

SEQUENCE LISTING

<110> Prothena Therapeutics Limited
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Robin Barbour

<120> Treatment And Prophylaxis Of Amyloidosis

<130> E090 1070US.P1

<160> 21

<170> PatentIn version 3.5

<210> 1

<211> 16

<212> PRT

<213> Mus musculus

<220>

<223> 2A4 VL CDR1

<400> 1

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1				5					10					15	

<210> 2

<211> 7

<212> PRT

<213> Mus musculus

<220>

<223> 2A4 VL CDR2

<400> 2

Lys	Val	Ser	Asn	Arg	Phe	Ser
1				5		

<210> 3

<211> 9

<212> PRT

<213> Mus musculus

<220>

<223> 2A4 VL CDR3

<400> 3

Ser Gln Ser Thr His Val Pro Phe Thr

1 5

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

<220>
<223> 2A4 VH CDR1

<400> 4

Gly Phe Thr Phe Asn Thr Tyr Ala Met Tyr
1 5 10

<210> 5
<211> 19
<212> PRT
<213> Mus musculus

<220>
<223> 2A4 VH CDR2

<400> 5

Arg Ile Arg Ser Lys Ser Asn Asn Tyr Ala Ile Tyr Tyr Ala Asp Ser
1 5 10 15

Val Lys Asp

<210> 6
<211> 8
<212> PRT
<213> Mus musculus

<220>
<223> 2A4 VH CDR3

<400> 6

Pro Tyr Ser Asp Ser Phe Ala Tyr
1 5

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

<220>

<223> Humanized 2A4 light chain variable region version 1

<400> 7

Asp Val 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 His Ser
20 25 30

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

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

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

<210> 8

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized 2A4 light chain variable region version 2

<400> 8

Asp Val 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 His Ser
20 25 30

Thr Gly Asn 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 Phe Cys Ser Gln Ser
85 90 95

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

<210> 9

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized 2A4 light chain variable region version 3

<400> 9

Asp Val 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 His Ser
20 25 30

Thr Gly Asn 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 Phe Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105 110

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

<220>
<223> Humanized 2A4 heavy chain variable region version 1

<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 Asn Thr Tyr
20 25 30

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

Ala Arg Ile Arg Ser Lys Ser Asn Asn Tyr Ala Ile Tyr Tyr Ala Asp
50 55 60

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

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

Tyr Cys Val Arg Pro Tyr Ser Asp Ser Phe Ala Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
115

<210> 11
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Humanized 2A4 heavy chain variable region version 2

<400> 11

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 Asn Thr Tyr
20 25 30

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

Ala Arg Ile Arg Ser Lys Ser Asn Asn Tyr Ala Ile Tyr Tyr Ala Asp
50 55 60

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

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

Tyr Cys Val Arg Pro Tyr Ser Asp Ser Phe Ala Tyr Trp Gly Gln Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
115

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

<220>
<223> Humanized 2A4 heavy chain variable region version 3

<400> 12

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 Asn Thr Tyr
20 25 30

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

Ala Arg Ile Arg Ser Lys Ser Asn Asn Tyr Ala Ile Tyr Tyr Ala Asp
50 55 60

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

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

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

Thr Leu Val Thr Val Ser Ser
115

<210> 13

<211> 219

<212> PRT

<213> Artificial Sequence

<220>

<223> Humanized 2A4 kappa light chain

<400> 13

Asp Val 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 His Ser
20 25 30

Thr Gly Asn 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 Phe Thr Phe Gly Gly 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> 14
<211> 449
<212> PRT
<213> Artificial Sequence

<220>
<223> Humanized 2A4 IgG1 heavy chain variant 2 (G1m3 allotype)

<400> 14

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 Asn Thr Tyr
20 25 30

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

Ala Arg Ile Arg Ser Lys Ser Asn Asn Tyr Ala Ile Tyr Tyr Ala Asp
50 55 60

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

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

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

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

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

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

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

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

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
260 265 270

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

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

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

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

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

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

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

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

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

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

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

Lys

<210> 15

<211> 660

<212> DNA

<213> Artificial Sequence

<220>

<223> Humanized antibody sequence containing murine and human residues

(Hu2A4 VH3VL3 hcg1,k cDNA sequence - light chain without signal sequence)

<400> 15

gacgtggtga tgaccagtc ccctctgtcc ctgcctgtga cccctggcga gcctgcctcc	60
atctcctgcc ggtcctccca gtccctggtg cactccaccg gcaacaccta tctgcactgg	120
tatctgcaga agcctggcca gtctcctcag ctgctgatct acaaggtgtc caaccggttc	180
tccggcgtgc ctgaccggtt ctctggctcc ggctccggca ccgacttcac cctgaagatc	240
tcccgggtgg aggccgagga cgtgggcgtg tactactgct cccagtccac ccacgtgcct	300
ttcaccttcg gcggaggtac caaggtggag atcaaacgaa ctgtggctgc accatctgtc	360
ttcatcttcc cgccatctga tgagcagttg aaatctggaa ctgcctctgt tgtgtgcctg	420
ctgaataact tctatcccag agaggccaaa gtacagtggga aggtggataa cgccctccaa	480
tcgggtaact cccaggagag tgtcacagag caggacagca aggacagcac ctacagcctc	540
agcagcacc tgacgtgag caaagcagac tacgagaaac acaaagtcta cgcctgcgaa	600
gtcacccatc agggcctgag ctcgcccgtc acaaagagct tcaacagggg agagtgttag	660

<210> 16

<211> 726

<212> DNA

<213> Artificial Sequence

<220>

<223> Humanized antibody sequence containing murine and human residues
(Hu2A4 VH3VL3 hcg1,k cDNA sequence - light chain)

<400> 16

atggacatgc gggtgccgc acagctgctg ggcctgctga tgctgtgggt gtccggctcc	60
tccggcgacg tggatgatgac ccagtcccct ctgtccctgc ctgtgacccc tggcgagcct	120
gcctccatct cctgccggtc ctcccagtcc ctggtgcact ccaccggcaa cacctatctg	180
cactggtatc tgcagaagcc tggccagtct cctcagctgc tgatctacaa ggtgtccaac	240
cggttctccg gcgtgcctga ccggttctct ggctccggct ccggcaccga cttcacctg	300
aagatctccc ggggtggaggc cgaggacgtg ggcgtgtact actgctcca gtccaccac	360
gtgcctttca ccttcggcgg aggcaccaag gtggagatca agcgaactgt ggctgcacca	420
tctgtcttca tcttcccgcc atctgatgag cagttgaaat ctggaactgc ctctgtttgtg	480

tgcttgctga ataacttcta tcccagagag gccaaagtac agtggaaggt ggataacgcc	540
ctccaatcgg gtaactccca ggagagtgtc acagagcagg acagcaagga cagcacctac	600
agcctcagca gcaccctgac gctgagcaaa gcagactacg agaaacacaa agtctacgcc	660
tgcgaagtca cccatcaggg cctgagctcg cccgtcacia agagcttcaa caggggagag	720
tgttag	726

<210> 17
 <211> 1347
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Humanized antibody sequence containing murine and human residues
 (Hu2A4 VH3VL3 hcg1,k cDNA sequence - heavy chain without signal
 sequence)

<400> 17

gaagtgcaat tggtcgagtc cggcggaggc ctggtgcagc ctggcggctc cctgagactg	60
tcctgcgccg cctccggctt caccttcaac acctacgcc tgtactggat caggcaggct	120
cctggcaagg gactggagtg ggtggcccgg atcaggtcca agtccaacaa ctacgctatc	180
tactacgccg actccgtgaa ggaccggttc accatctccc gggacgactc caagaactcc	240
ctgtatctgc agatgaactc cctgaaaacc gaggacaccg ccgtgtacta ctgcgctcgg	300
ccttactccg actccttcgc ctactggggc cagggcaccc tggtgaccgt gagctcagcc	360
tccaccaagg gtccatcggc cttccccctg gcaccctcct ccaagagcac ctctgggggc	420
acagcggccc tgggctgcct ggtcaaggac tacttccccg aaccggtgac ggtgtcgtgg	480
aactcaggcg ccctgaccag cggcgtgcac accttcccgg ctgtcctaca gtcctcagga	540
ctctactccc tcagcagcgt ggtgaccgtg ccctccagca gcttgggcac ccagacctac	600
atctgcaacg tgaatcacia gccagcaac accaaggtgg acaagagagt tgagcccaaa	660
tcttgtgaca aaactcacac atgcccaccg tgcccagcac ctgaactcct ggggggaccg	720
tcagtcttcc tcttcccccc aaaaccaag gacaccctca tgatctcccg gacccttag	780
gtcacatgcg tggtggtgga cgtgagccac gaagaccctg aggtcaagtt caactggtac	840
gtggacggcg tggaggtgca taatgccaag acaaagccgc gggaggagca gtacaacagc	900

acgtaccgtg tggtcagcgt cctcaccgtc ctgcaccagg actggctgaa tggcaaggag	960
tacaagtgca aggtctccaa caaagccctc ccagccccc tgcagaaaac catctccaaa	1020
gccaaagggc agccccgaga accacaggtg tacaccctgc ccccatcccg ggaggagatg	1080
accaagaacc aggtcagcct gacctgcctg gtcaaaggct tctatcccag cgacatcgcc	1140
gtggagtggg agagcaatgg gcagccggag aacaactaca agaccacgcc tcccgctgctg	1200
gactccgacg gctccttctt cctctatagc aagctcaccg tggacaagag caggtggcag	1260
caggggaacg tcttctcatg ctccgtgatg catgaggctc tgcacaacca ctacacgcag	1320
aagagcctct ccctgtcccc gggtaaa	1347

<210> 18

<211> 1404

<212> DNA

<213> Artificial Sequence

<220>

<223> Humanized antibody sequence containing murine and human residues
(Hu2A4 VH3VL3 hcg1,k cDNA sequence - heavy chain)

<400> 18

atggagttcg gcctgtcctg gctgttcctg gtggccatcc tgaagggcgt gcagtgcgaa	60
gtgcaattgg tcgagtccgg cggaggcctg gtgcagcctg gcggctccct gagactgtcc	120
tgcgccgcct ccggcttcac cttcaacacc tacgccatgt actggatcag gcaggctcct	180
ggcaagggac tggagtgggt ggccccgatc aggtccaagt ccaacaacta cgctatctac	240
tacgccgact ccgtgaagga ccggttcacc atctcccggg acgactccaa gaactccctg	300
tatctgcaga tgaactccct gaaaaccgag gacaccgccg tgtactactg cgctcggcct	360
tactccgact ctttcgccta ctggggccag ggcaccctgg tgaccgtgag ctcagcctcc	420
accaagggtc catcgggtctt ccccctggca ccctcctcca agagcacctc tgggggcaca	480
gcggccctgg gctgcctggg caaggactac ttccccgaac cggtgacggt gtcgtggaac	540
tcaggcgccc tgaccagcgg cgtgcacacc ttcccggtg tcctacagtc ctcaggactc	600
tactccctca gcagcgtggg gaccgtgccc tccagcagct tgggcaccca gacctacatc	660
tgcaacgtga atcacaagcc cagcaacacc aaggtggaca agagagttga gcccaaattc	720
tgtgacaaaa ctcacacatg cccaccgtgc ccagcacctg aactcctggg gggaccgtca	780

gtcttcctct tcccccaaa acccaaggac accctcatga tctcccggac ccctgaggtc	840
acatgcgtgg tggtaggacgt gagccacgaa gaccctgagg tcaagttcaa ctggtacgtg	900
gacggcgtgg aggtgcataa tgccaagaca aagccgcggg aggagcagta caacagcacg	960
taccgtgtgg tcagcgtcct caccgtcctg caccaggact ggctgaatgg caaggagtac	1020
aagtgaagg tctccaacaa agccctcca gccccatcg agaaaaccat ctccaaagcc	1080
aaagggcagc cccgagaacc acaggtgtac accctgcccc catcccggga ggagatgacc	1140
aagaaccagg tcagcctgac ctgcctggtc aaaggcttct atcccagcga catcgccgtg	1200
gagtgggaga gcaatgggca gccggagaac aactacaaga ccacgcctcc cgtgctggac	1260
tccgacggct ctttcttct ctatagcaag ctcaccgtgg acaagagcag gtggcagcag	1320
gggaacgtct tctcatgctc cgtgatgcat gaggctctgc acaaccacta cacgcagaag	1380
agcctctccc tgtccccggg taaa	1404

<210> 19
 <211> 4
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Immunoglobulin light chain sequence

<400> 19

His Glu Asp Thr
 1

<210> 20
 <211> 4
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Immunoglobulin light chain sequence

<400> 20

Ala Glu Asp Ser
 1

<210> 21
 <211> 4
 <212> PRT

<213> Artificial Sequence

<220>

<223> Immunoglobulin light chain sequence

<400> 21

His Gly Asp Thr

1