<110> AC Immune S.A. and Genentech, Inc.

<120> Safe and Functional Humanized Antibodies

<130> 12593-020-228

<140> To Be Determined
<141> To Be Determined

<150> 61/400,650
<151> 2010-07-30

<160> 22

<170> PatentIn version 3.3

<210> 1
<211> 10
<212> PRT
<213> Mus musculus

<220>
<223> MABT humanised heavy chain variable region (CDR1)

<400> 1

Gly Phe Thr Phe Ser Ser Tyr Gly Met Ser
1 5 10

<210> 2
<211> 17
<212> PRT
<213> Mus musculus

<220>
<223> MABT humanised heavy chain variable region (CDR2)

<400> 2

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

Gly

<210> 3
<211> 3
<212> PRT
<213> Mus musculus

<220>
<223> MABT humanised heavy chain variable region (CDR3)

<400> 3

Gly Asp Tyr
1

<210> 4
<211> 16
<212> PRT
<213> Mus musculus

<220>
<223> MABT humanised light chain variable region (CDR1)

<400> 4

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

<210> 5
<211> 7
<212> PRT
<213> Mus musculus

<220>
<223> MABT humanised light chain variable region (CDR2)

<400> 5

Lys Val Ser Asn Arg Phe Ser
1 5

<210> 6
<211> 9
<212> PRT
<213> Mus musculus

<220>
<223> MABT humanised light chain variable region (CDR3)

<400> 6

Ser Gln Ser Thr His Val Pro Trp Thr
1 5

<210> 7
<211> 112
<212> PRT
<213> Artificial sequence

<220>
<223> artificial humanized MABT variable light chain

<400> 7

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

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

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

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

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

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

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

<210> 8
<211> 219
<212> PRT
<213> artificial sequence

<220>
<223> artificial humanized MABT light chain

<400> 8

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

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

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

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

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

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

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

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
115 120 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
130 135 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
145 150 155 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
165 170 175

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

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

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 9
<211> 107
<212> PRT
<213> artificial sequence

<220>
<223> artificial humanized MABT light chain constant region

<400> 9

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

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

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

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

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

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

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

<210> 10
<211> 112
<212> PRT
<213> artificial sequence

<220>
<223> artificial humanized MABT variable heavy chain

<400> 10

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

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

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

Ala Ser 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 Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

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

Ala Ser Gly Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
            100                 105                 110
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<210> 11
<211> 439
<212> PRT
<213> artificial sequence

<220>
<223> artificial humanized MABT heavy chain

<400> 11

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

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

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

Ala Ser 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 Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

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

Ala Ser Gly Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
            100                 105                 110

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg
        115                 120                 125

Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
    130                 135                 140

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
145                 150                 155                 160

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
                165                 170                 175
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Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr
            180                 185                 190

Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys
        195                 200                 205

Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro
    210                 215                 220

Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
225                 230                 235                 240

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
                245                 250                 255

Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp
            260                 265                 270

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe
        275                 280                 285

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
    290                 295                 300

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu
305                 310                 315                 320

Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
                325                 330                 335

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys
            340                 345                 350

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
        355                 360                 365

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
    370                 375                 380

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
385                 390                 395                 400

Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser
                405                 410                 415

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
            420                 425                 430

Leu Ser Leu Ser Leu Gly Lys
        435
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<210> 12
<211> 326
<212> PRT
<213> Homo sapiens

<220>
<223> IG GAMMA-4 CHAIN C REGION modified

<400> 12

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys
225                 230                 235                 240
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Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
245 250 255

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

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

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

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

Leu Ser Leu Ser Leu Gly
325

<210> 13
<211> 51
<212> DNA
<213> Mus musculus

<220>
<223> MABT humanised heavy chain variable region (CDR2)

<400> 13
agcatcaata gtaatggtgg tagcacctat tatccagaca gtgtgaaggg c 51

<210> 14
<211> 9
<212> DNA
<213> Mus musculus

<220>
<223> MABT humanised heavy chain variable region (CDR3)

<400> 14
ggtgactac 9

<210> 15
<211> 49
<212> DNA
<213> Mus musculus

<220>
<223> MABT humanised light chain variable region (CDR1)

<400> 15
agatctagtc agagccttgt atatagtaat ggagacacct atttacatt 49

<210> 16
<211> 336
<212> DNA
<213> artificial sequence

<220>
<223> artificial humanized MABT variable light chain

<400> 16
gatattgtga tgacccaatc tccactctcc ctgcctgtca ctcctggtga gcctgcctcc 60

atctcttgca gatctagtca gagccttgta tatagtaatg gagacaccta tttacattgg 120

tacctgcaga agccaggcca gtctccacag ctcctgatct acaaagtttc caaccgattt 180

tctggggtcc cagacaggtt cagtggcagt ggatcaggga cagatttcac actcaagatc 240

agcagagtgg aggctgagga tgtgggagtt tattactgct ctcaaagtac acatgttcct 300

tggacgttcg gccaaggcac caaggtggaa atcaaa 336

<210> 17
<211> 657
<212> DNA
<213> artificial sequence

<220>
<223> artificial humanized MABT light chain

<400> 17
gatattgtga tgacccaatc tccactctcc ctgcctgtca ctcctggtga gcctgcctcc 60

atctcttgca gatctagtca gagccttgta tatagtaatg gagacaccta tttacattgg 120

tacctgcaga agccaggcca gtctccacag ctcctgatct acaaagtttc caaccgattt 180

tctggggtcc cagacaggtt cagtggcagt ggatcaggga cagatttcac actcaagatc 240

agcagagtgg aggctgagga tgtgggagtt tattactgct ctcaaagtac acatgttcct 300

tggacgttcg gccaaggcac caaggtggaa atcaaaagga ctgtggctgc accatctgtc 360

ttcatcttcc cgccatctga tgagcagttg aaatctggaa ctgcctctgt tgtgtgcctg 420

ctgaataact tctatcccag agaggccaaa gtacagtgga aggtggataa cgccctccaa 480

tcgggtaact cccaggagag tgtcacagag caggacagca aggacagcac ctacagcctc 540

agcagcaccc tgacgctgag caaagcagac tacgagaaac acaaagtcta cgcctgcgaa 600

gtcacccatc agggcctgag ctcgcccgtc acaaagagct tcaacagggg agagtgt 657

<210> 18
<211> 321
<212> DNA
<213> Homo sapiens

<220>
<223> artificial humanized MABT light chain constant region

<400> 18
aggactgtgg ctgcaccatc tgtcttcatc ttcccgccat ctgatgagca gttgaaatct 60

ggaactgcct ctgttgtgtg cctgctgaat aacttctatc ccagagaggc caaagtacag 120

tggaaggtgg ataacgccct ccaatcgggt aactcccagg agagtgtcac agagcaggac 180

agcaaggaca gcacctacag cctcagcagc accctgacgc tgagcaaagc agactacgag 240

aaacacaaag tctacgcctg cgaagtcacc catcagggcc tgagctcgcc cgtcacaaag 300

agcttcaaca ggggagagtg t 321

<210> 19
<211> 336
<212> DNA
<213> artificial sequence

<220>
<223> artificial humanized MABT variable heavy chain

<400> 19
gaggtgcagc tggtcgagtc tgggggaggc ttagtgcagc ctggagggtc cctgagactc 60

tcctgtgcag cctctggatt cactttcagt agctatggca tgtcttgggt tcgccaggct 120

ccaggcaagg gtctcgaatt ggtcgcaagc atcaatagta atggtggtag cacctattat 180

ccagacagtg tgaagggccg attcaccatc tccagagaca atgccaagaa ctccctgtac 240

ctgcaaatga acagtctgag agctgaggac accgccgtgt attactgtgc aagtggtgac 300

tactggggcc aaggcaccac tgtcacagtc tcctca 336

<210> 20
<211> 1317
<212> DNA
<213> artificial sequence

<220>
<223> artificial humanized MABT heavy chain

<400> 20
gaggtgcagc tggtcgagtc tgggggaggc ttagtgcagc ctggagggtc cctgagactc 60

tcctgtgcag cctctggatt cactttcagt agctatggca tgtcttgggt tcgccaggct 120

ccaggcaagg gtctcgaatt ggtcgcaagc atcaatagta atggtggtag cacctattat 180

ccagacagtg tgaagggccg attcaccatc tccagagaca atgccaagaa ctccctgtac 240

ctgcaaatga acagtctgag agctgaggac accgccgtgt attactgtgc aagtggtgac 300

tactggggcc aaggcaccac tgtcacagtc tcctcagctt ccaccaaggg cccatccgtc 360

ttcccctgg cgccctgctc cagatcgacc tccgagagca cagccgccct gggctgcctg 420

gtcaaggact acttccccga accggtgacg gtgtcgtgga actcaggcgc cctgaccagc 480

ggcgtgcaca ccttcccggc tgtcctacag tcctcaggac tctactccct cagcagcgtg 540

gtgaccgtgc cctccagcag cttgggcacg aagacctaca cctgcaacgt agatcacaag 600

cccagcaaca ccaaggtgga caagagagtt gagtccaaat atggtccccc gtgtccccca 660

tgcccagcac ctgagttcct gggggggacca tcagtcttcc tgttcccccc aaaacccaag 720

gacactctca tgatctcccg gacccctgag gtcacgtgcg tggtggtgga cgtgagccag 780

gaagaccccg aggtccagtt caactggtac gtggatggcg tggaggtgca taatgccaag 840

acaaagccgc gggaggagca gttcaacagc acgtaccgtg tggtcagcgt cctcaccgtc 900

ctgcaccagg actggctgaa cggcaaggag tacaagtgca aggtctccaa caaaggcctc 960

ccgtcctcca tcgagaaaac catctccaaa gccaaagggc agccccgaga gccacaggtg 1020

tacaccctgc ccccatccca ggaggagatg accaagaacc aggtcagcct gacctgcctg 1080

gtcaaaggct tctaccccag cgacatcgcc gtggagtggg agagcaatgg gcagccggag 1140

aacaactaca agaccacgcc tcccgtcctc gattccgacg gctccttctt cctctacagc 1200

aggctaaccg tggacaagag caggtggcag gaggggaatg tcttctcatg ctccgtgatg 1260

catgaggctc tgcacaacca ctacacacag aagagcctct ccctgtctct gggtaaa 1317

<210> 21
<211> 981
<212> DNA
<213> Homo sapiens

<220>
<223> artificial humanized MABT heavy chain constant region

<400> 21
gcttccacca agggcccatc cgtcttcccc ctggcgccct gctccagatc gacctccgag 60

agcacagccg ccctgggctg cctggtcaag gactacttcc ccgaaccggt gacggtgtcg 120

tggaactcag gcgccctgac cagcggcgtg cacaccttcc cggctgtcct acagtcctca 180

ggactctact ccctcagcag cgtggtgacc gtgccctcca gcagcttggg cacgaagacc 240

tacacctgca acgtagatca caagcccagc aacaccaagg tggacaagag agttgagtcc 300

aaatatggtc ccccgtgtcc cccatgccca gcacctgagt tcctgggggg accatcagtc 360

ttcctgttcc ccccaaaacc caaggacact ctcatgatct cccggacccc tgaggtcacg 420

tgcgtggtgg tggacgtgag ccaggaagac cccgaggtcc agttcaactg gtacgtggat 480

ggcgtggagg tgcataatgc caagacaaag ccgcgggagg agcagttcaa cagcacgtac 540

cgtgtggtca gcgtcctcac cgtcctgcac caggactggc tgaacggcaa ggagtacaag 600

tgcaaggtct ccaacaaagg cctcccgtcc tccatcgaga aaaccatctc caaagccaaa 660

gggcagcccc gagagccaca ggtgtacacc ctgccccccat cccaggagga gatgaccaag 720

aaccaggtca gcctgacctg cctggtcaaa ggcttctacc ccagcgacat cgccgtggag 780

tgggagagca atgggcagcc ggagaacaac tacaagacca cgcctcccgt cctcgattcc 840

gacggctcct tcttcctcta cagcaggcta accgtggaca agagcaggtg gcaggagggg 900

aatgtcttct catgctccgt gatgcatgag gctctgcaca accactacac acagaagagc 960

ctctccctgt ctctgggtaa a 981

<210> 22
<211> 5
<212> PRT
<213> Homo sapiens

<220>
<223> Typical amino acid sequence preceding HCDR2

<400> 22
Leu Glu Trp Ile Gly
1 5