

SEQUENCE LISTING

<110> DAIICHI SANKYO COMPANY, LIMITED

<120> Anti-HER2 antibody-Pyrrolobenzodiazepine Derivatives Conjugate

<130> SAP-858-PCT

<141> 2020-03-24

<150> JP 2019057128

<151> 2019-03-25

<160> 34

<170> PatentIn version 3.5

<210> 1

<211> 8

<212> PRT

<213> Mus musculus

<400> 1

Gly Phe Asn Ile Lys Asp Thr Tyr
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<210> 2

<211> 8

<212> PRT

<213> Mus musculus

<400> 2

Ile Tyr Pro Thr Asn Gly Tyr Thr
1 5

<210> 3

<211> 13

<212> PRT

<213> Mus musculus

<400> 3

Ser Arg Trp Gly Gly Asp Gly Phe Tyr Ala Met Asp Tyr
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<210> 4
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 <212> PRT
 <213> Artificial Sequence

<220>
 <223> CDRH3 of H01

<400> 4

Ser Arg Trp Gly Gly Asp Gly Phe Phe Ala Met Asp Tyr
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<400> 5

Gln Asp Val Asn Thr Ala
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 <213> Mus musculus

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Ser Ala Ser Phe Leu Tyr Ser
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<210> 7
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 <212> PRT
 <213> Mus musculus

<400> 7

Gln Gln His Tyr Thr Thr Pro Pro Thr
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<210> 8
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<213> Artificial Sequence

<220>

<223> CDRL3 of L02/L05

<400> 8

Gln Gln His Ala Thr Thr Pro Pro Thr

1 5

<210> 9

<211> 449

<212> DNA

<213> Homo sapiens

<400> 9

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cgtgttcattt tccccccct ccgacgagca gctgaagtcc ggcaccgcct ccgtggtgtg	180
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cctgagcagc accctgaccc tgagcaaagc cgactacgag aagcacaagg tgtacgctg	360
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ttaggggccc gtttaaaccg gggaggcta	449

<210> 10

<211> 1137

<212> DNA

<213> Homo sapiens

<400> 10

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aagggeccaa gcgtcttccc cctggcacc cctccaaga gcacctctgg cggcacagcc	180
gccctgggct gcctgtgcaa ggactacttc cccgaaccg tgaccgtgag ctggaactca	240
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tccctcagca gcggtgtgac cgtgccctcc agcagcttgg gcacccagac ctacatctgc 360
 aacgtgaatc acaagcccag caacaccaag gtggacaaga gatttgagcc caaatcttgt 420
 gacaaaactc acacatgccc accctgceca gcacctgaag ccgcgggggg accctcagtc 480
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<210> 11
 <211> 469
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Trastuzumab A-Hwt aa

<400> 11

Met Lys His Leu Trp Phe Phe Leu Leu Leu Val Ala Ala Pro Arg Trp
 1 5 10 15

Val Leu Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln
 20 25 30

Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile
 35 40 45

Lys Asp Thr Tyr Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
 50 55 60

Glu Trp Val Ala Arg Ile Tyr Pro Thr Asn Gly Tyr Thr Arg Tyr Ala
 65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn
 85 90 95

Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
 100 105 110

Tyr Tyr Cys Ser Arg Trp Gly Gly Asp Gly Phe Tyr Ala Met Asp Tyr
 115 120 125

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
 130 135 140

Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
 145 150 155 160

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
 165 170 175

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
 180 185 190

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
 195 200 205

Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
 210 215 220

Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
 225 230 235 240

Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala

245

250

255

Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
 260 265 270

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
 275 280 285

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
 290 295 300

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
 305 310 315 320

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
 325 330 335

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
 340 345 350

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
 355 360 365

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
 370 375 380

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
 385 390 395 400

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
 405 410 415

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
 420 425 430

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
 435 440 445

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
 450 455 460

Leu Ser Pro Gly Lys
 465

<210> 12
 <211> 1407
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Trastuzumab A-Hwt

<400> 12
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 tgtgccgcca gcggcttcaa catcaaggac acctacatcc actgggtccg acaggccctt 180
 ggcaaaggac ttgaatgggt cgccagaatc taccacacca acggctacac cagatacgcc 240
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 tccaccaagg gccaagcgt ctccccctg gcacctctct ccaagagcac ctctggcggc 480
 acagccgccc tgggtgcct ggtcaaggac tacttccccg aaccctgac cgtgagctgg 540
 aactcaggcg ccctgaccag cggcgtgcac accttccccg ctgtcctgca gtctcagga 600
 ctctactccc tcagcagcgt ggtgaccgtg ccttcagca gcttgggcac ccagacctac 660
 atctgcaacg tgaatcaca gcccagaac accaaggtgg acaagagagt tgagccaaa 720
 tcttgtgaca aaactcacac atgccacccc tgcccagcac ctgaagccgc ggggggaccc 780
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gccaaaggcc agccccggga accacaggtg tacacctgc ccccatcccg ggaggagatg 1140
accaagaacc aggtcagcct gacctgcctg gtcaaagget tctatcccag cgacatcgcc 1200
gtggagtggg agagcaatgg ccagcccgag aacaactaca agaccacccc tcccgtgctg 1260
gactccgacg gctccttctt cctctacagc aagctcaccg tggacaagag caggtggcag 1320
cagggcaacg tcttctcatg ctccgtgatg catgaggctc tgcacaacca ctacaccag 1380
aagagcctct ccctgtctcc cggcaaa 1407

<210> 13
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<223> Variable region of Hwt aa

<400> 13

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

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

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

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

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

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

Ser Arg Trp Gly Gly Asp Gly Phe Tyr Ala Met Asp Tyr Trp Gly Gln
 100 105 110

Gly Thr Leu Val Thr Val Ser Ser
 115 120

<210> 14
 <211> 360
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Variable region of Hwt

<400> 14
 gaggtgcagc tggttgaatc tggcggagga ctggttcagc ctggcggatc tctgagactg 60
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 cctggcaaag gacttgaatg ggtcgccaga atctacccca ccaacggcta caccagatac 180
 gccgactctg tgaagggcag attcaccatc agcgccgaca ccagcaagaa caccgcctac 240
 ctgcagatga acagcctgag agccgaggac accgccgtgt actactgttc tagatgggga 300
 ggcgacggct tctacgcat ggattattgg ggccaggga ccctggttac cgttagetca 360

<210> 15
 <211> 469
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> H01 aa

<400> 15

Met Lys His Leu Trp Phe Phe Leu Leu Leu Val Ala Ala Pro Arg Trp
 1 5 10 15

Val Leu Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln
 20 25 30

Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile

10

35

40

45

Lys Asp Thr Tyr Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50 55 60

Glu Trp Val Ala Arg Ile Tyr Pro Thr Asn Gly Tyr Thr Arg Tyr Ala
65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn
85 90 95

Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
100 105 110

Tyr Tyr Cys Ser Arg Trp Gly Gly Asp Gly Phe Phe Ala Met Asp Tyr
115 120 125

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
130 135 140

Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
145 150 155 160

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
165 170 175

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
180 185 190

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
195 200 205

Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
210 215 220

Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys
225 230 235 240

Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
 245 250 255

Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
 260 265 270

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
 275 280 285

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
 290 295 300

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
 305 310 315 320

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
 325 330 335

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
 340 345 350

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
 355 360 365

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
 370 375 380

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
 385 390 395 400

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
 405 410 415

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
 420 425 430

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

435 440 445
 Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
 450 455 460

Leu Ser Pro Gly Lys
 465

<210> 16
 <211> 1407
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> H01

<400> 16
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 tgtgccgcca ggggttcaa catcaaggac acctacatcc actgggtccg acagggccct 180
 ggcaaaggac ttgaatgggt cgccagaatc tacccacca acggctacac cagatacgcc 240
 gactctgtga agggcagatt caccatcagc gccgacacca gcaagaacac cgcctacctg 300
 cagatgaaca gcctgagagc cgaggacacc gccgtgtact actgttctag atggggaggc 360
 gagggcttct tcgcatgga ttattggggc cagggcaccc tggttaccgt tagctcagcc 420
 tccaccaagg gcccaagcgt ctccccctg gcacctcct ccaagagcac ctctggcggc 480
 acagccgccc tgggctgcct ggtcaaggac tacttccccg aaccctgac cgtgagctgg 540
 aactcaggcg ccctgaccag cggcgtgcac accttccccg ctgtcctgca gtcctcagga 600
 ctctactccc tcagcagcgt ggtgaccgtg ccctccagca gcttgggcac ccagacctac 660
 atctgcaacg tgaatcacia gccagcaac accaaggtgg acaagagagt tgagcccaaa 720
 tcttgtgaca aaactcacac atgccacccc tgcccagcac ctgaagccgc ggggggaccc 780
 tcagtcttcc tcttcccccc aaaaccaag gacacctca tgatctcccg gaccttgag 840
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gtggacggcg tggaggtgca taatgccaag acaaagcccc gggaggagca gtacaacagc 960
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 tacaagtgca aggtctccaa caaagccctc ccagcccca tcgagaaaac catctccaaa 1080
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 gtggagtggg agagcaatgg ccagcccgag aacaactaca agaccacccc tccgtgctg 1260
 gactccgacg gctcttctt cctctacagc aagctcaccg tggacaagag caggtggcag 1320
 cagggaacg tcttctcatg ctccgtgatg catgaggctc tgcacaacca ctacaccag 1380
 aagagcctct ccctgtctcc cggcaaa 1407

<210> 17
 <211> 120
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Variable region of H01 aa

<400> 17

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

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

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

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

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

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

14

85

90

95

Ser Arg Trp Gly Gly Asp Gly Phe Phe Ala Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 18
<211> 360
<212> DNA
<213> Artificial Sequence

<220>
<223> Variable region of H01

<400> 18
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tcttgtgccg ccagcggctt caacatcaag gacacctaca tccactgggt ccgacaggcc 120
cctggcaaag gacttgaatg ggtcgccaga atctacceca ccaacggcta caccagatac 180
gccgactctg tgaagggcag attcaccatc agcgccgaca ccagcaagaa caccgcctac 240
ctgcagatga acagcctgag agccgaggac accgccgtgt actactgttc tagatgggga 300
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<210> 19
<211> 234
<212> PRT
<213> Artificial Sequence

<220>
<223> Trastuzumab A-Lwt aa

<400> 19

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

Gly Ala Tyr Gly Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser
20 25 30

Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp
 35 40 45

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

Lys Leu Leu Ile Tyr Ser Ala Ser Phe Leu Tyr Ser Gly Val Pro Ser
 65 70 75 80

Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
 85 90 95

Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Tyr
 100 105 110

Thr Thr Pro Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
 115 120 125

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
 130 135 140

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
 145 150 155 160

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
 165 170 175

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
 180 185 190

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
 195 200 205

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
 210 215 220

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys

225

230

<210> 20
 <211> 702
 <212> DNA
 <213> Artificial Sequence

<220>

<223> Trastuzumab A-Lwt

<400> 20

atggtgctgc agaccaggt gttcatctcc ctgctgctgt ggatctccgg cgcgtacggc	60
gacatccaga tgacacagag ccctagcagc ctgtctgccg gcgtgggaga cagagtgacc	120
atcacctgta gagccagcca ggacgtgaac acagccgtgg cttggtatca gcagaagcct	180
ggcaaggccc ctaagetgct gatctacagc gccagctttc tgtacagcgg cgtgcccagc	240
agattcagcg gctctagaag cggcaccgac ttcacctga ccataagcag tctgcagccc	300
gaggacttcg ccacctacta ctgtcagcag cactacacca cacctccaac ctttggecag	360
ggcaccaagg tggaatcaa gcgtacggtg gccgccccct ccgtgttcat cttccccccc	420
tccgacgagc agctgaagtc cggcaccgcc tccgtggtgt gcctgctgaa taacttctac	480
cccagagagg ccaagtgca gtggaagggt gacaacgccc tgcagtccgg gaactcccag	540
gagagcgtga ccgagcagga cagcaaggac agcacctaca gcctgagcag caccctgacc	600
ctgagcaaag ccgactacga gaagcacaag gtgtacgcct gcgaggtgac ccaccagggc	660
ctgagctccc ccgtcaccaa gagcttcaac aggggggagt gt	702

<210> 21
 <211> 107
 <212> PRT
 <213> Artificial Sequence

<220>

<223> Variable region of Lwt aa

<400> 21

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

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

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

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

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

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

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

<210> 22
 <211> 321
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Variable region of Lwt

<400> 22
 gacatccaga tgacacagag ccctagcagc ctgtctgccg gcgtgggaga cagagtgacc 60
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 ggcaaggccc ctaagctgct gatctacagc gccagcttgc tgtacagcgg cgtgcccagc 180
 agattcagcg gctctagaag cggcaccgac ttcacctga ccataagcag tctgcagccc 240
 gaggacttcg ccacctacta ctgtcagcag cactacacca cacetccaac ctttggccag 300
 ggcaccaagg tggaatcaa g 321

<210> 23
 <211> 234
 <212> PRT

<213> Artificial Sequence

<220>

<223> L02 aa

<400> 23

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

Gly Ala Tyr Gly Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser
20 25 30

Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp
35 40 45

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

Lys Leu Leu Ile Tyr Ser Ala Ser Phe Leu Tyr Ser Gly Val Pro Ser
65 70 75 80

Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
85 90 95

Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Ala
100 105 110

Thr Thr Pro Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
115 120 125

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
130 135 140

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
145 150 155 160

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
165 170 175

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
 180 185 190

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
 195 200 205

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
 210 215 220

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
 225 230

<210> 24
 <211> 702
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> L02

<400> 24
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 gacatccaga tgacacagag ccctagcagc ctgtctgcca gcgtgggaga cagagtgacc 120
 atcacctgta gagccagcca ggacgtgaac acagccgtgg cttggtatca gcagaagcct 180
 ggcaaggccc ctaagctgct gatctacagc gccagctttc tgtacagcgg cgtgcccagc 240
 agattcagcg gctctagaag cggcaccgac ttcaccctga ccataagcag tctgcagccc 300
 gaggacttcg ccacctacta ctgtcagcag cagccacca cacetccaac atttgccag 360
 ggcaccaagg tggaaatcaa gcgtacggtg gccgccccct ccgtgttcat cttccccccc 420
 tccgacgagc agctgaagtc cggcaccgcc tccgtggtgt gcctgctgaa taacttctac 480
 cccagagagg ccaaggtgca gtggaagggt gacaacgccc tgcagtccgg gaactcccag 540
 gagagcgtga ccgagcagga cagcaaggac agcacctaca gcctgagcag caccctgacc 600
 ctgagcaaag ccgactacga gaagcacaag gtgtacgcct gcgaggtgac ccaccagggc 660
 ctgagctccc ccgtcaccaa gagcttcaac aggggggagt gt 702

<210> 25
 <211> 107
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Variable region of L02 aa

<400> 25

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

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

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

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

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

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

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

<210> 26
 <211> 321
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Variable region of L02

<400> 26

gacatccaga tgacacagag ccctagcagc ctgtctgccg gcgtgggaga cagagtgacc 60

atcacctgta gagccagcca ggacgtgaac acagccgtgg cttggtatca gcagaagcct 120
 ggcaaggccc ctaagctgct gatctacagc gccagctttc tgtacagcgg cgtgccccagc 180
 agattcagcg gctctagaag cggcacccgac ttcaccctga ccataagcag tctgcagccc 240
 gaggacttcg ccacctacta ctgtcagcag cagccacca cacctccaac atttggccag 300
 ggcaccaagg tggaaatcaa g 321

<210> 27
 <211> 234
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> L05 aa

<400> 27

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

Gly Ala Tyr Gly Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser
 20 25 30

Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp
 35 40 45

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

Lys Ala Leu Ile Tyr Ser Ala Ser Phe Leu Tyr Ser Gly Val Pro Ser
 65 70 75 80

Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
 85 90 95

Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Ala
 100 105 110

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

115	120	125
Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln		
130	135	140
Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr		
145	150	155
		160
Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser		
	165	170
		175
Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr		
	180	185
		190
Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys		
	195	200
		205
His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro		
	210	215
		220
Val Thr Lys Ser Phe Asn Arg Gly Glu Cys		
225	230	

<210> 28
 <211> 702
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> L05

<400> 28	
atggtgctgc agaccaggt gttcatctcc ctgctgctgt ggatctccgg cgcgtacggc	60
gacatccaga tgacacagag ccctagcagc ctgtctgcca gcgtgggaga cagagtgacc	120
atcacctgta gagccagcca ggacgtgaac acagccgtgg cttggtatca gcagaagcct	180
ggcaaagccc ctaaggtctt gatctacagc gccagctttc tgtacagcgg cgtgcccagc	240
agattcagcg gctctagaag cggcaccgac ttcacctga ccataagcag tctgcagccc	300

gaggacttcg ccacctacta ctgtcagcag cagccacca cacctccaac atttgccag 360
 ggcaccaagg tggaatcaa gcgtacggtg gccgcccct ccgtgttcat cttcccccc 420
 tccgacgagc agctgaagtc cggcacccgc tccgtggtgt gcctgtgaa taactttac 480
 cccagagagg ccaaggtgca gtggaagggtg gacaacgcc tgcagtccgg gaactcccag 540
 gagagcgtga ccgagcagga cagcaaggac agcacctaca gcctgagcag caccctgacc 600
 ctgagcaaag ccgactacga gaagcacaag gtgtacgcct gcgaggtgac ccaccagggc 660
 ctgagctccc ccgtcaccaa gagcttcaac aggggggagt gt 702

<210> 29
 <211> 107
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Variable region of L05 aa

<400> 29

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

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

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

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

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

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

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys

100

105

<210> 30
 <211> 321
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Variable region of L05

<400> 30
 gacatccaga tgacacagag ccctagcagc ctgtctgccg gcgtgggaga cagagtgacc 60
 atcacctgta gagccagcca ggacgtgaac acagccgtgg cttggtatca gcagaagcct 120
 ggcaaagccc ctaaggtctt gatctacagc gccagctttc tgtacagcgg cgtgcccagc 180
 agattcagcg gctctagaag cggcaccgac ttcacctga ccataagcag tctgcagccc 240
 gaggacttcg ccacctacta ctgtcagcag cagccacca cacctccaac atttgccag 300
 ggcaccaagg tggaaatcaa g 321

<210> 31
 <211> 469
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Heavy chain of Trastuzumab A2

<400> 31

Met Lys His Leu Trp Phe Phe Leu Leu Leu Val Ala Ala Pro Arg Trp
 1 5 10 15

Val Leu Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln
 20 25 30

Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile
 35 40 45

Lys Asp Thr Tyr Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
 50 55 60

Glu Trp Val Ala Arg Ile Tyr Pro Thr Asn Gly Tyr Thr Arg Tyr Ala
65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn
85 90 95

Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
100 105 110

Tyr Tyr Cys Ser Arg Trp Gly Gly Asp Gly Phe Tyr Ala Met Asp Tyr
115 120 125

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly
130 135 140

Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly
145 150 155 160

Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val
165 170 175

Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe
180 185 190

Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
195 200 205

Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val
210 215 220

Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys
225 230 235 240

Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala
245 250 255

Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr

260

265

270

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
 275 280 285

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
 290 295 300

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
 305 310 315 320

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
 325 330 335

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
 340 345 350

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
 355 360 365

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
 370 375 380

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
 385 390 395 400

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
 405 410 415

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
 420 425 430

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
 435 440 445

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
 450 455 460

Leu Ser Pro Gly Lys
465

<210> 32
<211> 234
<212> PRT
<213> Artificial Sequence

<220>
<223> Light chain of Trastuzumab A2

<400> 32

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

Gly Ala Tyr Gly Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser
20 25 30

Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp
35 40 45

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

Lys Leu Leu Ile Tyr Ser Ala Ser Phe Leu Tyr Ser Gly Val Pro Ser
65 70 75 80

Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
85 90 95

Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Tyr
100 105 110

Thr Thr Pro Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
115 120 125

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
130 135 140

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
 145 150 155 160

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
 165 170 175

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
 180 185 190

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
 195 200 205

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
 210 215 220

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
 225 230

<210> 33
 <211> 450
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Heavy chain of Trastuzumab

<400> 33

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

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

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

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

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

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

Ser Arg Trp Gly Gly Asp Gly Phe Tyr Ala Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
115 120 125

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

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

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

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

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

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

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

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu

260

265

270

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

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

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
 305 310 315 320

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

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

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

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

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

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

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
 420 425 430

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

Gly Lys
 450

<210> 34
 <211> 214
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Light chain of Trastuzumab

<400> 34

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

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

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

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

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

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

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

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

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

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

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

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

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

Phe Asn Arg Gly Glu Cys
210