

[0027] Examples of the disclosure relate to a method of inhibiting the growth of a tumor expressing a cancer or tumor antigen, by contacting the tumor with an effective amount of the isolated cells or compositions disclosed above. The contacting can be *in vitro* or *in vivo*. When the contacting is *in vitro*, the method can be used to test personalized therapy against a patient's tumor or to assay for combination therapies. When the contacting is *in vivo*, the method is useful to inhibit the growth of the tumor or cancer cell in a subject in need thereof, such as a human patient suffering from cancer and the patient receives an effective amount of the cells. In certain examples, the tumor is a solid tumor. An effective amount is administered alone or in combination with other therapies as described herein. In certain examples, the cancer/tumor targeted is a solid tumor or a cancer affecting the blood and/or bone marrow, e.g., multiple myeloma (MM). In certain examples the isolated cells are autologous to the subject being treated. In another example, the cells are allogeneic to the subject being treated. In another example, the method further comprises, or consists essentially of, or yet further consists of, administering to the subject an effective amount of a cytoreductive therapy. In a further example, the method further comprises the steps of isolating the cells to be administered to the subject, transducing the cells with an effective amount of an isolated nucleic acid encoding a CAR or BsAb-CAR as described herein, culturing the cells to obtain a population of CAR or BsAb-CAR encoding cells, that are optionally expanded and activated and then administering the cells to the patient.

[0027a] In another aspect, the present disclosure refers to an *in vitro* method of inhibiting the growth of a cancer cell or tumor expressing a cancer or tumor antigen, comprising contacting the cancer cell or tumor with the isolated cell as disclosed herein, wherein the isolated cell is a T cell and wherein the cancer cell or tumor antigen comprises BCMA or SLAMF7.

[0027b] In another aspect, the present disclosure refers to use of an isolated cell as disclosed herein in the manufacture of a medicament for inhibiting the growth of a cancer cell or tumor expressing a cancer or tumor antigen in a subject, wherein the isolated cell is a T cell and wherein the cancer cell or tumor antigen comprises BCMA or SLAMF7.

[0028] Also disclosed herein are kits comprising one or more of the above noted compositions and instructions for their use in the methods as disclosed herein.

[0028a] In another aspect, the present disclosure refers to a kit comprising a composition as disclosed herein and optionally, instructions for use.

[0029] The above compositions and methods are unique and overcome the limitation of the state of the art in that they provide a CAR cell that simultaneously secretes a NKG2D-based BsAb targeting a second tumor-associated antigen. The disclosed CAR NKG2D-based BsAb is exemplary only. This approach can be modified for any number of tumor antigens, as known in the art, e.g., EGFRVIII; CD70, mesothelin, CD123, CD19, CEA, CD133, Her2, see Townsend et al. (2018) J. Exp. & Clinical Cancer Res. 37:163.

[0030] The exemplary constructs were tested in a multiple myeloma model (MM). MM is a malignancy characterized by an accumulation of clonal plasma cells¹³. As noted above, current treatment regimens including chemotherapies, immunomodulatory drugs¹⁴, monoclonal antibodies¹⁵, and autologous or allogeneic transplantation often lead to remission, but nearly all patients eventually relapse and succumb to death due to return of

WHAT IS CLAIMED IS:

1. An isolated nucleic acid comprising:

a polynucleotide encoding a chimeric antigen receptor (CAR) comprising: (a) an antigen binding domain that targets B-cell maturation antigen (BCMA); (b) a hinge domain; (c) a transmembrane domain; (d) and an intracellular domain; and

a polynucleotide encoding a bispecific antibody comprising an antigen binding domain that recognizes and binds NKG2D and an antigen binding domain that recognizes and binds SLAMF7.

2. The isolated nucleic acid of claim 1, wherein the hinge domain comprises a CD8 α hinge domain.

3. The isolated nucleic acid of claim 1 or 2, wherein the transmembrane domain comprises a CD8 α transmembrane domain.

4. The isolated nucleic acid of any one of claims 1-3, wherein the intracellular domain comprises a CD28 costimulatory signaling region or a 4-1BB costimulatory signaling region; and a CD3 zeta signaling domain.

5. The isolated nucleic acid of any one of claims 1 to 4, wherein the antigen binding domain that recognizes and binds NKG2D comprises three complementarity determining regions (CDRs)

~~of SEQ ID NO: 27~~ of an anti-NKG2D heavy chain encoded by:

CAAGTGCAGC TGGTTGAATC CGGTGGCGGT CTGGTCAAGC CGGGCGGCTC
TTTGCGTCTG AGCTGTGCCG CGTCGGGTTT TACCTTCAGC TCTTATGGTA
TGCATTGGGT GCGTCAGGCG CCTGGCAAAG GTCTGGAGTG GGTTCGTTT
ATCCGCTACG ATGGGTCTAA CAAATATTAT GCCGACTCAG TAAAAGGACG
CTTCACTATT AGCCGCGACA ATAGCAAAAA TACCCTGTAC CTGCAAATGA
ATAGCCTGCG CGCCGAAGAT ACCGCCGTTT ACTATTGCGC TAAAGATCGT
GGCCTGGGTG ATGGTACGTA CTTGATTAC TGGGGTCAGG GCACCACCGT
TACCGTTAGT TCA,

and three CDRs ~~of SEQ ID NO: 28~~ of anti-NKG2D light chain encoded by:

CAGTCAGCGC TTACGCAGCC GCGGTCGGTG TCGGGTCCC CGGGTCAGTC
GATCACGATC AGCTGTAGTG GGAGCAGCTC CAACATCGGT AACAACGCAG
TGAACTGGTA TCAGCAACTG CCGGGAAAAG CGCCGAAACT GCTGATTTAC
TATGATGATT TGCTGCCAAG TGGAGTTAGT GACCGCTTTT CCGGCAGTAA
5 ATCGGGTACC TCGGCTTTTC TGGCTATTTC GGGTCTCCAG AGCGAGGATG
AAGCTGATTA TTATTGCGCC GCATGGGATG ATAGCTTAAA TGGCCCAGTT
TTTGGCGGCG GTACTAAACT GACCGTGCTG, or three CDRs ~~of SEQ ID NO: of anti-~~
NKG2D heavy chain encoded 30~~encoded by:~~

CAAGTGCAGCTGGTTGAATCCGGTGGCGGTCTGGTCAAGCCGGGCGGCTCTTTGCGT
10 CTGAGCTGTGCCGCGTCGGGTTTTACCTTCAGCTCTTATGGTATGCATTGGGTGCGTC
AGGCGCCTGGCAAAGGTCTGGAGTGGGTTCGTTTCATCCGCTACGATGGGTCTAACA
AATATTATGCCGACTCAGTAAAAGGACGCTTCACTATTAGCCGCGACAATAGCAAA
AATACCCTGTACCTGCAAATGAATAGCCTGCGCGCCGAAGATAACCGCCGTTTACTAT
TGCGCTAAAGATCGTGGCCTGGGTGATGGTACGTACTTCGATTACTGGGGTCAGGGC
15 ACCACCGTTACCGTTAGTTCAGGTGGGGGCGGCTCT and three CDRs ~~of SEQ ID NO: of~~
anti-NKG2D light chain encoded 31~~encoded by:~~

CAGCGCTTACGCAGCCGGCGTCGGTGTCGGGTCCCCGGGTCAGTCGATCACGATCA
GCTGTAGTGGGAGCAGCTCCAACATCGGTAACAACGCAGTGAAGTGGTATCAGCAA
CTGCCGGGAAAAGCGCCGAAACTGCTGATTTACTATGATGATTTGCTGCCAAGTGGA
20 GTTAGTGACCGCTTTTCCGGCAGTAAATCGGGTACCTCGGCTTTTCTGGCTATTTCCG
GTCTCCAGAGCGAGGATGAAGCTGATTATTATTGCGCCGCATGGGATGATAGCTTAA
ATGGCCCAGTTTTTGGCGGCGGTACTAAACTGACCGTGCTG.

6. The isolated nucleic acid of claim 5, wherein the antigen binding domain that recognizes and binds NKG2D comprises:

25 a heavy chain variable region comprising the amino acid sequence ~~of SEQ ID NO:~~
27~~encoded by:~~

CAAGTGCAGC TGGTTGAATC CGGTGGCGGT CTGGTCAAGC CGGGCGGCTC
TTTGCGTCTG AGCTGTGCCG CGTCGGGTTT TACCTTCAGC TCTTATGGTA

TGCATTGGGT GCGTCAGGCG CCTGGCAAAG GTCTGGAGTG GGTTCGCTTC
ATCCGCTACG ATGGGTCTAA CAAATATTAT GCCGACTCAG TAAAAGGACG
CTTCACTATT AGCCGCGACA ATAGCAAAAA TACCCTGTAC CTGCAAATGA
ATAGCCTGCG CGCCGAAGAT ACCGCCGTTT ACTATTGCGC TAAAGATCGT
5 GGCCTGGGTG ATGGTACGTA CTTGATTAC TGGGGTCAGG GCACCACCGT
TACCGTTAGT TCA,

and a light chain variable region comprising the amino acid sequence ~~of SEQ ID NO:~~
~~28~~encoded by:

CAGTCAGCGC TTACGCAGCC GCGTCGGTG TCGGGTTCCTT CGGGTCAGTC
10 GATCACGATC AGCTGTAGTG GGAGCAGCTC CAACATCGGT AACAACGCAG
TGAACTGGTA TCAGCAACTG CCGGGAAAAG CGCCGAAACT GCTGATTAC
TATGATGATT TGCTGCCAAG TGGAGTTAGT GACCGCTTTT CCGGCAGTAA
ATCGGGTACC TCGGCTTTTC TGGCTATTTC GGGTCTCCAG AGCGAGGATG
AAGCTGATTA TTATTGCGCC GCATGGGATG ATAGCTTAAA TGGCCAGTT
15 TTTGGCGGCG GTACTAAACT GACCGTGCTG; or

a heavy chain variable region comprising the amino acid sequence ~~of SEQ ID NO:~~
~~30~~encoded by:

CAAGTGCAGCTGGTTGAATCCGGTGGCGGTCTGGTCAAGCCGGGCGGCTCTT
TGCGTCTGAGCTGTGCCGCGTCGGGTTTTACCTTCAGCTCTTATGGTATGCATTGGGT
20 GCGTCAGGCGCCTGGCAAAGGTCTGGAGTGGGTTCGTTTCATCCGCTACGATGGGTC
TAACAAATATTATGCCGACTCAGTAAAAGGACGCTTCACTATTAGCCGCGACAATAG
CAAAAATACCCTGTACCTGCAAATGAATAGCCTGCGCGCCGAAGATACCGCCGTTT
ACTATTGCGCTAAAGATCGTGGCCTGGGTGATGGTACGTACTTCGATTACTGGGGTC
AGGGCACCAACGTTACCGTTAGTTCAGGTGGGGGCGGCTCT, and a light chain variable

25 region comprising the amino acid sequence ~~of SEQ ID NO:~~ ~~31~~encoded by:

CAGCGCTTACGCAGCCGGCGTCGGTGTCGGGTTCCTCGGGTCAGTCGATCAC
GATCAGCTGTAGTGGGAGCAGCTCCAACATCGGTAACAACGCAGTGAACCTGGTATC
AGCAACTGCCGGGAAAAGCGCCGAAACTGCTGATTACTATGATGATTTGCTGCCAA

GTGGAGTTAGTGACCGCTTTTCCGGCAGTAAATCGGGTACCTCGGCTTTTCTGGCTA
TTTCGGGTCTCCAGAGCGAGGATGAAGCTGATTATTATTGCGCCGCATGGGATGATA
GCTTAAATGGCCCAGTTTTTGGCGGCGGTACTAAACTGACCGTGCTG;or

an equivalent of each thereof, wherein an equivalent of a peptide has at least 90% amino acid identity to the peptide.

7. The isolated nucleic acid of any one of claims 1-6, wherein the antigen binding domain that recognizes and binds NKG2D comprises:

a heavy chain variable region comprising the amino acid sequence ~~of SEQ ID NO: 27~~ encoded by:

CAAGTGCAGC TGGTTGAATC CGGTGGCGGT CTGGTCAAGC CGGGCGGCTC
TTTGCGTCTG AGCTGTGCCG CGTCGGGTTT TACCTTCAGC TCTTATGGTA
TGCATTGGGT GCGTCAGGCG CCTGGCAAAG GTCTGGAGTG GGTTCGTTT
ATCCGCTACG ATGGGTCTAA CAAATATTAT GCCGACTCAG TAAAAGGACG
CTTCACTATT AGCCGCGACA ATAGCAAAAA TACCCTGTAC CTGCAAATGA
ATAGCCTGCG CGCCGAAGAT ACCGCCGTTT ACTATTGCGC TAAAGATCGT
GGCCTGGGTG ATGGTACGTA CTTCGATTAC TGGGGTCAGG GCACCACCGT
TACCGTTAGT TCA, and a light chain variable region comprising the amino acid sequence ~~of~~

~~SEQ ID NO: 28~~ encoded by:

CAGTCAGCGC TTACGCAGCC GCGTCGGTG TCGGGTTCCC CGGGTCAGTC
GATCACGATC AGCTGTAGTG GGAGCAGCTC CAACATCGGT AACAAACGCAG
TGAAGTGGTA TCAGCAACTG CCGGGAAAAG CGCCGAAACT GCTGATTTAC
TATGATGATT TGCTGCCAAG TGGAGTTAGT GACCGCTTTT CCGGCAGTAA
ATCGGGTACC TCGGCTTTTC TGGCTATTTT GGGTCTCCAG AGCGAGGATG
AAGCTGATTA TTATTGCGCC GCATGGGATG ATAGCTTAAA TGGCCCAGTT
TTTGGCGGCG GTACTAAACT GACCGTGCTG; or

a heavy chain variable region comprising the amino acid sequence ~~of SEQ ID NO: 30~~ encoded by:

CAAGTGCAGCTGGTTGAATCCGGTGGCGGTCTGGTCAAGCCGGGCGGCTCTT
TGCGTCTGAGCTGTGCCGCGTCGGGTTTTACCTTCAGCTCTTATGGTATGCATTGGGT
GCGTCAGGCGCCTGGCAAAGGTCTGGAGTGGGTTCGTTTCATCCGCTACGATGGGTC

TAACAAATATTATGCCGACTCAGTAAAAGGACGCTTCACTATTAGCCGCGACAATAG
CAAAAATACCCTGTACCTGCAAATGAATAGCCTGCGCGCCGAAGATACCGCCGTTT
ACTATTGCGCTAAAGATCGTGGCCTGGGTGATGGTACGTACTTCGATTACTGGGGTC
AGGGCACCAACCGTTACCGTTAGTTCAGGTGGGGGCGGCTCT, and a light chain variable

region comprising the amino acid sequence ~~of SEQ ID NO: 31~~ encoded by:

CAGCGCTTACGCAGCCGGCGTCGGTGTCTGGGTCCCCGGGTCAGTCGATCAC
GATCAGCTGTAGTGGGAGCAGCTCCAACATCGGTAACAACGCAGTGAAGTGGTATC
AGCAACTGCCGGGAAAAGCGCCGAAACTGCTGATTTACTATGATGATTTGCTGCCAA
GTGGAGTTAGTGACCGCTTTTCCGGCAGTAAATCGGGTACCTCGGCTTTTCTGGCTA
TTTCGGGTCTCCAGAGCGAGGATGAAGCTGATTATTATTGCGCCGCATGGGATGATA
GCTTAAATGGCCAGTTTTTGGCGGCGGTACTAAACTGACCGTGCTG.

8. The isolated nucleic acid of any one of claims 1-7, wherein the antigen binding domain that recognizes and binds SLAMF7 comprises three CDRs ~~of SEQ ID NO: 25~~ encoded by:

AGCGTTACCG TGAGTACAGG CCAGGGCTGG TATGACATGG CACGTACAGC
CATCATGACC TCGCGCGCAT GTTACTACGT CGCGTCAGAT GAATCGACGC
CTTCCTCGCT GCAAATGTAT GCAACCTCCA GCAGCAAAGA TGTTACCCTG
ACCGCAAAGG ACAAGTTTAA ACAGAATTTG CGTACGGAGA GTGACTCCCC
GCACATCATG GGAATCTGGG AGTTGGGTCA GGGGCCTCGT CAGAAGGTAT
GGAACATGTG GTATACAACT TTTTCGTACG GCTCAGCAA ATGCAGCTTG
AAAGTGTCGG CAGGTCCGCG CGTGCTGGAG GCCGGTCCGC AGCAGCTGCA
AGTCCAGTCT, and three CDRs ~~of SEQ ID NO: 26~~ encoded by:

AAACTTGAGT TGAAGACCGG TGCCGGCTTC ACCTTACCGA CCAGTTATCA
TCAACAATGC TATTACGTGG CCCTGGACGA AGCACAGGTG AATTCAATTA
CGTTTACGTT TGATACCGGC TCTGGCAGCG GTACATTTTCG TGATCCCGTG
GGCACTTACC GCTATTCGGC GAGTTATATC TTGCTGAAAC CTTCCCAAGG
TCCGAAACAG CAGTACTGGG CGGTTGGCAC CATTGTAGAC CAATCAGCCA
AATGTACAAT CTCGGTTCGC GATGGTGTCA GTACGTCGAT GTCTAAGCAG
TCACAGACAA TGGTTATCGA T or three CDRs ~~of SEQ ID NO: 33~~ encoded by:

CTCCGTGACGGTGTGCGACGGGCCAAGGATGGTACGATATGGCACGGACCGCGATTA
TGACATCGCGGGCGTGCTATTACGTGGCCAGCGATGAGTCGACCCCTTCCTCTCTGC
AAATGTATGCCACCTCCTCTTCAAAAGACGTGACTCTGACTGCGAAAGACAAATTTA
AACAGAATCTGCGCACCGAAAGCGATAGCCACATATCATGGGCATCTGGGAACTG
5 GGCCAGGGCCCCCGCCAGAAAGTGTGGAACATGTGGTACACCACCTTCAGCTATGG
TTCGGCCAAATGTTCCCTGAAGGTATCAGCCGGCCCCGCGCGTTCTTGAGGCGGGTCC
GCAGCAGCTGCAGGTACAGAGC, and three CDRs of ~~SEQ ID NO: 34~~ encoded by:
AAACTGGAActCAAGACGGGTGCGGGATTTACCCTCCCTACGAGCTATCACCAGCA
GTGCTATTACGTGGCGCTTGACGAAGCGCAGGTGAACTCTATTACCTTTACCTTTGA
10 TACAGGATCAGGCAGCGGTACGTTCCGTGATCCGGTAGGTACGTACCGGTATAGTGC
AAGCTATATCCTTCTGAAACCTTCTCAGGGTCCGAAACAGCAGTACTGGGCGGTGGG
AACGATCGTGACCAGTCTGCCAAATGTACAATTTCAGTTGCGGACGGAGTTAGCAC
CTCCATGAGCAAGCAGTCCCAAACCATGGTGATTGACTC.

9. The isolated nucleic acid of any one of claims 1-8, wherein the antigen binding domain that recognizes and binds SLAMF7 comprises:

a heavy chain variable region comprising the amino acid sequence ~~of SEQ ID NO: 25~~ encoded by:

AGCGTTACCG TGAGTACAGG CCAGGGCTGG TATGACATGG CACGTACAGC
20 CATCATGACC TCGCGCGCAT GTTACTACGT CGCGTCAGAT GAATCGACGC
CTTCCTCGCT GCAAATGTAT GCAACCTCCA GCAGCAAAGA TGTTACCCTG
ACCGCAAAGG ACAAGTTTAA ACAGAATTTG CGTACGGAGA GTGACTCCCC
GCACATCATG GGAATCTGGG AGTTGGGTCA GGGGCCTCGT CAGAAGGTAT
GGAACATGTG GTATACAACT TTTTCGTACG GCTCAGCAA ATGCAGCTTG
25 AAAGTGTCGG CAGGTCCGCG CGTGCTGGAG GCCGGTCCGC AGCAGCTGCA
AGTCCAGTCT, and a light chain variable region comprising the amino acid sequence ~~of SEQ ID NO: 26~~ encoded by:

AAACTTGAGT TGAAGACCGG TGCCGGCTTC ACCTTACCGA CCAGTTATCA
TCAACAATGC TATTACGTGG CCCTGGACGA AGCACAGGTG AATTCAATTA
30 CGTTTACGTT TGATACCGGC TCTGGCAGCG GTACATTTTCG TGATCCCGTG

GGCACTTACC GCTATTCGGC GAGTTATATC TTGCTGAAAC CTTCCCAAGG
TCCGAAACAG CAGTACTGGG CGGTTGGCAC CATTGTAGAC CAATCAGCCA
AATGTACAAT CTCGGTTCGC GATGGTGTCA GTACGTCGAT GTCTAAGCAG
TCACAGACAA TGGTTATCGA T; or

5 a heavy chain variable region comprising the amino acid sequence ~~of SEQ ID NO:~~
~~33~~encoded by:

CTCCGTGACGGTGTGACGGGCCAAGGATGGTACGATATGGCACGGACCGCG
ATTATGACATCGCGGGCGTGCTATTACGTGGCCAGCGATGAGTCGACCCCTTCCTCT
CTGCAAATGTATGCCACCTCCTCTTCAAAAGACGTGACTCTGACTGCGAAAGACAAA
10 TTTAAACAGAATCTGCGCACCGAAAGCGATAGCCACATATCATGGGCATCTGGGA
ACTGGGCCAGGGCCCCCGCCAGAAAGTGTGGAACATGTGGTACACCACCTTCAGCT
ATGGTTCGGCCAAATGTTCCCTGAAGGTATCAGCCGGCCCGCGCGTTCTTGAGGCGG
GTCCGCAGCAGCTGCAGGTACAGAGC, and a light chain variable region comprising the
amino acid sequence ~~of SEQ ID NO:~~ ~~34~~encoded by:

15 AAACTGGAActCAAGACGGGTGCGGGATTTACCCTCCCTACGAGCTATCACC
AGCAGTGCTATTACGTGGCGCTTGACGAAGCGCAGGTGAACTCTATTACCTTTACCT
TTGATACAGGATCAGGCAGCGGTACGTTCCGTGATCCGGTAGGTACGTACCGGTATA
GTGCAAGCTATATCCTTCTGAAACCTTCTCAGGGTCCGAAACAGCAGTACTGGGCGG
TGGGAACGATCGTGACAGTCTGCCAAATGTACAATTTAGTTTCGCGACGGAGTTA
20 GCACCTCCATGAGCAAGCAGTCCCAAACCATGGTGATTGACTCT; or

an equivalent of each thereof, wherein an equivalent of a peptide has at least 90% amino
acid identity to the peptide.

10. The isolated nucleic acid of any one of claims 1-9, wherein the antigen binding domain
25 that recognizes and binds SLAMF7 comprises:

a heavy chain variable region comprising the amino acid sequence ~~of SEQ ID NO:~~
~~25~~encoded by:

AGCGTTACCG TGAGTACAGG CCAGGGCTGG TATGACATGG CACGTACAGC
CATCATGACC TCGCGCGCAT GTTACTACGT CGCGTCAGAT GAATCGACGC
30 CTTCCTCGCT GCAAATGTAT GCAACCTCCA GCAGCAAAGA TGTTACCCTG

ACCGCAAAGG ACAAGTTTAA ACAGAATTTG CGTACGGAGA GTGACTCCCC
GCACATCATG GGAATCTGGG AGTTGGGTCA GGGGCCTCGT CAGAAGGTAT
GGAACATGTG GTATACAACT TTTTCGTACG GCTCAGCAAA ATGCAGCTTG
AAAGTGTCGG CAGGTCCGCG CGTGCTGGAG GCCGGTCCGC AGCAGCTGCA

5 AGTCCAGTCT and a light chain variable region comprising the amino acid sequence ~~of SEQ~~
~~ID NO: 26~~ encoded by:

AAACTTGAGT TGAAGACCGG TGCCGGCTTC ACCTTACCGA CCAGTTATCA
TCAACAATGC TATTACGTGG CCCTGGACGA AGCACAGGTG AATTCAATTA
CGTTTACGTT TGATACCGGC TCTGGCAGCG GTACATTTTCG TGATCCCGTG
10 GGCACTTACC GCTATTCGGC GAGTTATATC TTGCTGAAAC CTTCCCAAGG
TCCGAAACAG CAGTACTGGG CGGTTGGCAC CATTGTAGAC CAATCAGCCA
AATGTACAAT CTCGGTTCGC GATGGTGTCA GTACGTCGAT GTCTAAGCAG
TCACAGACAA TGGTTATCGA T; or

a heavy chain variable region comprising the amino acid sequence ~~of SEQ ID NO:~~
15 ~~33~~ encoded by:

CTCCGTGACGGTGTCGACGGGCCAAGGATGGTACGATATGGCACGGACCGCG
ATTATGACATCGCGGGCGTGCTATTACGTGGCCAGCGATGAGTCGACCCCTTCCTCT
CTGCAAATGTATGCCACCTCCTCTTCAAAAGACGTGACTCTGACTGCGAAAGACAAA
TTTAAACAGAATCTGCGCACCGAAAGCGATAGCCCACATATCATGGGCATCTGGGA
20 ACTGGGCCAGGGCCCCCGCCAGAAAGTGTGGAACATGTGGTACACCACCTTCAGCT
ATGGTTCGGCCAAATGTTCCCTGAAGGTATCAGCCGGCCCGCGCGTTCTTGAGGCGG
GTCCGCAGCAGCTGCAGGTACAGAGC, and a light chain variable region comprising the

amino acid sequence ~~of SEQ ID NO: 34~~ encoded by:

AAACTGGAActCAAGACGGGTGCGGGATTTACCCTCCCTACGAGCTATCACC
25 AGCAGTGCTATTACGTGGCGCTTGACGAAGCGCAGGTGAACTCTATTACCTTTACCT
TTGATACAGGATCAGGCAGCGGTACGTTCCGTGATCCGGTAGGTACGTACCGGTATA
GTGCAAGCTATATCCTTCTGAAACCTTCTCAGGGTCCGAAACAGCAGTACTGGGCGG
TGGGAACGATCGTGGACCAGTCTGCCAAATGTACAATTTTCAGTTCGCGACGGAGTTA
GCACCTCCATGAGCAAGCAGTCCCAAACCATGGTGATTGACTCT.

30

11. The isolated nucleic acid of any one of claims 1-10, wherein the antigen binding domain that recognizes and binds NKG2D is a single chain variable fragment (scFV) and the antigen binding domain that recognizes and binds SLAMF7 is a single chain variable fragment (scFv).

12. The isolated nucleic acid of any one of claims 1-11, wherein the antigen binding domain that targets BCMA comprises three CDRs ~~of SEQ ID NO: 21~~ encoded by:

ATGGGATGGAGCTCTATCATCCTCTTCTTGGTAGCAACAGCTACAGGTGTCCACCAG
ATTCAGCTGGTGCAGAGCGGCCCTGAGCTGAAGAAACCCGGCGAGACAGTGAAGAT
CAGCTGCAAGGCCTCCGGCTACACCTTCCGGCACTACAGCATGAACTGGGTGAAAC
AGGCCCTGGCAAGGGCCTGAAGTGGATGGGCCGGATCAACACCGAGAGCGGCGTG
CCCATCTACGCCGACGACTTCAAGGGCAGATTTCGCCTTCAGCGTGGAACACGCGC
CAGCACCGCCTACCTGGTGATCAACAACCTGAAGGACGAGGATACCGCCAGCTACT
TCTGCAGCAACGACTACCTGTACAGCCTGGACTTCTGGGGCCAGGGCACCGCCCTGA
CCGTGTCCAGC, and three CDRs ~~of SEQ ID NO: 22~~ encoded by:

GACATCGTGCTGACCCAGAGCCCCCCCAGCCTGGCCATGTCTCTGGGCAAGAGAGC
CACCATCAGCTGCCGGGCCAGCGAGAGCGTGACCATCCTGGGCAGCCACCTGATCT
ACTGGTATCAGCAGAAGCCTGGCCAGCCCCCCCACCCTGCTGATCCAGCTGGCTAGCA
ATGTGCAGACCGGCGTGCCCGCCAGATTCAGCGGCAGCGGCAGCAGAACCGACTTC
ACCCTGACCATCGACCCCGTGGAAGAGGACGACGTGGCCGTGTACTACTGCCTGCA
GAGCCGGACCATCCCCGGACCTTTGGCGGAGGAACAAAGCTGGAAATCAAG, three
CDRs ~~of SEQ ID NO: 23~~ encoded by:

ATGGGATGGAGCTCTATCATCCTCTTCTTGGTAGCAACAGCTACAGGTGTCCACCAG
ATTCAGCTGGTGCAGAGCGGCCCTGAGCTGAAGAAACCCGGCGAGACAGTGAAGAT
CAGCTGCAAGGCCTCCGGCTACACCTTCACCGACTACAGCATCAACTGGGTGAAAA
GAGCCCCTGGCAAGGGCCTGAAGTGGATGGGCTGGATCAACACCGAGACAAGAGA
GCCCGCCTACGCCTACGACTTCCGGGGCAGATTTCGCCTTCAGCCTGGAAACGAGCGC
CAGCACCGCCTACCTGCAGATCAACAACCTGAAGTACGAGGACACCGCCACCTACT
TTTGCGCCCTGGACTACAGCTACGCCATGGACTACTGGGGCCAGGGCACCGCGTG
ACCGTGTCCAGC, and three CDRs ~~of SEQ ID NO: 24~~ encoded by:

GACATCGTGCTGACCCAGAGCCCCCCCAGCCTGGCCATGTCTCTGGGCAAGAGAGC
CACCATCAGCTGCCGGGCCAGCGAGAGCGTGACCATCCTGGGCAGCCACCTGATCC
ACTGGTATCAGCAGAAGCCCGGCCAGCCCCCACCCTGCTGATCCAGCTCGCCAGC
AATGTGCAGACCGGCGTGCCCGCCAGATTCAGCGGCAGCGGCAGCAGAACCGACTT
5 CACCCTGACCATCGACCCCGTGGAAGAGGACGACGTGGCCGTGTACTACTGCCTGC
AGAGCCGGACCATCCCCGGACCTTTGGCGGAGGCACCAAACCTGGAAATCAAG, or

three CDRs ~~of SEQ ID NO: 20~~ encoded by:

CAGATTCAGCTGGTGCAGAGCGGCCCTGAGCTGAAGAAACCCGGCGAGACAGTGAA
GATCAGCTGCAAGGCCTCCGGCTACACCTTCACCGACTACAGCATCAACTGGGTGA
10 AAAGAGCCCCTGGCAAGGGCCTGAAGTGGATGGGCTGGATCAACACCGAGACAAG
AGAGCCCGCCTACGCCTACGACTTCCGGGGCAGATTGCCTTCAGCCTGGAAACCA
GCGCCAGCACCGCCTACCTGCAGATCAACAACCTGAAGTACGAGGACACCGCCACC
TACTTTTGCGCCCTGGACTACAGCTACGCCATGGACTACTGGGGCCAGGGCACCAGC
GTGACCGTGTCCAGC, and three CDRs ~~of SEQ ID NO: 24~~ encoded by:

15 GACATCGTGCTGACCCAGAGCCCCCCCAGCCTGGCCATGTCTCTGGGCAAGAGAGC
CACCATCAGCTGCCGGGCCAGCGAGAGCGTGACCATCCTGGGCAGCCACCTGATCC
ACTGGTATCAGCAGAAGCCCGGCCAGCCCCCACCCTGCTGATCCAGCTCGCCAGC
AATGTGCAGACCGGCGTGCCCGCCAGATTCAGCGGCAGCGGCAGCAGAACCGACTT
CACCCTGACCATCGACCCCGTGGAAGAGGACGACGTGGCCGTGTACTACTGCCTGC
20 AGAGCCGGACCATCCCCGGACCTTTGGCGGAGGCACCAAACCTGGAAATCAAG,

13. The isolated nucleic acid of any one of claims 1-12, wherein the antigen binding domain that targets BCMA comprises:

a heavy chain variable region comprising the amino acid sequence ~~of SEQ ID NO:~~

25 ~~24~~ encoded by:

ATGGGATGGAGCTCTATCATCCTCTTCTTGGTAGCAACAGCTACAGGTGTCCA
CCAGATTCAGCTGGTGCAGAGCGGCCCTGAGCTGAAGAAACCCGGCGAGACAGTGA
AGATCAGCTGCAAGGCCTCCGGCTACACCTTCCGGCACTACAGCATGAACTGGGTG
AAACAGGCCCCCTGGCAAGGGCCTGAAGTGGATGGGCCGGATCAACACCGAGAGCG
30 GCGTGCCCATCTACGCCGACGACTTCAAGGGCAGATTCGCCTTCAGCGTGGAACC

AGCGCCAGCACCGCCTACCTGGTGATCAACAACCTGAAGGACGAGGATACCGCCAG
CTACTTCTGCAGCAACGACTACCTGTACAGCCTGGACTTCTGGGGCCAGGGCACCGC
CCTGACCGTGTCCAGC, and a light chain variable region comprising the amino acid

sequence ~~of SEQ ID NO: 22~~ encoded by:

5 GACATCGTGCTGACCCAGAGCCCCCCCAGCCTGGCCATGTCTCTGGGCAAGA
GAGCCACCATCAGCTGCCGGGCCAGCGAGAGCGTGACCATCCTGGGCAGCCACCTG
ATCTACTGGTATCAGCAGAAGCCTGGCCAGCCCCCACCCTGCTGATCCAGCTGGCT
AGCAATGTGCAGACCGGCGTGCCCGCCAGATTCAGCGGCAGCGGCAGCAGAACCGA
CTTCACCCTGACCATCGACCCCGTGGAAGAGGACGACGTGGCCGTGTACTACTGCCT
10 GCAGAGCCGGACCATCCCCCGGACCTTTGGCGGAGGAACAAAGCTGGAAATCAAG;

or

a heavy chain variable region comprising the amino acid sequence ~~of SEQ ID NO:~~
23 encoded by:

15 ATGGGATGGAGCTCTATCATCCTCTTCTTGGTAGCAACAGCTACAGGTGTCCA
CCAGATTCAGCTGGTGCAGAGCGGCCCTGAGCTGAAGAAACCCGGCGAGACAGTGA
AGATCAGCTGCAAGGCCTCCGGCTACACCTTCACCGACTACAGCATCAACTGGGTG
AAAAGAGCCCCTGGCAAGGGCCTGAAGTGGATGGGCTGGATCAACACCGAGACAA
GAGAGCCCGCCTACGCCTACGACTTCCGGGGCAGATTCGCCTTCAGCCTGGAAACC
AGCGCCAGCACCGCCTACCTGCAGATCAACAACCTGAAGTACGAGGACACCGCCAC
20 CTACTTTTGCGCCCTGGACTACAGCTACGCCATGGACTACTGGGGCCAGGGCACCCAG
CGTGACCGTGTCCAGC, and a light chain variable region comprising the amino acid

sequence ~~of SEQ ID NO: 24~~ encoded by:

25 GACATCGTGCTGACCCAGAGCCCCCCCAGCCTGGCCATGTCTCTGGGCAAGA
GAGCCACCATCAGCTGCCGGGCCAGCGAGAGCGTGACCATCCTGGGCAGCCACCTG
ATCCACTGGTATCAGCAGAAGCCCGGCCAGCCCCCACCCTGCTGATCCAGCTCGCC
AGCAATGTGCAGACCGGCGTGCCCGCCAGATTCAGCGGCAGCGGCAGCAGAACCGA
CTTCACCCTGACCATCGACCCCGTGGAAGAGGACGACGTGGCCGTGTACTACTGCCT
GCAGAGCCGGACCATCCCCCGGACCTTTGGCGGAGGCACCAAACCTGGAAATCAAG;

or

a heavy chain variable region comprising the amino acid sequence ~~of SEQ ID NO:~~
20 encoded by:

CAGATTCAGCTGGTGCAGAGCGGCCCTGAGCTGAAGAAACCCGGCGAGACA
GTGAAGATCAGCTGCAAGGCCTCCGGCTACACCTTCACCGACTACAGCATCAACTG
5 GGTGAAGAGAGCCCCCTGGCAAGGGCCTGAAGTGGATGGGCTGGATCAACACCGAGA
CAAGAGAGCCCGCCTACGCCTACGACTTCCGGGGCAGATTCGCCTTCAGCCTGGAA
ACCAGCGCCAGCACCGCCTACCTGCAGATCAACAACCTGAAGTACGAGGACACCGC
CACCTACTTTTGCGCCCTGGACTACAGCTACGCCATGGACTACTGGGGCCAGGGCAC
CAGCGTGACCGTGTCCAGC, and a light chain variable region comprising the amino acid

10 sequence ~~of SEQ ID NO:~~ 24 encoded by:

GACATCGTGCTGACCCAGAGCCCCCCCAGCCTGGCCATGTCTCTGGGCAAGA
GAGCCACCATCAGCTGCCGGGCCAGCGAGAGCGTGACCATCCTGGGCAGCCACCTG
ATCCACTGGTATCAGCAGAAGCCCGGCCAGCCCCCACCCTGCTGATCCAGCTCGCC
AGCAATGTGCAGACCGGCGTGCCCGCCAGATTCAGCGGCAGCGGCAGCAGAACCGA
15 CTTCACCCTGACCATCGACCCCGTGGAAGAGGACGACGTGGCCGTGTACTACTGCCT
GCAGAGCCGGACCATCCCCCGGACCTTTGGCGGAGGCACCAAACCTGGAAATCAAG;

or

an equivalent of each thereof, wherein an equivalent of a peptide has at least 90% amino
acid identity to the peptide.

20 14. The isolated nucleic acid of any one of claims 1-13, wherein the antigen binding domain
that targets BCMA comprises:

a heavy chain variable region comprising the amino acid sequence ~~of SEQ ID NO:~~
24 encoded by:

ATGGGATGGAGCTCTATCATCCTCTTCTTGGTAGCAACAGCTACAGGTGTCCA
CCAGATTCAGCTGGTGCAGAGCGGCCCTGAGCTGAAGAAACCCGGCGAGACAGTGA
25 AGATCAGCTGCAAGGCCTCCGGCTACACCTTCCGGCACTACAGCATGAACTGGGTG
AAACAGGCCCTGGCAAGGGCCTGAAGTGGATGGGCCGATCAACACCGAGAGCG
GCGTGCCCATCTACGCCGACGACTTCAAGGGCAGATTCGCCTTCAGCGTGGAACC
30 AGCGCCAGCACCGCCTACCTGGTGATCAACAACCTGAAGGACGAGGATACCGCCAG

CTACTTCTGCAGCAACGACTACCTGTACAGCCTGGACTTCTGGGGCCAGGGCACCGC
CCTGACCGTGTCCAGC, and a light chain variable region comprising the amino acid
sequence ~~of SEQ ID NO: 22~~ encoded by:

GACATCGTGCTGACCCAGAGCCCCCCCAGCCTGGCCATGTCTCTGGGCAAGA
GAGCCACCATCAGCTGCCGGGCCAGCGAGAGCGTGACCATCCTGGGCAGCCACCTG
ATCTACTGGTATCAGCAGAAGCCTGGCCAGCCCCCACCCTGCTGATCCAGCTGGCT
AGCAATGTGCAGACCGGCGTGCCCGCCAGATTCAGCGGCAGCGGCAGCAGAACCGA
CTTCACCCTGACCATCGACCCCGTGGAAGAGGACGACGTGGCCGTGTACTACTGCCT
GCAGAGCCGGACCATCCCCCGGACCTTTGGCGGAGGAACAAAGCTGGAAATCAAG;

or

a heavy chain variable region comprising the amino acid sequence ~~of SEQ ID NO:~~
~~23~~ encoded by:

ATGGGATGGAGCTCTATCATCCTCTTCTTGGTAGCAACAGCTACAGGTGTCCA
CCAGATTCAGCTGGTGCAGAGCGGCCCTGAGCTGAAGAAACCCGGCGAGACAGTGA
AGATCAGCTGCAAGGCCTCCGGCTACACCTTCACCGACTACAGCATCAACTGGGTG
AAAAGAGCCCCTGGCAAGGGCCTGAAGTGGATGGGCTGGATCAACACCGAGACAA
GAGAGCCCGCCTACGCCTACGACTTCCGGGGCAGATTCGCCTTCAGCCTGGAAACC
AGCGCCAGCACCGCCTACCTGCAGATCAACAACCTGAAGTACGAGGACACCGCCAC
CTACTTTTGCGCCCTGGACTACAGCTACGCCATGGACTACTGGGGCCAGGGCACCCAG
CGTGACCGTGTCCAGC, and a light chain variable region comprising the amino acid

sequence ~~of SEQ ID NO: 24~~ encoded by:

GACATCGTGCTGACCCAGAGCCCCCCCAGCCTGGCCATGTCTCTGGGCAAGA
GAGCCACCATCAGCTGCCGGGCCAGCGAGAGCGTGACCATCCTGGGCAGCCACCTG
ATCCACTGGTATCAGCAGAAGCCCGGCCAGCCCCCACCCTGCTGATCCAGCTCGCC
AGCAATGTGCAGACCGGCGTGCCCGCCAGATTCAGCGGCAGCGGCAGCAGAACCGA
CTTCACCCTGACCATCGACCCCGTGGAAGAGGACGACGTGGCCGTGTACTACTGCCT
GCAGAGCCGGACCATCCCCCGGACCTTTGGCGGAGGCACCAAACTGGAAATCAAG;

or

a heavy chain variable region comprising the amino acid sequence ~~of SEQ ID NO:~~
~~20~~ encoded by:

CAGATTCAGCTGGTGCAGAGCGGCCCTGAGCTGAAGAAACCCGGCGAGACA
GTGAAGATCAGCTGCAAGGCCTCCGGCTACACCTTCACCGACTACAGCATCAACTG
GGTGAAAAGAGCCCCTGGCAAGGGCCTGAAGTGGATGGGCTGGATCAACACCGAGA
CAAGAGAGCCCGCCTACGCCTACGACTTCCGGGGCAGATTTCGCCTTCAGCCTGGAA
5 ACCAGCGCCAGCACCGCCTACCTGCAGATCAACAACCTGAAGTACGAGGACACCGC
CACCTACTTTTGCGCCCTGGACTACAGCTACGCCATGGACTACTGGGGCCAGGGCAC
CAGCGTGACCGTGTCCAGC, and a light chain variable region comprising the amino acid
sequence ~~of SEQ ID NO: 24~~ encoded by:

GACATCGTGCTGACCCAGAGCCCCCCCAGCCTGGCCATGTCTCTGGGCAAGA
10 GAGCCACCATCAGCTGCCGGGCCAGCGAGAGCGTGACCATCCTGGGCAGCCACCTG
ATCCACTGGTATCAGCAGAAGCCCGGCCAGCCCCCACCCTGCTGATCCAGCTCGCC
AGCAATGTGCAGACCGGCGTGCCCGCCAGATTCAGCGGCAGCGGCAGCAGAACCGA
CTTCACCCTGACCATCGACCCCGTGGAAGAGGACGACGTGGCCGTGTACTACTGCCT
GCAGAGCCGGACCATCCCCCGGACCTTTGGCGGAGGCACCAAACCTGGAAATCAAG.

15 15. The isolated nucleic acid of any one of claims 1-14, wherein the hinge domain comprises
CTCGAGCCCAAATCTTGTGACAAAACCTCACACATGCCACCGTGCCCG~~SEQ ID NO: 3~~,
the transmembrane domain comprises

TTTTGGGTGCTGGTGGTGGTTGGTGGAGTCCTGGCTTGCTATAGCTTGCTAGTAACA
20 GTGGCCTTTATTATTTTCTGGGTG~~SEQ ID NO: 4~~, the CD3 zeta signaling domain comprises
AGAGTGAAGTTCAGCAGGAGCGCAGACGCCCCCGCGTACCAGCAGGGCCAGAACC
AGCTCTATAACGAGCTCAATCTAGGACGAAGAGAGGAGTACGATGTTTTGGACAAG
AGACGTGGCCGGGACCCTGAGATGGGGGGAAAGCCGAGAAGGAAGAACCCTCAGG
AAGGCCTGTACAATGAACTGCAGAAAGATAAGATGGCGGAGGCCTACAGTGAGATT
25 GGGATGAAAGGCGAGCGCCGGAGGGGCAAGGGGCACGATGGCCTTTACCAGGGTCT
CAGTACAGCCACCAAGGACACCTACGACGCCCTTCACATGCAGGCCCTGCCCCCTCG
CTAA~~SEQ ID NO: 7~~, or an equivalent of each thereof, and optionally the intracellular domain
comprises a CD28 costimulatory signaling region comprising

AGGAGTAAGAGGAGCAGGCTCCTGCACAGTGACTACATGAACATGACTCCCCGCCG
30 CCCCGGGCCCCACCCGCAAGCATTACCAGCCCTATGCCCCACCACGCGACTTCGCAGC

CTATCGCTCC~~SEQ ID NO: 6~~ or an equivalent thereof, or a 4-1BB costimulatory signaling region comprising

AAACGGGGCAGAAAGAACTCCTGTATATATTCAAACAACCATTATGAGACCAGT
ACAACTACTCAAGAGGAAGATGGCTGTAGCTGCCGATTTCCAGAAGAAGAAG

5 GAGGATGTGAACTG~~SEQ ID NO: 5~~, or an equivalent thereof, wherein an equivalent of a peptide has at least 90% amino acid identity to the peptide.

16. A vector comprising the isolated nucleic acid of any one of claims 1-15.

10 17. The vector of claim 16, wherein the vector is a plasmid, and optionally further comprises a promoter to regulate expression of the polynucleotide.

18. The vector of claim 16, wherein the vector is a viral vector, optionally selected from the group of a retroviral vector, a lentiviral vector, an adenoviral vector, and an adeno-associated viral vector, and further optionally a promoter to regulate expression of the polynucleotide.

15 19. An isolated cell comprising the isolated nucleic acid of any one of claims 1-15 or the vector of any one of claims 16-18.

20. The isolated cell of claim 19, wherein the cell is a prokaryotic cell or a eukaryotic cell.

21. The isolated cell of claim 19 or 20, wherein the cell is an immune cell, optionally a T-cell, a B cell, a NK cell, a dendritic cell, a myeloid cell, a monocyte, or a macrophage.

20 22. The isolated cell of claim 19 or 20, wherein the cell is a stem cell, optionally an induced pluripotent stem cell (iPSC).

23. A composition comprising the isolated nucleic acid of any one of claims 1-15 or the vector of any one of claims 16-18 or the isolated cell of any one of claims 19-22, and optionally, a pharmaceutically acceptable carrier.

25 24. An isolated complex comprising an isolated cell comprising of any one of claims 19-22 bound to a cell expressing NKG2D.

25. An isolated complex comprising the isolated cell of any one of claims 19-22 bound to a cancer or tumor antigen or a fragment thereof, wherein the cancer or tumor antigen is BCMA or SLAMF7.

26. A method of producing a CAR expressing cell comprising transducing an isolated cell with the vector of any one of claims 16-18.

27. The method of claim 26, wherein the isolated cell is T-cells, B cells, NK cells, dendritic cells, myeloid cells, monocytes, or macrophages.

28. An *in vitro* method of inhibiting the growth of a cancer cell or tumor expressing a cancer or tumor antigen, comprising contacting the cancer cell or tumor with the isolated cell of ~~any one of claims 19 to 22~~claim 19 or claim 20, wherein the isolated cell is a T cell and wherein the cancer cell or tumor antigen comprises BCMA or SLAMF7.

29. Use of an isolated cell of ~~any one of claims 19 to 22~~claim 19 or claim 20 in the manufacture of a medicament for inhibiting the growth of a cancer cell or tumor expressing a cancer or tumor antigen in a subject, wherein the isolated cell is a T cell and wherein the cancer cell or tumor antigen comprises BCMA or SLAMF7.

30. The use of claim 29, wherein the isolated cells are autologous or allogeneic to the subject being treated.

31. The use of claim 29, wherein the isolated cells are allogenic to the subject being treated.

32. A kit comprising a composition of claim 23 and optionally, instructions for use.