGGSEVQLLESGGGLVQPGGSLRLSCAA
SGFTFSDYQMEWVRQAPGKGLEWVSYIYSSGGKTVYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARLPRVGATIINDYWGQGTLVTVSSASTGGGGSGG
GGSGGGGSGGGGSDIQMTQSPSSVSASVGDRVTITCRASRGISSSLAWYQQKPGRAPKLLIYAASSFHTGVPSRFSGSGSVTEFTLTISSLQPEDFATYYCQQTDSF
PLTFGGGTKVEIK
(SEQ ID NO:355)

Fig. 14
(sheet 3 of 24)

>sm3E-39Egy4-Onartuzumab
QVKLEQSGAEVVKPGASVKLSCKASGFNIKDSYMHWLRQGPGQRLEWIGWIDPENGDTEYAPKFQGKATFTTDTSANTAYLGLSSLRPEDTAVYYCNEGTPTGPYYF
DYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKV
DKKVEPKSCDKTHTCPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSKYRVVSVLTVLHQDWLNGKE
YKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSC
SVMHEALHNHYTQKSLSLSKSCDKTGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSCPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS
QEDPEVQFNWYVDGVEVHNAKTKPREEQFNSDYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVKGFYP
SDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSGECGGGGSGGGGSEVQLVESGGGLVQPGGSLRLSCAA
SGYTFTSYWLHWVRQAPGKGLEWVGMIDPSNSDTRFNPNFKDRFTISADTSKNTAYLQMNSLRAEDTAVYYCATYRSYVTPLDYWGQGTLVTVSSASTGGGGSGGGG
SGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCKSSQSLLYTSSQKNYLAWYQQKPGKAPKLLIYWASTRESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQ
YYAYPWTFGQGTKVEIK**
(SEQ ID NO:356)

>Onartuzumab-23E-sm3E
EVQLVESGGGLVQPGGSLRLSCAASGYTFTSYWLHWVRQAPGKGLEWVGMIDPSNSDTRFNPNFKDRFTISADTSKNTAYLQMNSLRAEDTAVYYCATYRSYVTPLD
YWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVD
KKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEY
KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS
VMHEALHNHYTQKSLSLSKSCDKTGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSGECGGGGSGGGGSQVKLEQSGAEVVKPGASVKLSCKAS
GFNIKDSYMHWLRQGPGQRLEWIGWIDPENGDTEYAPKFQGKATFTTDTSANTAYLGLSSLRPEDTAVYYCNEGTPTGPYYFDYWGQGTLVTVSSASTGGGGSGGGG
SGGGGSGGGGSENVLTQSPSSMSVSVGDRVTIACSASSSVPYMHWLQQKPGKSPKLLIYLTSNLASGVPSRFSGSGSGTDYSLTISSVQPEDAATYYCQQRSSYPLT
FGGGTKLEIK**
(SEQ ID NO:359)

Fig. 14
(sheet 4 of 24)

>Onartuzumab-39Egy4-sm3E
EVQLVESGGGLVQPGGSLRLSCAASGYTFTSYWLHWVRQAPGKGLEWVGMIDPSNSDTRFNPNFKDRFTISADTSKNTAYLQMNSLRAEDTAVYYCATYRSYVTPLD
YWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVD
KKVEPKSCDKTHTCPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSKYRVVSVLTVLHQDWLNGKEY
KCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS
VMHEALHNHYTQKSLSLSKSCDKTGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSCPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQ
EDPEVQFNWYVDGVEVHNAKTKPREEQFNSDYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSGECGGGGSGGGGSQVKLEQSGAEVVKPGASVKLSCKAS
GFNIKDSYMHWLRQGPGQRLEWIGWIDPENGDTEYAPKFQGKATFTTDTSANTAYLGLSSLRPEDTAVYYCNEGTPTGPYYFDYWGQGTLVTVSSASTGGGGSGGGG
SGGGGSGGGGSENVLTQSPSSMSVSVGDRVTIACSASSSVPYMHWLQQKPGKSPKLLIYLTSNLASGVPSRFSGSGSGTDYSLTISSVQPEDAATYYCQQRSSYPLT
FGGGTKLEIK**
(SEQ ID NO:360)

>Onartuzumab-39Egy4-Biwa6
EVQLVESGGGLVQPGGSLRLSCAASGYTFTSYWLHWVRQAPGKGLEWVGMIDPSNSDTRFNPNFKDRFTISADTSKNTAYLQMNSLRAEDTAVYYCATYRSYVTPLD
YWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVD
KKVEPKSCDKTHTCPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSKYRVVSVLTVLHQDWLNGKEY
KCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS
VMHEALHNHYTQKSLSLSKSCDKTGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSCPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQ
EDPEVQFNWYVDGVEVHNAKTKPREEQFNSDYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSGECGGGGSGGGGSEVQLVESGGGLVKPGGSLRLSCAAS
GFTFSSYDMSWVRQAPGKGLEWVSTISSGGSYTYYLDSIKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARQGLDYWGRGTLVTVSSASTGGGGSGGGGSGGGGS
GGGGSEIVLTQSPATLSLSPGERATLSCSASSSINYIYWYQQKPGQAPRLLIYLTSNLASGVPARFSGSGSGTDFTLTISSLEPEDFAVYYCLQWSSNPLTFGGGTK
VEIK**
(SEQ ID NO:361)

Fig. 14
(sheet 5 of 24)

>Onartuzumab-23E-Biwa6
EVQLVESGGGLVQPGGSLRLSCAASGYTFTSYWLHWVRQAPGKGLEWVGMIDPSNSDTRFNPNFKDRFTISADTSKNTAYLQMNSLRAEDTAVYYCATYRSYVTPLD
YWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVD
KKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEY
KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS
VMHEALHNHYTQKSLSLSKSCDKTGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSGECGGGGSGGGGSEVQLVESGGGLVKPGGSLRLSCAAS
GFTFSSYDMSWVRQAPGKGLEWVSTISSGGSYTYYLDSIKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARQGLDYWGRGTLVTVSSASTGGGGSGGGGSGGGGS
GGGGSEIVLTQSPATLSLSPGERATLSCSASSSINYIYWYQQKPGQAPRLLIYLTSNLASGVPARFSGSGSGTDFTLTISSLEPEDFAVYYCLQWSSNPLTFGGGTK
VEIK**
(SEQ ID NO:362)

>Onartuzumab-23E-ARH460-16-2-HC
EVQLVESGGGLVQPGGSLRLSCAASGYTFTSYWLHWVRQAPGKGLEWVGMIDPSNSDTRFNPNFKDRFTISADTSKNTAYLQMNSLRAEDTAVYYCATYRSYVTPLD
YWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVD
KKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEY
KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS
VMHEALHNHYTQKSLSLSKSCDKTGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSGECGGGGSGGGGSEVQLVESGGGLVQPGGSLRLSCAAS
GFDFSRYWMSWVRQAPGKGLVWVGEVNPDSTSINYTPSLKDRFTISRDNAKNTLYLQMNSLRAEDTAVYYCTRPNYYGSRYHYYAMDYWGQGTLVTVSSASTGGGGS
GGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQDINNYLNWYQQKPGKAPKLLIYYTSRLHSGVPSRFSGSGSGTDFTFTISSLQPEDIATYYCQQGS
TLPFTFGQGTKLEIK**
(SEQ ID NO:363)

Fig. 14
(sheet 6 of 24)

>Onartuzumab-39Egy4-ARH460-16-2-HC
EVQLVESGGGLVQPGGSLRLSCAASGYTFTSYWLHWVRQAPGKGLEWVGMIDPSNSDTRFNPNFKDRFTISADTSKNTAYLQMNSLRAEDTAVYYCATYRSYVTPLD
YWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVD
KKVEPKSCDKTHTCPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSKYRVVSVLTVLHQDWLNGKEY
KCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS
VMHEALHNHYTQKSLSLSKSCDKTGGGSGGGGSGGGGSGGGGSGGGGSCPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQ
EDPEVQFNWYVDGVEVHNAKTKPREEQFNSDYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSGECGGGGSGGGGSEVQLVESGGGLVQPGGSLRLSCAAS
GFDFSRYWMSWVRQAPGKGLVWVGEVNPDSTSINYTPSLKDRFTISRDNAKNTLYLQMNSLRAEDTAVYYCTRPNYYGSRYHYYAMDYWGQGTLVTVSSASTGGGGS
GGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQDINNYLNWYQQKPGKAPKLLIYYTSRLHSGVPSRFSGSGSGTDFTFTISSLQPEDIATYYCQQGS
TLPFTFGQGTKLEIK**
(SEQ ID NO:364)

>ARH460-16-2-23E-Onartuzumab
EVQLVESGGGLVQPGGSLRLSCAASGFDFSRYWMSWVRQAPGKGLVWVGEVNPDSTSINYTPSLKDRFTISRDNAKNTLYLQMNSLRAEDTAVYYCTRPNYYGSRYH
YYAMDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPS
NTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWL
NGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGN
VFSCSVMHEALHNHYTQKSLSLSKSCDKTGGGSGGGGSGGGGSGGGGSGGGGSCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVV
VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVK
GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSGECGGGGSGGGGEVQLVESGGGLVQPGGSLRLS
CAASGYTFTSYWLHWVRQAPGKGLEWVGMIDPSNSDTRFNPNFKDRFTISADTSKNTAYLQMNSLRAEDTAVYYCATYRSYVTPLDYWGQGTLVTVSSASTGGGGSG
GGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCKSSQSLLYTSSQKNYLAWYQQKPGKAPKLLIYWASTRESGVPSRFSGSGSGTDFTLTISSLQPEDFATYY
CQQYYAYPWTFGQGTKVEIK**
(SEQ ID NO:365)

Fig. 14
(sheet 7 of 24)

>ARH460-16-2-39Egy4-Onartuzumab
EVQLVESGGGLVQPGGSLRLSCAASGFDFSRYWMSWVRQAPGKGLVWVGEVNPDSTSINYTPSLKDRFTISRDNAKNTLYLQMNSLRAEDTAVYYCTRPNYYGSRYH
YYAMDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPS
NTKVDKKVEPKSCDKTHTCPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSKYRVVSVLTVLHQDWL
NGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGN
VFSCSVMHEALHNHYTQKSLSLSKSCDKTGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSCPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVV
VDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSDYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVK
GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSGECGGGGSGGGGSEVQLVESGGGLVQPGGSLRL
SCAASGYTFTSYWLHWVRQAPGKGLEWVGMIDPSNSDTRFNPNFKDRFTISADTSKNTAYLQMNSLRAEDTAVYYCATYRSYVTPLDYWGQGTLVTVSSASTGGGGS
GGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCKSSQSLLYTSSQKNYLAWYQQKPGKAPKLLIYWASTRESGVPSRFSGSGSGTDFTLTISSLQPEDFATY
YCQQYYAYPWTFGQGTKVEIK**
(SEQ ID NO:366)

>ARH460-16-2-LC
DIQMTQSPSSLSASVGDRVTITCRASQDINNYLNWYQQKPGKAPKLLIYYTSRLHSGVPSRFSGSGSGTDFTFTISSLQPEDIATYYCQQGSTLPFTFGQGTKLEIK
RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
**
(SEQ ID NO:367)

Fig. 14

(sheet 8 of 24)

Onartuzumab-23-HC

EVQLVESGGGLVQPGGSLRLSCAASGYTFTSYWLHWVRQAPGKGLEWVGMIDPSNSDTRFNPNFKDRFTISADTSKNTAYLQMNSLRAEDTAVYYCATYRSYVTPLD
YWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVD
KKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEY
KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS
VMHEALHNHYTQKSLSLSPGKGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDP
EVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVKGFYPSDIA
VEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK**
(SEQ ID NO:368)

gaggtgcagttggtagaatcaggaggggtctggtccaacccggaggaagcctcagactcagctgtgcggcttcgggttacacctttacctcctattggttgcactg
ggtgagacaggcacctggcaaagggctcgaatgggtcggaatgatcgacccctccaactcagatacgcggtttaacccgaatttcaaggatcgattcacgatctcag
cagacacatcgaaaaacacagcgtacctccagatgaattcgttgagggccgaggacacggcggtgtattactgcgccacgtatcgcagctatgtaactccattggat
tactgggggcagggtactcttgtgacagtctcctcggctagcaccaagggacccagcgtgtttccacttgcgccttcgtcaaagtccacaagcgggggaacggcagc
ccttggctgcctggtgaaagactactttcccgaacccgtgacagtatcgtggaatagcggagcgctcacatcgggcgtgcacacatttccggcggtgctgcagtcct
ccgggttgtattcgctgtcgagcgtagtcacggtgccgtcctcgtcactgggaactcagacatacatttgcaacgtcaatcacaaaccgtcaaacacgaaagtcgac
aagaaagtggaaccgaaatcatgcgacaagacccacacttgtccccatgtcctgccccagagcttctcgggggaccctcggtgttcttgttcccgccgaaaccgaa
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aaatgtaaggtatcaaacaaggccctcccagcgccgattgagaaaacgatctcgaaagcgaaaggacagcccagggagccgcaagtatacactcttccgccatcacg
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acaaaaccacgccacccgtcctcgacagcgacggatcgttctttctggtgagcaagttgaccgtcgataagtcgcggtggcaacagggtaatgtgttttcatgctca
gtgatgcatgaggccttgcacaatcattacacacagaagtccctcagcctttcgcctggcaaaggtgggggtgggtcgggaggggggaggatcaggtggtggagggtc
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gaggaccttcagtgtttctttttccgcccaaacccaaagataccttatgatctcgcgaacccctgaagtcacatgcgtggtcgtggatgtatcgcatgaggacccg
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ggtacttcatcaggattggctcaatgggaaagaatacaagtgcaaggtgtcgaataaggcgttgcctgcacccattgaaaagacgatttcgaaagctaagggtcaac
ccagagaaccccaagtctatacgcttccccttcccgcgaggaaatgacgaagaatcaggtcagcctctggtgcctggtgaaggggttctacccctccgacatcgcc
gtagagtgggaatccaatgggcagcccgaaaacaactacaagacgacaccgcctgtgttggattcagatgggagcttctttctctattccaaactgacggtggacaa
aagcaggtggcagcaaggaaatgtgttctcgtgctcggtaatgcacgaagcactgcacaaccactacacccagaagtccttgtccctttcgccaggaaaataatag
(SEQ ID NO:369)

Fig. 14

(sheet 9 of 24)

Onartuzumab-39-HC

EVQLVESGGGLVQPGGSLRLSCAASGYTFTSYWLHWVRQAPGKGLEWVGMIDPSNSDTRFNPNFKDRFTISADTSKNTAYLQMNSLRAEDTAVYYCATYRSYVTPLD
YWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVD
KKVEPKSCDKTHTCPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSKYRVVSVLTVLHQDWLNGKEY
KCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS
VMHEALHNHYTQKSLSLSPGKGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSCPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDP
EVQFNWYVDGVEVHNAKTKPREEQFNSKYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVKGFYPSDIA
VEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK**
(SEQ ID NO:370)

gaggtgcagttggtagaatcaggaggggtctggtccaacccggaggaagcctcagactcagctgtgcggcttcgggttacacctttacctcctattggttgcactg
ggtgagacaggcacctggcaaagggctcgaatgggtcggaatgatcgacccctccaactcagatacgcggtttaacccgaatttcaaggatcgattcacgatctcag
cagacacatcgaaaaacacagcgtacctccagatgaattcgttgagggccgaggacacggcggtgtattactgcgccacgtatcgcagctatgtaactccattggat
tactgggggcagggtactcttgtgacagtctcctcggctagcaccaagggacccagcgtgtttccacttgcgccttcgtcaaagtccacaagcgggggaacggcagc
ccttggctgcctggtgaaagactactttcccgaacccgtgacagtatcgtggaatagcggagcgctcacatcgggcgtgcacacatttccggcggtgctgcagtcct
ccgggttgtattcgctgtcgagcgtagtcacggtgccgtcctcgtcactgggaactcagacatacatttgcaacgtcaatcacaaaccgtcaaacacgaaagtcgac
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agacacgctcatgatttcgcgcacacccgaagtcacatgcgtggtggtggatgtgagccaggaagatccggaggtacagttcaattggtatgtcgatggggtggagg
tacataatgccaagacgaaaccgagggaggagcagttcaactccaagtatagggtggtgtcagtcttgactgtgttgcaccaagattggcttaacggaaaagagtat
aagtgtaaagtatcgaacaagggactccccagctcaatcgaaaagacgatctcaaaggcgaaaggtcagccacgagaaccccaagtatacacgctgcctccatcgcg
ggaagaaatgacgaaaaaccaagtatcgctttcatgcgctgtgaaggggttctacccgtcggacattgccgtggaatgggaaagcaatgggcagccagagaataact
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cgtccttcatcaggactggcttaatggaaaggaatacaaatgtaaagtctcgaataaggggttgcccagctcgattgagaaaaccatctccaaagcgaaagggcagc
caagagagcctcaagtctatacgcttcccccatcacgcgaagagatgactaagaatcaagtctccctgtggtgcctggtgaagggattctacccttcggatattgcg
gtggagtgggagtccaacggtcagccggagaacaattacaagacgactccgccggtactcgattcagatggatcattctttctctactccaaactcacagtagacaa
atcgaggtggcaacagggaaacgtcttttcatgttcggtaatgcacgaggcccttcacaatcattacacccagaaatcactcagcctgtccccgggaaataatag
(SEQ ID NO:371)

Fig. 14

(sheet 10 of 24)

Onartuzumab-23E-HC

EVQLVESGGGLVQPGGSLRLSCAASGYTFTSYWLHWVRQAPGKGLEWVGMIDPSNSDTRFNPNFKDRFTISADTSKNTAYLQMNSLRAEDTAVYYCATYRSYVTPLD
YWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVD
KKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEY
KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS
VMHEALHNHYTQKSLSLSKSCDKTGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSGEC**
(SEQ ID NO:372)

gaggtgcagttggtagaatcaggaggggtctggtccaacccggaggaagcctcagactcagctgtgcggcttcgggttacacctttacctcctattggttgcactg
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gcttggttgcctcgtcaaagactacttccccgagccggtaacggtgtcgtggaactccggtgcgctgacatcaggggtgcacacgttccctgctgtccttcagtcaa
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aaaaaggtcgaaccaaaatcgtgcgataagacgcacacctgcccaccttgtccggctccggaactcttgggtggtccgtccgtattcttgttcccgcctaagccgaa
ggacactcttatgatttcgaggaccccggaggtcacgtgcgtcgtggtggatgtctcgcatgaggacccggaagtcaaattcaactggtacgtagacggtgtcgagg
tgcataacgcaaagaccaagcccagggaagagcagtaccagtccacgtaccgggtagtgtcggtgctcaccgtgcttcaccaggactggcttaacgggaaggaatac
aagtgtaaagtctccaacaaagcgctccctgcccccatcgaaaagaccatttcgaaagcgaaagggcagccacgcgagcctcaagtgtacaccctgccgccgtcccg
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gaagatccggaggtgaagttcaattggtacgtagatggggtcgaagtgcataatgcaaagacgaaaccgcgagaggagcagtatcagtcaacgtatcgcgtagtaag
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aggggcaaccccgagagccccaagtatacactctcccgccttcgagagaggagatgactaaaaaccaggtgtcgctttggtgtttggtgaaggggttctatccctcg
gatatcgccgtcgagtgggaatccaatgggcaacccgaaaacaactataagacaacgcctccagtactggactccgacggctccttttttcttgtactccaaattgac
ggtggataagtcgcggtggcagcaggggaatgtgttttcgtgtagcgtgatgcatgaagccctgcataaccactatactcaaaagtcactttccctgtcgggtgaat
gctgataatct
(SEQ ID NO:373)

Fig. 14
(sheet 11 of 24)

Onartuzumab-39Egy4-HC

EVQLVESGGGLVQPGGSLRLSCAASGYTFTSYWLHWVRQAPGKGLEWVGMIDPSNSDTRFNPNFKDRFTISADTSKNTAYLQMNSLRAEDTAVYYCATYRSYVTPLD
YWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVD
KKVEPKSCDKTHTCPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSKYRVVSVLTVLHQDWLNGKEY
KCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS
VMHEALHNHYTQKSLSLSKSCDKTGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSCPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQ
EDPEVQFNWYVDGVEVHNAKTKPREEQFNSDYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSGEC**
(SEQ ID NO:374)

gaggtgcagttggtagaatcaggaggggtctggtccaacccggaggaagcctcagactcagctgtgcggcttcgggttacacctttacctcctattggttgcactg
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tccacaatgctaagacaaaaccaagagaggaacagttcaacagcaagtacagggtcgtgtccgtgctgactgtcctgcatcaggactggctgaacggaaaagagtat
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gaggatccagaggtccagtttaactggtatgtcgatggcgtggaggtccacaatgctaagaccaaacctcgcgaggaacagttcaactctgactaccgagtggtcag
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gacatcgccgtggagtgggaaagtaatggccagcctgaaaacaattacaagactacccctccagtgctggactcagatgggagcttctttctgtatagtaagctgac
cgtggataaatcacggtggcagcagggaaatgtgttctcttgcagtgtcatgcacgaggccctgcataaccattacacacagaagtcattaagcttatccggagagt
gttgataatctagactcgag
(SEQ ID NO:375)

Fig. 14

(sheet 12 of 24)

Onartuzumab-23E-Cetuximab-HC

EVQLVESGGGLVQPGGSLRLSCAASGYTFTSYWLHWVRQAPGKGLEWVGMIDPSNSDTRFNPNFKDRFTISADTSKNTAYLQMNSLRAEDTAVYYCATYRSYVTPLD
YWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVD
KKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEY
KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS
VMHEALHNHYTQKSLSLSKSCDKTGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSGECGGGGSGGGGSQVQLVESGGGVVQPGESLRISCAVS
GFSLTNYGVHWVRQAPGKGLEWLGVIWSGGNTDYNTPFTSRLTISKDNSKSTVYFQMNSLRAEDTAVYYCARALTYYDYEFAYWGQGTLVTVSSASTGGGGSGGGGS
GGGGSGGGGSDIVLTQSPSSLSVTPGEKVTFTCRASQSIGTNIHWYQQKPGQSPKLLIKYASESISGVPSRFSGSGSGTDFTLTINSVEAEDAATYYCQQNNNWPTT
FGQGTKLEIK**

(SEQ ID NO:376)

Fig. 14

(sheet 13 of 24)

gaggtgcagttggtagaatcaggagggggtctggtccaacccggaggaagcctcagactcagctgtgcggcttcgggttacacctttacctcctattggttgcactg
ggtgagacaggcacctggcaaagggctcgaatgggtcggaatgatcgacccctccaactcagatacgcggtttaacccgaatttcaaggatcgattcacgatctcag
cagacacatcgaaaaacacagcgtacctccagatgaattcgttgagggccgaggacacggcggtgtattactgcgccacgtatcgcagctatgtaactccattggat
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tcagcgggtctggaagtggcaccgacttacactgactatcaacagtgtggaggccgaagatgccgctacatactattgtcagcagaacaataactggcctaccaca
ttgggcagggaacaaagctggagatcaagtgataa
(SEQ ID NO:377)

Fig. 14
(sheet 14 of 24)

Onartuzumab-23E-Panitumumab-HC

EVQLVESGGGLVQPGGSLRLSCAASGYTFTSYWLHWVRQAPGKGLEWVGMIDPSNSDTRFNPNFKDRFTISADTSKNTAYLQMNSLRAEDTAVYYCATYRSYVTPLD
YWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVD
KKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEY
KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS
VMHEALHNHYTQKSLSLSKSCDKTGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSGECGGGGSGGGGSQVQLQESGPGLVKPSETLSLTCTVS
GGSVSSGDYYWTWIRQSPGKGLEWIGHIYYSGNTNYNPSLKSRLTISIDTSKTQFSLKLSSVTAADTAIYYCVRDRVTGAFDIWGQGTMVTSSASTGGGGSGGGGSG
GGGSGGGGSDIQMTQSPSSLSASVGDRVTITCQASQDISNYLNWYQQKPGKAPKLLIYDASNLETGVPSRFSGSGSGTDFTFTISSLQPEDEATYFCQHFDHLPLAF
GGGTKVEIKRT**
(SEQ ID NO:378)

Fig. 14
(sheet 15 of 24)

gaggtgcagttggtagaatcaggagggggtctggtccaacccggaggaagcctcagactcagctgtgcggcttcgggttacaccttacctcctattggttgcactg
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gaagatccggaggtgaagttcaattggtacgtagatgggggtcgaagtgcataatgcaaagacgaaaccgcgagaggagcagtatcagtcaacgtatcgcgtagtaag
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ccggttcagggtcgggaacggacttcacgtttacaatctccagcctgcagccggaggacgaagccacctactcttctgccaacacttcgacccattttgcctcttgcgttc
ggaggtgggacaaaggtggagatcaagcgaacttgataa
(SEQ ID NO:379)

Fig. 14
(sheet 16 of 24)

Onartuzumab-23E-2224-HC

EVQLVESGGGLVQPGGSLRLSCAASGYTFTSYWLHWVRQAPGKGLEWVGMIDPSNSDTRFNPNFKDRFTISADTSKNTAYLQMNSLRAEDTAVYYCATYRSYVTPLD
YWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVD
KKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEY
KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS
VMHEALHNHYTQKSLSLSKSCDKTGGGGSGGGGSGGGGSGGGGSGGGGSCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSGECGGGGSGGGGSEVQLVQSGAEVKKPGSSVKVSCKAS
GGTFSSYAIGWVRQAPGQGLEWMGGIIPIFGIANYAQKFQGRVTITADESTSSAYMELSSLRSEDTAVYYCAREEGPYCSSTSCYAAFDIWGQGTLVTVSSASTGGG
GSGGGGSGGGGSGGGGSQSVLTQDPAVSVALGQTVKITCQGDSLRSYFASWYQQKPGQAPTLVMYARNDRPAGVPDRFSGSKSGTSASLAISGLQPEDEADYYCAAW
DDSLNGYLFGAGTKLTVL**
(SEQ ID NO:380)

Fig. 14
(sheet 17 of 24)

gaggtgcagttggtagaatcaggagggggtctggtccaacccggaggaagcctcagactcagctgtgcggcttcgggttacacctttacctcctattggttgcactg
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gcttggttgcctcgtcaaagactacttcccgagccggtaacggtgtcgctgacatcagggggtgcacacgttccctgctgtcctttcagtcaa
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gatgactcattgaatgggtatcttcttcggtgcgggggacgaagttgacggtgctgtgataa
(SEQ ID NO:381)

Fig. 14
(sheet 18 of 24)

Onartuzumab-39Egy4-Cetuximab-HC

EVQLVESGGGLVQPGGSLRLSCAASGYTFTSYWLHWVRQAPGKGLEWVGMIDPSNSDTRFNPNFKDRFTISADTSKNTAYLQMNSLRAEDTAVYYCATYRSYVTPLD
YWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVD
KKVEPKSCDKTHTCPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSKYRVVSVLTVLHQDWLNGKEY
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DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSGECGGGSGGGGSQVQLVESGGGVVQPGESLRISCAVS
GFSLTNYGVHWVRQAPGKGLEWLGVIWSGGNTDYNTPFTSRLTISKDNSKSTVYFQMNSLRAEDTAVYYCARALTYYDYEFAYWGQGTLVTVSSASTGGGGSGGGGS
GGGGSGGGGSDIVLTQSPSSLSVTPGEKVTFTCRASQSIGTNIHWYQQKPGQSPKLLIKYASESISGVPSRFSGSGSGTDFTLTINSVEAEDAATYYCQQNNNWPTT
FGQGTKLEIK**
(SEQ ID NO:382)

Fig. 14
(sheet 19 of 24)

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tcagcgggtctggaagtggcaccgacttacactgactatcaacagtgtggaggccgaagatgccgctacatactattgtcagcagaacaataactggcctaccaca
ttgggcagggaacaaagctggagatcaagtgataa
(SEQ ID NO:383)

Fig. 14
(sheet 20 of 24)

Onartuzumab-39Egy4-Panitumumab-HC

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KKVEPKSCDKTHTCPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSKYRVVSVLTVLHQDWLNGKEY
KCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS
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GGGTKVEIKRT**
(SEQ ID NO:384)

Fig. 14
(sheet 21 of 24)

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(SEQ ID NO:385)

Fig. 14
(sheet 22 of 24)

Onartuzumab-39Egy4-2224-HC

EVQLVESGGGLVQPGGSLRLSCAASGYTFTSYWLHWVRQAPGKGLEWVGMIDPSNSDTRFNPNFKDRFTISADTSKNTAYLQMNSLRAEDTAVYYCATYRSYVTPLD
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KKVEPKSCDKTHTCPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSKYRVVSVLTVLHQDWLNGKEY
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GSGGGGSGGGGSGGGGSQSVLTQDPAVSVALGQTVKITCQGDSLRSYFASWYQQKPGQAPTLVMYARNDRPAGVPDRFSGSKSGTSASLAISGLQPEDEADYYCAAW
DDSLNGYLFGAGTKLTVL**
(SEQ ID NO:386)

Fig. 14
(sheet 23 of 24)

ggtaccatgggcttcggactgtcgtggcttttctggtggcgattcttaaggggtccagtgcgaggtgcagttggtagaatcaggaggggtctggtccaacccgg
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(SEQ ID NO:387)

Fig. 14
(sheet 24 of 24)

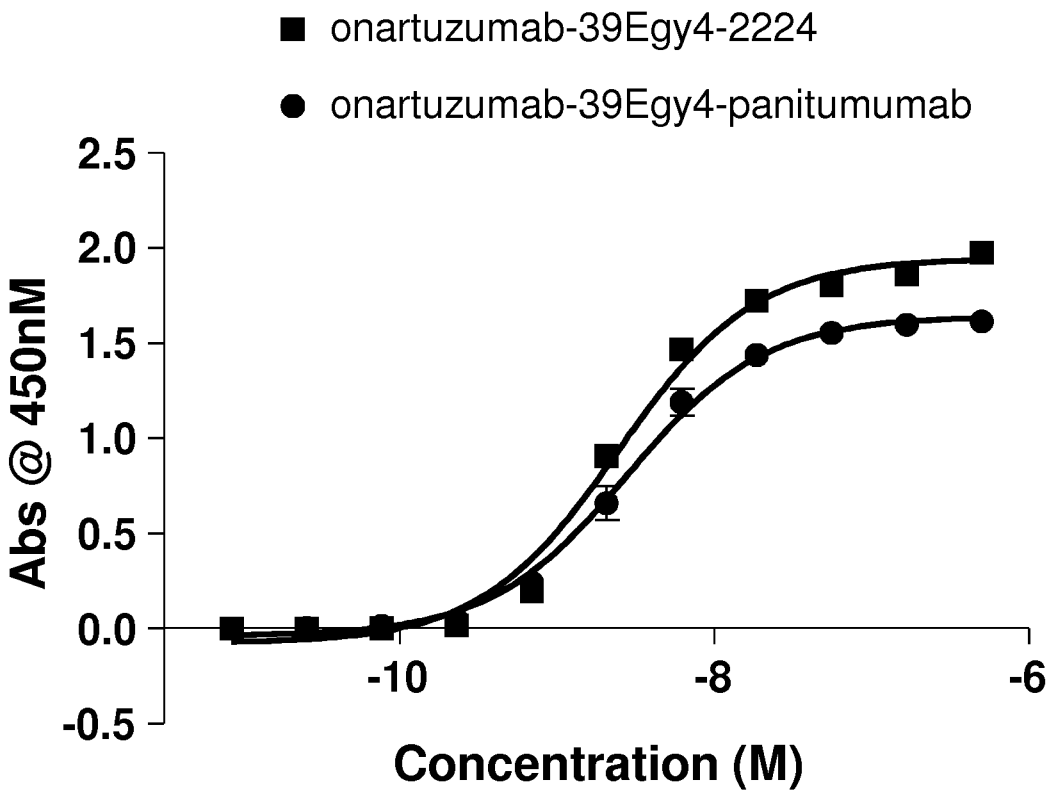

onartuzumab-39Egy4-2224
onartuzumab-39Egy4-panitumumab
Abs @ 450nM
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-10
-8
-6
Concentration (M)

Fig. 15

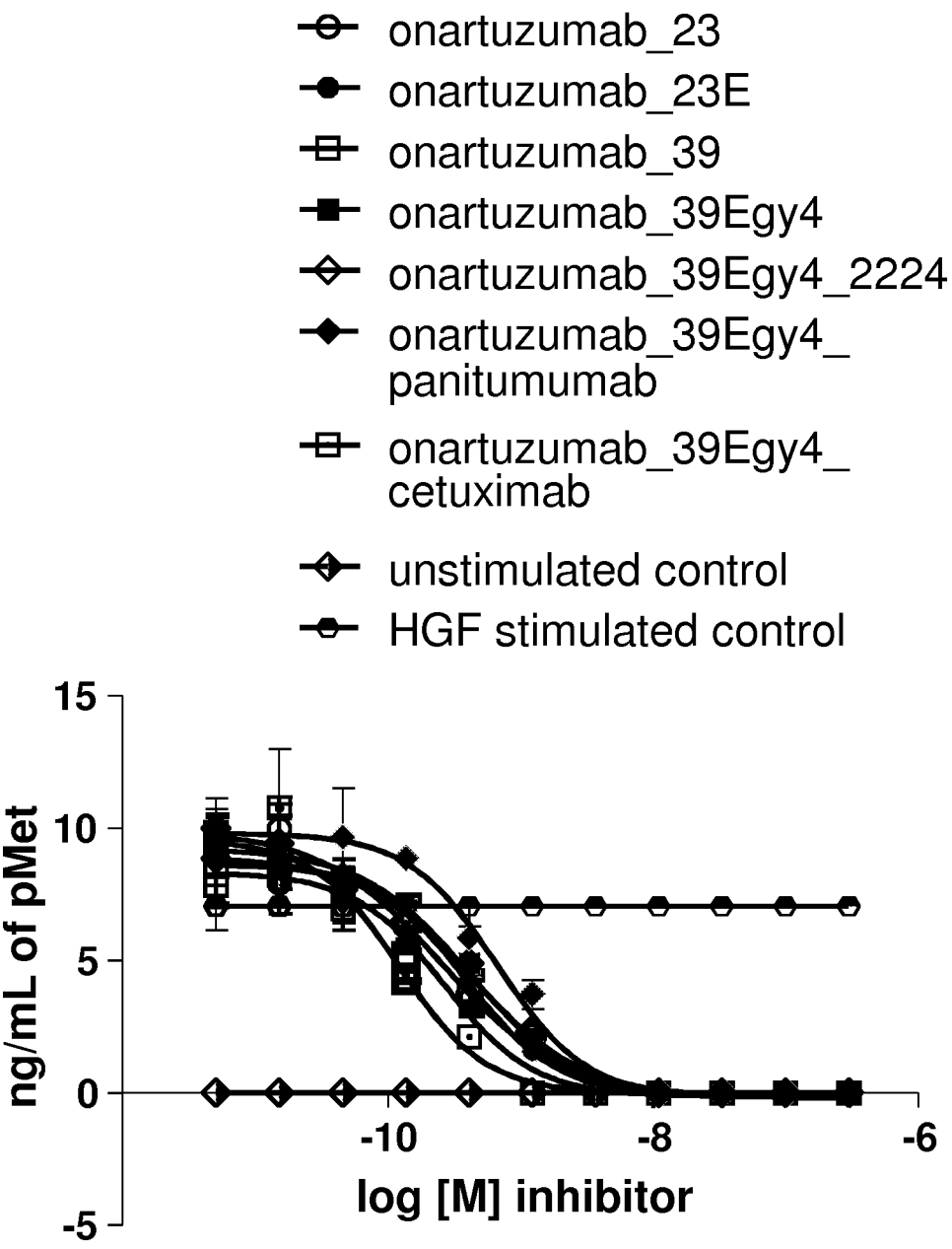

onartuzumab_23
onartuzumab_23E
onartuzumab_39
onartuzumab_39Egy4
onartuzumab_39Egy4_2224
onartuzumab_39Egy4_ panitumumab
onartuzumab_39Egy4_ cetuximab
unstimulated control
HGF stimulated control
15
10
5
0
-5
ng/mL of pMet
-10
-8
-6
log [M] inhibitor

Fig. 16

Glycosylation mutants

Glyco mutant 1
CH2: N297D/T299S::N297D/T299S
CH3: T366S/L368A/Y407V/CH3 C-terminal Cysteine KSCDKT::T366W/CH3 C-terminal Cysteine GEC

[DKTHTCPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKT
KPREEQF**D**S**S**YRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSREEMT
KNQVSL**S**C**A**VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL**V**SKLTVDKSRWQQGNVFSCSVMH
EALHNHYTQKSLSLS**KSCDKT**GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSCPSCPAPEF
LGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQF**D**S**S**YRVVS
VLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL**W**CLVKGFYP
SDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS
GEC
(SEQ ID No:388)

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gagtgctgataa
(SEQ ID No:389)

Fig. 17

Glyco mutant 2
CH2: T299K::N297D/T299S
CH3: T366S/L368A/Y407V/CH3 C-terminal Cysteine KSCDKT::T366W/CH3 C-terminal Cysteine GEC

DKTHTCPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTK
PREEQFNS**K**YRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSL**S**C**A**VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL**V**SKLTVDKSRWQQGNVFSCSVMHE
ALHNHYTQKSLSLS**KSCDKT**GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSCPSCPAPEFL
GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQF**D**S**S**YRVVSV
LTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL**W**CLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS**G**
EC
(SEQ ID No:390)

gataaaacgcacacgtgcccctcgtgtccggcaccggagtttcttggaggtccctcggtgttcctgttcc
ctcccaagccgaaggacacgttgatgatttcgaggacgccggaggtgacgtgtgtggtcgtagacgtgag
ccaggaggacccggaagtgcagtttaactggtacgtcgatggagtagaagtacataatgccaagacgaag
cccagggaggaacaattcaattcgaagtatcgcgtcgtatccgtgctgactgtgctccaccaggactggc
ttaacggaaaagaatacaagtgcaaggtatcaaataagggactcccctcgtcgatcgagaaaacaatcag
caaagcgaaaggacagccgagggaaccgcaagtgtacacattgccgccgtcgcgagaagaaatgaccaag
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acggtcaacccgagaataactacaaaactacaccgcccgtgctggattccgacggctcattctttctcgt
gtcaaaactgactgtggataagtcgcgctggcaacaggggaatgtgttctcgtgcagcgtcatgcatgaa
gctcttcataatcactacacccaaaaatccctgtcactctcgaaaagctgtgataagaccgggggtgggg
gctccggaggaggcggttcgggtggcggtgggtcgggtggaggcggatcgggcggtgggggaagcggtgg
tggtggaagcggaggggggtggatcaggtggaggggggcagctgtccatcctgccctgcaccagagtttttg
ggaggaccgtccgtatttctgtttccgcccaagcccaaagatactttgatgatcagcaggacgcctgagg
taacatgtgtagtggtcgatgtctcgcaagaggaccctgaggtccagttcaattggtacgtggacggggt
ggaagtccacaacgcgaaaacgaaaccacgcgaagaacagttcgacagcagttacagagtcgtgtcagtc
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gccctcgcgggaggagatgacaaagaatcaggtgtcgctgtggtgtctggtaaaaggattctatccatcc
gatatcgcggtagagtgggaatcaaacggccagccggagaacaattacaagaccacgccccctgtattgg
attcggacggatcgttcttcttgtattcgaaactcacggtggacaagtcgcggtggcagcagggtaatgt
gttttcatgctcagtcatgcacgaggcgctccataaccattatactcagaagtcgctgtccttgtccggg
gagtgctgataa
(SEQ ID No:391)

Fig. 17 (cont.)

Glyco mutant 3
CH2: N297D/T299S::T299K
CH3: T366S/L368A/Y407V/CH3 C-terminal Cysteine KSCDKT::T366W/CH3 C-terminal Cysteine GEC

DKTHTCPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTK
PREEQF**D**S**S**YRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSL**S**C**A**VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL**V**SKLTVDKSRWQQGNVFSCSVMHE
ALHNHYTQKSLSLS**KSCDKT**GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSCPSCPAPEFL
GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNS**K**YRVVSV
LTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL**W**CLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS**G**
EC
(SEQ ID No:392)

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ctcccaagccgaaggacacgttgatgatttcgaggacgccggaggtgacgtgtgtggtcgtagacgtgag
ccaggaggacccggaagtgcagtttaactggtacgtcgatggagtagaagtacataatgccaagacgaag
cccagggaggaacaattcgattcgagttatcgcgtcgtatccgtgctgactgtgctccaccaggactggc
ttaacggaaaagaatacaagtgcaaggtatcaaataagggactcccctcgtcgatcgagaaaacaatcag
caaagcgaaaggacagccgagggaaccgcaagtgtacacattgccgccgtcgcgagaagaaatgaccaag
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acggtcaacccgagaataactacaaaactacaccgcccgtgctggattccgacggctcattctttctcgt
gtcaaaactgactgtggataagtcgcgctggcaacaggggaatgtgttctcgtgcagcgtcatgcatgaa
gctcttcataatcactacacccaaaaatccctgtcactctcgaaaagctgtgataagaccgggggtgggg
gctccggaggaggcggttcgggtggcggtgggtcgggtggaggcggatcgggcggtgggggaagcggtgg
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ggaggaccgtccgtatttctgtttccgcccaagcccaaagatactttgatgatcagcaggacgcctgagg
taacatgtgtagtggtcgatgtctcgcaagaggaccctgaggtccagttcaattggtacgtggacggggt
ggaagtccacaacgcgaaaacgaaaccacgcgaagaacagttcaacagcaaatacagagtcgtgtcagtc
ttgacagtccttcaccaggattggttgaatggaaaggagtacaagtgtaaggtgtcaaacaaaggactgc
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gccctcgcgggaggagatgacaaagaatcaggtgtcgctgtggtgtctggtaaaaggattctatccatcc
gatatcgcggtagagtgggaatcaaacggccagccggagaacaattacaagaccacgccccctgtattgg
attcggacggatcgttcttcttgtattcgaaactcacggtggacaagtcgcggtggcagcagggtaatgt
gttttcatgctcagtcatgcacgaggcgctccataaccattatactcagaagtcgctgtccttgtccggg
gagtgctgataa
(SEQ ID No:393)

Fig. 17 (cont.)

Glyco mutant 4
CH2: T299K::T299D
CH3: T366S/L368A/Y407V/CH3 C-terminal Cysteine KSCDKT::T366W/CH3 C-terminal Cysteine GEC
DKTHTCPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTK
PREEQFNS**K**YRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSL**S**C**A**VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL**V**SKLTVDKSRWQQGNVFSCSVMHE
ALHNHYTQKSLSLS**KSCDKT**GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSCPSCPAPEFL
GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNS**D**YRVVSV
LTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL**W**CLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS**G**
EC
(SEQ ID No:394)

gataaaacgcacacgtgcccctcgtgtccggcaccggagtttcttggaggtccctcggtgttcctgttcc
ctcccaagccgaaggacacgttgatgatttcgaggacgccggaggtgacgtgtgtggtcgtagacgtgag
ccaggaggacccggaagtgcagtttaactggtacgtcgatggagtagaagtacataatgccaagacgaag
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ttaacggaaaagaatacaagtgcaaggtatcaaataagggactcccctcgtcgatcgagaaaacaatcag
caaagcgaaaggacagccgagggaaccgcaagtgtacacattgccgccgtcgcgagaagaaatgaccaag
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acggtcaacccgagaataactacaaaactacaccgcccgtgctggattccgacggctcattctttctcgt
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gatatcgcggtagagtgggaatcaaacggccagccggagaacaattacaagaccacgccccctgtattgg
attcggacggatcgttcttcttgtattcgaaactcacggtggacaagtcgcggtggcagcagggtaatgt
gttttcatgctcagtcatgcacgaggcgctccataaccattatactcagaagtcgctgtccttgtccggg
gagtgctgataa
(SEQ ID No:395)

Fig. 17 (cont.)

Glyco mutant 5
CH2: T299D::T299K
CH3: T366S/L368A/Y407V/CH3 C-terminal Cysteine KSCDKT::T366W/CH3 C-terminal Cysteine GEC

DKTHTCPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTK
PREEQFNS**D**YRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSL**S**C**A**VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL**V**SKLTVDKSRWQQGNVFSCSVMHE
ALHNHYTQKSLSLS**KSCDKT**GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSCPSCPAPEFL
GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNS**K**YRVVSV
LTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL**W**CLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS**G**
EC
(SEQ ID No:396)

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ctcccaagccgaaggacacgttgatgatttcgaggacgccggaggtgacgtgtgtggtcgtagacgtgag
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gtcaaaactgactgtggataagtcgcgctggcaacaggggaatgtgttctcgtgcagcgtcatgcatgaa
gctcttcataatcactacacccaaaaatccctgtcactctcgaaaagctgtgataagaccgggggtgggg
gctccggaggaggcggttcgggtggcggtgggtcgggtggaggcggatcgggcggtgggggaagcggtgg
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ggaagtccacaacgcgaaaacgaaaccacgcgaagaacagttcaacagcaaatacagagtcgtgtcagtc
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gttttcatgctcagtcatgcacgaggcgctccataaccattatactcagaagtcgctgtccttgtccggg
gagtgctgataa
(SEQ ID No:397)

Fig. 17 (cont.)

Glyco mutant 6
CH2: T299D::T299D
CH3: T366S/L368A/Y407V/CH3 C-terminal Cysteine KSCDKT::T366W/CH3 C-terminal Cysteine GEC

DKTHTCPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTK
PREEQFNS**D**YRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSL**S**C**A**VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL**V**SKLTVDKSRWQQGNVFSCSVMHE
ALHNHYTQKSLSLS**KSCDKT**GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSCPSCPAPEFL
GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNS**D**YRVVSV
LTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL**W**CLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS**G**
EC
(SEQ ID No:398)

gataaaacgcacacgtgcccctcgtgtccggcaccggagtttcttggaggtccctcggtgttcctgttcc
ctcccaagccgaaggacacgttgatgatttcgaggacgccggaggtgacgtgtgtggtcgtagacgtgag
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gagtgctgataa
(SEQ ID No:399)

Fig. 17 (cont.)

Glyco wt
CH2: wt
CH3: T366S/L368A/Y407V/CH3 C-terminal Cysteine KSCDKT::T366W/CH3 C-terminal Cysteine GEC

DKTHTCPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTK
PREEQFNS**T**YRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSREEMTK
NQVSL**S**C**A**VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFL**V**SKLTVDKSRWQQGNVFSCSVMHE
ALHNHYTQKSLSLS**KSCDKT**GGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSCPSCPAPEFL
GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNS**T**YRVVSV
LTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSL**W**CLVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS**G**
EC
(SEQ ID No:357)

gacaaaacccacacatgcccctcatgtccagctccagagttcctgggaggaccaagcgtgttcctgtttc
cacctaagcctaaagataccctgatgatttccaggactccagaagtgacctgcgtggtggtggacgtgtc
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cctcgggaggaacagtttaatagcacttacagagtggtgtctgtgctgactgtgctgcatcaggattggc
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acagtgatggctcattctttctgtattcaaagctgaccgtggataaaagcagatggcagcagggaaacgt
gttttcttgcagtgtgatgcatgaggctctgcacaatcattacacacagaagagcttaagcttaagcggc
gagtgctgataa
(SEQ ID No:358)

Fig. 17 (cont.)

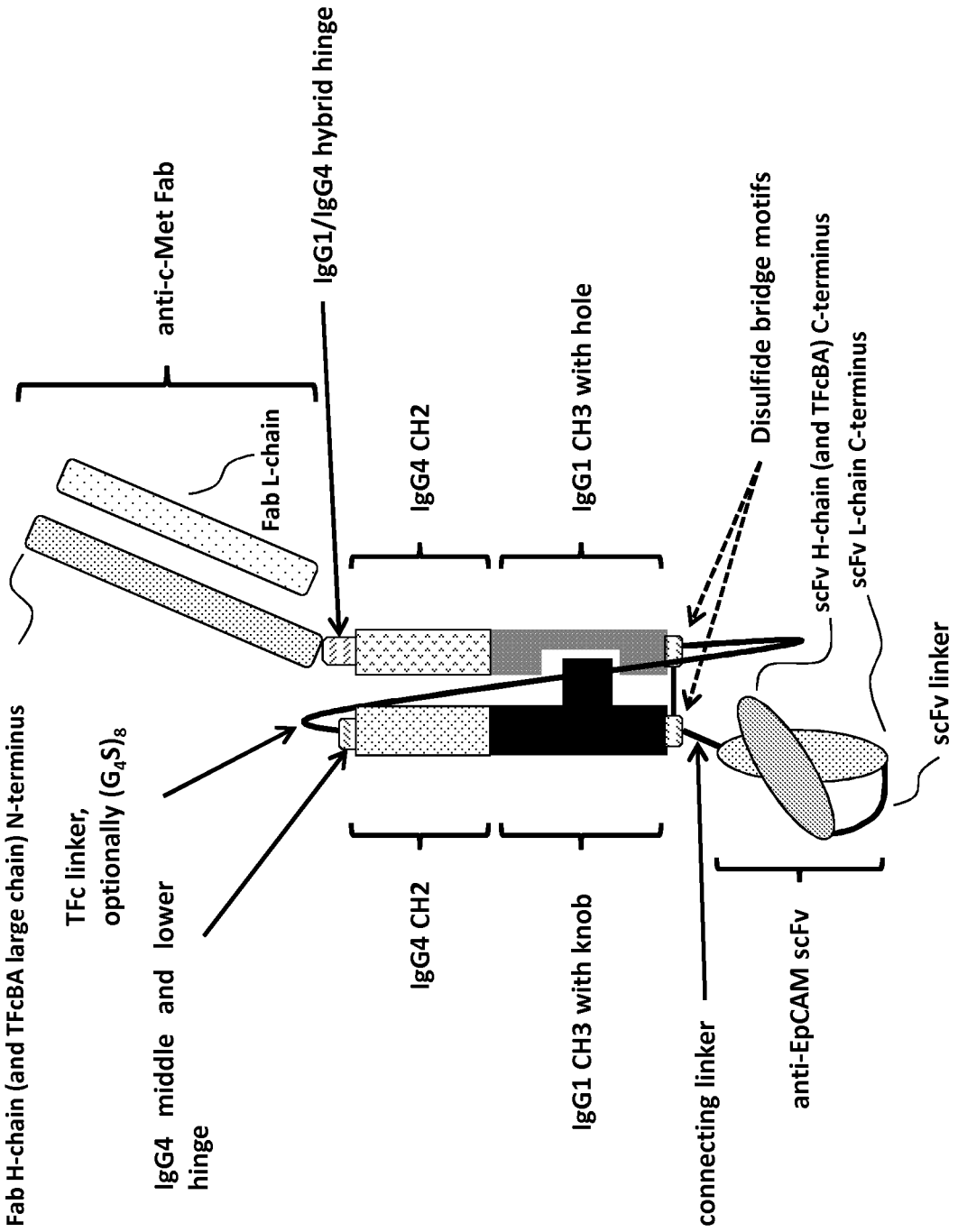

anti-c-Met Fab
IgG1/IgG4 hybrid hinge
Fab L-chain
IgG4 CH2
IgG1 CH3 with hole
Disulfide bridge motifs
scFv H-chain (and TFcBA) C-terminus
scFv L-chain C-terminus
scFv linker
Fab H-chain (and TFcBA large chain) N-terminus
TFc linker, optionally $(G_4S)_8$
IgG4 middle and lower hinge
IgG4 CH2
IgG1 CH3 with knob
connecting linker
anti-EpCAM scFv

Fig. 18

Bispecific antibody (MM131 alias)	scFv aa sequence (SEQ ID NO:)	Framework	Deamidation site removed	Methionine oxidation site removed	Orientation	Disulfide bridge	Linker
Ab# 1	SEQ ID NO:460	FR 1	yes	yes	VH/VL	yes	1
Ab# 2	SEQ ID NO:462	FR 1	yes	yes	VH/VL	no	1
Ab# 3	SEQ ID NO:464	FR 1	yes	yes	VH/VL	no	1
Ab# 4	SEQ ID NO:466	FR 1	yes	yes	VL/VH	no	1
Ab# 5 (131-3)	SEQ ID NO:468	FR 2	no	no	VL/VH	no	1
Ab# 6	SEQ ID NO:470	FR 2	yes	yes	VL/VH	no	1
Ab# 7 (131-4)	SEQ ID NO:472	FR 2	yes	yes	VL/VH	yes	1
Ab# 8	SEQ ID NO:474	FR 2	yes	no	VH/VL	no	1
Ab# 9	SEQ ID NO:476	FR 3	no	no	VH/VL	no	1
Ab# 10	SEQ ID NO:478	FR 3	yes	yes	VH/VL	no	1
Ab# 11	SEQ ID NO:480	FR 3	no	no	VL/VH	no	1
Ab# 12	SEQ ID NO:482	FR 3	yes	yes	VL/VH	no	1
Ab# 13 (131-5)	SEQ ID NO:484	FR 3	no	no	VL/VH	no	2

Fig. 19

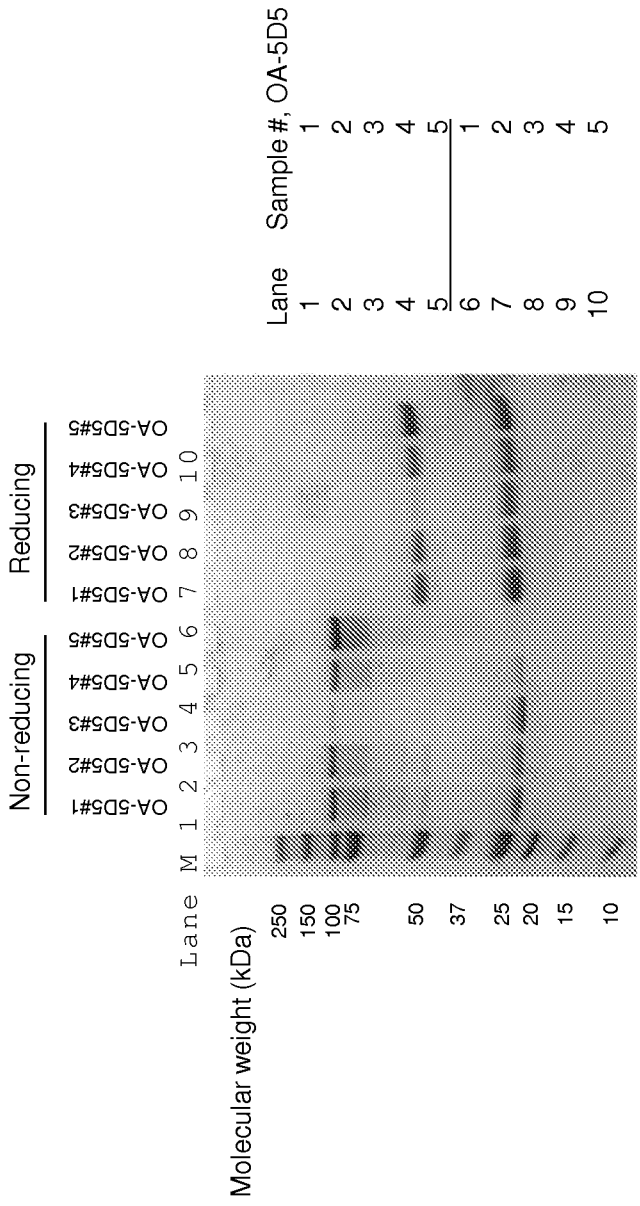

Non-reducing
Reducing
OA-5D5#1
OA-5D5#2
OA-5D5#3
OA-5D5#4
OA-5D5#5
OA-5D5#1
OA-5D5#2
OA-5D5#3
OA-5D5#4
OA-5D5#5
Lane M 1 2 3 4 5 6 7 8 9 10
Molecular weight (kDa)
250
150
100
75
50
37
25
20
15
10
Lane Sample #, OA-5D5
1 1
2 2
3 3
4 4
5 5
6 1
7 2
8 3
9 4
10 5

Fig. 20

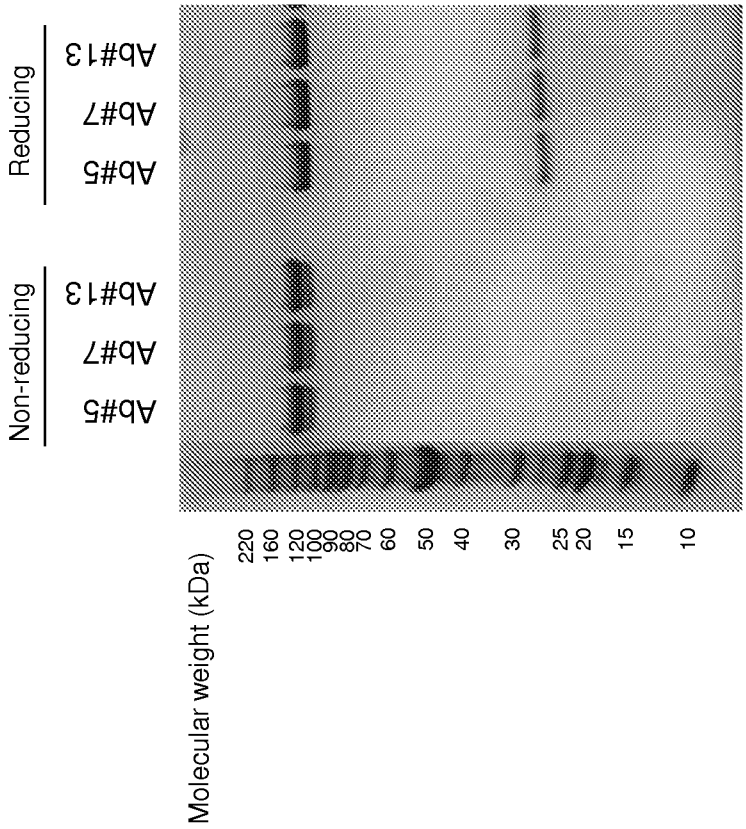

Non-reducing
Ab#5
Ab#7
Ab#13
Reducing
Ab#5
Ab#7
Ab#13
Molecular weight (kDa)
220
160
120
100
90
80
70
60
50
40
30
25
20
15
10

Fig. 21

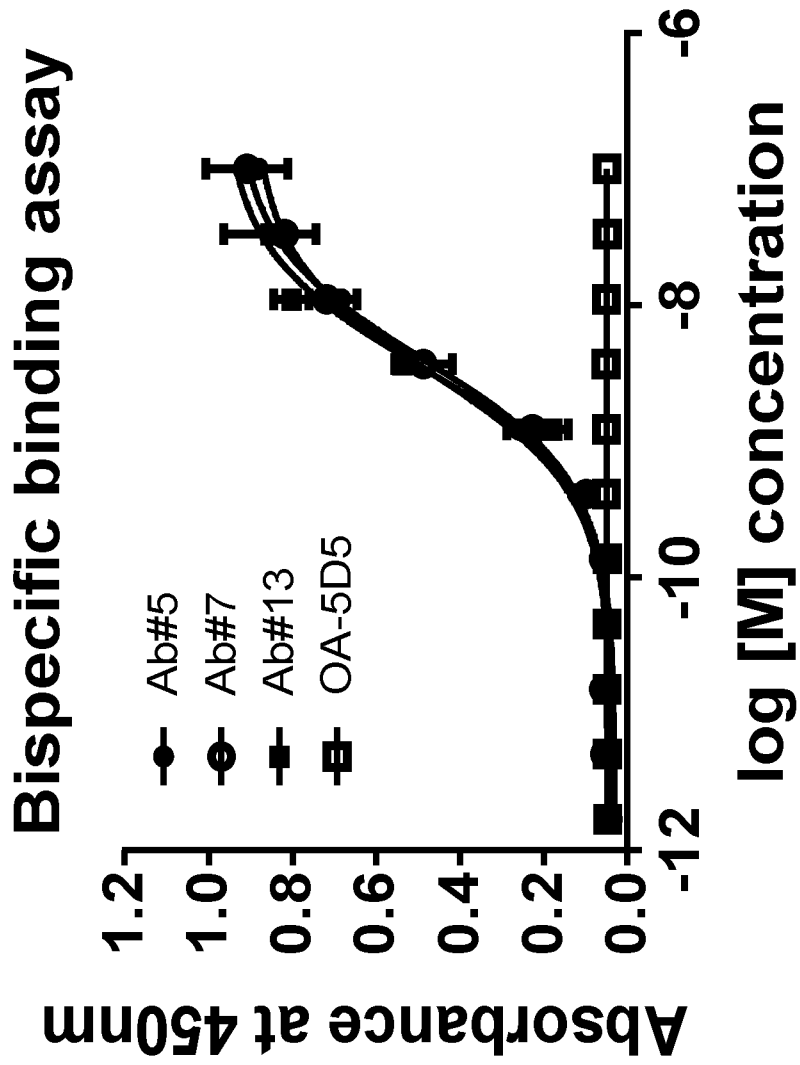

Bispecific binding assay
Ab#5
Ab#7
Ab#13
OA-5D5
Absorbance at 450nm
1.2
1.0
0.8
0.6
0.4
0.2
0.0
-12
-10
-8
-6
log [M] concentration

Fig. 22

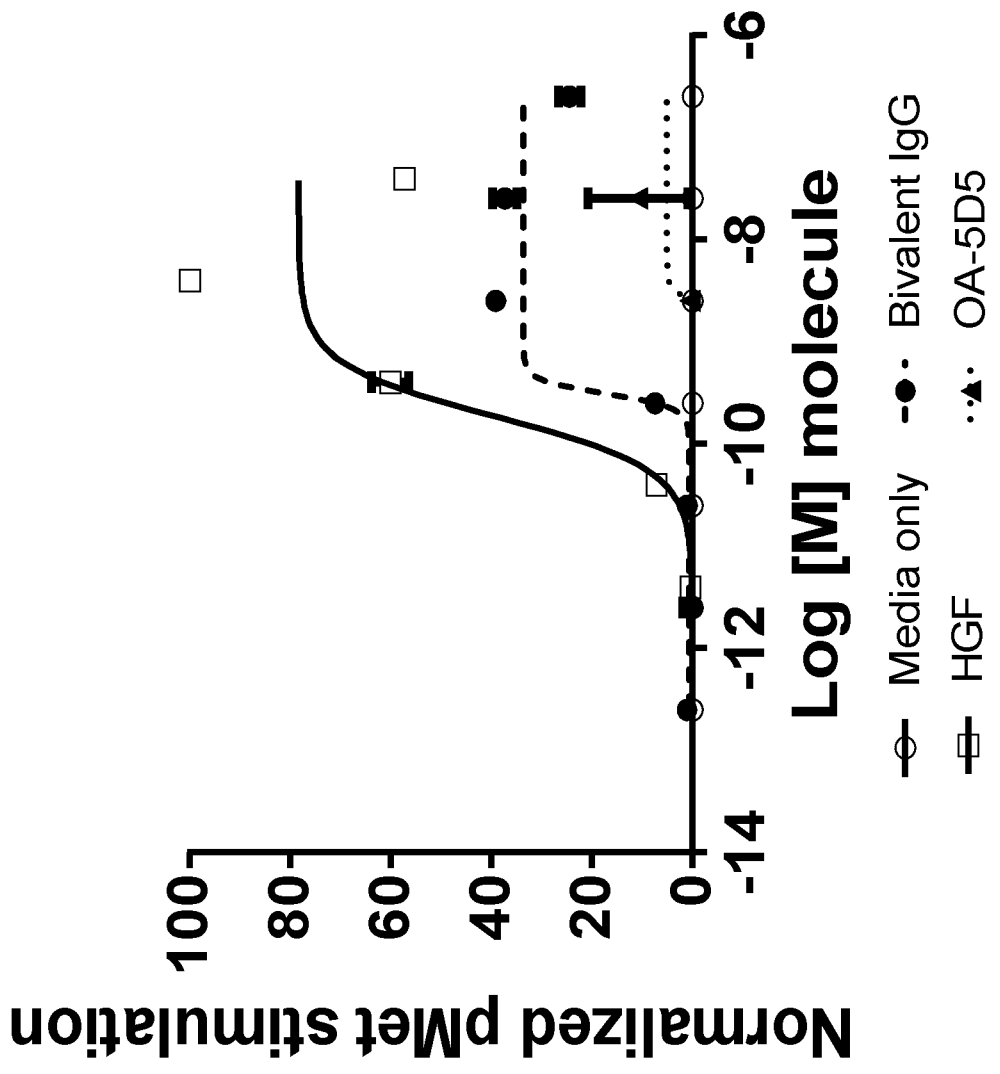

Normalized pMet stimulation
100
80
60
40
20
0
-14
-12
-10
-8
-6
Log [M] molecule
Media only
Bivalent IgG
HGF
OA-5D5

Fig. 23

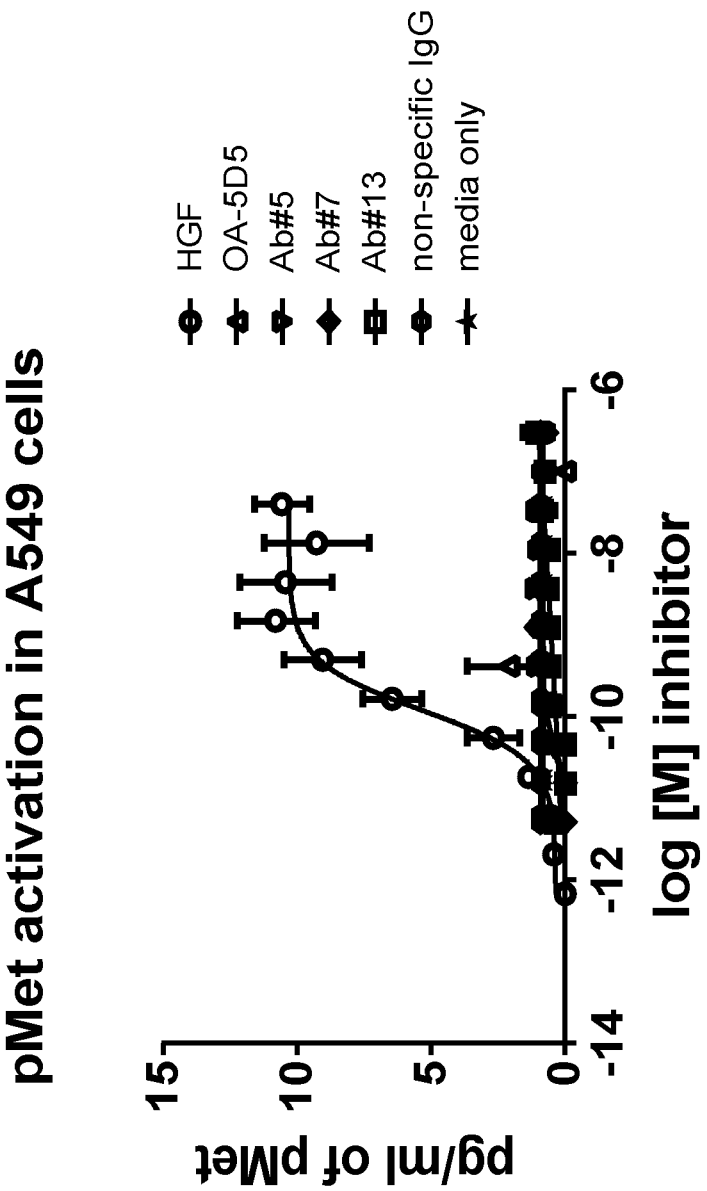

pMet activation in A549 cells
HGF
OA-5D5
Ab#5
Ab#7
Ab#13
non-specific IgG
media only
pg/ml of pMet
15
10
5
0
-14
-12
-10
-8
-6
log [M] inhibitor

Fig. 24

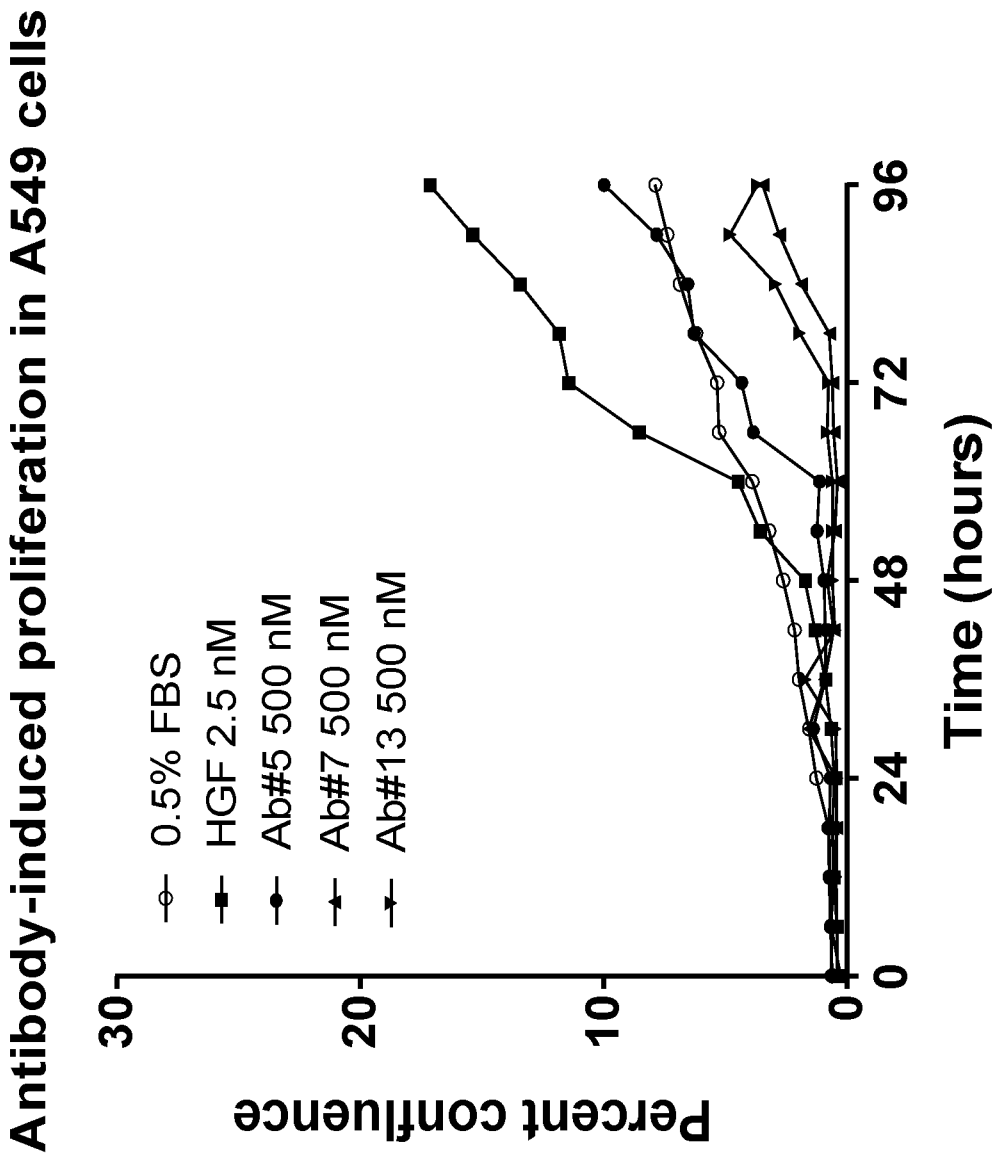

Antibody-induced proliferation in A549 cells
Percent confluence
30
20
10
0
0
24
48
72
96
Time (hours)
0.5% FBS
HGF 2.5 nM
Ab#5 500 nM
Ab#7 500 nM
Ab#13 500 nM

Fig. 25A

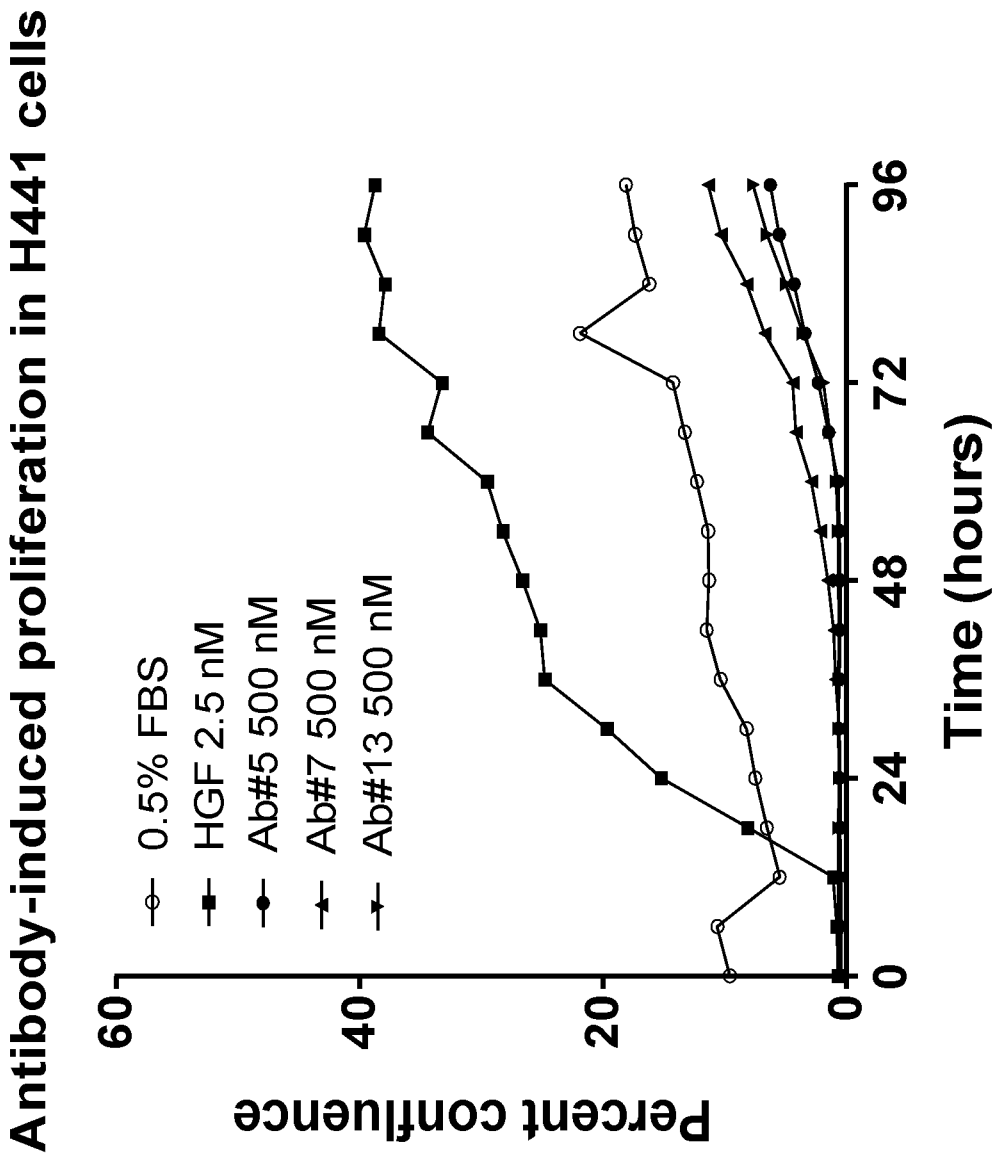

Antibody-induced proliferation in H441 cells
Percent confluence
60
40
20
0
0
24
48
72
96
Time (hours)
0.5% FBS
HGF 2.5 nM
Ab#5 500 nM
Ab#7 500 nM
Ab#13 500 nM

Fig. 25B

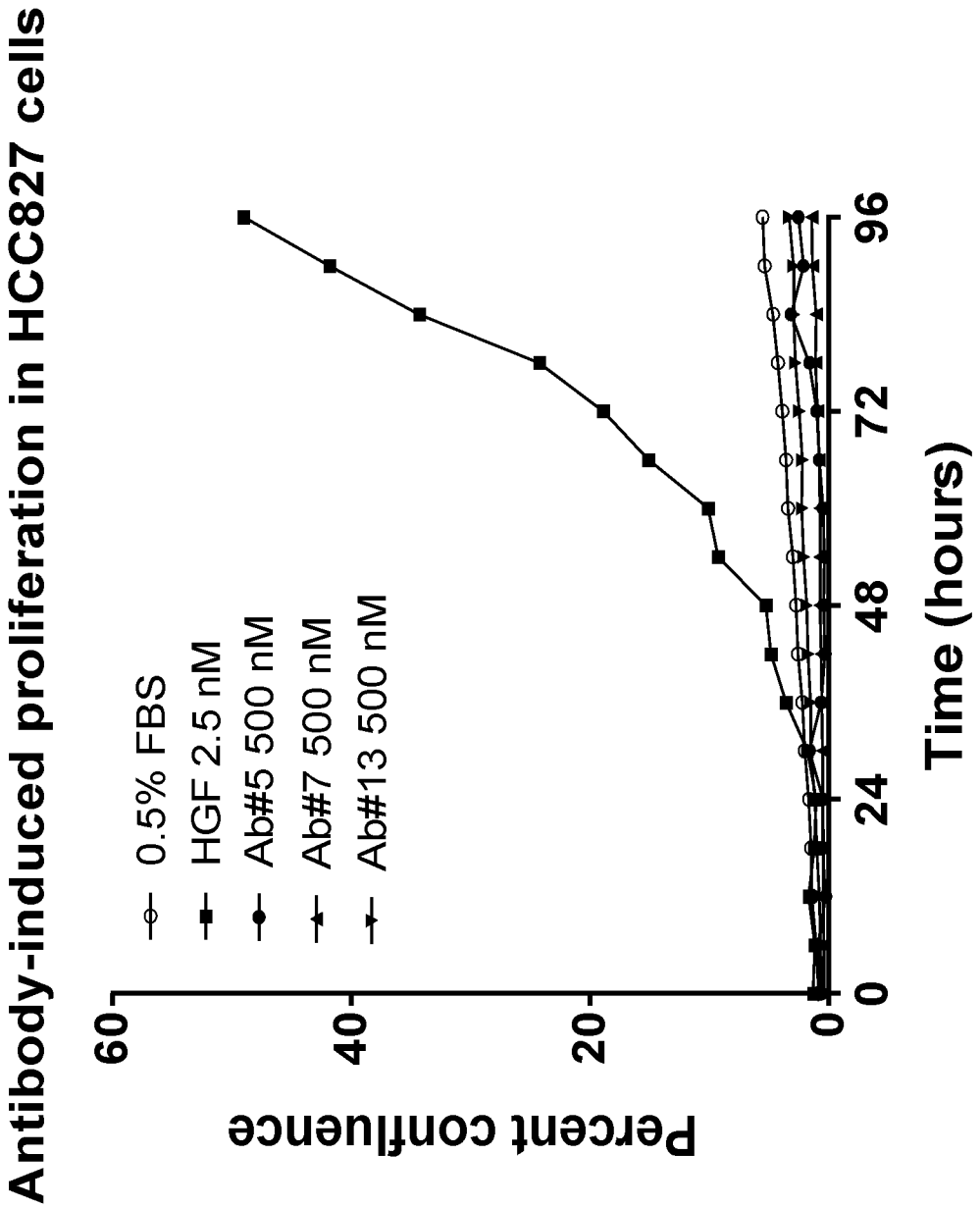

Antibody-induced proliferation in HCC827 cells
Percent confluence
60
40
20
0
0
24
48
72
96
Time (hours)
0.5% FBS
HGF 2.5 nM
Ab#5 500 nM
Ab#7 500 nM
Ab#13 500 nM

Fig. 25C

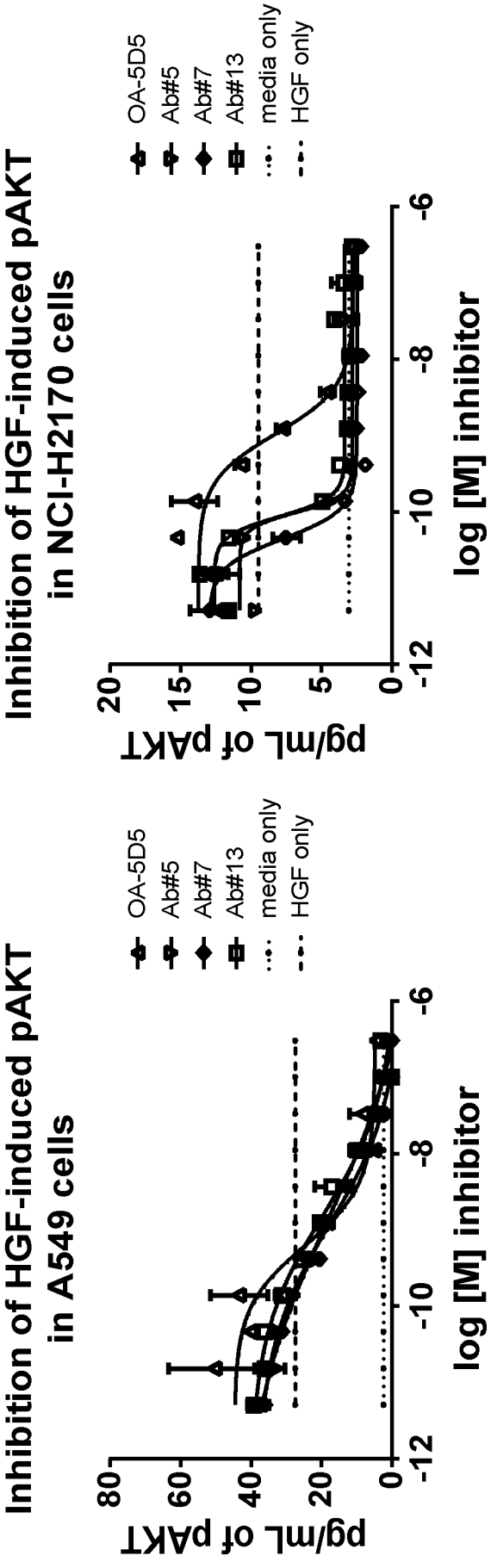
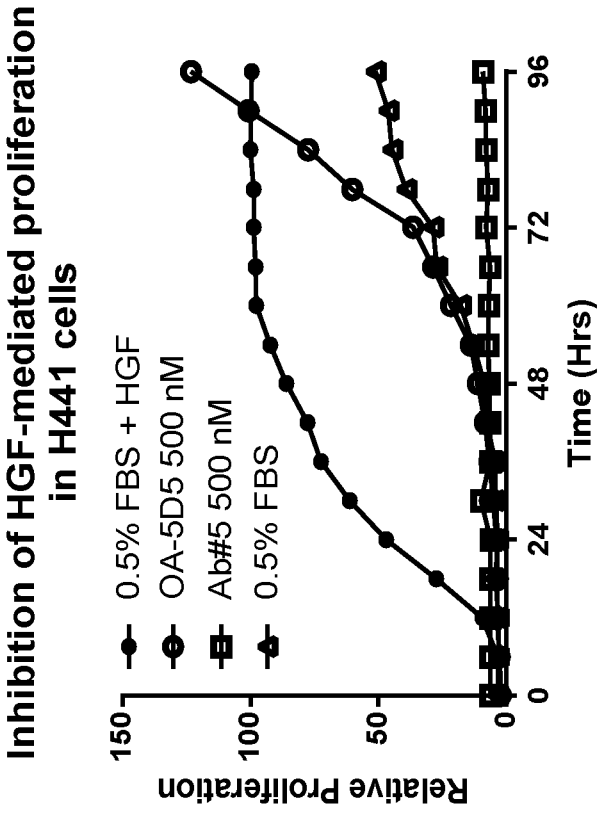

Inhibition of HGF-induced pAKT
in NCI-H2170 cells
pg/mL of pAKT
20
15
10
5
0
-12
-10
-8
-6
log [M] inhibitor
OA-5D5
Ab#5
Ab#7
Ab#13
media only
HGF only
Inhibition of HGF-induced pAKT
in A549 cells
pg/mL of pAKT
80
60
40
20
0
-12
-10
-8
-6
log [M] inhibitor
OA-5D5
Ab#5
Ab#7
Ab#13
media only
HGF only

Fig. 26


Inhibition of HGF-mediated proliferation in H441 cells
0.5% FBS + HGF
OA-5D5 500 nM
Ab#5 500 nM
0.5% FBS
Relative Proliferation
Time (Hrs)
0
50
100
150
0
24
48
72
96

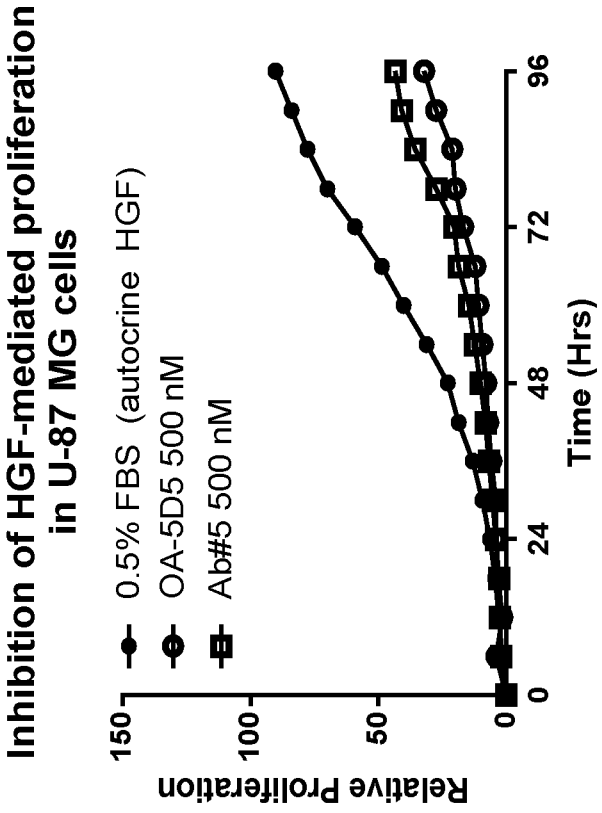
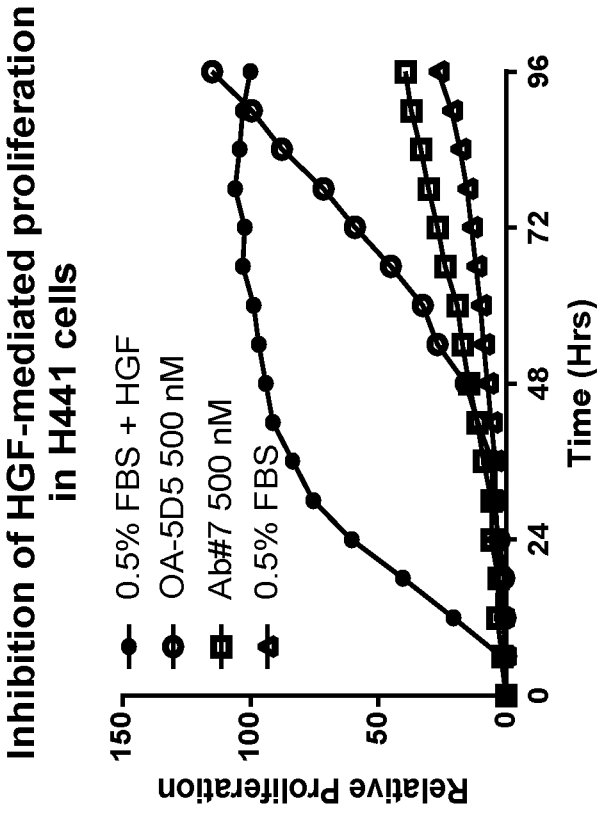

Inhibition of HGF-mediated proliferation in U-87 MG cells
0.5% FBS (autocrine HGF)
OA-5D5 500 nM
Ab#5 500 nM
Relative Proliferation
Time (Hrs)
0
50
100
150
0
24
48
72
96

Fig. 27


Inhibition of HGF-mediated proliferation in H441 cells
0.5% FBS + HGF
OA-5D5 500 nM
Ab#7 500 nM
0.5% FBS
Relative Proliferation
150
100
50
0
0
24
48
72
96
Time (Hrs)

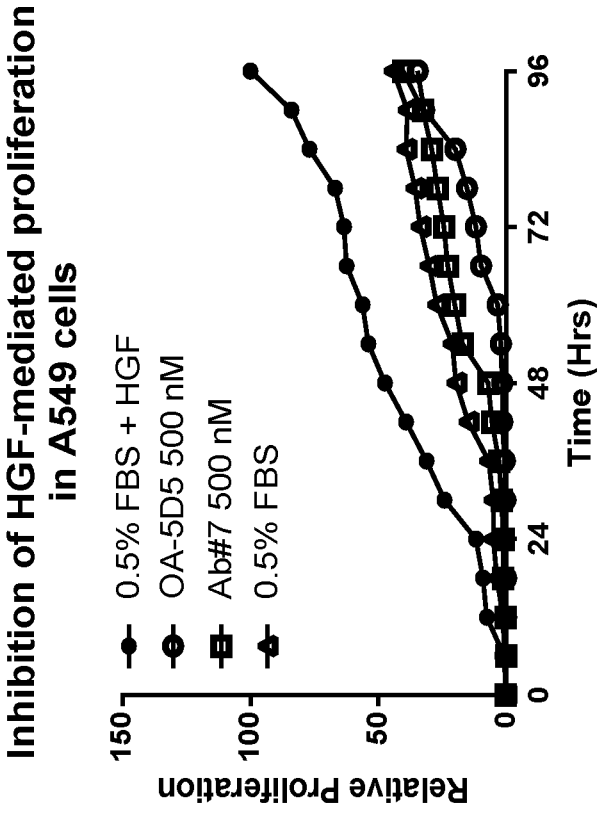

Inhibition of HGF-mediated proliferation in A549 cells
0.5% FBS + HGF
OA-5D5 500 nM
Ab#7 500 nM
0.5% FBS
Relative Proliferation
150
100
50
0
0
24
48
72
96
Time (Hrs)

Fig. 28

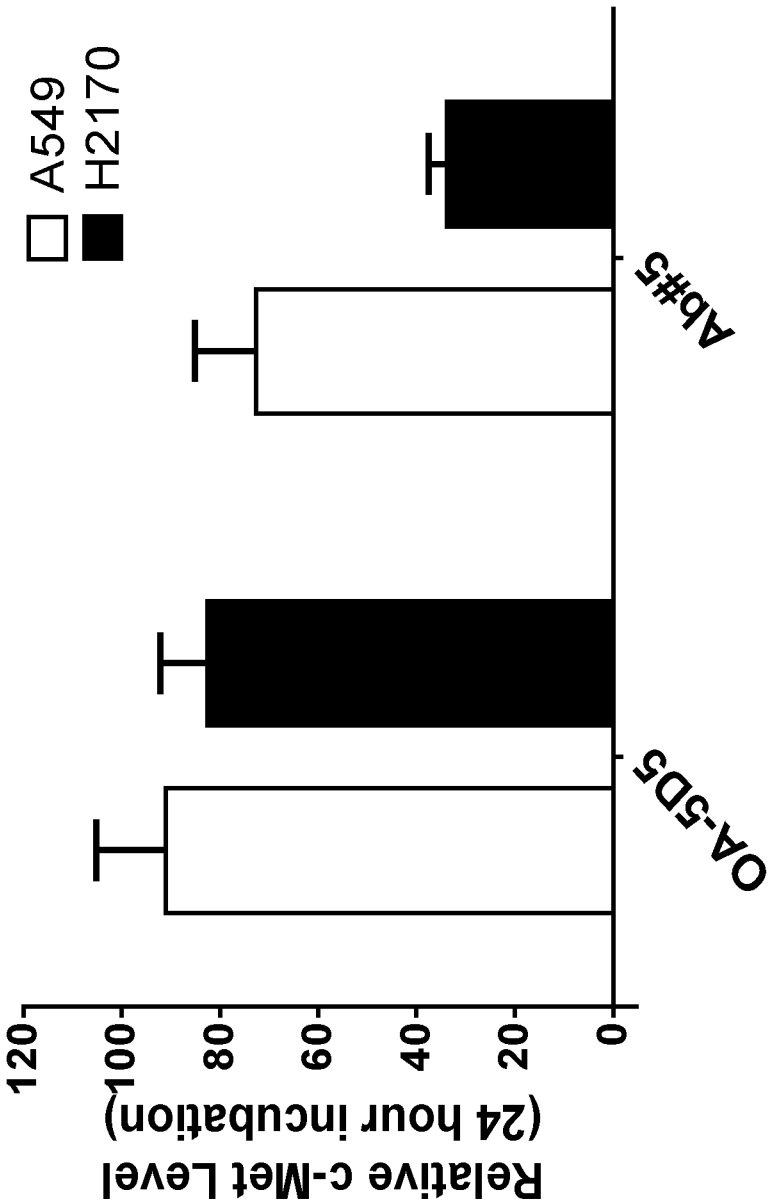

A549
H2170
Relative c-Met Level
(24 hour incubation)
0
20
40
60
80
100
120
OA-5D5
Ab#5

Fig. 29

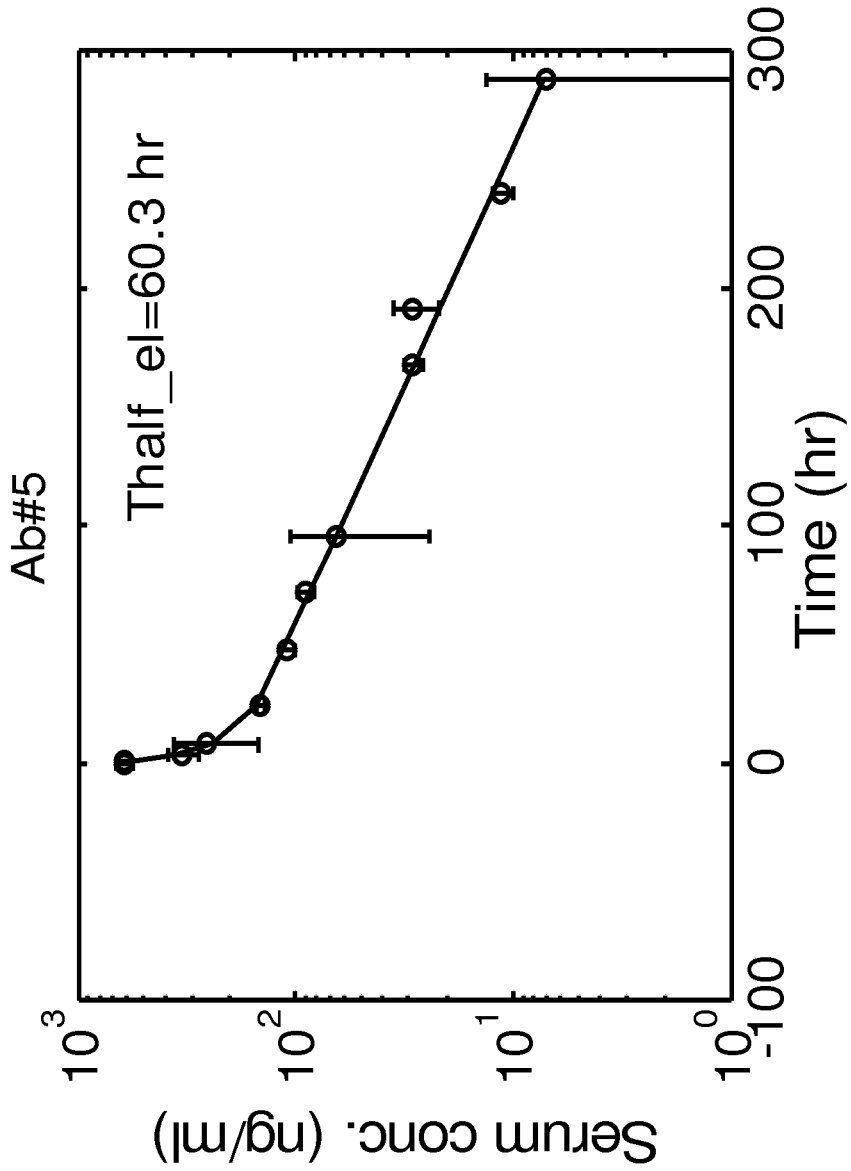

Ab#5
Thalf_el=60.3 hr
Serum conc. (ng/ml)
Time (hr)
10^3
10^2
10^1
10^0
-100
0
100
200
300

Fig. 30A

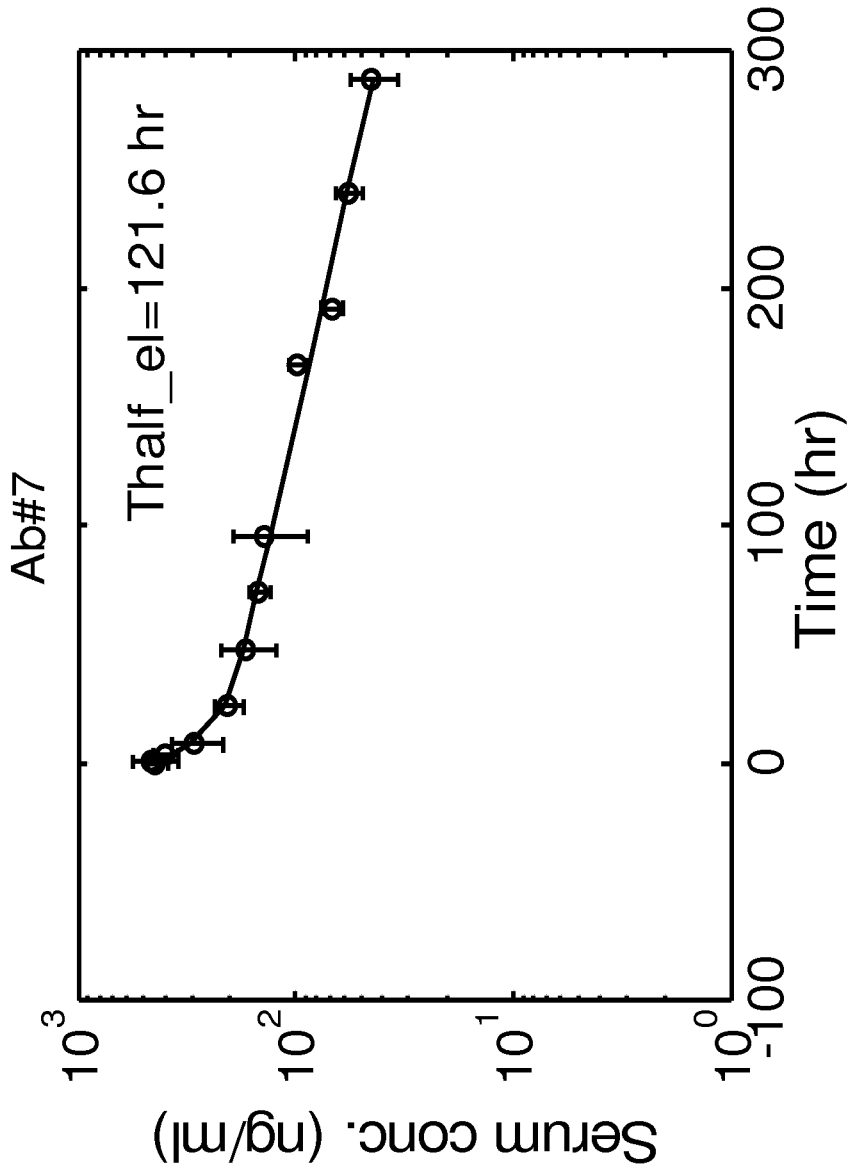

Ab#7
Thalf_el=121.6 hr
Serum conc. (ng/ml)
Time (hr)
10^3
10^2
10^1
10^0
-100
0
100
200
300

Fig. 30B

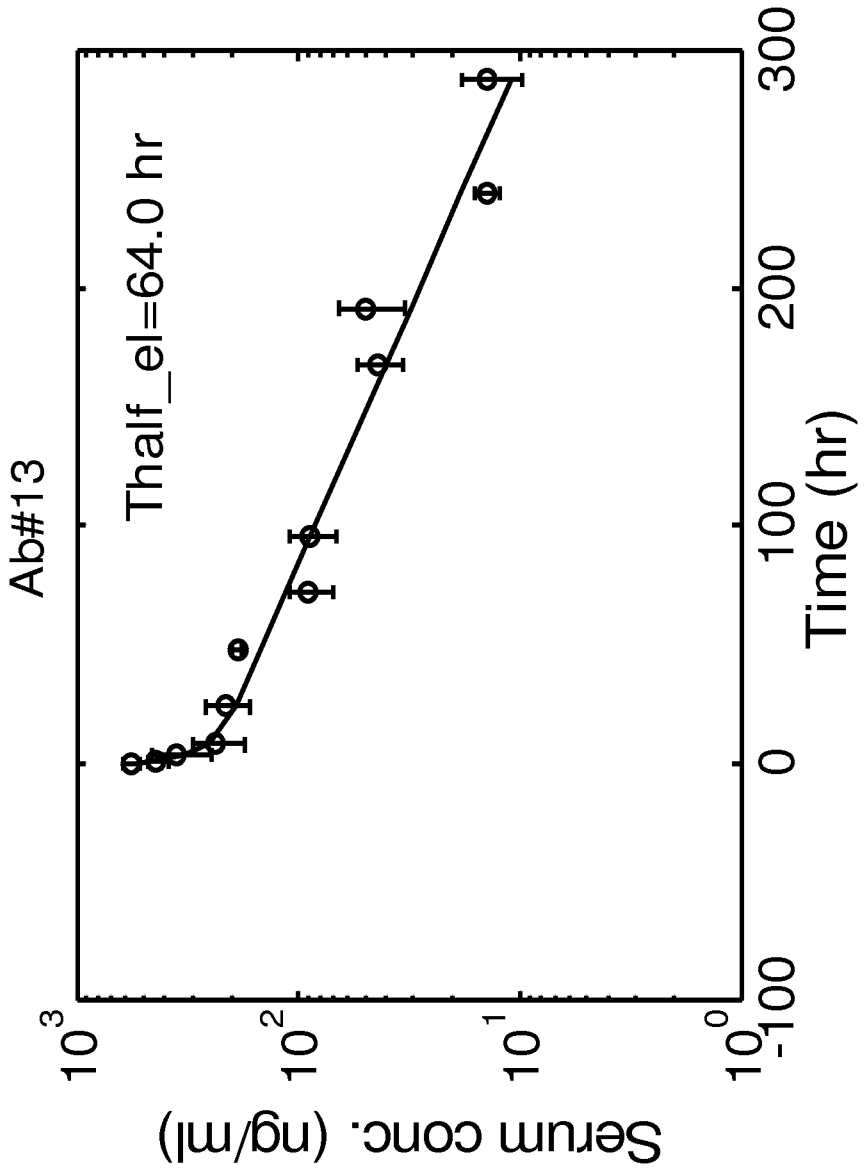

Ab#13
Thalf_el=64.0 hr
Serum conc. (ng/ml)
Time (hr)
10^3
10^2
10^1
10^0
-100
0
100
200
300

Fig. 30C

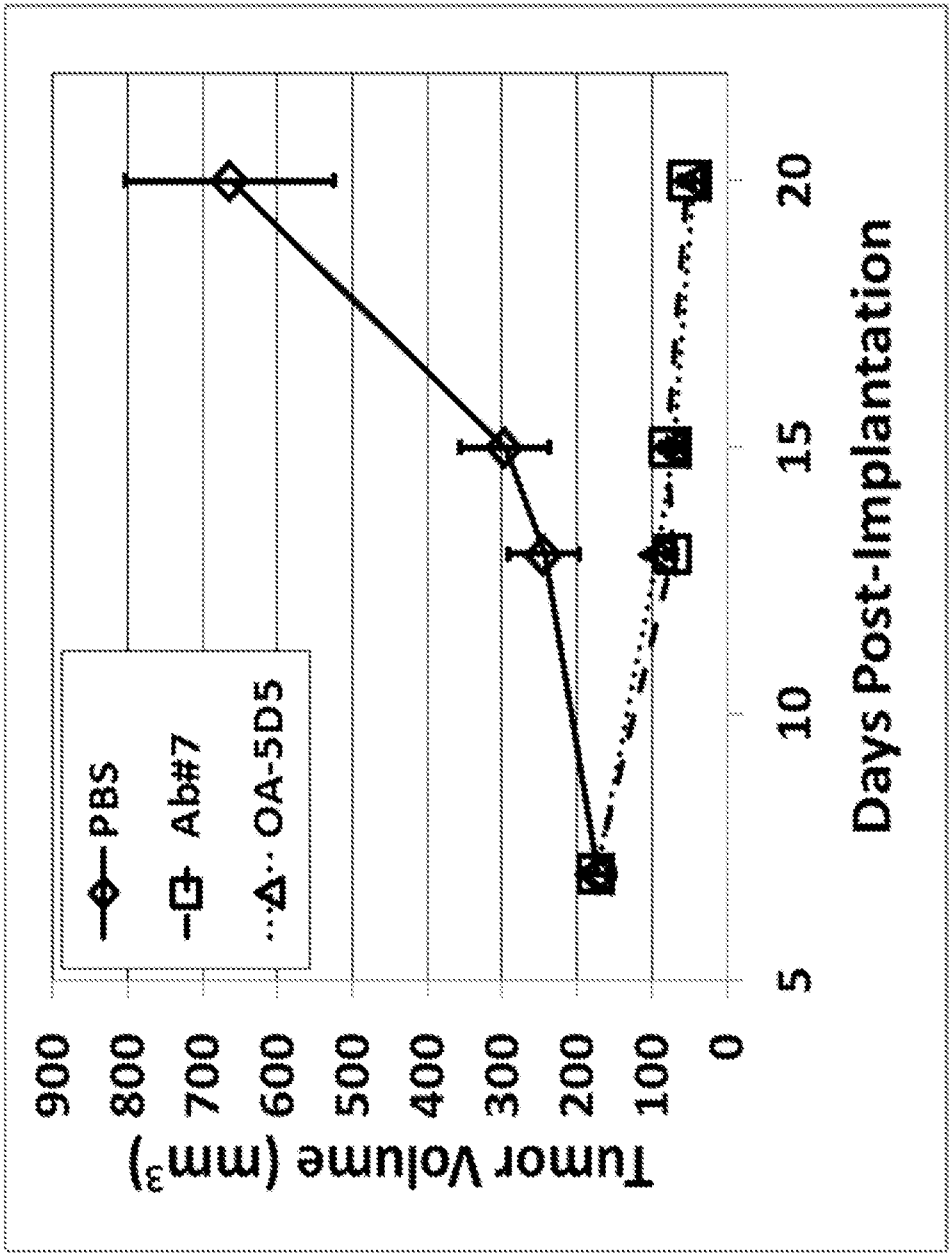

Tumor Volume (mm³)
900
800
700
600
500
400
300
200
100
0
5
10
15
20
Days Post-Implantation
PBS
Ab#7
OA-5D5

Fig. 31

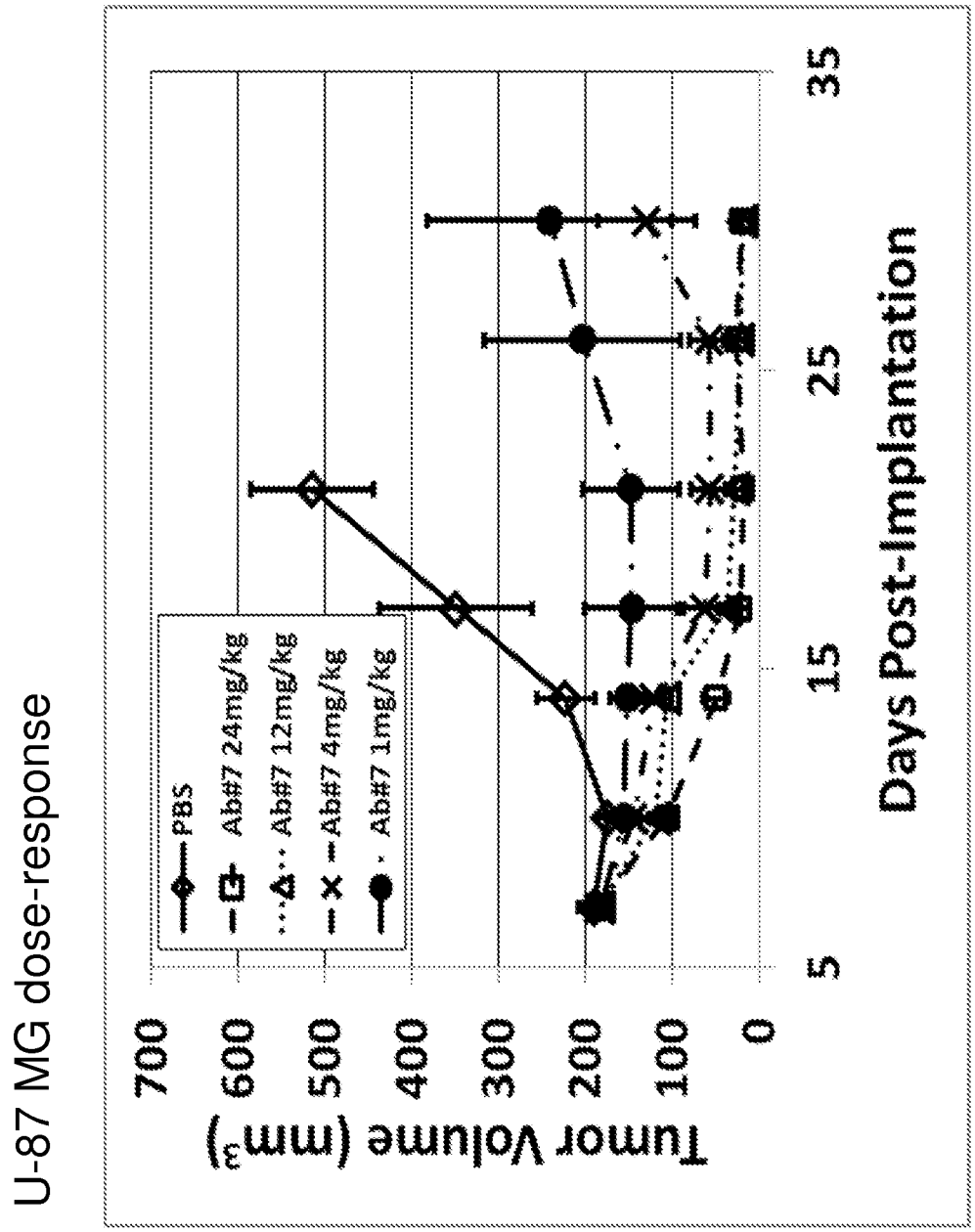

U-87 MG dose-response
Tumor Volume (mm3)
700
600
500
400
300
200
100
0
5
15
25
35
Days Post-Implantation
PBS
Ab#7 24mg/kg
Ab#7 12mg/kg
Ab#7 4mg/kg
Ab#7 1mg/kg

Fig. 32

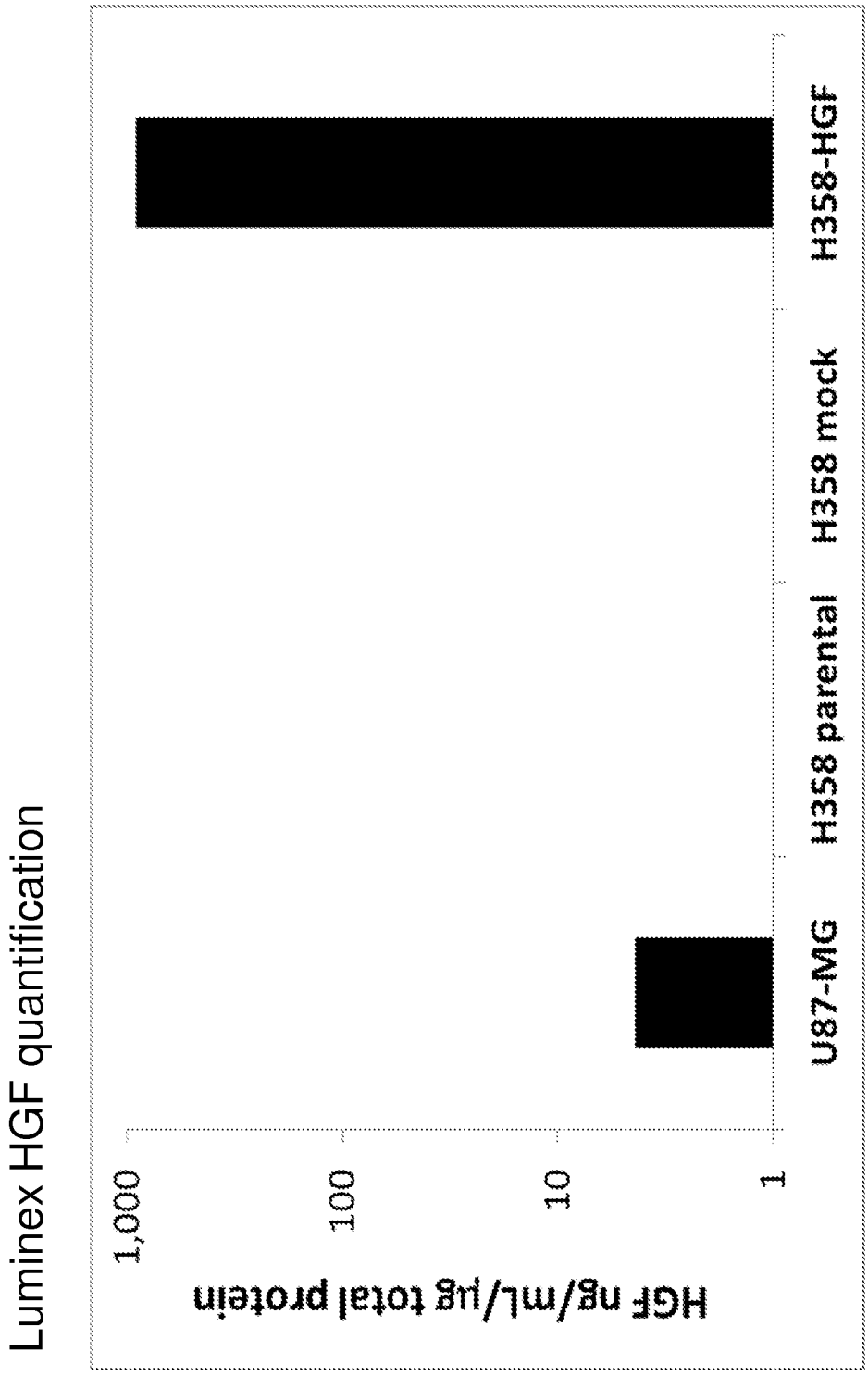

Luminex HGF quantification
HGF ng/mL/µg total protein
1,000
100
10
1
U87-MG
H358 parental
H358 mock
H358-HGF

Fig. 33

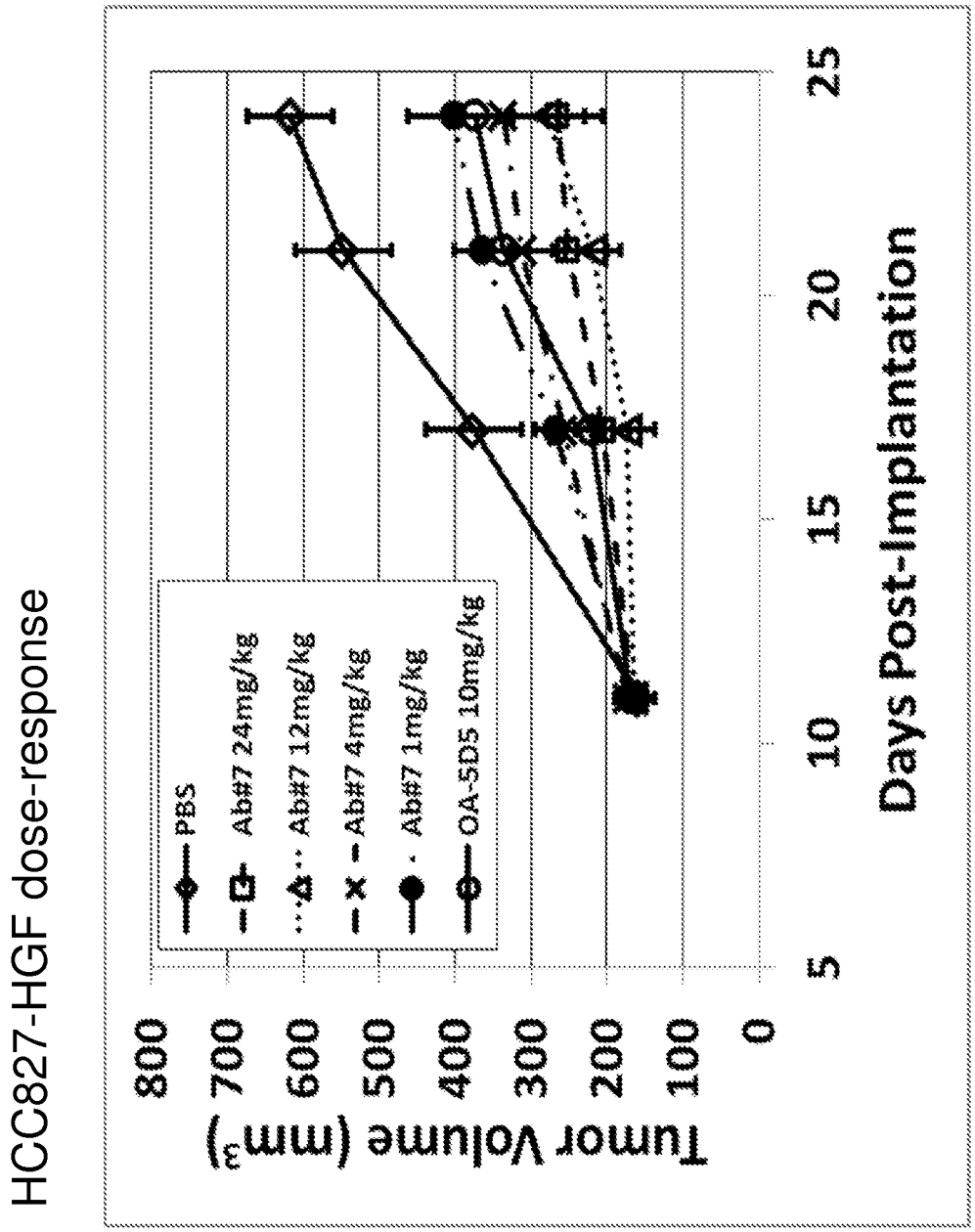

HCC827-HGF dose-response
Tumor Volume (mm3)
800
700
600
500
400
300
200
100
0
5
10
15
20
25
Days Post-Implantation
PBS
Ab#7 24mg/kg
Ab#7 12mg/kg
Ab#7 4mg/kg
Ab#7 1mg/kg
OA-5D5 10mg/kg

Fig. 34

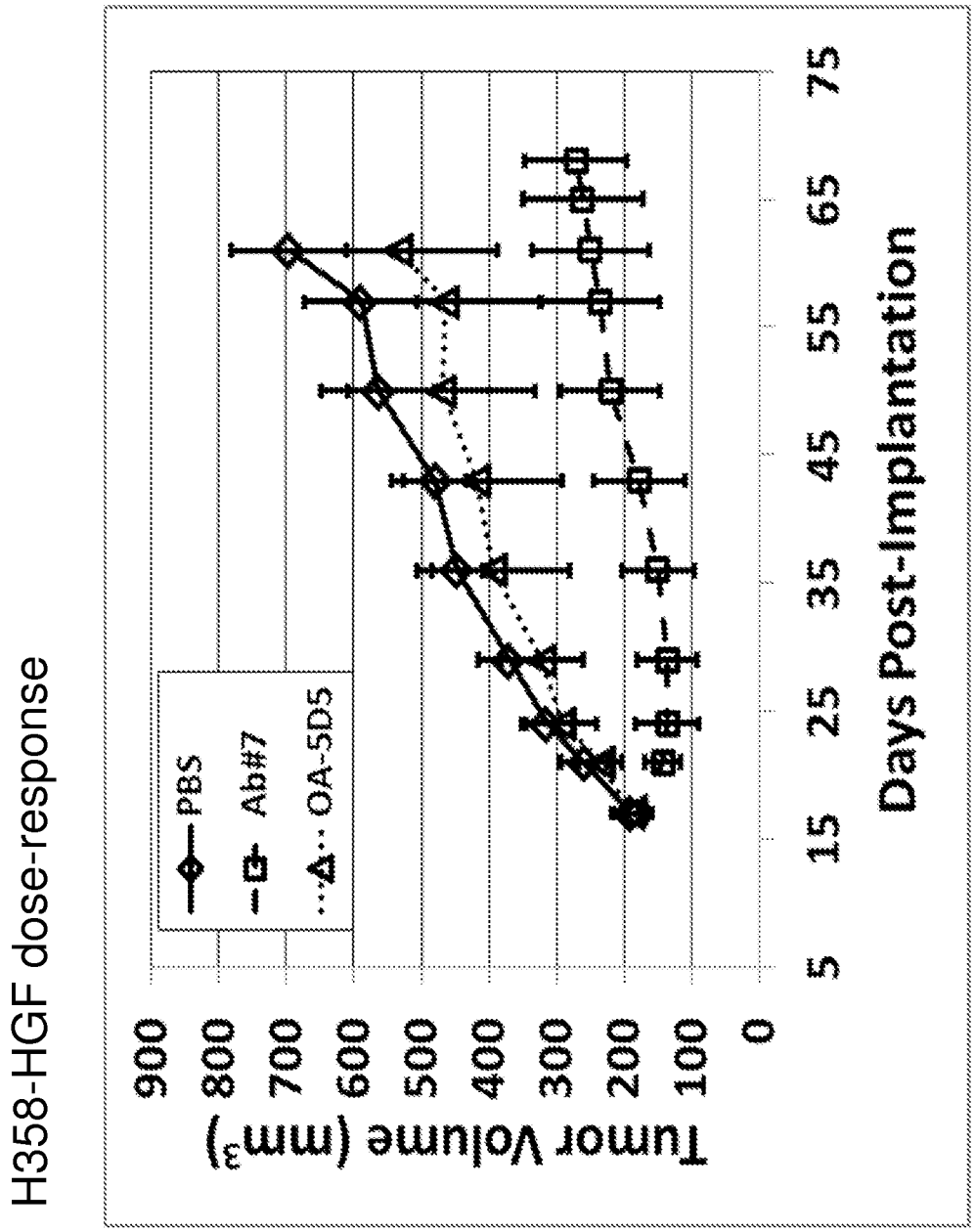

H358-HGF dose-response
Tumor Volume (mm3)
900
800
700
600
500
400
300
200
100
0
5
15
25
35
45
55
65
75
Days Post-Implantation
PBS
Ab#7
OA-5D5

Fig. 35

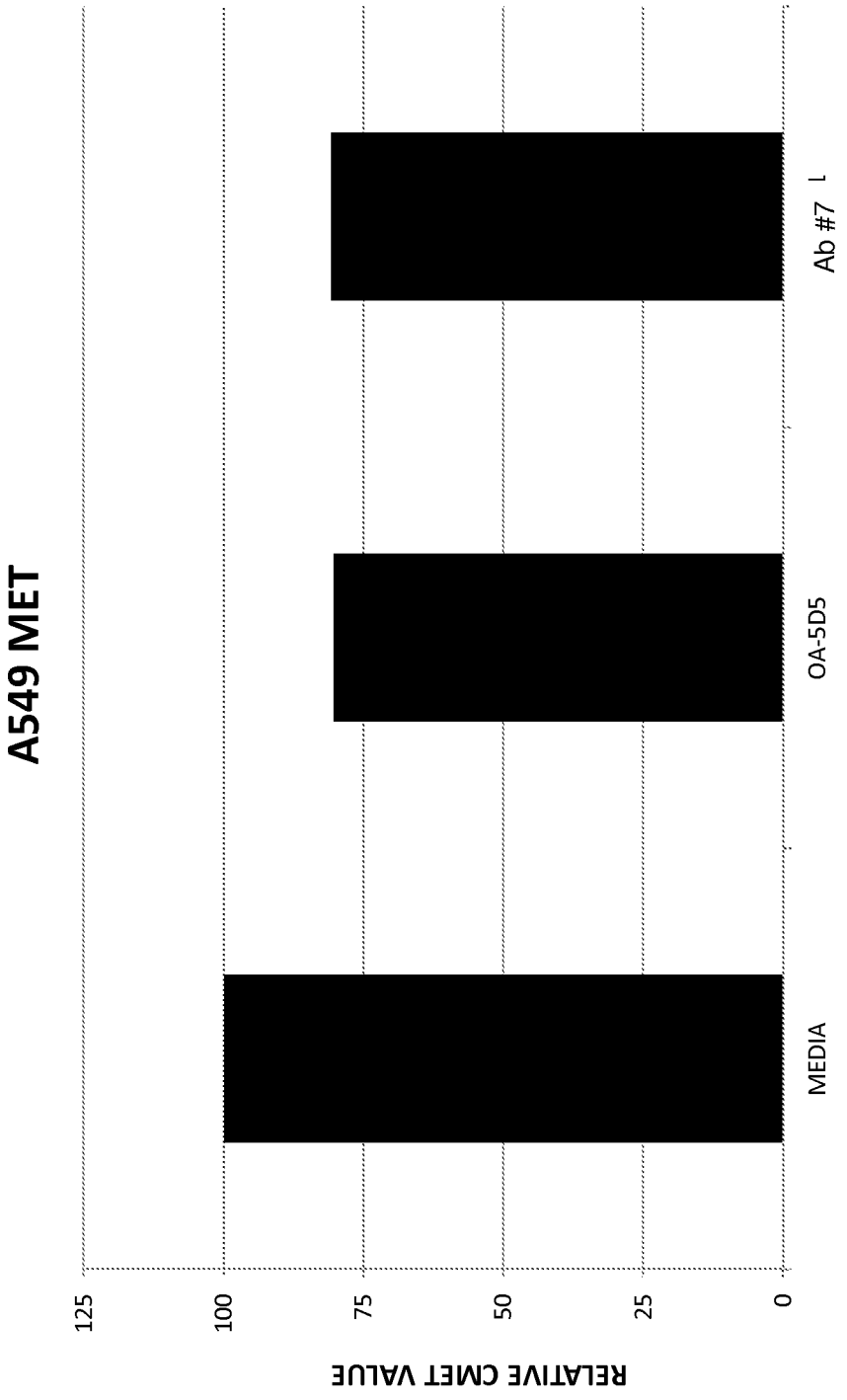
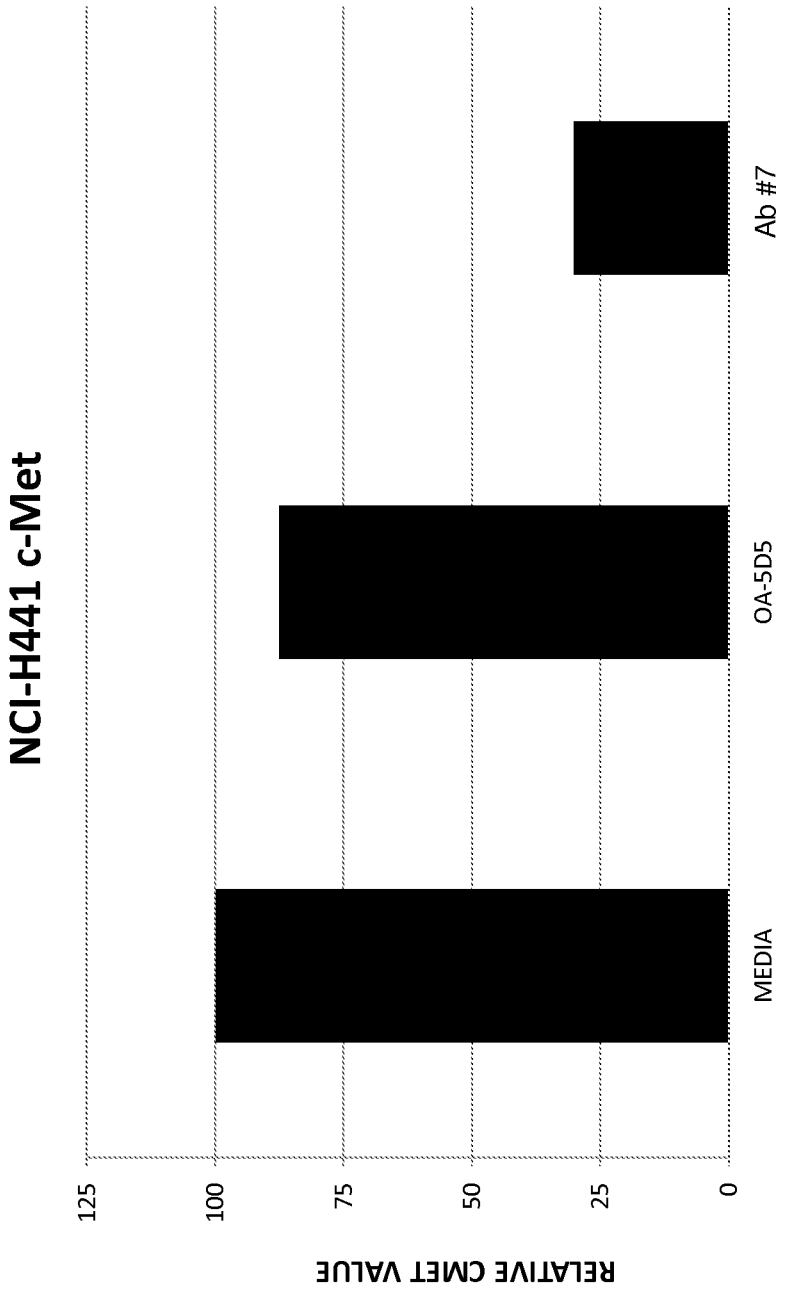
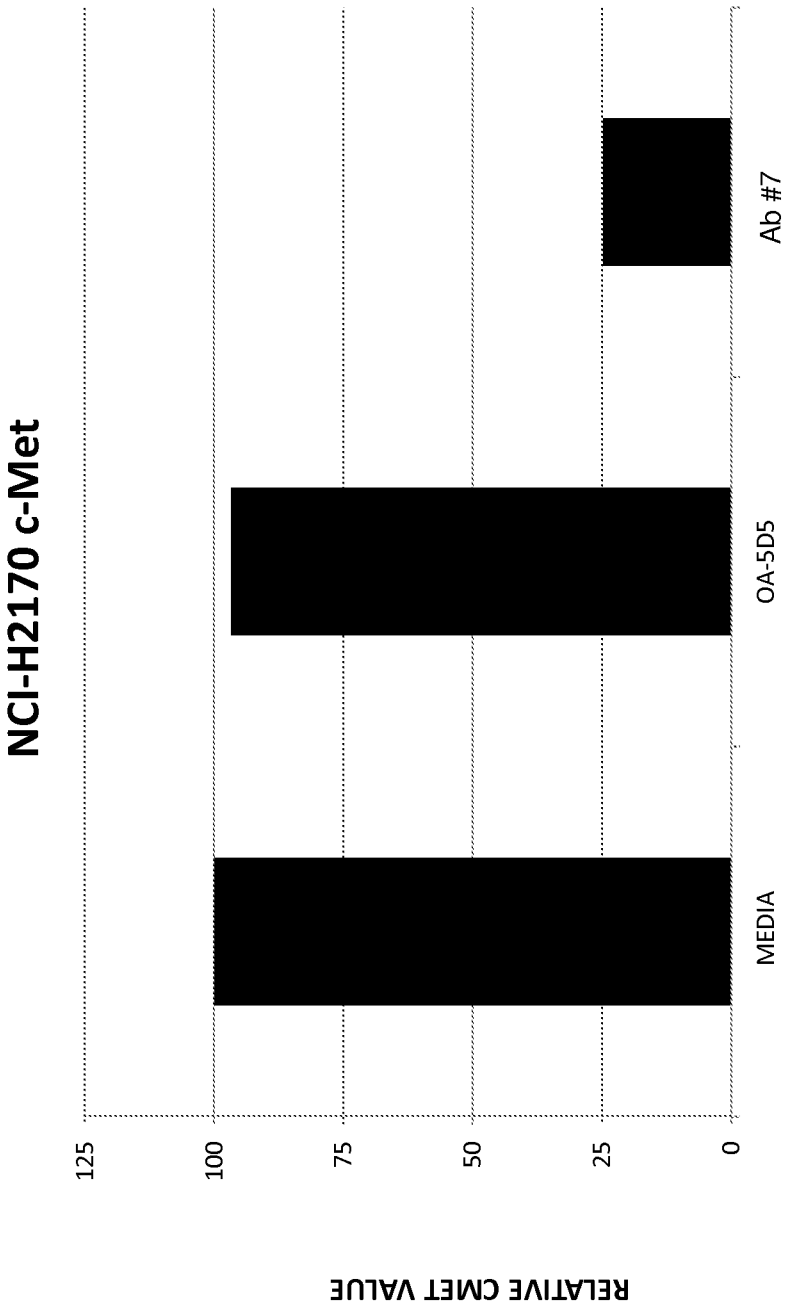

A549 MET
RELATIVE CMET VALUE
125
100
75
50
25
0
MEDIA
OA-5D5
Ab #7
A

Fig. 36



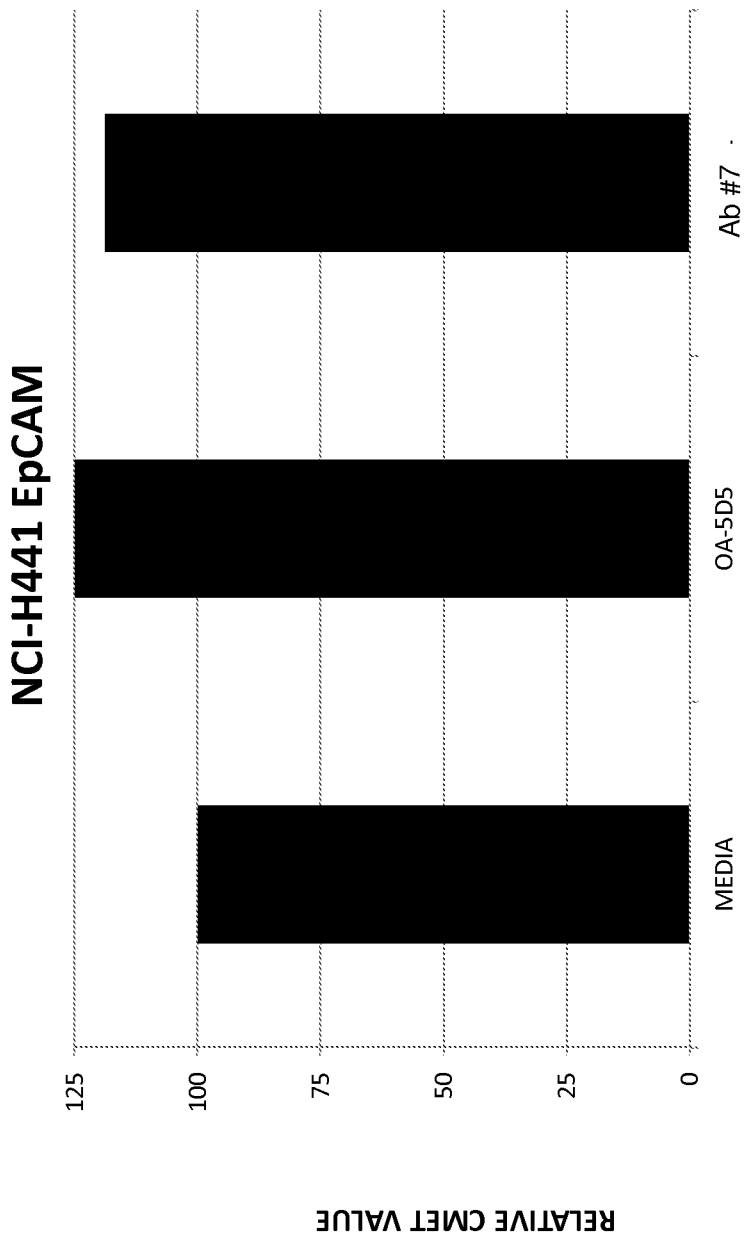
B

Fig. 36 (cont'd)



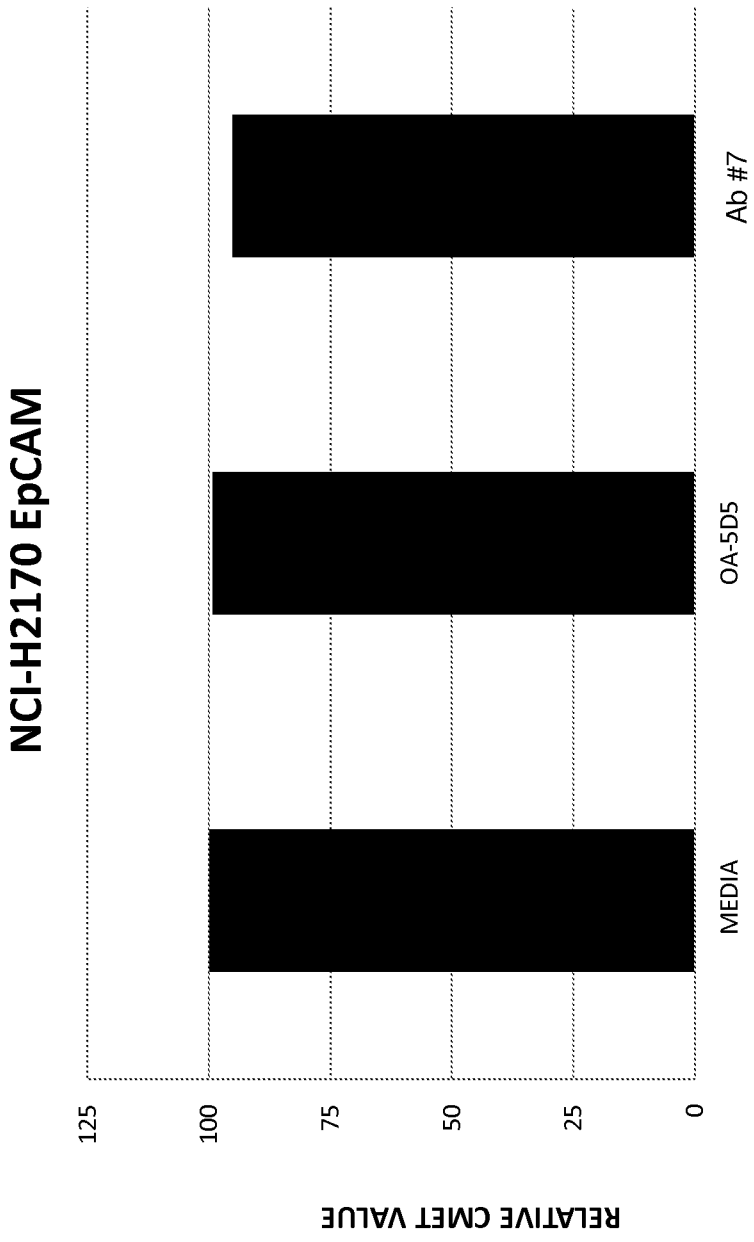
C

Fig. 36 (cont'd)



D

Fig. 36 (cont'd)



E

Fig. 36 (cont'd)