

SEQUENCE LISTING

<110> Amgen Inc.

<120> LOW-VISCOSITY, HIGH-CONCENTRATION EVOLOCUMAB FORMULATIONS AND METHODS OF MAKING THE SAME

<130> A-2112-WO-PCT

<150> 62/462,266

<151> 2017-02-22

<160> 17

<170> PatentIn version 3.5

<210> 1

<211> 441

<212> PRT

<213> Homo sapiens

<400> 1

Glu 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 Lys Ala Ser Gly Tyr Thr Leu Thr Ser Tyr
20 25 30

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

Gly Trp Val Ser Phe Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu
50 55 60

Gln Gly Arg Gly Thr Met Thr Thr Asp Pro Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Ala Arg Gly Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

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

Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val
130 135 140

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
145 150 155 160

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

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Asn Phe Gly
180 185 190

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

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

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

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

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

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

Gln Phe Asn Ser Thr Phe Arg Val Val Ser Val Leu Thr Val Val His
290 295 300

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys

305 310 315 320

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

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

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

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

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

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

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

Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440

<210> 2
<211> 215
<212> PRT
<213> Homo sapiens

<400> 2

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

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
20 25 30

Asn Ser Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Met Ile Tyr Glu Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

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

Ser Met Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln Pro
100 105 110

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

Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe Tyr Pro
130 135 140

Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro Val Lys Ala
145 150 155 160

Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys Tyr Ala
165 170 175

Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser His Arg
180 185 190

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

Val Ala Pro Thr Glu Cys Ser
210 215

<210> 3
<211> 692

<212> PRT

<213> Homo sapiens

<400> 3

Met Gly Thr Val Ser Ser Arg Arg Ser Trp Trp Pro Leu Pro Leu Leu
1 5 10 15

Leu Leu Leu Leu Leu Leu Leu Gly Pro Ala Gly Ala Arg Ala Gln Glu
20 25 30

Asp Glu Asp Gly Asp Tyr Glu Glu Leu Val Leu Ala Leu Arg Ser Glu
35 40 45

Glu Asp Gly Leu Ala Glu Ala Pro Glu His Gly Thr Thr Ala Thr Phe
50 55 60

His Arg Cys Ala Lys Asp Pro Trp Arg Leu Pro Gly Thr Tyr Val Val
65 70 75 80

Val Leu Lys Glu Glu Thr His Leu Ser Gln Ser Glu Arg Thr Ala Arg
85 90 95

Arg Leu Gln Ala Gln Ala Ala Arg Arg Gly Tyr Leu Thr Lys Ile Leu
100 105 110

His Val Phe His Gly Leu Leu Pro Gly Phe Leu Val Lys Met Ser Gly
115 120 125

Asp Leu Leu Glu Leu Ala Leu Lys Leu Pro His Val Asp Tyr Ile Glu
130 135 140

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

Ile Thr Pro Pro Arg Tyr Arg Ala Asp Glu Tyr Gln Pro Pro Asp Gly
165 170 175

Gly Ser Leu Val Glu Val Tyr Leu Leu Asp Thr Ser Ile Gln Ser Asp

180

185

190

His Arg Glu Ile Glu Gly Arg Val Met Val Thr Asp Phe Glu Asn Val
 195 200 205

Pro Glu Glu Asp Gly Thr Arg Phe His Arg Gln Ala Ser Lys Cys Asp
 210 215 220

Ser His Gly Thr His Leu Ala Gly Val Val Ser Gly Arg Asp Ala Gly
 225 230 235 240

Val Ala Lys Gly Ala Ser Met Arg Ser Leu Arg Val Leu Asn Cys Gln
 245 250 255

Gly Lys Gly Thr Val Ser Gly Thr Leu Ile Gly Leu Glu Phe Ile Arg
 260 265 270

Lys Ser Gln Leu Val Gln Pro Val Gly Pro Leu Val Val Leu Leu Pro
 275 280 285

Leu Ala Gly Gly Tyr Ser Arg Val Leu Asn Ala Ala Cys Gln Arg Leu
 290 295 300

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

Asp Ala Cys Leu Tyr Ser Pro Ala Ser Ala Pro Glu Val Ile Thr Val
 325 330 335

Gly Ala Thr Asn Ala Gln Asp Gln Pro Val Thr Leu Gly Thr Leu Gly
 340 345 350

Thr Asn Phe Gly Arg Cys Val Asp Leu Phe Ala Pro Gly Glu Asp Ile
 355 360 365

Ile Gly Ala Ser Ser Asp Cys Ser Thr Cys Phe Val Ser Gln Ser Gly
 370 375 380

Thr Ser Gln Ala Ala Ala His Val Ala Gly Ile Ala Ala Met Met Leu
385 390 395 400

Ser Ala Glu Pro Glu Leu Thr Leu Ala Glu Leu Arg Gln Arg Leu Ile
405 410 415

His Phe Ser Ala Lys Asp Val Ile Asn Glu Ala Trp Phe Pro Glu Asp
420 425 430

Gln Arg Val Leu Thr Pro Asn Leu Val Ala Ala Leu Pro Pro Ser Thr
435 440 445

His Gly Ala Gly Trp Gln Leu Phe Cys Arg Thr Val Trp Ser Ala His
450 455 460

Ser Gly Pro Thr Arg Met Ala Thr Ala Ile Ala Arg Cys Ala Pro Asp
465 470 475 480

Glu Glu Leu Leu Ser Cys Ser Ser Phe Ser Arg Ser Gly Lys Arg Arg
485 490 495

Gly Glu Arg Met Glu Ala Gln Gly Gly Lys Leu Val Cys Arg Ala His
500 505 510

Asn Ala Phe Gly Gly Glu Gly Val Tyr Ala Ile Ala Arg Cys Cys Leu
515 520 525

Leu Pro Gln Ala Asn Cys Ser Val His Thr Ala Pro Pro Ala Glu Ala
530 535 540

Ser Met Gly Thr Arg Val His Cys His Gln Gln Gly His Val Leu Thr
545 550 555 560

Gly Cys Ser Ser His Trp Glu Val Glu Asp Leu Gly Thr His Lys Pro
565 570 575

Pro Val Leu Arg Pro Arg Gly Gln Pro Asn Gln Cys Val Gly His Arg

580

585

590

Glu Ala Ser Ile His Ala Ser Cys Cys His Ala Pro Gly Leu Glu Cys
595 600 605

Lys Val Lys Glu His Gly Ile Pro Ala Pro Gln Gly Gln Val Thr Val
610 615 620

Ala Cys Glu Glu Gly Trp Thr Leu Thr Gly Cys Ser Ala Leu Pro Gly
625 630 635 640

Thr Ser His Val Leu Gly Ala Tyr Ala Val Asp Asn Thr Cys Val Val
645 650 655

Arg Ser Arg Asp Val Ser Thr Thr Gly Ser Thr Ser Glu Glu Ala Val
660 665 670

Thr Ala Val Ala Ile Cys Cys Arg Ser Arg His Leu Ala Gln Ala Ser
675 680 685

Gln Glu Leu Gln
690

<210> 4
<211> 14
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<213> Homo sapiens

<400> 4

Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn Ser Val Ser
1 5 10

<210> 5
<211> 7
<212> PRT
<213> Homo sapiens

<400> 5

Glu Val Ser Asn Arg Pro Ser

1 5

<210> 6
<211> 9
<212> PRT
<213> Homo sapiens

<400> 6

Asn Ser Tyr Thr Ser Thr Ser Met Val
1 5

<210> 7
<211> 10
<212> PRT
<213> Homo sapiens

<400> 7

Gly Tyr Thr Leu Thr Ser Tyr Gly Ile Ser
1 5 10

<210> 8
<211> 16
<212> PRT
<213> Homo sapiens

<400> 8

Trp Val Ser Phe Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu Gln
1 5 10 15

<210> 9
<211> 6
<212> PRT
<213> Homo sapiens

<400> 9

Gly Tyr Gly Met Asp Val
1 5

<210> 10
<211> 345
<212> DNA

<213> Homo sapiens

<400> 10

cagggttcagc tgggtgcagtc tggagctgag gtgaagaagc ctggggcctc agtgaaggtc	60
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cctggacaag ggcttgagtg gatgggatgg gtcagttttt ataatggtaa cacaaactat	180
gcacagaagc tccagggcag aggcaccatg accacagacc catccacgag cacagcctac	240
atggagctga ggagcctgag atctgacgac acggccgtgt attactgtgc gagaggctac	300
ggtatggacg tctggggcca agggaccacg gtcaccgtct cctct	345

<210> 11

<211> 327

<212> DNA

<213> Homo sapiens

<400> 11

cagtctgccc tgactcagcc tgcctccgtg tctgggtctc ctggacagtc gatcaccatc	60
tcctgcactg gaaccagcag tgacgttggg ggttataact ctgtctcctg gtaccaacag	120
cacccaggca aagcccccaa actcatgatt tatgagggtca gtaatcggcc ctcagggggtt	180
tctaatacgt tctctggctc caagtctggc aacacggcct ccctgaccat ctctgggctc	240
caggctgagg acgaggctga ttattactgc aattcatata caagcaccag catggtattc	300
ggcggaggga ccaagctgac cgtccta	327

<210> 12

<211> 1380

<212> DNA

<213> Homo sapiens

<400> 12

atggactgga cctggaggat ctttttcttg gtggcagcag ccacaggtgt ccactccgag	60
gttcagctgg tgcagtctgg agctgagggtg aagaagcctg gggcctcagt gaaggctctcc	120
tgcaaggctt ctggttacac cttaaccagc tatgggtatca gctgggtgcg acaggcccct	180
ggacaagggc ttgagtggat gggatgggtc agtttttata atggtaacac aaactatgca	240
cagaagctcc agggcagagg caccatgacc acagacccat ccacgagcac agcctacatg	300

gagctgagga gcctgagatc tgacgacacg gccgtgtatt actgtgcgag aggctacggt	360
atggacgtct ggggccaagg gaccacggtc accgtctcct ctgcctccac caagggccca	420
tcggtcttcc ccctggcgcc ctgctccagg agcacctccg agagcacagc ggccctgggc	480
tgcttggtca aggactactt cccgaaccg gtgacgggtg cgtggaactc aggcgctctg	540
accagcggcg tgcacacctt cccagctgtc ctacagtcct caggactcta ctccctcagc	600
agcgtgggtga ccgtgccctc cagcaacttc ggcacccaga cctacacctg caacgtagat	660
cacaagccca gcaacaccaa ggtggacaag acagttgagc gcaaagtgtg tgtcgagtgc	720
ccaccgtgcc cagcaccacc tgtggcagga ccgtcagtct tcctcttccc cccaaaaccc	780
aaggacaccc tcatgatctc ccggacccct gaggtcacgt gcgtgggtgg ggacgtgagc	840
cacgaagacc ccgaggtcca gttcaactgg tacgtggacg gcgtggaggt gcataatgcc	900
aagacaaagc cacgggagga gcagttcaac agcacgttcc gtgtggtcag cgtcctcacc	960
gttgtgcacc aggactggct gaacggcaag gagtacaagt gcaaggcttc caacaaaggc	1020
ctcccagccc ccatcgagaa aaccatctcc aaaaccaaag ggcagccccg agaaccacag	1080
gtgtacaccc tgccccatc ccgggaggag atgaccaaga accaggtcag cctgacctgc	1140
ctggtcaaag gcttctaccc cagcgacatc gccgtggagt gggagagcaa tgggcagccg	1200
gagaacaact acaagaccac acctcccatg ctggactccg acggctcctt cttcctctac	1260
agcaagctca ccgtggacaa gagcaggtgg cagcagggga acgtcttctc atgctccgtg	1320
atgcatgagg ctctgcacaa ccactacacg cagaagagcc tctccctgtc tccgggtaaa	1380

<210> 13
 <211> 711
 <212> DNA
 <213> Homo sapiens

<400> 13	
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agatgtgagt ctgccctgac tcagcctgcc tccgtgtctg ggtctcctgg acagtcgac	120
accatctcct gcactggaac cagcagtgac gttgggtggtt ataactctgt ctcttggtac	180

caacagcacc caggcaaagc ccccaaactc atgatttatg aggtcagtaa tcggccctca	240
ggggtttcta atcgcttctc tggctccaag tctggcaaca cggcctccct gaccatctct	300
gggctccagg ctgaggacga ggctgattat tactgcaatt catatacaag caccagcatg	360
gtattcggcg gagggaccaa gctgaccgtc ctaggtcagc ccaaggctgc cccctcggtc	420
actctgttcc cgccctcctc tgaggagctt caagccaaca aggccacact ggtgtgtctc	480
ataagtgact tctacccggg agccgtgaca gtggcctgga aggcagatag cagccccgtc	540
aaggcgggag tggagaccac cacaccctcc aaacaaagca acaacaagta cgcggccagc	600
agctatctga gcctgacgcc tgagcagtgg aagtcccaca gaagctacag ctgccaggtc	660
acgcatgaag ggagcaccgt ggagaagaca gtggccccta cagaatgttc a	711

<210> 14
 <211> 115
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<400> 14

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 Lys Ala Ser Gly Tyr Thr Leu Thr Ser Tyr	
20 25 30	

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

Gly Trp Val Ser Phe Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu	
50 55 60	

Gln Gly Arg Gly Thr Met Thr Thr Asp Pro Ser Thr Ser Thr Ala Tyr	
65 70 75 80	

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

Ala Arg Gly Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 15
<211> 109
<212> PRT
<213> Homo sapiens

<400> 15

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

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
20 25 30

Asn Ser Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Met Ile Tyr Glu Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

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

Ser Met Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 16
<211> 115
<212> PRT
<213> Homo sapiens

<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 Lys Ala Ser Gly Tyr Thr Leu Thr Ser Tyr
20 25 30

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

Gly Trp Val Ser Phe Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu
50 55 60

Gln Gly Arg Gly Thr Met Thr Thr Asp Pro Ser Thr Ser Thr Ala Tyr
65 70 75 80

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

Ala Arg Gly Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 17
<211> 109
<212> PRT
<213> Homo sapiens

<400> 17

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

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
20 25 30

Asn Ser Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Met Ile Tyr Glu Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

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

Ser Met Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105