

The presently disclosed subject matter further provides use of an effective amount of the immunoresponsive cell as described herein, in the manufacture of a medicament for reducing tumor burden in a subject.

5 The presently disclosed subject matter further provides use of an effective amount of the immunoresponsive cell as described herein, in the manufacture of a medicament for increasing or lengthening survival of a subject having neoplasia.

The presently disclosed subject matter further provides a chimeric antigen receptor (CAR), comprising an extracellular antigen-binding domain that binds to a G-protein coupled receptor, a transmembrane domain and an intracellular domain,  
10 wherein the extracellular antigen-binding domain comprises:

(a) a heavy chain variable region comprising the CDR1, CDR2 and CDR3 of the heavy chain variable region set forth in an amino acid sequence selected from the group consisting of SEQ ID NOS: 1, 5, 9, 13, 17, 21, 25, 29, 33, 37, 41, 45, 49, 53, 57, 61, 65, 69, 73, 77, 81, 85, 89, 93, 302, 314, 326, 338, 350, 362, 374, and 386; and

15 (a) a light chain variable region comprising the CDR1, CDR2 and CDR3 of the light chain variable region set forth in an amino acid sequence selected from the group consisting of SEQ ID NOS: 2, 6, 10, 14, 18, 22, 26, 30, 34, 38, 42, 46, 50, 54, 58, 62, 66, 70, 74, 78, 82, 86, 90, 94, 303, 315, 327, 339, 351, 363, 375, and 387.

The presently disclosed subject matter further provides a chimeric antigen receptor (CAR), comprising an extracellular antigen-binding domain that binds to a G-protein coupled receptor, a transmembrane domain and an intracellular domain,  
20 wherein the extracellular antigen-binding domain comprises:

(a) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 124, 125 and 126, and a light chain variable region comprising  
25 the amino acid sequences set forth in SEQ ID NOS: 127, 128 and 129;

(b) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 130, 131 and 132, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 133, 134 and 135;

(c) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 136, 137 and 138, and a light chain variable region comprising  
30 the amino acid sequences set forth in SEQ ID NOS: 139, 140 and 141;

(d) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 142, 143 and 144, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 145, 146 and 147;

(e) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 148, 149 and 150, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 151, 152 and 153;

5 (f) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 154, 155 and 156, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 157, 158 and 159;

(g) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 160, 161 and 162, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 163, 164 and 165;

10 (h) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 166, 167 and 168, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 169, 170 and 171;

(i) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 172, 173 and 174, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 175, 176 and 177;

(j) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 178, 179 and 180, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 181, 182 and 183;

20 (k) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 184, 185 and 186, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 187, 188 and 189;

(l) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 190, 191 and 192, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 193, 194 and 195;

25 (m) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 196, 197 and 198, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 199, 200 and 201;

(n) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 202, 203 and 204, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 205, 206 and 207;

30 (o) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 208, 209 and 210, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 211, 212 and 213;

(p) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 214, 215 and 216, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 217, 218 and 219;

5 (q) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 220, 221 and 222, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 223, 224 and 225;

(r) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 226, 227 and 228, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 229, 230 and 231;

10 (s) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 232, 233 and 234, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 235, 236 and 237;

(t) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 238, 239 and 240, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 241, 242 and 243;

15 (u) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 244, 245 and 246, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 247, 248 and 249;

(v) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 250, 251 and 252, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 253, 254 and 255;

(w) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 256, 257 and 258, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 259, 260 and 261;

25 (x) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 262, 263 and 264, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 265, 266 and 267;

(y) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 304, 305 and 306, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 307, 308 and 309;

30 (z) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 316, 317 and 318, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 319, 320 and 321;

(aa) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 328, 329 and 330, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 331, 332 and 333;

5 (ab) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 340, 341 and 342, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 343, 344 and 345;

(ac) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 352, 353 and 354, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 355, 356 and 357;

10 (ad) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 364, 365 and 366, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 367, 368 and 369;

(ae) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 376, 377 and 378, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 379, 380 and 381; or

15 (af) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 388, 389 and 390, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 391, 392 and 393.

The presently disclosed subject matter further provides an immunoresponsive cell comprising the CAR as described herein.

The presently disclosed subject matter further provides a nucleic acid molecule encoding the chimeric antigen receptor (CAR) as described herein.

The presently disclosed subject matter further provides a method for producing an immunoresponsive cell that binds to a G-protein coupled receptor, comprising introducing into the immunoresponsive cell a nucleic acid molecule as described herein.

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set forth in SEQ ID NO: 308, and a V<sub>L</sub> CDR3 comprising amino acids having the sequence set forth in SEQ ID NO: 309.

**Table 25**

| Antigen             | A GPRC5D polypeptide having the amino acid sequence of SEQ ID NO:97                                                                                                                                                                                                                                                                                                                                                                                 |                           |                             |
|---------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------|-----------------------------|
| CDRs                | 1                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 2                         | 3                           |
| V <sub>H</sub>      | GFTFGDYG [SEQ ID NO: 304]                                                                                                                                                                                                                                                                                                                                                                                                                           | INWNGGST [SEQ ID NO: 305] | ARSKQGY [SEQ ID NO: 306]    |
| V <sub>L</sub>      | SRDAGGYNY [SEQ ID NO: 307]                                                                                                                                                                                                                                                                                                                                                                                                                          | EVT [SEQ ID NO: 308]      | SSYGGSNFRV [SEQ ID NO: 309] |
| Full V <sub>H</sub> | EVQLVESGGGVVRPGGSLRLSCAASGFTFGDYGMSWVRQAPGK GLEWVSGINWNGGSTGYADSVKGRFTISRDNKNSLYLQMNSL RAEDTAVYYCARSKQDYWGQGLVTVSS [SEQ ID NO:302]                                                                                                                                                                                                                                                                                                                  |                           |                             |
| DNA                 | GAGGTGCAGCTGGTGGAGTCTGGGGGAGGTGTGGTACGGCCT GGGGGGTCCCTGAGACTCTCCTGTGCAGCCTCTGGATTACCT TTGGTGATTATGGCATGAGCTGGGTCCGCCAAGCTCCAGGGAA GGGGCTGGAGTGGGTCTCTGGTATTAATTGGAATGGTGGTAGC ACAGGTTATGCAGACTCTGTGAAGGGCCGATTACCATCTCCA GAGACAACGCCAAGAACTCCCTGTATCTGCAAATGAACAGTC TGAGAGCCGAGGACACGGCCGTATATTACTGTGCGCGCTCTAA ACAGGATTACTGGGGTCAAGGTACTCTGGTGACCGTCTCCTCA [SEQ ID NO:310]                                                                         |                           |                             |
| Full V <sub>L</sub> | MKKTAIAIAVALAGFATVAQAAELQSALTQPPSASGSPGQSVTIS CTGTSRDAGGYNYFSWYQQHPGKAPKLLIYEVTKRPSGVPDRFS GSKSGKTASLTVSGLQADDEAVYYCSSYGGSNFRVFGGGTKLT VLG [SEQ ID NO:303]                                                                                                                                                                                                                                                                                          |                           |                             |
| DNA                 | ATGAAAAAGACAGCTATCGCGATTGCAGTGGCACTGGCTGGT TTCGCTACCGTGGCCCAGGCGGCCGAGCTCCAGTCTGCCCTGA CTCAGCCTCCCTCCGCGTCCGGGTCTCCTGGACAGTCAGTCAC CATCTCCTGCACTGGAACAGCAGGGACGCTGGTGGTTATAAT TATTTCTCCTGGTACCAACAACACCCAGGCAAAGCCCCCAAAC TCCTGATTTATGAGGTCACCTAAGCGGCCCTCAGGGGTCCCTGA TCGCTTCTCTGGCTCCAAGTCTGGCAAGACGGCCTCCCTGACC GTCTCTGGGCTCCAGGCTGACGATGAGGCTGTATATTACTGCA GCTCATATGGAGGCAGCAACAACCTTTCGGGTGTTTCGGCGGAG GGACCAAGCTGACCGTCCTAGGT [SEQ ID NO:311] |                           |                             |
| scFv                | MKKTAIAIAVALAGFATVAQAAELQSALTQPPSASGSPGQSVTIS CTGTSRDAGGYNYFSWYQQHPGKAPKLLIYEVTKRPSGVPDRFS GSKSGKTASLTVSGLQADDEAVYYCSSYGGSNFRVFGGGTKLT VLGSRRGGGSGGGGSGGGGSLEMAEVQLVESGGGVVRPGGSLR LSCAASGFTFGDYGMSWVRQAPGKGLEWVSGINWNGGSTGYA DSVKGRFTISRDNKNSLYLQMNSLRAEDTAVYYCARSKQDYW GQGLVTVSS [SEQ ID NO:301]                                                                                                                                                  |                           |                             |
| DNA                 | ATGAAAAAGACAGCTATCGCGATTGCAGTGGCACTGGCTGGT TTCGCTACCGTGGCCCAGGCGGCCGAGCTCCAGTCTGCCCTGA CTCAGCCTCCCTCCGCGTCCGGGTCTCCTGGACAGTCAGTCAC CATCTCCTGCACTGGAACAGCAGGGACGCTGGTGGTTATAAT TATTTCTCCTGGTACCAACAACACCCAGGCAAAGCCCCCAAAC                                                                                                                                                                                                                           |                           |                             |

**What is claimed is:**

1. A chimeric antigen receptor (CAR), comprising an extracellular antigen-binding domain that binds to a G-protein coupled receptor, a transmembrane domain and an intracellular domain, wherein the extracellular antigen-binding domain comprises:

(a) a heavy chain variable region comprising the CDR1, CDR2 and CDR3 of the heavy chain variable region set forth in an amino acid sequence selected from the group consisting of SEQ ID NOS: 1, 5, 9, 13, 17, 21, 25, 29, 33, 37, 41, 45, 49, 53, 57, 61, 65, 69, 73, 77, 81, 85, 89, 93, 302, 314, 326, 338, 350, 362, 374, and 386; and

(a) a light chain variable region comprising the CDR1, CDR2 and CDR3 of the light chain variable region set forth in an amino acid sequence selected from the group consisting of SEQ ID NOS: 2, 6, 10, 14, 18, 22, 26, 30, 34, 38, 42, 46, 50, 54, 58, 62, 66, 70, 74, 78, 82, 86, 90, 94, 303, 315, 327, 339, 351, 363, 375, and 387.

2. A chimeric antigen receptor (CAR), comprising an extracellular antigen-binding domain that binds to a G-protein coupled receptor, a transmembrane domain and an intracellular domain, wherein the extracellular antigen-binding domain comprises:

(a) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 124, 125 and 126, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 127, 128 and 129;

(b) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 130, 131 and 132, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 133, 134 and 135;

(c) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 136, 137 and 138, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 139, 140 and 141;

(d) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 142, 143 and 144, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 145, 146 and 147;

(e) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 148, 149 and 150, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 151, 152 and 153;

(f) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 154, 155 and 156, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 157, 158 and 159;

(g) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 160, 161 and 162, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 163, 164 and 165;

(h) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 166, 167 and 168, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 169, 170 and 171;

(i) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 172, 173 and 174, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 175, 176 and 177;

(j) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 178, 179 and 180, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 181, 182 and 183;

(k) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 184, 185 and 186, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 187, 188 and 189;

(l) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 190, 191 and 192, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 193, 194 and 195;

(m) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 196, 197 and 198, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 199, 200 and 201;

(n) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 202, 203 and 204, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 205, 206 and 207;

(o) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 208, 209 and 210, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 211, 212 and 213;

(p) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 214, 215 and 216, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 217, 218 and 219;

(q) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 220, 221 and 222, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 223, 224 and 225;

(r) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 226, 227 and 228, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 229, 230 and 231;

(s) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 232, 233 and 234, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 235, 236 and 237;

(t) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 238, 239 and 240, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 241, 242 and 243;

(u) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 244, 245 and 246, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 247, 248 and 249;

(v) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 250, 251 and 252, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 253, 254 and 255;

(w) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 256, 257 and 258, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 259, 260 and 261;

(x) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 262, 263 and 264, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 265, 266 and 267;

(y) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 304, 305 and 306, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 307, 308 and 309;

(z) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 316, 317 and 318, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 319, 320 and 321;

(aa) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 328, 329 and 330, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 331, 332 and 333;

(ab) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 340, 341 and 342, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 343, 344 and 345;

(ac) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 352, 353 and 354, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 355, 356 and 357;

(ad) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 364, 365 and 366, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 367, 368 and 369;

(ae) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 376, 377 and 378, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 379, 380 and 381; or

(af) a heavy chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 388, 389 and 390, and a light chain variable region comprising the amino acid sequences set forth in SEQ ID NOS: 391, 392 and 393.

3. The CAR of claim 1 or 2, wherein the G protein receptor is a G-protein coupled receptor family C group 5 member D (GPRC5D).
4. The CAR of claim 3, wherein the extracellular antigen-binding domain of the CAR binds to GPRC5D with a binding affinity ( $K_d$ ) of from about  $1 \times 10^{-9}$  M to about  $3 \times 10^{-6}$  M.
5. The CAR of any one of claims 1-4, wherein the extracellular antigen-binding domain is a single-chain variable fragment (scFv).
6. The CAR of claim 5, wherein the extracellular antigen-binding domain is a murine scFv.
7. The CAR of claim 5, wherein the extracellular antigen-binding domain is a human scFv.

8. The CAR of any one of claims 1-4, wherein the extracellular antigen-binding domain is a Fab, which is optionally crosslinked.
9. The CAR of any one of claims 1-4, wherein the extracellular antigen-binding domain is a F(ab)<sub>2</sub>.
10. The CAR of any one of claims 3-9, one or more of the scFv, Fab and F(ab)<sub>2</sub> are comprised in a fusion protein with a heterologous sequence to form the extracellular antigen-binding domain.
11. The CAR of any one of claims 1-10, wherein the heavy chain variable region comprises an amino acid sequence that is at least about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, about 98% or about 99% homologous to an amino acid sequence selected from the group consisting of: SEQ ID NOS:1, 5, 9, 13, 17, 21, 25, 29, 33, 37, 41, 45, 49, 53, 57, 61, 65, 69, 73, 77, 81, 85, 89, 93, 302, 314, 326, 338, 350, 362, 374, and 386.
12. The CAR of any one of claims 1-11, wherein the heavy chain variable region comprises an amino acid sequence selected from the group consisting of SEQ ID NOS:1, 5, 9, 13, 17, 21, 25, 29, 33, 37, 41, 45, 49, 53, 57, 61, 65, 69, 73, 77, 81, 85, 89, 93, 302, 314, 326, 338, 350, 362, 374, and 386, and conservative modifications thereof.
13. The CAR of any one of claims 1-12, wherein the heavy chain variable region comprises the amino acid sequence selected from the group consisting of: SEQ ID NOS:1, 5, 9, 13, 17, 21, 25, 29, 33, 37, 41, 45, 49, 53, 57, 61, 65, 69, 73, 77, 81, 85, 89, 93, 302, 314, 326, 338, 350, 362, 374, and 386.
14. The CAR of any one of claims 1-13, wherein the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:53.
15. The CAR of any one of claims 1-13, wherein the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:57.
16. The CAR of any one of claims 1-13, wherein the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:61.

17. The CAR of any one of claims 1-13, wherein the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:65.
18. The CAR of any one of claims 1-13, wherein the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:69.
19. The CAR of any one of claims 1-18, wherein the light chain variable region comprises an amino acid sequence that is at least about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, about 98% or about 99% homologous to an amino acid sequence selected from the group consisting of SEQ ID NOS: 2, 6, 10, 14, 18, 22, 26, 30, 34, 38, 42, 46, 50, 54, 58, 62, 66, 70, 74, 78, 82, 86, 90, 94, 303, 315, 327, 339, 351, 363, 375, and 387.
20. The CAR of any one of claims 1-19, wherein the light chain variable region comprises an amino acid sequence selected from the group consisting of SEQ ID NOS: 2, 6, 10, 14, 18, 22, 26, 30, 34, 38, 42, 46, 50, 54, 58, 62, 66, 70, 74, 78, 82, 86, 90, 94, 303, 315, 327, 339, 351, 363, 375, and 387, and conservative modifications thereof.
21. The CAR of any one of claims 1-20, wherein the light chain variable region comprises the amino acid sequence selected from the group consisting of: SEQ ID NOS:2, 6, 10, 14, 18, 22, 26, 30, 34, 38, 42, 46, 50, 54, 58, 62, 66, 70, 74, 78, 82, 86, 90, 94, 303, 315, 327, 339, 351, 363, 375, and 387.
22. The CAR of any one of claims 1-21, wherein the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:54.
23. The CAR of any one of claims 1-21 20, wherein the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:58.
24. The CAR of any one of claims 1-21, wherein the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:62.
25. The CAR of any one of claims 1-21, wherein the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:66.
26. The CAR of any one of claims 1-21, wherein the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:70.

27. The CAR of any one of claims 1-26, wherein (a) the heavy chain variable region comprises an amino acid sequence that is at least about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, about 98% or about 99% homologous to an amino acid sequence selected from the group consisting of SEQ ID NO: 1, 5, 9, 13, 17, 21, 25, 29, 33, 37, 41, 45, 49, 53, 57, 61, 65, 69, 73, 77, 81, 85, 89, 93, 302, 314, 326, 338, 350, 362, 374, and 386; and (b) the light chain variable region comprises an amino acid sequence that is at least about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, about 98% or about 99% homologous to an amino acid sequence selected from the group consisting of SEQ ID NOS: 2, 6, 10, 14, 18, 22, 26, 30, 34, 38, 42, 46, 50, 54, 58, 62, 66, 70, 74, 78, 82, 86, 90, 94, 303, 315, 327, 339, 351, 363, 375, and 387.

28. The CAR of any one of claims 1-27, wherein (a) the heavy chain variable region comprises an amino acid sequence selected from the group consisting of SEQ ID NOS:1, 5, 9, 13, 17, 21, 25, 29, 33, 37, 41, 45, 49, 53, 57, 61, 65, 69, 73, 77, 81, 85, 89, 93, 302, 314, 326, 338, 350, 362, 374, and 386, and conservative modifications thereof, and (b) the light chain variable region comprises an amino acid sequence selected from the group consisting of SEQ ID NOS: 2, 6, 10, 14, 18, 22, 26, 30, 34, 38, 42, 46, 50, 54, 58, 62, 66, 70, 74, 78, 82, 86, 90, 94, 303, 315, 327, 339, 351, 363, 375, and 387, and conservative modifications thereof.

29. The CAR of any one of claims 1-28, wherein (a) the heavy chain variable region comprises the amino acid sequence selected from the group consisting of: SEQ ID NOS:1, 5, 9, 13, 17, 21, 25, 29, 33, 37, 41, 45, 49, 53, 57, 61, 65, 69, 73, 77, 81, 85, 89, 93, 302, 314, 326, 338, 350, 362, 374, and 386; and (b) the light chain variable region comprises the amino acid sequence selected from the group consisting of: SEQ ID NOS:2, 6, 10, 14, 18, 22, 26, 30, 34, 38, 42, 46, 50, 54, 58, 62, 66, 70, 74, 78, 82, 86, 90, 94, 303, 315, 327, 339, 351, 363, 375, and 387.

30. The CAR of any one of claims 1-29, wherein:

(a) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:1, and the light chain variable region comprising the amino acid sequence set forth in SEQ ID NO:2;

(b) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:5, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:6;

(c) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:9, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:10;

(d) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:13, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:14;

(e) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:17, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:18;

(f) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:21, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:22;

(g) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:25, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:26;

(h) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:29, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:30;

(i) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:33, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:34;

(j) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:37, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:38;

(k) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:41, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:42;

(l) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:45, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:46;

(m) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:49, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:50;

(n) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:53, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:54;

(o) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:57, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:58;

(p) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:61, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:62;

(q) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:65, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:66;

(r) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:69, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:70;

(s) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:73, the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:74;

(t) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:77, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:78;

(u) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:81, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:82;

(v) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:85, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:86;

(w) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:89, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:90;

(x) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:93, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:94;

(y) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:302, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:303;

(z) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:314, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:315;

(aa) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:326, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:327;

(ab) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:338, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:339;

(ac) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:350, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:351;

(ad) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:362, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:363;

(ae) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:374, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:375; or

(af) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:386, and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:387.

31. The CAR of claim 30, wherein heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:53; and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:54.

32. The CAR of claim 30, wherein the heavy chain variable region comprising comprises the amino acid sequence set forth in SEQ ID NO:57; and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:58.

33. The CAR of claim 30, wherein the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:61; and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:62.

34. The CAR of claim 30, wherein the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:65; and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:66.

35. The CAR of claim 30, wherein the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:69; and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:70.

36. The CAR of any one of claims 1-35, wherein the extracellular antigen-binding domain comprises a linker between the heavy chain variable region and the light chain variable region of the extracellular antigen-binding domain.

37. The CAR of any one of claims 1-36, wherein (a) the heavy chain variable region comprises the amino acid sequences set forth in SEQ ID NOs: 202, 203 and 204; and (b) the light chain variable region comprises the amino acid sequences set forth in SEQ ID NOs: 205, 206 and 207 .

38. The CAR of any one of claims 1-36, wherein (a) the heavy chain variable region comprises the amino acid sequences set forth in SEQ ID NOs: 208, 209 and 210; and (b) the light chain variable region comprises the amino acid sequences set forth in SEQ ID NOs: 211, 212 and 213 .

39. The CAR of any one of claims 1-36 , wherein (a) the heavy chain variable region comprises the amino acid sequences set forth in SEQ ID NOs: 214, 215 and 216; and (b) the

light chain variable region comprises the amino acid sequences set forth in SEQ ID NOs: 217, 218 and 219 .

40. The CAR of any one of claims 1-36, wherein (a) the heavy chain variable region comprises the amino acid sequences set forth in SEQ ID NOs: 220, 221 and 222; and (b) the light chain variable region comprises the amino acid sequences set forth in SEQ ID NOs: 223, 224 and 225 .

41. The CAR of any one of claims 1-36, wherein (a) the heavy chain variable region comprises the amino acid sequences set forth in SEQ ID NOs: 226, 227 and 228; and (b) the light chain variable region comprises the amino acid sequences set forth in SEQ ID NOs: 229, 230 and 231 .

42. The CAR of any one of claims 1-41, wherein the extracellular antigen-binding domain comprises a signal peptide that is covalently joined to the 5' terminus of the extracellular antigen-binding domain.

43. The CAR of any one of claims 1-42 , wherein the GPRC5D comprises the amino acid sequence set forth in SEQ ID NO:97.

44. The CAR of claim 43, wherein the extracellular antigen-binding domain binds to one, two, three or four epitope region selected from the group consisting of an epitope region in N-terminal region comprising amino acids 1-27 of SEQ ID NO:97, an epitope region in ECL1 region comprising amino acids 85-93 of SEQ ID NO:97, an epitope region in ECL2 region comprising amino acids 145-167 of SEQ ID NO:97, and an epitope region in ECL3 region comprising amino acids 226-239 of SEQ ID NO:97.

45. The CAR of claim 44, wherein the extracellular antigen-binding domain binds to an epitope region comprising amino acids 16-23 of SEQ ID NO:97.

46. The CAR of claim 45, wherein the extracellular antigen-binding domain binds to an epitope region comprising amino acids 15-23 of SEQ ID NO:97.

47. The CAR of claim 45, wherein the extracellular antigen-binding domain binds to an epitope region comprising amino acids 16-25 of SEQ ID NO:97.

48. The CAR of claim 44, wherein the extracellular antigen-binding domain binds to an epitope region comprising amino acids 10-17 of SEQ ID NO:97.
49. The CAR of claim 48, wherein the extracellular antigen-binding domain binds to an epitope region comprising amino acids 5-17 of SEQ ID NO:97.
50. The CAR of claim 44, wherein the extracellular antigen-binding domain binds to an epitope region comprising amino acids 85-95 of SEQ ID NO:97.
51. The CAR of claim 44, wherein the extracellular antigen-binding domain binds to an epitope region comprising amino acids 157-164 of SEQ ID NO:97.
52. The CAR of claim 51, wherein the extracellular antigen-binding domain binds to an epitope region comprising amino acids 157-167 of SEQ ID NO:97.
53. The CAR of claim 44, wherein the extracellular antigen-binding domain binds to an epitope region comprising amino acids 230-237 of SEQ ID NO:97.
54. The CAR of claim 53, wherein the extracellular antigen-binding domain binds to an epitope region comprising amino acids 229-237 of SEQ ID NO:97.
55. The CAR of claim 53, wherein the extracellular antigen-binding domain binds to an epitope region comprising amino acids 230-243 of SEQ ID NO:97.
56. The CAR of claim 53, wherein the extracellular antigen-binding domain binds to an epitope region comprising amino acids 227-237 of SEQ ID NO:97.
57. The CAR of claim 44, wherein the extracellular antigen-binding domain binds to one, two or three epitope region selected from the group consisting of an epitope region comprising amino acids 16-25 of SEQ ID NO:97, to an epitope region comprising amino acids 157-164 of SEQ ID NO:97, and an epitope region comprising amino acids 229-237 of SEQ ID NO:97.
58. The CAR of claim 57, wherein the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:57 and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:58.

59. The CAR of claim 57 or 58 , wherein (a) the heavy chain variable region comprises the amino acid sequences set forth in SEQ ID NOs: 208, 209 and 210; and (b) the light chain variable region comprises the amino acid sequences set forth in SEQ ID NOs: 211, 212 and 213.

60. The CAR of claim 44, wherein the extracellular antigen-binding domain binds to one, two or three epitope region selected from the group consisting of an epitope region comprising amino acids 5-17 of SEQ ID NO:97, an epitope region comprising amino acids 85-95 of SEQ ID NO:97, and an epitope region comprising amino acids 157-164 of SEQ ID NO:97.

61. The CAR of claim 60, wherein the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:61 and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:62.

62. The CAR of claim 60 or 61 , wherein (a) the heavy chain variable region comprises the amino acid sequences set forth in SEQ ID NOs: 214, 215 and 216; and (b) the light chain variable region comprises the amino acid sequences set forth in SEQ ID NOs: 217, 218 and 219.

63. The CAR of claim 44, wherein the extracellular antigen-binding domain binds to one or two epitope region selected from the group consisting of an epitope region comprising amino acids 15-23 of SEQ ID NO:97, and an epitope region comprising amino acids 230-243 of SEQ ID NO:97.

64. The CAR of claim 63, wherein the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:65 and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:66.

65. The CAR of claim 63 or 64 , wherein (a) the heavy chain variable region comprises the amino acid sequences set forth in SEQ ID NOs: 220, 221 and 222; and (b) the light chain variable region comprises the amino acid sequences set forth in SEQ ID NOs: 223, 224 and 225.

66. The CAR of claim 44, wherein the extracellular antigen-binding domain binds to one, two or three epitope region selected from the group consisting of an epitope region comprising amino acids 10-17 of SEQ ID NO:97, an epitope region comprising amino acids 157-167 of SEQ ID NO:97, and an epitope region comprising amino acids 227-237 of SEQ ID NO:97.

67. The CAR of claim 66, wherein the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:69 and the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:70.

68. The CAR of claim 66 or 67, wherein (a) the heavy chain variable region comprises the amino acid sequences set forth in SEQ ID NOs: 226, 227 and 228; and (b) the light chain variable region comprises the amino acid sequences set forth in SEQ ID NOs: 229, 230 and 231.

69. The CAR of any one of claims 1-68, wherein the transmembrane domain comprises a CD8 polypeptide, a CD28 polypeptide, a CD3 $\zeta$  polypeptide, a CD4 polypeptide, a 4-1BB polypeptide, an OX40 polypeptide, an ICOS polypeptide, a CTLA-4 polypeptide, a PD-1 polypeptide, a LAG-3 polypeptide, a 2B4 polypeptide, a BTLA polypeptide, or a combination thereof.

70. The CAR of claim 69, wherein the transmembrane domain comprises a CD8 polypeptide.

71. The CAR of claim 69, wherein the transmembrane domain comprises a CD28 polypeptide.

72. The CAR of any one of claims 1-71, wherein the intracellular domain comprises a CD3 $\zeta$  polypeptide.

73. The CAR of any one of claims 1-72, wherein the intracellular domain further comprises at least one signaling region.

74. The CAR of claim 73, wherein the at least one signaling region comprises a CD28 polypeptide, a 4-1BB polypeptide, an OX40 polypeptide, an ICOS polypeptide, a DAP-10 polypeptide, a PD-1 polypeptide, a CTLA-4 polypeptide, a LAG-3 polypeptide, a 2B4 polypeptide, a BTLA polypeptide, or a combination thereof.

75. The CAR of claim 73 or 74, wherein the signaling region is a co-stimulatory signaling region.

76. The CAR of claim 75, wherein the at least one co-stimulatory signaling region comprises a CD28 polypeptide, a 4-1BB polypeptide, an OX40 polypeptide, an ICOS polypeptide, a DAP-10 polypeptide, or a combination thereof.

77. The CAR of claim 76, wherein the at least one co-stimulatory signaling region comprises a CD28 polypeptide.
78. The CAR of claim 76, wherein the at least one co-stimulatory signaling region comprises a 4-1BB polypeptide.
79. The CAR of any one of claims 73-77, wherein the transmembrane domain comprises a CD28 polypeptide, the intracellular domain comprises a CD3 $\zeta$  polypeptide, and the signaling domain comprises a CD28 polypeptide.
80. The CAR of any one of claims 73-76 and 78, wherein the transmembrane domain comprises a CD8 polypeptide, the intracellular domain comprises a CD3 $\zeta$  polypeptide, and the signaling domain comprises a 4-1BB polypeptide.
81. The CAR of any one of claims 1-80, wherein the CAR is recombinantly expressed.
82. The CAR of any one of claims 1-81, wherein the CAR is expressed from a vector.
83. The CAR of claim 82, wherein the vector is a  $\gamma$ -retroviral vector.
84. An immunoresponsive cell comprising the CAR of any one of claims 1-83.
85. The immunoresponsive cell of claim 84, wherein the immunoresponsive cell is transduced with the CAR.
86. The immunoresponsive cell of claim 84 or 85, wherein the CAR is constitutively expressed on the surface of the immunoresponsive cell.
87. The immunoresponsive cell of any one of claims 84-86, wherein the immunoresponsive cell is further transduced with at least one co-stimulatory ligand such that the immunoresponsive cell expresses the at least one co-stimulatory ligand.
88. The immunoresponsive cell of claim 87, wherein the at least one co-stimulatory ligand is selected from the group consisting of 4-1BBL, CD80, CD86, CD70, OX40L, CD48, TNFRSF14, and combinations thereof.

89. The immunoresponsive cell of any one of claims 84-88, wherein the immunoresponsive cell is further transduced with at least one cytokine such that the immunoresponsive cell secretes the at least one cytokine.

90. The immunoresponsive cell of claim 89, wherein the at least one cytokine is selected from the group consisting of IL-2, IL-3, IL-6, IL-7, IL-11, IL-12, IL-15, IL-17, IL-21, and combinations thereof.

91. The immunoresponsive cell of any one of claims 84-90, wherein the immunoresponsive cell is selected from the group consisting of a T cell, a Natural Killer (NK) cell, a cytotoxic T lymphocyte (CTL), a regulatory T cell, a human embryonic stem cell, a lymphoid progenitor cell, a T cell-precursor cell, and a pluripotent stem cell from which lymphoid cells may be differentiated.

92. The immunoresponsive cell of claim 91, wherein the immunoresponsive cell is a T cell.

93. A nucleic acid molecule encoding the chimeric antigen receptor (CAR) of any one of claims 1-83.

94. The nucleic acid molecule of claim 93, comprising nucleic acids having the sequence set forth in SEQ ID NO:397.

95. The nucleic acid molecule of claim 93, comprising nucleic acids having the sequence set forth in SEQ ID NO:398.

96. The nucleic acid molecule of claim 93, comprising nucleic acids having the sequence set forth in SEQ ID NO:399.

97. The nucleic acid molecule of claim 93, comprising nucleic acids having the sequence set forth in SEQ ID NO:400.

98. The nucleic acid molecule of claim 93, comprising nucleic acids having the sequence set forth in SEQ ID NO:401.

99. The nucleic acid molecule of claim 93, comprising nucleic acids having the sequence set forth in SEQ ID NO:402.

100. The nucleic acid molecule of claim 93, comprising nucleic acids having the sequence set forth in SEQ ID NO:403.

101. The nucleic acid molecule of claim 93, comprising nucleic acids having the sequence set forth in SEQ ID NO:406.

102. The nucleic acid molecule of claim 93, comprising nucleic acids having the sequence set forth in SEQ ID NO:407.

103. The nucleic acid molecule of claim 93, comprising nucleic acids having the sequence set forth in SEQ ID NO:408.

104. A vector comprising the isolated nucleic acid molecule of any one of claims 93-103.

105. The vector of claim 104, wherein the vector is a  $\gamma$ -retroviral vector.

106. A host cell expressing the nucleic acid molecule of any one of claims 93-103.

107. The host cell of claim 106, wherein the host cell is a T cell.

108. Use of an effective amount of the immunoresponsive cell of any one of claims 84-92 in the manufacture of a medicament for reducing tumor burden in a subject.

109. The use of claim 108, wherein the immunoresponsive cell reduces the number of tumor cells.

110. The use of claim 108, wherein the immunoresponsive cell reduces tumor size.

111. The use of claim 108, wherein the immunoresponsive cell eradicates the tumor in the subject.

112. The use of any one of claims 108-111, wherein the tumor is multiple myeloma or Waldenstrom's Macroglobulinemia.

113. The use of claim 112, wherein the tumor is multiple myeloma.

114. The use of any one of claims 108-114, wherein the subject is a human.

115. The use of any one of claims 108-114, wherein the immunoresponsive cell is a T cell.

116. Use of an effective amount of the immunoresponsive cell of any one of claims 84-92 in the manufacture of a medicament for increasing or lengthening survival of a subject having neoplasia.

117. The use of claim 116, wherein the neoplasia is multiple myeloma or Waldenstrom's Macroglobulinemia.

118. The use of claim 117, wherein the neoplasia is multiple myeloma.

119. The use of any one of claims 116-118, wherein the immunoresponsive cell reduces or eradicates tumor burden in the subject.

120. A method for producing an immunoresponsive cell that binds to a G-protein coupled receptor, comprising introducing into the immunoresponsive cell  
a nucleic acid molecule of any one of claims 93-103.

121. A pharmaceutical composition comprising an effective amount of the immunoresponsive cell of any one of claims 84-92 and a pharmaceutically acceptable excipient.

122. The pharmaceutical composition of claim 121, wherein the pharmaceutical composition is for treating a neoplasia.

123. The pharmaceutical composition of claim 122, wherein the neoplasia is multiple myeloma or Waldenstrom's Macroglobulinemia.

124. The pharmaceutical composition of claim 123, wherein the neoplasia is multiple myeloma.

125. A kit for treating multiple myeloma, comprising the immunoresponsive cell of any one of claims 84-92.

126. The kit of claim 125, wherein the kit further comprises written instructions for using the immunoresponsive cell for treating a subject having a neoplasia.

127. The kit of claim 125 or 126, wherein the neoplasia is multiple myeloma or Waldenstrom's Macroglobulinemia.

128. The kit of claim 127, wherein the neoplasia is multiple myeloma.