

## Sequence Listing

<110> SHENZHEN PREGENE BIOPHARMA CO. LTD.

<120> BCMA CHIMERIC ANTIGEN RECEPTOR BASED ON SINGLE DOMAIN ANTIBODY AND USE THEREOF

<130> 0087-PA-003SG

<160> 16

<170> PatentIn version 3.5

<210> 1

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> amino acid sequence of HCDR1 of BCMA binding domain

<400> 1

Thr Tyr Phe Met Ala  
1 5

<210> 2

<211> 18

<212> PRT

<213> Artificial Sequence

<220>

<223> amino acid sequence of HCDR2 of BCMA binding domain

<400> 2

Gly Gly Ile Arg Trp Ser Asp Gly Val Pro His Tyr Ala Asp Ser Val  
1 5 10 15

Lys Gly

<210> 3

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> amino acid sequence of HCDR3 of BCMA binding domain

<400> 3

Cys Ala Ser Arg Gly Ile Ala Asp Gly Ser Asp Phe Gly Ser  
1 5 10

<210> 4

<211> 120

<212> PRT

<213> Artificial Sequence

<220>

<223> amino acid sequence of BCMA binding domain

<400> 4

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

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Arg Thr Phe Ser Thr Tyr  
20 25 30

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

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

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

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

Ala Ser Arg Gly Ile Ala Asp Gly Ser Asp Phe Gly Ser Tyr Gly Gln  
100 105 110

Gly Thr Gln Val Thr Val Ser Ser  
115 120

<210> 5  
<211> 21  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> amino acid sequence of transmembrane domain

<400> 5

Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu  
1 5 10 15

Ser Leu Val Ile Thr  
20

<210> 6  
<211> 49  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> amino acid sequence of hinge region

<400> 6

Pro Ala Lys Pro Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala  
1 5 10 15

Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg  
20 25 30

Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys  
35 40 45

Asp

<210> 7  
<211> 42  
<212> PRT  
<213> Artificial Sequence

<220>

<223> amino acid sequence of co-stimulatory domain

<400> 7

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met  
1 5 10 15

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe  
20 25 30

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu  
35 40

<210> 8

<211> 114

<212> PRT

<213> Artificial Sequence

<220>

<223> amino acid sequence of intracellular signaling domain

<400> 8

Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln  
1 5 10 15

Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu  
20 25 30

Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly  
35 40 45

Lys Pro Gln Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu  
50 55 60

Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly  
65 70 75 80

Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser  
85 90 95

Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro  
100 105 110

Pro Arg

<210> 9  
<211> 21  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> amino acid sequence of leader sequence

<400> 9

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu  
1 5 10 15

His Ala Ala Arg Pro  
20

<210> 10  
<211> 369  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> amino acid sequence of a complete CARF including a leader sequencef0

<400> 10

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu  
1 5 10 15

His Ala Ala Arg Pro Glu Val Gln Leu Gln Ala Ser Gly Gly Gly Leu  
20 25 30

Ala Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Arg  
35 40 45

Thr Phe Ser Thr Tyr Phe Met Ala Trp Phe Arg Gln Pro Pro Gly Lys

50

55

60

Gly Leu Glu Tyr Val Gly Gly Ile Arg Trp Ser Asp Gly Val Pro His  
 65 70 75 80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala  
 85 90 95

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

Ala Val Tyr Phe Cys Ala Ser Arg Gly Ile Ala Asp Gly Ser Asp Phe  
 115 120 125

Gly Ser Tyr Gly Gln Gly Thr Gln Val Thr Val Ser Ser Pro Ala Lys  
 130 135 140

Pro Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile  
 145 150 155 160

Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala  
 165 170 175

Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr  
 180 185 190

Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu  
 195 200 205

Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile  
 210 215 220

Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp  
 225 230 235 240

Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu  
 245 250 255

Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly  
260 265 270

Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr  
275 280 285

Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys  
290 295 300

Pro Gln Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln  
305 310 315 320

Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu  
325 330 335

Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr  
340 345 350

Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro  
355 360 365

Arg

<210> 11

<211> 348

<212> PRT

<213> Artificial Sequence

<220>

<223> amino acid sequence of a complete CARF not including a leader sequencef0

<400> 11

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

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Arg Thr Phe Ser Thr Tyr  
20 25 30

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

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

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

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

Ala Ser Arg Gly Ile Ala Asp Gly Ser Asp Phe Gly Ser Tyr Gly Gln  
100 105 110

Gly Thr Gln Val Thr Val Ser Ser Pro Ala Lys Pro Thr Thr Thr Pro  
115 120 125

Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu  
130 135 140

Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His  
145 150 155 160

Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu  
165 170 175

Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr  
180 185 190

Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe  
195 200 205

Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg  
210 215 220

Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser

225 230 235 240

Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu Tyr  
245 250 255

Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys  
260 265 270

Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Gln Arg Arg Lys  
275 280 285

Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala  
290 295 300

Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys  
305 310 315 320

Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr  
325 330 335

Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg  
340 345

<210> 12  
<211> 1110  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> nucleic sequence encoding CARF including a leader sequence

<400> 12  
atggccttac cagtgaccgc cttgctcctg ccgctggcct tgctgctcca cgccgccagg 60  
ccggaagtcc aactccaggc ttccgggtggc ggtctggcac agcctggagg gtccctgcgg 120  
ctctcctgcg cagcaagtgg caggactttc agtacctact ttatggcctg gttcagacag 180  
ccacctggca aaggcctcga atacgtcgga gggattaggt ggtctgacgg tgtccctcac 240  
tacgtgaca gtgtgaaggg tcggttcacc attagcagag acaacgctaa gaatacagtg 300

|                                                                    |      |
|--------------------------------------------------------------------|------|
| tacctgcaaa tgaactcact gagagctgag gatactgctg tgtacttctg cgcattctcgc | 360  |
| ggaatcgctg acgggtcaga ctttggctcc tatggacagg gcacccagggt gactgtgagt | 420  |
| tccccagcga agcccaccac gacgccagcg ccgcgaccac caacaccggc gcccaccatc  | 480  |
| gcgtcgcagc ccctgtccct gcgcccagag gcgtgccggc cagcggcggg gggcgcagtg  | 540  |
| cacacgaggg ggctggactt cgcctgtgat atctacatct gggcgccctt ggccgggact  | 600  |
| tgtgggggtcc ttctcctgtc actgggtatc accctttact gcaaacgggg cagaaagaaa | 660  |
| ctcctgtata tattcaaaca accatttatg agaccagtac aaactactca agaggaagat  | 720  |
| ggctgtagct gccgatttcc agaagaagaa gaaggaggat gtgaactgag agtgaagttc  | 780  |
| agcaggagcg cagacgcccc cgcgtaccag cagggccaga accagctcta taacgagctc  | 840  |
| aatctaggac gaagagagga gtacgatgtt ttggacaaga gacgtggccg ggaccctgag  | 900  |
| atgggggggaa agccgcagag aaggaagaac cctcaggaag gcctgtacaa tgaactgcag | 960  |
| aaagataaga tggcggaggc ctacagtgag attgggatga aaggcgagcg ccggaggggc  | 1020 |
| aaggggcacg atggccttta ccagggtctc agtacagcca ccaaggacac ctacgacgcc  | 1080 |
| cttcacatgc aggccctgcc ccctcgctaa                                   | 1110 |

<210> 13  
 <211> 1047  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> nucleic sequence encoding CARF not including a leader sequencef0

|                                                                     |     |
|---------------------------------------------------------------------|-----|
| <400> 13                                                            |     |
| gaagtccaac tccaggcttc cgggtggcgggt ctggcacagc ctggagggtc cctgcggctc | 60  |
| tcctgcgcag caagtggcag gactttcagt acctacttta tggcctgggtt cagacagcca  | 120 |
| cctggcaaag gcctcgaata cgtcggagggt attagggtggt ctgacggtgt ccctcactac | 180 |
| gctgacagtg tgaagggtcg gttcaccatt agcagagaca acgctaagaa tacagtgtac   | 240 |
| ctgcaaatga actcactgag agctgaggat actgctgtgt acttctgcgc atctcgcgga   | 300 |
| atcgctgacg ggtcagactt tggctcctat ggacagggca cccagggtgac tgtgagttcc  | 360 |

|                                                                     |      |
|---------------------------------------------------------------------|------|
| ccagcgaagc ccaccacgac gccagcgccg cgaccacca caccggcgcc caccatcgcg    | 420  |
| tcgcagcccc tgtccctgcg cccagaggcg tgccggccag cggcgggggg cgcagtgcac   | 480  |
| acgagggggc tggacttcgc ctgtgatatc tacatctggg cgcccttggc cgggacttgt   | 540  |
| ggggtccttc tcctgtcact ggttatcacc ctttactgca aacggggcag aaagaaactc   | 600  |
| ctgtatatat tcaaacaacc atttatgaga ccagtacaaa ctactcaaga ggaagatggc   | 660  |
| tgtagctgcc gatttccaga agaagaagaa ggaggatgtg aactgagagt gaagttcagc   | 720  |
| aggagcgcag acgccccgc gtaccagcag ggccagaacc agctctataa cgagctcaat    | 780  |
| ctaggacgaa gagaggagta cgatgttttg gacaagagac gtggccggga ccctgagatg   | 840  |
| gggggaaaagc cgcagagaag gaagaacctt caggaaaggcc tgtacaatga actgcagaaa | 900  |
| gataagatgg cggaggccta cagtgagatt gggatgaaag gcgagcgccg gaggggcaag   | 960  |
| gggcacgatg gcctttacca gggctctcagt acagccacca aggacaccta cgacgccctt  | 1020 |
| cacatgcagg ccctgcccc tcgctaa                                        | 1047 |

<210> 14

<211> 553

<212> DNA

<213> Artificial Sequence

<220>

<223> nucleic sequence of EF1 promoter

<400> 14

|                                                                   |     |
|-------------------------------------------------------------------|-----|
| aaggatctgc gatcgctccg gtgcccgtca gtgggcagag cgcacatcg cccacagtccc | 60  |
| cgagaagttg gggggagggg tcggcaattg aacgggtgcc tagagaagg ggcgcggggt  | 120 |
| aaactgggaa agtgatgtcg tgtactggct ccgccttttt cccgagggtg ggggagaacc | 180 |
| gtatataagt gcagtagtcg ccgtgaacgt tctttttcgc aacgggtttg ccgccagaac | 240 |
| acagctgaag cttcgagggg ctcgcatctc tccttcacgc gcccgccgcc ctacctgagg | 300 |
| ccgccatcca cgccggttga gtcgcgttct gccgcctccc gcctgtggtg cctcctgaac | 360 |
| tgcgtccgcc gtctaggtaa gtttaaagct caggctgaga ccgggccttt gtccggcgct | 420 |
| cccttgagag ctacctagac tcagccggct ctccacgctt tgccctgacc tgcttgctca | 480 |

|                                                                   |     |
|-------------------------------------------------------------------|-----|
| actctacgtc tttgtttcgt tttctgttct gcgccgttac agatccaagc tgtgaccggc | 540 |
| gcctacgcta gac                                                    | 553 |

<210> 15  
 <211> 423  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> nucleic sequence of BCMA sdAb I

|                                                                    |     |
|--------------------------------------------------------------------|-----|
| <400> 15                                                           |     |
| atggccttac cagtgaccgc cttgctcctg ccgctggcct tgctgctcca cgccgccagg  | 60  |
| ccggaagtcc aactccaggc ttccgggtggc ggtctggcac agcctggagg gtccctgcgg | 120 |
| ctctcctgcg cagcaagtgg caggactttc agtacctact ttatggcctg gttcagacag  | 180 |
| ccacctggca aaggcctcga atacgtcgga gggattaggt ggtctgacgg tgtccctcac  | 240 |
| tacgtgaca gtgtgaaggg tcggttcacc attagcagag acaacgctaa gaatacagtg   | 300 |
| tacctgcaaa tgaactcact gagagctgag gatactgctg tgtacttctg cgcatctcgc  | 360 |
| ggaatcgctg acgggtcaga ctttggctcc tatggacagg gcacccagggt gactgtgagt | 420 |
| tcc                                                                | 423 |

<210> 16  
 <211> 687  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> second generation CAR structure gene

|                                                                   |     |
|-------------------------------------------------------------------|-----|
| <400> 16                                                          |     |
| ccagcgaagc ccaccacgac gccagcgccg cgaccacca caccggcgcc caccatcgcg  | 60  |
| tcgcagcccc tgtccctgcg ccagaggcg tgccggccag cggcgggggg cgcagtgcac  | 120 |
| acgagggggc tggacttcgc ctgtgatatc tacatctggg cgcccttggc cgggacttgt | 180 |
| ggggtccttc tcctgtcact gggtatcacc ctttactgca aacggggcag aaagaaactc | 240 |
| ctgtatatat tcaaacaacc atttatgaga ccagtacaaa ctactcaaga ggaagatggc | 300 |

|                                                                    |     |
|--------------------------------------------------------------------|-----|
| tgtagctgcc gatttccaga agaagaagaa ggaggatgtg aactgagagt gaagttcagc  | 360 |
| aggagcgcag acgccccgc gtaccagcag ggccagaacc agctctataa cgagctcaat   | 420 |
| ctaggacgaa gagaggagta cgatgttttg gacaagagac gtggccggga ccctgagatg  | 480 |
| gggggaaagc cgcagagaag gaagaaccct caggaaggcc tgtacaatga actgcagaaa  | 540 |
| gataagatgg cggaggccta cagtgagatt gggatgaaag gcgagcgccg gaggggcaag  | 600 |
| gggcacgatg gcctttacca gggctctcagt acagccacca aggacaccta cgacgccctt | 660 |
| cacatgcagg ccctgcccc tcgctaa                                       | 687 |