

BCMA, including adoptive cell therapy methods involving engineered anti-BCMA CAR expressing cells. Provided herein are embodiments that meet such needs.

Summary

[0005] Provided herein are methods and uses for treating a subject having or suspected of having a disease or disorder associated with B-cell maturation antigen (BCMA) expression. Also provided are methods and uses for reducing the severity of, attenuating, and/or preventing the onset of a toxicity in a subject having or suspected of having a disease or disorder associated with B-cell maturation antigen (BCMA) expression to be treated with a cell therapy.

[0006] Provided herein are methods and uses for treating a subject having or suspected of having a disease or disorder associated with B-cell maturation antigen (BCMA) expression that involves administering to the subject a dose of an interleukin-1 receptor antagonist (IL-1Ra) and a cell therapy that includes a dose of engineered T cells that express a first chimeric antigen receptor (CAR) specific for BCMA, wherein at least one dose of the IL-1Ra is administered prior to the dose of engineered T cells.

[0007] Provided herein are methods and uses for treating a subject having or suspected of having a disease or disorder associated with B-cell maturation antigen (BCMA) expression that involves administering a cell therapy that includes a dose of engineered T cells that express a first chimeric antigen receptor (CAR) specific for BCMA to a subject that has been administered at least one dose of an interleukin-1 receptor antagonist (IL-1Ra).

[0008] Provided herein are methods and uses for treating a subject having or suspected of having a disease or disorder associated with B-cell maturation antigen (BCMA) expression, involving administering at least one dose of an interleukin-1 receptor antagonist (IL-1Ra) to a subject who is a candidate for a cell therapy that includes a dose of engineered T cells that express a first chimeric antigen receptor (CAR) specific for BCMA.

[0008a] In one aspect, the present disclosure refers to use of an interleukin-1 receptor antagonist (IL-1Ra) and a cell therapy in the manufacture of a medicament for the treatment of a subject having a disease or disorder associated with B-cell maturation antigen (BCMA) expression, wherein: the cell therapy is to be administered to the subject, said cell therapy comprising a dose of engineered T cells comprising a first chimeric antigen receptor (CAR) specific for BCMA; and the interleukin-1 receptor antagonist (IL-1Ra) is to be administered to the subject, wherein at least one dose of the IL-1Ra is to be administered within about or about 24 hours prior to the administration of the dose of engineered T cells; and at least one dose of the IL-1Ra is to be administered after the administration of the dose of engineered T cells.

[0008b] In one aspect, the present disclosure refers to use of an interleukin-1 receptor antagonist (IL-1Ra) in the manufacture of a medicament for the treatment of a subject having a disease or disorder associated with B-cell maturation antigen (BCMA) expression, wherein the IL-1Ra is to be administered to the subject in combination with a cell therapy, wherein; the cell therapy is to be administered to the subject, the cell therapy comprising a dose of engineered T cells comprising a first chimeric antigen receptor (CAR) specific for BCMA; and at least one dose of the IL-1Ra is to be administered within about or about 24 hours prior to the administration of the dose of engineered T cells; and at least one dose of the IL-1Ra is to be administered after the administration of the dose of engineered T cells.

[0008c] In one aspect, the present disclosure refers to use of a cell therapy in the manufacture of a medicament for the treatment of a subject having a disease or disorder associated with B-cell maturation antigen (BCMA) expression, wherein the cell therapy is to be administered to the subject in combination with an interleukin-1 receptor antagonist (IL-1Ra), wherein: the cell therapy comprises a dose of engineered T cells comprising a first chimeric antigen receptor (CAR) specific for BCMA; and at least one dose of the IL-1Ra is to be administered within about or about 24 hours prior to the administration of the dose of engineered T cells; and at least one dose of the IL-1Ra is to be administered after the administration of the dose of engineered T cells.

[0009] Provided herein are methods and uses for reducing the severity of, attenuating, and/or preventing the onset of a toxicity in a subject having or suspected of having a disease or disorder associated with B-cell maturation antigen (BCMA) expression to be treated with a cell therapy that involves administering to the subject a dose of an interleukin-1 receptor antagonist (IL-1Ra) and a cell therapy that includes a dose of engineered T cells that express a first chimeric antigen receptor (CAR) specific for BCMA, wherein at least one dose of the IL-1Ra is administered prior to the dose of engineered T cells.

[0010] Provided herein are methods and uses for reducing the severity of, attenuating, and/or preventing the onset of a toxicity in a subject having or suspected of having a disease or disorder

associated with B-cell maturation antigen (BCMA) expression to be treated with a cell therapy that involves administering a cell therapy that includes a dose of engineered T cells that express a first chimeric antigen receptor (CAR) specific for BCMA to a subject that has been administered at least one dose of an interleukin-1 receptor antagonist (IL-1Ra).

[0011] Provided herein are methods and uses for reducing the severity of, attenuating, and/or preventing the onset of a toxicity in a subject having or suspected of having a disease or disorder associated with B-cell maturation antigen (BCMA) expression to be treated with a cell therapy, including administering at least one dose of an interleukin-1 receptor antagonist (IL-1Ra) to a subject who is a candidate for a cell therapy including a dose of engineered T cells that express a first chimeric antigen receptor (CAR) specific for BCMA.

[0011a] In one aspect, the present disclosure refers to use of an interleukin-1 receptor antagonist (IL-1Ra) and a cell therapy in the manufacture of a medicament for reducing the severity of, attenuating, and/or preventing the onset of a toxicity to a cell therapy for treating a subject having a disease or disorder associated with B-cell maturation antigen (BCMA) expression, wherein: the cell therapy is to be administered to the subject, said cell therapy comprising a dose of engineered T cells comprising a first chimeric antigen receptor (CAR) specific for BCMA; and at least one dose of the IL-1Ra is to be administered within about or about 24 hours prior to the administration of the dose of engineered T cells; and at least one dose of the IL-1Ra is to be administered after the administration of the dose of engineered T cells.

[0011b] In one aspect, the present disclosure refers to use of an interleukin-1 receptor antagonist (IL-1Ra) in the manufacture of a medicament for reducing the severity of, attenuating, and/or preventing the onset of a toxicity to a cell therapy, wherein: the cell therapy is to be administered to the subject for treating a subject having a disease or disorder associated with B-cell maturation antigen (BCMA) expression, the cell therapy comprising a dose of engineered T cells comprising a first chimeric antigen receptor (CAR) specific for BCMA; and at least one dose of the IL-1Ra is to be administered within about or about 24 hours prior to the administration of the dose of engineered T cells; and at least one dose of the IL-1Ra is to be administered after the administration of the dose of engineered T cells.

[0011c] In one aspect, the present disclosure refers to use of a cell therapy in the manufacture of a medicament for treating a subject having a disease or disorder associated with B-cell maturation antigen (BCMA) expression in combination with an interleukin-1 receptor antagonist (IL-1Ra) for reducing the severity of, attenuating, and/or preventing the onset of a toxicity to the cell therapy, wherein: the cell therapy is to be administered to the subject, the cell therapy comprising a dose of engineered T cells comprising a first chimeric antigen receptor (CAR)

specific for BCMA; and at least one dose of the IL-1Ra is to be administered within about or about 24 hours prior to the administration of the dose of engineered T cells; and at least one dose of the IL-1Ra is to be administered after the administration of the dose of engineered T cells.

[0012] In some of any of the provided embodimentexamples, the subject has been administered the at least one dose of the IL-1Ra within at or about 24 hours prior to the dose of engineered T cells.

[0013] In some of any of the provided embodimentexamples, the at least one dose of the IL-1Ra includes at least two dose of the IL-1Ra.

[0014] Provided herein are methods and uses for treating a subject having or suspected of having a disease or disorder associated with B-cell maturation antigen (BCMA) expression that involves administering to the subject at least two doses of an interleukin-1 receptor antagonist (IL-1Ra) and a cell therapy that includes a dose of engineered T cells that express a first chimeric antigen receptor (CAR) specific for BCMA, wherein at least one dose of the IL-1Ra is administered within at or about 24 hours prior to the administration of the dose of engineered T cells; and at least one dose of the IL-1Ra is administered after the administration of the dose of engineered T cells.

[0015] Provided herein are methods and uses for treating a subject having or suspected of having a disease or disorder associated with B-cell maturation antigen (BCMA) expression, including administering to the subject at least two doses of an interleukin-1 receptor antagonist (IL-1Ra), wherein at least one dose of the IL-1Ra is administered within about or about 24 hours prior to administration of a cell therapy including a dose of engineered T cells that express a first chimeric antigen receptor (CAR) specific for BCMA to the subject; and at least one dose of the IL-1Ra is administered after the administration of the dose of engineered T cells.

[0016] Provided herein are methods and uses for treating a subject having or suspected of having a disease or disorder associated with B-cell maturation antigen (BCMA) expression, including administering to the subject a cell therapy including a dose of engineered T cells that express a first chimeric antigen receptor (CAR) specific for BCMA, wherein the subject has

been administered at least one dose of an interleukin-1 receptor antagonist (IL-1Ra) within about or about 24 hours prior to administration of the dose of engineered T cells; and the subject is to be administered at least one dose of the IL-1Ra after the administration of the dose of engineered T cells.

[0017] Provided herein are methods and uses for treating a subject having or suspected of having a disease or disorder associated with B-cell maturation antigen (BCMA) expression that involves administering a cell therapy that includes a dose of engineered T cells that express a first chimeric antigen receptor (CAR) specific for BCMA to a subject that has been administered at least one dose of an interleukin-1 receptor antagonist (IL-1Ra) within at or about 24 hour prior to the administration of the dose of engineered T cells; and administering at least one dose of the IL-1Ra after the administration of the dose of engineered T cells.

[0018] Provided herein are methods and uses for reducing the severity of, attenuating, and/or preventing the onset of a toxicity in a subject having or suspected of having a disease or disorder associated with B-cell maturation antigen (BCMA) expression to be treated with a cell therapy that involves administering to the subject at least two doses of an interleukin-1 receptor antagonist (IL-1Ra) and a cell therapy that includes a dose of engineered T cells that express a first chimeric antigen receptor (CAR) specific for BCMA, wherein at least one dose of the IL-1Ra is administered within at or about 24 hours prior to the administration of the dose of engineered T cells; and at least one dose of the IL-1Ra is administered after the administration of the dose of engineered T cells.

[0019] Provided herein are methods and uses for reducing the severity of, attenuating, and/or preventing the onset of a toxicity in a subject having or suspected of having a disease or disorder associated with B-cell maturation antigen (BCMA) expression to be treated with a cell therapy that involves administering a cell therapy that includes a dose of engineered T cells that express a first chimeric antigen receptor (CAR) specific for BCMA to a subject that has been administered at least one dose of an interleukin-1 receptor antagonist (IL-1Ra) within at or about 24 hour prior to the administration of the dose of engineered T cells; and administering at least one dose of the IL-1Ra is administered after the administration of the dose of engineered T cells.

[0020] In some of any of the provided [embodimentexamples](#), the at least one dose of IL-1Ra administered prior to the dose of engineered T cells is administered within at or about 21, 18, 15 or 12 hours prior to administration of the dose of engineered T cells. In some of any of the provided [embodimentexamples](#), the at least one dose of IL-1Ra administered prior to the dose of engineered T cells is administered within at or about 21 hours prior to administration of the dose of engineered T cells. In some of any of the provided [embodimentexamples](#), the at least one dose of IL-

IL-1Ra administered prior to the dose of engineered T cells is administered within at or about 18 hours prior to administration of the dose of engineered T cells. In some of any of the provided [embodimentexamples](#), the at least one dose of IL-1Ra administered prior to the dose of engineered T cells is administered within at or about 15 hours prior to administration of the dose of engineered T cells. In some of any of the provided [embodimentexamples](#), the at least one dose of IL-1Ra administered prior to the dose of engineered T cells is administered within at or about 12 hours prior to administration of the dose of engineered T cells.

[0021] In some of any of the provided [embodimentexamples](#), the at least one dose of the IL-1Ra administered prior to the dose of engineered cells includes at least two doses of the IL-1Ra administered prior to the administration of the dose of engineered T cells.

[0022] In some of any of the provided [embodimentexamples](#), one dose of the at least two doses of IL-1Ra is administered prior to the dose of engineered T cells. In some of any of the provided [embodimentexamples](#), one dose of the at least two doses of IL-1Ra is administered is administered within at or about 6, 5, 4, 3 or 2 hours prior to administration of the dose of engineered T cells. In some [embodimentexamples](#), one dose of the at least two doses of IL-1RA2 is administered at or about 6 hours prior to administration of the dose of engineered T cells. In some [embodimentexamples](#), one dose of the at least two doses of IL-1RA2 is administered at or about 5 hours prior to administration of the dose of engineered T cells. In some [embodimentexamples](#), one dose of the at least two doses of IL-1RA2 is administered at or about 4 hours prior to administration of the dose of engineered T cells. In some of any of the provided [embodimentexamples](#), one dose of the at least two doses of IL-1Ra is administered within at or about 3 hours prior to administration of the dose of engineered T cells. In some [embodimentexamples](#), one dose of the at least two doses of IL-1RA2 is administered at or about 2 hours prior to administration of the dose of engineered T cells. In some of any of the provided [embodimentexamples](#), one dose of the at least two doses of IL-1Ra is administered within at or about 24 hours prior to, and one dose of the at least two doses of IL-1Ra is administered within at or about 3 hours prior to, administration of the dose of engineered T cells.

[0023] In some of any of the provided [embodimentexamples](#), the methods and uses also involve administering at least one dose of the IL-1Ra after administering the dose of engineered T cells. In some of any of the provided [embodimentexamples](#), the at least one dose of the IL-1Ra administered after the dose of engineered cells includes at least 2, 3, 4, 5, 6, 7 or 8 doses of the IL-1Ra administered after administering the dose of engineered T cells. In some of any of the provided [embodimentexamples](#), the at least one dose of the IL-1Ra administered after the dose of engineered cells includes at least 2 doses of the IL-1Ra administered after administering the dose of engineered T

cells. In some of any of the provided [embodimentexamples](#), the at least one dose of the IL-1Ra administered after the dose of engineered cells includes 3, 4, 5, 6 or 7 doses of IL-1Ra administered after the administration of the dose of engineered T cells. In some of any of the provided [embodimentexamples](#), the at least one dose of the IL-1Ra administered after the dose of engineered cells includes at least 3 doses of the IL-1Ra administered after administering the dose of engineered T cells. In some of any of the provided [embodimentexamples](#), the at least one dose of the IL-1Ra administered after the dose of engineered cells includes at least 4 doses of the IL-1Ra administered after administering the dose of engineered T cells. In some of any of the provided [embodimentexamples](#), the at least one dose of the IL-1Ra administered after the dose of engineered cells includes 5 doses of IL-1Ra administered after the administration of the dose of engineered T cells. In some of any of the provided [embodimentexamples](#), the at least one dose of the IL-1Ra administered after the dose of engineered cells includes at least 6 doses of the IL-1Ra administered after administering the dose of engineered T cells. In some of any of the provided [embodimentexamples](#), the at least one dose of the IL-1Ra administered after the dose of engineered cells includes at least 7 doses of the IL-1Ra administered after administering the dose of engineered T cells. In some of any of the provided [embodimentexamples](#), the at least one dose of the IL-1Ra administered after the dose of engineered cells includes at least 8 doses of the IL-1Ra administered after administering the dose of engineered T cells.

[0024] In some of any of the provided [embodimentexamples](#), the at least one dose of the IL-1Ra administered after the dose of engineered cells is administered daily for consecutive days. In some of any of the provided [embodimentexamples](#), the at least one dose of IL-1Ra administered after the administration of the dose of engineered T cells is 4 doses, wherein one of the four doses is administered each day for 4 consecutive days after the administration of the dose of engineered T cells. . In some of any of the provided [embodimentexamples](#), the at least one dose of IL-1Ra administered after the administration of the dose of engineered T cells is 5 doses administered daily for 5 consecutive days after the administration of the dose of engineered T cells. In some [embodimentexamples](#), a dose of the IL-1Ra is administered every 24 hours (q24h) on Days 2-5.

[0025] Provided herein are methods and uses for reducing the severity of, attenuating, and/or preventing the onset of a toxicity in a subject having or suspected of having a disease or disorder associated with B-cell maturation antigen (BCMA) expression to be treated with a cell therapy, involving administering to the subject at least 6 doses of an interleukin-1 receptor antagonist (IL-1Ra) and a cell therapy including a dose of engineered T cells that express a first chimeric antigen receptor (CAR) specific for BCMA, wherein the cell therapy is administered on Day 1 and: (a) one dose of the IL-1Ra is administered within about or about 24 hours prior to the

administration of the dose of engineered T cells, optionally the night before the administration of the dose of the engineered T cells; (b) one dose of the IL-1Ra is administered within about or about 3 hours prior to the administration of the dose of engineered T cells on Day 1; (c) four doses of the IL-1Ra are administered after the administration of the dose of engineered T cells, wherein one dose of the four doses is administered each day on Days 2, 3, 4, and 5.

[0025a] In one aspect, the present disclosure refers to use of an interleukin-1 receptor antagonist (IL-1Ra) and a cell therapy in the manufacture of a medicament for reducing the severity of, attenuating, and/or preventing the onset of a toxicity in a subject having a disease or disorder associated with B-cell maturation antigen (BCMA) expression to be treated with a cell therapy, wherein the cell therapy is to be administered to a subject having a disease or disorder associated with BCMA expression to be treated with a cell therapy, said cell therapy comprising a dose of engineered T cells comprising a first chimeric antigen receptor (CAR) specific for BCMA; and at least six doses of an interleukin-1 receptor antagonist (IL-1Ra) are to be administered to the subject, wherein the cell therapy is to be administered on Day 1 and: (a) one dose of the IL-1Ra is to be administered within about or about 24 hours prior to the administration of the dose of engineered T cells, optionally the night before the administration of the dose of the engineered T cells; (b) one dose of the IL-1Ra is to be administered within about or about 3 hours prior to the administration of the dose of engineered T cells on Day 1; (c) four doses of the IL-1Ra are to be administered after the administration of the dose of engineered T cells, wherein one dose of the four doses is to be administered each day on Days 2, 3, 4, and 5.

[0026] In some of any of the provided embodimentexamples, methods and uses also involve administering at least one additional dose of the IL-1Ra after the administration of the dose of engineered cells if the subject exhibits symptoms or signs of a cytokine release syndrome (CRS). In some of any of the provided embodimentexamples, the at least one additional dose of the IL-1Ra includes administration of a plurality of doses. In some of any of the provided embodimentexamples, the plurality of doses is administered daily for consecutive days, until the symptoms or signs of CRS is resolved. In some of any of the provided embodimentexamples, the plurality of doses is administered twice daily for consecutive days, until the symptoms or signs of CRS is resolved. In some embodimentexamples, a dose of the IL-1Ra is administered every 12 hours (q12h). In some embodimentexamples, if the subject exhibits symptoms or signs of a cytokine release syndrome (CRS), a dose of IL-1Ra is administered every 12 hours (q12h) until the symptoms or signs of CRS resolve.

[0027] In some of any of the provided embodimentexamples, the daily administration of the IL-1Ra is administered at or at about the same time each day.

[0028] In some of any of the provided embodimentexamples, the IL-1Ra is a recombinant IL-1Ra. In some of any of the provided embodimentexamples, the IL-1Ra includes the sequence set forth in SEQ ID NO:256 or a sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or higher sequence identity to SEQ ID NO:256 that retains function as an IL-1R antagonist. In some of any of the provided embodimentexamples, the IL-1Ra includes the sequence set forth in SEQ ID NO:256. . In some of any of the provided embodimentexamples, the IL-1Ra includes a sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or higher sequence identity to SEQ ID NO:256 that retains function as an IL-1R antagonist. In some of any of the provided embodimentexamples, the IL-1Ra is anakinra. In some embodimentexamples, anakinra is recombinant anakinra.

[0029] In some of any of the provided embodimentexamples, each dose of the recombinant IL-1Ra is at or about 500 mg, at or about 400, at or about 300, at or about 200 mg, at or about 100 or at or about 50 mg, or a range defined by any of the foregoing. In some of any of the provided embodimentexamples, each dose of the IL-1Ra is at or about 500 mg, at or about 400, at or about 300, at or about 200 mg, at or about 100 or at or about 50 mg, or a range defined by any of the

foregoing. In some of any of the provided [embodimentexamples](#), each dose of the IL-1Ra is at or about 500 mg. In some of any of the provided [embodimentexamples](#), each dose of the IL-1Ra is at or about 400 mg. In some of any of the provided [embodimentexamples](#), each dose of the IL-1Ra is at or about 300 mg. In some of any of the provided [embodimentexamples](#), each dose of the IL-1Ra is at or about 200 mg. In some of any of the provided [embodimentexamples](#), each dose of the recombinant IL-1Ra is from at or about 50 mg to at or about 200 mg. In some of any of the provided [embodimentexamples](#), each dose of the recombinant IL-1Ra is at or about 100 mg. In some of any of the provided [embodimentexamples](#), each dose of the IL-1Ra is at or about 50 mg. In some of any of the provided [embodimentexamples](#), the IL-1Ra is administered subcutaneously.

[0030] In some of any of the provided [embodimentexamples](#), the methods and uses reduce the severity of, attenuates, and/or prevents the onset of a toxicity associated with administration of the cell therapy. In some of any of the provided [embodimentexamples](#), the methods and uses reduce the severity of the onset of a toxicity associated with administration of the cell therapy. In some of any of the provided [embodimentexamples](#), the methods and uses attenuates the onset of a toxicity associated with administration of the cell therapy. In some of any of the provided [embodimentexamples](#), the methods and uses prevents the onset of a toxicity associated with administration of the cell therapy.

[0031] In some of any of the provided [embodimentexamples](#), the toxicity is a cytokine release syndrome (CRS). In some of any of the provided [embodimentexamples](#), the CRS is a severe CRS or a grade 3 or higher CRS. In some of any of the provided [embodimentexamples](#), the CRS is a severe. In some of any of the provided [embodimentexamples](#), the CRS is a 3 or higher CRS. In some of any of the provided [embodimentexamples](#), the toxicity is a neurotoxicity (NT). In some of any of the provided [embodimentexamples](#), the NT is a severe NT or a grade 2 or higher NT or a grade 3 or higher NT. In some of any of the provided [embodimentexamples](#), the NT is a severe NT. In some of any of the provided [embodimentexamples](#), the NT is a grade 2 or higher NT. In some of any of the provided [embodimentexamples](#), the NT is a grade 3 or higher NT. In some of any of the provided [embodimentexamples](#), the toxicity is a macrophage activation syndrome (MAS) or a hemophagocytic lympho-histiocytosis (HLH). In some of any of the provided [embodimentexamples](#), the toxicity is a macrophage activation syndrome (MAS). In some of any of the provided [embodimentexamples](#), the toxicity is a hemophagocytic lympho-histiocytosis (HLH).

[0032] In some of any of the provided [embodimentexamples](#), at or prior to the administration of the dose of engineered T cells, the subject has been administered one or more prior BCMA-directed therapy selected from among: a prior dose of engineered T cells that express a second CAR specific for BCMA; a prior administration of a BCMA-directed T cell engager (TCE); and a

prior administration of a BCMA-directed antibody-drug conjugate (ADC).

[0033] Provided herein are methods and uses for treating a subject having or suspected of having a disease or disorder associated with B-cell maturation antigen (BCMA) expression that involves administering to the subject a cell therapy that includes a dose of engineered T cells that express a first chimeric antigen receptor (CAR) specific for BCMA, wherein at or prior to the administration of the dose of engineered T cells, the subject has been administered one or more prior BCMA-directed therapy selected from among: a prior dose of engineered T cells that express a second CAR specific for BCMA; a prior administration of a BCMA-directed T cell engager (TCE); and a prior administration of a BCMA-directed antibody-drug conjugate (ADC).

[0033a] In one aspect, the present disclosure refers to use of a cell therapy comprising a dose of engineered T cells comprising a first chimeric antigen receptor (CAR) specific for B-cell maturation antigen (BCMA) in the manufacture of a medicament to treat a subject having a disease or disorder associated with BCMA expression, wherein at or prior to the administration of the dose of engineered T cells, the subject has been administered one or more prior BCMA-directed therapy selected from among: a prior dose of engineered T cells comprising a second CAR specific for BCMA; a prior administration of a BCMA-directed T cell engager (TCE); and a prior administration of a BCMA-directed antibody-drug conjugate (ADC).

[0034] Provided herein are methods and uses for treating a subject having or suspected of having a disease or disorder associated with B-cell maturation antigen (BCMA) expression that involves administering to the subject a cell therapy that includes a dose of engineered T cells that express a first chimeric antigen receptor (CAR) specific for BCMA, to a subject that has previously received one or more prior BCMA-directed therapy selected from among: a prior dose of engineered T cells that express a second CAR specific for BCMA; a prior administration of a BCMA-directed T cell engager (TCE); and a prior administration of a BCMA-directed antibody-drug conjugate (ADC).

[0035] In some of any of the provided **embodimentexamples**, the subject has relapsed following or has been refractory to the one or more prior BCMA-directed therapy. In some of any of the provided **embodimentexamples**, the subject has relapsed following the one or more prior BCMA-directed therapy. In some of any of the provided **embodimentexamples**, the subject has been refractory to the one or more prior BCMA-directed therapy. In some of any of the provided **embodimentexamples**, the subject has relapsed following or has been refractory to the one or more prior BCMA-directed therapy within at or about 1 year prior to the administration of the dose of engineered T cells that express the first CAR. In some of any of the provided **embodimentexamples**, the subject has relapsed following the one or more prior BCMA-directed therapy within at or about 1 year prior to the administration of the dose of engineered T cells that express the first CAR. In some of any of the provided **embodimentexamples**, the subject has been refractory to the one or more prior BCMA-directed therapy within at or about 1 year prior to the administration of the dose of engineered T cells that express the first CAR. In some of any of the provided **embodimentexamples**, the subject has relapsed following or has been refractory to the one or more prior BCMA-directed therapy within at or about 6 months prior to the administration of the dose of engineered T cells that express the first CAR. In some of any of the provided **embodimentexamples**, the subject has relapsed following the one or more prior BCMA-directed therapy within at or about 6 months prior to the

administration of the dose of engineered T cells that express the first CAR. In some of any of the provided [embodimentexamples](#), the subject has been refractory to the one or more prior BCMA-directed therapy within at or about 6 months prior to the administration of the dose of engineered T cells that express the first CAR. In some of any of the provided [embodimentexamples](#), the subject has relapsed following or has been refractory to the one or more prior BCMA-directed therapy within at or about 3 months prior to the administration of the dose of engineered T cells that express the first CAR. In some of any of the provided [embodimentexamples](#), the subject has relapsed following the one or more prior BCMA-directed therapy within at or about 3 months prior to the administration of the dose of engineered T cells that express the first CAR. In some of any of the provided [embodimentexamples](#), the subject has been refractory to the one or more prior BCMA-directed therapy within at or about 3 months prior to the administration of the dose of engineered T cells that express the first CAR.

[0036] In some of any of the provided [embodimentexamples](#), the BCMA-directed TCE is or includes a bispecific antibody or a bispecific T cell engager (BiTE). In some of any of the provided [embodimentexamples](#), the BCMA-directed TCE is a bispecific antibody. In some of any of the provided [embodimentexamples](#), the BCMA-directed TCE includes a bispecific antibody. In some of any of the provided [embodimentexamples](#), the BCMA-directed TCE is a bispecific T cell engager (BiTE). In some of any of the provided [embodimentexamples](#), the BCMA-directed TCE includes a bispecific T cell engager (BiTE). In some of any of the provided [embodimentexamples](#), the BCMA-directed TCE is selected from among one or more of AMG 420/BI 836909, AMG 701, CC-93269, JNJ-64007957, PF-06863135 and REGN5458. In some of any of the provided [embodimentexamples](#), the BCMA-directed TCE is AMG 420/BI 836909. In some of any of the provided [embodimentexamples](#), the BCMA-directed TCE is AMG 701. In some of any of the provided [embodimentexamples](#), the BCMA-directed TCE is CC-93269. In some of any of the provided [embodimentexamples](#), the BCMA-directed TCE is JNJ-64007957. In some of any of the provided [embodimentexamples](#), the BCMA-directed TCE is PF-06863135. In some of any of the provided [embodimentexamples](#), the BCMA-directed TCE is REGN5458.

[0037] In some of any of the provided [embodimentexamples](#), the BCMA-directed ADC is selected from among one or more of Belantamab mafodotin (GSK2857916), MEDI2228, CC-99712 and AMG 224. In some of any of the provided [embodimentexamples](#), the BCMA-directed ADC is Belantamab mafodotin (GSK2857916). In some of any of the provided [embodimentexamples](#), the BCMA-directed ADC is MEDI2228. In some of any of the provided [embodimentexamples](#), the BCMA-directed ADC is CC-99712. In some of any of the provided [embodimentexamples](#), the BCMA-directed ADC is AMG 224.

[0038] In some of any of the provided [embodimentexamples](#), the first CAR contains: (a) an extracellular antigen-binding domain, comprising: a variable heavy chain (V_H) comprising a heavy chain complementarity determining region 1 (CDR-H1), a heavy chain complementarity determining region 2 (CDR-H2) and a heavy chain complementarity determining region 3 (CDR-H3) contained within the sequence set forth in SEQ ID NO: 116 and a variable light chain (V_L) comprising a light chain complementarity determining region 1 (CDR-L1), a light chain complementarity determining region 2 (CDR-L2) and a light chain complementarity determining region 3 (CDR-L3) contained within the sequence set forth in SEQ ID NO: 119; a V_H comprising a CDR-H1, a CDR-H2 and a CDR-H3 sequences set forth in SEQ ID NOS: 97, 101 and 103, respectively, and a V_L comprising a CDR-L1, a CDR-L2 and a CDR-L3 sequences set forth in SEQ ID NOS: 105, 107 and 108, respectively; a V_H comprising a CDR-H1, a CDR-H2 and a CDR-H3 sequences set forth in SEQ ID NOS: 96, 100 and 103, respectively, and a V_L comprising a CDR-L1, a CDR-L2 and a CDR-L3 sequences set forth in SEQ ID NOS: 105, 107 and 108, respectively; a V_H comprising a CDR-H1, a CDR-H2 and a CDR-H3 sequences set forth in SEQ ID NOS: 95, 99 and 103, respectively, and a V_L comprising a CDR-L1, a CDR-L2 and a CDR-L3 sequences set forth in SEQ ID NOS: 105, 107 and 108, respectively; a V_H comprising a CDR-H1, a CDR-H2 and a CDR-H3 sequences set forth in SEQ ID NOS: 94, 98 and 102, respectively, and a V_L comprising a CDR-L1, a CDR-L2 and a CDR-L3 sequences set forth in SEQ ID NOS: 104, 106 and 108, respectively; or a V_H comprising the amino acid sequence of SEQ ID NO: 116 and a V_L comprising the amino acid sequence of SEQ ID NO: 119; (b) a spacer comprising an IgG4/2 chimeric hinge or a modified IgG4 hinge; an IgG2/4 chimeric C_H2 region; and an IgG4 C_H3 region, such as a spacer that is about 228 amino acids in length; or a spacer set forth in SEQ ID NO: 174; (c) a transmembrane domain; and (d) an intracellular signaling region comprising a cytoplasmic signaling domain of a CD3-zeta ($CD3\zeta$) chain and a costimulatory signaling region comprising an intracellular signaling domain of a T cell costimulatory molecule or a signaling portion thereof.

[0039] In some of any of the provided [embodimentexamples](#), the V_H is or includes the amino acid sequence of SEQ ID NO: 116; and the V_L is or includes the amino acid sequence of SEQ ID NO: 119. In some of any of the provided [embodimentexamples](#), the V_H is the amino acid sequence of SEQ ID NO: 116; and the V_L is the amino acid sequence of SEQ ID NO: 119. In some of any of the provided [embodimentexamples](#), the V_H includes the amino acid sequence of SEQ ID NO: 116; and the V_L includes the amino acid sequence of SEQ ID NO: 119.

[0040] In some of any of the provided [embodimentexamples](#), the extracellular antigen-binding domain includes an scFv. In some of any of the provided [embodimentexamples](#), the extracellular

antigen-binding domain is an scFv. In some of any of the provided [embodimentexamples](#), the V_H and the V_L are joined by a flexible linker. In some of any of the provided [embodimentexamples](#), the flexible linker includes the amino acid sequence GGGGSGGGGSGGGGS (SEQ ID NO:1). In some of any of the provided [embodimentexamples](#), the flexible linker is the amino acid sequence GGGGSGGGGSGGGGS (SEQ ID NO:1). In some of any of the provided [embodimentexamples](#), the V_H is carboxy-terminal to the V_L.

[0041] In some of any of the provided [embodimentexamples](#), the extracellular antigen-binding domain includes the amino acid sequence of SEQ ID NO: 114 or an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 114. In some of any of the provided [embodimentexamples](#), the extracellular antigen-binding domain includes the amino acid sequence of SEQ ID NO: 114. In some of any of the provided [embodimentexamples](#), the extracellular antigen-binding domain includes an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 114.

[0042] In some of any of the provided [embodimentexamples](#), a nucleic acid encoding the extracellular antigen-binding domain includes (a) the sequence of nucleotides of SEQ ID NO:113; (b) a sequence of nucleotides that has at least 90% sequence identity thereto; or (c) a degenerate sequence of (a) or (b). In some of any of the provided [embodimentexamples](#), a nucleic acid encoding the extracellular antigen-binding domain includes the sequence of nucleotides of SEQ ID NO:113. In some of any of the provided [embodimentexamples](#), a nucleic acid encoding the extracellular antigen-binding domain includes a sequence of nucleotides that has at least 90% sequence identity to SEQ ID NO:113. In some of any of the provided [embodimentexamples](#), the nucleic acid encoding the extracellular antigen-binding domain includes the sequence of nucleotides of SEQ ID NO:115.

[0043] In some of any of the provided [embodimentexample](#), the transmembrane domain is or includes a transmembrane domain from human CD28. In some of any of the provided [embodimentexamples](#), the transmembrane domain is a transmembrane domain from human CD28. In some of any of the provided [embodimentexamples](#), the transmembrane domain includes a transmembrane domain from human CD28. In some of any of the provided [embodimentexamples](#), the transmembrane domain is or includes the sequence set forth in SEQ ID NO:138 or a sequence of amino acids that has at least 90% sequence identity to SEQ ID NO:138. In some of any of the provided [embodimentexamples](#), the transmembrane domain is or includes the sequence set forth in SEQ ID NO:138. In some of any of the provided [embodimentexamples](#), the transmembrane domain the sequence set forth in SEQ ID NO:138. In some of any of the provided [embodimentexamples](#), the

transmembrane domain includes the sequence set forth in SEQ ID NO:138. In some of any of the provided [embodimentexamples](#), the transmembrane domain is or includes a sequence of amino acids that has at least 90% sequence identity to SEQ ID NO:138. In some of any of the provided [embodimentexamples](#), the transmembrane domain is a sequence of amino acids that has at least 90% sequence identity to SEQ ID NO:138. In some of any of the provided [embodimentexample](#), the transmembrane domain includes a sequence of amino acids that has at least 90% sequence identity to SEQ ID NO:138.

[0044] In some [embodimentexamples](#), the first CAR contains an extracellular antigen-binding domain having: a variable heavy chain (VH) comprising a heavy chain complementarity determining region 1 (CDR-H1), a heavy chain complementarity determining region 2 (CDR-H2) and a heavy chain complementarity determining region 3 (CDR-H3) contained within the sequence set forth in SEQ ID NO: 125 and a variable light chain (VL) comprising a light chain complementarity determining region 1 (CDR-L1), a light chain complementarity determining region 2 (CDR-L2) and a light chain complementarity determining region 3 (CDR-L3) contained within the sequence set forth in SEQ ID NO: 127; and/or a VH comprising a CDR-H1, a CDR-H2 and a CDR-H3 sequences set forth in SEQ ID NOS: 260, 261, and 262, respectively, and a VL comprising a CDR-L1, a CDR-L2 and a CDR-L3 sequences set forth in SEQ ID NOS: 257, 258, and 259, respectively. In some [embodimentexamples](#), the V_H is or includes the amino acid sequence of SEQ ID NO: 125; and the V_L is or includes the amino acid sequence of SEQ ID NO: 127. In some [embodimentexamples](#), the extracellular antigen-binding domain includes the amino acid sequence of SEQ ID NO: 128 or an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 128.

[0045] In some of any of the provided [embodimentexamples](#), the cytoplasmic signaling domain is or includes the sequence set forth in SEQ ID NO:143 or a sequence of amino acids that has at least 90% sequence identity to SEQ ID NO:143. In some of any of the provided [embodimentexamples](#), the cytoplasmic signaling domain is or includes the sequence set forth in SEQ ID NO:143. In some of any of the provided [embodimentexamples](#), the cytoplasmic signaling domain is the sequence set forth in SEQ ID NO:143. In some of any of the provided [embodimentexamples](#), the cytoplasmic signaling domain includes the sequence set forth in SEQ ID NO:143. In some of any of the provided [embodimentexamples](#), the cytoplasmic signaling domain is or includes a sequence of amino acids that has at least 90% sequence identity to SEQ ID NO:143. In some of any of the provided [embodimentexamples](#), the cytoplasmic signaling domain is a sequence of amino acids that has at least 90% sequence identity to SEQ ID NO:143. In some of any of the provided [embodimentexamples](#), the

cytoplasmic signaling domain includes a sequence of amino acids that has at least 90% sequence identity to SEQ ID NO:143.

[0046] In some of any of the provided [embodimentexamples](#), the costimulatory signaling region includes an intracellular signaling domain of CD28, 4-1BB, or ICOS, or a signaling portion thereof. In some of any of the provided [embodimentexamples](#), the costimulatory signaling region includes an intracellular signaling domain of CD28. In some of any of the provided [embodimentexamples](#), the costimulatory signaling region includes an intracellular signaling domain of ICOS. In some of any of the provided [embodimentexamples](#), the costimulatory signaling region includes an intracellular signaling domain of 4-1BB. In some of any of the provided [embodimentexamples](#), the 4-1BB is human 4-1BB. In some of any of the provided [embodimentexamples](#), the costimulatory signaling region is or includes the sequence set forth in SEQ ID NO:4 or a sequence of amino acids that has at least 90% sequence identity to the sequence set forth in SEQ ID NO: 4. In some of any of the provided [embodimentexamples](#), the costimulatory signaling region is or includes the sequence set forth in SEQ ID NO: 4. In some of any of the provided [embodimentexamples](#), the costimulatory signaling region is the sequence set forth in SEQ ID NO: 4. In some of any of the provided [embodimentexamples](#), the costimulatory signaling region includes the sequence set forth in SEQ ID NO: 4. In some of any of the provided [embodimentexamples](#), the costimulatory signaling region is a sequence of amino acids that has at least 90% sequence identity to the sequence set forth in SEQ ID NO: 4. In some of any of the provided [embodimentexamples](#), the costimulatory signaling region includes a sequence of amino acids that has at least 90% sequence identity to the sequence set forth in SEQ ID NO: 4.

[0047] In some of any of the provided [embodimentexamples](#), the costimulatory signaling region is between the transmembrane domain and the cytoplasmic signaling domain of a CD3-zeta (CD3 ζ) chain.

[0048] In some of any of the provided [embodimentexamples](#), the first CAR contains from its N to C terminus, in order: the extracellular antigen-binding domain, the spacer, the transmembrane domain and the intracellular signaling region.

[0049] In some of any of the provided [embodimentexamples](#), the first CAR contains (a) an extracellular antigen-binding domain, comprising: a variable heavy chain (V_H) comprising a heavy chain complementarity determining region 1 (CDR-H1), a heavy chain complementarity determining region 2 (CDR-H2) and a heavy chain complementarity determining region 3 (CDR-H3) contained within the sequence set forth in SEQ ID NO: 116 and a variable light chain (V_L) comprising a light chain complementarity determining region 1 (CDR-L1), a light chain complementarity determining region 2 (CDR-L2) and a light chain complementarity

determining region 3 (CDR-L3) contained within the sequence set forth in SEQ ID NO: 119; (b) a spacer comprising a modified IgG4 hinge; an IgG2/4 chimeric C_H2 region; and an IgG4 C_H3 region, that is about 228 amino acids in length; (c) a transmembrane domain from a human CD28; and (d) an intracellular signaling region comprising a cytoplasmic signaling domain of a CD3-zeta (CD3ζ) chain and a costimulatory signaling region comprising an intracellular signaling domain of a 4-1BB.

[0050] In some of any of the provided [embodimentexamples](#), the first CAR contains (a) an extracellular antigen-binding domain, comprising the sequence set forth in SEQ ID NO: 114 or a sequence of amino acids having at least 90% sequence identity to the amino acid sequence of SEQ ID NO: 114; (b) a spacer comprising the sequence set forth in SEQ ID NO: 174 or a sequence of amino acids that has at least 90% sequence identity to SEQ ID NO:174; (c) a transmembrane domain comprising the sequence set forth in SEQ ID NO:138 or a sequence of amino acids that has at least 90% sequence identity to SEQ ID NO:138; and (d) an intracellular signaling region comprising a cytoplasmic signaling comprising the sequence set forth in SEQ ID NO:143 or a sequence of amino acids that has at least 90% sequence identity to SEQ ID NO:143 and a costimulatory signaling region comprising the sequence set forth in SEQ ID NO:4 or a sequence of amino acids that has at least 90% sequence identity to the sequence set forth in SEQ ID NO: 4.

[0051] In some of any of the provided [embodimentexamples](#), the first CAR contains (a) an extracellular antigen-binding domain, comprising the sequence set forth in SEQ ID NO: 114; (b) a spacer comprising the sequence set forth in SEQ ID NO: 174; (c) a transmembrane domain comprising the sequence set forth in SEQ ID NO:138; and (d) an intracellular signaling region comprising a cytoplasmic signaling comprising the sequence set forth in SEQ ID NO:143 and a costimulatory signaling region comprising the sequence set forth in SEQ ID NO:4.

[0052] In some of any of the provided [embodimentexamples](#), the first CAR contains the sequence set forth in SEQ ID NO:19. In some of any of the provided [embodimentexamples](#), the first CAR is encoded by a polynucleotide sequence comprising the sequence set forth in SEQ ID NO: 13 or a sequence that exhibits at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto. In some of any of the provided [embodimentexamples](#), the first CAR is encoded by a polynucleotide sequence comprising the sequence set forth in SEQ ID NO: 13. In some of any of the provided [embodimentexamples](#), the first CAR is encoded by a polynucleotide sequence that exhibits at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to SEQ ID NO: 13.

[0053] In some [embodimentexamples](#), wherein the first CAR contains the sequence set forth in SEQ

ID NO: 312.

[0054] In some of any of the provided [embodimentexamples](#), the first CAR and the second CAR bind to the same epitope of BCMA.

[0055] In some of any of the provided [embodimentexamples](#), the first CAR and the second CAR bind to different epitopes of BCMA.

[0056] In some of any of the provided [embodimentexamples](#), the first CAR and the second CAR are different.

[0057] In some of any of the provided [embodimentexamples](#), the second CAR includes: a V_H region comprising a CDR-H1, a CDR-H2, and a CDR-H3 comprising the amino acid sequence of SEQ ID NOs:257, 258, and 259, respectively; and a V_L region comprising a CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequence of SEQ ID NOs:260, 261, and 262, respectively; a V_H region comprising the sequence set forth in SEQ ID NO:125 and a V_L region comprising the sequence set forth in SEQ ID NO:127; the amino acid residues 22-493 of the sequence set forth in SEQ ID NO:265; and/or the sequence encoded by SEQ ID NO:266. In some of any of the provided [embodimentexamples](#), the second CAR includes a V_H region comprising a CDR-H1, a CDR-H2, and a CDR-H3 comprising the amino acid sequence of SEQ ID NOs: 260, 261, and 262, respectively; and a V_L region comprising a CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequence of SEQ ID NOs: 257, 258, and 259, respectively. In some of any of the provided [embodimentexamples](#), the second CAR includes a V_H region comprising the sequence set forth in SEQ ID NO:125 and a V_L region comprising the sequence set forth in SEQ ID NO:127. In some of any of the provided [embodimentexamples](#), the second CAR includes the amino acid residues 22-493 of the sequence set forth in SEQ ID NO:263. In some of any of the provided [embodimentexamples](#), the second CAR includes the sequence encoded by SEQ ID NO:264. In some of any of the provided [embodimentexamples](#), the second CAR includes the amino acid residues 22-493 of the sequence set forth in SEQ ID NO:263 and the sequence encoded by SEQ ID NO:264. In some of any of the provided [embodimentexamples](#), the second CAR includes the amino acid residues 22-493 of the sequence set forth in SEQ ID NO:263 and/or the sequence encoded by SEQ ID NO:264. In some of any of the provided [embodimentexamples](#), the second CAR includes the sequence encoded by SEQ ID NO:312.

[0058] In some of any of the provided [embodimentexamples](#), the second CAR is a multivalent CAR. In some of any of the provided [embodimentexamples](#), the second CAR includes the amino acid residues beginning at residue 22 to the end of the sequence set forth in any one of SEQ ID NOS: 267-304. In some of any of the provided [embodimentexamples](#), the second CAR is a multivalent CAR. In some of any of the provided [embodimentexamples](#), the second CAR includes the amino acid residues beginning at residue 22 to the end of the sequence set forth in any one of SEQ ID NOS: 265-

302.

[0059] In some of any of the provided [embodimentexamples](#), the second CAR includes a Centyrin-containing CAR. In some of any of the provided [embodimentexamples](#), the second CAR includes the amino acid residues 22-334 of the sequence set forth in SEQ ID NO: 310.

[0060] In some of any of the provided [embodimentexamples](#), the first CAR and the second CAR are the same.

[0061] In some of any of the provided [embodimentexample](#), the dose of engineered T cells that express the first CAR is generated from a sample comprising T cells obtained from the same subject that has previously been administered the prior dose of engineered T cells comprising the second CAR. In some of any of the provided [embodimentexamples](#), the dose of engineered T cells that express the first CAR is generated from a sample comprising T cells obtained from the subject after the subject has been administered the prior dose of engineered T cells comprising the second CAR.

[0062] In some of any of the provided [embodimentexample](#), prior to the administration of the dose of engineered T cells that express the first CAR, the method further includes assessing, in a test sample obtained from the subject, the presence or amount of (i) cells expressing the second CAR or (ii) a nucleotide sequence present in the construct encoding the second CAR. In some of any of the provided [embodimentexamples](#), prior to the administration of the dose of engineered T cells that express the first CAR, the method further includes assessing, in a test sample obtained from the subject, the presence or amount of cells expressing the second CAR. In some of any of the provided [embodimentexamples](#), prior to the administration of the dose of engineered T cells that express the first CAR, the method further includes assessing, in a test sample obtained from the subject, the presence or amount of a nucleotide sequence present in the construct encoding the second CAR. In some of any of the provided [embodimentexamples](#), the test sample is obtained from the subject at the same time as obtaining the sample comprising T cells for generating the dose of engineered T cells that express the first CAR from the same subject.

[0063] In some of any of the provided [embodimentexample](#), prior to administering the dose of engineered T cells that express the first CAR, the method further includes assessing the presence or amount of (i) cells expressing the second CAR or a (ii) nucleotide sequence present in the construct encoding the second CAR in a composition comprising the dose of engineered T cells that express the first CAR. In some of any of the provided [embodimentexamples](#), prior to administering the dose of engineered T cells that express the first CAR, the method further includes assessing the presence or amount of cells expressing the second CAR. In some of any of the provided [embodimentexamples](#), prior to administering the dose of engineered T cells that express the first CAR,

the method further includes assessing the presence or amount of a nucleotide sequence present in the construct encoding the second CAR in a composition comprising the dose of engineered T cells that express the first CAR. In some of any of the provided [embodimentexamples](#), the assessing the presence or amount of cells expressing the second CAR is carried out by contacting the sample or the dose of composition comprising the engineered T cells with a purified or recombinant BCMA. In some of any of the provided [embodimentexamples](#), the assessing the presence or amount of cells expressing the second CAR is carried out by contacting the sample or the dose of engineered T cells with a BCMA-Fc.

[0064] In some of any of the provided [embodimentexamples](#), the assessing the presence or amount of the nucleotide sequence present in a construct encoding the second CAR is carried out by quantitative polymerase chain reaction (qPCR).

[0065] In some of any of the provided [embodimentexamples](#), the binding of the extracellular antigen-binding domain and/or the first CAR, or a measure indicative of function or activity of the first CAR following exposure to cells expressing surface BCMA, is not reduced or blocked or is not substantially reduced or blocked in the presence of a soluble or shed form of BCMA. In some of any of the provided [embodimentexamples](#), the binding of the extracellular antigen-binding domain to cells expressing surface BCMA, is not reduced or blocked or is not substantially reduced or blocked in the presence of a soluble or shed form of BCMA. In some of any of the provided [embodimentexamples](#), the binding of the first CAR to cells expressing surface BCMA, is not reduced or blocked or is not substantially reduced or blocked in the presence of a soluble or shed form of BCMA. In some of any of the provided [embodimentexamples](#), a measure indicative of function or activity of the first CAR following exposure to cells expressing surface BCMA is not reduced or blocked or is not substantially reduced or blocked in the presence of a soluble or shed form of BCMA. In some of any of the provided [embodimentexamples](#), the concentration or amount of the soluble or shed form of the BCMA corresponds to a concentration or amount present in serum or blood or plasma of the subject or of a multiple myeloma patient, or on average in a multiple myeloma patient population, or at a concentration or amount of the soluble or shed BCMA at which the binding or measure is reduced or blocked, or is substantially reduced or blocked, for cells expressing a reference anti-BCMA recombinant receptor, such as a reference anti-BCMA CAR, in the same assay.

[0066] In some of any of the provided [embodimentexamples](#), the dose of engineered T cells that express the first CAR contains between at or about 1×10^7 CAR+ T cells and at or about 2×10^9 CAR+ T cells. In some of any of the provided [embodimentexamples](#), the dose of engineered T cells that express the first CAR contains between at or about 1×10^7 CAR+ T cells and at or about 1×10^9

CAR⁺ T cells. In some of any of the provided [embodimentexamples](#), the dose of engineered T cells that express the first CAR contains between at or about 1×10^8 CAR⁺ T cells and at or about 1×10^8 CAR⁺ T cells. In some of any of the provided [embodimentexamples](#), the dose of engineered T cells includes at or about 5×10^7 cells or CAR⁺ T cells. In some of any of the provided [embodimentexamples](#), the dose of engineered T cells that express the first CAR contains at or about 1×10^8 cells or CAR⁺ T cells. In some of any of the provided [embodimentexamples](#), the dose of engineered T cells that express the first CAR contains at or about 1.5×10^8 cells or CAR⁺ T cells. In some of any of the provided [embodimentexamples](#), the dose of engineered T cells that express the first CAR contains at or about 2×10^8 cells or CAR⁺ T cells. In some of any of the provided [embodimentexamples](#), the dose of engineered T cells that express the first CAR contains at or about 2.5×10^8 cells or CAR⁺ T cells. In some of any of the provided [embodimentexamples](#), the dose of engineered T cells that express the first CAR contains at or about 3×10^8 cells or CAR⁺ T cells. In some of any of the provided [embodimentexamples](#), the dose of engineered T cells that express the first CAR contains at or about 3.5×10^8 cells or CAR⁺ T cells. In some of any of the provided [embodimentexamples](#), the dose of engineered T cells that express the first CAR contains at or about 4×10^8 cells or CAR⁺ T cells. In some of any of the provided [embodimentexamples](#), the dose of engineered T cells that express the first CAR contains at or about 4.5×10^8 cells or CAR⁺ T cells. In some of any of the provided [embodimentexamples](#), the dose of engineered T cells that express the first CAR contains at or about 5×10^8 cells or CAR⁺ T cells. In some of any of the provided [embodimentexamples](#), the dose of engineered T cells that express the first CAR contains at or about 5.5×10^8 cells or CAR⁺ T cells. In some of any of the provided [embodimentexamples](#), the dose of engineered T cells that express the first CAR contains at or about 6×10^8 cells or CAR⁺ T cells. In some of any of the provided [embodimentexamples](#), the dose of engineered T cells that express the first CAR contains at or about 8×10^8 cells or CAR⁺ T cells. In some of any of the provided [embodimentexamples](#), the dose of engineered T cells that express the first CAR contains at or about 1×10^9 cells or CAR⁺ T cells. In some of any of the provided [embodimentexamples](#), the dose of engineered T cells that express the first CAR contains at or about 1.5×10^9 cells or CAR⁺ T cells. In some of any of the provided [embodimentexamples](#), the dose of engineered T cells that express the first CAR contains at or about 2×10^9 cells or CAR⁺ T cells.

[0067] In some of any of the provided [embodimentexamples](#), the dose of engineered T cells that express the first CAR contains a combination of CD4⁺ T cells and CD8⁺ T cells. In some of any of the provided [embodimentexamples](#), the dose of engineered T cells that express the first CAR includes a combination of CD4⁺ CAR⁺ T cells and CD8⁺ CAR⁺ T cells. In some of any of the provided [embodimentexamples](#), the ratio of CD4⁺ CAR⁺ T cells to CD8⁺ CAR⁺ T cells and/or of CD4⁺ T cells to CD8⁺ T cells is or is approximately 1:1 or is between at or approximately 1:3 and at or

approximately 3:1. In some of any of the provided [embodimentexamples](#), the ratio of CD4⁺ CAR⁺ T cells to CD8⁺ CAR⁺ T cells is or is approximately 1:1. In some of any of the provided [embodimentexamples](#), the ratio of CD4⁺ CAR⁺ T cells to CD8⁺ CAR⁺ T cells is or is between at or approximately 1:3 and at or approximately 3:1. In some of any of the provided [embodimentexamples](#), the dose of engineered T cells that express the first CAR includes a combination of CD4⁺ CAR⁺ T cells and CD8⁺ CAR⁺ T cells. In some of any of the provided [embodimentexamples](#), the ratio of CD4⁺ T cells to CD8⁺ T cells is or is approximately 1:1 or is between at or approximately 1:3 and at or approximately 3:1. In some of any of the provided [embodimentexamples](#), the ratio of CD4⁺ T cells to CD8⁺ T cells is or is approximately 1:1. In some of any of the provided [embodimentexamples](#), the ratio of CD4⁺ T cells to CD8⁺ T cells is or is between at or approximately 1:3 and at or approximately 3:1.

[0068] In some of any of the provided [embodimentexamples](#), the dose of engineered T cells that express the first CAR contains CD3⁺ CAR⁺ T cells.

[0069] In some of any of the provided [embodimentexamples](#), less than at or about 25%, 20%, 15%, 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2% or 1% of the CAR⁺ T cells in the dose of engineered T cells that express the first CAR express a marker of apoptosis, such as Annexin V or active Caspase 3. In some of any of the provided [embodimentexamples](#), less than at or about 25%, 20%, 15%, 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2% or 1% of the CAR⁺ T cells in the dose of engineered T cells that express the first CAR express a marker of apoptosis. In some [embodimentexamples](#), the marker of apoptosis is Annexin V. In some [embodimentexamples](#), the marker of apoptosis is active Caspase 3.

[0070] In some of any of the provided [embodimentexamples](#), prior to the administration of the dose of engineered T cells that express the first CAR, the subject has been administered a lymphodepleting therapy that includes the administration of fludarabine at or about 20-40 mg/m² body surface area of the subject. In some of any of the provided [embodimentexamples](#), prior to the administration of the dose of engineered T cells that express the first CAR, the subject has been administered a lymphodepleting therapy that includes the administration of fludarabine at or about 30 mg/m², daily, for 2-4 days. In some of any of the provided [embodimentexamples](#), prior to the administration of the dose of engineered T cells that express the first CAR, the subject has been administered a lymphodepleting therapy that includes the administration of cyclophosphamide at or about 200-400 mg/m² body surface area of the subject. In some of any of the provided [embodimentexamples](#), prior to the administration of the dose of engineered T cells that express the first CAR, the subject has been administered a lymphodepleting therapy that includes the administration of cyclophosphamide at or about 300 mg/m², daily, for 2-4 days. In some of any of the provided [embodimentexamples](#), the lymphodepleting therapy includes the administration of

fludarabine at or about 30 mg/m² body surface area of the subject, daily, and cyclophosphamide at or about 300 mg/m² body surface area of the subject, daily, for 3 days.

[0071] In some of any of the provided [embodimentexamples](#), the disease or disorder associated with BCMA expression is an autoimmune disease or disorder. In some of any of the provided [embodimentexamples](#), the disease or disorder associated with BCMAexpression is a cancer. In some of any of the provided [embodimentexample](#), a BCMA-expressing cancer.

[0072] In some of any of the provided [embodimentexamples](#), the cancer is a B cell malignancy. In some of any of the provided [embodimentexamples](#), the cancer is a lymphoma, a leukemia, or a plasma cell malignancy. In some of any of the provided [embodimentexamples](#), the cancer is a lymphoma and the lymphoma is Burkitt lymphoma, non-Hodgkin's lymphoma (NHL), Hodgkin's lymphoma, Waldenstrom macroglobulinemia, follicular lymphoma, small non-cleaved cell lymphoma, mucosa-associated lymphatic tissue lymphoma (MALT), marginal zone lymphoma, splenic lymphoma, nodal monocytoid B cell lymphoma, immunoblastic lymphoma, large cell lymphoma, diffuse mixed cell lymphoma, pulmonary B cell angiocentric lymphoma, small lymphocytic lymphoma, primary mediastinal B cell lymphoma, lymphoplasmacytic lymphoma (LPL), or mantle cell lymphoma (MCL). In some of any of the provided [embodimentexamples](#), the cancer is a leukemia and the leukemia is chronic lymphocytic leukemia (CLL), plasma cell leukemia or acute lymphocytic leukemia (ALL). In some of any of the provided [embodimentexamples](#), the cancer is a plasma cell malignancy and the plasma cell malignancy is multiple myeloma (MM) or plasmacytoma. In some of any of the provided [embodimentexamples](#), the cancer is multiple myeloma (MM). In some of any of the provided [embodimentexamples](#), the cancer is a relapsed and/or refractory multiple myeloma (R/R MM). In some of any of the provided [embodimentexamples](#), the cancer is a relapsed or refractory multiple myeloma (R/R MM). In some of any of the provided [embodimentexamples](#), the cancer is a relapsed multiple myeloma (MM). In some of any of the provided [embodimentexamples](#), the cancer is a refractory multiple myeloma (MM).

[0073] In some of any of the provided [embodimentexamples](#), the subject has been administered three or more prior therapies for the disease or disorder, such as four or more prior therapies. In some of any of the provided [embodimentexamples](#), the three or more prior therapies for the disease or disorder, or the four or more prior therapies are selected from among: autologous stem cell transplant (ASCT); an immunomodulatory agent; a proteasome inhibitor; and an anti-CD38 antibody. In some of any of the provided [embodimentexamples](#), the immunomodulatory agent is selected from among thalidomide, lenalidomide and pomalidomide. In some of any of the provided [embodimentexamples](#), the proteasome inhibitor is selected from among bortezomib, carfilzomib and ixazomib. In some of any of the provided [embodimentexamples](#), the anti-CD38 antibody is or includes

daratumumab.

[0074] In some of any of the provided [embodimentexamples](#), the subject has been administered between 3 and 15 or between 4 and 15 prior therapies or about 10 prior therapies. In some of any of the provided [embodimentexamples](#), the subject has relapsed following or has been refractory to the one or more of the three or more prior therapies. In some of any of the provided [embodimentexamples](#), the subject has relapsed following or has been refractory to the one or more prior therapies. In some of any of the provided [embodimentexamples](#), the subject has relapsed following or has been refractory to at least 3 or at least 4 prior therapies. In some of any of the provided [embodimentexamples](#), the subject has relapsed following or has been refractory to at least 3 prior therapies. In some of any of the provided [embodimentexamples](#), the subject has relapsed following or has been refractory to at least 4 prior therapies. In some of any of the provided [embodimentexamples](#), the subject has been refractory to or has not responded to bortezomib, carfilzomib, lenalidomide, pomalidomide and/or an anti-CD38 monoclonal antibody.

[0075] In some of any of the provided [embodimentexamples](#), the subject has had prior autologous stem cell transplant. In some of any of the provided [embodimentexamples](#), the subject has not had prior autologous stem cell transplant.

[0076] In some of any of the provided [embodimentexamples](#), the subject does not have an active or a history of plasma cell leukemia (PCL). In some of any of the provided [embodimentexamples](#), the subject has developed secondary plasma cell leukemia (PCL).

[0077] In some of any of the provided [embodimentexamples](#), the subject is an adult subject or is 25 or 35 years of age or older. In some of any of the provided [embodimentexamples](#), the subject is an adult subject. In some of any of the provided [embodimentexamples](#), the subject is 25 years of age or older. In some of any of the provided [embodimentexamples](#), the subject is 35 years of age or older.

[0078] In some of any of the provided [embodimentexamples](#), the subject has a time from diagnosis of the disease or disorder of approximately 4 years or between 2 and 15 years or between 2 and 12 years.

[0079] In some of any of the provided [embodimentexamples](#), the subject has IMWG high risk cytogenetics.

Brief Description of the Drawings

[0080] FIG. 1 shows the objective response rate (ORR), including rates of complete response (CR) and stringent complete response (sCR), very good partial response (VGPR), and partial response (PR) in human subjects with relapsed and/or refractory multiple myeloma (MM) that have been administered compositions containing autologous T cells expressing a CAR