

SEQUENCE LISTING

<110> F. Hoffmann-La Roche AG

<120> Bispecific anti-VEGF/anti-ANG-2 antibodies

<130> 25401 FT

<150> EP 08017607.6

<151> 2008-10-08

<150> EP 08021834.0

<151> 2008-12-16

<160> 136

<170> PatentIn version 3.2

<210> 1

<211> 14

<212> PRT

<213> Artificial

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Tyr Pro His Tyr Tyr Gly Ser Ser His Trp Tyr Phe Asp Val
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<400> 2

Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Ala Asp Phe Lys
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Arg

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<400> 3

Asn Tyr Gly Met Asn
1 5

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<400> 4

Gln Gln Tyr Ser Thr Val Pro Trp Thr
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Phe Thr Ser Ser Leu His Ser
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<400> 6

Ser Ala Ser Gln Asp Ile Ser Asn Tyr Leu Asn
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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Ala Asp Phe
50 55 60

Lys Arg Arg Phe Thr Phe Ser Leu Asp Thr Ser Lys Ser Thr Ala Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Tyr Pro His Tyr Tyr Gly Ser Ser His Trp Tyr Phe Asp Val
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Gln Asp Ile Ser Asn Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Val Leu Ile
35 40 45

Tyr Phe Thr Ser Ser Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Thr Val Pro Trp
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

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Tyr Pro Tyr Tyr Tyr Gly Thr Ser His Trp Tyr Phe Asp Val
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Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Ala Asp Phe Lys
1 5 10 15

Arg

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<400> 11

His Tyr Gly Met Asn
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Gln Gln Tyr Ser Thr Val Pro Trp Thr
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Phe Thr Ser Ser Leu His Ser
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Ser Ala Ser Gln Asp Ile Ser Asn Tyr Leu Asn
1 5 10

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<223> heavy chain variable domain, <VEGF>ranibizumab

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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Asp Phe Thr His Tyr
20 25 30

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Ala Asp Phe
50 55 60

Lys Arg Arg Phe Thr Phe Ser Leu Asp Thr Ser Lys Ser Thr Ala Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Tyr Pro Tyr Tyr Tyr Gly Thr Ser His Trp Tyr Phe Asp Val
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

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Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Gln Asp Ile Ser Asn Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Val Leu Ile
35 40 45

Tyr Phe Thr Ser Ser Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly

50

55

60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Thr Val Pro Trp
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

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Ser Ala Ser Gln Asp Ile Ser Asn Tyr Leu Asn
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<400> 18

Gly Ile Thr Pro Ala Gly Gly Tyr Thr Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

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<400> 19

Asp Tyr Trp Ile His
1 5

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Gln Gln Gly Tyr Gly Asn Pro Phe Thr
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Ser Ala Ser Phe Leu Tyr Ser
1 5

<210> 22
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<400> 22

Arg Ala Ser Gln Asp Val Ser Thr Ala Val Ala
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<400> 23

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly

1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Ile Ser Asp Tyr
20 25 30

Trp Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Gly Ile Thr Pro Ala Gly Gly Tyr Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Phe Val Phe Phe Leu Pro Tyr Ala Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Val Ser Thr Ala
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Ala Ser Phe Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Tyr Gly Asn Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

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<400> 25

Asp Leu Leu Asp Tyr Asp Ile Leu Thr Gly Tyr Gly Tyr
1 5 10

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<400> 26

Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

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<400> 27

Ser Tyr Gly Met His
1 5

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<223> light chain CDR3, <ANG-2> Mab 536

<400> 28

Met Gln Gly Thr His Trp Pro Pro Thr
1 5

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<400> 29

Leu Gly Ser Asn Arg Ala Ser
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Arg Ser Ser Gln Ser Leu Leu His Ser Asn Gly Tyr Asn Tyr Leu Asp
1 5 10 15

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<400> 31

Glu Val Gln Leu Val Gln Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Leu Leu Asp Tyr Asp Ile Leu Thr Gly Tyr Gly Tyr Trp
100 105 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

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<400> 32

Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
20 25 30

Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Gly
85 90 95

Thr His Trp Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 33
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<220>
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<400> 33

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser
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<210> 34
<211> 104
<212> PRT
<213> Homo sapiens

<400> 34

Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser Glu Glu
1 5 10 15

Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe Tyr
20 25 30

Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro Val Lys
35 40 45

Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys Tyr
50 55 60

Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser His
65 70 75 80

Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu Lys
85 90 95

Thr Val Ala Pro Thr Glu Cys Ser
100

<210> 35
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<212> PRT
<213> Homo sapiens

<400> 35

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65 70 75 80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95

Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
100 105 110

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
115 120 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
130 135 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145 150 155 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
165 170 175

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu

180 185 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
195 200 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
210 215 220

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu
225 230 235 240

Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
245 250 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
260 265 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
275 280 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
290 295 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305 310 315 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
325 330

<210> 36
<211> 327
<212> PRT
<213> Homo sapiens

<400> 36

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg
1 5 10 15

Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr
65 70 75 80

Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95

Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Ser Cys Pro Ala Pro
100 105 110

Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
115 120 125

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
130 135 140

Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp
145 150 155 160

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe
165 170 175

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
180 185 190

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu
195 200 205

Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
210 215 220

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys
225 230 235 240

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
245 250 255

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
260 265 270

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
275 280 285

Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser
290 295 300

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
305 310 315 320

Leu Ser Leu Ser Leu Gly Lys
325

<210> 37
<211> 107
<212> PRT
<213> Homo sapiens

<400> 37

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
1 5 10 15

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
20 25 30

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
35 40 45

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
50 55 60

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
65 70 75 80

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
85 90 95

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
100 105

<210> 38
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<223> heavy chain CDR3, <ANG-2> Ang2s_R3_LC03

<400> 38

Asp Leu Gly Tyr Asp Tyr Val
1 5

<210> 39

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<400> 39

Arg Ile Lys Ser Lys Thr Asp Gly Gly Thr Thr Asp Tyr Ala Ala Pro
1 5 10 15

Val Lys Gly

<210> 40

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<400> 40

Asn Ala Trp Met Ser
1 5

<210> 41

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<400> 41

Gln Gln Tyr Asp Asn Leu Pro Met Tyr Thr
1 5 10

<210> 42

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<400> 42

His Ala Ser Asn Leu Glu Thr
1 5

<210> 43

<211> 11

<212> PRT

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<400> 43

Gln Ala Ser Gln Asp Ile Ser Asn Arg Leu Asn
1 5 10

<210> 44

<211> 118

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<400> 44

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Ala
20 25 30

Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Gly Arg Ile Lys Ser Lys Thr Asp Gly Gly Thr Thr Asp Tyr Ala Ala
50 55 60

Pro Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Thr Thr Asp Leu Gly Tyr Asp Tyr Val Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115

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Asp Ile Gln Val Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Gln Ala Ser Gln Asp Ile Ser Asn Arg
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr His Ala Ser Asn Leu Glu Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Tyr Asp Asn Leu Pro Met
85 90 95

Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr
100 105 110

<210> 46
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<220>
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<400> 46

Ser Pro Asn Pro Tyr Tyr Tyr Asp Ser Ser Gly Tyr Tyr Tyr Pro Gly
1 5 10 15

Ala Phe Asp Ile
20

<210> 47
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<220>
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<400> 47

Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

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<400> 48

Gly Tyr Tyr Met His
1 5

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<400> 49

Gln Val Trp Asp Ser Ser Ser Asp His Tyr Val
1 5 10

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<400> 50

Asp Asp Ser Asp Arg Pro Ser
1 5

<210> 51
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<220>
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<400> 51

Gly Gly Asn Asn Ile Gly Ser Lys Ser Val His
1 5 10

<210> 52
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<400> 52

Gln Val Gln Leu Val Glu Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys

			85						90					95			
Ala	Arg	Ser	Pro	Asn	Pro	Tyr	Tyr	Tyr	Asp	Ser	Ser	Gly	Tyr	Tyr	Tyr		
			100					105					110				
Pro	Gly	Ala	Phe	Asp	Ile	Trp	Gly	Gln	Gly	Thr	Met	Val	Thr	Val	Ser		
		115					120					125					

Ser

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<400> 53

Gln	Pro	Gly	Leu	Thr	Gln	Pro	Pro	Ser	Val	Ser	Val	Ala	Pro	Gly	Gln		
1				5				10						15			
Thr	Ala	Arg	Ile	Thr	Cys	Gly	Gly	Asn	Asn	Ile	Gly	Ser	Lys	Ser	Val		
			20					25					30				
His	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ala	Pro	Val	Leu	Val	Val	Tyr		
		35					40					45					
Asp	Asp	Ser	Asp	Arg	Pro	Ser	Gly	Ile	Pro	Glu	Arg	Phe	Ser	Gly	Ser		
	50					55					60						
Asn	Ser	Gly	Asn	Thr	Ala	Thr	Leu	Thr	Ile	Ser	Arg	Val	Glu	Ala	Gly		
65					70					75					80		
Asp	Glu	Ala	Asp	Tyr	Tyr	Cys	Gln	Val	Trp	Asp	Ser	Ser	Ser	Asp	His		
			85						90					95			
Tyr	Val	Phe	Gly	Thr	Gly	Thr	Lys	Val	Thr	Val	Leu	Gly	Gln				
			100					105					110				

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<223> heavy chain CDR3, <ANG-2>Ang2i_LC07

<400> 54

Ser	Pro	Asn	Pro	Tyr	Tyr	Tyr	Asp	Ser	Ser	Gly	Tyr	Tyr	Tyr	Pro	Gly
1				5					10					15	

Ala	Phe	Asp	Ile
			20

<210> 55

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<212> PRT

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<220>

<223> heavy chain CDR2, <ANG-2>Ang2i_LC07

<400> 55

Trp	Ile	Asn	Pro	Asn	Ser	Gly	Gly	Thr	Asn	Tyr	Ala	Gln	Lys	Phe	Gln
1				5					10					15	

Gly

<210> 56

<211> 5

<212> PRT

<213> Artificial

<220>

<223> heavy chain CDR1, <ANG-2>Ang2i_LC07

<400> 56

Gly	Tyr	Tyr	Met	His
1				5

<210> 57

<211> 11

<212> PRT

<213> Artificial

<220>

<223> light chain CDR3, <ANG-2>Ang2i_LC07

<400> 57

Gln Val Trp Asp Ser Asp Ser Asp Gln Gly Val

1 5 10

<210> 58
<211> 7
<212> PRT
<213> Artificial

<220>
<223> light chain CDR2, <ANG-2>Ang2i_LC07

<400> 58

Asp Asp Ser Glu Arg Pro Ser
1 5

<210> 59
<211> 11
<212> PRT
<213> Artificial

<220>
<223> light chain CDR1, <ANG-2>Ang2i_LC07

<400> 59

Gly Gly Asn Phe Ile Gly Gly Lys Ser Val His
1 5 10

<210> 60
<211> 129
<212> PRT
<213> Artificial

<220>
<223> heavy chain variable domain, <ANG-2>Ang2i_LC07

<400> 60

Gln Val Gln Leu Val Glu Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Pro Asn Pro Tyr Tyr Tyr Asp Ser Ser Gly Tyr Tyr Tyr
100 105 110

Pro Gly Ala Phe Asp Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser
115 120 125

Ser

<210> 61
<211> 110
<212> PRT
<213> Artificial

<220>
<223> light chain variable domain, <ANG-2>Ang2i_LC07

<400> 61

Gln Pro Val Leu Thr Gln Ser Pro Ser Val Ser Val Ala Pro Gly Glu
1 5 10 15

Thr Ala Arg Val Ala Cys Gly Gly Asn Phe Ile Gly Gly Lys Ser Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr
35 40 45

Asp Asp Ser Glu Arg Pro Ser Gly Ile Pro Glu Arg Ile Ser Gly Ser
50 55 60

Asn Ser Gly Asn Thr Ala Thr Leu Ile Ile Thr Arg Ala Glu Ala Gly
65 70 75 80

Asp Glu Ala Asp Tyr His Cys Gln Val Trp Asp Ser Asp Ser Asp Gln
85 90 95

Gly Val Phe Gly Thr Gly Thr Lys Leu Thr Val Leu Gly Gln
100 105 110

<210> 62
<211> 15
<212> PRT
<213> Artificial

<220>
<223> heavy chain CDR3, <ANG-2>Ang2k_LC08

<400> 62

Pro	Thr	Leu	Asp	Ile	Tyr	Met	Gly	Tyr	Tyr	Tyr	Gly	Met	Asp	Val
1				5				10						15

<210> 63
<211> 17
<212> PRT
<213> Artificial

<220>
<223> heavy chain CDR2, <ANG-2>Ang2k_LC08

<400> 63

Val	Ile	Ser	Tyr	Asp	Gly	Ser	Asn	Lys	Tyr	Tyr	Ala	Asp	Ser	Val	Lys
1				5				10						15	

Gly

<210> 64
<211> 5
<212> PRT
<213> Artificial

<220>
<223> heavy chain CDR1, <ANG-2>Ang2k_LC08

<400> 64

Ser	Tyr	Gly	Met	His
1				5

<210> 65
<211> 11
<212> PRT
<213> Artificial

<220>
<223> light chain CDR3, <ANG-2>Ang2k_LC08

<400> 65

Ala Ala Trp Asp Asp Ser Leu Asn Gly Pro Val
1 5 10

<210> 66
<211> 7
<212> PRT
<213> Artificial

<220>
<223> light chain CDR2, <ANG-2>Ang2k_LC08

<400> 66

Asn Asn Asp Gln Arg Pro Ser
1 5

<210> 67
<211> 13
<212> PRT
<213> Artificial

<220>
<223> light chain CDR1, <ANG-2>Ang2k_LC08

<400> 67

Ser Gly Phe Ala Ser Asn Ile Gly Ser Asn Ser Val Asn
1 5 10

<210> 68
<211> 124
<212> PRT
<213> Artificial

<220>
<223> heavy chain variable domain, <ANG-2> Ang2k_LC08

<400> 68

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Val Ile Ser Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Pro Thr Leu Asp Ile Tyr Met Gly Tyr Tyr Tyr Gly Met Asp
100 105 110

Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 69
<211> 112
<212> PRT
<213> Artificial

<220>
<223> light chain variable domain, <ANG-2> Ang2k_LC08

<400> 69

Gln Pro Val Leu Thr Gln Pro Pro Ser Ala Ser Gly Ala Pro Gly Gln
1 5 10 15

Arg Val Thr Ile Ser Cys Ser Gly Phe Ala Ser Asn Ile Gly Ser Asn
20 25 30

Ser Val Asn Trp Tyr Gln Gln Val Pro Gly Thr Ala Pro Lys Leu Leu
35 40 45

Ile Tyr Asn Asn Asp Gln Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
50 55 60

Gly Ser Arg Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Gln
65 70 75 80

Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Ala Trp Asp Asp Ser Leu
85 90 95

Asn Gly Pro Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln
100 105 110

<210> 70
<211> 7

<212> PRT
<213> Artificial

<220>
<223> heavy chain CDR3, <ANG-2> Ang2s_LC09

<400> 70

Asp Leu Gly Tyr Asp Tyr Val
1 5

<210> 71
<211> 19
<212> PRT
<213> Artificial

<220>
<223> heavy chain CDR2, <ANG-2> Ang2s_LC09

<400> 71

Arg Ile Lys Ser Lys Thr Asp Gly Gly Thr Thr Asp Tyr Ala Ala Pro
1 5 10 15

Val Lys Gly

<210> 72
<211> 5
<212> PRT
<213> Artificial

<220>
<223> heavy chain CDR1, <ANG-2> Ang2s_LC09

<400> 72

Asn Ala Trp Met Ser
1 5

<210> 73
<211> 7
<212> PRT
<213> Artificial

<220>
<223> light chain CDR3, <ANG-2> Ang2s_LC09

<400> 73

Met Gln Ala Leu Gln Ile Pro
1 5

<210> 74
<211> 7
<212> PRT
<213> Artificial

<220>
<223> light chain CDR2, <ANG-2> Ang2s_LC09

<400> 74

Leu Gly Ser Asn Arg Ala Ser
1 5

<210> 75
<211> 16
<212> PRT
<213> Artificial

<220>
<223> light chain CDR1, <ANG-2> Ang2s_LC09

<400> 75

Arg Ser Ser Gln Ser Leu Leu His Ser Asn Gly Tyr Asn Tyr Leu Asp
1 5 10 15

<210> 76
<211> 119
<212> PRT
<213> Artificial

<220>
<223> heavy chain variable domain, <ANG-2> Ang2s_LC09

<400> 76

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Ala
20 25 30

Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Gly Arg Ile Lys Ser Lys Thr Asp Gly Gly Thr Thr Asp Tyr Ala Ala
50 55 60

Pro Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Thr Thr Asp Leu Gly Tyr Asp Tyr Val Trp Gly Ser Pro Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
115

<210> 77
<211> 109
<212> PRT
<213> Artificial

<220>
<223> light chain variable domain, <ANG-2> Ang2s_LC09
<400> 77

Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly Glu Pro Ala Ser Ile
1 5 10 15

Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser Asn Gly Tyr Asn Tyr
20 25 30

Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile
35 40 45

Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro Asp Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala
65 70 75 80

Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala Leu Gln Ile Pro Phe
85 90 95

Thr Phe Gly Pro Gly Thr Lys Val Thr Val Leu Arg Thr
100 105

<210> 78
<211> 20
<212> PRT
<213> Artificial

<220>
<223> heavy chain CDR3, <ANG-2> Ang2i_LC10

<400> 78

Ser	Pro	Asn	Pro	Tyr	Tyr	Tyr	Asp	Ser	Ser	Gly	Tyr	Tyr	Tyr	Pro	Gly
1				5					10					15	

Ala	Phe	Asp	Ile
			20

<210> 79
<211> 17
<212> PRT
<213> Artificial

<220>
<223> heavy chain CDR2, <ANG-2> Ang2i_LC10

<400> 79

Trp	Ile	Asn	Pro	Asn	Ser	Gly	Gly	Thr	Asn	Tyr	Ala	Gln	Lys	Phe	Gln
1				5					10					15	

Gly

<210> 80
<211> 5
<212> PRT
<213> Artificial

<220>
<223> heavy chain CDR1, <ANG-2> Ang2i_LC10

<400> 80

Gly	Tyr	Tyr	Met	His
1				5

<210> 81
<211> 11
<212> PRT
<213> Artificial

<220>
<223> light chain CDR3, <ANG-2> Ang2i_LC10

<400> 81

Gln	Val	Trp	Asp	Ser	Ser	Ser	Asp	His	Trp	Val
1				5					10	

<210> 82
<211> 7
<212> PRT
<213> Artificial

<220>
<223> light chain CDR2, <ANG-2> Ang2i_LC10

<400> 82

Asp Asp Ser Asp Arg Pro Ser
1 5

<210> 83
<211> 11
<212> PRT
<213> Artificial

<220>
<223> light chain CDR1, <ANG-2> Ang2i_LC10

<400> 83

Gly Gly Asn Asn Ile Gly Ser Lys Ser Val His
1 5 10

<210> 84
<211> 129
<212> PRT
<213> Artificial

<220>
<223> heavy chain variable domain, <ANG-2> Ang2i_LC10

<400> 84

Gln Val Gln Leu Val Glu Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr

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65              70              75              80
Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
      85              90              95

Ala Arg Ser Pro Asn Pro Tyr Tyr Tyr Asp Ser Ser Gly Tyr Tyr Tyr
      100             105             110

Pro Gly Ala Phe Asp Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser
      115             120             125

Ser

<210> 85
<211> 105
<212> PRT
<213> Artificial

<220>
<223> light chain variable domain, <ANG-2> Ang2i_LC10

<400> 85

Gln Pro Pro Ser Val Ser Val Ala Pro Gly Gln Thr Ala Arg Ile Thr
1              5              10              15

Cys Gly Gly Asn Asn Ile Gly Ser Lys Ser Val His Trp Tyr Gln Gln
      20              25              30

Lys Pro Gly Gln Ala Pro Val Leu Val Val Tyr Asp Asp Ser Asp Arg
      35              40              45

Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser Asn Ser Gly Asn Thr
      50              55              60

Ala Thr Leu Thr Ile Ser Arg Val Glu Ala Gly Asp Glu Ala Asp Tyr
65              70              75              80

Tyr Cys Gln Val Trp Asp Ser Ser Ser Asp His Trp Val Phe Gly Gly
      85              90              95

Gly Thr Lys Leu Thr Val Leu Gly Gln
      100             105

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<210> 86
<211> 15
<212> PRT
<213> Artificial

<220>
<223> heavy chain CDR3, <ANG-2> Ang2k_LC11

<400> 86

Pro	Thr	Leu	Asp	Ile	Tyr	Met	Gly	Tyr	Tyr	Tyr	Gly	Met	Asp	Val
1				5				10						15

<210> 87
<211> 17
<212> PRT
<213> Artificial

<220>
<223> heavy chain CDR2, <ANG-2> Ang2k_LC11

<400> 87

Val	Ile	Ser	Tyr	Asp	Gly	Ser	Asn	Lys	Tyr	Tyr	Ala	Asp	Ser	Val	Lys
1				5				10						15	

Gly

<210> 88
<211> 5
<212> PRT
<213> Artificial

<220>
<223> heavy chain CDR1, <ANG-2> Ang2k_LC11

<400> 88

Ser	Tyr	Gly	Met	His
1				5

<210> 89
<211> 12
<212> PRT
<213> Artificial

<220>
<223> light chain CDR3, <ANG-2> Ang2k_LC11

<400> 89

Gln Val Trp Asp Ser Ser Ser Asp His Pro Gly Val

1 5 10

<210> 90
<211> 7
<212> PRT
<213> Artificial

<220>
<223> light chain CDR2, <ANG-2> Ang2k_LC11

<400> 90

Asp Asp Ser Asp Arg Pro Ser
1 5

<210> 91
<211> 11
<212> PRT
<213> Artificial

<220>
<223> light chain CDR1, <ANG-2> Ang2k_LC11

<400> 91

Gly Gly Asn Asn Ile Gly Ser Lys Ser Val His
1 5 10

<210> 92
<211> 124
<212> PRT
<213> Artificial

<220>
<223> heavy chain variable domain, <ANG-2> Ang2k_LC11

<400> 92

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Val Ile Ser Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Pro Thr Leu Asp Ile Tyr Met Gly Tyr Tyr Tyr Gly Met Asp
100 105 110

Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 93
<211> 106
<212> PRT
<213> Artificial

<220>
<223> light chain variable domain, <ANG-2> Ang2k_LC11

<220>
<221> misc_feature
<222> (98)..(98)
<223> Xaa can be any naturally occurring amino acid

<220>
<221> misc_feature
<222> (102)..(102)
<223> Xaa can be any naturally occurring amino acid

<400> 93

Gln Pro Pro Ser Val Ser Val Ala Pro Gly Gln Thr Ala Arg Ile Thr
1 5 10 15

Cys Gly Gly Asn Asn Ile Gly Ser Lys Ser Val His Trp Tyr Gln Gln
20 25 30

Lys Pro Gly Gln Ala Pro Val Leu Val Val Tyr Asp Asp Ser Asp Arg
35 40 45

Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser Asn Ser Gly Asn Thr
50 55 60

Ala Thr Leu Thr Ile Ser Arg Val Glu Ala Gly Asp Glu Ala Asp Tyr
65 70 75 80

Tyr Cys Gln Val Trp Asp Ser Ser Ser Asp His Pro Gly Val Phe Gly
85 90 95

Gly Xaa Thr Lys Leu Xaa Val Leu Gly Gln
100 105

<210> 94
<211> 12
<212> PRT
<213> Artificial

<220>
<223> heavy chain CDR3, <VEGF>B20-4.1

<400> 94

Trp Gly His Ser Thr Ser Pro Trp Ala Met Asp Tyr
1 5 10

<210> 95
<211> 17
<212> PRT
<213> Artificial

<220>
<223> heavy chain CDR2, <VEGF>B20-4.1

<400> 95

Ala Ile Trp Pro Phe Gly Gly Tyr Thr His Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 96
<211> 8
<212> PRT
<213> Artificial

<220>
<223> heavy chain CDR1, <VEGF>B20-4.1

<400> 96

Phe Ser Ile Asn Gly Ser Trp Ile
1 5

<210> 97
<211> 9
<212> PRT

<213> Artificial

<220>

<223> light chain CDR3, <VEGF>B20-4.1

<400> 97

Gln Gln Ser Asn Thr Ser Pro Leu Thr
1 5

<210> 98

<211> 8

<212> PRT

<213> Artificial

<220>

<223> light chain CDR2, <VEGF>B20-4.1

<400> 98

Tyr Ala Ala Ser Asn Leu Ala Ser
1 5

<210> 99

<211> 11

<212> PRT

<213> Artificial

<220>

<223> light chain CDR1, <VEGF>B20-4.1

<400> 99

Arg Ala Ser Gln Val Ile Arg Arg Ser Leu Ala
1 5 10

<210> 100

<211> 117

<212> PRT

<213> Artificial

<220>

<223> heavy chain variable domain, <VEGF>B20-4.1

<400> 100

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Ile Asn Gly Ser
20 25 30

Trp Ile Phe Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Gly Ala Ile Trp Pro Phe Gly Gly Tyr Thr His Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Trp Gly His Ser Thr Ser Pro Trp Ala Met Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val
115

<210> 101

<211> 108

<212> PRT

<213> Artificial

<220>

<223> light chain variable domain, <VEGF>B20-4.1

<400> 101

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Val Ile Arg Arg Ser
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ala Ala Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Asn Thr Ser Pro Leu
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 102
<211> 730
<212> PRT
<213> Artificial

<220>
<223> bevacizumab heavy chain Ang2i LC06 scFv fusion peptide of
<VEGF-ANG-2> TvAb-2441-bevacizumab-LC06

<400> 102

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Ala Asp Phe
50 55 60

Lys Arg Arg Phe Thr Phe Ser Leu Asp Thr Ser Lys Ser Thr Ala Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Tyr Pro His Tyr Tyr Gly Ser Ser His Trp Tyr Phe Asp Val
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe

	165		170		175
Pro Ala Val	Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val				
	180		185		190
Thr Val Pro	Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val				
	195		200		205
Asn His Lys	Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys				
	210		215		220
Ser Cys Asp	Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu				
	225		230		235
Leu Gly Gly	Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr				
		245		250	255
Leu Met Ile	Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val				
		260		265	270
Ser His Glu	Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val				
		275		280	285
Glu Val His	Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser				
		290		295	300
Thr Tyr Arg	Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu				
		305		310	315
Asn Gly Lys	Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala				
		325		330	335
Pro Ile Glu	Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro				
		340		345	350
Gln Val Tyr	Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln				
		355		360	365
Val Ser Leu	Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala				
		370		375	380
Val Glu Trp	Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr				
		385		390	395

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445

Leu Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
450 455 460

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Val Glu Ser
465 470 475 480

Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys
485 490 495

Ala Ser Gly Tyr Thr Phe Thr Gly Tyr Tyr Met His Trp Val Arg Gln
500 505 510

Ala Pro Gly Gln Cys Leu Glu Trp Met Gly Trp Ile Asn Pro Asn Ser
515 520 525

Gly Gly Thr Asn Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Met Thr
530 535 540

Arg Asp Thr Ser Ile Ser Thr Ala Tyr Met Glu Leu Ser Arg Leu Arg
545 550 555 560

Ser Asp Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Pro Asn Pro Tyr
565 570 575

Tyr Tyr Asp Ser Ser Gly Tyr Tyr Tyr Pro Gly Ala Phe Asp Ile Trp
580 585 590

Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
595 600 605

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Pro
610 615 620

Gly Leu Thr Gln Pro Pro Ser Val Ser Val Ala Pro Gly Gln Thr Ala
625 630 635 640

Arg Ile Thr Cys Gly Gly Asn Asn Ile Gly Ser Lys Ser Val His Trp
645 650 655

Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Val Tyr Asp Asp
660 665 670

Ser Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser Asn Ser
675 680 685

Gly Asn Thr Ala Thr Leu Thr Ile Ser Arg Val Glu Ala Gly Asp Glu
690 695 700

Ala Asp Tyr Tyr Cys Gln Val Trp Asp Ser Ser Ser Asp His Tyr Val
705 710 715 720

Phe Gly Cys Gly Thr Lys Val Thr Val Leu
725 730

<210> 103

<211> 727

<212> PRT

<213> Artificial

<220>

<223> bevacizumab heavy chain Ang2i_LC08 scFv fusion peptide of
<VEGF-ANG-2> TvAb-2441-bevacizumab-LC08

<400> 103

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Ala Asp Phe
50 55 60

Lys Arg Arg Phe Thr Phe Ser Leu Asp Thr Ser Lys Ser Thr Ala Tyr

65		70		75		80									
Leu	Gln	Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
				85					90					95	
Ala	Lys	Tyr	Pro	His	Tyr	Tyr	Gly	Ser	Ser	His	Trp	Tyr	Phe	Asp	Val
			100					105					110		
Trp	Gly	Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser	Ala	Ser	Thr	Lys	Gly
		115					120					125			
Pro	Ser	Val	Phe	Pro	Leu	Ala	Pro	Ser	Ser	Lys	Ser	Thr	Ser	Gly	Gly
	130					135					140				
Thr	Ala	Ala	Leu	Gly	Cys	Leu	Val	Lys	Asp	Tyr	Phe	Pro	Glu	Pro	Val
145					150					155					160
Thr	Val	Ser	Trp	Asn	Ser	Gly	Ala	Leu	Thr	Ser	Gly	Val	His	Thr	Phe
				165					170					175	
Pro	Ala	Val	Leu	Gln	Ser	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val	Val
			180					185					190		
Thr	Val	Pro	Ser	Ser	Ser	Leu	Gly	Thr	Gln	Thr	Tyr	Ile	Cys	Asn	Val
		195					200					205			
Asn	His	Lys	Pro	Ser	Asn	Thr	Lys	Val	Asp	Lys	Lys	Val	Glu	Pro	Lys
	210					215					220				
Ser	Cys	Asp	Lys	Thr	His	Thr	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Glu	Leu
225					230					235					240
Leu	Gly	Gly	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr
				245					250					255	
Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val
			260					265					270		
Ser	His	Glu	Asp	Pro	Glu	Val	Lys	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val
		275					280					285			
Glu	Val	His	Asn	Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Tyr	Asn	Ser
	290					295					300				

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
325 330 335

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
355 360 365

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445

Leu Ser Pro Gly Lys Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
450 455 460

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Val Glu Ser
465 470 475 480

Gly Gly Gly Val Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala
485 490 495

Ala Ser Gly Phe Thr Phe Ser Ser Tyr Gly Met His Trp Val Arg Gln
500 505 510

Ala Pro Gly Lys Cys Leu Glu Trp Val Ala Val Ile Ser Tyr Asp Gly
515 520 525

Ser Asn Lys Tyr Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser
530 535 540

Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg
545 550 555 560

Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Lys Pro Thr Leu Asp Ile
565 570 575

Tyr Met Gly Tyr Tyr Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr
580 585 590

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
595 600 605

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Pro Val Leu Thr Gln Pro
610 615 620

Pro Ser Ala Ser Gly Ala Pro Gly Gln Arg Val Thr Ile Ser Cys Ser
625 630 635 640

Gly Phe Ala Ser Asn Ile Gly Ser Asn Ser Val Asn Trp Tyr Gln Gln
645 650 655

Val Pro Gly Thr Ala Pro Lys Leu Leu Ile Tyr Asn Asn Asp Gln Arg
660 665 670

Pro Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Arg Ser Gly Thr Ser
675 680 685

Ala Ser Leu Ala Ile Ser Gly Leu Gln Ser Glu Asp Glu Ala Asp Tyr
690 695 700

Tyr Cys Ala Ala Trp Asp Asp Ser Leu Asn Gly Pro Val Phe Gly Cys
705 710 715 720

Gly Thr Lys Leu Thr Val Leu
725

<210> 104

<211> 214

<212> PRT

<213> Artificial

<220>

<223> light chain of bevacizumab

<400> 104

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Gln Asp Ile Ser Asn Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Val Leu Ile
35 40 45

Tyr Phe Thr Ser Ser Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Thr Val Pro Trp
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 105
<211> 191
<212> PRT
<213> Homo sapiens

<400> 105

Met Asn Phe Leu Leu Ser Trp Val His Trp Ser Leu Ala Leu Leu Leu
1 5 10 15

Tyr Leu His His Ala Lys Trp Ser Gln Ala Ala Pro Met Ala Glu Gly
20 25 30

Gly Gly Gln Asn His His Glu Val Val Lys Phe Met Asp Val Tyr Gln
35 40 45

Arg Ser Tyr Cys His Pro Ile Glu Thr Leu Val Asp Ile Phe Gln Glu
50 55 60

Tyr Pro Asp Glu Ile Glu Tyr Ile Phe Lys Pro Ser Cys Val Pro Leu
65 70 75 80

Met Arg Cys Gly Gly Cys Cys Asn Asp Glu Gly Leu Glu Cys Val Pro
85 90 95

Thr Glu Glu Ser Asn Ile Thr Met Gln Ile Met Arg Ile Lys Pro His
100 105 110

Gln Gly Gln His Ile Gly Glu Met Ser Phe Leu Gln His Asn Lys Cys
115 120 125

Glu Cys Arg Pro Lys Lys Asp Arg Ala Arg Gln Glu Asn Pro Cys Gly
130 135 140

Pro Cys Ser Glu Arg Arg Lys His Leu Phe Val Gln Asp Pro Gln Thr
145 150 155 160

Cys Lys Cys Ser Cys Lys Asn Thr Asp Ser Arg Cys Lys Ala Arg Gln
165 170 175

Leu Glu Leu Asn Glu Arg Thr Cys Arg Cys Asp Lys Pro Arg Arg

180 185 190

<210> 106
<211> 504
<212> PRT
<213> Artificial

<220>
<223> Human angiopoietin-2 (ANG-2) with leader and His-tag

<400> 106

Met Trp Gln Ile Val Phe Phe Thr Leu Ser Cys Asp Leu Val Leu Ala
1 5 10 15

Ala Ala Tyr Asn Asn Phe Arg Lys Ser Met Asp Ser Ile Gly Lys Lys
20 25 30

Gln Tyr Gln Val Gln His Gly Ser Cys Ser Tyr Thr Phe Leu Leu Pro
35 40 45

Glu Met Asp Asn Cys Arg Ser Ser Ser Ser Pro Tyr Val Ser Asn Ala
50 55 60

Val Gln Arg Asp Ala Pro Leu Glu Tyr Asp Asp Ser Val Gln Arg Leu
65 70 75 80

Gln Val Leu Glu Asn Ile Met Glu Asn Asn Thr Gln Trp Leu Met Lys
85 90 95

Leu Glu Asn Tyr Ile Gln Asp Asn Met Lys Lys Glu Met Val Glu Ile
100 105 110

Gln Gln Asn Ala Val Gln Asn Gln Thr Ala Val Met Ile Glu Ile Gly
115 120 125

Thr Asn Leu Leu Asn Gln Thr Ala Glu Gln Thr Arg Lys Leu Thr Asp
130 135 140

Val Glu Ala Gln Val Leu Asn Gln Thr Thr Arg Leu Glu Leu Gln Leu
145 150 155 160

Leu Glu His Ser Leu Ser Thr Asn Lys Leu Glu Lys Gln Ile Leu Asp
165 170 175

Gln Thr Ser Glu Ile Asn Lys Leu Gln Asp Lys Asn Ser Phe Leu Glu
180 185 190

Lys Lys Val Leu Ala Met Glu Asp Lys His Ile Ile Gln Leu Gln Ser
195 200 205

Ile Lys Glu Glu Lys Asp Gln Leu Gln Val Leu Val Ser Lys Gln Asn
210 215 220

Ser Ile Ile Glu Glu Leu Glu Lys Lys Ile Val Thr Ala Thr Val Asn
225 230 235 240

Asn Ser Val Leu Gln Lys Gln Gln His Asp Leu Met Glu Thr Val Asn
245 250 255

Asn Leu Leu Thr Met Met Ser Thr Ser Asn Ser Ala Lys Asp Pro Thr
260 265 270

Val Ala Lys Glu Glu Gln Ile Ser Phe Arg Asp Cys Ala Glu Val Phe
275 280 285

Lys Ser Gly His Thr Thr Asn Gly Ile Tyr Thr Leu Thr Phe Pro Asn
290 295 300

Ser Thr Glu Glu Ile Lys Ala Tyr Cys Asp Met Glu Ala Gly Gly Gly
305 310 315 320

Gly Trp Thr Ile Ile Gln Arg Arg Glu Asp Gly Ser Val Asp Phe Gln
325 330 335

Arg Thr Trp Lys Glu Tyr Lys Val Gly Phe Gly Asn Pro Ser Gly Glu
340 345 350

Tyr Trp Leu Gly Asn Glu Phe Val Ser Gln Leu Thr Asn Gln Gln Arg
355 360 365

Tyr Val Leu Lys Ile His Leu Lys Asp Trp Glu Gly Asn Glu Ala Tyr
370 375 380

Ser Leu Tyr Glu His Phe Tyr Leu Ser Ser Glu Glu Leu Asn Tyr Arg
385 390 395 400

Ile His Leu Lys Gly Leu Thr Gly Thr Ala Gly Lys Ile Ser Ser Ile

	405		410		415
Ser Gln Pro Gly Asn Asp Phe Ser Thr Lys Asp Gly Asp Asn Asp Lys	420		425		430
Cys Ile Cys Lys Cys Ser Gln Met Leu Thr Gly Gly Trp Trp Phe Asp	435		440		445
Ala Cys Gly Pro Ser Asn Leu Asn Gly Met Tyr Tyr Pro Gln Arg Gln	450		455		460
Asn Thr Asn Lys Phe Asn Gly Ile Lys Trp Tyr Tyr Trp Lys Gly Ser	465		470		475
Gly Tyr Ser Leu Lys Ala Thr Thr Met Met Ile Arg Pro Ala Asp Phe	485		490		495
Ser Gly His His His His His His	500				

<210> 107
 <211> 506
 <212> PRT
 <213> Artificial

<220>
 <223> Human angiopoietin-1 (ANG-1) with leader and His-tag

<400> 107

Met Thr Val Phe Leu Ser Phe Ala Phe Leu Ala Ala Ile Leu Thr His	1	5	10	15
Ile Gly Cys Ser Asn Gln Arg Arg Ser Pro Glu Asn Ser Gly Arg Arg	20	25	30	
Tyr Asn Arg Ile Gln His Gly Gln Cys Ala Tyr Thr Phe Ile Leu Pro	35	40	45	
Glu His Asp Gly Asn Cys Arg Glu Ser Thr Thr Asp Gln Tyr Asn Thr	50	55	60	
Asn Ala Leu Gln Arg Asp Ala Pro His Val Glu Pro Asp Phe Ser Ser	65	70	75	80

Gln Lys Leu Gln His Leu Glu His Val Met Glu Asn Tyr Thr Gln Trp
85 90 95

Leu Gln Lys Leu Glu Asn Tyr Ile Val Glu Asn Met Lys Ser Glu Met
100 105 110

Ala Gln Ile Gln Gln Asn Ala Val Gln Asn His Thr Ala Thr Met Leu
115 120 125

Glu Ile Gly Thr Ser Leu Leu Ser Gln Thr Ala Glu Gln Thr Arg Lys
130 135 140

Leu Thr Asp Val Glu Thr Gln Val Leu Asn Gln Thr Ser Arg Leu Glu
145 150 155 160

Ile Gln Leu Leu Glu Asn Ser Leu Ser Thr Tyr Lys Leu Glu Lys Gln
165 170 175

Leu Leu Gln Gln Thr Asn Glu Ile Leu Lys Ile His Glu Lys Asn Ser
180 185 190

Leu Leu Glu His Lys Ile Leu Glu Met Glu Gly Lys His Lys Glu Glu
195 200 205

Leu Asp Thr Leu Lys Glu Glu Lys Glu Asn Leu Gln Gly Leu Val Thr
210 215 220

Arg Gln Thr Tyr Ile Ile Gln Glu Leu Glu Lys Gln Leu Asn Arg Ala
225 230 235 240

Thr Thr Asn Asn Ser Val Leu Gln Lys Gln Gln Leu Glu Leu Met Asp
245 250 255

Thr Val His Asn Leu Val Asn Leu Cys Thr Lys Glu Gly Val Leu Leu
260 265 270

Lys Gly Gly Lys Arg Glu Glu Glu Lys Pro Phe Arg Asp Cys Ala Asp
275 280 285

Val Tyr Gln Ala Gly Phe Asn Lys Ser Gly Ile Tyr Thr Ile Tyr Ile
290 295 300

Asn Asn Met Pro Glu Pro Lys Lys Val Phe Cys Asn Met Asp Val Asn

305		310		315		320
Gly Gly Gly Trp Thr Val Ile Gln His Arg Glu Asp Gly Ser Leu Asp						
		325		330		335
Phe Gln Arg Gly Trp Lys Glu Tyr Lys Met Gly Phe Gly Asn Pro Ser						
		340		345		350
Gly Glu Tyr Trp Leu Gly Asn Glu Phe Ile Phe Ala Ile Thr Ser Gln						
		355		360		365
Arg Gln Tyr Met Leu Arg Ile Glu Leu Met Asp Trp Glu Gly Asn Arg						
		370		375		380
Ala Tyr Ser Gln Tyr Asp Arg Phe His Ile Gly Asn Glu Lys Gln Asn						
		385		390		400
Tyr Arg Leu Tyr Leu Lys Gly His Thr Gly Thr Ala Gly Lys Gln Ser						
		405		410		415
Ser Leu Ile Leu His Gly Ala Asp Phe Ser Thr Lys Asp Ala Asp Asn						
		420		425		430
Asp Asn Cys Met Cys Lys Cys Ala Leu Met Leu Thr Gly Gly Trp Trp						
		435		440		445
Phe Asp Ala Cys Gly Pro Ser Asn Leu Asn Gly Met Phe Tyr Thr Ala						
		450		455		460
Gly Gln Asn His Gly Lys Leu Asn Gly Ile Lys Trp His Tyr Phe Lys						
		465		470		475
Gly Pro Ser Tyr Ser Leu Arg Ser Thr Thr Met Met Ile Arg Pro Leu						
		485		490		495
Asp Phe Ser Gly His His His His His His						
		500		505		

<210> 108
 <211> 1124
 <212> PRT
 <213> Homo sapiens
 <400> 108

Met	Asp	Ser	Leu	Ala	Ser	Leu	Val	Leu	Cys	Gly	Val	Ser	Leu	Leu	Leu	1	5	10	15
Ser	Gly	Thr	Val	Glu	Gly	Ala	Met	Asp	Leu	Ile	Leu	Ile	Asn	Ser	Leu	20	25	30	
Pro	Leu	Val	Ser	Asp	Ala	Glu	Thr	Ser	Leu	Thr	Cys	Ile	Ala	Ser	Gly	35	40	45	
Trp	Arg	Pro	His	Glu	Pro	Ile	Thr	Ile	Gly	Arg	Asp	Phe	Glu	Ala	Leu	50	55	60	
Met	Asn	Gln	His	Gln	Asp	Pro	Leu	Glu	Val	Thr	Gln	Asp	Val	Thr	Arg	65	70	75	80
Glu	Trp	Ala	Lys	Lys	Val	Val	Trp	Lys	Arg	Glu	Lys	Ala	Ser	Lys	Ile	85	90	95	
Asn	Gly	Ala	Tyr	Phe	Cys	Glu	Gly	Arg	Val	Arg	Gly	Glu	Ala	Ile	Arg	100	105	110	
Ile	Arg	Thr	Met	Lys	Met	Arg	Gln	Gln	Ala	Ser	Phe	Leu	Pro	Ala	Thr	115	120	125	
Leu	Thr	Met	Thr	Val	Asp	Lys	Gly	Asp	Asn	Val	Asn	Ile	Ser	Phe	Lys	130	135	140	
Lys	Val	Leu	Ile	Lys	Glu	Glu	Asp	Ala	Val	Ile	Tyr	Lys	Asn	Gly	Ser	145	150	155	160
Phe	Ile	His	Ser	Val	Pro	Arg	His	Glu	Val	Pro	Asp	Ile	Leu	Glu	Val	165	170	175	
His	Leu	Pro	His	Ala	Gln	Pro	Gln	Asp	Ala	Gly	Val	Tyr	Ser	Ala	Arg	180	185	190	
Tyr	Ile	Gly	Gly	Asn	Leu	Phe	Thr	Ser	Ala	Phe	Thr	Arg	Leu	Ile	Val	195	200	205	
Arg	Arg	Cys	Glu	Ala	Gln	Lys	Trp	Gly	Pro	Glu	Cys	Asn	His	Leu	Cys	210	215	220	

Thr Ala Cys Met Asn Asn Gly Val Cys His Glu Asp Thr Gly Glu Cys
225 230 235 240

Ile Cys Pro Pro Gly Phe Met Gly Arg Thr Cys Glu Lys Ala Cys Glu
245 250 255

Leu His Thr Phe Gly Arg Thr Cys Lys Glu Arg Cys Ser Gly Gln Glu
260 265 270

Gly Cys Lys Ser Tyr Val Phe Cys Leu Pro Asp Pro Tyr Gly Cys Ser
275 280 285

Cys Ala Thr Gly Trp Lys Gly Leu Gln Cys Asn Glu Ala Cys His Pro
290 295 300

Gly Phe Tyr Gly Pro Asp Cys Lys Leu Arg Cys Ser Cys Asn Asn Gly
305 310 315 320

Glu Met Cys Asp Arg Phe Gln Gly Cys Leu Cys Ser Pro Gly Trp Gln
325 330 335

Gly Leu Gln Cys Glu Arg Glu Gly Ile Pro Arg Met Thr Pro Lys Ile
340 345 350

Val Asp Leu Pro Asp His Ile Glu Val Asn Ser Gly Lys Phe Asn Pro
355 360 365

Ile Cys Lys Ala Ser Gly Trp Pro Leu Pro Thr Asn Glu Glu Met Thr
370 375 380

Leu Val Lys Pro Asp Gly Thr Val Leu His Pro Lys Asp Phe Asn His
385 390 395 400

Thr Asp His Phe Ser Val Ala Ile Phe Thr Ile His Arg Ile Leu Pro
405 410 415

Pro Asp Ser Gly Val Trp Val Cys Ser Val Asn Thr Val Ala Gly Met
420 425 430

Val Glu Lys Pro Phe Asn Ile Ser Val Lys Val Leu Pro Lys Pro Leu
435 440 445

Asn Ala Pro Asn Val Ile Asp Thr Gly His Asn Phe Ala Val Ile Asn

450		455		460
Ile Ser Ser Glu Pro Tyr Phe Gly Asp Gly Pro Ile Lys Ser Lys Lys				
465		470		475 480
Leu Leu Tyr Lys Pro Val Asn His Tyr Glu Ala Trp Gln His Ile Gln				
	485		490	495
Val Thr Asn Glu Ile Val Thr Leu Asn Tyr Leu Glu Pro Arg Thr Glu				
	500		505	510
Tyr Glu Leu Cys Val Gln Leu Val Arg Arg Gly Glu Gly Gly Glu Gly				
	515		520	525
His Pro Gly Pro Val Arg Arg Phe Thr Thr Ala Ser Ile Gly Leu Pro				
	530		535	540
Pro Pro Arg Gly Leu Asn Leu Leu Pro Lys Ser Gln Thr Thr Leu Asn				
545		550		555 560
Leu Thr Trp Gln Pro Ile Phe Pro Ser Ser Glu Asp Asp Phe Tyr Val				
	565		570	575
Glu Val Glu Arg Arg Ser Val Gln Lys Ser Asp Gln Gln Asn Ile Lys				
	580		585	590
Val Pro Gly Asn Leu Thr Ser Val Leu Leu Asn Asn Leu His Pro Arg				
	595		600	605
Glu Gln Tyr Val Val Arg Ala Arg Val Asn Thr Lys Ala Gln Gly Glu				
	610		615	620
Trp Ser Glu Asp Leu Thr Ala Trp Thr Leu Ser Asp Ile Leu Pro Pro				
625		630		635 640
Gln Pro Glu Asn Ile Lys Ile Ser Asn Ile Thr His Ser Ser Ala Val				
	645		650	655
Ile Ser Trp Thr Ile Leu Asp Gly Tyr Ser Ile Ser Ser Ile Thr Ile				
	660		665	670
Arg Tyr Lys Val Gln Gly Lys Asn Glu Asp Gln His Val Asp Val Lys				
	675		680	685

Ile	Lys	Asn	Ala	Thr	Ile	Thr	Gln	Tyr	Gln	Leu	Lys	Gly	Leu	Glu	Pro	
	690						695				700					
Glu	Thr	Ala	Tyr	Gln	Val	Asp	Ile	Phe	Ala	Glu	Asn	Asn	Ile	Gly	Ser	
705					710					715					720	
Ser	Asn	Pro	Ala	Phe	Ser	His	Glu	Leu	Val	Thr	Leu	Pro	Glu	Ser	Gln	
				725					730					735		
Ala	Pro	Ala	Asp	Leu	Gly	Gly	Gly	Lys	Met	Leu	Leu	Ile	Ala	Ile	Leu	
			740					745						750		
Gly	Ser	Ala	Gly	Met	Thr	Cys	Leu	Thr	Val	Leu	Leu	Ala	Phe	Leu	Ile	
	755						760					765				
Ile	Leu	Gln	Leu	Lys	Arg	Ala	Asn	Val	Gln	Arg	Arg	Met	Ala	Gln	Ala	
	770					775					780					
Phe	Gln	Asn	Val	Arg	Glu	Glu	Pro	Ala	Val	Gln	Phe	Asn	Ser	Gly	Thr	
785					790					795					800	
Leu	Ala	Leu	Asn	Arg	Lys	Val	Lys	Asn	Asn	Pro	Asp	Pro	Thr	Ile	Tyr	
				805					810					815		
Pro	Val	Leu	Asp	Trp	Asn	Asp	Ile	Lys	Phe	Gln	Asp	Val	Ile	Gly	Glu	
			820					825					830			
Gly	Asn	Phe	Gly	Gln	Val	Leu	Lys	Ala	Arg	Ile	Lys	Lys	Asp	Gly	Leu	
		835					840					845				
Arg	Met	Asp	Ala	Ala	Ile	Lys	Arg	Met	Lys	Glu	Tyr	Ala	Ser	Lys	Asp	
	850					855					860					
Asp	His	Arg	Asp	Phe	Ala	Gly	Glu	Leu	Glu	Val	Leu	Cys	Lys	Leu	Gly	
865					870					875					880	
His	His	Pro	Asn	Ile	Ile	Asn	Leu	Leu	Gly	Ala	Cys	Glu	His	Arg	Gly	
				885					890					895		
Tyr	Leu	Tyr	Leu	Ala	Ile	Glu	Tyr	Ala	Pro	His	Gly	Asn	Leu	Leu	Asp	
			900					905						910		

Phe Leu Arg Lys Ser Arg Val Leu Glu Thr Asp Pro Ala Phe Ala Ile
915 920 925

Ala Asn Ser Thr Ala Ser Thr Leu Ser Ser Gln Gln Leu Leu His Phe
930 935 940

Ala Ala Asp Val Ala Arg Gly Met Asp Tyr Leu Ser Gln Lys Gln Phe
945 950 955 960

Ile His Arg Asp Leu Ala Ala Arg Asn Ile Leu Val Gly Glu Asn Tyr
965 970 975

Val Ala Lys Ile Ala Asp Phe Gly Leu Ser Arg Gly Gln Glu Val Tyr
980 985 990

Val Lys Lys Thr Met Gly Arg Leu Pro Val Arg Trp Met Ala Ile Glu
995 1000 1005

Ser Leu Asn Tyr Ser Val Tyr Thr Thr Asn Ser Asp Val Trp Ser
1010 1015 1020

Tyr Gly Val Leu Leu Trp Glu Ile Val Ser Leu Gly Gly Thr Pro
1025 1030 1035

Tyr Cys Gly Met Thr Cys Ala Glu Leu Tyr Glu Lys Leu Pro Gln
1040 1045 1050

Gly Tyr Arg Leu Glu Lys Pro Leu Asn Cys Asp Asp Glu Val Tyr
1055 1060 1065

Asp Leu Met Arg Gln Cys Trp Arg Glu Lys Pro Tyr Glu Arg Pro
1070 1075 1080

Ser Phe Ala Gln Ile Leu Val Ser Leu Asn Arg Met Leu Glu Glu
1085 1090 1095

Arg Lys Thr Tyr Val Asn Thr Thr Leu Tyr Glu Lys Phe Thr Tyr
1100 1105 1110

Ala Gly Ile Asp Cys Ser Ala Glu Glu Ala Ala
1115 1120

<210> 109
<211> 946
<212> PRT
<213> Artificial

<220>
<223> Heavy chain 1 of bispecific, tetravalent single chain Fab
<VEGF-ANG-2> antibody molecule scFAB-Avastin-LC06-2620

<400> 109

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Ala Asp Phe
50 55 60

Lys Arg Arg Phe Thr Phe Ser Leu Asp Thr Ser Lys Ser Thr Ala Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Tyr Pro His Tyr Tyr Gly Ser Ser His Trp Tyr Phe Asp Val
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190

Thr	Val	Pro	Ser	Ser	Ser	Leu	Gly	Thr	Gln	Thr	Tyr	Ile	Cys	Asn	Val	195	200	205
Asn	His	Lys	Pro	Ser	Asn	Thr	Lys	Val	Asp	Lys	Lys	Val	Glu	Pro	Lys	210	215	220
Ser	Cys	Asp	Lys	Thr	His	Thr	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Glu	Leu	225	230	235
Leu	Gly	Gly	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr	245	250	255
Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val	260	265	270
Ser	His	Glu	Asp	Pro	Glu	Val	Lys	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	275	280	285
Glu	Val	His	Asn	Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Tyr	Asn	Ser	290	295	300
Thr	Tyr	Arg	Val	Val	Ser	Val	Leu	Thr	Val	Leu	His	Gln	Asp	Trp	Leu	305	310	315
Asn	Gly	Lys	Glu	Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys	Ala	Leu	Pro	Ala	325	330	335
Pro	Ile	Glu	Lys	Thr	Ile	Ser	Lys	Ala	Lys	Gly	Gln	Pro	Arg	Glu	Pro	340	345	350
Gln	Val	Tyr	Thr	Leu	Pro	Pro	Ser	Arg	Asp	Glu	Leu	Thr	Lys	Asn	Gln	355	360	365
Val	Ser	Leu	Thr	Cys	Leu	Val	Lys	Gly	Phe	Tyr	Pro	Ser	Asp	Ile	Ala	370	375	380
Val	Glu	Trp	Glu	Ser	Asn	Gly	Gln	Pro	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	385	390	395
Pro	Pro	Val	Leu	Asp	Ser	Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Lys	Leu	405	410	415

Thr	Val	Asp	Lys	Ser	Arg	Trp	Gln	Gln	Gly	Asn	Val	Phe	Ser	Cys	Ser		
			420					425					430				
Val	Met	His	Glu	Ala	Leu	His	Asn	His	Tyr	Thr	Gln	Lys	Ser	Leu	Ser		
		435					440					445					
Leu	Ser	Pro	Gly	Lys	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gln		
	450					455					460						
Pro	Gly	Leu	Thr	Gln	Pro	Pro	Ser	Val	Ser	Val	Ala	Pro	Gly	Gln	Thr		
465					470					475					480		
Ala	Arg	Ile	Thr	Cys	Gly	Gly	Asn	Asn	Ile	Gly	Ser	Lys	Ser	Val	His		
				485					490					495			
Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ala	Pro	Val	Leu	Val	Val	Tyr	Asp		
		500						505					510				
Asp	Ser	Asp	Arg	Pro	Ser	Gly	Ile	Pro	Glu	Arg	Phe	Ser	Gly	Ser	Asn		
		515					520					525					
Ser	Gly	Asn	Thr	Ala	Thr	Leu	Thr	Ile	Ser	Arg	Val	Glu	Ala	Gly	Asp		
	530					535					540						
Glu	Ala	Asp	Tyr	Tyr	Cys	Gln	Val	Trp	Asp	Ser	Ser	Ser	Asp	His	Tyr		
545					550					555				560			
Val	Phe	Gly	Thr	Gly	Thr	Lys	Val	Thr	Val	Leu	Arg	Thr	Val	Ala	Ala		
				565					570					575			
Pro	Ser	Val	Phe	Ile	Phe	Pro	Pro	Ser	Asp	Glu	Gln	Leu	Lys	Ser	Gly		
			580					585					590				
Thr	Ala	Ser	Val	Val	Cys	Leu	Leu	Asn	Asn	Phe	Tyr	Pro	Arg	Glu	Ala		
		595					600					605					
Lys	Val	Gln	Trp	Lys	Val	Asp	Asn	Ala	Leu	Gln	Ser	Gly	Asn	Ser	Gln		
	610					615					620						
Glu	Ser	Val	Thr	Glu	Gln	Asp	Ser	Lys	Asp	Ser	Thr	Tyr	Ser	Leu	Ser		
625					630					635					640		

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
645 650 655

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
660 665 670

Phe Asn Arg Gly Glu Cys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
675 680 685

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
690 695 700

Gly Gly Gly Ser Gly Gly Gln Val Gln Leu Val Glu Ser Gly Ala Glu
705 710 715 720

Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly
725 730 735

Tyr Thr Phe Thr Gly Tyr Tyr Met His Trp Val Arg Gln Ala Pro Gly
740 745 750

Gln Gly Leu Glu Trp Met Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr
755 760 765

Asn Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Met Thr Arg Asp Thr
770 775 780

Ser Ile Ser Thr Ala Tyr Met Glu Leu Ser Arg Leu Arg Ser Asp Asp
785 790 795 800

Thr Ala Val Tyr Tyr Cys Ala Arg Ser Pro Asn Pro Tyr Tyr Tyr Asp
805 810 815

Ser Ser Gly Tyr Tyr Tyr Pro Gly Ala Phe Asp Ile Trp Gly Gln Gly
820 825 830

Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
835 840 845

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
850 855 860

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp

865		870		875		880
Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu						
		885		890		895
Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser						
		900		905		910
Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro						
		915		920		925
Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys						
		930		935		940
Thr His						
945						
<210>	110					
<211>	214					
<212>	PRT					
<213>	Artificial					
<220>						
<223>	Light chain of bispecific, tetravalent single chain Fab					
	<VEGF-ANG-2> antibody molecule scFAB-Avastin-LC06-2620					
<400>	110					
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly						
1		5		10		15
Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Gln Asp Ile Ser Asn Tyr						
		20		25		30
Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Val Leu Ile						
		35		40		45
Tyr Phe Thr Ser Ser Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly						
		50		55		60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro						
65			70		75	80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Thr Val Pro Trp						
		85		90		95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 111

<211> 956

<212> PRT

<213> Artificial

<220>

<223> Heavy chain 1 of bispecific, tetravalent single chain Fab
<VEGF-ANG-2> antibody molecule scFab-Avastin-Ang2i-LC06-2640

<400> 111

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Ala Asp Phe

50	55	60
Lys Arg Arg Phe Thr Phe Ser Leu Asp Thr Ser Lys Ser Thr Ala Tyr 65 70 75 80		
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys 85 90 95		
Ala Lys Tyr Pro His Tyr Tyr Gly Ser Ser His Trp Tyr Phe Asp Val 100 105 110		
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly 115 120 125		
Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly 130 135 140		
Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val 145 150 155 160		
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe 165 170 175		
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val 180 185 190		
Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val 195 200 205		
Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys 210 215 220		
Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu 225 230 235 240		
Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr 245 250 255		
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val 260 265 270		
Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val 275 280 285		

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
325 330 335

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
355 360 365

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445

Leu Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
450 455 460

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Pro Gly Leu Thr Gln Pro
465 470 475 480

Pro Ser Val Ser Val Ala Pro Gly Gln Thr Ala Arg Ile Thr Cys Gly
485 490 495

Gly Asn Asn Ile Gly Ser Lys Ser Val His Trp Tyr Gln Gln Lys Pro
500 505 510

Gly Gln Ala Pro Val Leu Val Val Tyr Asp Asp Ser Asp Arg Pro Ser
515 520 525

Gly Ile Pro Glu Arg Phe Ser Gly Ser Asn Ser Gly Asn Thr Ala Thr
530 535 540

Leu Thr Ile Ser Arg Val Glu Ala Gly Asp Glu Ala Asp Tyr Tyr Cys
545 550 555 560

Gln Val Trp Asp Ser Ser Ser Asp His Tyr Val Phe Gly Thr Gly Thr
565 570 575

Lys Val Thr Val Leu Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe
580 585 590

Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys
595 600 605

Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val
610 615 620

Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln
625 630 635 640

Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser
645 650 655

Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His
660 665 670

Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
675 680 685

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
690 695 700

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
705 710 715 720

Gln Val Gln Leu Val Glu Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
725 730 735

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
740 745 750

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
755 760 765

Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
770 775 780

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
785 790 795 800

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
805 810 815

Ala Arg Ser Pro Asn Pro Tyr Tyr Tyr Asp Ser Ser Gly Tyr Tyr Tyr
820 825 830

Pro Gly Ala Phe Asp Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser
835 840 845

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser
850 855 860

Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
865 870 875 880

Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
885 890 895

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
900 905 910

Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln
915 920 925

Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp
930 935 940

Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His
945 950 955

<210> 112

<211> 214
<212> PRT
<213> Artificial

<220>
<223> Light chain of bispecific, tetravalent single chain Fab
<VEGF-ANG-2> antibody molecule scFab-Avastin-Ang2i-LC06-2640

<400> 112

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Gln Asp Ile Ser Asn Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Val Leu Ile
35 40 45

Tyr Phe Thr Ser Ser Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Thr Val Pro Trp
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 113

<211> 956

<212> PRT

<213> Artificial

<220>

<223> Heavy chain 1 of bispecific, tetravalent single chain Fab
<VEGF-ANG-2> antibody molecule scFab-Avastin-Ang2i-LC06-2641

<400> 113

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Ala Asp Phe
50 55 60

Lys Arg Arg Phe Thr Phe Ser Leu Asp Thr Ser Lys Ser Thr Ala Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Tyr Pro His Tyr Tyr Gly Ser Ser His Trp Tyr Phe Asp Val
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val

145		150		155		160
Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe						
		165		170		175
Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val						
		180		185		190
Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val						
		195		200		205
Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys						
		210		215		220
Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu						
		225		230		235
Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr						
		245		250		255
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val						
		260		265		270
Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val						
		275		280		285
Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser						
		290		295		300
Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu						
		305		310		315
Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala						
		325		330		335
Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro						
		340		345		350
Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln						
		355		360		365
Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala						
		370		375		380

Val	Glu	Trp	Glu	Ser	Asn	Gly	Gln	Pro	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	385	390	395	400
Pro	Pro	Val	Leu	Asp	Ser	Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Lys	Leu	405	410	415	
Thr	Val	Asp	Lys	Ser	Arg	Trp	Gln	Gln	Gly	Asn	Val	Phe	Ser	Cys	Ser	420	425	430	
Val	Met	His	Glu	Ala	Leu	His	Asn	His	Tyr	Thr	Gln	Lys	Ser	Leu	Ser	435	440	445	
Leu	Ser	Pro	Gly	Lys	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	450	455	460	
Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gln	Pro	Gly	Leu	Thr	Gln	Pro	465	470	475	480
Pro	Ser	Val	Ser	Val	Ala	Pro	Gly	Gln	Thr	Ala	Arg	Ile	Thr	Cys	Gly	485	490	495	
Gly	Asn	Asn	Ile	Gly	Ser	Lys	Ser	Val	His	Trp	Tyr	Gln	Gln	Lys	Pro	500	505	510	
Gly	Gln	Ala	Pro	Val	Leu	Val	Val	Tyr	Asp	Asp	Ser	Asp	Arg	Pro	Ser	515	520	525	
Gly	Ile	Pro	Glu	Arg	Phe	Ser	Gly	Ser	Asn	Ser	Gly	Asn	Thr	Ala	Thr	530	535	540	
Leu	Thr	Ile	Ser	Arg	Val	Glu	Ala	Gly	Asp	Glu	Ala	Asp	Tyr	Tyr	Cys	545	550	555	560
Gln	Val	Trp	Asp	Ser	Ser	Ser	Asp	His	Tyr	Val	Phe	Gly	Cys	Gly	Thr	565	570	575	
Lys	Val	Thr	Val	Leu	Arg	Thr	Val	Ala	Ala	Pro	Ser	Val	Phe	Ile	Phe	580	585	590	
Pro	Pro	Ser	Asp	Glu	Gln	Leu	Lys	Ser	Gly	Thr	Ala	Ser	Val	Val	Cys	595	600	605	

Leu	Leu	Asn	Asn	Phe	Tyr	Pro	Arg	Glu	Ala	Lys	Val	Gln	Trp	Lys	Val
610						615					620				
Asp	Asn	Ala	Leu	Gln	Ser	Gly	Asn	Ser	Gln	Glu	Ser	Val	Thr	Glu	Gln
625					630					635					640
Asp	Ser	Lys	Asp	Ser	Thr	Tyr	Ser	Leu	Ser	Ser	Thr	Leu	Thr	Leu	Ser
				645					650					655	
Lys	Ala	Asp	Tyr	Glu	Lys	His	Lys	Val	Tyr	Ala	Cys	Glu	Val	Thr	His
			660					665					670		
Gln	Gly	Leu	Ser	Ser	Pro	Val	Thr	Lys	Ser	Phe	Asn	Arg	Gly	Glu	Cys
		675					680					685			
Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly
	690					695					700				
Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly
705					710					715					720
Gln	Val	Gln	Leu	Val	Glu	Ser	Gly	Ala	Glu	Val	Lys	Lys	Pro	Gly	Ala
				725					730					735	
Ser	Val	Lys	Val	Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Thr	Phe	Thr	Gly	Tyr
			740					745					750		
Tyr	Met	His	Trp	Val	Arg	Gln	Ala	Pro	Gly	Gln	Cys	Leu	Glu	Trp	Met
		755					760					765			
Gly	Trp	Ile	Asn	Pro	Asn	Ser	Gly	Gly	Thr	Asn	Tyr	Ala	Gln	Lys	Phe
	770					775					780				
Gln	Gly	Arg	Val	Thr	Met	Thr	Arg	Asp	Thr	Ser	Ile	Ser	Thr	Ala	Tyr
785					790					795					800
Met	Glu	Leu	Ser	Arg	Leu	Arg	Ser	Asp	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
				805					810					815	
Ala	Arg	Ser	Pro	Asn	Pro	Tyr	Tyr	Tyr	Asp	Ser	Ser	Gly	Tyr	Tyr	Tyr
			820					825					830		

Pro Gly Ala Phe Asp Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser
835 840 845

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser
850 855 860

Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
865 870 875 880

Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
885 890 895

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
900 905 910

Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln
915 920 925

Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp
930 935 940

Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His
945 950 955

<210> 114

<211> 214

<212> PRT

<213> Artificial

<220>

<223> Light chain of bispecific, tetravalent single chain Fab
<VEGF-ANG-2> antibody molecule scFab-Avastin-Ang2i-LC06-2641

<400> 114

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Gln Asp Ile Ser Asn Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Val Leu Ile
35 40 45

Tyr Phe Thr Ser Ser Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Thr Val Pro Trp
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 115
<211> 946
<212> PRT
<213> Artificial

<220>
<223> Heavy chain 1 of bispecific, trivalent single chain Fab
<VEGF-ANG-2> antibody molecule Avastin-LC06-KiH-C-scFab

<400> 115

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Tyr	Thr	Phe	Thr	Asn	Tyr	20	25	30
Gly	Met	Asn	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val	35	40	45
Gly	Trp	Ile	Asn	Thr	Tyr	Thr	Gly	Glu	Pro	Thr	Tyr	Ala	Ala	Asp	Phe	50	55	60
Lys	Arg	Arg	Phe	Thr	Phe	Ser	Leu	Asp	Thr	Ser	Lys	Ser	Thr	Ala	Tyr	65	70	75
Leu	Gln	Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys	85	90	95
Ala	Lys	Tyr	Pro	His	Tyr	Tyr	Gly	Ser	Ser	His	Trp	Tyr	Phe	Asp	Val	100	105	110
Trp	Gly	Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser	Ala	Ser	Thr	Lys	Gly	115	120	125
Pro	Ser	Val	Phe	Pro	Leu	Ala	Pro	Ser	Ser	Lys	Ser	Thr	Ser	Gly	Gly	130	135	140
Thr	Ala	Ala	Leu	Gly	Cys	Leu	Val	Lys	Asp	Tyr	Phe	Pro	Glu	Pro	Val	145	150	155
Thr	Val	Ser	Trp	Asn	Ser	Gly	Ala	Leu	Thr	Ser	Gly	Val	His	Thr	Phe	165	170	175
Pro	Ala	Val	Leu	Gln	Ser	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val	Val	180	185	190
Thr	Val	Pro	Ser	Ser	Ser	Leu	Gly	Thr	Gln	Thr	Tyr	Ile	Cys	Asn	Val	195	200	205
Asn	His	Lys	Pro	Ser	Asn	Thr	Lys	Val	Asp	Lys	Lys	Val	Glu	Pro	Lys	210	215	220
Ser	Cys	Asp	Lys	Thr	His	Thr	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Glu	Leu	225	230	235
Leu	Gly	Gly	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr			

245										250					255				
Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val				
			260					265					270						
Ser	His	Glu	Asp	Pro	Glu	Val	Lys	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val				
		275					280					285							
Glu	Val	His	Asn	Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Tyr	Asn	Ser				
	290					295					300								
Thr	Tyr	Arg	Val	Val	Ser	Val	Leu	Thr	Val	Leu	His	Gln	Asp	Trp	Leu				
305					310					315					320				
Asn	Gly	Lys	Glu	Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys	Ala	Leu	Pro	Ala				
				325					330					335					
Pro	Ile	Glu	Lys	Thr	Ile	Ser	Lys	Ala	Lys	Gly	Gln	Pro	Arg	Glu	Pro				
			340					345					350						
Gln	Val	Tyr	Thr	Leu	Pro	Pro	Cys	Arg	Asp	Glu	Leu	Thr	Lys	Asn	Gln				
		355					360					365							
Val	Ser	Leu	Trp	Cys	Leu	Val	Lys	Gly	Phe	Tyr	Pro	Ser	Asp	Ile	Ala				
	370					375					380								
Val	Glu	Trp	Glu	Ser	Asn	Gly	Gln	Pro	Glu	Asn	Asn	Tyr	Lys	Thr	Thr				
385					390					395					400				
Pro	Pro	Val	Leu	Asp	Ser	Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Lys	Leu				
				405					410					415					
Thr	Val	Asp	Lys	Ser	Arg	Trp	Gln	Gln	Gly	Asn	Val	Phe	Ser	Cys	Ser				
			420					425					430						
Val	Met	His	Glu	Ala	Leu	His	Asn	His	Tyr	Thr	Gln	Lys	Ser	Leu	Ser				
		435					440					445							
Leu	Ser	Pro	Gly	Lys	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gln				
	450					455					460								
Pro	Gly	Leu	Thr	Gln	Pro	Pro	Ser	Val	Ser	Val	Ala	Pro	Gly	Gln	Thr				
465					470					475					480				

Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile Gly Ser Lys Ser Val His
485 490 495

Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Val Tyr Asp
500 505 510

Asp Ser Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser Asn
515 520 525

Ser Gly Asn Thr Ala Thr Leu Thr Ile Ser Arg Val Glu Ala Gly Asp
530 535 540

Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp Ser Ser Ser Asp His Tyr
545 550 555 560

Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Arg Thr Val Ala Ala
565 570 575

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
580 585 590

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
595 600 605

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
610 615 620

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
625 630 635 640

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
645 650 655

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
660 665 670

Phe Asn Arg Gly Glu Cys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
675 680 685

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
690 695 700

Gly	Gly	Gly	Ser	Gly	Gly	Gln	Val	Gln	Leu	Val	Glu	Ser	Gly	Ala	Glu
705					710					715					720
Val	Lys	Lys	Pro	Gly	Ala	Ser	Val	Lys	Val	Ser	Cys	Lys	Ala	Ser	Gly
				725					730					735	
Tyr	Thr	Phe	Thr	Gly	Tyr	Tyr	Met	His	Trp	Val	Arg	Gln	Ala	Pro	Gly
			740					745					750		
Gln	Gly	Leu	Glu	Trp	Met	Gly	Trp	Ile	Asn	Pro	Asn	Ser	Gly	Gly	Thr
		755					760					765			
Asn	Tyr	Ala	Gln	Lys	Phe	Gln	Gly	Arg	Val	Thr	Met	Thr	Arg	Asp	Thr
	770					775					780				
Ser	Ile	Ser	Thr	Ala	Tyr	Met	Glu	Leu	Ser	Arg	Leu	Arg	Ser	Asp	Asp
785					790					795					800
Thr	Ala	Val	Tyr	Tyr	Cys	Ala	Arg	Ser	Pro	Asn	Pro	Tyr	Tyr	Tyr	Asp
				805					810					815	
Ser	Ser	Gly	Tyr	Tyr	Tyr	Pro	Gly	Ala	Phe	Asp	Ile	Trp	Gly	Gln	Gly
			820					825					830		
Thr	Met	Val	Thr	Val	Ser	Ser	Ala	Ser	Thr	Lys	Gly	Pro	Ser	Val	Phe
		835					840					845			
Pro	Leu	Ala	Pro	Ser	Ser	Lys	Ser	Thr	Ser	Gly	Gly	Thr	Ala	Ala	Leu
	850					855					860				
Gly	Cys	Leu	Val	Lys	Asp	Tyr	Phe	Pro	Glu	Pro	Val	Thr	Val	Ser	Trp
865					870					875					880
Asn	Ser	Gly	Ala	Leu	Thr	Ser	Gly	Val	His	Thr	Phe	Pro	Ala	Val	Leu
				885					890					895	
Gln	Ser	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val	Val	Thr	Val	Pro	Ser
			900					905					910		
Ser	Ser	Leu	Gly	Thr	Gln	Thr	Tyr	Ile	Cys	Asn	Val	Asn	His	Lys	Pro
		915					920					925			

Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
930 935 940

Thr His
945

<210> 116
<211> 453
<212> PRT
<213> Artificial

<220>
<223> Heavy chain 2 of bispecific, trivalent single chain Fab
<VEGF-ANG-2> antibody molecule Avastin-LC06-KiH-C-scFab

<400> 116

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Ala Asp Phe
50 55 60

Lys Arg Arg Phe Thr Phe Ser Leu Asp Thr Ser Lys Ser Thr Ala Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Tyr Pro His Tyr Tyr Gly Ser Ser His Trp Tyr Phe Asp Val
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160

Thr	Val	Ser	Trp	Asn	Ser	Gly	Ala	Leu	Thr	Ser	Gly	Val	His	Thr	Phe
				165					170					175	
Pro	Ala	Val	Leu	Gln	Ser	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val	Val
			180					185					190		
Thr	Val	Pro	Ser	Ser	Ser	Leu	Gly	Thr	Gln	Thr	Tyr	Ile	Cys	Asn	Val
		195					200					205			
Asn	His	Lys	Pro	Ser	Asn	Thr	Lys	Val	Asp	Lys	Lys	Val	Glu	Pro	Lys
	210					215					220				
Ser	Cys	Asp	Lys	Thr	His	Thr	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Glu	Leu
225					230					235					240
Leu	Gly	Gly	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp	Thr
				245					250					255	
Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp	Val
			260					265					270		
Ser	His	Glu	Asp	Pro	Glu	Val	Lys	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val
		275					280					285			
Glu	Val	His	Asn	Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Tyr	Asn	Ser
	290					295					300				
Thr	Tyr	Arg	Val	Val	Ser	Val	Leu	Thr	Val	Leu	His	Gln	Asp	Trp	Leu
305					310					315					320
Asn	Gly	Lys	Glu	Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys	Ala	Leu	Pro	Ala
				325					330					335	
Pro	Ile	Glu	Lys	Thr	Ile	Ser	Lys	Ala	Lys	Gly	Gln	Pro	Arg	Glu	Pro
			340					345					350		
Gln	Val	Cys	Thr	Leu	Pro	Pro	Ser	Arg	Asp	Glu	Leu	Thr	Lys	Asn	Gln
		355					360					365			
Val	Ser	Leu	Ser	Cys	Ala	Val	Lys	Gly	Phe	Tyr	Pro	Ser	Asp	Ile	Ala
	370					375					380				

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu
405 410 415

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445

Leu Ser Pro Gly Lys
450

<210> 117
<211> 214
<212> PRT
<213> Artificial

<220>
<223> Light chain of bispecific, trivalent single chain Fab
<VEGF-ANG-2> antibody molecule Avastin-LC06-KiH-C-scFab

<400> 117

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Gln Asp Ile Ser Asn Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Val Leu Ile
35 40 45

Tyr Phe Thr Ser Ser Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Thr Val Pro Trp
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala

100	105	110
Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly		
115	120	125
Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala		
130	135	140
Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln		
145	150	155
Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser		
165	170	175
Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr		
180	185	190
Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser		
195	200	205
Phe Asn Arg Gly Glu Cys		
210		

<210> 118
 <211> 698
 <212> PRT
 <213> Artificial

<220>
 <223> Heavy chain 1 of bispecific, trivalent <VEGF-ANG-2> antibody molecule Avastin-LC06-C-Fab-6CSS

<400> 118

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30
Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Ala Asp Phe
50 55 60

Lys Arg Arg Phe Thr Phe Ser Leu Asp Thr Ser Lys Ser Thr Ala Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Tyr Pro His Tyr Tyr Gly Ser Ser His Trp Tyr Phe Asp Val
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
115 120 125

Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
130 135 140

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
145 150 155 160

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
165 170 175

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
180 185 190

Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
195 200 205

Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys
210 215 220

Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
225 230 235 240

Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
325 330 335

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350

Gln Val Tyr Thr Leu Pro Pro Cys Arg Asp Glu Leu Thr Lys Asn Gln
355 360 365

Val Ser Leu Trp Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
405 410 415

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445

Leu Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
450 455 460

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
465 470 475 480

Gly Gly Ser Gln Pro Gly Leu Thr Gln Pro Pro Ser Val Ser Val Ala
485 490 495

Pro Gly Gln Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile Gly Ser
500 505 510

Lys Ser Val His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu

515					520					525					
Val	Val	Tyr	Asp	Asp	Ser	Asp	Arg	Pro	Ser	Gly	Ile	Pro	Glu	Arg	Phe
530					535						540				
Ser	Gly	Ser	Asn	Ser	Gly	Asn	Thr	Ala	Thr	Leu	Thr	Ile	Ser	Arg	Val
545					550					555					560
Glu	Ala	Gly	Asp	Glu	Ala	Asp	Tyr	Tyr	Cys	Gln	Val	Trp	Asp	Ser	Ser
				565					570					575	
Ser	Asp	His	Tyr	Val	Phe	Gly	Cys	Gly	Thr	Lys	Val	Thr	Val	Leu	Arg
			580					585					590		
Thr	Val	Ala	Ala	Pro	Ser	Val	Phe	Ile	Phe	Pro	Pro	Ser	Asp	Glu	Gln
		595					600						605		
Leu	Lys	Ser	Gly	Thr	Ala	Ser	Val	Val	Cys	Leu	Leu	Asn	Asn	Phe	Tyr
	610					615					620				
Pro	Arg	Glu	Ala	Lys	Val	Gln	Trp	Lys	Val	Asp	Asn	Ala	Leu	Gln	Ser
625					630					635					640
Gly	Asn	Ser	Gln	Glu	Ser	Val	Thr	Glu	Gln	Asp	Ser	Lys	Asp	Ser	Thr
				645					650					655	
Tyr	Ser	Leu	Ser	Ser	Thr	Leu	Thr	Leu	Ser	Lys	Ala	Asp	Tyr	Glu	Lys
			660					665					670		
His	Lys	Val	Tyr	Ala	Cys	Glu	Val	Thr	His	Gln	Gly	Leu	Ser	Ser	Pro
		675					680					685			
Val	Thr	Lys	Ser	Phe	Asn	Arg	Gly	Glu	Cys						
	690					695									
<210> 119															
<211> 719															
<212> PRT															
<213> Artificial															
<220>															
<223> Heavy chain 2 of bispecific, trivalent <VEGF-ANG-2> antibody molecule Avastin-LC06-C-Fab-6CSS															
<400> 119															

Glu	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Leu	Val	Gln	Pro	Gly	Gly	1	5	10	15
Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Tyr	Thr	Phe	Thr	Asn	Tyr	20	25	30	
Gly	Met	Asn	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val	35	40	45	
Gly	Trp	Ile	Asn	Thr	Tyr	Thr	Gly	Glu	Pro	Thr	Tyr	Ala	Ala	Asp	Phe	50	55	60	
Lys	Arg	Arg	Phe	Thr	Phe	Ser	Leu	Asp	Thr	Ser	Lys	Ser	Thr	Ala	Tyr	65	70	75	80
Leu	Gln	Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys	85	90	95	
Ala	Lys	Tyr	Pro	His	Tyr	Tyr	Gly	Ser	Ser	His	Trp	Tyr	Phe	Asp	Val	100	105	110	
Trp	Gly	Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser	Ala	Ser	Thr	Lys	Gly	115	120	125	
Pro	Ser	Val	Phe	Pro	Leu	Ala	Pro	Ser	Ser	Lys	Ser	Thr	Ser	Gly	Gly	130	135	140	
Thr	Ala	Ala	Leu	Gly	Cys	Leu	Val	Lys	Asp	Tyr	Phe	Pro	Glu	Pro	Val	145	150	155	160
Thr	Val	Ser	Trp	Asn	Ser	Gly	Ala	Leu	Thr	Ser	Gly	Val	His	Thr	Phe	165	170	175	
Pro	Ala	Val	Leu	Gln	Ser	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val	Val	180	185	190	
Thr	Val	Pro	Ser	Ser	Ser	Leu	Gly	Thr	Gln	Thr	Tyr	Ile	Cys	Asn	Val	195	200	205	
Asn	His	Lys	Pro	Ser	Asn	Thr	Lys	Val	Asp	Lys	Lys	Val	Glu	Pro	Lys	210	215	220	

Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
225 230 235 240

Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
245 250 255

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
260 265 270

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
275 280 285

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
290 295 300

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
305 310 315 320

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
325 330 335

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
340 345 350

Gln Val Cys Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
355 360 365

Val Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
370 375 380

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
385 390 395 400

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu
405 410 415

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
420 425 430

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
435 440 445

Leu Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly

450				455				460							
Gly 465	Gly	Gly	Ser	Gly	Gly 470	Gly	Gly	Ser	Gly	Gly 475	Gly	Gly	Ser	Gly	Gly 480
Gly	Gly	Ser	Gln	Val 485	Gln	Leu	Val	Glu	Ser 490	Gly	Ala	Glu	Val	Lys 495	Lys
Pro	Gly	Ala	Ser 500	Val	Lys	Val	Ser	Cys 505	Lys	Ala	Ser	Gly	Tyr 510	Thr	Phe
Thr	Gly	Tyr 515	Tyr	Met	His	Trp	Val 520	Arg	Gln	Ala	Pro	Gly 525	Gln	Cys	Leu
Glu	Trp 530	Met	Gly	Trp	Ile	Asn 535	Pro	Asn	Ser	Gly	Gly 540	Thr	Asn	Tyr	Ala
Gln 545	Lys	Phe	Gln	Gly	Arg 550	Val	Thr	Met	Thr	Arg 555	Asp	Thr	Ser	Ile	Ser 560
Thr	Ala	Tyr	Met	Glu 565	Leu	Ser	Arg	Leu	Arg 570	Ser	Asp	Asp	Thr	Ala 575	Val
Tyr	Tyr	Cys	Ala 580	Arg	Ser	Pro	Asn	Pro 585	Tyr	Tyr	Tyr	Asp	Ser 590	Ser	Gly
Tyr	Tyr	Tyr 595	Pro	Gly	Ala	Phe	Asp 600	Ile	Trp	Gly	Gln	Gly 605	Thr	Met	Val
Thr	Val 610	Ser	Ser	Ala	Ser	Thr 615	Lys	Gly	Pro	Ser	Val 620	Phe	Pro	Leu	Ala
Pro 625	Ser	Ser	Lys	Ser	Thr 630	Ser	Gly	Gly	Thr	Ala 635	Ala	Leu	Gly	Cys	Leu 640
Val	Lys	Asp	Tyr	Phe 645	Pro	Glu	Pro	Val	Thr 650	Val	Ser	Trp	Asn	Ser 655	Gly
Ala	Leu	Thr	Ser 660	Gly	Val	His	Thr	Phe 665	Pro	Ala	Val	Leu	Gln 670	Ser	Ser
Gly	Leu	Tyr 675	Ser	Leu	Ser	Ser	Val 680	Val	Thr	Val	Pro	Ser 685	Ser	Ser	Leu

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr
690 695 700

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His
705 710 715

<210> 120

<211> 214

<212> PRT

<213> Artificial

<220>

<223> Light chain of bispecific, trivalent <VEGF-ANG-2> antibody
molecule Avastin-LC06-C-Fab-6CSS

<400> 120

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Gln Asp Ile Ser Asn Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Val Leu Ile
35 40 45

Tyr Phe Thr Ser Ser Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Thr Val Pro Trp
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys
210

<210> 121
<211> 459
<212> PRT
<213> Artificial

<220>
<223> Heavy chain 1 of bispecific, bivalent domain exchanged
<VEGF-ANG-2> antibody molecule Avastin-LC06-CH1-CL

<400> 121

Gln Val Gln Leu Val Glu Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Pro Asn Pro Tyr Tyr Tyr Asp Ser Ser Gly Tyr Tyr Tyr
100 105 110

Pro Gly Ala Phe Asp Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser
115 120 125

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser
130 135 140

Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
145 150 155 160

Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
165 170 175

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
180 185 190

Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln
195 200 205

Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp
210 215 220

Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro
225 230 235 240

Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro
245 250 255

Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr
260 265 270

Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn
275 280 285

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
290 295 300

Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
305 310 315 320

Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
325 330 335

Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys
340 345 350

Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Cys Arg Asp
355 360 365

Glu Leu Thr Lys Asn Gln Val Ser Leu Trp Cys Leu Val Lys Gly Phe
370 375 380

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
385 390 395 400

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
405 410 415

Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
420 425 430

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
435 440 445

Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
450 455

<210> 122

<211> 457

<212> PRT

<213> Artificial

<220>

<223> Heavy chain 2 of bispecific, bivalent domain exchanged
<VEGF-ANG-2> antibody molecule Avastin-LC06-CH1-CL

<400> 122

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Asp Phe Thr His Tyr
20 25 30

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val
35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Ala Asp Phe

50						55						60					
Lys	Arg	Arg	Phe	Thr	Phe	Ser	Leu	Asp	Thr	Ser	Lys	Ser	Thr	Ala	Tyr		
65					70					75					80		
Leu	Gln	Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys		
				85					90					95			
Ala	Lys	Tyr	Pro	Tyr	Tyr	Tyr	Gly	Thr	Ser	His	Trp	Tyr	Phe	Asp	Val		
			100					105					110				
Trp	Gly	Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ser	Ala	Ser	Val	Ala	Ala		
		115					120						125				
Pro	Ser	Val	Phe	Ile	Phe	Pro	Pro	Ser	Asp	Glu	Gln	Leu	Lys	Ser	Gly		
	130					135					140						
Thr	Ala	Ser	Val	Val	Cys	Leu	Leu	Asn	Asn	Phe	Tyr	Pro	Arg	Glu	Ala		
145					150					155					160		
Lys	Val	Gln	Trp	Lys	Val	Asp	Asn	Ala	Leu	Gln	Ser	Gly	Asn	Ser	Gln		
				165					170					175			
Glu	Ser	Val	Thr	Glu	Gln	Asp	Ser	Lys	Asp	Ser	Thr	Tyr	Ser	Leu	Ser		
			180					185					190				
Ser	Thr	Leu	Thr	Leu	Ser	Lys	Ala	Asp	Tyr	Glu	Lys	His	Lys	Val	Tyr		
		195					200					205					
Ala	Cys	Glu	Val	Thr	His	Gln	Gly	Leu	Ser	Ser	Pro	Val	Thr	Lys	Ser		
	210					215					220						
Phe	Asn	Arg	Gly	Glu	Cys	Asp	Lys	Thr	His	Thr	Cys	Pro	Pro	Cys	Pro		
225					230					235					240		
Ala	Pro	Glu	Leu	Leu	Gly	Gly	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys		
			245						250					255			
Pro	Lys	Asp	Thr	Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val		
			260					265					270				
Val	Val	Asp	Val	Ser	His	Glu	Asp	Pro	Glu	Val	Lys	Phe	Asn	Trp	Tyr		
		275					280					285					

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
290 295 300

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
305 310 315 320

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
325 330 335

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
340 345 350

Pro Arg Glu Pro Gln Val Cys Thr Leu Pro Pro Ser Arg Asp Glu Leu
355 360 365

Thr Lys Asn Gln Val Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro
370 375 380

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
385 390 395 400

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
405 410 415

Val Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
420 425 430

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
435 440 445

Lys Ser Leu Ser Leu Ser Pro Gly Lys
450 455

<210> 123

<211> 215

<212> PRT

<213> Artificial

<220>

<223> Light chain 1 of bispecific, bivalent domain exchanged
<VEGF-ANG-2> antibody molecule Avastin-LC06-CH1-CL

<400> 123

Gln Pro Gly Leu Thr Gln Pro Pro Ser Val Ser Val Ala Pro Gly Gln
1 5 10 15

Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile Gly Ser Lys Ser Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Val Tyr
35 40 45

Asp Asp Ser Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50 55 60

Asn Ser Gly Asn Thr Ala Thr Leu Thr Ile Ser Arg Val Glu Ala Gly
65 70 75 80

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp Ser Ser Ser Asp His
85 90 95

Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Arg Thr Val Ala
100 105 110

Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser
115 120 125

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
130 135 140

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
145 150 155 160

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
165 170 175

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
180 185 190

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
195 200 205

Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 124

<211> 212
<212> PRT
<213> Artificial

<220>
<223> Light chain 2 of bispecific, bivalent domain exchanged
<VEGF-ANG-2> antibody molecule Avastin-LC06-CH1-CL

<400> 124

Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Gln Asp Ile Ser Asn Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Val Leu Ile
35 40 45

Tyr Phe Thr Ser Ser Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Thr Val Pro Trp
85 90 95

Thr Phe Gly Cys Gly Thr Lys Val Glu Ile Lys Ser Ser Ala Ser Thr
100 105 110

Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser
115 120 125

Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu
130 135 140

Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His
145 150 155 160

Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser
165 170 175

Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys
180 185 190

Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu
195 200 205

Pro Lys Ser Cys
210

<210> 125
<211> 459
<212> PRT
<213> Artificial

<220>
<223> Heavy chain 1 of bispecific, bivalent domain exchanged
<VEGF-ANG-2> antibody molecule Avastin-LC06-VH-VL

<400> 125

Gln Val Gln Leu Val Glu Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Pro Asn Pro Tyr Tyr Tyr Asp Ser Ser Gly Tyr Tyr Tyr
100 105 110

Pro Gly Ala Phe Asp Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser
115 120 125

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser
130 135 140

Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp

145					150					155				160	
Tyr	Phe	Pro	Glu	Pro	Val	Thr	Val	Ser	Trp	Asn	Ser	Gly	Ala	Leu	Thr
				165					170					175	
Ser	Gly	Val	His	Thr	Phe	Pro	Ala	Val	Leu	Gln	Ser	Ser	Gly	Leu	Tyr
			180					185					190		
Ser	Leu	Ser	Ser	Val	Val	Thr	Val	Pro	Ser	Ser	Ser	Leu	Gly	Thr	Gln
		195					200					205			
Thr	Tyr	Ile	Cys	Asn	Val	Asn	His	Lys	Pro	Ser	Asn	Thr	Lys	Val	Asp
	210					215					220				
Lys	Lys	Val	Glu	Pro	Lys	Ser	Cys	Asp	Lys	Thr	His	Thr	Cys	Pro	Pro
225					230					235					240
Cys	Pro	Ala	Pro	Glu	Leu	Leu	Gly	Gly	Pro	Ser	Val	Phe	Leu	Phe	Pro
				245					250					255	
Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr
			260					265					270		
Cys	Val	Val	Val	Asp	Val	Ser	His	Glu	Asp	Pro	Glu	Val	Lys	Phe	Asn
		275					280					285			
Trp	Tyr	Val	Asp	Gly	Val	Glu	Val	His	Asn	Ala	Lys	Thr	Lys	Pro	Arg
	290					295					300				
Glu	Glu	Gln	Tyr	Asn	Ser	Thr	Tyr	Arg	Val	Val	Ser	Val	Leu	Thr	Val
305					310					315					320
Leu	His	Gln	Asp	Trp	Leu	Asn	Gly	Lys	Glu	Tyr	Lys	Cys	Lys	Val	Ser
				325					330					335	
Asn	Lys	Ala	Leu	Pro	Ala	Pro	Ile	Glu	Lys	Thr	Ile	Ser	Lys	Ala	Lys
			340					345					350		
Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val	Tyr	Thr	Leu	Pro	Pro	Cys	Arg	Asp
		355					360					365			
Glu	Leu	Thr	Lys	Asn	Gln	Val	Ser	Leu	Trp	Cys	Leu	Val	Lys	Gly	Phe
	370					375					380				

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
385 390 395 400

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
405 410 415

Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
420 425 430

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
435 440 445

Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
450 455

<210> 126

<211> 439

<212> PRT

<213> Artificial

<220>

<223> Heavy chain 2 of bispecific, bivalent domain exchanged
<VEGF-ANG-2> antibody molecule Avastin-LC06-VH-VL

<400> 126

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Gln Asp Ile Ser Asn Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Val Leu Ile
35 40 45

Tyr Phe Thr Ser Ser Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Thr Val Pro Trp
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Ser Ser Ala Ser Thr
100 105 110

Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser
115 120 125

Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu
130 135 140

Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His
145 150 155 160

Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser
165 170 175

Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys
180 185 190

Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu
195 200 205

Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
210 215 220

Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
225 230 235 240

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
245 250 255

Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
260 265 270

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
275 280 285

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
290 295 300

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
305 310 315 320

Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg

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<210> 127
<211> 215
<212> PRT
<213> Artificial

<220>
<223> Light chain 1 of bispecific, bivalent domain exchanged
<VEGF-ANG-2> antibody molecule Avastin-LC06- VH-VL

<400> 127

Gln Pro Gly Leu Thr Gln Pro Pro Ser Val Ser Val Ala Pro Gly Gln
1          5          10          15

Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile Gly Ser Lys Ser Val
          20          25          30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Val Tyr
          35          40          45

Asp Asp Ser Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50          55          60

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Asn Ser Gly Asn Thr Ala Thr Leu Thr Ile Ser Arg Val Glu Ala Gly
65 70 75 80

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp Ser Ser Ser Asp His
85 90 95

Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Arg Thr Val Ala
100 105 110

Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser
115 120 125

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
130 135 140

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
145 150 155 160

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
165 170 175

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
180 185 190

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
195 200 205

Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 128

<211> 230

<212> PRT

<213> Artificial

<220>

<223> Light chain 2 of bispecific, bivalent domain exchanged
<VEGF-ANG-2> antibody molecule Avastin-LC06- VH-VL

<400> 128

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Asn Tyr

$\langle 210 \rangle$	129
$\langle 211 \rangle$	459

<212> PRT

<213> Artificial

<220>

<223> Heavy chain 1 of bispecific, bivalent domain exchanged
<VEGF-ANG-2> antibody molecule Avastin-LC06-VH-VL-SS

<400> 129

Gln Val Gln Leu Val Glu Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Cys Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Pro Asn Pro Tyr Tyr Tyr Asp Ser Ser Gly Tyr Tyr Tyr
100 105 110

Pro Gly Ala Phe Asp Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser
115 120 125

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser
130 135 140

Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
145 150 155 160

Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
165 170 175

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
180 185 190

Ser	Leu	Ser	Ser	Val	Val	Thr	Val	Pro	Ser	Ser	Ser	Leu	Gly	Thr	Gln
	195						200					205			
Thr	Tyr	Ile	Cys	Asn	Val	Asn	His	Lys	Pro	Ser	Asn	Thr	Lys	Val	Asp
	210					215					220				
Lys	Lys	Val	Glu	Pro	Lys	Ser	Cys	Asp	Lys	Thr	His	Thr	Cys	Pro	Pro
225					230					235					240
Cys	Pro	Ala	Pro	Glu	Leu	Leu	Gly	Gly	Pro	Ser	Val	Phe	Leu	Phe	Pro
				245					250					255	
Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr
			260					265					270		
Cys	Val	Val	Val	Asp	Val	Ser	His	Glu	Asp	Pro	Glu	Val	Lys	Phe	Asn
		275					280					285			
Trp	Tyr	Val	Asp	Gly	Val	Glu	Val	His	Asn	Ala	Lys	Thr	Lys	Pro	Arg
	290					295					300				
Glu	Glu	Gln	Tyr	Asn	Ser	Thr	Tyr	Arg	Val	Val	Ser	Val	Leu	Thr	Val
305					310					315					320
Leu	His	Gln	Asp	Trp	Leu	Asn	Gly	Lys	Glu	Tyr	Lys	Cys	Lys	Val	Ser
				325					330					335	
Asn	Lys	Ala	Leu	Pro	Ala	Pro	Ile	Glu	Lys	Thr	Ile	Ser	Lys	Ala	Lys
			340					345					350		
Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val	Tyr	Thr	Leu	Pro	Pro	Cys	Arg	Asp
		355					360					365			
Glu	Leu	Thr	Lys	Asn	Gln	Val	Ser	Leu	Trp	Cys	Leu	Val	Lys	Gly	Phe
	370					375					380				
Tyr	Pro	Ser	Asp	Ile	Ala	Val	Glu	Trp	Glu	Ser	Asn	Gly	Gln	Pro	Glu
385					390					395					400
Asn	Asn	Tyr	Lys	Thr	Thr	Pro	Pro	Val	Leu	Asp	Ser	Asp	Gly	Ser	Phe
				405					410					415	
Phe	Leu	Tyr	Ser	Lys	Leu	Thr	Val	Asp	Lys	Ser	Arg	Trp	Gln	Gln	Gly

420 425 430

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
435 440 445

Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
450 455

<210> 130
<211> 439
<212> PRT
<213> Artificial

<220>
<223> Heavy chain 2 of bispecific, bivalent domain exchanged
<VEGF-ANG-2> antibody molecule Avastin-LC06-VH-VL-SS

<400> 130

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Gln Asp Ile Ser Asn Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Val Leu Ile
35 40 45

Tyr Phe Thr Ser Ser Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Thr Val Pro Trp
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Ser Ser Ala Ser Thr
100 105 110

Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser
115 120 125

Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu
130 135 140

Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His
145 150 155 160

Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser
165 170 175

Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys
180 185 190

Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu
195 200 205

Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
210 215 220

Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
225 230 235 240

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
245 250 255

Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
260 265 270

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
275 280 285

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
290 295 300

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
305 310 315 320

Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
325 330 335

Glu Pro Gln Val Cys Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys
340 345 350

Asn Gln Val Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp
355 360 365

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
370 375 380

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser
385 390 395 400

Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
405 410 415

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
420 425 430

Leu Ser Leu Ser Pro Gly Lys
435

<210> 131
<211> 215
<212> PRT
<213> Artificial

<220>
<223> Light chain 1 of bispecific, bivalent domain exchanged
<VEGF-ANG-2> antibody molecule Avastin-LC06- VH-VL-SS

<400> 131

Gln Pro Gly Leu Thr Gln Pro Pro Ser Val Ser Val Ala Pro Gly Gln
1 5 10 15

Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile Gly Ser Lys Ser Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Val Tyr
35 40 45

Asp Asp Ser Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50 55 60

Asn Ser Gly Asn Thr Ala Thr Leu Thr Ile Ser Arg Val Glu Ala Gly
65 70 75 80

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp Ser Ser Ser Asp His
85 90 95

Tyr Val Phe Gly Cys Gly Thr Lys Val Thr Val Leu Arg Thr Val Ala
100 105 110

Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser
115 120 125

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
130 135 140

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
145 150 155 160

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
165 170 175

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
180 185 190

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
195 200 205

Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 132

<211> 230

<212> PRT

<213> Artificial

<220>

<223> Light chain 2 of bispecific, bivalent domain exchanged
<VEGF-ANG-2> antibody molecule Avastin-LC06- VH-VL-SS

<400> 132

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro Thr Tyr Ala Ala Asp Phe
50 55 60

Lys Arg Arg Phe Thr Phe Ser Leu Asp Thr Ser Lys Ser Thr Ala Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Tyr Pro His Tyr Tyr Gly Ser Ser His Trp Tyr Phe Asp Val
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Val Ala Ala
115 120 125

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
130 135 140

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
145 150 155 160

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
165 170 175

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
180 185 190

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
195 200 205

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
210 215 220

Phe Asn Arg Gly Glu Cys
225 230

<210> 133

<211> 706

<212> PRT

<213> Artificial

<220>

<223> Heavy chain 1 of bispecific, bivalent ScFab-Fc fusion
<VEGF-ANG-2> antibody molecule Avastin-LC06-N-scFab

<400> 133

Gln Pro Gly Leu Thr Gln Pro Pro Ser Val Ser Val Ala Pro Gly Gln
1 5 10 15

Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile Gly Ser Lys Ser Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Val Tyr
35 40 45

Asp Asp Ser Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50 55 60

Asn Ser Gly Asn Thr Ala Thr Leu Thr Ile Ser Arg Val Glu Ala Gly
65 70 75 80

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp Ser Ser Ser Asp His
85 90 95

Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Arg Thr Val Ala
100 105 110

Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser
115 120 125

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
130 135 140

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
145 150 155 160

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
165 170 175

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
180 185 190

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys
195 200 205

Ser Phe Asn Arg Gly Glu Cys Gly Gly Gly Gly Ser Gly Gly Gly Gly
210 215 220

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
225 230 235 240

Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gln	Val	Gln	Leu	Val	Glu	Ser	Gly	Ala	245	250	255
Glu	Val	Lys	Lys	Pro	Gly	Ala	Ser	Val	Lys	Val	Ser	Cys	Lys	Ala	Ser	260	265	270
Gly	Tyr	Thr	Phe	Thr	Gly	Tyr	Tyr	Met	His	Trp	Val	Arg	Gln	Ala	Pro	275	280	285
Gly	Gln	Gly	Leu	Glu	Trp	Met	Gly	Trp	Ile	Asn	Pro	Asn	Ser	Gly	Gly	290	295	300
Thr	Asn	Tyr	Ala	Gln	Lys	Phe	Gln	Gly	Arg	Val	Thr	Met	Thr	Arg	Asp	305	310	315
Thr	Ser	Ile	Ser	Thr	Ala	Tyr	Met	Glu	Leu	Ser	Arg	Leu	Arg	Ser	Asp	325	330	335
Asp	Thr	Ala	Val	Tyr	Tyr	Cys	Ala	Arg	Ser	Pro	Asn	Pro	Tyr	Tyr	Tyr	340	345	350
Asp	Ser	Ser	Gly	Tyr	Tyr	Tyr	Pro	Gly	Ala	Phe	Asp	Ile	Trp	Gly	Gln	355	360	365
Gly	Thr	Met	Val	Thr	Val	Ser	Ser	Ala	Ser	Thr	Lys	Gly	Pro	Ser	Val	370	375	380
Phe	Pro	Leu	Ala	Pro	Ser	Ser	Lys	Ser	Thr	Ser	Gly	Gly	Thr	Ala	Ala	385	390	395
Leu	Gly	Cys	Leu	Val	Lys	Asp	Tyr	Phe	Pro	Glu	Pro	Val	Thr	Val	Ser	405	410	415
Trp	Asn	Ser	Gly	Ala	Leu	Thr	Ser	Gly	Val	His	Thr	Phe	Pro	Ala	Val	420	425	430
Leu	Gln	Ser	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val	Val	Thr	Val	Pro	435	440	445
Ser	Ser	Ser	Leu	Gly	Thr	Gln	Thr	Tyr	Ile	Cys	Asn	Val	Asn	His	Lys	450	455	460

Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp
465 470 475 480

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
485 490 495

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
500 505 510

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
515 520 525

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
530 535 540

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
545 550 555 560

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
565 570 575

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
580 585 590

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
595 600 605

Thr Leu Pro Pro Cys Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu
610 615 620

Trp Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
625 630 635 640

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
645 650 655

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
660 665 670

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
675 680 685

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro

690

695

700

Gly Lys
705

<210> 134
<211> 699
<212> PRT
<213> Artificial

<220>
<223> Heavy chain 2 of bispecific, bivalent ScFab-Fc fusion
<VEGF-ANG-2> antibody molecule Avastin-LC06-N-scFab

<400> 134

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
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Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Gln Asp Ile Ser Asn Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Val Leu Ile
35 40 45

Tyr Phe Thr Ser Ser Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Thr Val Pro Trp
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205

Phe Asn Arg Gly Glu Cys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
210 215 220

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
225 230 235 240

Gly Gly Gly Ser Gly Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly
245 250 255

Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly
260 265 270

Tyr Thr Phe Thr Asn Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly
275 280 285

Lys Gly Leu Glu Trp Val Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro
290 295 300

Thr Tyr Ala Ala Asp Phe Lys Arg Arg Phe Thr Phe Ser Leu Asp Thr
305 310 315 320

Ser Lys Ser Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
325 330 335

Thr Ala Val Tyr Tyr Cys Ala Lys Tyr Pro His Tyr Tyr Gly Ser Ser
340 345 350

His Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser
355 360 365

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser
370 375 380

Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
385 390 395 400

Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
405 410 415

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
420 425 430

Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln
435 440 445

Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp
450 455 460

Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro
465 470 475 480

Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro
485 490 495

Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr
500 505 510

Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn
515 520 525

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
530 535 540

Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
545 550 555 560

Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
565 570 575

Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys
580 585 590

Gly Gln Pro Arg Glu Pro Gln Val Cys Thr Leu Pro Pro Ser Arg Asp
595 600 605

Glu Leu Thr Lys Asn Gln Val Ser Leu Ser Cys Ala Val Lys Gly Phe

610	615	620
Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu		
625	630	635 640
Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe		
	645	650 655
Phe Leu Val Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly		
	660	665 670
Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr		
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Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile Gly Ser Lys Ser Val		
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His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Val Tyr		
	35	40 45
Asp Asp Ser Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser		
	50	55 60
Asn Ser Gly Asn Thr Ala Thr Leu Thr Ile Ser Arg Val Glu Ala Gly		
	65	70 75 80
Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp Ser Ser Ser Asp His		
	85	90 95

Tyr	Val	Phe	Gly	Cys	Gly	Thr	Lys	Val	Thr	Val	Leu	Arg	Thr	Val	Ala	
			100					105						110		
Ala	Pro	Ser	Val	Phe	Ile	Phe	Pro	Pro	Ser	Asp	Glu	Gln	Leu	Lys	Ser	
		115					120					125				
Gly	Thr	Ala	Ser	Val	Val	Cys	Leu	Leu	Asn	Asn	Phe	Tyr	Pro	Arg	Glu	
	130					135					140					
Ala	Lys	Val	Gln	Trp	Lys	Val	Asp	Asn	Ala	Leu	Gln	Ser	Gly	Asn	Ser	
145					150					155					160	
Gln	Glu	Ser	Val	Thr	Glu	Gln	Asp	Ser	Lys	Asp	Ser	Thr	Tyr	Ser	Leu	
				165					170					175		
Ser	Ser	Thr	Leu	Thr	Leu	Ser	Lys	Ala	Asp	Tyr	Glu	Lys	His	Lys	Val	
			180					185					190			
Tyr	Ala	Cys	Glu	Val	Thr	His	Gln	Gly	Leu	Ser	Ser	Pro	Val	Thr	Lys	
		195					200					205				
Ser	Phe	Asn	Arg	Gly	Glu	Cys	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	
	210					215					220					
Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	
225					230					235					240	
Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gln	Val	Gln	Leu	Val	Glu	Ser	Gly	Ala	
				245					250					255		
Glu	Val	Lys	Lys	Pro	Gly	Ala	Ser	Val	Lys	Val	Ser	Cys	Lys	Ala	Ser	
			260					265					270			
Gly	Tyr	Thr	Phe	Thr	Gly	Tyr	Tyr	Met	His	Trp	Val	Arg	Gln	Ala	Pro	
		275					280					285				
Gly	Gln	Cys	Leu	Glu	Trp	Met	Gly	Trp	Ile	Asn	Pro	Asn	Ser	Gly	Gly	
	290					295					300					
Thr	Asn	Tyr	Ala	Gln	Lys	Phe	Gln	Gly	Arg	Val	Thr	Met	Thr	Arg	Asp	
305					310					315					320	

Thr Ser Ile Ser Thr Ala Tyr Met Glu Leu Ser Arg Leu Arg Ser Asp
325 330 335

Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ser Pro Asn Pro Tyr Tyr Tyr
340 345 350

Asp Ser Ser Gly Tyr Tyr Tyr Pro Gly Ala Phe Asp Ile Trp Gly Gln
355 360 365

Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
370 375 380

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
385 390 395 400

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
405 410 415

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
420 425 430

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
435 440 445

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
450 455 460

Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp
465 470 475 480

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
485 490 495

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
500 505 510

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
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Leu	Asn	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Ala	Pro	Lys	Val	Leu	Ile	35	40	45	
Tyr	Phe	Thr	Ser	Ser	Leu	His	Ser	Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly	50	55	60	
Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Ser	Ser	Leu	Gln	Pro	65	70	75	80
Glu	Asp	Phe	Ala	Thr	Tyr	Tyr	Cys	Gln	Gln	Tyr	Ser	Thr	Val	Pro	Trp	85	90	95	
Thr	Phe	Gly	Cys	Gly	Thr	Lys	Val	Glu	Ile	Lys	Arg	Thr	Val	Ala	Ala	100	105	110	
Pro	Ser	Val	Phe	Ile	Phe	Pro	Pro	Ser	Asp	Glu	Gln	Leu	Lys	Ser	Gly	115	120	125	
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Lys	Val	Gln	Trp	Lys	Val	Asp	Asn	Ala	Leu	Gln	Ser	Gly	Asn	Ser	Gln	145	150	155	160
Glu	Ser	Val	Thr	Glu	Gln	Asp	Ser	Lys	Asp	Ser	Thr	Tyr	Ser	Leu	Ser	165	170	175	
Ser	Thr	Leu	Thr	Leu	Ser	Lys	Ala	Asp	Tyr	Glu	Lys	His	Lys	Val	Tyr	180	185	190	
Ala	Cys	Glu	Val	Thr	His	Gln	Gly	Leu	Ser	Ser	Pro	Val	Thr	Lys	Ser	195	200	205	
Phe	Asn	Arg	Gly	Glu	Cys	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	210	215	220	
Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	225	230	235	240

Gly Gly Gly Ser Gly Gly Glu Val Gln Leu Val Glu Ser Gly Gly Gly
245 250 255

Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly
260 265 270

Tyr Thr Phe Thr Asn Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly
275 280 285

Lys Cys Leu Glu Trp Val Gly Trp Ile Asn Thr Tyr Thr Gly Glu Pro
290 295 300

Thr Tyr Ala Ala Asp Phe Lys Arg Arg Phe Thr Phe Ser Leu Asp Thr
305 310 315 320

Ser Lys Ser Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp
325 330 335

Thr Ala Val Tyr Tyr Cys Ala Lys Tyr Pro His Tyr Tyr Gly Ser Ser
340 345 350

His Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser
355 360 365

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser
370 375 380

Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
385 390 395 400

Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
405 410 415

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
420 425 430

Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln
435 440 445

Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp
450 455 460

Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro

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Cys	Pro	Ala	Pro	Glu 485	Leu	Leu	Gly	Gly	Pro 490	Ser	Val	Phe	Leu	Phe 495	Pro
Pro	Lys	Pro	Lys 500	Asp	Thr	Leu	Met	Ile 505	Ser	Arg	Thr	Pro	Glu 510	Val	Thr
Cys	Val	Val 515	Val	Asp	Val	Ser	His 520	Glu	Asp	Pro	Glu	Val 525	Lys	Phe	Asn
Trp	Tyr 530	Val	Asp	Gly	Val	Glu 535	Val	His	Asn	Ala	Lys 540	Thr	Lys	Pro	Arg
Glu 545	Glu	Gln	Tyr	Asn	Ser 550	Thr	Tyr	Arg	Val	Val 555	Ser	Val	Leu	Thr	Val 560
Leu	His	Gln	Asp	Trp 565	Leu	Asn	Gly	Lys	Glu 570	Tyr	Lys	Cys	Lys	Val 575	Ser
Asn	Lys	Ala	Leu 580	Pro	Ala	Pro	Ile	Glu 585	Lys	Thr	Ile	Ser	Lys 590	Ala	Lys
Gly	Gln	Pro 595	Arg	Glu	Pro	Gln	Val 600	Cys	Thr	Leu	Pro	Pro 605	Ser	Arg	Asp
Glu 610	Leu	Thr	Lys	Asn	Gln	Val 615	Ser	Leu	Ser	Cys	Ala 620	Val	Lys	Gly	Phe
Tyr 625	Pro	Ser	Asp	Ile	Ala 630	Val	Glu	Trp	Glu	Ser 635	Asn	Gly	Gln	Pro	Glu 640
Asn	Asn	Tyr	Lys	Thr 645	Thr	Pro	Pro	Val	Leu 650	Asp	Ser	Asp	Gly	Ser 655	Phe
Phe	Leu	Val	Ser 660	Lys	Leu	Thr	Val	Asp 665	Lys	Ser	Arg	Trp	Gln 670	Gln	Gly
Asn	Val	Phe 675	Ser	Cys	Ser	Val	Met 680	His	Glu	Ala	Leu	His 685	Asn	His	Tyr
Thr	Gln 690	Lys	Ser	Leu	Ser	Leu	Ser	Pro	Gly	Lys					

