

SEQUENCE LISTING

<110> Regeneron Pharmaceuticals, Inc.

<120> Combination of Anti-PD-1 Antibodies and
Bispecific Anti-CD20/Anti-CD3 Antibodies to Treat Cancer

<130> 10221W001

<160> 22

<170> FastSEQ for windows Version 4.0

<210> 1

<211> 117

<212> PRT

<213> Artificial Sequence

<220>

<223> anti-PD-1 HCVR

<400> 1

Glu	Val	Gln	Leu	Leu	Glu	Ser	Gly	Gly	Val	Leu	Val	Gln	Pro	Gly	Gly	1	5	10	15
Ser	Leu	Arg	Leu	Ser	Cys	Ala	Ala	Ser	Gly	Phe	Thr	Phe	Ser	Asn	Phe	20	25	30	
Gly	Met	Thr	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val	35	40	45	
Ser	Gly	Ile	Ser	Gly	Gly	Gly	Arg	Asp	Thr	Tyr	Phe	Ala	Asp	Ser	Val	50	55	60	
Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ser	Lys	Asn	Thr	Leu	Tyr	65	70	75	80
Leu	Gln	Met	Asn	Ser	Leu	Lys	Gly	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys	85	90	95	
Val	Lys	Trp	Gly	Asn	Ile	Tyr	Phe	Asp	Tyr	Trp	Gly	Gln	Gly	Thr	Leu	100	105	110	
Val	Thr	Val	Ser	Ser												115			

<210> 2

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> anti-PD-1 LCVR

<400> 2

Asp	Ile	Gln	Met	Thr	Gln	Ser	Pro	Ser	Ser	Leu	Ser	Ala	Ser	Val	Gly	1	5	10	15
Asp	Ser	Ile	Thr	Ile	Thr	Cys	Arg	Ala	Ser	Leu	Ser	Ile	Asn	Thr	Phe	20	25	30	
Leu	Asn	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Ala	Pro	Asn	Leu	Leu	Ile	35	40	45	
Tyr	Ala	Ala	Ser	Ser	Leu	His	Gly	Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly	50	55	60	
Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Arg	Thr	Leu	Gln	Pro	65	70	75	80
Glu	Asp	Phe	Ala	Thr	Tyr	Tyr	Cys	Gln	Gln	Ser	Ser	Asn	Thr	Pro	Phe	85	90	95	
Thr	Phe	Gly	Pro	Gly	Thr	Val	Val	Asp	Phe	Arg						100	105		

<210> 3

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

<220>
 <223> anti-PD-1 HCDR1

<400> 3
 Gly Phe Thr Phe Ser Asn Phe Gly
 1 5

<210> 4
 <211> 8
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> anti-PD-1 HCDR2

<400> 4
 Ile Ser Gly Gly Gly Arg Asp Thr
 1 5

<210> 5
 <211> 10
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> anti-PD-1 HCDR3

<400> 5
 Val Lys Trp Gly Asn Ile Tyr Phe Asp Tyr
 1 5 10

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

<220>
 <223> anti-PD-1 LCDR1

<400> 6
 Leu Ser Ile Asn Thr Phe
 1 5

<210> 7
 <211> 3
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> anti-PD-1 LCDR2

<400> 7
 Ala Ala Ser
 1

<210> 8
 <211> 9
 <212> PRT
 <213> Artificial Sequence

<220>

<223> anti-PD-1 LCDR3

<400> 8

Gln Gln Ser Ser Asn Thr Pro Phe Thr
 1 5

<210> 9

<211> 444

<212> PRT

<213> Artificial Sequence

<220>

<223> anti-PD-1 HC

aa 1-117: Variable region

aa 118-444: Constant region

<400> 9

Glu Val Gln Leu Leu Glu Ser Gly Gly Val Leu Val Gln Pro Gly Gly
 1 5 10 15
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Phe
 20 25 30
 Gly Met Thr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45
 Ser Gly Ile Ser Gly Gly Gly Arg Asp Thr Tyr Phe Ala Asp Ser Val
 50 55 60
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
 65 70 75 80
 Leu Gln Met Asn Ser Leu Lys Gly Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Val Lys Trp Gly Asn Ile Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu
 100 105 110
 Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
 115 120 125
 Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys
 130 135 140
 Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
 145 150 155 160
 Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
 165 170 175
 Ser Gly Leu Tyr Ser Leu Ser Ser Val Thr Val Pro Ser Ser Ser
 180 185 190
 Leu Gly Thr Lys Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn
 195 200 205
 Thr Lys Val Asp Lys Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro
 210 215 220
 Pro Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe
 225 230 235 240
 Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val
 245 250 255
 Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe
 260 265 270
 Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro
 275 280 285
 Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr
 290 295 300
 Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val
 305 310 315 320
 Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala
 325 330 335
 Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln
 340 345 350
 Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly
 355 360 365
 Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro
 370 375 380

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Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser
 385 390 395 400
 Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu
 405 410 415
 Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His
 420 425 430
 Tyr Thr Gln Lys Ser Leu Ser Leu Ser Leu Gly Lys
 435 440

<210> 10

<211> 214

<212> PRT

<213> Artificial Sequence

<220>

<223> anti-PD-1 LC

aa 1-108: Variable region

aa 109-214: Constant region

<400> 10

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
 1 5 10 15
 Asp Ser Ile Thr Ile Thr Cys Arg Ala Ser Leu Ser Ile Asn Thr Phe
 20 25 30
 Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Asn Leu Leu Ile
 35 40 45
 Tyr Ala Ala Ser Ser Leu His Gly Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60
 Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Arg Thr Leu Gln Pro
 65 70 75 80
 Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Ser Asn Thr Pro Phe
 85 90 95
 Thr Phe Gly Pro Gly Thr Val Val Asp Phe Arg Arg Thr Val Ala Ala
 100 105 110
 Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
 115 120 125
 Thr Ala Ser Val Val Cys Leu Asn Asn Phe Tyr Pro Arg Glu Ala
 130 135 140
 Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
 145 150 155 160
 Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
 165 170 175
 Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
 180 185 190
 Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
 195 200 205
 Phe Asn Arg Gly Glu Cys
 210

<210> 11

<211> 127

<212> PRT

<213> Artificial Sequence

<220>

<223> anti-CD20/anti-CD3 A-HCVR

<400> 11

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1 5 10 15
 Ser Leu Arg Leu Ser Cys Val Ala Ser Gly Phe Thr Phe Asn Asp Tyr
 20 25 30
 Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45
 Ser Val Ile Ser Trp Asn Ser Asp Ser Ile Gly Tyr Ala Asp Ser Val
 50 55 60

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Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
 65 70 75 80
 Leu Gln Met His Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
 85 90 95
 Ala Lys Asp Asn His Tyr Gly Ser Gly Ser Tyr Tyr Tyr Tyr Gln Tyr
 100 105 110
 Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
 115 120 125

<210> 12
 <211> 108
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> anti-CD20/anti-CD3 LCVR

<400> 12
 Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
 1 5 10 15
 Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Asn
 20 25 30
 Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
 35 40 45
 Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
 50 55 60
 Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Ser
 65 70 75 80
 Glu Asp Phe Ala Val Tyr Tyr Cys Gln His Tyr Ile Asn Trp Pro Leu
 85 90 95
 Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg
 100 105

<210> 13
 <211> 123
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> anti-CD20/anti-CD3 B-HCVR

<400> 13
 Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1 5 10 15
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
 20 25 30
 Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45
 Ser Gly Ile Ser Trp Asn Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val
 50 55 60
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Lys Ser Leu Tyr
 65 70 75 80
 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Leu Tyr Tyr Cys
 85 90 95
 Ala Lys Asp Asn Ser Gly Tyr Gly His Tyr Tyr Tyr Gly Met Asp Val
 100 105 110
 Trp Gly Gln Gly Thr Thr Val Thr Val Ala Ser
 115 120

<210> 14
 <211> 8
 <212> PRT
 <213> Artificial Sequence

<220>

<223> anti-CD20/anti-CD3 A-HCDR1

<400> 14

Gly Phe Thr Phe Asn Asp Tyr Ala
1 5

<210> 15

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> anti-CD20/anti-CD3 A-HCDR2

<400> 15

Ile Ser Trp Asn Ser Asp Ser Ile
1 5

<210> 16

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> anti-CD20/anti-CD3 A-HCDR3

<400> 16

Ala Lys Asp Asn His Tyr Gly Ser Gly Ser Tyr Tyr Tyr Tyr Gln Tyr
1 5 10 15
Gly Met Asp Val
20

<210> 17

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> anti-CD20/anti-CD3 LCDR1

<400> 17

Gln Ser Val Ser Ser Asn
1 5

<210> 18

<211> 3

<212> PRT

<213> Artificial Sequence

<220>

<223> anti-CD20/anti-CD3 LCDR2

<400> 18

Gly Ala Ser
1

<210> 19

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> anti-CD20/anti-CD3 LCDR3

<400> 19

Gln His Tyr Ile Asn Trp Pro Leu Thr
1 5

<210> 20

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> anti-CD20/anti-CD3 B-HCDR1

<400> 20

Gly Phe Thr Phe Asp Asp Tyr Thr
1 5

<210> 21

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> anti-CD20/anti-CD3 B-HCDR2

<400> 21

Ile Ser Trp Asn Ser Gly Ser Ile
1 5

<210> 22

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> anti-CD20/anti-CD3 B-HCDR3

<400> 22

Ala Lys Asp Asn Ser Gly Tyr Gly His Tyr Tyr Tyr Gly Met Asp Val
1 5 10 15