CLAIMS

The claims defining the invention are as follows:

1. An isolated immune cell comprising a chimeric antigen receptor (CAR) comprising:
   (i) an anti-CLL-1 scFv;
   (ii) a hinge domain;
   (iii) a CD8 transmembrane domain;
   (iv) a CD28 co-stimulatory domain; and
   (v) a CD3 zeta domain,
   the immune cell further comprising armoring genomic modifications comprising inactivation of the *PDCD1* gene and inactivation of the beta-2 microglobulin (*B2M*) gene.

2. The immune cell of claim 1, wherein the anti-CLL-1 scFv is represented by a formula V_H-L_n-V_L, wherein V_H comprises SEQ ID NO: 7, V_L comprises SEQ ID NO: 11, and L_n is a peptide linker having the sequence GGGGSGGGGSGGGGSGGGSGGGGS.

3. The immune cell of claim 2, wherein the anti-CLL-1 scFv comprises or consists essentially of SEQ ID NO: 5.

4. The immune cell of claim 1, wherein the hinge domain comprises a CD8 hinge domain consisting essentially of SEQ ID NO. 15.

5. The immune cell of claim 1, wherein the hinge domain comprises or consists essentially of a CD28 hinge domain.

6. The immune cell of claim 1, wherein the CAR comprises or consists essentially of SEQ ID NO: 22.

7. The immune cell of claim 1, wherein the chimeric antigen receptor (CAR) is inserted into the T-cell receptor alpha chain (*TRAC*) locus on human chromosome 14 between nucleotides 22547538 and 22547539.

8. The immune cell of claim 1, wherein the *PDCD1* gene is cleaved between nucleotides 241852860 and 241852883.

9. The immune cell of claim 1, wherein the armoring genomic modification further comprises insertion of an HLA-E-B2M fusion coding sequence into the *B2M* locus on human chromosome 15 between nucleotides 44715624 and 44715625.

10. An *in vitro* method of making the immune cell of claim 1, the method comprising introducing into a cell a nucleic acid comprising SEQ ID NO: 27 and a nucleic acid encoding SEQ ID NO: 40 and further comprising disrupting the *PDCD1* gene, the *TRAC* gene and the *B2M* gene in the cell.

11. The method of claim 10, wherein the introducing step comprises introducing into the cell a sequence-dependent endonuclease.

12. The method of claim 11, wherein the introducing step comprises introducing into the cell a CRISPR Cas12a system comprising a nucleic acid-guided endonuclease and nucleic acidtargeting nucleic acid (NATNA).

13. The method of claim 12, wherein the endonuclease cleaves the *TRAC* locus between nucleotides 22547538 and 22547539 and the endonuclease forms a nucleoprotein complex with a NATNA comprising a targeting region having SEQ ID NO: 37.

14. The method of claim 10, wherein SEQ ID NO: 27 is inserted into the cleaved *TRAC* locus.

15. The method of claim 12, wherein the endonuclease cleaves the *B2M* locus on human chromosome 15 between nucleotides 44715624 and 44715625 and the endonuclease forms a nucleoprotein complex with a NATNA comprising a targeting region having SEQ ID NO: 38.

16. The method of claim 15, wherein a sequence encoding the HLA-E-B2M fusion of SEQ ID NO: 40 is inserted into the cleaved *B2M* locus.

17. The method of claim 10, wherein the disrupting of the *PDCD1* gene comprises introducing into the cell a CRISPR Cas12a endonuclease and NATNA comprising

SEQ ID NO: 39 wherein the endonuclease cleaves the *PDCD1* locus on human chromosome 2 between nucleotides 241852860 and 241852883.

18. The immune cell of claim 1 present in a pharmaceutically acceptable excipient.

19. Use of the immune cell of claim 18 in the manufacture of a medicament for use in a method of inhibiting the growth of a CLL-1 expressing tumor selected from acute myeloblastic leukemia (AML) and myelodysplastic syndrome (MDS).