

SEQUENCE LISTING

<110> Amgen Inc.

<120> C-Terminal Antibody Variants

<130> 31173/52080

<150> US 62/650,762

<151> 2018-03-30

<150> US 62/812,741

<151> 2019-03-01

<160> 16

<170> PatentIn version 3.5

<210> 1

<211> 190

<212> PRT

<213> Homo sapiens

<220>

<221> MISC_FEATURE

<223> Human Sclerostin

<400> 1

Gln Gly Trp Gln Ala Phe Lys Asn Asp Ala Thr Glu Ile Ile Pro Glu
1 5 10 15

Leu Gly Glu Tyr Pro Glu Pro Pro Pro Glu Leu Glu Asn Asn Lys Thr
20 25 30

Met Asn Arg Ala Glu Asn Gly Gly Arg Pro Pro His His Pro Phe Glu
35 40 45

Thr Lys Asp Val Ser Glu Tyr Ser Cys Arg Glu Leu His Phe Thr Arg
50 55 60

Tyr Val Thr Asp Gly Pro Cys Arg Ser Ala Lys Pro Val Thr Glu Leu
65 70 75 80

Val Cys Ser Gly Gln Cys Gly Pro Ala Arg Leu Leu Pro Asn Ala Ile
85 90 95

Gly Arg Gly Lys Trp Trp Arg Pro Ser Gly Pro Asp Phe Arg Cys Ile
100 105 110

Pro Asp Arg Tyr Arg Ala Gln Arg Val Gln Leu Leu Cys Pro Gly Gly
115 120 125

Glu Ala Pro Arg Ala Arg Lys Val Arg Leu Val Ala Ser Cys Lys Cys
130 135 140

Lys Arg Leu Thr Arg Phe His Asn Gln Ser Glu Leu Lys Asp Phe Gly
145 150 155 160

Thr Glu Ala Ala Arg Pro Gln Lys Gly Arg Lys Pro Arg Pro Arg Ala
165 170 175

Arg Ser Ala Lys Ala Asn Gln Ala Glu Leu Glu Asn Ala Tyr
180 185 190

<210> 2
<211> 5
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<223> romo HCDR1

<400> 2

Asp Tyr Asn Met His
1 5

<210> 3
<211> 17
<212> PRT
<213> Mus musculus

<220>

<221> MISC_FEATURE

<223> romo HCDR2

<400> 3

Glu Ile Asn Pro Asn Ser Gly Gly Ala Gly Tyr Asn Gln Lys Phe Lys
1 5 10 15

Gly

<210> 4

<211> 14

<212> PRT

<213> Mus musculus

<220>

<221> MISC_FEATURE

<223> romo HCDR3

<400> 4

Leu Gly Tyr Asp Asp Ile Tyr Asp Asp Trp Tyr Phe Asp Val
1 5 10

<210> 5

<211> 11

<212> PRT

<213> Mus musculus

<220>

<221> MISC_FEATURE

<223> romoLCDR1

<400> 5

Arg Ala Ser Gln Asp Ile Ser Asn Tyr Leu Asn
1 5 10

<210> 6

<211> 7

<212> PRT

<213> Mus musculus

<220>
<221> MISC_FEATURE
<223> romo LCDR2

<400> 6

Tyr Thr Ser Arg Leu Leu Ser
1 5

<210> 7
<211> 9
<212> PRT
<213> Mus musculus

<220>
<221> MISC_FEATURE
<223> romo LCD3

<400> 7

Gln Gln Gly Asp Thr Leu Pro Tyr Thr
1 5

<210> 8
<211> 4
<212> PRT
<213> Homo sapiens

<220>
<221> MISC_FEATURE
<223> C-Terminal variant sequence

<400> 8

Pro Ala Arg Gly
1

<210> 9
<211> 123
<212> PRT
<213> Mus musculus

<220>
 <221> MISC_FEATURE
 <223> romo light chain variable region

<400> 9

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 Phe Thr Asp Tyr
 20 25 30

Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45

Gly Glu Ile Asn Pro Asn Ser Gly Gly Ala Gly Tyr Asn Gln Lys Phe
 50 55 60

Lys Gly Arg Val Thr Met Thr Thr Asp Thr 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 Leu Gly Tyr Asp Asp Ile Tyr Asp Asp Trp Tyr Phe Asp Val
 100 105 110

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
 115 120

<210> 10
 <211> 107
 <212> PRT
 <213> Mus musculus

<220>
 <221> MISC_FEATURE
 <223> romo heavy chain variable region

<400> 10

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 Ile Ser Asn Tyr
 20 25 30

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

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

Ser Gly 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 Gly Asp Thr Leu Pro Tyr
 85 90 95

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

<210> 11
 <211> 5
 <212> PRT
 <213> Homo sapiens

<220>
 <221> MISC_FEATURE
 <223> C-terminal variant sequence

<400> 11

Pro Ala Arg Gly Lys
 1 5

<210> 12
 <211> 236
 <212> PRT
 <213> Artificial Sequence

<220>

<223> Humanized antibody sequence

<220>

<221> MISC_FEATURE

<223> romo light chain

<400> 12

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

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

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

Gln Asp Ile Ser Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys
50 55 60

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

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

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

Gly Asp Thr Leu Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
115 120 125

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

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

Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu

165 170 175
 Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp
 180 185 190
 Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr
 195 200 205
 Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser
 210 215 220
 Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
 225 230 235

<210> 13
 <211> 469
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Humanized antibody sequence

<220>
 <221> MISC_FEATURE
 <223> romo heavy chain variant without lysine

<400> 13

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

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

Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe
 35 40 45

Thr Asp Tyr Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu
 50 55 60

Glu Trp Met Gly Glu Ile Asn Pro Asn Ser Gly Gly Ala Gly Tyr Asn
65 70 75 80

Gln Lys Phe Lys Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser
85 90 95

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

Tyr Tyr Cys Ala Arg Leu Gly Tyr Asp Asp Ile Tyr Asp Asp Trp Tyr
115 120 125

Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser
130 135 140

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

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

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

His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser
195 200 205

Ser Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr
210 215 220

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

Glu Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val
245 250 255

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

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

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

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

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

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

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

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

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

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

Pro Met Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
420 425 430

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

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

Ser Pro Ala Arg Gly
465

<210> 14
<211> 470
<212> PRT
<213> Artificial Sequence

<220>
<223> Humanized antibody sequence

<220>
<221> MISC_FEATURE
<223> romo heavy chain variant with lysine

<400> 14

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

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

Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe
35 40 45

Thr Asp Tyr Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu
50 55 60

Glu Trp Met Gly Glu Ile Asn Pro Asn Ser Gly Gly Ala Gly Tyr Asn
65 70 75 80

Gln Lys Phe Lys Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser
85 90 95

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

Tyr Tyr Cys Ala Arg Leu Gly Tyr Asp Asp Ile Tyr Asp Asp Trp Tyr
115 120 125

Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser
 130 135 140

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

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

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

His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser
 195 200 205

Ser Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr
 210 215 220

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

Glu Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val
 245 250 255

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

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

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

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

Phe Arg Val Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn

	325		330		335										
Gly	Lys	Glu	Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys	Gly	Leu	Pro	Ala	Pro
			340					345					350		
Ile	Glu	Lys	Thr	Ile	Ser	Lys	Thr	Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln
		355					360					365			
Val	Tyr	Thr	Leu	Pro	Pro	Ser	Arg	Glu	Glu	Met	Thr	Lys	Asn	Gln	Val
	370					375					380				
Ser	Leu	Thr	Cys	Leu	Val	Lys	Gly	Phe	Tyr	Pro	Ser	Asp	Ile	Ala	Val
385					390					395					400
Glu	Trp	Glu	Ser	Asn	Gly	Gln	Pro	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	Pro
				405					410					415	
Pro	Met	Leu	Asp	Ser	Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Lys	Leu	Thr
			420					425					430		
Val	Asp	Lys	Ser	Arg	Trp	Gln	Gln	Gly	Asn	Val	Phe	Ser	Cys	Ser	Val
		435					440					445			
Met	His	Glu	Ala	Leu	His	Asn	His	Tyr	Thr	Gln	Lys	Ser	Leu	Ser	Leu
	450					455					460				
Ser	Pro	Ala	Arg	Gly	Lys										
465					470										

<210> 15
 <211> 26
 <212> PRT
 <213> Homo sapiens

<220>
 <221> MISC_FEATURE
 <223> amino acids 86-111 of SEQ ID NO: 1

<400> 15

Cys Gly Pro Ala Arg Leu Leu Pro Asn Ala Ile Gly Arg Gly Lys Trp
 1 5 10 15

Trp Arg Pro Ser Gly Pro Asp Phe Arg Cys
 20 25

<210> 16
 <211> 468
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Humanized Antibody sequence

<220>
 <221> MISC_FEATURE
 <223> romo heavy chain wild type

<400> 16

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

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

Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe
 35 40 45

Thr Asp Tyr Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu
 50 55 60

Glu Trp Met Gly Glu Ile Asn Pro Asn Ser Gly Gly Ala Gly Tyr Asn
 65 70 75 80

Gln Lys Phe Lys Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser
 85 90 95

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

Tyr Tyr Cys Ala Arg Leu Gly Tyr Asp Asp Ile Tyr Asp Asp Trp Tyr
115 120 125

Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser
130 135 140

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

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

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

His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser
195 200 205

Ser Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr
210 215 220

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

Glu Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val
245 250 255

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

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

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

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

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

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

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

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

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

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

Pro Met Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
 420 425 430

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

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

Ser Pro Gly Lys
 465