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<110> Avipep Pty Ltd

<120> IMMUNO-CONJUGATES AND METHODS FOR PRODUCING THEM 2

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<150> US61/289497
<151> 2009-12-23

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<170> PatentIn version 3.5

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<400> 11

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<400> 12

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<210> 22
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<400> 26

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Met Ser Ser Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
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<400> 28

Arg Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr Leu Gln
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Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys Ala Arg
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Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
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Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys Ala Lys
20 25 30

Asp

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Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr Met Glu
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Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
20 25 30

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

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<400> 33

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

<210> 34
<211> 33
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<400> 34

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Met Asn Ser Leu Arg Thr Glu Asp Thr Ala Leu Tyr Tyr Cys Ala Lys

20 25 30

Asp

<210> 35
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<212> PRT
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<220>
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<400> 35

Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln
1 5 10 15

Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
20 25 30

<210> 36
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<220>
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<400> 36

Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val Val Leu Thr
1 5 10 15

Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr Cys Ala Arg
20 25 30

Ile

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<400> 37

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

<210> 38
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<400> 38

Arg Ile Thr Ile Asn Pro Asp Thr Ser Lys Asn Gln Phe Ser Leu Gln
1 5 10 15

Leu Asn Ser Val Thr Pro Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
20 25 30

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<400> 39

His Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr Leu Gln
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Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys Ala Arg
20 25 30

<210> 40
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<400> 40

Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Ala Tyr Met Glu
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Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
20 25 30

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<400> 41

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
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Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
20 25 30

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<400> 42

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
1 5 10 15

Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala Thr Tyr Tyr Cys
20 25 30

<210> 43
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<400> 43

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr
1 5 10 15

Leu Thr Ile Ser Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr Tyr Cys
20 25 30

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Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr
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Leu Thr Ile Ser Ser Leu Gln Ser Glu Asp Phe Ala Val Tyr Tyr Cys
20 25 30

<210> 45
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<400> 45

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

<210> 46
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<400> 46

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

<210> 47
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<400> 47

Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
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Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys
20 25 30

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<220>
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<400> 48

Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
1 5 10 15

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

<210> 49
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<400> 49

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
1 5 10 15

Leu Thr Ile Ser Cys Leu Gln Ser Glu Asp Phe Ala Thr Tyr Tyr Cys
20 25 30

<210> 50
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<212> PRT
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Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr
1 5 10 15

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
20 25 30

<210> 51
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<400> 51

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

Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys
20 25 30

<210> 52
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<400> 52

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
1 5 10 15

Leu Thr Ile Asn Ser Leu Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys
20 25 30

<210> 53
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<220>
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<400> 53

Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
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Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Tyr Cys
20 25 30

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<400> 54

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
1 5 10 15

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

<210> 55
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<400> 55

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

Leu Thr Ile Asn Asn Ile Glu Ser Glu Asp Ala Ala Tyr Tyr Phe Cys
20 25 30

<210> 56
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<220>
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<400> 56

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
1 5 10 15

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Val Ala Thr Tyr Tyr Cys
20 25 30

<210> 57

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<220>
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<400> 57

Gly Gly Gly Gly Ser
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<210> 58
<211> 711
<212> DNA
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<220>
<223> nucleotide sequence encoding AVP04-07 anti TAG72 diabody

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ccggaacagg gcctggaatg gattggctat tttagcccgg gcaacgatga ttttaaatat 180

aacgaacgtt ttaaaggcaa agcgaccctg accgcggata aaagcagcag caccgcgtat 240

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aatatggcgt attggggtca gggcacctcg gtcaccgtga gcagcggtgg cggcggcagc 360

gatatcgtga tgacccagag cccgagcagc ctgccggtga gcgtgggcga aaaagtgacc 420

ctgagctgca aaagcagcca gagcctgctg tatagcggca atcagaaaaa ctatctggcg 480

tggtatcagc agaaaccggg tcagagcccg aaactgctga tttattgggc gagcacccgt 540

gaaagcggcg tgccggatcg ttttaccggc agcggtagcg gcaccgattt taccctgagc 600

attagcagcg tggaaaccga agatctggcg gtgtattatt gccagcagta ttatagctat 660

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20 25 30

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

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

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

Thr Arg Ser Leu Asn Met Ala Tyr Trp Gly Gln Gly Thr Ser Val Thr
            100                 105                 110

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

Ser Ser Leu Pro Val Ser Val Gly Glu Lys Val Thr Leu Ser Cys Lys
    130                 135                 140

Ser Ser Gln Ser Leu Leu Tyr Ser Gly Asn Gln Lys Asn Tyr Leu Ala
145                 150                 155                 160

Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Trp
                165                 170                 175

Ala Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly
            180                 185                 190

Ser Gly Thr Asp Phe Thr Leu Ser Ile Ser Ser Val Glu Thr Glu Asp
        195                 200                 205

Leu Ala Val Tyr Tyr Cys Gln Gln Tyr Tyr Ser Tyr Pro Leu Thr Phe
    210                 215                 220

Gly Ala Gly Thr Lys Leu Val Leu Lys Arg Ala Ala Ala Leu Glu His
225                 230                 235                 240

His His His His His
                245
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<211> 804
<212> DNA
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cccgggaaag gcctggagta catggggctc atctatcctg gtgactctga caccaaatac      180
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gtgggatatt gcagtagttc caactgcgca aagtggcctg aatacttcca gcattggggc 360

cagggcaccc tggtcaccgt ttcctcaggt ggaggcggtt cacagtctgt gttgacgcag 420

ccgccctcag tgtctgcggc cccaggacag aaggtcacca tctcctgctc tggaagcagc 480

tccaacattg ggaataatta tgtatcctgg taccagcagc tcccaggaac agtccccaaa 540

ctcctcatct atggtcacac caatcggccc gcaggggtcc ctgaccgatt ctctggctcc 600

aagtctggca cctcagcctc cctggccatc agtgggttcc ggtccgagga tgaggctgat 660

tattactgtg cagcatggga tgacagcctg agtggttggg tgttcggcgg agggaccaag 720

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<212> PRT
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<400> 61

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Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
20 25 30

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

Gly Leu Ile Tyr Pro Gly Asp Ser Asp Thr Lys Tyr Ser Pro Ser Phe
50 55 60

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

Leu Gln Trp Ser Ser Leu Lys Pro Ser Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg His Asp Val Gly Tyr Cys Ser Ser Ser Asn Cys Ala Lys Trp
100 105 110

Pro Glu Tyr Phe Gln His Trp Gly Gln Gly Thr Leu Val Thr Val Ser
115 120 125

Ser Gly Gly Gly Gly Ser Gln Ser Val Leu Thr Gln Pro Pro Ser Val
130 135 140

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145                 150                 155                 160

Ser Asn Ile Gly Asn Asn Tyr Val Ser Trp Tyr Gln Gln Leu Pro Gly
                165                 170                 175

Thr Val Pro Lys Leu Leu Ile Tyr Gly His Thr Asn Arg Pro Ala Gly
            180                 185                 190

Val Pro Asp Arg Phe Ser Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu
        195                 200                 205

Ala Ile Ser Gly Phe Arg Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala
    210                 215                 220

Ala Trp Asp Asp Ser Leu Ser Gly Trp Val Phe Gly Gly Gly Thr Lys
225                 230                 235                 240

Leu Thr Val Leu Gly Ala Ala Ala Glu Gln Lys Leu Ile Ser Glu Glu
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Asp Leu Asn Gly Ala Ala His His His His His His
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<220>
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<400> 62

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ccggataaag gcctggaact ggtggcgacc attaacagca acggtggaag cacctattat      180
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ctgcagatga acagcctgcg taccgaagat accgcggtgt attattgcgc gcgtgatcgt      300
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ggtgatcgtg tgaccattac ctgcagcgcg agcagcagcg tgagctatat gcattggtat      480
cagcagaaac cgggcaaagc gccgaaacgt tggatttatg ataccagcaa actggcgagc      540
ggcgtgccga gccgttttag cggcagcggc agcggcaccg attatacctt taccattagc      600
agcctgcagc cggaagatat tgcgacctat tattgccagc agtggagcag caacccgccg      660
acctttggcc agggcaccaa actgcagatt aaacgtgcgg ccgcactcga gcaccaccac      720
caccaccac                                                              729
```

<210> 63
<211> 243
<212> PRT
<213> Artificial

<220>
<223> amino acid sequence of AVP02-60 anti-MucI diabody

<400> 63

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

Ala Thr Ile Asn Ser Asn Gly Gly Ser Thr Tyr Tyr Pro 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 Thr Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Arg Asp Gly Tyr Asp Glu Gly Phe Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gln Ile Gln
115 120 125

Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
130 135 140

Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met His Trp Tyr
145 150 155 160

Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser
165 170 175

Lys Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
180 185 190

Thr Asp Tyr Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
195 200 205

Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Pro Thr Phe Gly Gln
210 215 220

Gly Thr Lys Leu Gln Ile Lys Arg Ala Ala Ala Leu Glu His His His

225 230 235 240

His His His

<210> 64
<211> 804
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence encoding a modified AVP07-17 anti-HER2 diabody replacing CDR3H Cysteine residues Cys104 (Kabat numbering H100) and Cys109 (H100E) with Alanines and comprising a N-terminal serine designated AVP07-86

<400> 64
agcgtgcagc tggtgcagtc tggggcagag gtgaaaaagc ccggggagtc tctgaagatc 60

tcctgtaagg gttctggata cagctttacc agctactgga tcgcctgggt gcgccagatg 120

cccgggaaag gcctggagta catggggctc atctatcctg gtgactctga caccaaatac 180

agcccgtcct tccaaggcca ggtcaccatc tcagtcgaca agtccgtcag cactgcctac 240

ttgcaatgga gcagtctgaa gccctcggac agcgccgtgt atttttgtgc gagacatgac 300

gtgggatatg cgagtagttc caacgcggca aagtggcctg aatacttcca gcattggggc 360

cagggcaccc tggtcaccgt ttcctcaggt ggaggcggtt cacagtctgt gttgacgcag 420

ccgccctcag tgtctgcggc cccaggacag aaggtcacca tctcctgctc tggaagcagc 480

tccaacattg ggaataatta tgtatcctgg taccagcagc tcccaggaac agtccccaaa 540

ctcctcatct atggtcacac caatcggccc gcaggggtcc ctgaccgatt ctctggctcc 600

aagtctggca cctcagcctc cctggccatc agtgggttcc ggtccgagga tgaggctgat 660

tattactgtg cagcatggga tgacagcctg agtggttggg tgttcggcgg agggaccaag 720

ctgaccgtcc taggtgcggc cgcagaacaa aaactcatct cagaagagga tctgaatggg 780

gccgcacatc accatcatca ccat 804

<210> 65
<211> 268
<212> PRT
<213> Artificial

<220>
<223> amino acid sequence of modified AVP07-17 anti-HER2 diabody replacing CDR3H Cysteine residues Cys104 (Kabat numbering H100) and Cys109 (H100E) with Alanines and comprising a N-terminal serine designated AVP07-86

<400> 65

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

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
20 25 30

```
Trp Ile Ala Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Tyr Met
        35                  40                  45

Gly Leu Ile Tyr Pro Gly Asp Ser Asp Thr Lys Tyr Ser Pro Ser Phe
    50                  55                  60

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

Leu Gln Trp Ser Ser Leu Lys Pro Ser Asp Ser Ala Val Tyr Phe Cys
                85                  90                  95

Ala Arg His Asp Val Gly Tyr Ala Ser Ser Ser Asn Ala Ala Lys Trp
            100                 105                 110

Pro Glu Tyr Phe Gln His Trp Gly Gln Gly Thr Leu Val Thr Val Ser
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gln Ser Val Leu Thr Gln Pro Pro Ser Val
    130                 135                 140

Ser Ala Ala Pro Gly Gln Lys Val Thr Ile Ser Cys Ser Gly Ser Ser
145                 150                 155                 160

Ser Asn Ile Gly Asn Asn Tyr Val Ser Trp Tyr Gln Gln Leu Pro Gly
                165                 170                 175

Thr Val Pro Lys Leu Leu Ile Tyr Gly His Thr Asn Arg Pro Ala Gly
            180                 185                 190

Val Pro Asp Arg Phe Ser Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu
        195                 200                 205

Ala Ile Ser Gly Phe Arg Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala
    210                 215                 220

Ala Trp Asp Asp Ser Leu Ser Gly Trp Val Phe Gly Gly Gly Thr Lys
225                 230                 235                 240

Leu Thr Val Leu Gly Ala Ala Ala Glu Gln Lys Leu Ile Ser Glu Glu
                245                 250                 255

Asp Leu Asn Gly Ala Ala His His His His His His
            260                 265
```

<210> 66
<211> 39
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of mutagenic primer for substituting the

N-terminal Gln residue with a Ser residue in AVP04-07

<400> 66
cccagccggc catggcgagc gtgcagctgc agcagagcg 39

<210> 67
<211> 39
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of mutagenic primer for substituting the N-terminal Gln residue with a Ser residue in AVP04-07

<400> 67
cgctctgctg cagctgcacg ctcgccatgg ccggctggg 39

<210> 68
<211> 66
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of mutagenic primer for introducing cysteine residue substitutions at positions 38 and 42 in the VL FR2 of AVP04-07

<400> 68
cagaaaaact atctggcgtg gtatcagtgc aaaccgggtt gcagcccgaa actgctgatt 60

tattgg 66

<210> 69
<211> 66
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of mutagenic primer for introducing cysteine residue substitutions at positions 38 and 42 in the VL FR2 of AVP04-07

<400> 69
ccaataaatc agcagtttcg ggctgcaacc cggtttgcac tgataccacg ccagatagtt 60

tttctg 66

<210> 70
<211> 72
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of mutagenic primer for introducing cysteine residue substitutions at positions 38 and 44 in the VL FR2 of AVP04-07

<400> 70
cagaaaaact atctggcgtg gtatcagtgc aaaccgggtc agagctgcaa actgctgatt 60

tattgggcga gc 72

<210> 71

<211> 72
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of mutagenic primer for introducing cysteine residue substitutions at positions 38 and 44 in the VL FR2 of AVP04-07

<400> 71
gctcgcccaa taaatcagca gtttgcagct ctgacccggt ttgcactgat accacgccag 60

atagtttttc tg 72

<210> 72
<211> 65
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of mutagenic primer for introducing cysteine residue substitutions at positions 78 and 82 in the VL FR3 of AVP04-07

<400> 72
ccgattttac cctgagcatt agcagctgcg aaaccgaatg cctggcggtg tattattgcc 60

agcag 65

<210> 73
<211> 65
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of mutagenic primer for introducing cysteine residue substitutions at positions 78 and 82 in the VL FR3 of AVP04-07

<400> 73
ctgctggcaa taatacaccg ccaggcattc ggtttcgcag ctgctaatgc tcagggtaaa 60

atcgg 65

<210> 74
<211> 67
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of mutagenic primer for introducing cysteine residue substitutions at positions 39 and 43 in the VH FR2 of AVP04-07

<400> 74
cgatcatgcg attcattggg tgaaatgcaa tccggaatgc ggcctggaat ggattggcta 60

ttttagc 67

<210> 75
<211> 67
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of mutagenic primer for introducing cysteine residue substitutions at positions 39 and 43 in the VH FR2 of AVP04-07

<400> 75
gctaaaatag ccaatccatt ccaggccgca ttccggattg catttcaccc aatgaatcgc 60

atgatcg 67

<210> 76
<211> 70
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of mutagenic primer for introducing cysteine residue substitutions at positions 39 and 45 in the VH FR2 of AVP04-07

<400> 76
cgatcatgcg attcattggg tgaaatgcaa tccggaacag ggctgcgaat ggattggcta 60

ttttagcccg 70

<210> 77
<211> 70
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of mutagenic primer for introducing cysteine residue substitutions at positions 39 and 45 in the VH FR2 of AVP04-07

<400> 77
cgggctaaaa tagccaatcc attcgcagcc ctgttccgga ttgcatttca cccaatgaat 60

cgcatgatcg 70

<210> 78
<211> 58
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of mutagenic primer for introducing cysteine residue substitutions at positions 82C and 86 in the VH FR3 of AVP04-07

<400> 78
gcgtatctgc agctgaacag ctgcaccagc gaatgcagcg cggtgtattt ttgcaccc 58

<210> 79
<211> 58
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of mutagenic primer for introducing cysteine residue substitutions at positions 82C and 86 in the VH FR3 of AVP04-07

<400> 79

gggtgcaaaa atacaccgcg ctgcattcgc tggtgcagct gttcagctgc agatacgc 58

<210> 80
<211> 60
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of mutagenic primer for introducing cysteine residue substitutions at positions 70 and 79 in the VH FR3 of AVP04-07

<400> 80
ggcaaagcga ccctgtgcgc ggataaaagc agcagcaccg cgtgcctgca gctgaacagc 60

<210> 81
<211> 56
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of mutagenic primer for introducing cysteine residue substitutions at positions 70 and 79 in the VH FR3 of AVP04-07

<400> 81
cgctgctaat gcacagggta aaatcggtgc cgctaccgct gccgcaaaaa cgatcc 56

<210> 82
<211> 54
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of mutagenic primer for introducing cysteine residue substitutions at positions 72 and 75 in the VH FR3 of AVP04-07

<400> 82
ggcaaagcga ccctgaccgc gtgcaaaagc tgcagcaccg cgtatctgca gctg 54

<210> 83
<211> 54
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of mutagenic primer for introducing cysteine residue substitutions at positions 72 and 75 in the VH FR3 of AVP04-07

<400> 83
cagctgcaga tacgcggtgc tgcagctttt gcacgcggtc agggtcgctt tgcc 54

<210> 84
<211> 48
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of mutagenic primer for introducing cysteine residue substitutions at positions 65 and 72 in the VL FR3 of AVP04-07

<400> 84
cgttttaccg gctgcggtag cggcaccgat ttttgcctga gcattagc 48

<210> 85
<211> 48
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of mutagenic primer for introducing cysteine residue substitutions at positions 65 and 72 in the VL FR3 of AVP04-07

<400> 85
gctaatgctc aggcaaaaat cggtgccgct accgcagccg gtaaaacg 48

<210> 86
<211> 50
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of mutagenic primer for modification of linker residues of AVP04-79 for scFv expression

<400> 86
ctcggtcacc gtgagcagcg gtggcggcgg cagcggtggc ggcggcagcg 50

<210> 87
<211> 50
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of mutagenic primer for modification of linker residues of AVP04-79 for scFv expression

<400> 87
cgctgccgcc gccaccgctg ccgccgccac cgctgctcac ggtgaccgag 50

<210> 88
<211> 42
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of mutagenic primer for modification of linker residues of AVP04-79 for triabody expression

<400> 88
ggcacctcgg tcaccgtgag cgatatcgtg atgacccaga gc 42

<210> 89
<211> 42
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of mutagenic primer for modification of linker residues of AVP04-79 for triabody expression

<400> 89

gctctgggtc atcacgatat cgctcacggt gaccgaggtg cc 42

<210> 90
<211> 39
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of mutagenic primer for AVP07-17 anti-HER2 diabody replacing CDR3H Cysteine residues with alanines designated AVP07-86

<400> 90
cccagccggc catggcgagc gtgcagctgg tgcagtctg 39

<210> 91
<211> 39
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of mutagenic primer for AVP07-17 anti-HER2 diabody replacing CDR3H Cysteine residues with alanines designated AVP07-86

<400> 91
cagactgcac cagctgcacg ctcgccatgg ccggctggg 39

<210> 92
<211> 66
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of mutagenic primer for introducing cysteine residue substitutions at positions 38 and 42 in the VL FR2 of AVP02-60

<400> 92
cgtgagctat atgcattggt atcagtgcaa accgggctgc gcgccgaaac gttggattta 60

tgatac 66

<210> 93
<211> 66
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of mutagenic primer for introducing cysteine residue substitutions at positions 38 and 42 in the VL FR2 of AVP02-60

<400> 93
gtatcataaa tccaacgttt cggcgcgcag cccggtttgc actgatacca atgcatatag 60

ctcacg 66

<210> 94
<211> 55
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of mutagenic primer for introducing cysteine residue substitutions at positions 39 and 43 in the VH FR2 of AVP02-60

<400> 94
ctatggcatg agctgggtgc gttgcgcgcc ggattgcggc ctggaactgg tggcg 55

<210> 95
<211> 55
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of mutagenic primer for introducing cysteine residue substitutions at positions 39 and 43 in the VH FR2 of AVP02-60

<400> 95
cgccaccagt tccaggccgc aatccggcgc gcaacgcacc cagctcatgc catag 55

<210> 96
<211> 65
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of mutagenic primer for introducing cysteine residue substitutions at positions 38 and 42 in the VL FR2 of AVP07-86

<400> 96
gggaataatt atgtatcctg gtaccagtgc ctcccaggat gcgtccccaa actcctcatc 60

tatgg 65

<210> 97
<211> 65
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of mutagenic primer for introducing cysteine residue substitutions at positions 38 and 42 in the VL FR2 of AVP07-86

<400> 97
ccatagatga ggagtttggg gacgcatcct gggaggcact ggtaccagga tacataatta 60

ttccc 65

<210> 98
<211> 51
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of mutagenic primer for introducing cysteine residue substitutions at positions 39 and 43 in the VH FR2 of AVP07-86

<400> 98
ggatcgcctg ggtgcgctgc atgcccgggt gcggcctgga gtacatgggg c 51

<210> 99
<211> 51
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of mutagenic primer for introducing cysteine residue substitutions at positions 39 and 43 in the VH FR2 of AVP07-86

<400> 99
gccccatgta ctccaggccg cacccgggca tgcagcgcac ccaggcgatc c 51

<210> 100
<211> 735
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of an anti-TAG72 diabody comprising cysteine replacement mutations in the VL FR2 Kabat positions 38 and 42 designated AVP04-79.

<400> 100
agcgtgcagc tgcagcagag cgatgcggaa ctggtgaaac cgggcgcgag cgtgaaaatt 60

agctgcaaag cgagcggcta tacctttacc gatcatgcga ttcattgggt gaaacagaat 120

ccggaacagg gcctggaatg gattggctat tttagcccgg gcaacgatga ttttaaatat 180

aacgaacgtt ttaaaggcaa agcgaccctg accgcggata aaagcagcag caccgcgtat 240

ctgcagctga acagcctgac cagcgaagat agcgcggtgt atttttgcac ccgtagcctg 300

aatatggcgt attggggtca gggcacctcg gtcaccgtga gcagcggtgg cggcggcagc 360

gatatcgtga tgacccagag cccgagcagc ctgccggtga gcgtgggcga aaaagtgacc 420

ctgagctgca aaagcagcca gagcctgctg tatagcggca atcagaaaaa ctatctggcg 480

tggtatcagt gcaaaccggg ttgcagcccg aaactgctga tttattgggc gagcacccgt 540

gaaagcggcg tgccggatcg ttttaccggc agcggtagcg gcaccgattt taccctgagc 600

attagcagcg tggaaaccga agatctggcg gtgtattatt gccagcagta ttatagctat 660

ccgctgacct ttggtgcggg caccaaactg gtgctgaaac gtgcggccgc actcgagcac 720

caccaccacc accac 735

<210> 101
<211> 245
<212> PRT
<213> Artificial

<220>
<223> amino acid sequence of an anti-TAG72 diabody comprising cysteine replacement mutations in the VL FR2 Kabat positions 38 and 42 designated AVP04-79.

<400> 101

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

```
Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp His
            20                  25                  30

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

Gly Tyr Phe Ser Pro Gly Asn Asp Asp Phe Lys Tyr Asn Glu Arg Phe
    50                  55                  60

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

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

Thr Arg Ser Leu Asn Met Ala Tyr Trp Gly Gln Gly Thr Ser Val Thr
            100                 105                 110

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

Ser Ser Leu Pro Val Ser Val Gly Glu Lys Val Thr Leu Ser Cys Lys
    130                 135                 140

Ser Ser Gln Ser Leu Leu Tyr Ser Gly Asn Gln Lys Asn Tyr Leu Ala
145                 150                 155                 160

Trp Tyr Gln Cys Lys Pro Gly Cys Ser Pro Lys Leu Leu Ile Tyr Trp
                165                 170                 175

Ala Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly
            180                 185                 190

Ser Gly Thr Asp Phe Thr Leu Ser Ile Ser Ser Val Glu Thr Glu Asp
        195                 200                 205

Leu Ala Val Tyr Tyr Cys Gln Gln Tyr Tyr Ser Tyr Pro Leu Thr Phe
    210                 215                 220

Gly Ala Gly Thr Lys Leu Val Leu Lys Arg Ala Ala Ala Leu Glu His
225                 230                 235                 240

His His His His His
                245
```

<210> 102
<211> 735
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of an anti-TAG72 diabody comprising cysteine

replacement mutations in the VL FR2 Kabat positions 38 and 44 is designated AVP04-80.

<400> 102
agcgtgcagc tgcagcagag cgatgcggaa ctggtgaaac cgggcgcgag cgtgaaaatt 60

agctgcaaag cgagcggcta tacctttacc gatcatgcga ttcattgggt gaaacagaat 120

ccggaacagg gcctggaatg gattggctat tttagcccgg gcaacgatga ttttaaatat 180

aacgaacgtt ttaaaggcaa agcgaccctg accgcggata aaagcagcag caccgcgtat 240

ctgcagctga acagcctgac cagcgaagat agcgcggtgt atttttgcac ccgtagcctg 300

aatatggcgt attggggtca gggcacctcg gtcaccgtga gcagcggtgg cggcggcagc 360

gatatcgtga tgacccagag cccgagcagc ctgccggtga gcgtgggcga aaaagtgacc 420

ctgagctgca aaagcagcca gagcctgctg tatagcggca atcagaaaaa ctatctggcg 480

tggtatcagt gcaaaccggg tcagagctgc aaactgctga tttattgggc gagcacccgt 540

gaaagcggcg tgccggatcg ttttaccggc agcggtagcg gcaccgattt taccctgagc 600

attagcagcg tggaaaccga agatctggcg gtgtattatt gccagcagta ttatagctat 660

ccgctgacct ttggtgcggg caccaaactg gtgctgaaac gtgcggccgc actcgagcac 720

caccaccacc accac 735

<210> 103
<211> 245
<212> PRT
<213> Artificial

<220>
<223> amino acid sequence of an anti-TAG72 diabody comprising cysteine replacement mutations in the VL FR2 Kabat positions 38 and 44 is designated AVP04-80.

<400> 103

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

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

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

Gly Tyr Phe Ser Pro Gly Asn Asp Asp Phe Lys Tyr Asn Glu Arg Phe
50 55 60

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

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

Thr Arg Ser Leu Asn Met Ala Tyr Trp Gly Gln Gly Thr Ser Val Thr

100 105 110

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

Ser Ser Leu Pro Val Ser Val Gly Glu Lys Val Thr Leu Ser Cys Lys
130 135 140

Ser Ser Gln Ser Leu Leu Tyr Ser Gly Asn Gln Lys Asn Tyr Leu Ala
145 150 155 160

Trp Tyr Gln Cys Lys Pro Gly Gln Ser Cys Lys Leu Leu Ile Tyr Trp
165 170 175

Ala Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly
180 185 190

Ser Gly Thr Asp Phe Thr Leu Ser Ile Ser Ser Val Glu Thr Glu Asp
195 200 205

Leu Ala Val Tyr Tyr Cys Gln Gln Tyr Tyr Ser Tyr Pro Leu Thr Phe
210 215 220

Gly Ala Gly Thr Lys Leu Val Leu Lys Arg Ala Ala Ala Leu Glu His
225 230 235 240

His His His His His
245

<210> 104
<211> 735
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of an anti-TAG72 diabody comprising cysteine replacement mutations in the VL FR3 Kabat positions 78 and 82 designated AVP04-83.

<400> 104
agcgtgcagc tgcagcagag cgatgcggaa ctggtgaaac cgggcgcgag cgtgaaaatt 60

agctgcaaag cgagcggcta tacctttacc gatcatgcga ttcattgggt gaaacagaat 120

ccggaacagg gcctggaatg gattggctat tttagcccgg gcaacgatga ttttaaatat 180

aacgaacgtt ttaaaggcaa agcgaccctg accgcggata aaagcagcag caccgcgtat 240

ctgcagctga acagcctgac cagcgaagat agcgcggtgt atttttgcac ccgtagcctg 300

aatatggcgt attggggtca gggcacctcg gtcaccgtga gcagcggtgg cggcggcagc 360

gatatcgtga tgacccagag cccgagcagc ctgccggtga gcgtgggcga aaaagtgacc 420

ctgagctgca aaagcagcca gagcctgctg tatagcggca atcagaaaaa ctatctggcg 480

tggtatcagc agaaaccggg tcagagcccg aaactgctga tttattgggc gagcacccgt 540

gaaagcggcg tgccggatcg ttttaccggc agcggtagcg gcaccgattt taccctgagc 600

attagcagct gcgaaaccga atgcctggcg gtgtattatt gccagcagta ttatagctat 660

ccgctgacct ttggtgcggg caccaaactg gtgctgaaac gtgcggccgc actcgagcac 720

caccaccacc accac 735

<210> 105
<211> 245
<212> PRT
<213> Artificial

<220>
<223> amino acid sequence of an anti-TAG72 diabody comprising cysteine replacement mutations in the VL FR3 Kabat positions 78 and 82 designated AVP04-83.

<400> 105

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

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

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

Gly Tyr Phe Ser Pro Gly Asn Asp Asp Phe Lys Tyr Asn Glu Arg Phe
50 55 60

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

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

Thr Arg Ser Leu Asn Met Ala Tyr Trp Gly Gln Gly Thr Ser Val Thr
100 105 110

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

Ser Ser Leu Pro Val Ser Val Gly Glu Lys Val Thr Leu Ser Cys Lys
130 135 140

Ser Ser Gln Ser Leu Leu Tyr Ser Gly Asn Gln Lys Asn Tyr Leu Ala
145 150 155 160

Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Trp
165 170 175

Ala Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly
180 185 190

Ser Gly Thr Asp Phe Thr Leu Ser Ile Ser Ser Cys Glu Thr Glu Cys
195 200 205

Leu Ala Val Tyr Tyr Cys Gln Gln Tyr Tyr Ser Tyr Pro Leu Thr Phe
210 215 220

Gly Ala Gly Thr Lys Leu Val Leu Lys Arg Ala Ala Ala Leu Glu His
225 230 235 240

His His His His His
245

<210> 106
<211> 735
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of an anti-TAG72 diabody comprising cysteine replacement mutations in the VH FR2 Kabat positions 39 and 43 designated AVP04-111.

<400> 106
agcgtgcagc tgcagcagag cgatgcggaa ctggtgaaac cgggcgcgag cgtgaaaatt 60

agctgcaaag cgagcggcta tacctttacc gatcatgcga ttcattgggt gaaatgcaat 120

ccggaatgcg gcctggaatg gattggctat ttagcccgg gcaacgatga ttttaaatat 180

aacgaacgtt ttaaaggcaa agcgaccctg accgcggata aaagcagcag caccgcgtat 240

ctgcagctga acagcctgac cagcgaagat agcgcggtgt atttttgcac ccgtagcctg 300

aatatggcgt attggggtca gggcacctcg gtcaccgtga gcagcggtgg cggcggcagc 360

gatatcgtga tgacccagag cccgagcagc ctgccggtga gcgtgggcga aaaagtgacc 420

ctgagctgca aaagcagcca gagcctgctg tatagcggca atcagaaaaa ctatctggcg 480

tggtatcagc agaaaccggg tcagagcccg aaactgctga tttattgggc gagcacccgt 540

gaaagcggcg tgccggatcg ttttaccggc agcggtagcg gcaccgattt taccctgagc 600

attagcagcg tggaaaccga agatctggcg gtgtattatt gccagcagta ttatagctat 660

ccgctgacct ttggtgcggg caccaaactg gtgctgaaac gtgcggccgc actcgagcac 720

caccaccacc accac 735

<210> 107
<211> 245
<212> PRT
<213> Artificial

<220>
<223> amino acid sequence of an anti-TAG72 diabody comprising cysteine replacement mutations in the VH FR2 Kabat positions 39 and 43 designated AVP04-111.

<400> 107

Ser Val Gln Leu Gln Gln Ser Asp Ala Glu Leu Val Lys Pro Gly Ala

1 5 10 15

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

Ala Ile His Trp Val Lys Cys Asn Pro Glu Cys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Phe Ser Pro Gly Asn Asp Asp Phe Lys Tyr Asn Glu Arg Phe
50 55 60

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

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

Thr Arg Ser Leu Asn Met Ala Tyr Trp Gly Gln Gly Thr Ser Val Thr
100 105 110

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

Ser Ser Leu Pro Val Ser Val Gly Glu Lys Val Thr Leu Ser Cys Lys
130 135 140

Ser Ser Gln Ser Leu Leu Tyr Ser Gly Asn Gln Lys Asn Tyr Leu Ala
145 150 155 160

Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Trp
165 170 175

Ala Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly
180 185 190

Ser Gly Thr Asp Phe Thr Leu Ser Ile Ser Ser Val Glu Thr Glu Asp
195 200 205

Leu Ala Val Tyr Tyr Cys Gln Gln Tyr Tyr Ser Tyr Pro Leu Thr Phe
210 215 220

Gly Ala Gly Thr Lys Leu Val Leu Lys Arg Ala Ala Ala Leu Glu His
225 230 235 240

His His His His His
245

<210> 108
<211> 735
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of an anti-TAG72 diabody comprising cysteine replacement mutations in the VH FR2 Kabat positions 39 and 45 designated AVP04-112.

<400> 108

agcgtgcagc tgcagcagag cgatgcggaa ctggtgaaac cgggcgcgag cgtgaaaatt 60

agctgcaaag cgagcggcta tacctttacc gatcatgcga ttcattgggt gaaatgcaat 120

ccggaacagg gctgcgaatg gattggctat ttagcccgg gcaacgatga ttttaaatat 180

aacgaacgtt ttaaaggcaa agcgaccctg accgcggata aaagcagcag caccgcgtat 240

ctgcagctga acagcctgac cagcgaagat agcgcggtgt atttttgcac ccgtagcctg 300

aatatggcgt attggggtca gggcacctcg gtcaccgtga gcagcggtgg cggcggcagc 360

gatatcgtga tgacccagag cccgagcagc ctgccggtga gcgtgggcga aaaagtgacc 420

ctgagctgca aaagcagcca gagcctgctg tatagcggca atcagaaaaa ctatctggcg 480

tggtatcagc agaaaccggg tcagagcccg aaactgctga tttattgggc gagcacccgt 540

gaaagcggcg tgccggatcg ttttaccggc agcggtagcg gcaccgattt taccctgagc 600

attagcagcg tggaaaccga agatctggcg gtgtattatt gccagcagta ttatagctat 660

ccgctgacct ttggtgcggg caccaaactg gtgctgaaac gtgcggccgc actcgagcac 720

caccaccacc accac 735

<210> 109
<211> 245
<212> PRT
<213> Artificial

<220>
<223> amino acid sequence of an anti-TAG72 diabody comprising cysteine replacement mutations in the VH FR2 Kabat positions 39 and 45 designated AVP04-112.

<400> 109

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

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

Ala Ile His Trp Val Lys Cys Asn Pro Glu Gln Gly Cys Glu Trp Ile
35 40 45

Gly Tyr Phe Ser Pro Gly Asn Asp Asp Phe Lys Tyr Asn Glu Arg Phe
50 55 60

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

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

```
Thr Arg Ser Leu Asn Met Ala Tyr Trp Gly Gln Gly Thr Ser Val Thr
            100                 105                 110

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

Ser Ser Leu Pro Val Ser Val Gly Glu Lys Val Thr Leu Ser Cys Lys
    130                 135                 140

Ser Ser Gln Ser Leu Leu Tyr Ser Gly Asn Gln Lys Asn Tyr Leu Ala
145                 150                 155                 160

Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Trp
                165                 170                 175

Ala Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly
            180                 185                 190

Ser Gly Thr Asp Phe Thr Leu Ser Ile Ser Ser Val Glu Thr Glu Asp
        195                 200                 205

Leu Ala Val Tyr Tyr Cys Gln Gln Tyr Tyr Ser Tyr Pro Leu Thr Phe
    210                 215                 220

Gly Ala Gly Thr Lys Leu Val Leu Lys Arg Ala Ala Ala Leu Glu His
225                 230                 235                 240

His His His His His
                245
```

<210> 110
<211> 735
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of an anti-TAG72 diabody comprising cysteine replacement mutations in the VH FR3 Kabat positions 82C and 86 designated AVP04-114

<400> 110

```
agcgtgcagc tgcagcagag cgatgcggaa ctggtgaaac cgggcgcgag cgtgaaaatt       60

agctgcaaag cgagcggcta tacctttacc gatcatgcga ttcattgggt gaaacagaat      120

ccggaacagg gcctggaatg gattggctat tttagcccgg gcaacgatga ttttaaatat      180

aacgaacgtt ttaaaggcaa agcgaccctg accgcggata aaagcagcag caccgcgtat      240

ctgcagctga acagctgcac cagcgaatgc agcgcggtgt atttttgcac ccgtagcctg      300

aatatggcgt attggggtca gggcacctcg gtcaccgtga gcagcggtgg cggcggcagc      360

gatatcgtga tgacccagag cccgagcagc ctgccggtga gcgtgggcga aaaagtgacc      420

ctgagctgca aaagcagcca gagcctgctg tatagcggca atcagaaaaa ctatctggcg      480
```

tggtatcagc agaaaccggg tcagagcccg aaactgctga tttattgggc gagcacccgt 540

gaaagcggcg tgccggatcg ttttaccggc agcggtagcg gcaccgattt taccctgagc 600

attagcagcg tggaaaccga agatctggcg gtgtattatt gccagcagta ttatagctat 660

ccgctgacct ttggtgcggg caccaaactg gtgctgaaac gtgcggccgc actcgagcac 720

caccaccacc accac 735

<210> 111
<211> 245
<212> PRT
<213> Artificial

<220>
<223> amino acid sequence of an anti-TAG72 diabody comprising cysteine replacement mutations in the VH FR3 Kabat positions 82C and 86 designated AVP04-114.

<400> 111

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

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

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

Gly Tyr Phe Ser Pro Gly Asn Asp Asp Phe Lys Tyr Asn Glu Arg Phe
50 55 60

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

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

Thr Arg Ser Leu Asn Met Ala Tyr Trp Gly Gln Gly Thr Ser Val Thr
100 105 110

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

Ser Ser Leu Pro Val Ser Val Gly Glu Lys Val Thr Leu Ser Cys Lys
130 135 140

Ser Ser Gln Ser Leu Leu Tyr Ser Gly Asn Gln Lys Asn Tyr Leu Ala
145 150 155 160

Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Trp
165 170 175

Ala Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly

180 185 190

Ser Gly Thr Asp Phe Thr Leu Ser Ile Ser Ser Val Glu Thr Glu Asp
195 200 205

Leu Ala Val Tyr Tyr Cys Gln Gln Tyr Tyr Ser Tyr Pro Leu Thr Phe
210 215 220

Gly Ala Gly Thr Lys Leu Val Leu Lys Arg Ala Ala Ala Leu Glu His
225 230 235 240

His His His His His
245

<210> 112
<211> 735
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of an anti-TAG72 diabody comprising cysteine replacement mutations in the VH FR3 Kabat positions 70 and 79 designated AVP04-120

<400> 112
agcgtgcagc tgcagcagag cgatgcggaa ctggtgaaac cgggcgcgag cgtgaaaatt 60

agctgcaaag cgagcggcta tacctttacc gatcatgcga ttcattgggt gaaacagaat 120

ccggaacagg gcctggaatg gattggctat ttagcccgg gcaacgatga ttttaaatat 180

aacgaacgtt ttaaaggcaa agcgaccctg tgcgcggata aaagcagcag caccgcgtgc 240

ctgcagctga acagcctgac cagcgaagat agcgcggtgt atttttgcac ccgtagcctg 300

aatatggcgt attggggtca gggcacctcg gtcaccgtga gcagcggtgg cggcggcagc 360

gatatcgtga tgacccagag cccgagcagc ctgccggtga gcgtgggcga aaaagtgacc 420

ctgagctgca aaagcagcca gagcctgctg tatagcggca atcagaaaaa ctatctggcg 480

tggtatcagc agaaaccggg tcagagcccg aaactgctga tttattgggc gagcacccgt 540

gaaagcggcg tgccggatcg ttttaccggc agcggtagcg gcaccgattt taccctgagc 600

attagcagcg tggaaaccga agatctggcg gtgtattatt gccagcagta ttatagctat 660

ccgctgacct ttggtgcggg caccaaactg gtgctgaaac gtgcggccgc actcgagcac 720

caccaccacc accac 735

<210> 113
<211> 245
<212> PRT
<213> Artificial

<220>
<223> amino acid sequence of an anti-TAG72 diabody comprising cysteine replacement mutations in the VH FR3 Kabat positions 70 and 79 designated AVP04-120

<400> 113

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

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

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

Gly Tyr Phe Ser Pro Gly Asn Asp Asp Phe Lys Tyr Asn Glu Arg Phe
    50                  55                  60

Lys Gly Lys Ala Thr Leu Cys Ala Asp Lys Ser Ser Ser Thr Ala Cys
65                  70                  75                  80

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

Thr Arg Ser Leu Asn Met Ala Tyr Trp Gly Gln Gly Thr Ser Val Thr
            100                 105                 110

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

Ser Ser Leu Pro Val Ser Val Gly Glu Lys Val Thr Leu Ser Cys Lys
    130                 135                 140

Ser Ser Gln Ser Leu Leu Tyr Ser Gly Asn Gln Lys Asn Tyr Leu Ala
145                 150                 155                 160

Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Trp
                165                 170                 175

Ala Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly
            180                 185                 190

Ser Gly Thr Asp Phe Thr Leu Ser Ile Ser Ser Val Glu Thr Glu Asp
        195                 200                 205

Leu Ala Val Tyr Tyr Cys Gln Gln Tyr Tyr Ser Tyr Pro Leu Thr Phe
    210                 215                 220

Gly Ala Gly Thr Lys Leu Val Leu Lys Arg Ala Ala Ala Leu Glu His
225                 230                 235                 240

His His His His His
                245
```

<210> 114
<211> 735
<212> DNA

<213> Artificial

<220>
<223> nucleotide sequence of an anti-TAG72 diabody comprising cysteine replacement mutations in the VH FR3 Kabat positions 72 and 75 designated AVP04-121

<400> 114
agcgtgcagc tgcagcagag cgatgcggaa ctggtgaaac cgggcgcgag cgtgaaaatt 60

agctgcaaag cgagcggcta tacctttacc gatcatgcga ttcattgggt gaaacagaat 120

ccggaacagg gcctggaatg gattggctat ttagcccgg gcaacgatga ttttaaatat 180

aacgaacgtt ttaaaggcaa agcgaccctg accgcgtgca aaagctgcag caccgcgtat 240

ctgcagctga acagcctgac cagcgaagat agcgcggtgt atttttgcac ccgtagcctg 300

aatatggcgt attggggtca gggcacctcg gtcaccgtga gcagcggtgg cggcggcagc 360

gatatcgtga tgacccagag cccgagcagc ctgccggtga gcgtgggcga aaaagtgacc 420

ctgagctgca aaagcagcca gagcctgctg tatagcggca atcagaaaaa ctatctggcg 480

tggtatcagc agaaaccggg tcagagcccg aaactgctga tttattgggc gagcacccgt 540

gaaagcggcg tgccggatcg ttttaccggc agcggtagcg gcaccgattt taccctgagc 600

attagcagcg tggaaaccga agatctggcg gtgtattatt gccagcagta ttatagctat 660

ccgctgacct ttggtgcggg caccaaactg gtgctgaaac gtgcggccgc actcgagcac 720

caccaccacc accac 735

<210> 115
<211> 245
<212> PRT
<213> Artificial

<220>
<223> amino acid sequence of an anti-TAG72 diabody comprising cysteine replacement mutations in the VH FR3 Kabat positions 72 and 75 designated AVP04-121

<400> 115

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

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

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

Gly Tyr Phe Ser Pro Gly Asn Asp Asp Phe Lys Tyr Asn Glu Arg Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Cys Lys Ser Cys Ser Thr Ala Tyr
65 70 75 80

Leu Gln Leu Asn Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys

85 90 95

Thr Arg Ser Leu Asn Met Ala Tyr Trp Gly Gln Gly Thr Ser Val Thr
100 105 110

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

Ser Ser Leu Pro Val Ser Val Gly Glu Lys Val Thr Leu Ser Cys Lys
130 135 140

Ser Ser Gln Ser Leu Leu Tyr Ser Gly Asn Gln Lys Asn Tyr Leu Ala
145 150 155 160

Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Trp
165 170 175

Ala Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly
180 185 190

Ser Gly Thr Asp Phe Thr Leu Ser Ile Ser Ser Val Glu Thr Glu Asp
195 200 205

Leu Ala Val Tyr Tyr Cys Gln Gln Tyr Tyr Ser Tyr Pro Leu Thr Phe
210 215 220

Gly Ala Gly Thr Lys Leu Val Leu Lys Arg Ala Ala Ala Leu Glu His
225 230 235 240

His His His His His
245

<210> 116
<211> 735
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of an anti-TAG72 diabody comprising cysteine replacement mutations in the VL FR3 Kabat positions 65 and 72 designated AVP04-123.

<400> 116
agcgtgcagc tgcagcagag cgatgcggaa ctggtgaaac cgggcgcgag cgtgaaaatt 60

agctgcaaag cgagcggcta tacctttacc gatcatgcga ttcattgggt gaaacagaat 120

ccggaacagg gcctggaatg gattggctat ttagcccgg gcaacgatga ttttaaatat 180

aacgaacgtt ttaaaggcaa agcgaccctg accgcggata aaagcagcag caccgcgtat 240

ctgcagctga acagcctgac cagcgaagat agcgcggtgt atttttgcac ccgtagcctg 300

aatatggcgt attggggtca gggcacctcg gtcaccgtga gcagcggtgg cggcggcagc 360

gatatcgtga tgacccagag cccgagcagc ctgccggtga gcgtgggcga aaaagtgacc 420

ctgagctgca aaagcagcca gagcctgctg tatagcggca atcagaaaaa ctatctggcg 480

tggtatcagc agaaaccggg tcagagcccg aaactgctga tttattgggc gagcacccgt 540

gaaagcggcg tgccggatcg ttttaccggc tgcggtagcg gcaccgattt ttgcctgagc 600

attagcagcg tggaaaccga agatctggcg gtgtattatt gccagcagta ttatagctat 660

ccgctgacct ttggtgcggg caccaaactg gtgctgaaac gtgcggccgc actcgagcac 720

caccaccacc accac 735

<210> 117
<211> 245
<212> PRT
<213> Artificial

<220>
<223> amino acid sequence of an anti-TAG72 diabody comprising cysteine replacement mutations in the VL FR3 Kabat positions 65 and 72 designated AVP04-123.

<400> 117

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

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

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

Gly Tyr Phe Ser Pro Gly Asn Asp Asp Phe Lys Tyr Asn Glu Arg Phe
50 55 60

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

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

Thr Arg Ser Leu Asn Met Ala Tyr Trp Gly Gln Gly Thr Ser Val Thr
100 105 110

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

Ser Ser Leu Pro Val Ser Val Gly Glu Lys Val Thr Leu Ser Cys Lys
130 135 140

Ser Ser Gln Ser Leu Leu Tyr Ser Gly Asn Gln Lys Asn Tyr Leu Ala
145 150 155 160

Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Trp
165 170 175

Ala Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Cys Gly
180 185 190

Ser Gly Thr Asp Phe Cys Leu Ser Ile Ser Ser Val Glu Thr Glu Asp
195 200 205

Leu Ala Val Tyr Tyr Cys Gln Gln Tyr Tyr Ser Tyr Pro Leu Thr Phe
210 215 220

Gly Ala Gly Thr Lys Leu Val Leu Lys Arg Ala Ala Ala Leu Glu His
225 230 235 240

His His His His His
245

<210> 118
<211> 765
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of an anti-TAG72 scFv comprising cysteine replacement mutations in the VL FR2 Kabat positions 38 and 42 designated AVP04-124

<400> 118
agcgtgcagc tgcagcagag cgatgcggaa ctggtgaaac cgggcgcgag cgtgaaaatt 60

agctgcaaag cgagcggcta tacctttacc gatcatgcga ttcattgggt gaaacagaat 120

ccggaacagg gcctggaatg gattggctat ttagcccgg gcaacgatga ttttaaatat 180

aacgaacgtt ttaaaggcaa agcgaccctg accgcggata aaagcagcag caccgcgtat 240

ctgcagctga acagcctgac cagcgaagat agcgcggtgt atttttgcac ccgtagcctg 300

aatatggcgt attggggtca gggcacctcg gtcaccgtga gcagcggtgg cggcggcagc 360

ggtggcggcg gcagcggtgg cggcggcagc gatatcgtga tgacccagag cccgagcagc 420

ctgccggtga gcgtgggcga aaaagtgacc ctgagctgca aaagcagcca gagcctgctg 480

tatagcggca atcagaaaaa ctatctggcg tggtatcagt gcaaaccggg ttgcagcccg 540

aaactgctga tttattgggc gagcacccgt gaaagcggcg tgccggatcg ttttaccggc 600

agcggtagcg gcaccgattt taccctgagc attagcagcg tggaaaccga agatctggcg 660

gtgtattatt gccagcagta ttatagctat ccgctgacct ttggtgcggg caccaaactg 720

gtgctgaaac gtgcggccgc actcgagcac caccaccacc accac 765

<210> 119
<211> 260
<212> PRT
<213> Artificial

<220>
<223> amino acid sequence of an anti-TAG72 scFv comprising cysteine replacement mutations in the VL FR2 Kabat positions 38 and 42 designated AVP04-124.

<400> 119

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

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

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

Gly Tyr Phe Ser Pro Gly Asn Asp Asp Phe Lys Tyr Asn Glu Arg Phe
    50                  55                  60

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

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

Thr Arg Ser Leu Asn Met Ala Tyr Trp Gly Gln Gly Thr Ser Val Thr
            100                 105                 110

Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115                 120                 125

Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Ser Pro Ser
    130                 135                 140

Ser Leu Pro Val Ser Val Gly Glu Lys Val Thr Leu Ser Cys Lys Ser
145                 150                 155                 160

Ser Gln Ser Leu Leu Tyr Ser Gly Asn Gln Lys Asn Tyr Leu Ala Trp
                165                 170                 175

Tyr Gln Cys Lys Pro Gly Cys Ser Pro Lys Leu Leu Ile Tyr Trp Ala
            180                 185                 190

Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser
        195                 200                 205

Gly Thr Asp Phe Thr Leu Ser Ile Ser Ser Val Glu Thr Glu Asp Leu
    210                 215                 220

Ala Val Tyr Tyr Cys Gln Gln Tyr Tyr Ser Tyr Pro Leu Thr Phe Gly
225                 230                 235                 240

Ala Gly Thr Lys Leu Val Leu Lys Arg Ala Ala Ala Leu Glu His His
                245                 250                 255

His His His His
```

260

<210> 120
<211> 717
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of an anti-TAG72 triabody comprising cysteine replacement mutations in the VL FR2 Kabat positions 38 and 42 designated AVP04-125.

<400> 120
caggtgcagc tgcagcagag cgatgcggaa ctggtgaaac cgggcgcgag cgtgaaaatt 60

agctgcaaag cgagcggcta tacctttacc gatcatgcga ttcattgggt gaaacagaat 120

ccggaacagg gcctggaatg gattggctat tttagcccgg gcaacgatga ttttaaatat 180

aacgaacgtt ttaaaggcaa agcgaccctg accgcggata aaagcagcag caccgcgtat 240

ctgcagctga acagcctgac cagcgaagat agcgcggtgt atttttgcac ccgtagcctg 300

aatatggcgt attggggtca gggcacctcg gtcaccgtga gcgatatcgt gatgacccag 360

agcccgagca gcctgccggt gagcgtgggc gaaaaagtga ccctgagctg caaaagcagc 420

cagagcctgc tgtatagcgg caatcagaaa aactatctgg cgtggtatca gtgcaaaccg 480

ggttgcagcc cgaaactgct gatttattgg gcgagcaccc gtgaaagcgg cgtgccggat 540

cgttttaccg gcagcggtag cggcaccgat tttaccctga gcattagcag cgtggaaacc 600

gaagatctgg cggtgtatta ttgccagcag tattatagct atccgctgac ctttggtgcg 660

ggcaccaaac tggtgctgaa acgtgcggcc gcactcgagc accaccacca ccaccac 717

<210> 121
<211> 239
<212> PRT
<213> Artificial

<220>
<223> amino acid sequence of an anti-TAG72 triabody comprising cysteine replacement mutations in the VL FR2 Kabat positions 38 and 42 designated AVP04-125

<400> 121

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

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

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

Gly Tyr Phe Ser Pro Gly Asn Asp Asp Phe Lys Tyr Asn Glu Arg Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr

65 70 75 80

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

Thr Arg Ser Leu Asn Met Ala Tyr Trp Gly Gln Gly Thr Ser Val Thr
100 105 110

Val Ser Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Pro Val Ser
115 120 125

Val Gly Glu Lys Val Thr Leu Ser Cys Lys Ser Ser Gln Ser Leu Leu
130 135 140

Tyr Ser Gly Asn Gln Lys Asn Tyr Leu Ala Trp Tyr Gln Cys Lys Pro
145 150 155 160

Gly Cys Ser Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser
165 170 175

Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr
180 185 190

Leu Ser Ile Ser Ser Val Glu Thr Glu Asp Leu Ala Val Tyr Tyr Cys
195 200 205

Gln Gln Tyr Tyr Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu
210 215 220

Val Leu Lys Arg Ala Ala Ala Leu Glu His His His His His His
225 230 235

<210> 122
<211> 729
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of an anti-MucI diabody comprising cysteine replacement mutations in the VL FR2 Kabat positions 38 and 42 designated AVP02-115

<400> 122
agcgtgcagc tggttgaaag cggtggcgga gtggtgcagc caggtggaag cctgcgtctg 60

agctgcgcag caagcggttt acctttagc agctatggca tgagctgggt gcgtcaggcg 120

ccggataaag gcctggaact ggtggcgacc attaacagca acggtggaag cacctattat 180

ccggatagcg tgaaaggccg ttttaccatt agccgtgata acagcaaaaa caccctgtat 240

ctgcagatga acagcctgcg taccgaagat accgcggtgt attattgcgc gcgtgatcgt 300

gatggctatg atgaaggctt tgattattgg ggccagggca ccctggtgac cgtgagcagc 360

ggtgggggcg gaagccagat tcagctgacc cagagcccga gcagcctgag cgcaagcgtg 420

ggtgatcgtg tgaccattac ctgcagcgcg agcagcagcg tgagctatat gcattggtat 480

cagtgcaaac cgggctgcgc gccgaaacgt tggatttatg ataccagcaa actggcgagc 540

ggcgtgccga gccgttttag cggcagcggc agcggcaccg attatacctt taccattagc 600

agcctgcagc cggaagatat tgcgacctat tattgccagc agtggagcag caacccgccg 660

acctttggcc agggcaccaa actgcagatt aaacgtgcgg ccgcactcga gcaccaccac 720

caccaccac 729

<210> 123
<211> 243
<212> PRT
<213> Artificial

<220>
<223> amino acid sequence of an anti-MucI diabody comprising cysteine replacement mutations in the VL FR2 Kabat positions 38 and 42 designated AVP02-115

<400> 123

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

Ala Thr Ile Asn Ser Asn Gly Gly Ser Thr Tyr Tyr Pro 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 Thr Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Arg Asp Gly Tyr Asp Glu Gly Phe Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gln Ile Gln
115 120 125

Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
130 135 140

Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met His Trp Tyr
145 150 155 160

Gln Cys Lys Pro Gly Cys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser
165 170 175

Lys Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
180 185 190

Thr Asp Tyr Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
195 200 205

Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Pro Thr Phe Gly Gln
210 215 220

Gly Thr Lys Leu Gln Ile Lys Arg Ala Ala Ala Leu Glu His His His
225 230 235 240

His His His

<210> 124
<211> 729
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of an anti-MucI diabody comprising cysteine replacement mutations in the VH FR2 Kabat positions 39 and 43 designated AVP02-116.

<400> 124
agcgtgcagc tggttgaaag cggtggcgga gtggtgcagc caggtggaag cctgcgtctg 60

agctgcgcag caagcggttt acctttagc agctatggca tgagctgggt gcgttgcgcg 120

ccggattgcg gcctggaact ggtggcgacc attaacagca acggtggaag cacctattat 180

ccggatagcg tgaaaggccg ttttaccatt agccgtgata acagcaaaaa caccctgtat 240

ctgcagatga acagcctgcg taccgaagat accgcggtgt attattgcgc gcgtgatcgt 300

gatggctatg atgaaggctt tgattattgg ggccagggca ccctggtgac cgtgagcagc 360

ggtgggggcg gaagccagat tcagctgacc cagagcccga gcagcctgag cgcaagcgtg 420

ggtgatcgtg tgaccattac ctgcagcgcg agcagcagcg tgagctatat gcattggtat 480

cagcagaaac cgggcaaagc gccgaaacgt tggatttatg ataccagcaa actggcgagc 540

ggcgtgccga gccgttttag cggcagcggc agcggcaccg attatacctt taccattagc 600

agcctgcagc cggaagatat tgcgacctat tattgccagc agtggagcag caacccgccg 660

acctttggcc agggcaccaa actgcagatt aaacgtgcgg ccgcactcga gcaccaccac 720

caccaccac 729

<210> 125
<211> 243
<212> PRT
<213> Artificial

<220>
<223> amino acid sequence of an anti-MucI diabody comprising cysteine replacement mutations in the VH FR2 Kabat positions 39 and 43 designated AVP02-116.

<400> 125

```
Ser 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 Ser Trp Val Arg Cys Ala Pro Asp Cys Gly Leu Glu Leu Val
        35                  40                  45

Ala Thr Ile Asn Ser Asn Gly Gly Ser Thr Tyr Tyr Pro 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 Thr Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Asp Arg Asp Gly Tyr Asp Glu Gly Phe Asp Tyr Trp Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gln Ile Gln
        115                 120                 125

Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
    130                 135                 140

Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met His Trp Tyr
145                 150                 155                 160

Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser
                165                 170                 175

Lys Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
            180                 185                 190

Thr Asp Tyr Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
        195                 200                 205

Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Pro Thr Phe Gly Gln
    210                 215                 220

Gly Thr Lys Leu Gln Ile Lys Arg Ala Ala Ala Leu Glu His His His
225                 230                 235                 240

His His His
```

<210> 126

<211> 804
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of an anti-Her2 diabody comprising cysteine replacement mutations in the VL FR2 Kabat positions 38 and 42 designated AVP07-117.

<400> 126
agcgtgcagc tggtgcagtc tggggcagag gtgaaaaagc ccggggagtc tctgaagatc 60

tcctgtaagg gttctggata cagctttacc agctactgga tcgcctgggt gcgccagatg 120

cccgggaaag gcctggagta catggggctc atctatcctg gtgactctga caccaaatac 180

agcccgtcct tccaaggcca ggtcaccatc tcagtcgaca agtccgtcag cactgcctac 240

ttgcaatgga gcagtctgaa gccctcggac agcgccgtgt atttttgtgc gagacatgac 300

gtgggatatg cgagtagttc caacgcggca aagtggcctg aatacttcca gcattggggc 360

cagggcaccc tggtcaccgt ttcctcaggt ggaggcggtt cacagtctgt gttgacgcag 420

ccgccctcag tgtctgcggc cccaggacag aaggtcacca tctcctgctc tggaagcagc 480

tccaacattg ggaataatta tgtatcctgg taccagtgcc tcccaggatg cgtccccaaa 540

ctcctcatct atggtcacac caatcggccc gcaggggtcc ctgaccgatt ctctggctcc 600

aagtctggca cctcagcctc cctggccatc agtgggttcc ggtccgagga tgaggctgat 660

tattactgtg cagcatggga tgacagcctg agtggttggg tgttcggcgg agggaccaag 720

ctgaccgtcc taggtgcggc cgcagaacaa aaactcatct cagaagagga tctgaatggg 780

gccgcacatc accatcatca ccat 804

<210> 127
<211> 268
<212> PRT
<213> Artificial

<220>
<223> amino acid sequence of an anti-Her2 diabody comprising cysteine replacement mutations in the VL FR2 Kabat positions 38 and 42 designated AVP07-117.

<400> 127

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

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
20 25 30

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

Gly Leu Ile Tyr Pro Gly Asp Ser Asp Thr Lys Tyr Ser Pro Ser Phe
50 55 60

Gln Gly Gln Val Thr Ile Ser Val Asp Lys Ser Val Ser Thr Ala Tyr

65 70 75 80

Leu Gln Trp Ser Ser Leu Lys Pro Ser Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg His Asp Val Gly Tyr Ala Ser Ser Ser Asn Ala Ala Lys Trp
100 105 110

Pro Glu Tyr Phe Gln His Trp Gly Gln Gly Thr Leu Val Thr Val Ser
115 120 125

Ser Gly Gly Gly Gly Ser Gln Ser Val Leu Thr Gln Pro Pro Ser Val
130 135 140

Ser Ala Ala Pro Gly Gln Lys Val Thr Ile Ser Cys Ser Gly Ser Ser
145 150 155 160

Ser Asn Ile Gly Asn Asn Tyr Val Ser Trp Tyr Gln Cys Leu Pro Gly
165 170 175

Cys Val Pro Lys Leu Leu Ile Tyr Gly His Thr Asn Arg Pro Ala Gly
180 185 190

Val Pro Asp Arg Phe Ser Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu
195 200 205

Ala Ile Ser Gly Phe Arg Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala
210 215 220

Ala Trp Asp Asp Ser Leu Ser Gly Trp Val Phe Gly Gly Gly Thr Lys
225 230 235 240

Leu Thr Val Leu Gly Ala Ala Ala Glu Gln Lys Leu Ile Ser Glu Glu
245 250 255

Asp Leu Asn Gly Ala Ala His His His His His His
260 265

<210> 128
<211> 804
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of an anti-Her2 diabody comprising cysteine replacement mutations in the VH FR2 Kabat positions 39 and 43 designated AVP07-118.

<400> 128
agcgtgcagc tggtgcagtc tggggcagag gtgaaaaagc ccggggagtc tctgaagatc 60

tcctgtaagg gttctggata cagctttacc agctactgga tcgcctgggt gcgctgcatg 120

cccgggtgcg gcctggagta catggggctc atctatcctg gtgactctga caccaaatac 180

agcccgtcct tccaaggcca ggtcaccatc tcagtcgaca agtccgtcag cactgcctac 240

ttgcaatgga gcagtctgaa gccctcggac agcgccgtgt atttttgtgc gagacatgac 300

gtgggatatg cgagtagttc caacgcggca aagtggcctg aatacttcca gcattggggc 360

cagggcaccc tggtcaccgt ttcctcaggt ggaggcggtt cacagtctgt gttgacgcag 420

ccgccctcag tgtctgcggc cccaggacag aaggtcacca tctcctgctc tggaagcagc 480

tccaacattg ggaataatta tgtatcctgg taccagcagc tcccaggaac agtccccaaa 540

ctcctcatct atggtcacac caatcggccc gcaggggtcc ctgaccgatt ctctggctcc 600

aagtctggca cctcagcctc cctggccatc agtgggttcc ggtccgagga tgaggctgat 660

tattactgtg cagcatggga tgacagcctg agtggttggg tgttcggcgg agggaccaag 720

ctgaccgtcc taggtgcggc cgcagaacaa aaactcatct cagaagagga tctgaatggg 780

gccgcacatc accatcatca ccat 804

<210> 129
<211> 268
<212> PRT
<213> Artificial

<220>
<223> amino acid sequence of an anti-Her2 diabody comprising cysteine replacement mutations in the VH FR2 Kabat positions 39 and 43 designated AVP07-118.

<400> 129

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

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
20 25 30

Trp Ile Ala Trp Val Arg Cys Met Pro Gly Cys Gly Leu Glu Tyr Met
35 40 45

Gly Leu Ile Tyr Pro Gly Asp Ser Asp Thr Lys Tyr Ser Pro Ser Phe
50 55 60

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

Leu Gln Trp Ser Ser Leu Lys Pro Ser Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg His Asp Val Gly Tyr Ala Ser Ser Ser Asn Ala Ala Lys Trp
100 105 110

Pro Glu Tyr Phe Gln His Trp Gly Gln Gly Thr Leu Val Thr Val Ser
115 120 125

Ser Gly Gly Gly Gly Ser Gln Ser Val Leu Thr Gln Pro Pro Ser Val

130 135 140

Ser Ala Ala Pro Gly Gln Lys Val Thr Ile Ser Cys Ser Gly Ser Ser
145 150 155 160

Ser Asn Ile Gly Asn Asn Tyr Val Ser Trp Tyr Gln Gln Leu Pro Gly
165 170 175

Thr Val Pro Lys Leu Leu Ile Tyr Gly His Thr Asn Arg Pro Ala Gly
180 185 190

Val Pro Asp Arg Phe Ser Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu
195 200 205

Ala Ile Ser Gly Phe Arg Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala
210 215 220

Ala Trp Asp Asp Ser Leu Ser Gly Trp Val Phe Gly Gly Gly Thr Lys
225 230 235 240

Leu Thr Val Leu Gly Ala Ala Ala Glu Gln Lys Leu Ile Ser Glu Glu
245 250 255

Asp Leu Asn Gly Ala Ala His His His His His His
260 265

<210> 130
<211> 729
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of an anti-MucI diabody comprising cysteine replacement mutations in the VL FR2 Kabat positions 38 and 44 designated AVP02-126

<400> 130
agcgtgcagc tggttgaaag cggtggcgga gtggtgcagc caggtggaag cctgcgtctg 60

agctgcgcag caagcggttt acctttagc agctatggca tgagctgggt gcgtcaggcg 120

ccggataaag gcctggaact ggtggcgacc attaacagca acggtggaag cacctattat 180

ccggatagcg tgaaaggccg ttttaccatt agccgtgata acagcaaaaa caccctgtat 240

ctgcagatga acagcctgcg taccgaagat accgcggtgt attattgcgc gcgtgatcgt 300

gatggctatg atgaaggctt tgattattgg ggccagggca ccctggtgac cgtgagcagc 360

ggtgggggcg gaagccagat tcagctgacc cagagcccga gcagcctgag cgcaagcgtg 420

ggtgatcgtg tgaccattac ctgcagcgcg agcagcagcg tgagctatat gcattggtat 480

cagtgcaaac cgggcaaagc gtgcaaacgt tggatttatg ataccagcaa actggcgagc 540

ggcgtgccga gccgttttag cggcagcggc agcggcaccg attatacctt taccattagc 600

agcctgcagc cggaagatat tgcgacctat tattgccagc agtggagcag caacccgccg 660

acctttggcc agggcaccaa actgcagatt aaacgtgcgg ccgcactcga gcaccaccac 720

caccaccac 729

<210> 131
<211> 243
<212> PRT
<213> Artificial

<220>
<223> amino acid sequence of an anti-MucI diabody comprising cysteine replacement mutations in the VL FR2 Kabat positions 38 and 44 designated AVP02-126.

<400> 131

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

Ala Thr Ile Asn Ser Asn Gly Gly Ser Thr Tyr Tyr Pro 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 Thr Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Arg Asp Gly Tyr Asp Glu Gly Phe Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gln Ile Gln
115 120 125

Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
130 135 140

Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met His Trp Tyr
145 150 155 160

Gln Cys Lys Pro Gly Lys Ala Cys Lys Arg Trp Ile Tyr Asp Thr Ser
165 170 175

Lys Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
180 185 190

Thr Asp Tyr Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
195 200 205

Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Pro Thr Phe Gly Gln
210 215 220

Gly Thr Lys Leu Gln Ile Lys Arg Ala Ala Ala Leu Glu His His His
225 230 235 240

His His His

<210> 132
<211> 729
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of an anti-MucI diabody comprising cysteine replacement mutations in the VH FR2 Kabat positions 39 and 45 designated AVP02-127

<400> 132
agcgtgcagc tggttgaaag cggtggcgga gtggtgcagc caggtggaag cctgcgtctg 60

agctgcgcag caagcggttt acctttagc agctatggca tgagctgggt gcgttgcgcg 120

ccggataaag gctgcgaact ggtggcgacc attaacagca acggtggaag cacctattat 180

ccggatagcg tgaaaggccg ttttaccatt agccgtgata acagcaaaaa caccctgtat 240

ctgcagatga acagcctgcg taccgaagat accgcggtgt attattgcgc gcgtgatcgt 300

gatggctatg atgaaggctt tgattattgg ggccagggca ccctggtgac cgtgagcagc 360

ggtgggggcg gaagccagat tcagctgacc cagagcccga gcagcctgag cgcaagcgtg 420

ggtgatcgtg tgaccattac ctgcagcgcg agcagcagcg tgagctatat gcattggtat 480

cagcagaaac cgggcaaagc gccgaaacgt tggatttatg ataccagcaa actggcgagc 540

ggcgtgccga gccgttttag cggcagcggc agcggcaccg attatacctt taccattagc 600

agcctgcagc cggaagatat tgcgacctat tattgccagc agtggagcag caacccgccg 660

acctttggcc agggcaccaa actgcagatt aaacgtgcgg ccgcactcga gcaccaccac 720

caccaccac 729

<210> 133
<211> 243
<212> PRT
<213> Artificial

<220>
<223> amino acid sequence of an anti-MucI diabody comprising cysteine replacement mutations in the VH FR2 Kabat positions 39 and 45 designated AVP02-127.

<400> 133

Ser 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 Ser Trp Val Arg Cys Ala Pro Asp Lys Gly Cys Glu Leu Val
35 40 45

Ala Thr Ile Asn Ser Asn Gly Gly Ser Thr Tyr Tyr Pro 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 Thr Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Arg Asp Gly Tyr Asp Glu Gly Phe Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gln Ile Gln
115 120 125

Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
130 135 140

Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met His Trp Tyr
145 150 155 160

Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser
165 170 175

Lys Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
180 185 190

Thr Asp Tyr Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
195 200 205

Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Pro Thr Phe Gly Gln
210 215 220

Gly Thr Lys Leu Gln Ile Lys Arg Ala Ala Ala Leu Glu His His His
225 230 235 240

His His His

<210> 134
<211> 729
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of an anti-MucI diabody comprising cysteine replacement mutations in the VL FR3 Kabat positions 65 and 72 designated AVP02-128

<400> 134
agcgtgcagc tggttgaaag cggtggcgga gtggtgcagc caggtggaag cctgcgtctg 60

agctgcgcag caagcggttt acctttagc agctatggca tgagctgggt gcgtcaggcg 120

ccggataaag gcctggaact ggtggcgacc attaacagca acggtggaag cacctattat 180

ccggatagcg tgaaaggccg ttttaccatt agccgtgata acagcaaaaa caccctgtat 240

ctgcagatga acagcctgcg taccgaagat accgcggtgt attattgcgc gcgtgatcgt 300

gatggctatg atgaaggctt tgattattgg ggccagggca ccctggtgac cgtgagcagc 360

ggtgggggcg gaagccagat tcagctgacc cagagcccga gcagcctgag cgcaagcgtg 420

ggtgatcgtg tgaccattac ctgcagcgcg agcagcagcg tgagctatat gcattggtat 480

cagcagaaac cgggcaaagc gccgaaacgt tggatttatg ataccagcaa actggcgagc 540

ggcgtgccga gccgttttag cggctgcggc agcggcaccg attattgctt taccattagc 600

agcctgcagc cggaagatat tgcgacctat tattgccagc agtggagcag caacccgccg 660

acctttggcc agggcaccaa actgcagatt aaacgtgcgg ccgcactcga gcaccaccac 720

caccaccac 729

<210> 135
<211> 243
<212> PRT
<213> Artificial

<220>
<223> amino acid sequence of an anti-MucI diabody comprising cysteine replacement mutations in the VL FR3 Kabat positions 65 and 72 designated AVP02-128.

<400> 135

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

Ala Thr Ile Asn Ser Asn Gly Gly Ser Thr Tyr Tyr Pro 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 Thr Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Arg Asp Gly Tyr Asp Glu Gly Phe Asp Tyr Trp Gly Gln
100 105 110

```
Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gln Ile Gln
        115                 120                 125

Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
    130                 135                 140

Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met His Trp Tyr
145                 150                 155                 160

Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser
                165                 170                 175

Lys Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Cys Gly Ser Gly
            180                 185                 190

Thr Asp Tyr Cys Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
        195                 200                 205

Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Pro Thr Phe Gly Gln
    210                 215                 220

Gly Thr Lys Leu Gln Ile Lys Arg Ala Ala Ala Leu Glu His His His
225                 230                 235                 240

His His His
```

<210> 136
<211> 729
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of an anti-MucI diabody comprising cysteine replacement mutations in the VH FR3 Kabat positions 70 and 79 designated AVP02-129.

<400> 136

```
agcgtgcagc tggttgaaag cggtggcgga gtggtgcagc caggtggaag cctgcgtctg       60

agctgcgcag caagcggttt acctttagc agctatggca tgagctgggt gcgtcaggcg      120

ccggataaag gcctggaact ggtggcgacc attaacagca acggtggaag cacctattat      180

ccggatagcg tgaaaggccg ttttaccatt tgccgtgata acagcaaaaa caccctgtgc      240

ctgcagatga acagcctgcg taccgaagat accgcggtgt attattgcgc gcgtgatcgt      300

gatggctatg atgaaggctt tgattattgg ggccagggca ccctggtgac cgtgagcagc      360

ggtgggggcg gaagccagat tcagctgacc cagagcccga gcagcctgag cgcaagcgtg      420

ggtgatcgtg tgaccattac ctgcagcgcg agcagcagcg tgagctatat gcattggtat      480

cagcagaaac cgggcaaagc gccgaaacgt tggatttatg ataccagcaa actggcgagc      540

ggcgtgccga gccgttttag cggcagcggc agcggcaccg attatacctt taccattagc      600
```

agcctgcagc cggaagatat tgcgacctat tattgccagc agtggagcag caacccgccg 660

acctttggcc agggcaccaa actgcagatt aaacgtgcgg ccgcactcga gcaccaccac 720

caccaccac 729

<210> 137
<211> 243
<212> PRT
<213> Artificial

<220>
<223> amino acid sequence of an anti-MucI diabody comprising cysteine replacement mutations in the VH FR3 Kabat positions 70 and 79 designated AVP02-129

<400> 137

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

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

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

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

Ala Arg Asp Arg Asp Gly Tyr Asp Glu Gly Phe Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gln Ile Gln
115 120 125

Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
130 135 140

Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met His Trp Tyr
145 150 155 160

Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser
165 170 175

Lys Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
180 185 190

Thr Asp Tyr Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala

195 200 205

Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Pro Thr Phe Gly Gln
210 215 220

Gly Thr Lys Leu Gln Ile Lys Arg Ala Ala Ala Leu Glu His His His
225 230 235 240

His His His

<210> 138
<211> 729
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of an anti-MucI diabody comprising cysteine replacement mutations in the VH FR3 Kabat positions 72 and 75 designated AVP02-130

<400> 138
agcgtgcagc tggttgaaag cggtggcgga gtggtgcagc caggtggaag cctgcgtctg 60

agctgcgcag caagcggttt acctttagc agctatggca tgagctgggt gcgtcaggcg 120

ccggataaag gcctggaact ggtggcgacc attaacagca acggtggaag cacctattat 180

ccggatagcg tgaaaggccg ttttaccatt agccgttgca acagctgcaa caccctgtat 240

ctgcagatga acagcctgcg taccgaagat accgcggtgt attattgcgc gcgtgatcgt 300

gatggctatg atgaaggctt tgattattgg ggccagggca ccctggtgac cgtgagcagc 360

ggtgggggcg gaagccagat tcagctgacc cagagcccga gcagcctgag cgcaagcgtg 420

ggtgatcgtg tgaccattac ctgcagcgcg agcagcagcg tgagctatat gcattggtat 480

cagcagaaac cgggcaaagc gccgaaacgt tggatttatg ataccagcaa actggcgagc 540

ggcgtgccga gccgttttag cggcagcggc agcggcaccg attatacctt taccattagc 600

agcctgcagc cggaagatat tgcgacctat tattgccagc agtggagcag caacccgccg 660

acctttggcc agggcaccaa actgcagatt aaacgtgcgg ccgcactcga gcaccaccac 720

caccaccac 729

<210> 139
<211> 243
<212> PRT
<213> Artificial

<220>
<223> amino acid sequence of an anti-MucI diabody comprising cysteine replacement mutations in the VH FR3 Kabat positions 72 and 75 designated AVP02-130.

<400> 139

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

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

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

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

Ala Arg Asp Arg Asp Gly Tyr Asp Glu Gly Phe Asp Tyr Trp Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gln Ile Gln
        115                 120                 125

Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
    130                 135                 140

Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met His Trp Tyr
145                 150                 155                 160

Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser
                165                 170                 175

Lys Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
            180                 185                 190

Thr Asp Tyr Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
        195                 200                 205

Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Pro Thr Phe Gly Gln
    210                 215                 220

Gly Thr Lys Leu Gln Ile Lys Arg Ala Ala Ala Leu Glu His His His
225                 230                 235                 240

His His His
```

<210> 140
<211> 804
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of an anti-Her2 diabody comprising cysteine

replacement mutations in the VL FR2 Kabat positions 38 and 44 designated AVP07-131.

<400> 140
agcgtgcagc tggtgcagtc tggggcagag gtgaaaaagc ccggggagtc tctgaagatc 60

tcctgtaagg gttctggata cagctttacc agctactgga tcgcctgggt gcgccagatg 120

cccgggaaag gcctggagta catggggctc atctatcctg gtgactctga caccaaatac 180

agcccgtcct tccaaggcca ggtcaccatc tcagtcgaca agtccgtcag cactgcctac 240

ttgcaatgga gcagtctgaa gccctcggac agcgccgtgt atttttgtgc gagacatgac 300

gtgggatatg cgagtagttc caacgcggca aagtggcctg aatacttcca gcattggggc 360

cagggcaccc tggtcaccgt ttcctcaggt ggaggcggtt cacagtctgt gttgacgcag 420

ccgccctcag tgtctgcggc cccaggacag aaggtcacca tctcctgctc tggaagcagc 480

tccaacattg ggaataatta tgtatcctgg taccagtgcc tcccaggaac agtctgcaaa 540

ctcctcatct atggtcacac caatcggccc gcaggggtcc ctgaccgatt ctctggctcc 600

aagtctggca cctcagcctc cctggccatc agtgggttcc ggtccgagga tgaggctgat 660

tattactgtg cagcatggga tgacagcctg agtggttggg tgttcggcgg agggaccaag 720

ctgaccgtcc taggtgcggc cgcagaacaa aaactcatct cagaagagga tctgaatggg 780

gccgcacatc accatcatca ccat 804

<210> 141
<211> 268
<212> PRT
<213> Artificial

<220>
<223> amino acid sequence of an anti-Her2 diabody comprising cysteine replacement mutations in the VL FR2 Kabat positions 38 and 44 designated AVP07-131.

<400> 141

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

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
20 25 30

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

Gly Leu Ile Tyr Pro Gly Asp Ser Asp Thr Lys Tyr Ser Pro Ser Phe
50 55 60

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

Leu Gln Trp Ser Ser Leu Lys Pro Ser Asp Ser Ala Val Tyr Phe Cys
85 90 95

```
Ala Arg His Asp Val Gly Tyr Ala Ser Ser Ser Asn Ala Ala Lys Trp
            100                 105                 110

Pro Glu Tyr Phe Gln His Trp Gly Gln Gly Thr Leu Val Thr Val Ser
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gln Ser Val Leu Thr Gln Pro Pro Ser Val
    130                 135                 140

Ser Ala Ala Pro Gly Gln Lys Val Thr Ile Ser Cys Ser Gly Ser Ser
145                 150                 155                 160

Ser Asn Ile Gly Asn Asn Tyr Val Ser Trp Tyr Gln Cys Leu Pro Gly
                165                 170                 175

Thr Val Cys Lys Leu Leu Ile Tyr Gly His Thr Asn Arg Pro Ala Gly
            180                 185                 190

Val Pro Asp Arg Phe Ser Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu
        195                 200                 205

Ala Ile Ser Gly Phe Arg Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala
    210                 215                 220

Ala Trp Asp Asp Ser Leu Ser Gly Trp Val Phe Gly Gly Gly Thr Lys
225                 230                 235                 240

Leu Thr Val Leu Gly Ala Ala Ala Glu Gln Lys Leu Ile Ser Glu Glu
                245                 250                 255

Asp Leu Asn Gly Ala Ala His His His His His His
            260                 265
```

<210> 142
<211> 804
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of an anti-Her2 diabody comprising cysteine replacement mutations in the VH FR2 Kabat positions 39 and 45 designated AVP07-132.

<400> 142

```
agcgtgcagc tggtgcagtc tggggcagag gtgaaaaagc ccggggagtc tctgaagatc       60

tcctgtaagg gttctggata cagctttacc agctactgga tcgcctgggt gcgctgcatg      120

cccgggaaag gctgcgagta catggggctc atctatcctg gtgactctga caccaaatac      180

agcccgtcct tccaaggcca ggtcaccatc tcagtcgaca agtccgtcag cactgcctac      240

ttgcaatgga gcagtctgaa gccctcggac agcgccgtgt atttttgtgc gagacatgac      300

gtgggatatg cgagtagttc caacgcggca aagtggcctg aatacttcca gcattggggc      360
```

cagggcaccc tggtcaccgt ttcctcaggt ggaggcggtt cacagtctgt gttgacgcag 420

ccgccctcag tgtctgcggc cccaggacag aaggtcacca tctcctgctc tggaagcagc 480

tccaacattg ggaataatta tgtatcctgg taccagcagc tcccaggaac agtccccaaa 540

ctcctcatct atggtcacac caatcggccc gcaggggtcc ctgaccgatt ctctggctcc 600

aagtctggca cctcagcctc cctggccatc agtgggttcc ggtccgagga tgaggctgat 660

tattactgtg cagcatggga tgacagcctg agtggttggg tgttcggcgg agggaccaag 720

ctgaccgtcc taggtgcggc cgcagaacaa aaactcatct cagaagagga tctgaatggg 780

gccgcacatc accatcatca ccat 804

<210> 143
<211> 268
<212> PRT
<213> Artificial

<220>
<223> amino acid sequence of an anti-Her2 diabody comprising cysteine replacement mutations in the VH FR2 Kabat positions 39 and 45 designated AVP07-132.

<400> 143

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

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
20 25 30

Trp Ile Ala Trp Val Arg Cys Met Pro Gly Lys Gly Cys Glu Tyr Met
35 40 45

Gly Leu Ile Tyr Pro Gly Asp Ser Asp Thr Lys Tyr Ser Pro Ser Phe
50 55 60

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

Leu Gln Trp Ser Ser Leu Lys Pro Ser Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg His Asp Val Gly Tyr Ala Ser Ser Ser Asn Ala Ala Lys Trp
100 105 110

Pro Glu Tyr Phe Gln His Trp Gly Gln Gly Thr Leu Val Thr Val Ser
115 120 125

Ser Gly Gly Gly Gly Ser Gln Ser Val Leu Thr Gln Pro Pro Ser Val
130 135 140

Ser Ala Ala Pro Gly Gln Lys Val Thr Ile Ser Cys Ser Gly Ser Ser
145 150 155 160

```
Ser Asn Ile Gly Asn Asn Tyr Val Ser Trp Tyr Gln Gln Leu Pro Gly
                165                 170                 175

Thr Val Pro Lys Leu Leu Ile Tyr Gly His Thr Asn Arg Pro Ala Gly
            180                 185                 190

Val Pro Asp Arg Phe Ser Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu
        195                 200                 205

Ala Ile Ser Gly Phe Arg Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala
    210                 215                 220

Ala Trp Asp Asp Ser Leu Ser Gly Trp Val Phe Gly Gly Gly Thr Lys
225                 230                 235                 240

Leu Thr Val Leu Gly Ala Ala Ala Glu Gln Lys Leu Ile Ser Glu Glu
                245                 250                 255

Asp Leu Asn Gly Ala Ala His His His His His His
            260                 265
```

<210> 144
<211> 804
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of an anti-Her2 diabody comprising cysteine replacement mutations in the VL FR3 Kabat positions 65 and 72 designated AVP07-133.

<400> 144

```
agcgtgcagc tggtgcagtc tggggcagag gtgaaaaagc ccggggagtc tctgaagatc       60

tcctgtaagg gttctggata cagctttacc agctactgga tcgcctgggt gcgccagatg      120

cccgggaaag gcctggagta catggggctc atctatcctg gtgactctga caccaaatac      180

agcccgtcct tccaaggcca ggtcaccatc tcagtcgaca agtccgtcag cactgcctac      240

ttgcaatgga gcagtctgaa gccctcggac agcgccgtgt atttttgtgc gagacatgac      300

gtgggatatg cgagtagttc caacgcggca aagtggcctg aatacttcca gcattggggc      360

cagggcaccc tggtcaccgt ttcctcaggt ggaggcggtt cacagtctgt gttgacgcag      420

ccgccctcag tgtctgcggc cccaggacag aaggtcacca tctcctgctc tggaagcagc      480

tccaacattg ggaataatta tgtatcctgg taccagcagc tcccaggaac agtccccaaa      540

ctcctcatct atggtcacac caatcggccc gcaggggtcc ctgaccgatt ctctggctgc      600

aagtctggca cctcagcctg cctggccatc agtgggttcc ggtccgagga tgaggctgat      660

tattactgtg cagcatggga tgacagcctg agtggttggg tgttcggcgg agggaccaag      720

ctgaccgtcc taggtgcggc cgcagaacaa aaactcatct cagaagagga tctgaatggg      780
```

gccgcacatc accatcatca ccat 804

<210> 145
<211> 268
<212> PRT
<213> Artificial

<220>
<223> amino acid sequence of an anti-Her2 diabody comprising cysteine replacement mutations in the VL FR3 Kabat positions 65 and 72 designated AVP07-133.

<400> 145

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

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
20 25 30

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

Gly Leu Ile Tyr Pro Gly Asp Ser Asp Thr Lys Tyr Ser Pro Ser Phe
50 55 60

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

Leu Gln Trp Ser Ser Leu Lys Pro Ser Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg His Asp Val Gly Tyr Ala Ser Ser Ser Asn Ala Ala Lys Trp
100 105 110

Pro Glu Tyr Phe Gln His Trp Gly Gln Gly Thr Leu Val Thr Val Ser
115 120 125

Ser Gly Gly Gly Gly Ser Gln Ser Val Leu Thr Gln Pro Pro Ser Val
130 135 140

Ser Ala Ala Pro Gly Gln Lys Val Thr Ile Ser Cys Ser Gly Ser Ser
145 150 155 160

Ser Asn Ile Gly Asn Asn Tyr Val Ser Trp Tyr Gln Gln Leu Pro Gly
165 170 175

Thr Val Pro Lys Leu Leu Ile Tyr Gly His Thr Asn Arg Pro Ala Gly
180 185 190

Val Pro Asp Arg Phe Ser Gly Cys Lys Ser Gly Thr Ser Ala Cys Leu
195 200 205

Ala Ile Ser Gly Phe Arg Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala

210 215 220

Ala Trp Asp Asp Ser Leu Ser Gly Trp Val Phe Gly Gly Gly Thr Lys
225 230 235 240

Leu Thr Val Leu Gly Ala Ala Ala Glu Gln Lys Leu Ile Ser Glu Glu
245 250 255

Asp Leu Asn Gly Ala Ala His His His His His His
260 265

<210> 146
<211> 804
<212> DNA
<213> Artificial

<220>
<223> nucleotide sequence of an anti-Her2 diabody comprising cysteine replacement mutations in the VH FR3 Kabat positions 70 and 79 designated AVP07-134.

<400> 146
agcgtgcagc tggtgcagtc tggggcagag gtgaaaaagc ccggggagtc tctgaagatc 60

tcctgtaagg gttctggata cagctttacc agctactgga tcgcctgggt gcgccagatg 120

cccgggaaag gcctggagta catggggctc atctatcctg gtgactctga caccaaatac 180

agcccgtcct tccaaggcca ggtcaccatc tgcgtcgaca agtccgtcag cactgcctgc 240

ttgcaatgga gcagtctgaa gccctcggac agcgccgtgt atttttgtgc gagacatgac 300

gtgggatatg cgagtagttc caacgcggca aagtggcctg aatacttcca gcattggggc 360

cagggcaccc tggtcaccgt ttcctcaggt ggaggcggtt cacagtctgt gttgacgcag 420

ccgccctcag tgtctgcggc cccaggacag aaggtcacca tctcctgctc tggaagcagc 480

tccaacattg ggaataatta tgtatcctgg taccagcagc tcccaggaac agtccccaaa 540

ctcctcatct atggtcacac caatcggccc gcaggggtcc ctgaccgatt ctctggctcc 600

aagtctggca cctcagcctc cctggccatc agtgggttcc ggtccgagga tgaggctgat 660

tattactgtg cagcatggga tgacagcctg agtggttggg tgttcggcgg agggaccaag 720

ctgaccgtcc taggtgcggc cgcagaacaa aaactcatct cagaagagga tctgaatggg 780

gccgcacatc accatcatca ccat 804

<210> 147
<211> 268
<212> PRT
<213> Artificial

<220>
<223> amino acid sequence of an anti-Her2 diabody comprising cysteine replacement mutations in the VH FR3 Kabat positions 70 and 79 designated AVP07-134

<400> 147

Ser Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu

1 5 10 15

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
20 25 30

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

Gly Leu Ile Tyr Pro Gly Asp Ser Asp Thr Lys Tyr Ser Pro Ser Phe
50 55 60

Gln Gly Gln Val Thr Ile Cys Val Asp Lys Ser Val Ser Thr Ala Cys
65 70 75 80

Leu Gln Trp Ser Ser Leu Lys Pro Ser Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg His Asp Val Gly Tyr Ala Ser Ser Ser Asn Ala Ala Lys Trp
100 105 110

Pro Glu Tyr Phe Gln His Trp Gly Gln Gly Thr Leu Val Thr Val Ser
115 120 125

Ser Gly Gly Gly Gly Ser Gln Ser Val Leu Thr Gln Pro Pro Ser Val
130 135 140

Ser Ala Ala Pro Gly Gln Lys Val Thr Ile Ser Cys Ser Gly Ser Ser
145 150 155 160

Ser Asn Ile Gly Asn Asn Tyr Val Ser Trp Tyr Gln Gln Leu Pro Gly
165 170 175

Thr Val Pro Lys Leu Leu Ile Tyr Gly His Thr Asn Arg Pro Ala Gly
180 185 190

Val Pro Asp Arg Phe Ser Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu
195 200 205

Ala Ile Ser Gly Phe Arg Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala
210 215 220

Ala Trp Asp Asp Ser Leu Ser Gly Trp Val Phe Gly Gly Gly Thr Lys
225 230 235 240

Leu Thr Val Leu Gly Ala Ala Ala Glu Gln Lys Leu Ile Ser Glu Glu
245 250 255

Asp Leu Asn Gly Ala Ala His His His His His His
260 265

<210> 148

<211> 804
<212> DNA
<213> Artificial

<220>
<223> SEQ ID NO: 148 - nucleotide sequence of an anti-Her2 diabody comprising cysteine replacement mutations in the VH FR3 Kabat positions 72 and 75 designated AVP07-135.

<400> 148
agcgtgcagc tggtgcagtc tggggcagag gtgaaaaagc ccggggagtc tctgaagatc 60

tcctgtaagg gttctggata cagctttacc agctactgga tcgcctgggt gcgccagatg 120

cccgggaaag gcctggagta catggggctc atctatcctg gtgactctga caccaaatac 180

agcccgtcct tccaaggcca ggtcaccatc tcagtctgca agtcctgcag cactgcctac 240

ttgcaatgga gcagtctgaa gccctcggac agcgccgtgt atttttgtgc gagacatgac 300

gtgggatatg cgagtagttc caacgcggca aagtggcctg aatacttcca gcattggggc 360

cagggcaccc tggtcaccgt ttcctcaggt ggaggcggtt cacagtctgt gttgacgcag 420

ccgccctcag tgtctgcggc cccaggacag aaggtcacca tctcctgctc tggaagcagc 480

tccaacattg ggaataatta tgtatcctgg taccagcagc tcccaggaac agtccccaaa 540

ctcctcatct atggtcacac caatcggccc gcaggggtcc ctgaccgatt ctctggctcc 600

aagtctggca cctcagcctc cctggccatc agtgggttcc ggtccgagga tgaggctgat 660

tattactgtg cagcatggga tgacagcctg agtggttggg tgttcggcgg agggaccaag 720

ctgaccgtcc taggtgcggc cgcagaacaa aaactcatct cagaagagga tctgaatggg 780

gccgcacatc accatcatca ccat 804

<210> 149
<211> 268
<212> PRT
<213> Artificial

<220>
<223> amino acid sequence of an anti-Her2 diabody comprising cysteine replacement mutations in the VH FR3 Kabat positions 72 and 75 designated AVP07-135.

<400> 149

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

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
20 25 30

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

Gly Leu Ile Tyr Pro Gly Asp Ser Asp Thr Lys Tyr Ser Pro Ser Phe
50 55 60

Gln Gly Gln Val Thr Ile Ser Val Cys Lys Ser Cys Ser Thr Ala Tyr

65 70 75 80

Leu Gln Trp Ser Ser Leu Lys Pro Ser Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg His Asp Val Gly Tyr Ala Ser Ser Ser Asn Ala Ala Lys Trp
100 105 110

Pro Glu Tyr Phe Gln His Trp Gly Gln Gly Thr Leu Val Thr Val Ser
115 120 125

Ser Gly Gly Gly Gly Ser Gln Ser Val Leu Thr Gln Pro Pro Ser Val
130 135 140

Ser Ala Ala Pro Gly Gln Lys Val Thr Ile Ser Cys Ser Gly Ser Ser
145 150 155 160

Ser Asn Ile Gly Asn Asn Tyr Val Ser Trp Tyr Gln Gln Leu Pro Gly
165 170 175

Thr Val Pro Lys Leu Leu Ile Tyr Gly His Thr Asn Arg Pro Ala Gly
180 185 190

Val Pro Asp Arg Phe Ser Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu
195 200 205

Ala Ile Ser Gly Phe Arg Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala
210 215 220

Ala Trp Asp Asp Ser Leu Ser Gly Trp Val Phe Gly Gly Gly Thr Lys
225 230 235 240

Leu Thr Val Leu Gly Ala Ala Ala Glu Gln Lys Leu Ile Ser Glu Glu
245 250 255

Asp Leu Asn Gly Ala Ala His His His His His His
260 265

<210> 150
<211> 1255
<212> PRT
<213> Homo sapiens

<400> 150

Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu
1 5 10 15

Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys
20 25 30

Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
35 40 45

```
Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
    50                  55                  60

Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
65                  70                  75                  80

Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
                85                  90                  95

Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
            100                 105                 110

Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
        115                 120                 125

Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
    130                 135                 140

Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
145                 150                 155                 160

Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn
                165                 170                 175

Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
            180                 185                 190

His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
        195                 200                 205

Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
    210                 215                 220

Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
225                 230                 235                 240

Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
                245                 250                 255

His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
            260                 265                 270

Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
        275                 280                 285

Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu
    290                 295                 300

Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln
305                 310                 315                 320
```

Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys
325 330 335

Pro Cys Ala Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Glu
340 345 350

Val Arg Ala Val Thr Ser Ala Asn Ile Gln Glu Phe Ala Gly Cys Lys
355 360 365

Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly Asp
370 375 380

Pro Ala Ser Asn Thr Ala Pro Leu Gln Pro Glu Gln Leu Gln Val Phe
385 390 395 400

Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro
405 410 415

Asp Ser Leu Pro Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg
420 425 430

Gly Arg Ile Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu
435 440 445

Gly Ile Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly
450 455 460

Leu Ala Leu Ile His His Asn Thr His Leu Cys Phe Val His Thr Val
465 470 475 480

Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His Thr
485 490 495

Ala Asn Arg Pro Glu Asp Glu Cys Val Gly Glu Gly Leu Ala Cys His
500 505 510

Gln Leu Cys Ala Arg Gly His Cys Trp Gly Pro Gly Pro Thr Gln Cys
515 520 525

Val Asn Cys Ser Gln Phe Leu Arg Gly Gln Glu Cys Val Glu Glu Cys
530 535 540

Arg Val Leu Gln Gly Leu Pro Arg Glu Tyr Val Asn Ala Arg His Cys
545 550 555 560

Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Gly Ser Val Thr Cys
565 570 575

Phe Gly Pro Glu Ala Asp Gln Cys Val Ala Cys Ala His Tyr Lys Asp
580 585 590

```
Pro Pro Phe Cys Val Ala Arg Cys Pro Ser Gly Val Lys Pro Asp Leu
        595                 600                 605

Ser Tyr Met Pro Ile Trp Lys Phe Pro Asp Glu Glu Gly Ala Cys Gln
    610                 615                 620

Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Asp Lys
625                 630                 635                 640

Gly Cys Pro Ala Glu Gln Arg Ala Ser Pro Leu Thr Ser Ile Val Ser
                645                 650                 655

Ala Val Val Gly Ile Leu Leu Val Val Val Leu Gly Val Val Phe Gly
            660                 665                 670

Ile Leu Ile Lys Arg Arg Gln Gln Lys Ile Arg Lys Tyr Thr Met Arg
        675                 680                 685

Arg Leu Leu Gln Glu Thr Glu Leu Val Glu Pro Leu Thr Pro Ser Gly
    690                 695                 700

Ala Met Pro Asn Gln Ala Gln Met Arg Ile Leu Lys Glu Thr Glu Leu
705                 710                 715                 720

Arg Lys Val Lys Val Leu Gly Ser Gly Ala Phe Gly Thr Val Tyr Lys
                725                 730                 735

Gly Ile Trp Ile Pro Asp Gly Glu Asn Val Lys Ile Pro Val Ala Ile
            740                 745                 750

Lys Val Leu Arg Glu Asn Thr Ser Pro Lys Ala Asn Lys Glu Ile Leu
        755                 760                 765

Asp Glu Ala Tyr Val Met Ala Gly Val Gly Ser Pro Tyr Val Ser Arg
    770                 775                 780

Leu Leu Gly Ile Cys Leu Thr Ser Thr Val Gln Leu Val Thr Gln Leu
785                 790                 795                 800

Met Pro Tyr Gly Cys Leu Leu Asp His Val Arg Glu Asn Arg Gly Arg
                805                 810                 815

Leu Gly Ser Gln Asp Leu Leu Asn Trp Cys Met Gln Ile Ala Lys Gly
            820                 825                 830

Met Ser Tyr Leu Glu Asp Val Arg Leu Val His Arg Asp Leu Ala Ala
        835                 840                 845

Arg Asn Val Leu Val Lys Ser Pro Asn His Val Lys Ile Thr Asp Phe
    850                 855                 860
```

```
Gly Leu Ala Arg Leu Leu Asp Ile Asp Glu Thr Glu Tyr His Ala Asp
865                 870                 875                 880

Gly Gly Lys Val Pro Ile Lys Trp Met Ala Leu Glu Ser Ile Leu Arg
                885                 890                 895

Arg Arg Phe Thr His Gln Ser Asp Val Trp Ser Tyr Gly Val Thr Val
            900                 905                 910

Trp Glu Leu Met Thr Phe Gly Ala Lys Pro Tyr Asp Gly Ile Pro Ala
        915                 920                 925

Arg Glu Ile Pro Asp Leu Leu Glu Lys Gly Glu Arg Leu Pro Gln Pro
    930                 935                 940

Pro Ile Cys Thr Ile Asp Val Tyr Met Ile Met Val Lys Cys Trp Met
945                 950                 955                 960

Ile Asp Ser Glu Cys Arg Pro Arg Phe Arg Glu Leu Val Ser Glu Phe
                965                 970                 975

Ser Arg Met Ala Arg Asp Pro Gln Arg Phe Val Val Ile Gln Asn Glu
            980                 985                 990

Asp Leu Gly Pro Ala Ser Pro Leu  Asp Ser Thr Phe Tyr  Arg Ser Leu
        995                 1000                1005

Leu Glu  Asp Asp Asp Met Gly  Asp Leu Val Asp Ala  Glu Glu Tyr
    1010                1015                1020

Leu Val  Pro Gln Gln Gly Phe  Phe Cys Pro Asp Pro  Ala Pro Gly
    1025                1030                1035

Ala Gly  Gly Met Val His His  Arg His Arg Ser Ser  Ser Thr Arg
    1040                1045                1050

Ser Gly  Gly Gly Asp Leu Thr  Leu Gly Leu Glu Pro  Ser Glu Glu
    1055                1060                1065

Glu Ala  Pro Arg Ser Pro Leu  Ala Pro Ser Glu Gly  Ala Gly Ser
    1070                1075                1080

Asp Val  Phe Asp Gly Asp Leu  Gly Met Gly Ala Ala  Lys Gly Leu
    1085                1090                1095

Gln Ser  Leu Pro Thr His Asp  Pro Ser Pro Leu Gln  Arg Tyr Ser
    1100                1105                1110

Glu Asp  Pro Thr Val Pro Leu  Pro Ser Glu Thr Asp  Gly Tyr Val
    1115                1120                1125
```

```
Ala Pro  Leu Thr Cys Ser Pro  Gln Pro Glu Tyr Val  Asn Gln Pro
    1130                1135                1140

Asp Val  Arg Pro Gln Pro Pro  Ser Pro Arg Glu Gly  Pro Leu Pro
    1145                1150                1155

Ala Ala  Arg Pro Ala Gly Ala  Thr Leu Glu Arg Ala  Lys Thr Leu
    1160                1165                1170

Ser Pro  Gly Lys Asn Gly Val  Val Lys Asp Val Phe  Ala Phe Gly
    1175                1180                1185

Gly Ala  Val Glu Asn Pro Glu  Tyr Leu Thr Pro Gln  Gly Gly Ala
    1190                1195                1200

Ala Pro  Gln Pro His Pro Pro  Pro Ala Phe Ser Pro  Ala Phe Asp
    1205                1210                1215

Asn Leu  Tyr Tyr Trp Asp Gln  Asp Pro Pro Glu Arg  Gly Ala Pro
    1220                1225                1230

Pro Ser  Thr Phe Lys Gly Thr  Pro Thr Ala Glu Asn  Pro Glu Tyr
    1235                1240                1245

Leu Gly  Leu Asp Val Pro Val
    1250                1255
```

<210> 151
<211> 750
<212> PRT
<213> Homo sapiens

<400> 151

```
Met Trp Asn Leu Leu His Glu Thr Asp Ser Ala Val Ala Thr Ala Arg
1               5                  10                  15

Arg Pro Arg Trp Leu Cys Ala Gly Ala Leu Val Leu Ala Gly Gly Phe
            20                  25                  30

Phe Leu Leu Gly Phe Leu Phe Gly Trp Phe Ile Lys Ser Ser Asn Glu
        35                  40                  45

Ala Thr Asn Ile Thr Pro Lys His Asn Met Lys Ala Phe Leu Asp Glu
    50                  55                  60

Leu Lys Ala Glu Asn Ile Lys Lys Phe Leu His Asn Phe Thr Gln Ile
65                  70                  75                  80

Pro His Leu Ala Gly Thr Glu Gln Asn Phe Gln Leu Ala Lys Gln Ile
                85                  90                  95
```

```
Gln Ser Gln Trp Lys Glu Phe Gly Leu Asp Ser Val Glu Leu Ala His
            100                 105                 110

Tyr Asp Val Leu Leu Ser Tyr Pro Asn Lys Thr His Pro Asn Tyr Ile
        115                 120                 125

Ser Ile Ile Asn Glu Asp Gly Asn Glu Ile Phe Asn Thr Ser Leu Phe
    130                 135                 140

Glu Pro Pro Pro Pro Gly Tyr Glu Asn Val Ser Asp Ile Val Pro Pro
145                 150                 155                 160

Phe Ser Ala Phe Ser Pro Gln Gly Met Pro Glu Gly Asp Leu Val Tyr
                165                 170                 175

Val Asn Tyr Ala Arg Thr Glu Asp Phe Phe Lys Leu Glu Arg Asp Met
            180                 185                 190

Lys Ile Asn Cys Ser Gly Lys Ile Val Ile Ala Arg Tyr Gly Lys Val
        195                 200                 205

Phe Arg Gly Asn Lys Val Lys Asn Ala Gln Leu Ala Gly Ala Lys Gly
    210                 215                 220

Val Ile Leu Tyr Ser Asp Pro Ala Asp Tyr Phe Ala Pro Gly Val Lys
225                 230                 235                 240

Ser Tyr Pro Asp Gly Trp Asn Leu Pro Gly Gly Gly Val Gln Arg Gly
                245                 250                 255

Asn Ile Leu Asn Leu Asn Gly Ala Gly Asp Pro Leu Thr Pro Gly Tyr
            260                 265                 270

Pro Ala Asn Glu Tyr Ala Tyr Arg Arg Gly Ile Ala Glu Ala Val Gly
        275                 280                 285

Leu Pro Ser Ile Pro Val His Pro Ile Gly Tyr Tyr Asp Ala Gln Lys
    290                 295                 300

Leu Leu Glu Lys Met Gly Gly Ser Ala Pro Pro Asp Ser Ser Trp Arg
305                 310                 315                 320

Gly Ser Leu Lys Val Pro Tyr Asn Val Gly Pro Gly Phe Thr Gly Asn
                325                 330                 335

Phe Ser Thr Gln Lys Val Lys Met His Ile His Ser Thr Asn Glu Val
            340                 345                 350

Thr Arg Ile Tyr Asn Val Ile Gly Thr Leu Arg Gly Ala Val Glu Pro
        355                 360                 365
```

```
Asp Arg Tyr Val Ile Leu Gly Gly His Arg Asp Ser Trp Val Phe Gly
    370                 375                 380

Gly Ile Asp Pro Gln Ser Gly Ala Ala Val Val His Glu Ile Val Arg
385                 390                 395                 400

Ser Phe Gly Thr Leu Lys Lys Glu Gly Trp Arg Pro Arg Arg Thr Ile
                405                 410                 415

Leu Phe Ala Ser Trp Asp Ala Glu Glu Phe Gly Leu Leu Gly Ser Thr
            420                 425                 430

Glu Trp Ala Glu Glu Asn Ser Arg Leu Leu Gln Glu Arg Gly Val Ala
        435                 440                 445

Tyr Ile Asn Ala Asp Ser Ser Ile Glu Gly Asn Tyr Thr Leu Arg Val
    450                 455                 460

Asp Cys Thr Pro Leu Met Tyr Ser Leu Val His Asn Leu Thr Lys Glu
465                 470                 475                 480

Leu Lys Ser Pro Asp Glu Gly Phe Glu Gly Lys Ser Leu Tyr Glu Ser
                485                 490                 495

Trp Thr Lys Lys Ser Pro Ser Pro Glu Phe Ser Gly Met Pro Arg Ile
            500                 505                 510

Ser Lys Leu Gly Ser Gly Asn Asp Phe Glu Val Phe Phe Gln Arg Leu
        515                 520                 525

Gly Ile Ala Ser Gly Arg Ala Arg Tyr Thr Lys Asn Trp Glu Thr Asn
    530                 535                 540

Lys Phe Ser Gly Tyr Pro Leu Tyr His Ser Val Tyr Glu Thr Tyr Glu
545                 550                 555                 560

Leu Val Glu Lys Phe Tyr Asp Pro Met Phe Lys Tyr His Leu Thr Val
                565                 570                 575

Ala Gln Val Arg Gly Gly Met Val Phe Glu Leu Ala Asn Ser Ile Val
            580                 585                 590

Leu Pro Phe Asp Cys Arg Asp Tyr Ala Val Val Leu Arg Lys Tyr Ala
        595                 600                 605

Asp Lys Ile Tyr Ser Ile Ser Met Lys His Pro Gln Glu Met Lys Thr
    610                 615                 620

Tyr Ser Val Ser Phe Asp Ser Leu Phe Ser Ala Val Lys Asn Phe Thr
625                 630                 635                 640
```

```
Glu Ile Ala Ser Lys Phe Ser Glu Arg Leu Gln Asp Phe Asp Lys Ser
                645                 650                 655

Asn Pro Ile Val Leu Arg Met Met Asn Asp Gln Leu Met Phe Leu Glu
            660                 665                 670

Arg Ala Phe Ile Asp Pro Leu Gly Leu Pro Asp Arg Pro Phe Tyr Arg
        675                 680                 685

His Val Ile Tyr Ala Pro Ser Ser His Asn Lys Tyr Ala Gly Glu Ser
    690                 695                 700

Phe Pro Gly Ile Tyr Asp Ala Leu Phe Asp Ile Glu Ser Lys Val Asp
705                 710                 715                 720

Pro Ser Lys Ala Trp Gly Glu Val Lys Arg Gln Ile Tyr Val Ala Ala
                725                 730                 735

Phe Thr Val Gln Ala Ala Ala Glu Thr Leu Ser Glu Val Ala
            740                 745                 750
```

<210> 152
<211> 475
<212> PRT
<213> Homo sapiens

<400> 152

```
Met Thr Pro Gly Thr Gln Ser Pro Phe Phe Leu Leu Leu Leu Leu Thr
1               5                   10                  15

Val Leu Thr Val Val Thr Gly Ser Gly His Ala Ser Ser Thr Pro Gly
            20                  25                  30

Gly Glu Lys Glu Thr Ser Ala Thr Gln Arg Ser Ser Val Pro Ser Ser
        35                  40                  45

Thr Glu Lys Asn Ala Val Ser Met Thr Ser Ser Val Leu Ser Ser His
    50                  55                  60

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

Ala Pro Ala Thr Glu Pro Ala Ser Gly Ser Ala Ala Thr Trp Gly Gln
                85                  90                  95

Asp Val Thr Ser Val Pro Val Thr Arg Pro Ala Leu Gly Ser Thr Thr
            100                 105                 110

Pro Pro Ala His Asp Val Thr Ser Ala Pro Asp Asn Lys Pro Ala Pro
        115                 120                 125
```

```
Gly Ser Thr Ala Pro Pro Ala His Gly Val Thr Ser Ala Pro Asp Thr
    130                 135                 140

Arg Pro Ala Pro Gly Ser Thr Ala Pro Pro Ala His Gly Val Thr Ser
145                 150                 155                 160

Ala Pro Asp Asn Arg Pro Ala Leu Gly Ser Thr Ala Pro Pro Val His
                165                 170                 175

Asn Val Thr Ser Ala Ser Gly Ser Ala Ser Gly Ser Ala Ser Thr Leu
            180                 185                 190

Val His Asn Gly Thr Ser Ala Arg Ala Thr Thr Thr Pro Ala Ser Lys
        195                 200                 205

Ser Thr Pro Phe Ser Ile Pro Ser His His Ser Asp Thr Pro Thr Thr
    210                 215                 220

Leu Ala Ser His Ser Thr Lys Thr Asp Ala Ser Ser Thr His His Ser
225                 230                 235                 240

Thr Val Pro Pro Leu Thr Ser Ser Asn His Ser Thr Ser Pro Gln Leu
                245                 250                 255

Ser Thr Gly Val Ser Phe Phe Phe Leu Ser Phe His Ile Ser Asn Leu
            260                 265                 270

Gln Phe Asn Ser Ser Leu Glu Asp Pro Ser Thr Asp Tyr Tyr Gln Glu
        275                 280                 285

Leu Gln Arg Asp Ile Ser Glu Met Phe Leu Gln Ile Tyr Lys Gln Gly
    290                 295                 300

Gly Phe Leu Gly Leu Ser Asn Ile Lys Phe Arg Pro Gly Ser Val Val
305                 310                 315                 320

Val Gln Leu Thr Leu Ala Phe Arg Glu Gly Thr Ile Asn Val His Asp
                325                 330                 335

Val Glu Thr Gln Phe Asn Gln Tyr Lys Thr Glu Ala Ala Ser Arg Tyr
            340                 345                 350

Asn Leu Thr Ile Ser Asp Val Ser Val Ser Asp Val Pro Phe Pro Phe
        355                 360                 365

Ser Ala Gln Ser Gly Ala Gly Val Pro Gly Trp Gly Ile Ala Leu Leu
    370                 375                 380

Val Leu Val Cys Val Leu Val Ala Leu Ala Ile Val Tyr Leu Ile Ala
385                 390                 395                 400
```

Leu Ala Val Cys Gln Cys Arg Arg Lys Asn Tyr Gly Gln Leu Asp Ile
405 410 415

Phe Pro Ala Arg Asp Thr Tyr His Pro Met Ser Glu Tyr Pro Thr Tyr
420 425 430

His Thr His Gly Arg Tyr Val Pro Pro Ser Ser Thr Asp Arg Ser Pro
435 440 445

Tyr Glu Lys Val Ser Ala Gly Asn Gly Gly Ser Ser Leu Ser Tyr Thr
450 455 460

Asn Pro Ala Val Ala Ala Thr Ser Ala Asn Leu
465 470 475

<210> 153
<211> 307
<212> PRT
<213> Homo sapiens

<400> 153

Met Thr Pro Gly Thr Gln Ser Pro Phe Phe Leu Leu Leu Leu Leu Thr
1 5 10 15

Val Leu Thr Val Val Thr Gly Ser Gly His Ala Ser Ser Thr Pro Gly
20 25 30

Gly Glu Lys Glu Thr Ser Ala Thr Gln Arg Ser Ser Val Pro Ser Ser
35 40 45

Thr Glu Lys Asn Ala Val Ser Met Thr Ser Ser Val Leu Ser Ser His
50 55 60

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

Ala Pro Ala Thr Glu Pro Ala Ser Gly Ser Ala Ala Thr Trp Gly Gln
85 90 95

Asp Val Thr Ser Val Pro Val Thr Arg Pro Ala Leu Gly Ser Thr Thr
100 105 110

Pro Pro Ala His Asp Val Thr Ser Ala Pro Asp Asn Lys Pro Ala Pro
115 120 125

Gly Ser Thr Ala Pro Pro Ala Gln Gly Val Thr Ser Ala Pro Glu Thr
130 135 140

Arg Pro Pro Pro Gly Ser Thr Ala Pro Pro Ala His Gly Val Thr Ser
145 150 155 160

Ala Pro Asp Asn Arg Pro Ala Leu Ala Ser Thr Ala Pro Pro Val His

165 170 175

Asn Val Thr Ser Ala Ser Gly Ser Ala Ser Gly Ser Ala Ser Thr Leu
180 185 190

Val His Asn Gly Thr Ser Ala Arg Ala Thr Thr Thr Pro Ala Ser Lys
195 200 205

Ser Thr Pro Phe Ser Ile Pro Ser His His Ser Asp Thr Pro Thr Thr
210 215 220

Leu Ala Ser His Ser Thr Lys Thr Asp Ala Ser Ser Thr His His Ser
225 230 235 240

Thr Val Pro Pro Leu Thr Ser Ser Asn His Ser Thr Ser Pro Gln Leu
245 250 255

Ser Thr Gly Val Ser Phe Phe Phe Leu Ser Phe His Ile Ser Asn Leu
260 265 270

Gln Phe Asn Ser Ser Leu Glu Asp Pro Ser Thr Asp Tyr Tyr Gln Glu
275 280 285

Leu Gln Arg Asp Ile Ser Glu Met Val Ser Ile Gly Leu Ser Phe Pro
290 295 300

Met Leu Pro
305

<210> 154
<211> 735
<212> DNA
<213> artificial

<220>
<223> nucleotide sequence encoding AVP04-50 diabody

<400> 154
agcgtgcagc tgcagcagag cgatgcggaa ctggtgaaac cgggcgcgag cgtgaaaatt 60

agctgcaaag cgagcggcta tacctttacc gatcatgcga ttcattgggt gaaacagaat 120

ccggaacagg gcctggaatg gattggctat tttagcccgg gcaacgatga ttttaaatat 180

aacgaacgtt ttaaaggcaa agcgaccctg accgcggata aaagcagcag caccgcgtat 240

ctgcagctga acagcctgac cagcgaagat agcgcggtgt atttttgcac ccgtagcctg 300

aatatggcgt attggggtca gggcacctcg gtcaccgtga gcagcggtgg cggcggcagc 360

gatatcgtga tgacccagag ctgcagcagc tgcccggtga gcgtgggcga aaaagtgacc 420

ctgagctgca aaagcagcca gagcctgctg tatagcggca atcagaaaaa ctatctggcg 480

tggtatcagc agaaaccggg tcagagcccg aaactgctga tttattgggc gagcacccgt 540

gaaagcggcg tgccggatcg ttttaccggc agcggtagcg gcaccgattt taccctgagc 600

attagcagcg tggaaaccga agatctggcg gtgtattatt gccagcagta ttatagctat 660

ccgctgacct ttggtgcggg caccaaactg gtgctgaaac gtgcggccgc actcgagcac 720

caccaccacc accac 735

<210> 155
<211> 245
<212> PRT
<213> artificial

<220>
<223> amino acid sequence of AVP04-50 diabody

<400> 155

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

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

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

Gly Tyr Phe Ser Pro Gly Asn Asp Asp Phe Lys Tyr Asn Glu Arg Phe
50 55 60

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

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

Thr Arg Ser Leu Asn Met Ala Tyr Trp Gly Gln Gly Thr Ser Val Thr
100 105 110

Val Ser Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Ser Cys
115 120 125

Ser Ser Cys Pro Val Ser Val Gly Glu Lys Val Thr Leu Ser Cys Lys
130 135 140

Ser Ser Gln Ser Leu Leu Tyr Ser Gly Asn Gln Lys Asn Tyr Leu Ala
145 150 155 160

Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Trp
165 170 175

Ala Ser Thr Arg Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly
180 185 190

Ser Gly Thr Asp Phe Thr Leu Ser Ile Ser Ser Val Glu Thr Glu Asp
195 200 205

```
Leu Ala Val Tyr Tyr Cys Gln Gln Tyr Tyr Ser Tyr Pro Leu Thr Phe
    210                 215                 220

Gly Ala Gly Thr Lys Leu Val Leu Lys Arg Ala Ala Ala Leu Glu His
225                 230                 235                 240

His His His His His
                245
```

<210> 156
<211> 804
<212> DNA
<213> artificial

<220>
<223> nucleotide sequence encoding AVP07-63 diabody

<400> 156

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agcgtgcagc tggtgcagtc tggggcagag gtgaaaaagc ccggggagtc tctgaagatc       60

tcctgtaagg gttctggata cagctttacc agctactgga tcgcctgggt gcgccagatg      120

cccgggaaag gcctggagta catggggctc atctatcctg gtgactctga caccaaatac      180

agcccgtcct tccaaggcca ggtcaccatc tcagtcgaca agtccgtcag cactgcctac      240

ttgcaatgga gcagtctgaa gccctcggac agcgccgtgt atttttgtgc gagacatgac      300

gtgggatatg cgagtagttc caacgcggca aagtggcctg aatacttcca gcattggggc      360

cagggcaccc tggtcaccgt ttcctcaggt ggaggcggtt cacagtctgt gttgacgcag      420

ccgtgcagca gctgcgcggc cccaggacag aaggtcacca tctcctgctc tggaagcagc      480

tccaacattg ggaataatta tgtatcctgg taccagcagc tcccaggaac agtccccaaa      540

ctcctcatct atggtcacac caatcggccc gcaggggtcc ctgaccgatt ctctggctcc      600

aagtctggca cctcagcctc cctggccatc agtgggttcc ggtccgagga tgaggctgat      660

tattactgtg cagcatggga tgacagcctg agtggttggg tgttcggcgg agggaccaag      720

ctgaccgtcc taggtgcggc cgcagaacaa aaactcatct cagaagagga tctgaatggg      780

gccgcacatc accatcatca ccat                                             804
```

<210> 157
<211> 268
<212> PRT
<213> artificial

<220>
<223> amino acid sequence of AVP07-63 diabody

<400> 157

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

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
            20                  25                  30
```

```
Trp Ile Ala Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Tyr Met
        35                  40                  45

Gly Leu Ile Tyr Pro Gly Asp Ser Asp Thr Lys Tyr Ser Pro Ser Phe
    50                  55                  60

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

Leu Gln Trp Ser Ser Leu Lys Pro Ser Asp Ser Ala Val Tyr Phe Cys
                85                  90                  95

Ala Arg His Asp Val Gly Tyr Ala Ser Ser Ser Asn Ala Ala Lys Trp
            100                 105                 110

Pro Glu Tyr Phe Gln His Trp Gly Gln Gly Thr Leu Val Thr Val Ser
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gln Ser Val Leu Thr Gln Pro Cys Ser Ser
    130                 135                 140

Cys Ala Ala Pro Gly Gln Lys Val Thr Ile Ser Cys Ser Gly Ser Ser
145                 150                 155                 160

Ser Asn Ile Gly Asn Asn Tyr Val Ser Trp Tyr Gln Gln Leu Pro Gly
                165                 170                 175

Thr Val Pro Lys Leu Leu Ile Tyr Gly His Thr Asn Arg Pro Ala Gly
            180                 185                 190

Val Pro Asp Arg Phe Ser Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu
        195                 200                 205

Ala Ile Ser Gly Phe Arg Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala
    210                 215                 220

Ala Trp Asp Asp Ser Leu Ser Gly Trp Val Phe Gly Gly Gly Thr Lys
225                 230                 235                 240

Leu Thr Val Leu Gly Ala Ala Ala Glu Gln Lys Leu Ile Ser Glu Glu
                245                 250                 255

Asp Leu Asn Gly Ala Ala His His His His His His
            260                 265
```