

SEQUENCE LISTING

<110> BeiGene, Ltd.

<120> Anti-TIGIT antibodies and their use as therapeutics and diagnostics

<130> F18W0462

<160> 24

<170> PatentIn version 3.5

<210> 1

<211> 244

<212> PRT

<213> Homo sapiens

<400> 1

Met Arg Trp Cys Leu Leu Leu Ile Trp Ala Gln Gly Leu Arg Gln Ala
1 5 10 15

Pro Leu Ala Ser Gly Met Met Thr Gly Thr Ile Glu Thr Thr Gly Asn
20 25 30

Ile Ser Ala Glu Lys Gly Gly Ser Ile Ile Leu Gln Cys His Leu Ser
35 40 45

Ser Thr Thr Ala Gln Val Thr Gln Val Asn Trp Glu Gln Gln Asp Gln
50 55 60

Leu Leu Ala Ile Cys Asn Ala Asp Leu Gly Trp His Ile Ser Pro Ser
65 70 75 80

Phe Lys Asp Arg Val Ala Pro Gly Pro Gly Leu Gly Leu Thr Leu Gln
85 90 95

Ser Leu Thr Val Asn Asp Thr Gly Glu Tyr Phe Cys Ile Tyr His Thr
100 105 110

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

Ser Ser Val Ala Glu His Gly Ala Arg Phe Gln Ile Pro Leu Leu Gly
130 135 140

Ala Met Ala Ala Thr Leu Val Val Ile Cys Thr Ala Val Ile Val Val
145 150 155 160

Val Ala Leu Thr Arg Lys Lys Lys Ala Leu Arg Ile His Ser Val Glu
165 170 175

Gly Asp Leu Arg Arg Lys Ser Ala Gly Gln Glu Glu Trp Ser Pro Ser
180 185 190

Ala Pro Ser Pro Pro Gly Ser Cys Val Gln Ala Glu Ala Ala Pro Ala
195 200 205

Gly Leu Cys Gly Glu Gln Arg Gly Glu Asp Cys Ala Glu Leu His Asp
210 215 220

Tyr Phe Asn Val Leu Ser Tyr Arg Ser Leu Gly Asn Cys Ser Phe Phe
225 230 235 240

Thr Glu Thr Gly

<210> 2
<211> 120
<212> PRT
<213> Homo sapiens

<400> 2

Met Met Thr Gly Thr Ile Glu Thr Thr Gly Asn Ile Ser Ala Glu Lys
1 5 10 15

Gly Gly Ser Ile Ile Leu Gln Cys His Leu Ser Ser Thr Thr Ala Gln
20 25 30

Val Thr Gln Val Asn Trp Glu Gln Gln Asp Gln Leu Leu Ala Ile Cys
35 40 45

Asn Ala Asp Leu Gly Trp His Ile Ser Pro Ser Phe Lys Asp Arg Val
50 55 60

Ala Pro Gly Pro Gly Leu Gly Leu Thr Leu Gln Ser Leu Thr Val Asn
65 70 75 80

Asp Thr Gly Glu Tyr Phe Cys Ile Tyr His Thr Tyr Pro Asp Gly Thr
85 90 95

Tyr Thr Gly Arg Ile Phe Leu Glu Val Leu Glu Ser Ser Val Ala Glu

100

105

110

His Gly Ala Arg Phe Gln Ile Pro
 115 120

<210> 3
 <211> 5
 <212> PRT
 <213> Mus musculus

<400> 3

Asp Tyr Tyr Met Tyr
 1 5

<210> 4
 <211> 17
 <212> PRT
 <213> Mus musculus

<400> 4

Tyr Ile Thr Lys Gly Gly Gly Ser Thr Tyr Tyr Pro Asp Thr Val Lys
 1 5 10 15

Gly

<210> 5
 <211> 10
 <212> PRT
 <213> Mus musculus

<400> 5

Gln Thr Asn Tyr Asp Phe Thr Met Asp Tyr
 1 5 10

<210> 6
 <211> 11
 <212> PRT
 <213> Mus musculus

<400> 6

Lys Ala Ser Gln Asp Val Gly Thr Ser Val Ala
 1 5 10

<210> 7
 <211> 7
 <212> PRT

<213> Mus musculus

<400> 7

Trp Ala Ser Ala Arg His Thr
1 5

<210> 8

<211> 9

<212> PRT

<213> Mus musculus

<400> 8

Gln Gln Tyr Ser Ser Tyr Pro Leu Thr
1 5

<210> 9

<211> 119

<212> PRT

<213> Mus musculus

<400> 9

Glu Val Lys Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Thr Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30

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

Ala Tyr Ile Thr Lys Gly Gly Gly Ser Thr Tyr Tyr Pro Asp Thr Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Val Ser Arg Leu Lys Ser Glu Asp Thr Ala Ile Tyr Tyr Cys
85 90 95

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

Thr Ser Val Thr Val Ser Ser
115

<210> 10
 <211> 357
 <212> DNA
 <213> Mus musculus

<400> 10
 gaagtgaagc tgggtggagtc tgggggaggc ttagtgcagc ctggaggggc cctgaaactc 60
 tcctgtgcaa cctctggatt cactttcagt gactattaca tgtattggat tcggcagact 120
 ccagagaaga ggctggagtg ggtcgcatac attactaagg gtgggtggtag cacctattat 180
 ccagacactg taaagggccg attcaccatc tccagagaca atgccaagaa caccctgtac 240
 ctgcaagtga gccgtctgaa gtctgaggac acagccatat attactgtgc aagacagact 300
 aactacgact ttactatgga ctactggggc caaggaacct cagtcacggc ctcctca 357

<210> 11
 <211> 107
 <212> PRT
 <213> Mus musculus

<400> 11

Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser Thr Ser Val Gly
 1 5 10 15

Asp Arg Val Ser Ile Ile Cys Lys Ala Ser Gln Asp Val Gly Thr Ser
 20 25 30

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

Tyr Trp Ala Ser Ala Arg His Thr Gly Val Pro Asp Arg Phe Thr Gly
 50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Asn Val Gln Ser
 65 70 75 80

Glu Asp Leu Ala Asp Tyr Phe Cys Gln Gln Tyr Ser Ser Tyr Pro Leu
 85 90 95

Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
 100 105

<210> 12
 <211> 321
 <212> DNA
 <213> Mus musculus

<400> 12
gacattgtga tgacccagtc tcacaaattc atgtccacat cagtaggaga cagggtcagc 60
atcatctgca aggccagtca ggatgtgggt acttctgtag cctgggtatca acagaaacca 120
gggcaatctc ctaacctact gatttactgg gcatccgccc ggcacactgg agtccttgat 180
cgcttcacag gcagtggatc tgggacagat ttcactctca ccattagcaa tgtacagtct 240
gaagacttgg cagattatatt ctgtcagcaa tatagcagtt atcctctcac gttcgggtgct 300
gggaccaagc tggagctgaa a 321

<210> 13
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> hu1217-1-1 HCDR2

<400> 13

Tyr Ile Thr Lys Gly Gly Gly Ser Thr Tyr Tyr Pro Asp Ser Val Lys
1 5 10 15

Gly

<210> 14
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> hu1217-1-1 VH pro

<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 Thr Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30

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

Ala Tyr Ile Thr Lys Gly Gly Gly Ser Thr Tyr Tyr Pro Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr
65 70 75 80

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

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

Thr Leu Val Thr Val Ser Ser
115

<210> 15
<211> 357
<212> DNA
<213> Artificial Sequence

<220>
<223> hu1217-1-1 VH DNA

<400> 15
gaggtgcagc tggtggagag cggaggagga ctggtgcagc ctggaggcag cctgagactg 60
agctgcgcca ccagcggcctt caccttctcc gactactaca tgtactggat caggcaggcc 120
cctggcaaag gcctggagtg ggtggcctac atcaccaagg gcggcggcag cacctactac 180
cccgatagcg tgaagggcag gttcaccatc agcagggaca acgccaagaa caccctgtac 240
ctgcagatga acagcctgag ggccgaggat accgccgtgt actactgcgc caggcagacc 300
aactacgact tcaccatgga ctactggggc cagggcacac tggtgaccgt gagcagc 357

<210> 16
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> hu1217-1-1 VK pro

<400> 16

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 Lys Ala Ser Gln Asp Val Gly Thr Ser
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile

35

40

45

Tyr Trp Ala Ser Ala Arg His Thr Gly Val 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 Gln Tyr Ser Ser Tyr Pro Leu
85 90 95

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

<210> 17
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> hul217-1-1 VK DNA

<400> 17
gagatcgtga tgaccagag ccctgccaca ctgagcgtga gccctggcga gagagccacc 60
ctgagctgca aggccagcca ggatgtgggc accagcgtgg cctggtacca gcagaaaccc 120
ggccaggctc ccaggctgct gatctactgg gccagcgcca gacacacagg cgtgcctgcc 180
agatttagcg gcagcggcag cggcaccgag tttaccctga ccatcagcag cctgcagtcc 240
gaggacttcg ccgtgtacta ctgccagcag tacagcagct accccctgac attcggcggc 300
ggcaccaagg tggagatcaa g 321

<210> 18
<211> 329
<212> PRT
<213> Artificial Sequence

<220>
<223> IgG1mf

<400> 18

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 Pro Ala Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
115 120 125
Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
130 135 140
Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
145 150 155 160
Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
165 170 175
Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
180 185 190
Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
195 200 205
Ala Leu Ala Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
210 215 220
Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu
225 230 235 240
Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
245 250 255
Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn

260 265 270
 Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
 275 280 285
 Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
 290 295 300
 Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
 305 310 315 320
 Lys Ser Leu Ser Leu Ser Pro Gly Lys
 325
 <210> 19
 <211> 119
 <212> PRT
 <213> Artificial Sequence
 <220>
 <223> hul217-2-2 VH pro
 <400> 19
 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 Ser Asp Tyr
 20 25 30
 Tyr Met Tyr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45
 Ala Tyr Ile Thr Lys Gly Gly Gly Ser Thr Tyr Tyr Pro Asp Ser Val
 50 55 60
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr
 65 70 75 80
 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Ala Arg Gln Thr Asn Tyr Asp Phe Thr Met Asp Tyr Trp Gly Gln Gly
 100 105 110
 Thr Leu Val Thr Val Ser Ser

<210> 20
 <211> 357
 <212> DNA
 <213> Artificial Sequence

<220>

<223> hu1217-2-2 VH DNA

<400> 20
 gaggtgcagc tgggtggagag cggaggagga ctgggtgcagc ctggaggcag cctgagactg 60
 agctgcgccg ccagcgggctt caccttctcc gactactaca tgtactgggt caggcaggcc 120
 cctggcaaag gcctggagtg ggtggcctac atcaccaagg gcggcggcag cacctactac 180
 cccgatagcg tgaagggcag gttcaccatc agcagggaca acgccaagaa caccctgtac 240
 ctgcagatga acagcctgag ggccgaggat accgccgtgt actactgcgc caggcagacc 300
 aactacgact tcaccatgga ctactggggc cagggcacac tggtgaccgt gagcagc 357

<210> 21
 <211> 107
 <212> PRT
 <213> Artificial Sequence

<220>

<223> hu1217-2-2 VK pro

<400> 21

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 Lys Ala Ser Gln Asp Val Gly Thr Ser
 20 25 30

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

Tyr Trp Ala Ser Ala Arg His 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 Gln Tyr Ser Ser Tyr Pro Leu
 85 90 95

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

<210> 22
 <211> 321
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> hu1217-2-2 VK DNA

<400> 22
 gagatcgtga tgaccagag ccctgccaca ctgagcgtga gccctggcga gagagccacc 60
 ctgagctgca aggccagcca ggatgtgggc accagcgtgg cctggtacca gcagaaaccc 120
 ggccaggctc ccaggctgct gatctactgg gccagcgcca gacacacagg catccctgcc 180
 agatttagcg gcagcggcag cggcaccgag ttaccctga ccatcagcag cctgcagtcc 240
 gaggacttcg ccgtgtacta ctgccagcag tacagcagct accccctgac attcggcggc 300
 ggcaccaagg tggagatcaa g 321

<210> 23
 <211> 119
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> murinized 10A7 VH pro

<400> 23

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
 1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Phe
 20 25 30

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

Ala Tyr Ile Arg Ser Gly Ser Gly Ile Val Phe Tyr Ala Asp Thr Val
 50 55 60

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

Leu Gln Met Thr Ser Leu Arg Ser Glu Asp Thr Ala Met Tyr Tyr Cys

85

90

95

Ala Arg Arg Pro Leu Gly His Asn Thr Phe Asp Ser Trp Gly Gln Gly
 100 105 110

Thr Leu Val Thr Val Ser Ser
 115

<210> 24

<211> 113

<212> PRT

<213> Artificial Sequence

<220>

<223> murinized 10A7 VK pro

<400> 24

Asp Ile Val Met Ser Gln Ser Pro Ser Ser Leu Ala Val Ser Ala Gly
 1 5 10 15

Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Tyr Tyr Ser
 20 25 30

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

Ser Pro Lys Leu Leu Ile Tyr Tyr Ala Ser Ile Arg Phe Ser Gly Val
 50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
 65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln
 85 90 95

Gly Ile Asn Asn Pro Leu Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
 100 105 110

Lys