

[0006] There is an unmet medical need for interventions that can effectively treat MM, including relapsed/refractory MM. Provided herein are methods and compositions that address this need.

SUMMARY

[0007] Chimeric antigen receptors (CARs) that bind to BCMA are provided herein; as well as dosing paradigms for use in the treatment of multiple (MM), including relapsed and/or refractory MM.

[0008] More specifically, in one example provided herein is a method of treating MM in a subject comprising administering to the subject at least one dose of allogeneic chimeric antigen receptor (CAR)-T cells comprising an anti-human BCMA CAR (BCMA CAR-T cells), wherein the at least one dose is about 7×10^6 cells/dose to about 480×10^6 cells/dose.

[0008a] In one aspect, the present disclosure refers to use of at least one flat dose of allogeneic chimeric antigen receptor (CAR)-T cells comprising an anti-human BCMA CAR (BCMA CAR-T cells) in the manufacture of a medicament for treating multiple myeloma in a subject, wherein the at least one flat dose is about 7-160 $\times 10^6$ cells/dose to about 480×10^6 cells/dose.

[0009] In some examples, the weight of the subject is ≥ 50 kg, and the method comprises administering at least one dose of BCMA CAR-T cells, wherein the dose ranges from about 20×10^6 cells/dose to about 480×10^6 cells/dose. In some examples, the at least one dose is about 20×10^6 cells/dose, about 40×10^6 cells/dose, about 120×10^6 cells/dose, about 360×10^6 cells/dose, or about 480×10^6 cells/dose. In some examples, the at least one dose is from about 20×10^6 cells/dose to about 40×10^6 cells/dose, from about 40×10^6 cells/dose to about 120×10^6 cells/dose, from about 120×10^6 cells/dose to about 360×10^6 cells/dose, or from about 360×10^6 cells/dose to about 480×10^6 cells/dose.

[0010] In some examples, the weight of the subject is >50 kg, and the method comprises administering at least one dose of BCMA CAR-T cells, wherein the dose ranges from about 20×10^6 cells/dose to about 480×10^6 cells/dose. In some examples, the at least one dose is about 20×10^6 cells/dose, about 40×10^6 cells/dose, about 160×10^6 cells/dose, about 240×10^6 cells/dose, about 320×10^6 cells/dose, or about 480×10^6 cells/dose. In some examples, the at least one dose is from about 20×10^6 cells/dose to about 40×10^6 cells/dose, from about 40×10^6 cells/dose to about 160×10^6 cells/dose, from about 160×10^6 cells/dose to about 240×10^6 cells/dose, from about 240×10^6 cells/dose to about 320×10^6 cells/dose, from about 160×10^6 cells/dose to about 320×10^6 cells/dose, or from about 320×10^6 cells/dose to about 480×10^6 cells/dose.

[0028a] In another aspect, the present disclosure refers to a formulation comprising BCMA CAR-T cells, wherein the cells are formulated in a solution comprising about 5% dimethyl sulfoxide, wherein the dosage strength of the formulation is 14×10^6 cells /mL, wherein the genotype of the cells is BCMA-CAR+ _TCR $\alpha\beta$ - _CD52+/-, and wherein the BCMA

5 CAR-T cells comprise a CAR comprising an extracellular ligand-binding domain, two ~~CD20 epitope rituximab-binding~~ domains (SEQ ID NO: 397), a first transmembrane domain, and an intracellular signaling domain, wherein the extracellular domain comprises a scFv comprising a sequence: a heavy chain variable (VH) region comprising a sequence shown in SEQ ID NO: 33 of Table 1 and a light chain variable (VL) region comprising a
10 sequence shown in SEQ ID NO: 34 of Table 1, a VH region comprising a sequence shown in SEQ ID NO: 72 of Table 1 and a VL region comprising a sequence shown in SEQ ID NO: 73 of Table 1, a VH region comprising a sequence shown in SEQ ID NO: 39 of Table 1 and a VL region comprising a sequence shown in SEQ ID NO: 40 of Table 1, a VH region comprising a sequence shown in SEQ ID NO: 76 of Table 1 and a VL region comprising a
15 sequence shown in SEQ ID NO: 77 of Table 1, a VH region comprising a sequence shown in SEQ ID NO: 83 of Table 1 and a VL region comprising a sequence shown in SEQ ID NO: 84 of Table 1, a VH region comprising a sequence shown in SEQ ID NO: 92 of Table 1 and a VL region comprising a sequence shown in SEQ ID NO: 93 of Table 1, a VH region comprising a sequence shown in SEQ ID NO: 25 of Table 1 and a VL region comprising a
20 sequence shown in SEQ ID NO: 18 of Table 1, a VH region comprising a sequence shown in SEQ ID NO: 112 of Table 1 and a VL region comprising a sequence shown in SEQ ID NO: 38 of Table 1, or a VH region comprising a sequence shown in SEQ ID NO: 8 of Table 1 and a VL region comprising a sequence shown in SEQ ID NO: 80 of Table 1;~~a heavy chain variable (VH) region comprising a sequence shown in SEQ ID NO: 33, 72, 39, 76, 83, 92, 25, 112, or 8 of Table 1; and a light chain variable (VL) region comprising a sequence shown in SEQ ID NO: 34, 73, 40, 77, 84, 93, 18, 38, or 80 of Table 1~~, wherein the first transmembrane domain comprises a CD8 α chain transmembrane domain, and wherein the intracellular signaling domain comprises a CD3 ζ signaling domain and/or a 4-1BB signaling domain.

30 [0028b] In another aspect, the present disclosure refers to a formulation comprising BCMA CAR-T cells, wherein the cells are formulated in a 1:1 mixture of CryoStor® Basal Solution and CryoStor® CS10 resulting in a 5% final concentration of dimethyl sulfoxide, wherein the dosage strength of the formulation is 14×10^6 cells /mL, wherein the genotype of the

cells is BCMA-CAR+_{TCRαβ}-_{CD52}+/-, and wherein the BCMA CAR-T cells comprise a CAR comprising an extracellular ligand-binding domain, two CD20 epitope rituximab-binding domains (SEQ ID NO: 397), a first transmembrane domain, and an intracellular signaling domain, wherein the extracellular domain comprises a scFv comprising a

5 sequence: a heavy chain variable (VH) region comprising a sequence shown in SEQ ID NO: 33 of Table 1 and a light chain variable (VL) region comprising a sequence shown in SEQ ID NO: 34 of Table 1, a VH region comprising a sequence shown in SEQ ID NO: 72 of Table 1 and a VL region comprising a sequence shown in SEQ ID NO: 73 of Table 1, a VH region comprising a sequence shown in SEQ ID NO: 39 of Table 1 and a VL region

10 comprising a sequence shown in SEQ ID NO: 40 of Table 1, a VH region comprising a sequence shown in SEQ ID NO: 76 of Table 1 and a VL region comprising a sequence shown in SEQ ID NO: 77 of Table 1, a VH region comprising a sequence shown in SEQ ID NO: 83 of Table 1 and a VL region comprising a sequence shown in SEQ ID NO: 84 of Table 1, a VH region comprising a sequence shown in SEQ ID NO: 92 of Table 1 and a VL region comprising a sequence shown in SEQ ID NO: 93 of Table 1, a VH region comprising a sequence shown in SEQ ID NO: 25 of Table 1 and a VL region comprising a sequence shown in SEQ ID NO: 18 of Table 1, a VH region comprising a sequence shown in SEQ ID NO: 112 of Table 1 and a VL region comprising a sequence shown in SEQ ID NO: 38 of Table 1, or a VH region comprising a sequence shown in SEQ ID NO: 8 of Table 1 and a

15 VL region comprising a sequence shown in SEQ ID NO: 80 of Table 1; a heavy chain variable (VH) region comprising a sequence shown in SEQ ID NO: 33, 72, 39, 76, 83, 92, 25, 112, or 8 of Table 1; and a light chain variable (VL) region comprising a sequence shown in SEQ ID NO: 34, 73, 40, 77, 84, 93, 18, 38, or 80 of Table 1, wherein the first

20 transmembrane domain comprises a CD8α chain transmembrane domain, and wherein the

25 intracellular signaling domain comprises a CD3ζ signaling domain and/or a 4-1BB signaling domain.

WHAT IS CLAIMED IS:

1. Use of at least one flat dose of allogeneic chimeric antigen receptor (CAR)-T cells comprising an anti-human BCMA CAR (BCMA CAR-T cells) in the manufacture of a medicament for treating multiple myeloma in a subject, wherein the at least one flat dose is about ~~7-160~~ 20-160 $\times 10^6$ cells/dose to about 480×10^6 cells/dose.

~~2. The use of claim 1, wherein the weight of the subject is ≥ 50 kg, and at least one dose of BCMA CAR-T cells is to be administered, wherein the dose ranges from about 20×10^6 cells/dose to about 480×10^6 cells/dose.~~

~~3.2. The use of claim 11, wherein the at least one flat dose is about $20-160 \times 10^6$ cells/dose, about 40×10^6 cells/dose, about 120×10^6 cells/dose, about 360×10^6 cells/dose, or about 480×10^6 cells/dose.~~

~~4.3. The use of claim 21, wherein the at least one flat dose is from about $20-320 \times 10^6$ cells/dose to about 40×10^6 cells/dose, from about 40×10^6 cells/dose to about 120×10^6 cells/dose, from about 120×10^6 cells/dose to about 360×10^6 cells/dose, or from about 360×10^6 cells/dose to about 480×10^6 cells/dose.~~

~~5. The use of claim 1, wherein the weight of the subject is < 50 kg, and at least one dose of BCMA CAR-T cells is to be administered, wherein the dose ranges from about 7×10^6 cells/dose to about 360×10^6 cells/dose.~~

~~6.4. The use of claim 51, wherein the at least one flat dose is about $7-480 \times 10^6$ cells/dose, about 14×10^6 cells/dose, about 20×10^6 cells/dose, about 80×10^6 cells/dose, about 240×10^6 cells/dose, or about 360×10^6 cells/dose.~~

~~7.5. The use of claim 51, wherein the at least one flat dose is from about 160×10^6 cells/dose to about 320×10^6 cells/dose, or about 320×10^6 cells/dose to about 480×10^6 cells/dose, 7×10^6 or 14×10^6 cells/dose to about 20×10^6 cells/dose, from about 20×10^6 cells/dose to about 80×10^6 cells/dose, from about 80×10^6 cells/dose to about 240×10^6 cells/dose, or from about 240×10^6 cells/dose to about 360×10^6 cells/dose.~~

~~8. The use of claim 1, wherein the weight of the subject is > 50 kg, and at least one dose of BCMA CAR-T cells is to be administered, wherein the dose ranges from about 20×10^6 cells/dose to about 480×10^6 cells/dose.~~

~~9. The use of claim 8, wherein the at least one dose is about 20×10^6 cells/dose, about~~

~~40 x 10⁶ cells/dose, about 160 x 10⁶ cells/dose, about 240 x 10⁶ cells/dose, about 320 x 10⁶ cells/dose, or about 480 x 10⁶ cells/dose.~~

~~10. The use of claim 8, wherein the at least one dose is from about 20 x 10⁶ cells/dose to about 40 x 10⁶ cells/dose, from about 40 x 10⁶ cells/dose to about 160 x 10⁶ cells/dose, from about 160 x 10⁶ cells/dose to about 240 x 10⁶ cells/dose, from about 240 x 10⁶ cells/dose to about 320 x 10⁶ cells/dose, from about 160 x 10⁶ cells/dose to about 320 x 10⁶ cells/dose, or from about 320 x 10⁶ cells/dose to about 480 x 10⁶ cells/dose.~~

~~11. The use of claim 1, wherein the weight of the subject is ≤50 kg, and at least one dose of BCMA CAR-T cells is to be administered, wherein the dose ranges from about 14 x 10⁶ cells/dose to about 320 x 10⁶ cells/dose.~~

~~12. The use of claim 11, where in the at least one dose is about 14 x 10⁶ cells/dose, about 20 x 10⁶ cells/dose, about 80 x 10⁶ cells/dose, about 160 x 10⁶ cells/dose, about 200 x 10⁶ cells/dose, or about 320 x 10⁶ cells/dose.~~

~~13. The use of claim 12, where in the at least one dose is from about 14 x 10⁶ cells/dose to about 20 x 10⁶ cells/dose, from about 20 x 10⁶ cells/dose to about 80 x 10⁶ cells/dose, from about 80 x 10⁶ cells/dose to about 200 x 10⁶ cells/dose, from about 80 x 10⁶ cells/dose to about 160 x 10⁶ cells/dose, from about 160 x 10⁶ cells/dose to about 200 x 10⁶ cells/dose, or from about 200 x 10⁶ cells/dose to about 320 x 10⁶ cells/dose.~~

14.6. The use of any one of claims 1 to 135, wherein the multiple myeloma is refractory multiple myeloma.

15.7. The use of any one of claims 1 to 146, wherein the multiple myeloma is relapsed multiple myeloma.

16.8. The use of any one of claims 1 to 135, wherein the multiple myeloma is refractory and relapsed multiple myeloma.

17.9. The use of any one of claims 1 to 135, wherein the subject is one that has not received any prior therapy for multiple myeloma.

18.10. The use of any one of claims 1 to 135, wherein the subject is one that has received at least one, two, or three prior therapies for multiple myeloma.

19.11. The use of any one of claims 1 to 1810, wherein the BCMA CAR-T cells comprise a CAR comprising an extracellular binding domain comprising a single chain Fv fragment

(scFv), wherein the scFv comprises a heavy chain variable (VH) region and a light chain variable (VL) region, wherein the VH region comprises a VH complementary determining region 1 (VH CDR1), a VH complementary determining region 2 (VH CDR2), and a VH complementary determining region 3 (VH CDR3) and the VL region comprises a VL complementary determining region 1 (VL CDR1), a VL complementary determining region 2 (VL CDR2), and a VL complementary determining region 3 (VL CDR3), wherein:

(a) the VH CDR1 comprises the amino acid sequence of SEQ ID NO: 150, 151, or 152; the VH CDR2 comprises the amino acid sequence of SEQ ID NO: 153 or 154; the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 155; the VL CDR1 comprises the amino acid sequence of SEQ ID NO: 209; the VL CDR2 comprises the amino acid sequence of SEQ ID NO: 221; and the VL CDR3 comprises the amino acid sequence of SEQ ID NO: 222;

(b) the VH CDR1 comprises the amino acid sequence of SEQ ID NO: 150, 151, or 152; the VH CDR2 comprises the amino acid sequence of SEQ ID NO: 187 or 188; the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 155; the VL CDR1 comprises the amino acid sequence of SEQ ID NO: 249; the VL CDR2 comprises the amino acid sequence of SEQ ID NO: 221; and the VL CDR3 comprises the amino acid sequence of SEQ ID NO: 225;

(c) the VH CDR1 comprises the amino acid sequence of SEQ ID NO: 150, 151, or 152; the VH CDR2 comprises the amino acid sequence of SEQ ID NO: 165 or 166; the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 155; the VL CDR1 comprises the amino acid sequence of SEQ ID NO: 226; the VL CDR2 comprises the amino acid sequence of SEQ ID NO: 221; and the VL CDR3 comprises the amino acid sequence of SEQ ID NO: 227;

(d) the VH CDR1 comprises the amino acid sequence of SEQ ID NO: 151, 156, or 157; the VH CDR2 comprises the amino acid sequence of SEQ ID NO: 159 or 162; the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 161; the VL CDR1 comprises the amino acid sequence of SEQ ID NO: 251; the VL CDR2 comprises the amino acid sequence of SEQ ID NO: 252; and the VL CDR3 comprises the amino acid sequence of SEQ ID NO: 253;

(e) the VH CDR1 comprises the amino acid sequence of SEQ ID NO: 151, 156, or 157; the VH CDR2 comprises the amino acid sequence of SEQ ID NO: 190 or 191; the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 161; the VL CDR1 comprises the amino acid sequence of SEQ ID NO: 262; the VL CDR2 comprises the amino acid sequence of SEQ ID NO: 252; and the VL CDR3 comprises the amino acid sequence of SEQ ID NO: 263;

(f) the VH CDR1 comprises the amino acid sequence of SEQ ID NO: 150, 151, or 152; the VH CDR2 comprises the amino acid sequence of SEQ ID NO: 154 or 169; the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 155; the VL CDR1 comprises the amino acid sequence of SEQ ID NO: 271; the VL CDR2 comprises the amino acid sequence of SEQ ID NO: 221; and the VL CDR3 comprises the amino acid sequence of SEQ ID NO: 272;

(g) the VH CDR1 comprises the amino acid sequence of SEQ ID NO: 129, 130, or 131; the VH CDR2 comprises the amino acid sequence of SEQ ID NO: 139 or 140; the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 134; the VL CDR1 comprises the amino acid sequence of SEQ ID NO: 217; the VL CDR2 comprises the amino acid sequence of SEQ ID NO: 210; and the VL CDR3 comprises the amino acid sequence of SEQ ID NO: 216;

(h) the VH CDR1 comprises the amino acid sequence of SEQ ID NO: 151, 156, or 157; the VH CDR2 comprises the amino acid sequence of SEQ ID NO: 158 or 159; the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 155; the VL CDR1 comprises the amino acid sequence of SEQ ID NO: 209; the VL CDR2 comprises the amino acid sequence of SEQ ID NO: 221; and the VL CDR3 comprises the amino acid sequence of SEQ ID NO: 225; or

(i) the VH CDR1 comprises the amino acid sequence of SEQ ID NO: 129, 130, or 131; the VH CDR2 comprises the amino acid sequence of SEQ ID NO: 132 or 133; the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 137; the VL CDR1 comprises the amino acid sequence of SEQ ID NO: 377; the VL CDR2 comprises the amino acid sequence of SEQ ID NO: 210; and the VL CDR3 comprises the amino acid sequence of SEQ ID NO: 214.

20-12. The use of claim ~~19~~11, wherein the VH region comprises a VH CDR1 comprising the amino acid sequence of SEQ ID NO: 150, 151, or 152; a VH CDR2 comprising the amino acid sequence of SEQ ID NO: 153 or 154; and a VH CDR3 comprising the amino acid sequence of SEQ ID NO: 155; and the VL region comprises a VL CDR1 comprising the amino acid sequence of SEQ ID NO: 209; a VL CDR2 comprising the amino acid sequence of SEQ ID NO: 221; and a VL CDR3 comprising the amino acid sequence of SEQ ID NO: 222.

21-13. The use of claim ~~19~~11, wherein the VH region comprises a VH CDR1 comprising the amino acid sequence of SEQ ID NO: 151, 156, or 157; a VH CDR2 comprising the amino acid sequence of SEQ ID NO: 158 or 159; and a VH CDR3 comprising the amino acid sequence of SEQ ID NO: 155; and the VL region comprises a VL CDR1 comprising the

amino acid sequence of SEQ ID NO: 209; a VL CDR2 comprising the amino acid sequence of SEQ ID NO: 221; and a VL CDR3 comprising the amino acid sequence of SEQ ID NO: 225.

22-14. The use of any one of claims 1 to ~~18~~10, wherein the BCMA CAR-T cells comprise a CAR comprising an extracellular binding domain comprising a single chain Fv fragment (scFv), wherein the scFv comprises a VH region and a VL region, wherein the combination of VH and VL regions are chosen from the combinations presented in Table 1.

23-15. The use of any one of claims 1 to ~~18~~10, wherein the BCMA CAR-T cells comprise a CAR comprising an extracellular ligand-binding domain, a first transmembrane domain, and an intracellular signaling domain, wherein the extracellular domain comprises a scFv comprising a sequence: a heavy chain variable (VH) region comprising a sequence shown in SEQ ID NO: 33, ~~72, 39, 76, 83, 92, 25, 112, or 8~~ of Table 1; and a light chain variable (VL) region comprising a sequence shown in SEQ ID NO: 34, ~~73, 40, 77, 84, 93, 18, 38, or 80~~ of Table 1, a VH region comprising a sequence shown in SEQ ID NO: 72 of Table 1 and a VL region comprising a sequence shown in SEQ ID NO: 73 of Table 1, a VH region comprising a sequence shown in SEQ ID NO: 39 of Table 1 and a VL region comprising a sequence shown in SEQ ID NO: 40 of Table 1, a VH region comprising a sequence shown in SEQ ID NO: 76 of Table 1 and a VL region comprising a sequence shown in SEQ ID NO: 77 of Table 1, a VH region comprising a sequence shown in SEQ ID NO: 83 of Table 1 and a VL region comprising a sequence shown in SEQ ID NO: 84 of Table 1, a VH region comprising a sequence shown in SEQ ID NO: 92 of Table 1 and a VL region comprising a sequence shown in SEQ ID NO: 93 of Table 1, a VH region comprising a sequence shown in SEQ ID NO: 25 of Table 1 and a VL region comprising a sequence shown in SEQ ID NO: 18 of Table 1, a VH region comprising a sequence shown in SEQ ID NO: 112 of Table 1 and a VL region comprising a sequence shown in SEQ ID NO: 38 of Table 1, or a VH region comprising a sequence shown in SEQ ID NO: 8 of Table 1 and a VL region comprising a sequence shown in SEQ ID NO: 80 of Table 1; wherein the first transmembrane domain comprises a CD8 α chain transmembrane domain, and wherein the intracellular signaling domain comprises a CD3 ζ signaling domain and/or a 4-1BB signaling domain.

24-16. The use of claim ~~23~~15, wherein the VH comprises SEQ ID NO: 33 and the VL comprises SEQ ID NO: 34.

25-17. The use of claim ~~23~~15, wherein the VH comprises SEQ ID NO: 112 and the VL

comprises SEQ ID NO: 38.

26-18. The use of any one of claims 1 to ~~18~~10, wherein the BCMA CAR-T cells comprise a CAR comprising the amino acid sequence shown in SEQ ID NO: 344.

27-19. The use of claim ~~26~~18, wherein the CAR further comprises a CD20 epitope, wherein the CD20 epitope comprises the amino acid sequence shown in SEQ ID NO: 397 or SEQ ID NO: 398.

~~28.—The use of claim 27, wherein the CD20 epitope comprises the amino acid sequence shown in SEQ ID NO: 397 or SEQ ID NO: 398.~~

29-20. The use of any one of claims 1 to ~~18~~10, wherein the BCMA CAR-T cells comprise a CAR comprising a CD8 α signal peptide having the sequence of SEQ ID NO: 318; a VH region having the sequence of SEQ ID NO: 112; a GS linker having the sequence of SEQ ID NO: 333; a VL region having the sequence of SEQ ID NO: 38; a CD8 α hinge having the sequence of SEQ ID NO: 320; a CD8 α transmembrane domain having the sequence of SEQ ID NO: 322; a 4-1BB intracellular signaling domain having the sequence of SEQ ID NO: 323; and a CD3 ζ intracellular signaling domain having the sequence of SEQ ID NO: 324.

30-21. The use of any one of claims 1 to ~~18~~10, wherein the BCMA CAR-T cells comprise a CAR comprising a CD8 α signal peptide having the sequence of SEQ ID NO: 318; a VH region having the sequence of SEQ ID NO: 112; a GS linker having the sequence of SEQ ID NO: 333; a VL region having the sequence of SEQ ID NO: 38; a CD20 epitope having the sequence of SEQ ID NO: 398; a CD8 α hinge having the sequence of SEQ ID NO: 320; a CD8 α transmembrane domain having the sequence of SEQ ID NO: 322; a 4-1BB intracellular signaling domain having the sequence of SEQ ID NO: 323; and a CD3 ζ intracellular signaling domain having the sequence of SEQ ID NO: 324.

31-22. The use of any one of claims 1 to ~~18~~10, wherein the BCMA CAR-T cells comprise a CAR comprising a CD8 α signal peptide having the sequence of SEQ ID NO: 318; a VH region having the sequence of SEQ ID NO: 33; a GS linker having the sequence of SEQ ID NO: 333; a VL region having the sequence of SEQ ID NO: 34; a CD8 α hinge having the sequence of SEQ ID NO: 320; a CD8 α transmembrane domain having the sequence of SEQ ID NO: 322; a 4-1BB intracellular signaling domain having the sequence of SEQ ID NO: 323; and a CD3 ζ intracellular signaling domain having the sequence of SEQ ID NO: 324.

32-23. The use of any one of claims 1 to ~~18~~10, wherein the BCMA CAR-T cells comprise a

CAR comprising a CD8 α signal peptide having the sequence of SEQ ID NO: 318; a VH region having the sequence of SEQ ID NO: 33; a GS linker having the sequence of SEQ ID NO: 333; a VL region having the sequence of SEQ ID NO: 34; a CD20 epitope having the sequence of SEQ ID NO: 398; a CD8 α hinge having the sequence of SEQ ID NO: 320; a
5 CD8 α transmembrane domain having the sequence of SEQ ID NO: 322; a 4-1BB intracellular signaling domain having the sequence of SEQ ID NO: 323; and a CD3 ζ intracellular signaling domain having the sequence of SEQ ID NO: 324.

33-24. The use of any one of claims 1 to 3223, wherein the CAR-T cells are deficient in CD52.

10 34-25. The use of any one of claims 1 to 3023, wherein the CAR-T cells are deficient in TCR α and/or TCR β .

35-26. The use of any one of claims 1 to 3425, wherein the genotype of the cells is TCR $\alpha\beta^-$ and CD52 $^{+/-}$.

15 36-27. The use of any one of claims 1 to 3223, wherein the CAR-T cells do not express a safety switch.

37-28. The use of any one of claims 1 to 3223, wherein the CAR-T cells express a CD20rituximab epitope, wherein the CD20 epitope comprises the amino acid sequence shown in SEQ ID NO: 397 or SEQ ID NO: 398.

20 38-29. The use of any one of claims 1 to 3728, wherein a first lymphodepletion regimen is to be administered to the subject prior to administration of the at least one dose.

39-30. The use of claim 3829, wherein in the first lymphodepletion regimen fludarabine and cyclophosphamide are to be administered.

40-31. The use of claim 3829, wherein in the first lymphodepletion regimen fludarabine, cyclophosphamide, and an anti-CD52 antibody are to be administered.

25 41-32. The use of claim 3829, wherein in the first lymphodepletion regimen an anti-CD52 antibody is to be administered.

42-33. The use of claim 3829, wherein in the first lymphodepletion regimen only an anti-CD52 antibody is to be administered.

43-34. The use of claim 3829, wherein fludarabine is to be administered at a dosage of about

30 mg/m²/day; cyclophosphamide is to be administered at a dosage of about 300 mg/m²/day; and the anti-CD52 antibody is to be administered at a dosage of about 10 to about 13 mg/day.

44.35. The use of claim 4031, wherein fludarabine is to be administered at a dosage of about 30 mg/m²/day; cyclophosphamide is to be administered at a dosage of about 300 mg/m²/day; and the anti-CD52 antibody is to be administered at a dosage of about 13 to about 30 mg/day, about 13 to 20 mg/day, about 13 to 30 mg/day, or about 20 to 30 mg/day.

45.36. The use of claim 4435, wherein the anti-CD52 antibody is to be administered at a dosage of about 13 mg/day, about 20 mg/day or about 30 mg/day.

46.37. The use of any one of claims 38-29 to 4536, wherein the first lymphodepletion regimen is to be initiated between about 1 to 15 days prior to administration of the at least one dose.

47.38. The use of any one of claims 38-29 to 4637, wherein the first lymphodepletion regimen is to be administered over the course of 1, 2, 3, 4, or 5 days.

48.39. The use of any one of claims 3627 to -4738, wherein the first lymphodepletion regimen is to be administered 5 days prior to administration of the at least one dose in the course of 3 days.

49.40. The use of any one of claims 1 to 4839, wherein a subsequent dose of the CAR-T cells is to be administered to the subject.

50.41. A formulation comprising BCMA CAR-T cells, wherein the cells are formulated in a solution comprising about 5% dimethyl sulfoxide, wherein the dosage strength of the formulation is 14×10^6 cells /mL, wherein the genotype of the cells is BCMA-CAR+_TCR $\alpha\beta$ -CD52+/-, and wherein the BCMA CAR-T cells comprise a CAR comprising an extracellular ligand-binding domain, two CD20 epitope rituximab-binding domains (SEQ ID NO: 397), a first transmembrane domain, and an intracellular signaling domain, wherein the extracellular domain comprises a scFv comprising a sequence: a heavy chain variable (VH) region comprising a sequence shown in SEQ ID NO: 33 of Table 1 and a light chain variable (VL) region comprising a sequence shown in SEQ ID NO: 34 of Table 1, a VH region comprising a sequence shown in SEQ ID NO: 72 of Table 1 and a VL region comprising a sequence shown in SEQ ID NO: 73 of Table 1, a VH region comprising a sequence shown in SEQ ID NO: 39 of Table 1 and a VL region comprising a sequence shown in SEQ ID NO: 40 of Table 1, a VH region comprising a sequence shown in SEQ ID NO: 76 of Table 1 and a VL region comprising a sequence shown in SEQ ID NO: 77 of Table 1, a

VH region comprising a sequence shown in SEQ ID NO: 83 of Table 1 and a VL region comprising a sequence shown in SEQ ID NO: 84 of Table 1, a VH region comprising a sequence shown in SEQ ID NO: 92 of Table 1 and a VL region comprising a sequence shown in SEQ ID NO: 93 of Table 1, a VH region comprising a sequence shown in SEQ ID NO: 25 of Table 1 and a VL region comprising a sequence shown in SEQ ID NO: 18 of Table 1, a VH region comprising a sequence shown in SEQ ID NO: 112 of Table 1 and a VL region comprising a sequence shown in SEQ ID NO: 38 of Table 1, or a VH region comprising a sequence shown in SEQ ID NO: 8 of Table 1 and a VL region comprising a sequence shown in SEQ ID NO: 80 of Table 1; ~~a heavy chain variable (VH) region comprising a sequence shown in SEQ ID NO: 33, 72, 39, 76, 83, 92, 25, 112, or 8 of Table 1; and a light chain variable (VL) region comprising a sequence shown in SEQ ID NO: 34, 73, 40, 77, 84, 93, 18, 38, or 80 of Table 1,~~ wherein the first transmembrane domain comprises a CD8 α chain transmembrane domain, and wherein the intracellular signaling domain comprises a CD3 ζ signaling domain and/or a 4-1BB signaling domain.

51.42. A formulation comprising BCMA CAR-T cells, wherein the cells are formulated in a 1:1 mixture of CryoStor® Basal Solution and CryoStor® CS10 resulting in a 5% final concentration of dimethyl sulfoxide, wherein the dosage strength of the formulation is 14×10^6 cells /mL, wherein the genotype of the cells is BCMA-CAR+ _TCR $\alpha\beta$ - _CD52+/-, and wherein the BCMA CAR-T cells comprise a CAR comprising an extracellular ligand-binding domain, two CD20 epitope rituximab-binding domains (SEQ ID NO: 397), a first transmembrane domain, and an intracellular signaling domain, wherein the extracellular domain comprises a scFv comprising a sequence: a heavy chain variable (VH) region comprising a sequence shown in SEQ ID NO: 33 of Table 1 and a light chain variable (VL) region comprising a sequence shown in SEQ ID NO: 34 of Table 1, a VH region comprising a sequence shown in SEQ ID NO: 72 of Table 1 and a VL region comprising a sequence shown in SEQ ID NO: 73 of Table 1, a VH region comprising a sequence shown in SEQ ID NO: 39 of Table 1 and a VL region comprising a sequence shown in SEQ ID NO: 40 of Table 1, a VH region comprising a sequence shown in SEQ ID NO: 76 of Table 1 and a VL region comprising a sequence shown in SEQ ID NO: 77 of Table 1, a VH region comprising a sequence shown in SEQ ID NO: 83 of Table 1 and a VL region comprising a sequence shown in SEQ ID NO: 84 of Table 1, a VH region comprising a sequence shown in SEQ ID NO: 92 of Table 1 and a VL region comprising a sequence shown in SEQ ID NO: 93 of Table 1, a VH region comprising a sequence shown in SEQ ID NO: 25 of Table 1 and a VL region

comprising a sequence shown in SEQ ID NO: 18 of Table 1, a VH region comprising a sequence shown in SEQ ID NO: 112 of Table 1 and a VL region comprising a sequence shown in SEQ ID NO: 38 of Table 1, or a VH region comprising a sequence shown in SEQ ID NO: 8 of Table 1 and a VL region comprising a sequence shown in SEQ ID NO: 80 of Table 1;
5 a heavy chain variable (VH) region comprising a sequence shown in SEQ ID NO: 33, 72, 39, 76, 83, 92, 25, 112, or 8 of Table 1; and a light chain variable (VL) region comprising a sequence shown in SEQ ID NO: 34, 73, 40, 77, 84, 93, 18, 38, or 80 of Table 1,
wherein the first transmembrane domain comprises a CD8 α chain transmembrane domain, and wherein the intracellular signaling domain comprises a CD3 ζ signaling domain and/or a
10 4-1BB signaling domain.

43. The formulation of claim 41 or 42, wherein the two CD20 epitope domains are provided as the amino acid sequence shown in SEQ ID NO: 398.