

SEQUENCE LISTING

<110> BIOVERATIV USA INC.
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PARRU, GRAHAM
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<120> ANTI-C1s ANTIBODIES AND METHODS OF USE THEREOF

<130> 4159.504PC01/C-K/BMD

<150> US 62/407,390

<151> 2016-10-12

<160> 54

<170> PatentIn version 3.5

<210> 1

<211> 15

<212> PRT

<213> Artificial Sequence

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<223> VL CDR1

<400> 1

Lys	Ala	Ser	Gln	Ser	Val	Asp	Tyr	Asp	Gly	Asp	Ser	Tyr	Met	Asn
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<211> 7

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<223> VL CDR2

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Asp	Ala	Ser	Asn	Leu	Glu	Ser
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<211> 9

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<223> VL CDR3

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Gln Gln Ser Asn Glu Asp Pro Trp Thr
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<210> 4

<211> 5

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<223> VH CDR1

<400> 4

Asp Asp Tyr Ile His
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<210> 5

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<223> VH CDR2

<400> 5

Arg Ile Asp Pro Ala Asp Gly His Thr Lys Tyr Ala Pro Lys Phe Gln
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Val

<210> 6

<211> 10

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<213> Artificial Sequence

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<223> VH CDR3

<400> 6

Tyr Gly Tyr Gly Arg Glu Val Phe Asp Tyr
1 5 10

<210> 7

<211> 111

<212> PRT
<213> Artificial Sequence

<220>
<223> Parental Murine anti-C1s VL Variable Light

<400> 7

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

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

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

Lys Ile Leu Ile Tyr Asp Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
50 55 60

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

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

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

<210> 8
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> VH CDR of an anti-C1s antibody

<400> 8

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

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

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

Gly Arg Ile Asp Pro Ala Asp Gly His Thr Lys Tyr Ala Pro Lys Phe
50 55 60

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

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

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

Thr Thr Leu Thr Val Ser Ser
115

<210> 9
<211> 673
<212> PRT
<213> Artificial Sequence

<220>
<223> Human C1s

<400> 9

Glu Pro Thr Met Tyr Gly Glu Ile Leu Ser Pro Asn Tyr Pro Gln Ala
1 5 10 15

Tyr Pro Ser Glu Val Glu Lys Ser Trp Asp Ile Glu Val Pro Glu Gly
20 25 30

Tyr Gly Ile His Leu Tyr Phe Thr His Leu Asp Ile Glu Leu Ser Glu
35 40 45

Asn Cys Ala Tyr Asp Ser Val Gln Ile Ile Ser Gly Asp Thr Glu Glu
50 55 60

Gly Arg Leu Cys Gly Gln Arg Ser Ser Asn Asn Pro His Ser Pro Ile
65 70 75 80

Val Glu Glu Phe Gln Val Pro Tyr Asn Lys Leu Gln Val Ile Phe Lys
85 90 95

Ser Asp Phe Ser Asn Glu Glu Arg Phe Thr Gly Phe Ala Ala Tyr Tyr
100 105 110

Val Ala Thr Asp Ile Asn Glu Cys Thr Asp Phe Val Asp Val Pro Cys
115 120 125

Ser His Phe Cys Asn Asn Phe Ile Gly Gly Tyr Phe Cys Ser Cys Pro
130 135 140

Pro Glu Tyr Phe Leu His Asp Asp Met Lys Asn Cys Gly Val Asn Cys
145 150 155 160

Ser Gly Asp Val Phe Thr Ala Leu Ile Gly Glu Ile Ala Ser Pro Asn
165 170 175

Tyr Pro Lys Pro Tyr Pro Glu Asn Ser Arg Cys Glu Tyr Gln Ile Arg
180 185 190

Leu Glu Lys Gly Phe Gln Val Val Val Thr Leu Arg Arg Glu Asp Phe
195 200 205

Asp Val Glu Ala Ala Asp Ser Ala Gly Asn Cys Leu Asp Ser Leu Val
210 215 220

Phe Val Ala Gly Asp Arg Gln Phe Gly Pro Tyr Cys Gly His Gly Phe
225 230 235 240

Pro Gly Pro Leu Asn Ile Glu Thr Lys Ser Asn Ala Leu Asp Ile Ile
245 250 255

Phe Gln Thr Asp Leu Thr Gly Gln Lys Lys Gly Trp Lys Leu Arg Tyr
260 265 270

His Gly Asp Pro Met Pro Cys Pro Lys Glu Asp Thr Pro Asn Ser Val
275 280 285

Trp Glu Pro Ala Lys Ala Lys Tyr Val Phe Arg Asp Val Val Gln Ile
290 295 300

Thr Cys Leu Asp Gly Phe Glu Val Val Glu Gly Arg Val Gly Ala Thr
305 310 315 320

Ser Phe Tyr Ser Thr Cys Gln Ser Asn Gly Lys Trp Ser Asn Ser Lys
325 330 335

Leu Lys Cys Gln Pro Val Asp Cys Gly Ile Pro Glu Ser Ile Glu Asn
340 345 350

Gly Lys Val Glu Asp Pro Glu Ser Thr Leu Phe Gly Ser Val Ile Arg
355 360 365

Tyr Thr Cys Glu Glu Pro Tyr Tyr Tyr Met Glu Asn Gly Gly Gly Gly
370 375 380

Glu Tyr His Cys Ala Gly Asn Gly Ser Trp Val Asn Glu Val Leu Gly
385 390 395 400

Pro Glu Leu Pro Lys Cys Val Pro Val Cys Gly Val Pro Arg Glu Pro
405 410 415

Phe Glu Glu Lys Gln Arg Ile Ile Gly Gly Ser Asp Ala Asp Ile Lys
420 425 430

Asn Phe Pro Trp Gln Val Phe Phe Asp Asn Pro Trp Ala Gly Gly Ala
435 440 445

Leu Ile Asn Glu Tyr Trp Val Leu Thr Ala Ala His Val Val Glu Gly
450 455 460

Asn Arg Glu Pro Thr Met Tyr Val Gly Ser Thr Ser Val Gln Thr Ser
465 470 475 480

Arg Leu Ala Lys Ser Lys Met Leu Thr Pro Glu His Val Phe Ile His
485 490 495

Pro Gly Trp Lys Leu Leu Glu Val Pro Glu Gly Arg Thr Asn Phe Asp
500 505 510

Asn Asp Ile Ala Leu Val Arg Leu Lys Asp Pro Val Lys Met Gly Pro
515 520 525

Thr Val Ser Pro Ile Cys Leu Pro Gly Thr Ser Ser Asp Tyr Asn Leu
530 535 540

Met Asp Gly Asp Leu Gly Leu Ile Ser Gly Trp Gly Arg Thr Glu Lys
545 550 555 560

Arg Asp Arg Ala Val Arg Leu Lys Ala Ala Arg Leu Pro Val Ala Pro
565 570 575

Leu Arg Lys Cys Lys Glu Val Lys Val Glu Lys Pro Thr Ala Asp Ala
580 585 590

Glu Ala Tyr Val Phe Thr Pro Asn Met Ile Cys Ala Gly Gly Glu Lys
595 600 605

Gly Met Asp Ser Cys Lys Gly Asp Ser Gly Gly Ala Phe Ala Val Gln
610 615 620

Asp Pro Asn Asp Lys Thr Lys Phe Tyr Ala Ala Gly Leu Val Ser Trp
625 630 635 640

Gly Pro Gln Cys Gly Thr Tyr Gly Leu Tyr Thr Arg Val Lys Asn Tyr
645 650 655

Val Asp Trp Ile Met Lys Thr Met Gln Glu Asn Ser Thr Pro Arg Glu
660 665 670

Asp

<210> 10
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> VH1 Variant

<400> 10

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

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

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

Gly Arg Ile Asp Pro Ala Asp Gly His Thr Lys Tyr Ala Pro Lys Phe
50 55 60

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

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

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

Thr Thr Val Thr Val Ser Ser
115

<210> 11
<211> 357
<212> DNA
<213> Artificial Sequence

<220>
<223> VH variant 1

<400> 11
gaggttcagc tgggtgcagtc tggggctgag cttaagaagc caggggcctc agtcaagttg 60
tcctgcacag cttctggctt taacattaaa gacgactata tacactgggt gaagcaggcc 120
cctggacagg gcctggagtg gattggaagg attgatacctg cggatgggtca tactaaatat 180
gccccgaagt tccaagtcaa ggccactata actgcagaca catccaccaa cacagcctac 240
ctgcagctca gcagcctgac atctgaggac actgccgtct attactgtgc tagatatggt 300
tacgggaggg aggtctttga ctactggggc caaggcacca ctgtcacagt ctcctca 357

<210> 12
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> VH2 variant

<400> 12

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

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

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

Gly Arg Ile Asp Pro Ala Asp Gly His Thr Lys Tyr Ala Pro Lys Phe
50 55 60

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

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

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

Thr Thr Val Thr Val Ser Ser
115

<210> 13
<211> 357
<212> DNA
<213> Artificial Sequence

<220>
<223> VH variant 2

<400> 13

gaggttcagc tgggtgcagtc tggggctgag gtgaagaagc caggggcctc agtcaagttg 60

tcctgcacag cttctggctt taacattaaa gacgactata tacactgggt gaagcaggcc 120

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cctggacagg gcctggagtg gattggaagg attgatcctg cggatggtca tactaaatat 180
gccccgaagt tccaagtcaa ggccactata actgcagaca catccaccaa cacagcctac 240
ctggagctca gcagcctgag atctgaggac actgccgtct attactgtgc tagatatggt 300
tacgggaggg aggtctttga ctactggggc caaggcacca ctgtcacagt ctcctca 357
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<220>
<223> VH3 variant

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

$\langle 210 \rangle$	15
$\langle 211 \rangle$	357

<212> DNA
<213> Artificial Sequence

<220>
<223> VH variant 3

<400> 15
caggttcagc tggtgcagtc tggggctgag gtgaagaagc caggggcctc agtcaagttg 60
tcctgcacag cttctggctt taacattaaa gacgactata tacactgggt gaagcaggcc 120
cctggacagg gcctggagtg gattggaagg attgatacctg cggatgggtca tactaaatat 180
gccccgaagt tccaagtcaa agtcactata actgcagaca catccaccag cacagcctac 240
ctggagctca gcagcctgag atctgaggac actgccgtct attactgtgc tagatatggt 300
tacgggaggg aggtctttga ctactggggc caaggcacca ctgtcacagt ctcctca 357

<210> 16
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> VH4 variant

<400> 16

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

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

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

Gly Arg Ile Asp Pro Ala Asp Gly His Thr Lys Tyr Ala Pro Lys Phe
50 55 60

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

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

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

Thr Thr Val Thr Val Ser Ser
115

<210> 17
<211> 357
<212> DNA
<213> Artificial Sequence

<220>
<223> VH variant 4

<400> 17
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tcctgcacag cttctggcctt taacattaaa gacgactata tacactgggt gcgccaggcc 120
cctggacagg gcctggagtg gattggaagg attgacctg cggatgggtca tactaaatat 180
gccccgaagt tccaagtcaa agtcactata actgcagaca catccaccag cacagcctac 240
atggagctca gcagcctgag atctgaggac actgccgtct attactgtgc tagatatggt 300
tacgggaggg aggtctttga ctactggggc caaggcacca ctgtcacagt ctcctca 357

<210> 18
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> VH5 variant

<400> 18

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

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

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

Gly Arg Ile Asp Pro Ala Asp Gly His Thr Lys Tyr Ala Pro Lys Phe
50 55 60

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

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

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

Thr Thr Val Thr Val Ser Ser
115

<210> 19
<211> 357
<212> DNA
<213> Artificial Sequence

<220>
<223> VH variant 5

<400> 19
caggttcagc tgggtgcagtc tggggctgag gtgaagaagc caggggcctc agtcaaggtc 60
tcctgcgag cttctggctt taacattaaa gacgactata tacactgggt gcgccaggcc 120
cctggacagg gcctggagtg gattggaagg attgatacctg cggatgggtca tactaaatat 180
gccccgaagt tccaagtcaa agtcactata actgcagaca catccaccag cacagcctac 240
atggagctca gcagcctgag atctgaggac actgccgtct attactgtgc tagatatggt 300
tacgggaggg aggtctttga ctactggggc caaggcacca ctgtcacagt ctcctca 357

<210> 20
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<223> Vkappa1 variant Variable Light

<400> 20

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

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

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

Lys Ile Leu Ile Tyr Asp Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
50 55 60

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

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

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

<210> 21
<211> 333
<212> DNA
<213> Artificial Sequence

<220>
<223> Vkappa variant 1

<400> 21
gacattgtgc tgaccaatc tccagactct ttggctgtgt ctctcgggga gagggccacc 60
atctcctgca aggccagcca aagtgttgat tatgatggtg atagttatat gaactggtac 120
caacaaaaaa caggacagcc acccaaaatc ctcatattatg atgcatccaa tttggaatct 180
ggcatcccag ccaggttttag tggcagtggg tctgggacag acttcaccct caccatcagc 240
agcctggagg aggaggattt tgcaatctat tactgtcagc aaagtaatga agaccctggg 300
acgttcggtg gaggcaccaa ggtggaaatc aaa 333

<210> 22
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<223> Vkappa2 variant Variable Light

<400> 22

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

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

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

Lys Ile Leu Ile Tyr Asp Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
50 55 60

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

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

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

<210> 23

<211> 333

<212> DNA

<213> Artificial Sequence

<220>

<223> Vkappa variant 2

<400> 23

gacattgtgc tgaccaatc tccagactct ttggctgtgt ctctcgggga gagggccacc 60
atctcctgca aggccagcca aagtgttgat tatgatgggtg atagttatat gaactggtac 120
caacaaaaac caggacagcc acccaaaatc ctcatTTatg atgcatccaa tttggaatct 180
ggcatcccag ccaggtttag tggcagtggg tctgggacag acttcaccct caccatcagc 240
agcctgggagc ctgaggattt tgcaatctat tactgtcagc aaagtaatga agaccctggg 300
acgttcggtg gaggcaccaa ggtggaaatc aaa 333

<210> 24

<211> 111

<212> PRT
<213> Artificial Sequence

<220>
<223> Vkappa5 variant Variable Light

<400> 24

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

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

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

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
50 55 60

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

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

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

<210> 25
<211> 333
<212> DNA
<213> Artificial Sequence

<220>
<223> Vkappa variant 5

<400> 25

gacattgtgc tgaccaatc tccagactct ttggctgtgt ctctcgggga gagggccacc	60
atctcctgca aggccagcca aagtgttgat tatgatggtg atagttatat gaactggtac	120
caacaaaaac caggacagcc acccaaactc ctcatztatg atgcatcaa tttggaatct	180
ggcatcccag ccaggtttag tggcagtggg tctgggacag acttcaccct caccatcagc	240
agcctggagc ctgaggattt tgcagtctat tactgtcagc aaagtaatga agaccctggg	300

acgttcggtg gaggcaccaa ggtggaaatc aaa

333

<210> 26
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> VH region of anti-C1s antibody

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> may be Gln or Glu

<220>
<221> MISC_FEATURE
<222> (5)..(5)
<223> may be Val or Gln

<220>
<221> MISC_FEATURE
<222> (11)..(11)
<223> may be Val or Leu

<220>
<221> MISC_FEATURE
<222> (20)..(20)
<223> may be Leu or Val

<220>
<221> MISC_FEATURE
<222> (23)..(23)
<223> may be Thr or Ala

<220>
<221> MISC_FEATURE
<222> (38)..(38)
<223> may be Lys or Arg

<220>
<221> MISC_FEATURE
<222> (68)..(68)
<223> may be Val or Ala

<220>
<221> MISC_FEATURE
<222> (77)..(77)
<223> may be Ser or Asn

<220>

<221> MISC_FEATURE
<222> (81)..(81)
<223> may be Leu or Met

<220>
<221> MISC_FEATURE
<222> (82)..(82)
<223> may be Glu or Gln

<220>
<221> MISC_FEATURE
<222> (87)..(87)
<223> may be Arg or Thr

<400> 26

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

Ser Val Lys Xaa Ser Cys Xaa Ala Ser Gly Phe Asn Ile Lys Asp Asp
20 25 30

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

Gly Arg Ile Asp Pro Ala Asp Gly His Thr Lys Tyr Ala Pro Lys Phe
50 55 60

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

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

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

Thr Thr Val Thr Val Ser Ser
115

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

<220>

<223> VL region of anti-C1s antibody

<220>

<221> MISC_FEATURE

<222> (44)..(44)

<223> may be Thr or Pro

<220>

<221> MISC_FEATURE

<222> (50)..(50)

<223> may be Ile or Leu

<220>

<221> MISC_FEATURE

<222> (84)..(84)

<223> may be Glu or Pro

<220>

<221> MISC_FEATURE

<222> (89)..(89)

<223> may be Ile or Val

<400> 27

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

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

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

Lys Xaa Leu Ile Tyr Asp Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
50 55 60

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

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

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

<210> 28

<211> 327
<212> PRT
<213> Artificial Sequence

<220>
<223> Human IgG4 Constant Region (Fc) Variant 2

<400> 28

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

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

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

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

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp

180

185

190

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

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

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

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

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

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

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

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

Leu Ser Leu Ser Leu Gly Lys
 325

<210> 29

<211> 446

<212> PRT

<213> Artificial Sequence

<220>

<223> VH3 Mature Heavy Chain

<400> 29

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

Ser Val Lys Leu Ser Cys Thr Ala Ser Gly Phe Asn Ile Lys Asp Asp

20

25

30

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

Gly Arg Ile Asp Pro Ala Asp Gly His Thr Lys Tyr Ala Pro Lys Phe
 50 55 60

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

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

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

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

Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu
 130 135 140

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

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

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

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

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro
 210 215 220

Cys Pro Pro Cys Pro Ala Pro Glu Phe Glu Gly Gly Pro Ser Val Phe
 225 230 235 240

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

Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val
260 265 270

Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
275 280 285

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

Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
305 310 315 320

Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser
325 330 335

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

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

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

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

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

Gln Glu Gly Asn Val Phe Ser Cys Ser Val Leu His Glu Ala Leu His
420 425 430

Ser His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
435 440 445

<211> 218
<212> PRT
<213> Artificial Sequence

<220>
<223> Vkappa2 variant Mature Light Chain

<400> 30

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

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

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

Lys Ile Leu Ile Tyr Asp Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
50 55 60

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

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

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg
100 105 110

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

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

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

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

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys

180

185

190

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

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

<210> 31

<211> 465

<212> PRT

<213> Artificial Sequence

<220>

<223> synthetic amino acid sequence

<400> 31

Met Gly Trp Ser Leu Ile Leu Leu Phe Leu Val Ala Val Ala Thr Arg
 1 5 10 15

Val His Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
 20 25 30

Pro Gly Ala Ser Val Lys Leu Ser Cys Thr Ala Ser Gly Phe Asn Ile
 35 40 45

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

Glu Trp Ile Gly Arg Ile Asp Pro Ala Asp Gly His Thr Lys Tyr Ala
 65 70 75 80

Pro Lys Phe Gln Val Lys Val Thr Ile Thr Ala Asp Thr Ser Thr Ser
 85 90 95

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

Tyr Tyr Cys Ala Arg Tyr Gly Tyr Gly Arg Glu Val Phe Asp Tyr Trp
 115 120 125

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro

130

135

140

Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr
 145 150 155 160

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

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

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

Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp
 210 215 220

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

Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe Glu Gly Gly Pro
 245 250 255

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
 260 265 270

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp
 275 280 285

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

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

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
 325 330 335

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

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

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

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

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

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys
420 425 430

Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Leu His Glu
435 440 445

Ala Leu His Ser His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly
450 455 460

Lys
465

<210> 32
<211> 238
<212> PRT
<213> Artificial Sequence

<220>
<223> synthetic amino acid sequence

<400> 32

Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp Leu Pro
1 5 10 15

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

Val Ser Leu Gly Glu Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser
35 40 45

Val Asp Tyr Asp Gly Asp Ser Tyr Met Asn Trp Tyr Gln Gln Lys Pro
50 55 60

Gly Gln Pro Pro Lys Ile Leu Ile Tyr Asp Ala Ser Asn Leu Glu Ser
65 70 75 80

Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
85 90 95

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

Gln Gln Ser Asn Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Val
115 120 125

Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro
130 135 140

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

Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn
165 170 175

Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser
180 185 190

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

Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly
210 215 220

Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
225 230 235

<210> 33
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> VL CDR1 (CDR-L1) of anti-C1s antibody

<400> 33

Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr
1 5 10

<210> 34
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> VL CDR2 (CDR-L2) of anti-C1s antibody

<400> 34

Asp Ala Ser
1

<210> 35
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> VL CDR3 (CDR-L3) of anti-C1s antibody

<400> 35

Ser Asn Glu Asp Pro Trp
1 5

<210> 36
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> VH CDR1 (CDR-H1) of anti-C1s antibody

<400> 36

Gly Phe Asn Ile Lys Asp Asp
1 5

<210> 37
<211> 3
<212> PRT

<213> Artificial Sequence

<220>

<223> VH CDR2 (CDR-H2) of anti-C1s antibody

<400> 37

Ala Asp Gly

1

<210> 38

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> VH CDR3 (CDR-H3) of anti-C1s antibody

<400> 38

Gly Tyr Gly Arg Glu Val Phe Asp

1

5

<210> 39

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> VL CDR1 (CDR-L1) of anti-C1s antibody

<400> 39

Asp Ser Tyr Met Asn Trp Tyr

1

5

<210> 40

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> VL CDR2 (CDR-L2) of anti-C1s antibody

<400> 40

Ile Leu Ile Tyr Asp Ala Ser Asn Leu Glu

1

5

10

<210> 41

<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> VL CDR3 (CDR-L3) of anti-C1s antibody

<400> 41

Gln Gln Ser Asn Glu Asp Pro Trp
1 5

<210> 42
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> VH CDR1 (CDR-H1) of anti-C1s antibody

<400> 42

Lys Asp Asp Tyr Ile His
1 5

<210> 43
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> VH CDR2 (CDR-H2) of anti-C1s antibody

<400> 43

Trp Ile Gly Arg Ile Asp Pro Ala Asp Gly His Thr Lys
1 5 10

<210> 44
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> VH CDR3 (CDR-H3) of anti-C1s antibody

<400> 44

Ala Arg Tyr Gly Tyr Gly Arg Glu Val Phe Asp
1 5 10

<210> 45
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> TNT020 VH3/VK2-Fc-sub4

<400> 45

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> 46
<211> 446
<212> PRT
<213> Artificial Sequence

<220>
<223> VH1 Mature Heavy Chain

<400> 46

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

Ser Val Lys Leu Ser Cys Thr Ala Ser Gly Phe Asn Ile Lys Asp Asp

20

25

30

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

Gly Arg Ile Asp Pro Ala Asp Gly His Thr Lys Tyr Ala Pro Lys Phe
 50 55 60

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

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

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

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

Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu
 130 135 140

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

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

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

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

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro
 210 215 220

Cys Pro Pro Cys Pro Ala Pro Glu Phe Glu Gly Gly Pro Ser Val Phe
 225 230 235 240

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

Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val
260 265 270

Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
275 280 285

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

Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
305 310 315 320

Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser
325 330 335

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

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

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

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

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

Gln Glu Gly Asn Val Phe Ser Cys Ser Val Leu His Glu Ala Leu His
420 425 430

Ser His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
435 440 445

<211> 446
<212> PRT
<213> Artificial Sequence

<220>
<223> VH2 Mature Heavy Chain

<400> 47

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

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

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

Gly Arg Ile Asp Pro Ala Asp Gly His Thr Lys Tyr Ala Pro Lys Phe
50 55 60

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

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

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

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

Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu
130 135 140

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

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

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

180

185

190

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

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro
 210 215 220

Cys Pro Pro Cys Pro Ala Pro Glu Phe Glu Gly Gly Pro Ser Val Phe
 225 230 235 240

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

Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val
 260 265 270

Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
 275 280 285

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

Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
 305 310 315 320

Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser
 325 330 335

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

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

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

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

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

Gln Glu Gly Asn Val Phe Ser Cys Ser Val Leu His Glu Ala Leu His
420 425 430

Ser His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
435 440 445

<210> 48

<211> 446

<212> PRT

<213> Artificial Sequence

<220>

<223> VH4 Mature Heavy Chain

<400> 48

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

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

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

Gly Arg Ile Asp Pro Ala Asp Gly His Thr Lys Tyr Ala Pro Lys Phe
50 55 60

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

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

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

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

Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu
130 135 140

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

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

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

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

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro
210 215 220

Cys Pro Pro Cys Pro Ala Pro Glu Phe Glu Gly Gly Pro Ser Val Phe
225 230 235 240

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

Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val
260 265 270

Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
275 280 285

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

Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
305 310 315 320

Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser
325 330 335

Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro

340

345

350

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

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

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

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

Gln Glu Gly Asn Val Phe Ser Cys Ser Val Leu His Glu Ala Leu His
 420 425 430

Ser His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
 435 440 445

<210> 49

<211> 446

<212> PRT

<213> Artificial Sequence

<220>

<223> VH5 Mature Heavy Chain

<400> 49

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

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

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

Gly Arg Ile Asp Pro Ala Asp Gly His Thr Lys Tyr Ala Pro Lys Phe
 50 55 60

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

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

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

Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
305 310 315 320

Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser
325 330 335

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

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

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

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

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

Gln Glu Gly Asn Val Phe Ser Cys Ser Val Leu His Glu Ala Leu His
420 425 430

Ser His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
435 440 445

<210> 50

<211> 218

<212> PRT

<213> Artificial Sequence

<220>

<223> Vkappa1 variant Mature Light Chain

<400> 50

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

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

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

Lys Ile Leu Ile Tyr Asp Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
50 55 60

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

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

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg
100 105 110

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

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

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

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

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

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

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

<210> 51

<211> 218
<212> PRT
<213> Artificial Sequence

<220>
<223> Vkappa5 variant Mature Light Chain

<400> 51

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

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

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

Lys Leu Leu Ile Tyr Asp Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
50 55 60

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

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

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg
100 105 110

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

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

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

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

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys

180

185

190

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

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

<210> 52

<211> 327

<212> PRT

<213> Artificial Sequence

<220>

<223> Human IgG4 Constant Region (Fc)

<400> 52

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

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

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

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

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

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

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

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

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val

130

135

140

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

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

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

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

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

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

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

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

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

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

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

Leu Ser Leu Ser Leu Gly Lys
 325

<210> 53

<211> 327

<212> PRT

<213> Artificial Sequence

<220>

<223> Human IgG4 Constant Region (Fc) Variant 1

<400> 53

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

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

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

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

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

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

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

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

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

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

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

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

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

Leu Ser Leu Ser Leu Gly Lys
325

<210> 54
<211> 218
<212> PRT
<213> Artificial Sequence

<220>
<223> Parental Murine anti-C1s VL Mature Light Chain

<400> 54

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

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

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

Lys Ile Leu Ile Tyr Asp Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
50 55 60

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

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

Glu Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg
100 105 110

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

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

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

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

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

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

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