of administration to subjects, articles of manufacture and kits for use in the methods. In some aspects, features of the methods and cells provide for increased or improved activity, efficacy, persistence, expansion and/or proliferation of T cells for adoptive cell therapy or endogenous T cells recruited by immunotherapeutic agents.

Background

[0004] Various strategies are available for immunotherapy, for example administering engineered T cells for adoptive therapy. For example, strategies are available for engineering T cells expressing genetically engineered antigen receptors, such as CARs, and administering compositions containing such cells to subjects. Improved strategies are needed to improve efficacy of the cells, for example, improving the persistence, activity and/or proliferation of the cells upon administration to subjects. Provided are methods, compositions, kits, and systems that meet such needs.

Summary

[0005] Provided herein are combination therapies involving administration of an immunotherapy involving T cell function or activity, such as a T cell therapy, and an immunomodulatory compound, such as a structural or functional analog or derivative of thalidomide and/or an inhibitor of E3-ubiquitin ligase. In some examples, the provided methods enhance or modulate proliferation and/or activity of T cell activity associated with administration of an immunotherapy or immunotherapeutic agent, such as a composition including cells for adoptive cell therapy, e.g., such as a T cell therapy (e.g. CAR-expressing T cells). In some examples, the combination therapy generally involves administration of an immunomodulatory compound, such as a structural or functional analog of thalidomide and/or an inhibitor of E3-ubiquitin ligase (e.g. lenalidomide (3-(4-amino-1-oxo-1,3-dihydro-2H-isoindol-2-yl)piperidine-2,6-dione)), and administration of the T cell therapy, such as a composition including cells for adoptive cell therapy, e.g., such as a T cell therapy (e.g. CAR-expressing T cells).

[0006] Provided herein are methods of treatment that involve: (a) administering a T cell therapy to a subject having a disease or condition; and (b) administering to the subject an immunomodulatory compound.

[0007] Provided herein are methods of treatment that involve administering a T cell therapy to a subject having a disease or condition, wherein, at the time of initiation of the administration of the T cell therapy, the subject has been administered, and/or is undergoing treatment with, an immunomodulatory compound and/or a blood or biopsy sample of the subject contains detectable levels of T cells of an engineered T cell therapy.

[0008] Provided herein are methods of treatment that involve administering an immunomodulatory compound to a subject having a disease or condition, wherein, at the time of initiation of administration of the immunomodulatory compound, the subject has been previously administered a T cell therapy for treatment of the disease or condition and/or a blood or biopsy sample of the subject contains detectable levels of T cells of an engineered T cell therapy. In some examples, the method thereby prevents, reduces or ameliorates one or more symptoms or outcomes of the disease or condition.

[0008a] In one aspect, the present disclosure refers to use of an immunomodulatory compound in the manufacture of a medicament for the treatment of a disease or condition in a subject, wherein the subject has been previously administered a T cell therapy for treatment of the disease or condition at the time of initiation of administration of the immunomodulatory compound, wherein said immunomodulatory compound is selected from the group consisting of: thalidomide analogs; thalidomide derivatives; compounds that interact with and/or bind to cereblon (CRBN) and/or one or more members of the CRBN E3 ubiquitin-ligase complex; inhibitors of Ikaros (IKZF1); inhibitors of Aiolos (IKZF3); and compounds that enhance or promote ubiquitination and/or degradation of Ikaros (IKZF1) and/or Aiolos (IKZF3).

[0008b] In another aspect, the present disclosure refers to use of a combination comprising a T cell therapy and an immunomodulatory compound in the manufacture of a medicament for the treatment of a disease or condition, wherein:

(a) the T cell therapy is to be administered to a subject having a disease or condition; and

(b) a therapeutically effective amount of the immunomodulatory compound is to be administered to the subject, wherein said immunomodulatory compound is selected from the group consisting of: thalidomide analogs; thalidomide derivatives; compounds that interact with and/or bind to cereblon (CRBN) and/or one or more members of the CRBN E3 ubiquitin-ligase complex; inhibitors of Ikaros (IKZF1); inhibitors of Aiolos (IKZF3); and compounds that enhance or promote ubiquitination and/or degradation of Ikaros (IKZF1) and/or Aiolos (IKZF3).

[0009] In some examples of any of the methods provided herein, (a) the amount of the immunomodulatory compound administered is insufficient, as a single agent and/or in the absence of administration of the T cell therapy, to ameliorate, reduce or prevent the disease or condition or a symptom or outcome thereof; and/or (b) the amount of the immunomodulatory compound administered is insufficient, as a single agent and/or in the absence of administration of the T cell therapy, to ameliorate, reduce or prevent the disease or condition in the subject or a symptom or outcome thereof; and/or (c) the method thereby reduces or ameliorates a symptom or outcome or burden of the disease or condition to a degree that is greater than the combination of (i) the degree of reduction or amelioration effected by the administration of the immunomodulatory agent alone, optionally on average in a population of subjects having the disease or condition, and (ii) the degree of reduction or amelioration by the administration of the T cell therapy alone, optionally on average in a population of subjects having the disease or condition; and/or (d) the amount of the immunomodulatory compound administered in the method, or administered in one or more doses, is a maintenance-level dose of the compound, or corresponds to a dose of the compound administered to subjects having exhibited a response, optionally a complete response, following administration of the compound for treatment.

[0010] In some examples of any of the methods provided herein, the disease or condition is refractory or resistant to the immunomodulatory compound and/or has become refractory or resistant thereto following treatment with the immunomodulatory compound; and/or the subject or disease or condition has been determined to have a mutation or factor

conferring resistance of the disease or condition to treatment with the immunomodulatory compound.

[0011] In some examples of any of the methods provided herein, the immunomodulatory compound is selected from: immunomodulatory drugs (IMiDs), thalidomide analogs, thalidomide derivatives, compounds that interact with and/or bind to cereblon (CRBN) and/or one or more members of the CRBN E3 ubiquitin-ligase complex, inhibitors of Ikaros (IKZF1), inhibitors of Aiolos (IKZF3), compounds that enhance or promote ubiquitination and/or degradation of Ikaros (IKZF1) and/or Aiolos (IKZF3).

[0012] Provided herein are methods of treatment that involves (a) administering a T cell therapy to a subject having a disease or condition; and (b) administering to the subject an immunomodulatory compound, wherein said immunomodulatory compound is selected from the group consisting of lenalidomide (3-(4-amino-1-oxo-1,3-dihydro-2H-isoindol-2-yl)piperidine-2,6-dione), pomalidomide (4-amino-2-(2,6-dioxopiperidin-3-yl)isoindole-1,3-dione), or avadomide (3-(5-amino-2-methyl-4-oxo-4H-quinazolin-3-yl)-piperidine-2,6-dione), a stereoisomer, an enantiomer or a mixture of enantiomers thereof, or a pharmaceutically acceptable salt, solvate, hydrate, co-crystal, clathrate, or polymorph thereof.

[0013] Provided herein are methods of treatment that involves administering a T cell therapy to a subject having a disease or condition, wherein, at the time of initiation of the administration of the T cell therapy, the subject has been administered, and/or is undergoing treatment with, an immunomodulatory compound and/or a blood or biopsy sample of the subject contains detectable levels of T cells of an engineered T cell therapy, wherein said immunomodulatory compound is selected from the group consisting of lenalidomide (3-(4-amino-1-oxo-1,3-dihydro-2H-isoindol-2-yl)piperidine-2,6-dione), pomalidomide (4-amino-2-(2,6-dioxopiperidin-3-yl)isoindole-1,3-dione), or avadomide (3-(5-amino-2-methyl-4-oxo-4H-quinazolin-3-yl)-piperidine-2,6-dione), a stereoisomer, an enantiomer or a mixture of enantiomers thereof, or a pharmaceutically acceptable salt, solvate, hydrate, co-crystal, clathrate, or polymorph thereof.

[0014] Provided herein are methods of treatment that involves administering an immunomodulatory compound to a subject having a disease or condition, wherein, at the time of initiation of administration of the immunomodulatory compound, the subject has been previously administered a T cell therapy for treatment of the disease or condition and/or a blood or biopsy sample of the subject contains detectable levels of T cells of an engineered T cell therapy, wherein said immunomodulatory compound is selected from the group consisting of

(2,6-dioxopiperidin-3-yl)isoindole-1,3-dione), or avadomide (3-(5-amino-2-methyl-4-oxo-4H-quinazolin-3-yl)-piperidine-2,6-dione), a stereoisomer, an enantiomer or a mixture of enantiomers thereof, or a pharmaceutically acceptable salt, solvate, hydrate, co-crystal, clathrate, or polymorph thereof, to a subject having been administered, prior to initiation of administration of the immunomodulatory compound, a T cell therapy for treating a disease or condition, wherein the subject is one in which at or about at day 12 to 15, optionally at or about day 14, after initiation of administration of a T cell therapy for treating a disease or condition: (i) the number of cells of the T cell therapy in the subject is less than 75% of the average number of cells of the T cell therapy at the same time in a plurality of subjects administered the same or similar dose of the T cell therapy; and/or (ii) the number of CD3+ or CD8+ cells of the T cell therapy, optionally CAR+ T cells, in the blood is less than 10 cells per μL, less than 5 cells per μL or less than per 1 cells per μL.

[0018] Provided herein are methods of treatment that involves (a) selecting a subject in which at or about at day 12 to 15, optionally at or about day 14, after initiation of administration of a T cell therapy for treating a disease or condition: (i) the number of cells of the T cell therapy in the subject is less than 75% of the average number of cells of the T cell therapy at the same time in a plurality of subjects administered the same or similar dose of the T cell therapy; and/or (ii) the number of CD3+ or CD8+ cells of the T cell therapy, optionally CAR+ T cells, in the blood is less than 10 cells per μL, less than 5 cells per μL or less than per 1 cells per μL; and (b) administering a therapeutically effective amount of an immunomodulatory compound to the subject, wherein said immunomodulatory compound is selected from the group consisting of lenalidomide (3-(4-amino-1-oxo-1,3-dihydro-2H-isoindol-2-yl)piperidine-2,6-dione), pomalidomide (4-amino-2-(2,6-dioxopiperidin-3-yl)isoindole-1,3-dione), or avadomide (3-(5-amino-2-methyl-4-oxo-4H-quinazolin-3-yl)-piperidine-2,6-dione), a stereoisomer, an enantiomer or a mixture of enantiomers thereof, or a pharmaceutically acceptable salt, solvate, hydrate, co-crystal, clathrate, or polymorph thereof.

[0018a] In another aspect, the present disclosure refers to use of an immunomodulatory compound in the manufacture of a medicament for the treatment of a disease or condition in a subject, wherein:

the immunomodulatory compound is to be administered to a subject in which at or about at day 12 to 15 after initiation of administration of the T cell therapy for treating the disease or condition:

(i) the number of cells of the T cell therapy in the subject is less than 75% of the average number of cells of the T cell therapy at the same time in a plurality of subjects administered the same or similar dose of the T cell therapy; and/or

(ii) the number of CD3+ or CD8+ cells of the T cell therapy, optionally CAR+ T cells, in the blood is less than 10 cells per μL, less than 5 cells per μL or less than per 1 cells per μL; and

the immunomodulatory compound is selected from the group consisting of: thalidomide analogs; thalidomide derivatives; compounds that interact with and/or bind to cereblon (CRBN) and/or one or more members of the CRBN E3 ubiquitin-ligase complex; inhibitors of Ikaros (IKZF1); inhibitors of Aiolos (IKZF3); and compounds that enhance or promote ubiquitination and/or degradation of Ikaros (IKZF1) and/or Aiolos (IKZF3).

[0019] Provided herein are methods of treatment that involves administering a T cell therapy to a subject having a disease or condition, wherein the subject has been administered, prior to initiation of the T cell therapy, an immunomodulatory compound, wherein said immunomodulatory compound is selected from the group consisting of: lenalidomide (3-(4-amino-1-oxo-1,3-dihydro-2H-isoindol-2-yl)piperidine-2,6-dione), pomalidomide (4-amino-2-(2,6-dioxopiperidin-3-yl)isoindole-1,3-dione), or avadomide (3-(5-amino-2-methyl-4-oxo-4H-

quinazolin-3-yl)-piperidine-2,6-dione), a stereoisomer, an enantiomer or a mixture of enantiomers thereof, or a pharmaceutically acceptable salt, solvate, hydrate, co-crystal, clathrate, or polymorph thereof, and wherein the immunomodulatory compound is administered in a cycle comprising: (i) administration for up to 21 consecutive days, wherein the cycle comprises greater than 30 days beginning upon initiation of the administration of the immunomodulatory compound; and/or (ii) administration for a plurality of consecutive days followed by a rest period during which the immunomodulatory compound is not administered, wherein the rest period is greater than 14 consecutive days; and/or (iii) administration for no more than 14 consecutive days.

[0019a] In another aspect, the present disclosure refers to use of a T cell therapy in the manufacture of a medicament for the treatment of a disease or condition in a subject, wherein the subject has been administered, prior to initiation of the T cell therapy, an immunomodulatory compound, wherein said immunomodulatory compound is selected from the group consisting of: thalidomide analogs; thalidomide derivatives; compounds that bind to cereblon (CRBN) and/or one or more members of the CRBN E3 ubiquitin-ligase complex; inhibitors of Ikaros (IKZF1); inhibitors of Aiolos (IKZF3); and compounds that enhance or promote ubiquitination and/or degradation of Ikaros (IKZF1) and/or Aiolos (IKZF3).

[0020] Provided herein are methods of treatment that involves comprising administering an immunomodulatory compound to a subject, the subject having a disease or condition and having been administered, a T cell therapy, wherein said immunomodulatory compound is selected from the group consisting of: lenalidomide (3-(4-amino-1-oxo-1,3-dihydro-2H-isoindol-2-yl)piperidine-2,6-dione), pomalidomide (4-amino-2-(2,6-dioxopiperidin-3-yl)isoindole-1,3-dione), or avadomide (3-(5-amino-2-methyl-4-oxo-4H-quinazolin-3-yl)-piperidine-2,6-dione), a stereoisomer, an enantiomer or a mixture of enantiomers thereof, or a pharmaceutically acceptable salt, solvate, hydrate, co-crystal, clathrate, or polymorph thereof, and wherein the immunomodulatory compound is administered in a cycle comprising: (i) administration of the immunomodulatory compound for up to 21 consecutive days, wherein the cycle comprises greater than 30 days beginning upon initiation of the administration of the immunomodulatory compound; and/or (ii) administration of the immunomodulatory compound for a plurality of consecutive days followed by a rest period during which the immunomodulatory compound is not administered, wherein the rest period is greater than 14 consecutive days; and/or (iii) administration of the immunomodulatory compound for no more than 14 consecutive days.

[0021] In some examples of any of the methods provided herein, the administration of the immunomodulatory compound includes: (i) at least one cycle of greater than 30 days beginning upon initiation of the administration of the immunomodulatory compound, wherein the cycle includes administration of the compound, optionally daily or at least daily, for up to 21 consecutive days and/or wherein the last administration of the compound in the cycle is at or less than 21 days after the first administration of the compound in the cycle; and/or (ii) at least two cycles, each of the at least two cycles including administration of the compound for a plurality of consecutive days followed by a rest period during which the immunomodulatory

compound is not administered, wherein the rest period is greater than 14 consecutive days; and/or (iii) administration, optionally daily or at least daily, for no more than 14 consecutive days.

[0022] In some examples of any of the methods provided herein, initiation of administration of the immunomodulatory compound, or initiation of administration of the compound in at least one cycle, and initiation of administration of the T cell therapy are carried out on the same day or consecutive days, optionally concurrently; and/or at least one dose of the immunomodulatory compound is administered on the same day or within one or two days, prior or subsequent to, administration of a dose of the T cell therapy.

[0023] In some examples of any of the methods provided herein, initiation of administration of the immunomodulatory compound, or initiation of administration of the compound in at least one cycle, is prior to initiation of administration of the T cell therapy.

[0024] Provided herein are methods of treatment that involve administering a T cell therapy to a subject having a disease or condition, wherein the subject has been administered, prior to initiation of the T cell therapy, an immunomodulatory compound, wherein the cycle includes: (i) administration for up to 21 consecutive days, wherein the cycle includes greater than 30 days beginning upon initiation of the administration of the immunomodulatory compound; and/or (ii) administration for a plurality of consecutive days followed by a rest period during which the immunomodulatory compound is not administered, wherein the rest period is greater than 14 consecutive days; and/or (iii) administration for no more than 14 consecutive days. In some examples, initiation of administration of the immunomodulatory compound is within 14 days prior to initiation of the T cell therapy.

[0025] In some of any of the examples provided herein, the immunomodulatory compound is selected from the group consisting of: thalidomide analogs; thalidomide derivatives; compounds that interact with and/or bind to cereblon (CRBN) and/or one or more members of the CRBN E3 ubiquitin-ligase complex; inhibitors of Ikaros (IKZF1); inhibitors of Aiolos (IKZF3); and compounds that enhance or promote ubiquitination and/or degradation of Ikaros (IKZF1) and/or Aiolos (IKZF3).

[0026] In some examples of any of the methods provided herein, administration of the immunomodulatory compound is initiated prior to administration of the T cell therapy beginning: (i) at or within one week prior to or subsequent to collecting, from the subject, a sample containing T cells to be processed and/or engineered to produce the therapy, optionally

wherein the sample is an apheresis sample; and/or (ii) within 14 days prior to initiation of the administration of the T cell therapy.

[0027] In some examples of any of the methods provided herein, the T cell therapy includes cells engineered to express a recombinant receptor. In some examples, the engineering includes one or more steps of the ex vivo manufacturing process, optionally selected from among: (1) isolating cells from a biological sample by leukapheresis or apheresis; (2) selecting or enriching cells by immunoaffinity-based methods; (3) introducing a recombinant nucleic acid, optionally a viral vector, into cells; (4) incubating cells, optionally engineered cells, in the presence of one or more stimulating conditions; (5) formulating cells in the presence of a cryoprotectant; and/or (6) formulating cells for administration to a subject, optionally in the presence of a pharmaceutically acceptable excipient.

[0028] In some examples of any of the methods provided herein, the method includes carrying out the manufacturing process and/or further including engineering T cells to express a recombinant receptor, thereby generating the T cell therapy. In some examples of any of the methods provided herein, the method includes contacting cells with an immunomodulatory compound during one or more of the steps of the ex vivo manufacturing process.

[0029] In some examples of any of the methods provided herein, the T cell therapy includes engineered T cells produced by a manufacturing process including incubation of cells, ex vivo, in the presence of the immunomodulatory compound.

[0030] In some examples of any of the methods provided herein, the method involves incubating cells in the presence of one or more stimulating conditions, which is carried out in the presence of an immunomodulatory compound.

[0031] In some examples of any of the methods provided herein, initiation of administration of the immunomodulatory compound is within 10 days, 7 days, 4 days, 3 days or 2 days prior to initiation of administration of the T cell therapy. In some examples of any of the methods provided herein, initiation of administration of the immunomodulatory compound in at least one cycle is after initiation of administration of the T cell therapy.

[0032] Provided herein are methods of treatment that involve administering an immunomodulatory compound to a subject, the subject having a disease or condition and having been administered, a T cell therapy, wherein the immunomodulatory compound is administered in a cycle including: (i) administration of the immunomodulatory compound for up to 21 consecutive days, wherein the cycle includes greater than 30 days beginning upon initiation of

the administration of the immunomodulatory compound; and/or (ii) administration of the immunomodulatory compound for a plurality of consecutive days followed by a rest period during which the immunomodulatory compound is not administered, wherein the rest period is greater than 14 consecutive days; and/or (iii) administration of the immunomodulatory compound for no more than 14 consecutive days.

[0033] In some examples of any of the methods provided herein, the T cell therapy is one in which the peak number of a population of cells of the therapy, which optionally are CD3+ or CD8+ cells of the T cell therapy and/or are optionally CAR+ T cells, in the blood is ((a) on average in a plurality of subjects treated with the T cell therapy in the absence of administration of the immunomodulatory compound, or (b) in the subject following administration of the T cell therapy) less than 10 cells per μL, less than 5 cells per μL or less than per 1 cells per μL.

[0034] In some examples of any of the methods provided herein, the T cell therapy includes cells expressing a recombinant receptor, optionally a CAR. In some examples of any of the methods provided herein, the recombinant receptor includes an antigen-binding domain specific for a B cell maturation antigen (BCMA).

[0035] In some examples of any of the methods provided herein, initiation of administration of the immunomodulatory compound in at least one cycle is carried out after initiation of administration of the T cell therapy. In some examples of any of the methods provided herein, initiation of administration of the immunomodulatory compound is carried out at least 2 days after, at least 1 week after, at least 2 weeks after, at least 3 weeks after, or at least 4 weeks after, the initiation of the administration of, or after the last dose of, the T cell therapy, and/or is carried out 2 to 28 days or 7 to 21 days after initiation of administration of, or after the last dose of, the T cell therapy.

[0036] Provided herein are methods of treatment that involve (a) administering a T cell therapy to a subject having a disease or condition; and (b) administering to the subject an immunomodulatory compound, wherein initiation of administration of the immunomodulatory compound is at a time: (a) at least 2 days after, at least 1 week after, at least 2 weeks after, at least 3 weeks after, or at least 4 weeks after, the initiation of the administration of the T cell therapy, and/or is carried out 2 to 28 days or 7 to 21 days after the initiation of administration of the T cell therapy; and/or (b) at or after, optionally immediately after or within 1 to 3 days after: (i) peak or maximum level of the cells of the T cell therapy are detectable in the blood of the subject; (ii) the number of cells of the T cell therapy detectable in the blood, after having been

progression and/or has relapsed following remission after treatment with the T cell therapy; and/or (iv) the subject exhibits increased tumor burden as compared to tumor burden at a time prior to or after administration of the T cells and prior to initiation of administration of the immunomodulatory compound.

[0038] In some examples of any of the methods provided herein, initiation of administration of the immunomodulatory compound is carried out at a time that is greater than or greater than about 14 days, 15 days, 16 days, 17 days, 18 days, 19, days, 20 days, 21 days, 24 days, or 28 days after initiation of the administration of the T cell therapy.

[0039] In some examples of any of the methods provided herein, prior to initiation of administration of the immunomodulatory compound, selecting a subject in which: (i) peak or maximum level of the cells of the T cell therapy are detectable in the blood of the subject; (ii) the number of cells of the T cell therapy detectable in the blood, after having been detectable in the blood, is not detectable or is reduced, optionally reduced compared to a preceding time point after administration of the T cell therapy; (iii) the number of cells of the T cell therapy detectable in the blood is decreased by or more than 1.5-fold, 2.0-fold, 3.0-fold, 4.0-fold, 5.0-fold, 10-fold or more the peak or maximum number cells of the T cell therapy detectable in the blood of the subject after initiation of administration of the T cell therapy; (iv) at a time after a peak or maximum level of the cells of the T cell therapy are detectable in the blood of the subject, the number of cells of or derived from the T cells detectable in the blood from the subject is less than less than 10%, less than 5%, less than 1% or less than 0.1% of total peripheral blood mononuclear cells (PBMCs) in the blood of the subject; (v) the subject exhibits disease progression and/or has relapsed following remission after treatment with the T cell therapy; and/or (iv) the subject exhibits increased tumor burden as compared to tumor burden at a time prior to or after administration of the T cells and prior to initiation of administration of the immunomodulatory compound.

[0040] Provided herein are methods of treatment that involve administering a therapeutically effective amount of an immunomodulatory compound to a subject having been administered, prior to initiation of administration of the immunomodulatory compound, a T cell therapy for treating a disease or condition, wherein the subject is one in which at or about at day 12 to 15, optionally at or about day 14, after initiation of administration of a T cell therapy for treating a disease or condition: (i) the number of cells of the T cell therapy in the subject is less than 75% of the average number of cells of the T cell therapy at the same time in a plurality of subjects

administered the same or similar dose of the T cell therapy; and/or (ii) the number of CD3+ or CD8+ cells of the T cell therapy, optionally CAR+ T cells, in the blood is less than 10 cells per µL, less than 5 cells per µL or less than per 1 cells per µL.

[0041] Provided herein are methods of treatment that involve (a) selecting a subject in which at or about at day 12 to 15, optionally at or about day 14, after initiation of administration of a T cell therapy for treating a disease or condition: (i) the number of cells of the T cell therapy in the subject is less than 75% of the average number of cells of the T cell therapy at the same time in a plurality of subjects administered the same or similar dose of the T cell therapy; and/or (ii) the number of CD3+ or CD8+ cells of the T cell therapy, optionally CAR+ T cells, in the blood is less than 10 cells per µL, less than 5 cells per µL or less than per 1 cells per µL; and (b) administering a therapeutically effective amount of an immunomodulatory compound to the subject. In some examples of any of the methods provided herein, the immunomodulatory compound is administered daily, optionally once daily.

[0042] In some examples of any of the methods provided herein, the immunomodulatory compound is administered for greater than or greater than about 7 consecutive days, greater than or greater than about 14 consecutive days, greater than or greater than about 21 consecutive days, greater than or greater than about 21 consecutive days, or greater than or greater than about 28 consecutive days. In some examples of any of the methods provided herein, the immunomodulatory compound is administered in a cycle including administration daily for a plurality of consecutive days followed by a rest period during which the immunomodulatory compound is not administered. In some examples, the rest period during with the immunomodulatory compound is not administered is greater than 7 consecutive days, greater than 14 consecutive days, greater than 21 days, or greater than 28 days.

[0043] In some examples of any of the methods provided herein, the cycle of administration of the immunomodulatory compound is repeated at least one time. In some examples, the immunomodulatory compound is administered for at least 2 cycles, at least 3 cycles, at least 4 cycles, at least 5 cycles, at least 6 cycles, at least 7 cycles, at least 8 cycles, at least 9 cycles, at least 10 cycles, at least 11 cycles, or at least 12 cycles.

[0044] In some examples of any of the methods provided herein, the administration of the immunomodulatory compound is continued, from at least after initiation of administration of the T cells, until: the number of cells of or derived from the administered T cell therapy detectable in the blood from the subject is increased compared to in the subject at a preceding

time point just prior to administration of the immunomodulatory compound or compared to a preceding time point after administration of the T-cell therapy; the number of cells of or derived from the T cell therapy detectable in the blood is within 2.0-fold (greater or less) the peak or maximum number observed in the blood of the subject after initiation of administration of the T cells; the number of cells of the T cell therapy detectable in the blood from the subject is greater than or greater than about 10%, 15%, 20%, 30%, 40%, 50%, or 60% total peripheral blood mononuclear cells (PBMCs) in the blood of the subject; and/or the subject exhibits a reduction in tumor burden as compared to tumor burden at a time immediately prior to the administration of the T cell therapy or at a time immediately prior to the administration of the immunomodulatory compound; and/or the subject exhibits complete or clinical remission.

[0045] In some examples of any of the methods provided herein, the immunomodulatory compound binds to cereblon (CRBN) and/or the CRBN E3 ubiquitin-ligase complex; and/or is an inhibitor of Ikaros (IKZF1) or Aiolos (IKZF3) transcription factor; and/or enhances ubiquitination or degradation of Ikaros (IKZF1) or Aiolos (IKZF3).

[0046] In some examples of any of the methods provided herein, the immunomodulatory compound is thalidomide or is a derivative or analogue of thalidomide. In some examples, the immunomodulatory compound is lenalidomide (3-(4-amino-1-oxo-1,3-dihydro-2H-isoindol-2-yl)piperidine-2,6-dione) or pomalidomide (4-amino-2-(2,6-dioxopiperidin-3-yl)isoindole-1,3-dione), avadomide (3-(5-amino-2-methyl-4-oxo-4H-quinazolin-3-yl)-piperidine-2,6-dione), a stereoisomer of lenalidomide (3-(4-amino-1-oxo-1,3-dihydro-2H-isoindol-2-yl)piperidine-2,6-dione), pomalidomide (4-amino-2-(2,6-dioxopiperidin-3-yl)isoindole-1,3-dione), avadomide (3-(5-amino-2-methyl-4-oxo-4H-quinazolin-3-yl)-piperidine-2,6-dione) or a pharmaceutically acceptable salt, solvate, hydrate, co-crystal, clathrate, or polymorph thereof. In some examples, the immunomodulatory compound is lenalidomide (3-(4-amino-1-oxo-1,3-dihydro-2H-isoindol-2-yl)piperidine-2,6-dione), a stereoisomer of lenalidomide (3-(4-amino-1-oxo-1,3-dihydro-2H-isoindol-2-yl)piperidine-2,6-dione) or a pharmaceutically acceptable salt, solvate, hydrate, co-crystal, clathrate, or polymorph thereof.

[0047] In some of any of the examples provided herein, the immunomodulatory compound is lenalidomide (3-(4-amino-1-oxo-1,3-dihydro-2H-isoindol-2-yl)piperidine-2,6-dione), pomalidomide (4-amino-2-(2,6-dioxopiperidin-3-yl)isoindole-1,3-dione), or avadomide (3-(5-amino-2-methyl-4-oxo-4H-quinazolin-3-yl)-piperidine-2,6-dione), a stereoisomer of lenalidomide (3-(4-amino-1-oxo-1,3-dihydro-2H-isoindol-2-yl)piperidine-2,6-dione),

pomalidomide (4-amino-2-(2,6-dioxopiperidin-3-yl)isoindole-1,3-dione), or avadomide (3-(5-amino-2-methyl-4-oxo-4H-quinazolin-3-yl)-piperidine-2,6-dione), or a pharmaceutically acceptable salt, solvate, hydrate, co-crystal, clathrate, or polymorph thereof.

[0048] In some examples, the immunomodulatory compound is 3-(4-amino-1-oxo-1,3-dihydro-2H-isoindol-2-yl)piperidine-2,6-dione, or a stereoisomer thereof, or a pharmaceutically acceptable salt, solvate, hydrate, co-crystal, clathrate, or polymorph thereof. In some examples, the immunomodulatory compound is 3-(4-amino-1-oxo-1,3-dihydro-2H-isoindol-2-yl)piperidine-2,6-dione. In some examples, the immunomodulatory compound is 3-(5-amino-2-methyl-4-oxo-4H-quinazolin-3-yl)-piperidine-2,6-dione, or a stereoisomer thereof, or a pharmaceutically acceptable salt, solvate, hydrate, co-crystal, clathrate, or polymorph thereof. In some examples, the immunomodulatory compound is 3-(5-amino-2-methyl-4-oxo-4H-quinazolin-3-yl)-piperidine-2,6-dione.

[0049] In some examples of any of the methods provided herein, the immunomodulatory compound is administered orally, subcutaneously, or intravenously. In some examples, the immunomodulatory compound is administered orally. In some examples, the immunomodulatory compound is administered in a capsule or a tablet.

[0050] In some examples of any of the methods provided herein, the immunomodulatory compound is administered in an amount from or from about 0.1 mg to about 100 mg, from or from about 0.1 mg to 50 mg, from or from about 0.1 mg to 25 mg, from or from about 0.1 mg to 10 mg, from or from about 0.1 mg to 5 mg, from or from about 0.1 mg to 1 mg, from or from about 1 mg to 100 mg, from or from about 1 mg to 50 mg, from or from about 1 mg to 25 mg, from or from about 1 mg to 10 mg, from or from about 1 mg to 5 mg, from or from about 5 mg to 100 mg, from or from about 5 mg to 50 mg, from or from about 5 mg to 25 mg, from or from about 5 mg to 10 mg, from or from about 10 mg to 100 mg, from or from about 10 mg to 50 mg, from or from 10 mg to 25 mg, from or from about 25 mg to 100 mg, from or from about 25 mg to 50 mg or from or from about 50 mg to 100 mg, each inclusive.

[0051] In some examples of any of the methods provided herein, the immunomodulatory compound is administered once daily, twice daily, three times daily, four times daily, five times daily, or six times daily. In some examples, the immunomodulatory compound is administered at a total daily dosage amount of at least or at least about 0.1 mg per day, 0.5 mg per day, 1.0 mg per day, 2.5 mg per day, 5 mg per day, 10 mg per day, 25 mg per day, 50 mg per day or 100 mg per day.

[0052] In some examples of any of the methods provided herein, the immunomodulatory compound is administered in an amount greater than or greater than about 1 mg, 2.5 mg, 5 mg, 7.5 mg, 10 mg, 15 mg and less than 25 mg; or the immunomodulatory compound is administered in an amount greater than or greater than about 1 mg per day, 2.5 mg per day, 5 mg per day, 7.5 mg per day, 10 mg per day, 15 mg per day and less than 25 mg per day.

[0053] In some examples of any of the methods provided herein, the administration of the therapeutically effective amount of immunomodulatory compound stimulates an increased expansion of T cells associated with the T cell therapy compared to the expansion of following administration of the T cell therapy in absence of the immunomodulatory compound.

[0054] In some examples of any of the methods provided herein, the administration of the therapeutically effective amount of immunomodulatory compound stimulates an increase in T cell-mediated cytolytic activity of T cells associated with the T cell therapy compared to the cytolytic activity following the administration of the T cells in absence of the immunomodulatory compound.

[0055] In some examples of any of the methods provided herein, the administration of the therapeutically effective amount of immunomodulatory compound stimulates an increase in the cytokine production of T cells associated with the T cell therapy compared to cytokine production following the administration of the T cells in absence of the immunomodulatory compound. In some examples, the increase is greater than or greater than about 1.5-fold, 2.0-fold, 3.0-fold, 4.0-fold, 5.0-fold, 10.0-fold or more.

[0056] In some examples of any of the methods provided herein, the T cell therapy is or includes tumor infiltrating lymphocytic (TIL) therapy or genetically engineered cells expressing a recombinant receptor that specifically binds to an antigen. In some examples of any of the methods provided herein, the T cell therapy is or includes genetically engineered cells expressing a recombinant receptor that specifically binds to an antigen. In some examples, the T cell therapy includes cells expressing a recombinant receptor that is or includes a functional non-TCR antigen receptor or a TCR or antigen-binding fragment thereof. In some examples, the recombinant antigen receptor is a chimeric antigen receptor (CAR).

[0057] In some examples of any of the methods provided herein, the T cell therapy includes a recombinant antigen receptor, which includes an extracellular domain containing an antigen-binding domain that specifically binds to an antigen. In some examples, the antigen is associated with, specific to, and/or expressed on a cell or tissue of a disease, disorder or

condition. In some examples, the disease, disorder or condition is an infectious disease or disorder, an autoimmune disease, an inflammatory disease, or a tumor or a cancer. In some examples, the antigen is a tumor antigen.

[0058] In some examples of any of the methods provided herein, the antigen is selected from among ROR1, B cell maturation antigen (BCMA), carbonic anhydrase 9 (CAIX), tEGFR, Her2/neu (receptor tyrosine kinase erbB2), L1-CAM, CD19, CD20, CD22, mesothelin, CEA, and hepatitis B surface antigen, anti-folate receptor, CD23, CD24, CD30, CD33, CD38, CD44, EGFR, epithelial glycoprotein 2 (EPG-2), epithelial glycoprotein 40 (EPG-40), EPHa2, erb-B2, erb-B3, erb-B4, erbB dimers, EGFR vIII, folate binding protein (FBP), FCRL5, FCRH5, fetal acetylcholine receptor, GD2, GD3, HMW-MAA, IL-22R-alpha, IL-13R-alpha2, kinase insert domain receptor (kdr), kappa light chain, Lewis Y, L1-cell adhesion molecule, (L1-CAM), Melanoma-associated antigen (MAGE)-A1, MAGE-A3, MAGE-A6, Preferentially expressed antigen of melanoma (PRAME), survivin, TAG72, B7-H6, IL-13 receptor alpha 2 (IL-13Ra2), CA9, GD3, HMW-MAA, CD171, G250/CAIX, HLA-AI MAGE Al, HLA-A2 NY-ESO-1, PSCA, folate receptor-a, CD44v6, CD44v7/8, avb6 integrin, 8H9, NCAM, VEGF receptors, 5T4, Foetal AchR, NKG2D ligands, CD44v6, dual antigen, a cancer-testes antigen, mesothelin, murine CMV, mucin 1 (MUC1), MUC16, PSCA, NKG2D, NY-ESO-1, MART-1, gp100, G Protein Coupled Receptor 5D (GPCR5D), oncofetal antigen, ROR1, TAG72, VEGF-R2, carcinoembryonic antigen (CEA), Her2/neu, estrogen receptor, progesterone receptor, ephrinB2, CD123, c-Met, GD-2, O-acetylated GD2 (OGD2), CE7, Wilms Tumor 1 (WT-1), a cyclin, cyclin A2, CCL-1, CD138, optionally a human antigen of any of the foregoing; a pathogen-specific antigen; and an antigen associated with a universal tag. In some examples, the antigen is or includes CD19, optionally human CD19. In some examples, the antigen is or includes a multiple myeloma-associated antigen, optionally a BCMA, optionally human BCMA.

[0059] In some examples of any of the methods provided herein, the antigen-binding domain is or includes an antibody or an antibody fragment thereof, which optionally is a single chain fragment. In some examples, the fragment includes antibody variable regions joined by a flexible linker. In some examples, the fragment includes an scFv.

[0060] In some examples of any of the methods provided herein, the T cell therapy includes a recombinant receptor that further includes a spacer, optionally derived from an immunoglobulin, optionally containing a hinge region. In some examples, the recombinant antigen receptor includes an intracellular signaling region. In some examples, the

intracellular signaling region includes an intracellular signaling domain. In some examples, the intracellular signaling domain is or includes a primary signaling domain, a signaling domain that is capable of inducing a primary activation signal in a T cell, a signaling domain of a T cell receptor (TCR) component, and/or a signaling domain containing an immunoreceptor tyrosine-based activation motif (ITAM). In some examples of any of the methods provided herein, the intracellular signaling domain is or includes an intracellular signaling domain of a CD3 chain, optionally a CD3-zeta (CD3ζ) chain, or a signaling portion thereof.

[0061] In some examples of any of the methods provided herein, the recombinant receptor further includes a transmembrane domain disposed between the extracellular domain and the intracellular signaling region, wherein the transmembrane domain is optionally transmembrane domain of CD8 or CD28. In some examples, the intracellular signaling region further includes a costimulatory signaling region. In some examples, costimulatory signaling region includes an intracellular signaling domain of a T cell costimulatory molecule or a signaling portion thereof. In some examples, the costimulatory signaling region includes an intracellular signaling domain of a CD28, a 4-1BB or an ICOS or a signaling portion thereof. In some examples, the costimulatory signaling region containing an intracellular signaling domain of 4-1BB. In some examples of any of the methods provided herein, the costimulatory signaling region is between the transmembrane domain and the intracellular signaling region.

[0062] In some examples of any of the methods provided herein, the T cell therapy includes: T cells selected from central memory T cells, effector memory T cells, naïve T cells, stem central memory T cells, effector T cells and regulatory T cells; and/or a plurality of cells, the plurality containing at least 50 % of a population of cells selected from CD4+ T cells, CD8+ T cells, central memory T cells, effector memory T cells, naïve T cells, stem central memory T cells, effector T cells and regulatory T cells.

[0063] In some examples of any of the methods provided herein, the T cell therapy includes T cells that are CD4+ or CD8+. In some examples, the T cell therapy includes primary cells derived from a subject. In some examples, the T cell therapy includes cells that are autologous to the subject. In some examples, the T cell therapy includes T cells that are allogeneic to the subject. In some examples of any of the methods provided herein, the subject is a human.

[0064] In some examples of any of the methods provided herein, the T cell therapy includes the administration of from or from about 1 x 105 to 1 x 108 total recombinant receptor-expressing cells, total T cells, or total peripheral blood mononuclear cells (PBMCs), from or from about 5 x 10^5 to 1 x 10^7 total recombinant receptor-expressing cells, total T cells, or total peripheral blood mononuclear cells (PBMCs) or from or from about 1 x 10^6 to 1 x 10^7 total recombinant receptor-expressing cells, total T cells, or total peripheral blood mononuclear cells (PBMCs), each inclusive.

[0065] In some examples of any of the methods provided herein, the T cell therapy includes the administration of no more than 1 x 10^8 total recombinant receptor-expressing cells, total T cells, or total peripheral blood mononuclear cells (PBMCs), no more than 1 x 10^7 total recombinant receptor-expressing cells, total T cells, or total peripheral blood mononuclear cells (PBMCs), no more than 0.5 x 10^7 total recombinant receptor-expressing cells, total T cells, or total peripheral blood mononuclear cells (PBMCs), no more than 1 x 10^6 total recombinant receptor-expressing cells, total T cells, or total peripheral blood mononuclear cells (PBMCs), no more than 0.5 x 10^6 total recombinant receptor-expressing cells, total T cells, or total peripheral blood mononuclear cells (PBMCs).

[0066] In some examples of any of the methods provided herein, the amount of cells administered in the T cell therapy is less than the amount in another method in which the T cell therapy is administered without administration of the immunomodulatory compound, optionally which other method results in a similar or lower degree of amelioration or reduction or prevention of the disease or condition or symptom or burden thereof, as compared to that resulting from the method. In some examples, the amount of cells administered is 1.5-fold, 2-fold, 3-fold, 4-fold, 5-fold, or 10-fold less than that administered in the other method.

[0067] In some examples of any of the methods provided herein, the T cell therapy is administered as a single pharmaceutical composition containing the cells. In some examples of any of the methods provided herein, the T cell therapy includes a dose of cell that is a split dose, wherein the cells of the dose are administered in a plurality of compositions, collectively containing the cells of the dose, over a period of no more than three days.

[0068] In some examples of any of the methods provided herein, the method further includes administering a lymphodepleting chemotherapy prior to administration of the T cell therapy.

[0069] In some examples of any of the methods provided herein, the disease or condition is cancer. In some examples, the cancer is a B cell malignancy and/or a myeloma, lymphoma or leukemia. In some examples, the cancer is mantle cell lymphoma (MCL), multiple myeloma (MM), acute lymphoblastic leukemia (ALL), adult ALL, chronic lymphoblastic leukemia (CLL), non-Hodgkin lymphoma (NHL), or Diffuse Large B-Cell Lymphoma (DLBCL). In some examples, cancer is a non-hematological cancer or is a solid tumor.

[0070] In some examples of any of the methods provided herein, the T cell therapy exhibits increased or prolonged expansion and/or persistence in the subject as compared to a method in which the T cell therapy is administered to the subject in the absence of the immunomodulatory compound.

[0071] In some examples of any of the methods provided herein, the method reduces tumor burden to a greater degree and/or for a greater period of time as compared to the reduction that would be observed with a comparable method in which the T cell therapy is administered to the subject in the absence of the immunomodulatory compound and/or in which the immunomodulatory compound is administered in the absence of the T cell therapy, optionally at the same dose or dosing schedule.

[0072] Provided herein is a kit containing a pharmaceutical composition including a unit dose of a T cell therapy; and instructions for administration of the composition to a subject having a disease or condition in combination with administration of a composition containing an immunomodulatory compound, wherein the instructions specify administering the immunomodulatory compound in one or more unit doses according to an administration cycle including administration of the immunomodulatory compound for up to 21 consecutive days, wherein the cycle includes greater than 30 days beginning upon initiation of the administration of the immunomodulatory compound; and/or administration of the immunomodulatory compound for a plurality of consecutive days followed by a rest period during which the immunomodulatory compound is not administered, wherein the rest period is greater than 14 consecutive days; and/or administration of the immunomodulatory compound for no more than 14 consecutive days.

[0072a] In another aspect, the present disclosure refers to a kit, comprising:

(a) a pharmaceutical composition comprising a unit dose of a T cell therapy; and

(b) instructions for administration of the composition to a subject having a disease or condition in combination with administration of a composition comprising an immunomodulatory compound, wherein said immunomodulatory compound is selected from the group consisting of: thalidomide analogs; thalidomide derivatives; compounds that bind to cereblon (CRBN) and/or one or more members of the CRBN E3 ubiquitin-ligase complex; inhibitors of Ikaros (IKZF1); inhibitors of Aiolos (IKZF3); and compounds that enhance or promote ubiquitination and/or degradation of Ikaros (IKZF1) and/or Aiolos (IKZF3), and wherein the instructions specify initiation of the administration of the immunomodulatory compound in one or more unit doses at a time:

(1) at least 2 days after, at least 1 week after, at least 2 weeks after, at least 3 weeks after, or at least 4 weeks after, initiating the administration of the T cell therapy, and/or is carried out 2 to 28 days or 7 to 21 days after initiating the administration of the T cell therapy; and/or

(2) at or after, optionally immediately after or within 1 to 3 days after: (i) peak or maximum level of the cells of the T cell therapy are detectable in the blood of the subject; (ii) the number of cells of the T cell therapy detectable in the blood, after having been detectable in the blood, is not detectable or is reduced, optionally reduced compared to a preceding time point after administration of the T cell therapy; (iii) the number of cells of the T cell therapy detectable in the blood is decreased by or more than 1.5-fold, 2.0-fold, 3.0-fold, 4.0-fold, 5.0-fold, 10-fold or more the peak or maximum number cells of the T cell therapy detectable in the blood of the subject after initiation of administration of the T cell therapy; (iv) at a time after a peak or maximum level of the cells of the T cell therapy are detectable in the blood of the subject, the number of cells of or derived from the T cells detectable in the blood from the subject is less than less than 10%, less than 5%, less than 1% or less than 0.1% of total peripheral blood mononuclear cells (PBMCs) in the blood of the subject; (v) the subject exhibits disease progression and/or has relapsed following remission after treatment with the T cell therapy; and/or (iv) the subject exhibits increased tumor burden as compared to tumor burden at a time prior to or after administration of the T cells and prior to initiation of administration of the immunomodulatory compound.

[0073] Also provided herein is a kit containing a pharmaceutical composition containing one or more unit doses of an immunomodulatory compound; and instructions for administration of the immunomodulatory compound to a subject having a disease or condition in combination

with administration of a unit dose of a pharmaceutical composition including a T cell therapy, wherein the instructions specify administering the one or more unit doses of the immunomodulatory compound according to an administration cycle including administration of the immunomodulatory compound for up to 21 consecutive days, wherein the cycle includes greater than 30 days beginning upon initiation of the administration of the immunomodulatory compound; and/or administration of the immunomodulatory compound for a plurality of consecutive days followed by a rest period during which the immunomodulatory compound is not administered, wherein the rest period is greater than 14 consecutive days; and/or administration of the immunomodulatory compound for no more than 14 consecutive days.

[0073a] In another aspect, the present disclosure refers to a kit, comprising:

(a) a pharmaceutical composition comprising one or more unit doses of an immunomodulatory compound, wherein said immunomodulatory compound is selected from the group consisting of: thalidomide analogs; thalidomide derivatives; compounds that bind to cereblon (CRBN) and/or one or more members of the CRBN E3 ubiquitin-ligase complex; inhibitors of Ikaros (IKZF1); inhibitors of Aiolos (IKZF3); and compounds that enhance or promote ubiquitination and/or degradation of Ikaros (IKZF1) and/or Aiolos (IKZF3); and

(b) instructions for administration of the immunomodulatory compound to a subject having a disease or condition in combination with administration of a unit dose of a pharmaceutical composition comprising a T cell therapy, wherein the instructions specify initiation of administration of the one or more unit doses of the immunomodulatory compound at a time:

(1) at least 2 days after, at least 1 week after, at least 2 weeks after, at least 3 weeks after, or at least 4 weeks after, initiating the administration of the T cell therapy, and/or is carried out 2 to 28 days or 7 to 21 days after initiating the administration of the T cell therapy; and/or

(2) at or after, optionally immediately after or within 1 to 3 days after: (i) peak or maximum level of the cells of the T cell therapy are detectable in the blood of the subject; (ii) the number of cells of the T cell therapy detectable in the blood, after having been detectable in the blood, is not detectable or is reduced, optionally reduced compared to a preceding time point after administration of the T cell therapy; (iii) the number of cells of the T cell therapy detectable in the blood is decreased by or more than 1.5-fold, 2.0-fold, 3.0-fold, 4.0-fold, 5.0-fold, 10-fold or more the peak or maximum number cells of the T cell therapy detectable in the blood of the subject after initiation of administration of the T cell therapy; (iv) at a time after a peak or maximum level of the cells of the T cell therapy are detectable in the blood of the subject, the

number of cells of or derived from the T cells detectable in the blood from the subject is less than less than 10%, less than 5%, less than 1% or less than 0.1% of total peripheral blood mononuclear cells (PBMCs) in the blood of the subject; (v) the subject exhibits disease progression and/or has relapsed following remission after treatment with the T cell therapy; and/or (iv) the subject exhibits increased tumor burden as compared to tumor burden at a time prior to or after administration of the T cells and prior to initiation of administration of the immunomodulatory compound.

[0074] In some of any such examples, the instructions specify initiating administration of the one or more unit doses of the immunomodulatory compound on the same day, optionally concurrently, as initiating administration of the T cell therapy. In some of any such examples, the instructions specify initiating administration of the one or more unit doses of the immunomodulatory compound prior to initiating administration of the T cell therapy.

[0075] In some examples, the instructions specify initiating administration of the one or more unit doses of the immunomodulatory compound at or within one week prior to collecting, from the subject, a sample containing T cells to be engineered, optionally wherein the sample is an apheresis sample; and/or at a time when one or more steps of an ex vivo manufacturing process for producing the engineered T cell therapy; and/or within 14 days prior to administering the T cell therapy.

[0076] In some examples, the one or more steps of the ex vivo manufacturing process is selected from isolating cells from a biological sample by leukapheresis or apheresis; selecting or enriching cells by immunoaffinity-based methods; introducing a recombinant nucleic acid, optionally a viral vector, into cells; incubating cells, optionally engineered, in the presence of one or more stimulating conditions; formulating cells in the presence of a cryoprotectant; and/or formulating cells for administration to a subject, optionally in the presence of a pharmaceutically acceptable excipient.

[0077] In some of any such examples, the instructions specify initiating administration of the one or more unit doses of the immunomodulatory compound within 10 days, 7 days, 4 days, 3 days or 2 days prior to initiating administration of the T cell therapy. In some examples, the instructions specify initiating administration of the one or more unit doses of the immunomodulatory compound after initiating administration of the T cell therapy. In some

examples, the instructions specify initiating administration of the one or more unit doses of the immunomodulatory compound at least 2 days after, at least 1 week after, at least 2 weeks after, at least 3 weeks after, or at least 4 weeks after, the initiating administration of the T cell therapy, and/or 2 to 28 days or 7 to 21 days after initiating administration of the T cell therapy.

[0078] Also provided herein is a kit containing a pharmaceutical composition containing a unit dose of a T cell therapy; and instructions for administration of the composition to a subject having a disease or condition in combination with administration of an immunomodulatory compound, wherein the instructions specify initiation of the administration of the immunomodulatory compound in one or more unit doses at a time at least 2 days after, at least 1 week after, at least 2 weeks after, at least 3 weeks after, or at least 4 weeks after, initiating the administration of the T cell therapy, and/or is carried out 2 to 28 days or 7 to 21 days after initiating the administration of the T cell therapy; and/or at or after, optionally immediately after or within 1 to 3 days after: (i) peak or maximum level of the cells of the T cell therapy are detectable in the blood of the subject; (ii) the number of cells of the T cell therapy detectable in the blood, after having been detectable in the blood, is not detectable or is reduced, optionally reduced compared to a preceding time point after administration of the T cell therapy; (iii) the number of cells of the T cell therapy detectable in the blood is decreased by or more than 1.5-fold, 2.0-fold, 3.0-fold, 4.0-fold, 5.0-fold, 10-fold or more the peak or maximum number cells of the T cell therapy detectable in the blood of the subject after initiation of administration of the T cell therapy; (iv) at a time after a peak or maximum level of the cells of the T cell therapy are detectable in the blood of the subject, the number of cells of or derived from the T cells detectable in the blood from the subject is less than less than 10%, less than 5%, less than 1% or less than 0.1% of total peripheral blood mononuclear cells (PBMCs) in the blood of the subject; (v) the subject exhibits disease progression and/or has relapsed following remission after treatment with the T cell therapy; and/or (iv) the subject exhibits increased tumor burden as compared to tumor burden at a time prior to or after administration of the T cells and prior to initiation of administration of the immunomodulatory compound.

[0079] Provided herein is a kit containing a pharmaceutical composition containing one or more unit doses of an immunomodulatory compound; and instructions for administration of the immunomodulatory compound to a subject having a disease or condition in combination with administration of a unit dose of a pharmaceutical composition including a T cell therapy, wherein the instructions specify initiation of administration of the one or more unit doses of the

immunomodulatory compound at a time at least 2 days after, at least 1 week after, at least 2 weeks after, at least 3 weeks after, or at least 4 weeks after, initiating the administration of the T cell therapy, and/or is carried out 2 to 28 days or 7 to 21 days after initiating the administration of the T cell therapy; and/or at or after, optionally immediately after or within 1 to 3 days after: (i) peak or maximum level of the cells of the T cell therapy are detectable in the blood of the subject; (ii) the number of cells of the T cell therapy detectable in the blood, after having been detectable in the blood, is not detectable or is reduced, optionally reduced compared to a preceding time point after administration of the T cell therapy; (iii) the number of cells of the T cell therapy detectable in the blood is decreased by or more than 1.5-fold, 2.0-fold, 3.0-fold, 4.0-fold, 5.0-fold, 10-fold or more the peak or maximum number cells of the T cell therapy detectable in the blood of the subject after initiation of administration of the T cell therapy; (iv) at a time after a peak or maximum level of the cells of the T cell therapy are detectable in the blood of the subject, the number of cells of or derived from the T cells detectable in the blood from the subject is less than less than 10%, less than 5%, less than 1% or less than 0.1% of total peripheral blood mononuclear cells (PBMCs) in the blood of the subject; (v) the subject exhibits disease progression and/or has relapsed following remission after treatment with the T cell therapy; and/or (iv) the subject exhibits increased tumor burden as compared to tumor burden at a time prior to or after administration of the T cells and prior to initiation of administration of the immunomodulatory compound.

[0080] In some of any such examples, the instructions specify initiating administration of the one or more unit doses of the immunomodulatory compound at a time that is greater than or greater than about 14 days, 15 days, 16 days, 17 days, 18 days, 19, days, 20 days, 21 days, 24 days, or 28 days after initiating the administration of the T cell therapy. In some of any such examples, the instructions specify selecting a subject for the administration of the one or more unit doses of the immunomodulatory compound, after having been administered the T cell therapy, in which: (i) peak or maximum level of the cells of the T cell therapy are detectable in the blood of the subject; (ii) the number of cells of the T cell therapy detectable in the blood, after having been detectable in the blood, is not detectable or is reduced, optionally reduced compared to a preceding time point after administration of the T cell therapy; (iii) the number of cells of the T cell therapy detectable in the blood is decreased by or more than 1.5-fold, 2.0-fold, 3.0-fold, 4.0-fold, 5.0-fold, 10-fold or more the peak or maximum number cells of the T cell therapy detectable in the blood of the subject after initiation of administration of the T cell

[0089] In some of any such examples, the immunomodulatory compound is formulated in an amount for daily administration and/or the instructions specify administering the immunomodulatory compound daily. In some of any such examples, the instructions specify administering the immunomodulatory compound for greater than or greater than about 7 consecutive days, greater than or greater than about 14 consecutive days, greater than or greater than about 21 consecutive days, greater than or greater than about 21 consecutive days, or greater than or greater than about 28 consecutive days.

[0090] In some of any such examples, the instructions specify administering the immunomodulatory compound in an administration cycle including daily administration for a plurality of consecutive days followed by a rest period during which the immunomodulatory compound is not administered. In some examples, the instructions specify the rest period during with the immunomodulatory compound is not administered is greater than 7 consecutive days, greater than 14 consecutive days, greater than 21 days, or greater than 28 days. In some of any such examples, the instructions specify the administration cycle of the immunomodulatory compound is repeated at least one time.

[0091] In some of any such examples, the instructions specify continuing administration of the immunomodulatory compound, from at least after initiation of administration of the T cells, until the number of cells of or derived from the administered T cell therapy detectable in the blood from the subject is increased compared to in the subject at a preceding time point just prior to administration of the immunomodulatory compound or compared to a preceding time point after administration of the T-cell therapy; the number of cells of or derived from the T cell therapy detectable in the blood is within 2.0-fold (greater or less) the peak or maximum number observed in the blood of the subject after initiation of administration of the T cells; the number of cells of the T cell therapy detectable in the blood from the subject is greater than or greater than about 10%, 15%, 20%, 30%, 40%, 50%, or 60% total peripheral blood mononuclear cells (PBMCs) in the blood of the subject; and/or the subject exhibits a reduction in tumor burden as compared to tumor burden at a time immediately prior to the administration of the T cell therapy or at a time immediately prior to the administration of the immunomodulatory compound; and/or the subject exhibits complete or clinical remission.

[0092] In some of any such examples, the immunomodulatory compound binds to cereblon (CRBN) and/or the CRBN E3 ubiquitin-ligase complex; and/or is an inhibitor of Ikaros (IKZF1) or Aiolos (IKZF3) transcription factor; and/or enhances ubiquitination or degradation

of Ikaros (IKZF1) or Aiolos (IKZF3). In some of any such examples, the immunomodulatory compound is thalidomide or is a derivative or analogue of thalidomide. In some of any such examples, the immunomodulatory compound is lenalidomide (3-(4-amino-1-oxo-1,3-dihydro-2H-isoindol-2-yl)piperidine-2,6-dione) or pomalidomide (4-amino-2-(2,6-dioxopiperidin-3-yl)isoindole-1,3-dione), avadomide (3-(5-amino-2-methyl-4-oxo-4H-quinazolin-3-yl)-piperidine-2,6-dione), a stereoisomer of lenalidomide (3-(4-amino-1-oxo-1,3-dihydro-2H-isoindol-2-yl)piperidine-2,6-dione), pomalidomide (4-amino-2-(2,6-dioxopiperidin-3-yl)isoindole-1,3-dione), avadomide (3-(5-amino-2-methyl-4-oxo-4H-quinazolin-3-yl)-piperidine-2,6-dione) or a pharmaceutically acceptable salt, solvate, hydrate, co-crystal, clathrate, or polymorph thereof. In some of any such examples, the immunomodulatory compound is lenalidomide (3-(4-amino-1-oxo-1,3-dihydro-2H-isoindol-2-yl)piperidine-2,6-dione), a stereoisomer of lenalidomide (3-(4-amino-1-oxo-1,3-dihydro-2H-isoindol-2-yl)piperidine-2,6-dione) or a pharmaceutically acceptable salt, solvate, hydrate, co-crystal, clathrate, or polymorph thereof.

[0093] In some of any such examples, the immunomodulatory compound is formulated for administration orally, subcutaneously, or intravenously. In some examples, the immunomodulatory compound is formulated for oral administration. In some of any such examples, the immunomodulatory compound is formulated in a capsule or a tablet.

[0094] In some of any such examples, each of the one or more unit dose of the immunomodulatory compound contains an amount from or from about 0.1 mg to about 100 mg, from or from about 0.1 mg to 50 mg, from or from about 0.1 mg to 25 mg, from or from about 0.1 mg to 10 mg, from or from about 0.1 mg to 5 mg, from or from about 0.1 mg to 1 mg, from or from about 1 mg to 100 mg, from or from about 1 mg to 50 mg, from or from about 1 mg to 25 mg, from or from about 1 mg to 10 mg, from or from about 1 mg to 5 mg, from or from about 5 mg to 100 mg, from or from about 5 mg to 50 mg, from or from about 5 mg to 25 mg, from or from about 5 mg to 10 mg, from or from about 10 mg to 100 mg, from or from about 10 mg to 50 mg, from or from 10 mg to 25 mg, from or from about 25 mg to 100 mg, from or from about 25 mg to 50 mg or from or from about 50 mg to 100 mg, each inclusive; and/or each of the one or more unit doses of the immunomodulatory compound contains an amount of at least or at least about 0.1 mg, 0.5 mg, 1.0 mg, 2.5 mg, 5 mg, 10 mg, 25 mg, 50 mg or 100 mg. In some of any such examples, the one or more unit dose of the immunomodulatory compound contains

an amount greater than or greater than about 1 mg, 2.5 mg, 5 mg, 7.5 mg, 10 mg, 15 mg and less than 25 mg.

[0095] In some of any such examples, the T cell therapy is or includes tumor infiltrating lymphocytic (TIL) therapy or genetically engineered cells expressing a recombinant receptor that specifically binds to an antigen. In some of any such examples, the T cell therapy is or includes genetically engineered cells expressing a recombinant receptor that specifically binds to an antigen.

[0096] In some of any such examples, the recombinant receptor is or contains a functional non-TCR antigen receptor or a TCR or antigen-binding fragment thereof. In some of any such examples, the recombinant antigen receptor is a chimeric antigen receptor (CAR). In some of any such examples, the recombinant antigen receptor contains an extracellular domain containing an antigen-binding domain that specifically binds to an antigen.

[0097] In some of any such examples, the antigen is associated with, specific to, and/or expressed on a cell or tissue of a disease, disorder or condition. In some instances, the disease, disorder or condition is an infectious disease or disorder, an autoimmune disease, an inflammatory disease, or a tumor or a cancer.

[0098] In some of any such examples, the antigen is a tumor antigen. In some of any such examples, the antigen is selected from among ROR1, B cell maturation antigen (BCMA), carbonic anhydrase 9 (CAIX), tEGFR, Her2/neu (receptor tyrosine kinase erbB2), L1-CAM, CD19, CD20, CD22, mesothelin, CEA, and hepatitis B surface antigen, anti-folate receptor, CD23, CD24, CD30, CD33, CD38, CD44, EGFR, epithelial glycoprotein 2 (EPG-2), epithelial glycoprotein 40 (EPG-40), EPHa2, erb-B2, erb-B3, erb-B4, erbB dimers, EGFR vIII, folate binding protein (FBP), FCRL5, FCRH5, fetal acetylcholine receptor, GD2, GD3, HMW-MAA, IL-22R-alpha, IL-13R-alpha2, kinase insert domain receptor (kdr), kappa light chain, Lewis Y, L1-cell adhesion molecule, (L1-CAM), Melanoma-associated antigen (MAGE)-A1, MAGE-A3, MAGE-A6, Preferentially expressed antigen of melanoma (PRAME), survivin, TAG72, B7-H6, IL-13 receptor alpha 2 (IL-13Ra2), CA9, GD3, HMW-MAA, CD171, G250/CAIX, HLA-AI MAGE Al, HLA-A2 NY-ESO-1, PSCA, folate receptor-a, CD44v6, CD44v7/8, avb6 integrin, 8H9, NCAM, VEGF receptors, 5T4, Foetal AchR, NKG2D ligands, CD44v6, dual antigen, a cancer-testes antigen, mesothelin, murine CMV, mucin 1 (MUC1), MUC16, PSCA, NKG2D, NY-ESO-1, MART-1, gp100, G Protein Coupled Receptor 5D (GPCR5D), oncofetal antigen, ROR1, TAG72, VEGF-R2, carcinoembryonic antigen (CEA),

Her2/neu, estrogen receptor, progesterone receptor, ephrinB2, CD123, c-Met, GD-2, O-acetylated GD2 (OGD2), CE7, Wilms Tumor 1 (WT-1), a cyclin, cyclin A2, CCL-1, CD138, optionally a human antigen of any of the foregoing; a pathogen-specific antigen; and an antigen associated with a universal tag. In some examples, the antigen is or includes CD19, optionally human CD19. In some examples, the antigen is or includes BCMA, optionally human BCMA.

[0099] In some of any such examples, the antigen-binding domain is or contains an antibody or an antibody fragment thereof, which optionally is a single chain fragment. In some cases, the fragment contains antibody variable regions joined by a flexible linker. In some examples, the fragment contains an scFv. In some of any such examples, the recombinant receptor further contains a spacer, optionally derived from an immunoglobulin, optionally containing a hinge region.

[0100] In some of any such examples, the recombinant antigen receptor contains an intracellular signaling region. In some of any such examples, the intracellular signaling region contains an intracellular signaling domain. In some examples, the intracellular signaling domain is or contains a primary signaling domain, a signaling domain that is capable of inducing a primary activation signal in a T cell, a signaling domain of a T cell receptor (TCR) component, and/or a signaling domain including an immunoreceptor tyrosine-based activation motif (ITAM).

[0101] In some of any such examples, the intracellular signaling domain is or contains an intracellular signaling domain of a CD3 chain, optionally a CD3-zeta (CD3ζ) chain, or a signaling portion thereof. In some of any such examples, the recombinant receptor further contains a transmembrane domain disposed between the extracellular domain and the intracellular signaling region, wherein the transmembrane domain is optionally transmembrane domain of CD8 or CD28.

[0102] In some of any such examples, the intracellular signaling region further contains a costimulatory signaling region. In some cases, the costimulatory signaling region contains an intracellular signaling domain of a T cell costimulatory molecule or a signaling portion thereof. In some examples, the costimulatory signaling region contains an intracellular signaling domain of a CD28, a 4-1BB or an ICOS or a signaling portion thereof. In some examples, the costimulatory signaling region containing an intracellular signaling domain of 4-1BB. In some

of any such examples, the costimulatory signaling region is between the transmembrane domain and the intracellular signaling region.

[0103] In some of any such examples, the T cell therapy includes T cells selected from the group consisting of central memory T cells, effector memory T cells, naïve T cells, stem central memory T cells, effector T cells and regulatory T cells; and/or a plurality of cells, the plurality including at least 50 % of a population of cells selected from the group consisting of CD4+ T cells, CD8+ T cells, central memory T cells, effector memory T cells, naïve T cells, stem central memory T cells, effector T cells and regulatory T cells. In some of any such examples, the T cell therapy contains T cells that are CD4+ or CD8+.

[0104] In some of any such examples, the T cell therapy contains primary cells derived from a subject. In some of any such examples, the T cell therapy is autologous to the subject. In some of any such examples, the T cell therapy is allogeneic to the subject. In some of any such examples, the subject is a human.

[0105] In some of any such examples, the unit dose of the T cell therapy contains from or from about 1×10^5 to 1×10^8 total recombinant receptor-expressing cells, total T cells, or total peripheral blood mononuclear cells (PBMCs), from or from about 5×10^5 to 1×10^7 total recombinant receptor-expressing cells, total T cells, or total peripheral blood mononuclear cells (PBMCs) or from or from about 1×10^6 to 1×10^7 total recombinant receptor-expressing cells, total T cells, or total peripheral blood mononuclear cells (PBMCs), each inclusive. In some of any such examples, the unit dose of the T cell therapy includes the administration of no more than 1×10^8 total recombinant receptor-expressing cells, total T cells, or total peripheral blood mononuclear cells (PBMCs), no more than 1×10^7 total recombinant receptor-expressing cells, total T cells, or total peripheral blood mononuclear cells (PBMCs), no more than 0.5×10^7 total recombinant receptor-expressing cells, total T cells, or total peripheral blood mononuclear cells (PBMCs), no more than 1×10^6 total recombinant receptor-expressing cells, total T cells, or total peripheral blood mononuclear cells (PBMCs), no more than 0.5×10^6 total recombinant receptor-expressing cells, total T cells, or total peripheral blood mononuclear cells (PBMCs).

[0106] In some of any such examples, the unit dose of the T cell therapy contains a dose of cell that is a split dose, wherein the cells of the dose are administered in a plurality of compositions, collectively containing the cells of the dose, over a period of no more than three days.

[0107] In some of any such examples, the instructions further specify administering a lymphodepleting chemotherapy prior to administration of the T cell therapy. In some of any such examples, the disease or condition is cancer. In some of any such examples, the cancer is a B cell malignancy and/or a myeloma, lymphoma or leukemia. In some examples, the cancer is mantle cell lymphoma (MCL), multiple myeloma (MM), acute lymphoblastic leukemia (ALL), adult ALL, chronic lymphoblastic leukemia (CLL), non-Hodgkin lymphoma (NHL), or Diffuse Large B-Cell Lymphoma (DLBCL). In some cases, the cancer is a non-hematological cancer or is a solid tumor.

[0108] Provided herein is an article of manufacture, containing any of the kits described herein.

[0108a] In another aspect, the present disclosure refers to an article of manufacture, comprising the kit as disclosed herein.

[0109] Also provided herein is pharmaceutical composition containing a T cell therapy, an immunomodulatory compound and a pharmaceutically acceptable carrier. In some examples, the T cell therapy is formulated in a unit dose amount. In some cases, the unit dose of the T cell therapy contains from or from about 1 x 10^5 to 1 x 10^8 total recombinant receptor-expressing cells, total T cells, or total peripheral blood mononuclear cells (PBMCs), from or from about 5 x 10^5 to 1 x 10^7 total recombinant receptor-expressing cells, total T cells, or total peripheral blood mononuclear cells (PBMCs) or from or from about 1 x 10^6 to 1 x 10^7 total recombinant receptor-expressing cells, total T cells, or total peripheral blood mononuclear cells (PBMCs), each inclusive.

[0109a] In another aspect, the present disclosure refers to a pharmaceutical composition comprising a T cell therapy, an immunomodulatory compound and a pharmaceutically acceptable carrier, wherein said immunomodulatory compound is selected from the group consisting of: thalidomide analogs; thalidomide derivatives; compounds that bind to cereblon (CRBN) and/or one or more members of the CRBN E3 ubiquitin-ligase complex; inhibitors of Ikaros (IKZF1); inhibitors of Aiolos (IKZF3); and compounds that enhance or promote ubiquitination and/or degradation of Ikaros (IKZF1) and/or Aiolos (IKZF3).

[0110] Provided herein are pharmaceutical compositions that include a T cell therapy, an immunomodulatory compound and a pharmaceutically acceptable carrier, wherein said immunomodulatory compound is selected from the group consisting of: lenalidomide (3-(4-amino-1-oxo-1,3-dihydro-2H-isoindol-2-yl)piperidine-2,6-dione), pomalidomide (4-amino-2-(2,6-dioxopiperidin-3-yl)isoindole-1,3-dione), or avadomide (3-(5-amino-2-methyl-4-oxo-4H-quinazolin-3-yl)-piperidine-2,6-dione), a stereoisomer, an enantiomer or a mixture of enantiomers thereof, or a pharmaceutically acceptable salt, solvate, hydrate, co-crystal, clathrate, or polymorph thereof.

[0111] In some examples, the unit dose of the T cell therapy contains the administration of no more than 1 x 10^8 total recombinant receptor-expressing cells, total T cells, or total peripheral blood mononuclear cells (PBMCs), no more than 1 x 10^7 total recombinant receptor-expressing cells, total T cells, or total peripheral blood mononuclear cells (PBMCs), no more than 0.5 x 10^7 total recombinant receptor-expressing cells, total T cells, or total peripheral blood

mononuclear cells (PBMCs), no more than 1×10^6 total recombinant receptor-expressing cells, total T cells, or total peripheral blood mononuclear cells (PBMCs), no more than 0.5×10^6 total recombinant receptor-expressing cells, total T cells, or total peripheral blood mononuclear cells (PBMCs).

[0112] In some of any such examples, the immunomodulatory compound binds to cereblon (CRBN) and/or the CRBN E3 ubiquitin-ligase complex; and/or is an inhibitor of Ikaros (IKZF1) or Aiolos (IKZF3) transcription factor; and/or enhances ubiquitination or degradation of Ikaros (IKZF1) or Aiolos (IKZF3). In some of any such examples, the immunomodulatory compound is thalidomide or is a derivative or analogue of thalidomide. In some of any such examples, the immunomodulatory compound is lenalidomide (3-(4-amino-1-oxo-1,3-dihydro-2H-isoindol-2-yl)piperidine-2,6-dione) or pomalidomide (4-amino-2-(2,6-dioxopiperidin-3-yl)isoindole-1,3-dione), avadomide (3-(5-amino-2-methyl-4-oxo-4H-quinazolin-3-yl)-piperidine-2,6-dione), a stereoisomer of lenalidomide (3-(4-amino-1-oxo-1,3-dihydro-2H-isoindol-2-yl)piperidine-2,6-dione), pomalidomide (4-amino-2-(2,6-dioxopiperidin-3-yl)isoindole-1,3-dione), avadomide (3-(5-amino-2-methyl-4-oxo-4H-quinazolin-3-yl)-piperidine-2,6-dione) or a pharmaceutically acceptable salt, solvate, hydrate, co-crystal, clathrate, or polymorph thereof. In some of any such examples, the immunomodulatory compound is lenalidomide (3-(4-amino-1-oxo-1,3-dihydro-2H-isoindol-2-yl)piperidine-2,6-dione), a stereoisomer of lenalidomide (3-(4-amino-1-oxo-1,3-dihydro-2H-isoindol-2-yl)piperidine-2,6-dione) or a pharmaceutically acceptable salt, solvate, hydrate, co-crystal, clathrate, or polymorph thereof.

[0113] In some of any such examples, the immunomodulatory compound is formulated in a unit dose amount. In some of any such examples, the amount of the immunomodulatory compound in the composition is from or from about 0.1 mg to about 100 mg, from or from about 0.1 mg to 50 mg, from or from about 0.1 mg to 25 mg, from or from about 0.1 mg to 10 mg, from or from about 0.1 mg to 5 mg, from or from about 0.1 mg to 1 mg, from or from about 1 mg to 100 mg, from or from about 1 mg to 50 mg, from or from about 1 mg to 25 mg, from or from about 1 mg to 10 mg, from or from about 1 mg to 5 mg, from or from about 5 mg to 100 mg, from or from about 5 mg to 50 mg, from or from about 5 mg to 25 mg, from or from about 5 mg to 10 mg, from or from about 10 mg to 100 mg, from or from about 10 mg to 50 mg, from or from 10 mg to 25 mg, from or from about 25 mg to 100 mg, from or from about 25 mg to 50 mg or from or from about 50 mg to 100 mg, each inclusive;

and/or the amount of the immunomodulatory compound in the composition is at least or at least about 0.1 mg, 0.5 mg, 1.0 mg, 2.5 mg, 5 mg, 10 mg, 25 mg, 50 mg or 100 mg. In some of any such examples, the amount of the immunomodulatory compound in the composition is greater than or greater than about 1 mg, 2.5 mg, 5 mg, 7.5 mg, 10 mg, 15 mg and less than 25 mg.

[0114] In some of any such examples, the T cell therapy is or contains tumor infiltrating lymphocytic (TIL) therapy or genetically engineered cells expressing a recombinant receptor that specifically binds to an antigen. In some of any such examples, the T cell therapy is or contains genetically engineered cells expressing a recombinant receptor that specifically binds to an antigen. In some of any such examples, the recombinant receptor is or contains a functional non-TCR antigen receptor or a TCR or antigen-binding fragment thereof. In some of any such examples, the recombinant antigen receptor is a chimeric antigen receptor (CAR).

[0115] In some of any such examples, the recombinant antigen receptor contains an extracellular domain containing an antigen-binding domain that specifically binds to an antigen. In some of any such examples, the antigen is associated with, specific to, and/or expressed on a cell or tissue of a disease, disorder or condition. In some cases, the disease, disorder or condition is an infectious disease or disorder, an autoimmune disease, an inflammatory disease, or a tumor or a cancer.

[0116] In some of any such examples, the antigen is a tumor antigen. In some of any such examples, the antigen is selected from among ROR1, B cell maturation antigen (BCMA), carbonic anhydrase 9 (CAIX), tEGFR, Her2/neu (receptor tyrosine kinase erbB2), L1-CAM, CD19, CD20, CD22, mesothelin, CEA, and hepatitis B surface antigen, anti-folate receptor, CD23, CD24, CD30, CD33, CD38, CD44, EGFR, epithelial glycoprotein 2 (EPG-2), epithelial glycoprotein 40 (EPG-40), EPHa2, erb-B2, erb-B3, erb-B4, erbB dimers, EGFR vIII, folate binding protein (FBP), FCRL5, FCRH5, fetal acetylcholine receptor, GD2, GD3, HMW-MAA, IL-22R-alpha, IL-13R-alpha2, kinase insert domain receptor (kdr), kappa light chain, Lewis Y, L1-cell adhesion molecule, (L1-CAM), Melanoma-associated antigen (MAGE)-A1, MAGE-A3, MAGE-A6, Preferentially expressed antigen of melanoma (PRAME), survivin, TAG72, B7-H6, IL-13 receptor alpha 2 (IL-13Ra2), CA9, GD3, HMW-MAA, CD171, G250/CAIX, HLA-AI MAGE Al, HLA-A2 NY-ESO-1, PSCA, folate receptor-a, CD44v6, CD44v7/8, avb6 integrin, 8H9, NCAM, VEGF receptors, 5T4, Foetal AchR, NKG2D ligands, CD44v6, dual antigen, a cancer-testes antigen, mesothelin, murine CMV, mucin 1 (MUC1),

MUC16, PSCA, NKG2D, NY-ESO-1, MART-1, gp100, G Protein Coupled Receptor 5D (GPCR5D), oncofetal antigen, ROR1, TAG72, VEGF-R2, carcinoembryonic antigen (CEA), Her2/neu, estrogen receptor, progesterone receptor, ephrinB2, CD123, c-Met, GD-2, O-acetylated GD2 (OGD2), CE7, Wilms Tumor 1 (WT-1), a cyclin, cyclin A2, CCL-1, CD138, optionally a human antigen of any of the foregoing; a pathogen-specific antigen; and an antigen associated with a universal tag. In some of any such examples, the antigen is or contains CD19, optionally human CD19. In some examples, the antigen is or contains BCMA, optionally human BCMA.

[0117] In some of any such examples, the antigen-binding domain is or contains an antibody or an antibody fragment thereof, which optionally is a single chain fragment. In some examples, the fragment contains antibody variable regions joined by a flexible linker. In some examples, the fragment contains an scFv. In some of any such examples, the recombinant receptor further contains a spacer, optionally derived from an immunoglobulin, optionally containing a hinge region.

[0118] In some of any such examples, the recombinant antigen receptor contains an intracellular signaling region. In some examples, the intracellular signaling region contains an intracellular signaling domain. In some instances, the intracellular signaling domain is or contains a primary signaling domain, a signaling domain that is capable of inducing a primary activation signal in a T cell, a signaling domain of a T cell receptor (TCR) component, and/or a signaling domain containing an immunoreceptor tyrosine-based activation motif (ITAM). In some examples, the intracellular signaling domain is or contains an intracellular signaling domain of a CD3 chain, optionally a CD3-zeta (CD3ζ) chain, or a signaling portion thereof.

[0119] In some of any such examples, the recombinant receptor further contains a transmembrane domain disposed between the extracellular domain and the intracellular signaling region, wherein the transmembrane domain is optionally transmembrane domain of CD8, CD28, CTLA-4, or PD-1. In some of any such examples, the intracellular signaling region further contains a costimulatory signaling region.

[0120] In some of any such examples, the costimulatory signaling region contains an intracellular signaling domain of a T cell costimulatory molecule or a signaling portion thereof. In some examples, the costimulatory signaling region contains an intracellular signaling domain of a CD28, a 4-1BB or an ICOS or a signaling portion thereof. In some examples, the costimulatory signaling region contains an intracellular signaling domain of 4-1BB. In some of

any such examples, the costimulatory signaling region is between the transmembrane domain and the intracellular signaling region. In some of any such examples, the recombinant receptor is or comprises a chimeric antigen receptor containing an antigen-binding domain, a spacer, a transmembrane domain from CD28, an intracellular signaling domain containing the CD3-zeta (CD3ζ) chain and an intracellular signaling domain from 4-1BB.

[0121] In some of any such examples, the T cell therapy includes T cells selected from the group consisting of central memory T cells, effector memory T cells, naïve T cells, stem central memory T cells, effector T cells and regulatory T cells; and/or a plurality of cells, the plurality including at least 50 % of a population of cells selected from the group consisting of CD4+ T cells, CD8+ T cells, central memory T cells, effector memory T cells, naïve T cells, stem central memory T cells, effector T cells and regulatory T cells. In some of any such examples, the T cell therapy contains T cells that are CD4+ or CD8+. In some examples, the ratio of CD4+ to CD8+ T cells is from or from about 1:3 to 3:1, optionally 1:1.

[0122] In some of any such examples, the T cell therapy contains primary cells derived from a subject. In some instances, the subject is a human.

[0123] In some of any such examples, the pharmaceutical composition contains a volume from or from about 1 mL to 100 mL, 1 mL to 75 mL, 1 mL to 50 mL, 1 mL to 25 mL, 1 mL to 10 mL, 1 mL to 5 mL, 5 mL to 100 mL, 5 mL to 75 mL, 5 mL to 50 mL, 5 mL to 25 mL, 5 mL to 10 mL, 10 mL to 100 mL, 10 mL to 75 mL, 10 mL to 50 mL, 10 mL to 25 mL, 25 mL to 100 mL, 25 mL to 75 mL, 25 mL to 50 mL, 50 mL to 100 mL, 50 mL to 75 mL or 75 mL to 100 mL. In some of any such examples, the pharmaceutical composition contains a volume of at least or about at least or about 1 mL, 5 mL, 10 mL, 20 mL, 25 mL, 30 mL, 40 mL, 50 mL, 60 mL, 70 mL, 80 mL, 90 mL or 100 mL.

[0124] In some of any such examples, the pharmaceutical composition further contains a cryoprotectant. In some of any such examples, the pharmaceutical composition is sterile.

[0125] Provided herein is an article of manufacture containing any of the pharmaceutical compositions described herein.

[0126] Also provided is a method of treatment including administering any of the pharmaceutical compositions described herein to a subject for treating a disease or condition. In some cases, the disease or condition is cancer. In some instances, the cancer is a B cell malignancy and/or a myeloma, lymphoma or leukemia. In some examples, the cancer is mantle cell lymphoma (MCL), multiple myeloma (MM), acute lymphoblastic leukemia (ALL),

adult ALL, chronic lymphoblastic leukemia (CLL), non-Hodgkin lymphoma (NHL), Diffuse Large B-Cell Lymphoma (DLB) or follicular lymphoma (FL).

[0126a] In another aspect, the present disclosure refers to use of the pharmaceutical composition as disclosed herein in the manufacture of a medicament for treating a disease or condition in a subject.

Brief Description of the Drawings

[0127] **FIG.1A** shows the surface BCMA expression of multiple myeloma cells lines (RPMI-8226, MM1.S, and OPM-2). The dotted line indicates background and BCMA-negative cell lines were stained with anti-BCMA antibody. MFI, median fluorescence intensity.

[0128] **FIG.1B** shows the percent of reduction of BCMA-expressing target cells (RPMI-8226) by anti-BCMA CAR+ T cells in the presence and absence of lenalidomide (10 μM) after 6 days of co-culture. **FIG. 1C** shows the effect of lenalidomide on the cytolytic activity of anti-BCMA CAR+ T cells against RPMI-8226 target cells.

[0129] **FIGs. 2A-2C** show the amount of IL-2 (FIG. 2A), IFNγ (FIG. 2B), and TNF-α (FIG. 2C) observed in supernatants after incubation of RPMI-8226 target cells with anti-BCMA CAR T cells in the presence and absence of lenalidomide.

[0130] **FIG. 3A** shows the effect of increasing concentrations of lenalidomide on the cytolytic activity of anti-BCMA CAR+ T cells against OPM2 target cells.

[0131] **FIGs. 3B-D** show the amount of IFNγ (FIG. 3B), IL-2 (FIG. 3C), and TNF-α (FIG. 3D) observed in supernatants after incubation of OPM2 target cells with anti-BCMA CAR T cells in the presence of increasing concentrations of lenalidomide, or in the absence of lenalidomide.

[0132] **FIG. 3E** shows the antigen-specific anti-BCMA CAR-T cytolytic activity and cytokine production of anti-BCMA CAR+ T cells derived from representative healthy donors and multiple myeloma patients against OPM-2 target cells in the presence of varying concentrations of lenalidomide (0.01 μM, 0.1 μM, 1.0 μM or 10 μM lenalidomide) or in the absence of lenalidomide.

[0133] **FIG. 3F** shows the antigen-specific anti-BCMA CAR-T cytolytic activity of anti-BCMA CAR+ T cells derived from three healthy donors and one multiple myeloma patient against OPM-2 and RPMI-8226 target cells in the presence of varying concentrations of lenalidomide (0.01 μM, 0.1 μM, 1.0 μM or 10 μM lenalidomide) or in the absence of lenalidomide. **FIG. 3G** shows cytokine production of anti-BCMA CAR+ T cells derived from three healthy donors and one multiple myeloma patient against OPM-2 target cells in the presence of varying concentrations of lenalidomide (0.01 μM, 0.1 μM, 1.0 μM or 10 μM

WHAT IS CLAIMED:

1. Use of an immunomodulatory compound in the manufacture of a medicament for the treatment of a disease or condition in a subject, wherein the subject has been previously administered a T cell therapy for treatment of the disease or condition at the time of initiation of administration of the immunomodulatory compound, wherein said immunomodulatory compound is selected from the group consisting of: thalidomide analogs; thalidomide derivatives; compounds that interact with and/or bind to cereblon (CRBN) and/or one or more members of the CRBN E3 ubiquitin-ligase complex; inhibitors of Ikaros (IKZF1); inhibitors of Aiolos (IKZF3); and compounds that enhance or promote ubiquitination and/or degradation of Ikaros (IKZF1) and/or Aiolos (IKZF3).

2. Use of a combination comprising a T cell therapy and an immunomodulatory compound in the manufacture of a medicament for the treatment of a disease or condition, wherein:

(a) the T cell therapy is to be administered to a subject having a disease or condition; and

(b) a therapeutically effective amount of the immunomodulatory compound is to be administered to the subject, wherein said immunomodulatory compound is selected from the group consisting of: thalidomide analogs; thalidomide derivatives; compounds that interact with and/or bind to cereblon (CRBN) and/or one or more members of the CRBN E3 ubiquitin-ligase complex; inhibitors of Ikaros (IKZF1); inhibitors of Aiolos (IKZF3); and compounds that enhance or promote ubiquitination and/or degradation of Ikaros (IKZF1) and/or Aiolos (IKZF3).

3. The use of claim 2, wherein initiation of administration of the immunomodulatory compound in at least one cycle is to be carried out after initiation of administration of the T cell therapy.

4. The use of any of claims 1-3, wherein initiation of administration of the immunomodulatory compound is to be carried out 2 to 28 days after the initiation of administration of the T cell therapy.

5. The use of any of claims 1-4, wherein initiation of administration of the immunomodulatory compound is to be carried out 7 to 21 days after the initiation of administration of the T cell therapy.

6. The use of any of claims 1-5, wherein initiation of administration of the immunomodulatory compound is to be at a time immediately after or within 1 to 3 days after:

(i) peak or maximum level of the cells of the T cell therapy are detectable in the blood of the subject;

(ii) the number of cells of the T cell therapy detectable in the blood, after having been detectable in the blood, is not detectable or is reduced compared to a preceding time point after administration of the T cell therapy;

(iii) the number of cells of the T cell therapy detectable in the blood is decreased by or more than 1.5-fold, 2.0-fold, 3.0-fold, 4.0-fold, 5.0-fold, 10-fold or more the peak or maximum number cells of the T cell therapy detectable in the blood of the subject after initiation of administration of the T cell therapy;

(iv) at a time after a peak or maximum level of the cells of the T cell therapy are detectable in the blood of the subject, the number of cells of or derived from the T cells detectable in the blood from the subject is less than less than 10%, less than 5%, less than 1% or less than 0.1% of total peripheral blood mononuclear cells (PBMCs) in the blood of the subject;

(v) the subject exhibits disease progression and/or has relapsed following remission after treatment with the T cell therapy; and/or

(iv) the subject exhibits increased tumor burden as compared to tumor burden at a time prior to or after administration of the T cells and prior to initiation of administration of the immunomodulatory compound.

7. The use of any of claims 1-5, wherein initiation of administration of the immunomodulatory compound is to be carried out:

(1) 2 to 28 days after the initiation of administration of the T cell therapy; and/or

(2) immediately after or within 1 to 3 days after:

(i) peak or maximum level of the cells of the T cell therapy are detectable in the blood of the subject;

(ii) the number of cells of the T cell therapy detectable in the blood, after having been detectable in the blood, is not detectable or is reduced compared to a preceding time point after administration of the T cell therapy;

(iii) the number of cells of the T cell therapy detectable in the blood is decreased by or more than 1.5-fold, 2.0-fold, 3.0-fold, 4.0-fold, 5.0-fold, 10-fold or more the peak or maximum number cells of the T cell therapy detectable in the blood of the subject after initiation of administration of the T cell therapy;

(iv) at a time after a peak or maximum level of the cells of the T cell therapy are detectable in the blood of the subject, the number of cells of or derived from the T cells detectable in the blood from the subject is less than less than 10%, less than 5%, less than 1% or less than 0.1% of total peripheral blood mononuclear cells (PBMCs) in the blood of the subject;

(v) the subject exhibits disease progression and/or has relapsed following remission after treatment with the T cell therapy; and/or

(iv) the subject exhibits increased tumor burden as compared to tumor burden at a time prior to or after administration of the T cells and prior to initiation of administration of the immunomodulatory compound.

8. The use of any one of claims 1-7, wherein the immunomodulatory compound is to be administered to the subject at a time in which:

(i) peak or maximum level of the cells of the T cell therapy are detectable in the blood of the subject;

(ii) the number of cells of the T cell therapy detectable in the blood, after having been detectable in the blood, is not detectable or is reduced compared to a preceding time point after administration of the T cell therapy;

(iii) the number of cells of the T cell therapy detectable in the blood is decreased by or more than 1.5-fold, 2.0-fold, 3.0-fold, 4.0-fold, 5.0-fold, 10-fold or more the peak or maximum number cells of the T cell therapy detectable in the blood of the subject after initiation of administration of the T cell therapy;

(iv) at a time after a peak or maximum level of the cells of the T cell therapy are detectable in the blood of the subject, the number of cells of or derived from the T cells detectable in the blood from the subject is less than less than 10%, less than 5%, less than 1% or less than 0.1% of total peripheral blood mononuclear cells (PBMCs) in the blood of the subject;

(v) the subject exhibits disease progression and/or has relapsed following remission after treatment with the T cell therapy; and/or

(iv) the subject exhibits increased tumor burden as compared to tumor burden at a time prior to or after administration of the T cells and prior to initiation of administration of the immunomodulatory compound.

9. Use of an immunomodulatory compound in the manufacture of a medicament for the treatment of a disease or condition in a subject, wherein:

the immunomodulatory compound is to be administered to a subject in which at or about at day 12 to 15 after initiation of administration of the T cell therapy for treating the disease or condition:

(i) the number of cells of the T cell therapy in the subject is less than 75% of the average number of cells of the T cell therapy at the same time in a plurality of subjects administered the same or similar dose of the T cell therapy; and/or

(ii) the number of CD3+ or CD8+ cells of the T cell therapy, optionally CAR+ T cells, in the blood is less than 10 cells per μL, less than 5 cells per μL or less than per 1 cells per μL; and

the immunomodulatory compound is selected from the group consisting of: thalidomide analogs; thalidomide derivatives; compounds that interact with and/or bind to cereblon (CRBN) and/or one or more members of the CRBN E3 ubiquitin-ligase complex; inhibitors of Ikaros (IKZF1); inhibitors of Aiolos (IKZF3); and compounds that enhance or promote ubiquitination and/or degradation of Ikaros (IKZF1) and/or Aiolos (IKZF3).

10. The use of claim 2, wherein:

initiation of administration of the immunomodulatory compound, or initiation of administration of the compound in at least one cycle, and initiation of administration of the T cell therapy are to be carried out on the same day or consecutive days; and/or

at least one dose of the immunomodulatory compound is to be administered on the same day or within one or two days, prior or subsequent to, administration of a dose of the T cell therapy.

11. The use of claim 2, wherein initiation of administration of the immunomodulatory compound, or initiation of administration of the compound in at least one cycle, is to be prior to initiation of administration of the T cell therapy.

12. Use of a T cell therapy in the manufacture of a medicament for the treatment of a disease or condition in a subject, wherein the subject has been administered, prior to initiation of the T cell therapy, an immunomodulatory compound, wherein said immunomodulatory compound is selected from the group consisting of: thalidomide analogs; thalidomide derivatives; compounds that bind to cereblon (CRBN) and/or one or more members of the CRBN E3 ubiquitin-ligase complex; inhibitors of Ikaros (IKZF1); inhibitors of Aiolos (IKZF3); and compounds that enhance or promote ubiquitination and/or degradation of Ikaros (IKZF1) and/or Aiolos (IKZF3).

13. The use of any of claims 1-12, wherein the immunomodulatory compound is to be administered in a cycle comprising:

(i) administration for up to 21 consecutive days, wherein the cycle comprises greater than 30 days beginning upon initiation of the administration of the immunomodulatory compound; and/or

(ii) administration for a plurality of consecutive days followed by a rest period during which the immunomodulatory compound is not administered, wherein the rest period is greater than 14 consecutive days; and/or

(iii) administration for no more than 14 consecutive days.

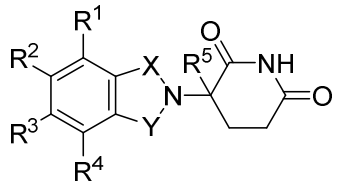
14. The use of any of claims 2 and 11-13, wherein administration of the immunomodulatory compound is initiated prior to administration of the T cell therapy beginning:

(i) at or within one week prior to or subsequent to collecting, from the subject, a sample comprising T cells to be processed and/or engineered to produce the therapy; and/or

(ii) within 14 days prior to initiation of the administration of the T cell therapy.

15. The use of any of claims 1-14, wherein the disease or condition is refractory or resistant to the immunomodulatory compound; and/or the subject or disease or condition has been determined to have a mutation or factor conferring resistance of the disease or condition to treatment with the immunomodulatory compound.

16. The use of any of claims 1-15, wherein the immunomodulatory compound is a compound of the following formula:



wherein

one of X and Y is –C(O)- and the other of X and Y is –C(O)- or –CH_2-;

(1) each of R^1, R^2, R^3, and R^4 are independently halo, alkyl of 1 to 4 carbon atoms, or alkoxy or 1 to 4 carbon atoms, or

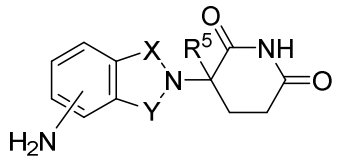
(2) one of R^1, R^3 , R^4 , and R^5 is –NHR^a and the remaining of R^1, R^2, R^3, and R^4 is are hydrogen, wherein R^a is hydrogen or alkyl of 1 to 8 carbon atoms;

R^5 is hydrogen or alkyl of 1 to 8 carbon atoms, benzyl, or halo;

provided that R^5 is other than hydrogen if X and Y are –C(O)- and (i) each of R^1, R^2, R^3, and R^4 is fluoro; or (ii) one of R^1, R^2, R^3, and R^4 is amino;

or a pharmaceutically acceptable salt thereof.

17. The use of any of claims 1-15, wherein the immunomodulatory compound is a compound of the following formula:



wherein one of X and Y is –C(O)- and the other of X and Y is –C(O)- or –CH_2-, and R^5 is hydrogen or lower alkyl, or a pharmaceutically acceptable salt thereof.

18. The use of any of claims 1-17, wherein the immunomodulatory compound is 3-(4-amino-1-oxo-1,3-dihydro-2H-isoindol-2-yl)piperidine-2,6-dione, pomalidomide, 3-(5-amino-2-methyl-4-oxo-4H-quinazolin-3-yl)-piperidine-2,6-dione, a stereoisomer of 3-(4-amino-1-oxo-1,3-dihydro-2H-isoindol-2-yl)piperidine-2,6-dione, a stereoisomer of pomalidomide, a stereoisomer of 3-(5-amino-2-methyl-4-oxo-4H-quinazolin-3-yl)-piperidine-2,6-dione, or a pharmaceutically acceptable salt, solvate, hydrate, co-crystal, clathrate, or polymorph thereof.

19. The use of any of claims 1-18, wherein the immunomodulatory compound is 3-(4-amino-1-oxo-1,3-dihydro-2H-isoindol-2-yl)piperidine-2,6-dione.

20. The use of any of claims 1-18, wherein the immunomodulatory compound is 3-(5-amino-2-methyl-4-oxo-4H-quinazolin-3-yl)-piperidine-2,6-dione.

21. The use of any of claims 1-20, wherein the immunomodulatory compound is to be administered in an amount from or from about 0.1 mg to about 100 mg.

22. The use of any of claims 1-21, wherein the administration of the immunomodulatory compound:

stimulates an increased expansion of T cells associated with the T cell therapy compared to the expansion of T cells associated with the T cell therapy following administration of the T cell therapy in absence of the immunomodulatory compound; or

stimulates an increase in T cell-mediated cytolytic activity of T cells associated with the T cell therapy compared to the cytolytic activity following the administration of the T cells in absence of the immunomodulatory compound; or

stimulates an increase in the cytokine production of T cells associated with the T cell therapy compared to cytokine production following the administration of the T cells in absence of the immunomodulatory compound.

23. The use of any of claims 1-22, wherein the T cell therapy is or comprises tumor infiltrating lymphocytic (TIL) therapy or genetically engineered cells expressing a recombinant receptor that specifically binds to an antigen.

24. The use of any of claims 1-23, wherein the T cell therapy is or comprises genetically engineered cells expressing a recombinant receptor that specifically binds to an antigen expressed by cells of the disease or condition

25. The use of claim 23 or claim 24, wherein the recombinant receptor is or comprises a functional non-TCR antigen receptor or a TCR or antigen-binding fragment thereof.

26. The use of any of claims 23-25, wherein the recombinant antigen receptor is a chimeric antigen receptor (CAR).

27. The use of any of claims 24-26, wherein the antigen is selected from among ROR1, B cell maturation antigen (BCMA), carbonic anhydrase 9 (CAIX), Her2/neu (receptor tyrosine kinase erbB2), L1-CAM, CD19, CD20, CD22, mesothelin, CEA, and hepatitis B surface antigen, anti-folate receptor, CD23, CD24, CD30, CD33, CD38, CD44, EGFR, epithelial glycoprotein 2 (EPG-2), epithelial glycoprotein 40 (EPG-40), EPHa2, erb-B2, erb-B3, erb-B4, erbB dimers, EGFR vIII, folate binding protein (FBP), FCRL5, FCRH5, fetal acetylcholine receptor, GD2, GD3, HMW-MAA, IL-22R-alpha, IL-13R-alpha2, kinase insert domain receptor (kdr), kappa light chain, Lewis Y, L1-cell adhesion molecule, (L1-CAM), Melanoma-associated antigen (MAGE)-A1, MAGE-A3, MAGE-A6, Preferentially expressed antigen of melanoma (PRAME), survivin, TAG72, B7-H6, IL-13 receptor alpha 2 (IL-13Ra2), CA9, GD3, HMW-MAA, CD171, G250/CAIX, HLA-AI MAGE Al, HLA-A2 NY-ESO-1, PSCA, folate receptor-a, CD44v6, CD44v7/8, avb6 integrin, 8H9, NCAM, VEGF receptors, 5T4, Fetal AchR, NKG2D ligands, CD44v6, dual antigen, a cancer-testes antigen, mesothelin, murine CMV, mucin 1 (MUC1), MUC16, PSCA, NKG2D, NY-ESO-1, MART-1, gp100, G Protein Coupled Receptor 5D (GPCR5D), oncofetal antigen, ROR1, TAG72, VEGF-R2, carcinoembryonic antigen (CEA), Her2/neu, estrogen receptor, progesterone receptor, ephrinB2, CD123, c-Met, GD-2, O-acetylated GD2 (OGD2), CE7, Wilms Tumor 1 (WT-1), a cyclin, cyclin A2, CCL-1, CD138,

optionally a human antigen of any of the foregoing; a pathogen-specific antigen; and an antigen associated with a universal tag.

28. The use of claim 27, wherein the antigen is CD19.

29. The use of claim 27, wherein the antigen is BCMA.

30. The use of any of claims 1-29, wherein the T cell therapy comprises:

T cells selected from the group consisting of central memory T cells, effector memory T cells, naïve T cells, stem central memory T cells, effector T cells and regulatory T cells; and/or

a plurality of cells, the plurality comprising at least 50 % of a population of cells selected from the group consisting of CD4+ T cells, CD8+ T cells, central memory T cells, effector memory T cells, naïve T cells, stem central memory T cells, effector T cells and regulatory T cells.

31. The use of any of claims 1-30, wherein the T cell therapy comprises T cells that are CD4+ or CD8+.

32. The use of any of claims 1-31, wherein the T cell therapy comprises cells that are autologous to the subject.

33. The use of any of claims 1-31, wherein the T cell therapy comprises T cells that are allogeneic to the subject.

34. The use of any of claims 1-33, wherein the T cell therapy is to be administered in an amount of from or from about 1×10^5 to 1×10^8 total recombinant receptor-expressing cells, total T cells, or total peripheral blood mononuclear cells (PBMCs).

35. The use of any of claims 1-34, wherein the subject is to be administered a lymphodepleting chemotherapy prior to administration of the T cell therapy.

36. The use of any of claims 1-35, wherein the disease or condition is cancer.

37. The use of any of claims 1-36, wherein the disease or condition is a B cell malignancy and/or a myeloma, lymphoma or leukemia.

38. The use of claim 36 or claim 37, wherein the cancer is mantle cell lymphoma (MCL), multiple myeloma (MM), acute lymphoblastic leukemia (ALL), adult ALL, chronic lymphoblastic leukemia (CLL), non-Hodgkin lymphoma (NHL), Diffuse Large B-Cell Lymphoma (DLBCL) or follicular lymphoma (FL).

39. The use of claim 36, wherein the cancer is a non-hematological cancer or is a solid tumor.

40. A kit, comprising:

(a) a pharmaceutical composition comprising a unit dose of a T cell therapy; and

(b) instructions for administration of the composition to a subject having a disease or condition in combination with administration of a composition comprising an immunomodulatory compound, wherein said immunomodulatory compound is selected from the group consisting of: thalidomide analogs; thalidomide derivatives; compounds that bind to cereblon (CRBN) and/or one or more members of the CRBN E3 ubiquitin-ligase complex; inhibitors of Ikaros (IKZF1); inhibitors of Aiolos (IKZF3); and compounds that enhance or promote ubiquitination and/or degradation of Ikaros (IKZF1) and/or Aiolos (IKZF3), and wherein the instructions specify initiation of the administration of the immunomodulatory compound in one or more unit doses at a time:

(1) at least 2 days after, at least 1 week after, at least 2 weeks after, at least 3 weeks after, or at least 4 weeks after, initiating the administration of the T cell therapy, and/or is carried out 2 to 28 days or 7 to 21 days after initiating the administration of the T cell therapy; and/or

(2) at or after, optionally immediately after or within 1 to 3 days after: (i) peak or maximum level of the cells of the T cell therapy are detectable in the blood of the subject; (ii) the number of cells of the T cell therapy detectable in the blood, after having been detectable in

the blood, is not detectable or is reduced, optionally reduced compared to a preceding time point after administration of the T cell therapy; (iii) the number of cells of the T cell therapy detectable in the blood is decreased by or more than 1.5-fold, 2.0-fold, 3.0-fold, 4.0-fold, 5.0-fold, 10-fold or more the peak or maximum number cells of the T cell therapy detectable in the blood of the subject after initiation of administration of the T cell therapy; (iv) at a time after a peak or maximum level of the cells of the T cell therapy are detectable in the blood of the subject, the number of cells of or derived from the T cells detectable in the blood from the subject is less than less than 10%, less than 5%, less than 1% or less than 0.1% of total peripheral blood mononuclear cells (PBMCs) in the blood of the subject; (v) the subject exhibits disease progression and/or has relapsed following remission after treatment with the T cell therapy; and/or (iv) the subject exhibits increased tumor burden as compared to tumor burden at a time prior to or after administration of the T cells and prior to initiation of administration of the immunomodulatory compound.

41. A kit, comprising:

(a) a pharmaceutical composition comprising one or more unit doses of an immunomodulatory compound, wherein said immunomodulatory compound is selected from the group consisting of: thalidomide analogs; thalidomide derivatives; compounds that bind to cereblon (CRBN) and/or one or more members of the CRBN E3 ubiquitin-ligase complex; inhibitors of Ikaros (IKZF1); inhibitors of Aiolos (IKZF3); and compounds that enhance or promote ubiquitination and/or degradation of Ikaros (IKZF1) and/or Aiolos (IKZF3); and

(b) instructions for administration of the immunomodulatory compound to a subject having a disease or condition in combination with administration of a unit dose of a pharmaceutical composition comprising a T cell therapy, wherein the instructions specify initiation of administration of the one or more unit doses of the immunomodulatory compound at a time:

(1) at least 2 days after, at least 1 week after, at least 2 weeks after, at least 3 weeks after, or at least 4 weeks after, initiating the administration of the T cell therapy, and/or is

carried out 2 to 28 days or 7 to 21 days after initiating the administration of the T cell therapy; and/or

(2) at or after, optionally immediately after or within 1 to 3 days after: (i) peak or maximum level of the cells of the T cell therapy are detectable in the blood of the subject; (ii) the number of cells of the T cell therapy detectable in the blood, after having been detectable in the blood, is not detectable or is reduced, optionally reduced compared to a preceding time point after administration of the T cell therapy; (iii) the number of cells of the T cell therapy detectable in the blood is decreased by or more than 1.5-fold, 2.0-fold, 3.0-fold, 4.0-fold, 5.0-fold, 10-fold or more the peak or maximum number cells of the T cell therapy detectable in the blood of the subject after initiation of administration of the T cell therapy; (iv) at a time after a peak or maximum level of the cells of the T cell therapy are detectable in the blood of the subject, the number of cells of or derived from the T cells detectable in the blood from the subject is less than less than 10%, less than 5%, less than 1% or less than 0.1% of total peripheral blood mononuclear cells (PBMCs) in the blood of the subject; (v) the subject exhibits disease progression and/or has relapsed following remission after treatment with the T cell therapy; and/or (iv) the subject exhibits increased tumor burden as compared to tumor burden at a time prior to or after administration of the T cells and prior to initiation of administration of the immunomodulatory compound.

42. An article of manufacture, comprising the kit of claim 40 or claim 41.

43. A pharmaceutical composition comprising a T cell therapy, an immunomodulatory compound and a pharmaceutically acceptable carrier, wherein said immunomodulatory compound is selected from the group consisting of: thalidomide analogs; thalidomide derivatives; compounds that bind to cereblon (CRBN) and/or one or more members of the CRBN E3 ubiquitin-ligase complex; inhibitors of Ikaros (IKZF1); inhibitors of Aiolos (IKZF3); and compounds that enhance or promote ubiquitination and/or degradation of Ikaros (IKZF1) and/or Aiolos (IKZF3).

44. The pharmaceutical composition of claim 43, wherein the immunomodulatory compound is 3-(4-amino-1-oxo-1,3-dihydro-2H-isoindol-2-yl)piperidine-2,6-dione, pomalidomide, or 3-(5-amino-2-methyl-4-oxo-4H-quinazolin-3-yl)-piperidine-2,6-dione, a stereoisomer of 3-(4-amino-1-oxo-1,3-dihydro-2H-isoindol-2-yl)piperidine-2,6-dione, a stereoisomer of pomalidomide, a stereoisomer of 3-(5-amino-2-methyl-4-oxo-4H-quinazolin-3-yl)-piperidine-2,6-dione, or a pharmaceutically acceptable salt, solvate, hydrate, co-crystal, clathrate, or polymorph thereof.

45. The pharmaceutical composition of claim 43 or claim 44, wherein the immunomodulatory compound is 3-(4-amino-1-oxo-1,3-dihydro-2H-isoindol-2-yl)piperidine-2,6-dione.

46. The pharmaceutical composition of claim 43 or claim 44, wherein the immunomodulatory compound is 3-(5-amino-2-methyl-4-oxo-4H-quinazolin-3-yl)-piperidine-2,6-dione.

47. Use of the pharmaceutical composition of any of claims 43-46 in the manufacture of a medicament for treating a disease or condition in a subject.