

Sequence Listing

<110> BEIJING HANMI PHARMACEUTICAL CO., LTD.

<120> An anti-PD-L1/anti-4-1BB bispecific antibody in the form of an anti-PD-L1/anti-4-1BB natural antibody structure-like heterodimer and its preparation thereof

<130> LZ2120047CN07

<160> 26

<170> SIPOSequenceListing 1.0

<210> 1

<211> 321

<212> DNA

<213> Artificial Sequence

<220>

<223> light chain variable region

<400> 1

gacatccaga tgaccagtc cccttctctc ctgtccgcct ctgtgggcga cagggtgacc	60
atcacctgca aggcctccca ggatgtgcac accgccgtgg cttggattca gcagaagccc	120
ggcaagtccc ccaagctgct gatctactcc gcctccaacc ggtacaccgg cgtgcctagc	180
aggttcagcg gaagcggcag cggcaccgac ttcaccttca ccatctcttc cctgcagcct	240
gaggacatcg ccacctatta ctgccagcag cactacatca cccccctgac cttcggccag	300
ggcaccaagc tggagatcaa g	321

<210> 2

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> light chain variable region

<400> 2

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

<210> 3

<211> 321
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> light chain constant region

<400> 3
 cgtacggtgg ccgccccag cgtcttcatt tttccaccct ctgacgaaca gctgaagtca 60
 gggacagctt ccgtggtctg tctgctgaac aatttttacc ccaggaggagc caaagtgcag 120
 tggaaggtcg ataacgtct gcagagcgga aattctcagg agagtgtgac agaacaggac 180
 tcaaaagatt ccacttatag cctgtctagt accctgacac tgtccaaggc agactacgaa 240
 aagcataaag tgtatgcctg tgaggtcaca catcagggtc tgtcaagccc cgtcactaag 300
 tccttcaacc ggggagaatg c 321

<210> 4
 <211> 107
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> light chain constant region

<400> 4
 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> 5
 <211> 351
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> heavy chain variable region

<400> 5
 gaagtgcagc tgggtgcagtc cggcgccgag gtgaagaagc ctggctcctc cgtgaaggtg 60
 tcctgcaagg cctccggctt caacatcgag gacacctaca tccactgggt gaggcaggct 120
 cccggacagg gactggagt gatgggcagg atcgatcccc ccaacgcaa caccaagtac 180
 gacccaagt tccagggcag ggtgaccatc accgccgata ccagcaccaa caccgcctac 240
 atggagctgt cctccctgag gtccgaggac acagccgtgt actactgtgg caggggactg 300
 ggcgcttgtt ttgcctactg gggacagggc accctggtga ccgtgtcctc c 351

<210> 6
 <211> 117
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> heavy chain variable region

<400> 6
 Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
 1 5 10 15
 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Phe Asn Ile Glu Asp Thr
 20 25 30
 Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45
 Gly Arg Ile Asp Pro Ala Asn Ala Asn Thr Lys Tyr Asp Pro Lys Phe
 50 55 60
 Gln Gly Arg Val Thr Ile Thr Ala Asp Thr Ser Thr Asn 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
 Gly Arg Gly Leu Gly Ala Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu
 100 105 110
 Val Thr Val Ser Ser
 115

<210> 7
 <211> 990
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> heavy chain constant region

<400> 7
 gctagcaciaa aaggaccttc cgtgtttcca ctggcaccct ctagtaagag tacttcagga 60
 ggaaccgcag cactgggatg tctggtgaag gactacttcc cagagcccgt caccgtgtct 120
 tggaacagtg gagcactgac ctccggggtc catacatttc ctgccgtgct gcagtcatcc 180
 ggtctgtata gcctgagctc tgtggtcaca gtcccaagtt catccctggg caccagaca 240
 tacatctgca acgtgaatca caaaccttcc aatactaagg tcgacaagaa agtggaaacc 300
 aagtcctgcg ataagacca cacatgcctt cctgtcctg ctcccgaact gctgggagga 360
 ccctccgtct tcctgttccc ccccaagccc aaagacacac tgatgatcag caggaccctt 420
 gaagtgcctt gcgtggctgt ggacgtgagc cacgaggacc ccgaggtcaa gtttaactgg 480
 tacgtggacg gcgtggaggt ccacaacgcc aagaccaagc ccaggaggag gacgtacaac 540
 agcacctaca gggctcgtgtc cgtgctgacc gtgctccacc aagattggct caacggcaag 600
 gagtataagt gcaaagtcag caacaaggcc ctccccgccc ccatcgagaa aaccatcagc 660
 aaggccaagg gccaaccgcg ggaacctcaa gtgtataccc tccctcccag ccgggatgag 720
 ctgaccaaga accaagtctc cctcttgtgc ctgggtcaagg gattctaccc ttccgacatt 780
 gccgtcgaat gggagagcaa tggccagccc gagaacaact acaagacaac ccccccgctc 840
 ctgcgcagcg acggatcctt ctctctgtac tccaagctca ccgtggacaa gagccggtgg 900
 caacagggca acgtgttctc ctgtagcgtg atgcacgaag ccctccacaa ccactatacc 960
 cagaagagcc tgagcctcag ccccgcaaaa 990

<210> 8

<211> 330
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> heavy chain constant region

<400> 8
 Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
 1 5 10 15
 Ser Thr Ser Gly Gly 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 Gln Thr
 65 70 75 80
 Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
 85 90 95
 Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
 100 105 110
 Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
 115 120 125
 Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
 130 135 140
 Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
 145 150 155 160
 Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
 165 170 175
 Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
 180 185 190
 His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
 195 200 205
 Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
 210 215 220
 Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu
 225 230 235 240
 Leu Thr Lys Asn Gln Val Ser Leu Leu Cys Leu Val Lys Gly Phe Tyr
 245 250 255
 Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
 260 265 270
 Asn Tyr Lys Thr Thr Pro Pro Val Leu Arg Ser Asp Gly Ser Phe Phe
 275 280 285
 Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
 290 295 300
 Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
 305 310 315 320
 Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
 325 330

<210> 9
 <211> 321
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> light chain variable region

<400> 9
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 atcacctgca gagccagcca ggacatcagc aattacctga attggtacca gcagaagcct 120
 ggcaaggtgc ctaagctgct gatctaccac accagcagac tgcacagcgg cgtgcctagc 180
 agattcagcg gcagcggcag cggcaccgac ttcaccctga ccatcagcag cctgcagcct 240
 gaggacgtgg ccacctacta ctgccagcag ggccacaccc tgcctagaac cttcggcggc 300
 ggcaccaagg tggagatcaa g 321

<210> 10
 <211> 107
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> light 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 Val Pro Lys Leu Leu Ile
 35 40 45
 Tyr His Thr Ser Arg Leu His 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 Val Ala Thr Tyr Tyr Cys Gln Gln Gly His Thr Leu Pro Arg
 85 90 95
 Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 100 105

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

<220>
 <223> heavy chain variable region

<400> 11
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 agctgcaagg ccagcggcta caccctcacc agctactgga tcaattgggt gagacaggct 120
 ccgggccaag ggctggagt gatgggcaat atctacccta gcgacagcta caccaattac 180
 aatcagaagt tcaaggacag agtgaccatc accgccgaca agagcaccag caccgcctac 240
 atggagctga gcagcctgag aagcgaggac accgccgtgt actactgcgc cagactgtac 300
 tacggcagca gccctttcga ctactgggga caaggcacca ccgtgaccgt gagcagc 357

<210> 12
 <211> 119
 <212> PRT

<213> Artificial Sequence

<220>

<223> heavy chain variable region

<400> 12

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

<210> 13

<211> 990

<212> DNA

<213> Artificial Sequence

<220>

<223> heavy chain constant region

<400> 13

gctagcacia	aaggaccttc	cgtgtttcca	ctggcaccct	ctagtaagag	tacttcagga	60
ggaaccgcag	cactgggatg	tctgggtgaag	gactacttcc	cagagcccgt	caccgtgtct	120
tggaacagtg	gagcactgac	ctccggggtc	catacatttc	ctgccgtgct	gcagtcaccc	180
ggctctgtata	gcctgagctc	tgtggtcaca	gtcccaagtt	catccctggg	caccagaca	240
tacatctgca	acgtgaatca	caaaccttcc	aatactaagg	tcgacaagaa	agtggaaccc	300
aagtcctgcg	ataagaccca	cacatgcctt	ccctgtcctg	ctcccgaact	gctgggagga	360
ccctccgtct	tcctgttccc	ccccaaagcc	aaagacacac	tgatgatcag	caggaccctt	420
gaagtgcact	gcgtggtcgt	ggacgtgagc	cacgaggacc	ccgaggtcaa	gtttaactgg	480
tacgtggacg	gcgtggaggt	ccacaacgcc	aagaccaagc	ccaggagga	gcagtacgcc	540
agcacctaca	gggtggtcag	cgtgctgacc	gtgctgcacc	aggattggct	caacggcaag	600
gagtacaagt	gcaaagtctc	caacaaggcc	ctgccccgcc	ccatcgagaa	gaccatctcc	660
aaggctaagg	gacagcccag	ggagccccc	gtgtacaccg	agcctcccag	ccgggatgag	720
ctgaccaaga	accaagtctc	cctcacctgc	ctgggtcaagg	gattctaccc	ttccgacatt	780
gccgtcgaat	gggagagcaa	tggccagccc	gagaacaact	acaagacaac	cccccccgctc	840
ctggatagcg	acggatcctt	cttctgtctc	tccgtgtctc	ccgtcgacaa	gagcagatgg	900
cagcagggca	acgtgttcag	ctgtagcgtg	atgcacgagg	ccctgcacaa	ccactacacc	960
cagaagagcc	tgtccctcag	ccccggcaag				990

<210> 14

<211> 330

<212> PRT

<213> Artificial Sequence

<220>

<223> heavy chain constant region

<400> 14

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

<210> 15

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> PD-L1 HCDR1

<400> 15
Gly Phe Asn Ile Glu Asp Thr Tyr Ile His
1 5 10

<210> 16
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> PD-L1 HCDR2

<400> 16
Arg Ile Asp Pro Ala Asn Ala Asn Thr Lys Tyr Asp Pro Lys Phe Gln
1 5 10 15
Gly

<210> 17
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> PD-L1 HCDR3

<400> 17
Gly Leu Gly Ala Trp Phe Ala Tyr
1 5

<210> 18
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> PD-L1 LCDR1

<400> 18
Lys Ala Ser Gln Asp Val His Thr Ala Val Ala
1 5 10

<210> 19
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> PD-L1 LCDR2

<400> 19
Ser Ala Ser Asn Arg Tyr Thr
1 5

<210> 20
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> PD-L1 LCDR3

<400> 20
Gln Gln His Tyr Ile Thr Pro Leu Thr
1 5

<210> 21
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> 4-1BB HCDR1

<400> 21
Gly Tyr Thr Phe Thr Ser Tyr Trp Ile Asn
1 5 10

<210> 22
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> 4-1BB HCDR2

<400> 22
Asn Ile Tyr Pro Ser Asp Ser Tyr Thr Asn Tyr Asn Gln Lys Phe Lys
1 5 10 15
Asp

<210> 23
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> 4-1BB HCDR3

<400> 23
Leu Tyr Tyr Gly Ser Ser Pro Phe Asp Tyr
1 5 10

<210> 24
<211> 11

<212> PRT
<213> Artificial Sequence

<220>
<223> 4-1BB LCDR1

<400> 24
Arg Ala Ser Gln Asp Ile Ser Asn Tyr Leu Asn
1 5 10

<210> 25
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> 4-1BB LCDR2

<400> 25
His Thr Ser Arg Leu His Ser
1 5

<210> 26
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> 4-1BB LCDR3

<400> 26
Gln Gln Gly His Thr Leu Pro Arg Thr
1 5