We Claim:

1. An invention not claimed in any divisional application.~~A composition comprising a JAK-STAT inhibitor (e.g., ruxolitinib), in combination with a CAR therapy (e.g., a CD123 CAR therapy), for use in preventing cytokine release syndrome (CRS), in a subject in need thereof.~~

~~2. A method of preventing cytokine release syndrome (CRS) with a CAR therapy (e.g., a CD123 CAR therapy) in a subject in need thereof, comprising administering a JAK-STAT inhibitor (e.g., ruxolitinib), in combination with the CAR therapy, to the subject, thereby preventing CRS in the subject.~~

~~3. A composition comprising:~~

~~(i) a cell, e.g., a population of immune effector cells, expressing, a chimeric antigen receptor (CAR), wherein the CAR comprises a CD123 binding domain, a transmembrane domain, and an intracellular signaling domain; and~~

~~(ii) a JAK-STAT inhibitor, e.g., ruxolitinib,~~

~~for use in treating a subject having a disease associated with expression of CD123.~~

~~4. A method of treating a subject having a disease associated with expression of CD123, comprising administering to the subject:~~

~~(i) a cell, e.g., a population of immune effector cells, expressing a chimeric antigen receptor (CAR), wherein the CAR comprises a CD123 binding domain, a transmembrane domain, and an intracellular signaling domain; and~~

~~(ii) a JAK-STAT inhibitor, e.g., ruxolitinib.~~

~~5. The method or composition for use of any of the preceding claims, wherein the subject (i) is at risk of developing, has, or is diagnosed with CRS; (ii) is identified or has previously been identified as being at risk for CRS; and/or (iii) has been, is being, or will be administered a CAR therapy, e.g., a CD123 CAR-expressing cell.~~

6. The method or composition for use of any of the preceding claims, wherein the JAK-STAT inhibitor is chosen from: ruxolitinib, AG490, AZD1480, tofacitinib (tasocitinib or CP-690550), CYT387, fedratinib, baricitinib (INCB039110), lestaurtinib (CEP701), pacritinib (SB1518), XL019, gandotinib (LY2784544), BMS911543, fedratinib (SAR302503), decemotinib (V-509), INCB39110, GEN1, GEN2, GLPG0634, NS018, and N-(cyanomethyl)-4-[2-(4-morpholinoanilino)pyrimidin-4-yl]benzamide, or a pharmaceutically acceptable salt thereof, e.g., wherein the JAK-STAT inhibitor is ruxolitinib or a pharmaceutically acceptable salt thereof.

7. The method or composition for use of any of claims 1-2 or 5-6, wherein the CAR therapy comprises a CD123 CAR-expressing cell.

8. The method or composition for use of any of the preceding claims, further comprising selecting the subject for administration of the JAK-STAT inhibitor (e.g., ruxolitinib).

9. The method or composition for use of any of the preceding claims, wherein the subject is selected based on

(i) his or her risk of developing CRS,

(ii) his or her diagnosis of CRS, and/or

(iii) whether he or she has been, is being, or will be administered a CAR therapy (e.g., CD123 CAR-expressing cell).

10. The method of or composition for use of any of the preceding claims, wherein the subject is selected for administration of the JAK-STAT inhibitor (e.g., ruxolitinib), if the subject is diagnosed with CRS, e.g., severe or non-severe CRS.

11. The method or composition for use of any of the preceding claims, wherein the subject is selected for administration of the JAK-STAT inhibitor (e.g., ruxolitinib), if the subject is at risk of developing CRS.

12. The method or composition for use of any of the preceding claims, wherein the subject is selected for administration of the JAK-STAT inhibitor (e.g., ruxolitinib), if the subject has been, is being, or will be administered a CAR therapy (e.g., CD123 CAR-expressing cell).

13. The method or composition for use of any of the preceding claims, wherein the JAK-STAT inhibitor is ruxolitinib and the CAR therapy is a CD123 CAR-expressing cell.

14. The method or composition for use of any of the preceding claims, wherein the CAR therapy (e.g., CD123 CAR-expressing cell) and the JAK-STAT inhibitor (e.g., ruxolitinib) are administered sequentially.

15. The method or composition for use of any of the preceding claims, wherein the JAK-STAT inhibitor (e.g., ruxolitinib) is administered prior to the CAR therapy (e.g., CD123 CAR-expressing cell).

16. The method or composition for use of any of claims 1-12, wherein the JAK-STAT inhibitor (e.g., ruxolitinib) and the CAR therapy (e.g., CD123 CAR-expressing cell) are administered simultaneously or concurrently.

17. The method or composition for use of any of the preceding claims, wherein the CAR therapy (e.g., CD123 CAR-expressing cell) and the JAK-STAT inhibitor (e.g., ruxolitinib) are administered for a treatment interval, and wherein the treatment interval comprises a single dose of the CAR therapy and multiple doses (e.g., a first and second, and optionally a subsequent dose) of the JAK-STAT inhibitor.

18. The method or composition for use of any of claims 1-15 or 17 wherein the dose of the CAR therapy is administered after (e.g., at least 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 7 days, 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, or more, after) administration of the first dose of the JAK-STAT inhibitor, e.g., but before administration of the second dose of the inhibitor.

19. The method or composition for use of any of claims 1-13 and 16-17, wherein the dose of the CAR therapy is administered concurrently with (e.g., within 2 days (e.g., within 2 days, 1 day, 24 hours, 12 hours, 6 hours, 4 hours, 2 hours, or less) of), the administration of the first dose of the JAK-STAT inhibitor.

20. The method or composition for use of any of claims 17-19, wherein one or more subsequent doses of the JAK-STAT inhibitor are administered after the second dose of the JAK-STAT inhibitor.

21. The method or composition for use of any of claims 17-20, wherein the doses of the JAK-STAT inhibitor are administered twice a day (BID).

22. The method or composition for use of any of preceding claims, wherein the treatment interval comprises a duration of at least 7 days, e.g., at least 7 days, 8 days, 9 days, 10 days, 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, 6 weeks, 1 month, 2 months, 3 months, 4 months, 5 months, 6 months, 7 months, 8 months, or more.

23. The method or composition for use of any of claims 17-22, wherein the treatment interval is repeated, e.g., one or more times, e.g., 1, 2, 3, 4, or 5 more times, e.g., the treatment interval is followed by one or more, e.g., 1, 2, 3, 4, or 5, subsequent treatment intervals.

24. The method or compositon for use of any of the preceding claims, wherein the CD123 binding domain comprises:

a heavy chain complementary determining region 1 (HC CDR1), a heavy chain complementary determining region 2 (HC CDR2), and a heavy chain complementary determining region 3 (HC CDR3) of any CD123 heavy chain binding domain amino acid sequence listed in Table 12B, Table 11A, or Table 12A; and

a light chain complementary determining region 1 (LC CDR1), a light chain complementary determining region 2 (LC CDR2), and a light chain complementary determining region 3 (LC CDR3) of any CD19 light chain binding domain amino acid sequence listed in Table 12B, Table 11A, or Table 12A.

25. The method or composition for use of any of the preceding claims, wherein the CD123 binding domain comprises a HC CDR1, a HC CDR2, and a HC CDR3 according to the HC CDR amino acid sequences in Tables 5A, 7A, 1A, or 3A, and a LC CDR1, a LC CDR2, and a LC CDR3 according to the LC CDR amino acid sequences in Tables 6A, 8A, 2A or 4A.

26. The method or composition for use of any of the preceding claims, wherein the CD123 binding domain comprises:

i) the amino acid sequence of any heavy chain variable region of a CD123 binding domain listed in Table 12B or 11A;

ii) an amino acid sequence having at least one, two or three modifications but not more than 30, 20 or 10 modifications to the amino acid sequence of any heavy chain variable region of a CD123 binding domain provided in Table 12B or 11A; or

iii) an amino acid sequence with at least 95% identity to the amino acid sequence of any heavy chain variable region of a CD123 binding domain provided in Table 12B or 11A.

27. The method or composition for use of any of the preceding claims, wherein the CD123 binding domain comprises:

(i) the amino acid sequence of any heavy chain of a CD123 binding domain provided in Table 12B, Table 11A, or Table 12A;

(ii) an amino acid sequence having at least one, two or three modifications but not more than 30, 20 or 10 modifications to any heavy chain of a CD123 binding domain provided in Table 12B, Table 11A, or Table 12A; or

(iii) an amino acid sequence with at least 95% identity to the amino acid sequence to any heavy chain of a CD123 binding domain provided in Table 12B, Table 11A, or Table 12A.

28. The method or composition for use of any of the preceding claims, wherein the CD123 binding domain comprises:

(i) the amino acid sequence of any light chain variable region of a CD123 binding domain provided in Table 12B, Table 11A, or Table 12A;

(ii) an amino acid sequence having at least one, two or three modifications but not more than 30, 20 or 10 modifications to the amino acid sequence of any light chain variable region of a CD123 binding domain provided in Table 12B, Table 11A, or Table 12A; or

(iii) an amino acid sequence with at least 95% identity to the amino acid sequence of any light chain variable region of a CD123 binding domain provided in Table 12B, Table 11A, or Table 12A.

29. The method or composition for use of any of the preceding claims, wherein the CD123 binding domain comprises:

(i) the amino acid sequence of any light chain of a CD123 binding domain provided in Table12B, Table 11A, or Table 12A;

(ii) the amino acid sequence having at least one, two or three modifications but not more than 30, 20 or 10 modifications to any light chain of a CD123 binding domain provided in Table 12B, Table 11A, or Table 12A; or

(iii)an amino acid sequence with at least 95% identity to the amino acid sequence to any light chain of a CD123 binding domain provided in Table 12B, Table 11A, or Table 12A.

30. The method o or composition for use f any of the preceding claims, wherein the CD123 binding domain comprises the amino acid sequence of any heavy chain variable region listed in Table 12B or 11A, and the amino acid sequence of any light chain variable region listed in Table 12B or 11A.

31. The method or composition for use of any of the preceding claims, wherein the CD123 binding domain comprises:

(i) the amino acid sequence selected from a group consisting of SEQ ID NO:480, 483, 485, 478, 158, 159, 160, 157, 217, 218, 219, 216, 276, 277, 278, or 275;

(ii) an amino acid sequence having at least one, two or three modifications but not more than 30, 20 or 10 modifications to any of SEQ ID NO: 480, 483, 485, 478, 158, 159, 160, 157, 217, 218, 219, 216, 276, 277, 278, or 275; or

(iii) an amino acid sequence with at least 95% identity to any of SEQ ID NO: 480, 483, 485, 478, 158, 159, 160, 157, 217, 218, 219, 216, 276, 277, 278, or 275.

32. The method or composition for use of any of the preceding claims, wherein the transmembrane domain comprises a transmembrane domain from a protein selected from the group consisting of the alpha, beta or zeta chain of the T-cell receptor, CD28, CD3 epsilon, CD45, CD4, CD5, CD8, CD9, CD16, CD22, CD33, CD37, CD64, CD80, CD86, CD134, CD137 and CD154.

33. The method or composition for use of any of the preceding claims, wherein the transmembrane domain comprises

(i) the amino acid sequence of SEQ ID NO: 6,

(ii) an amino acid sequence comprises at least one, two or three modifications but not more than 20, 10 or 5 modifications of the amino acid sequence of SEQ ID NO:6, or

(iii) a sequence with at least 95% identity to the amino acid sequence of SEQ ID NO:6.

34. The method or composition for use of any of the preceding claims, wherein the CD123 binding domain is connected to the transmembrane domain by a hinge region.

35. The method or composition for use of any of the preceding claims, wherein the hinge region comprises SEQ ID NO:2, or a sequence with at least 95% identity thereof.

36. The method or composition for use of any of the preceding claims, wherein the intracellular signaling domain comprises a costimulatory signaling domain comprising a functional signaling domain obtained from a protein selected from the group consisting of a MHC class I molecule, a TNF receptor protein, an Immunoglobulin-like protein, a cytokine receptor, an integrin, a signaling lymphocytic activation molecule (SLAM protein), an activating NK cell receptor, BTLA, a Toll ligand receptor, OX40, CD2, CD7, CD27, CD28, CD30, CD40, CDS, ICAM-1, LFA-1 (CD11a/CD18), 4-1BB (CD137), B7-H3, CDS, ICAM-1, ICOS (CD278), GITR, BAFFR, LIGHT, HVEM (LIGHTR), KIRDS2, SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD19, CD4, CD8alpha, CD8beta, IL2R beta, IL2R gamma, IL7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CD11d,

ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, NKG2C, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRTAM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Ly108), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, and a ligand that specifically binds with CD83.

37. The method or composition for use of any of the preceding claims, wherein the costimulatory domain comprises the amino acid sequence of SEQ ID NO:7, or an amino acid sequence having at least one, two or three modifications but not more than 20, 10 or 5 modifications of the amino acid sequence of SEQ ID NO:7, or an amino acid sequence with at least 95% identity to the amino acid sequence of SEQ ID NO:7.

38. The method or composition for use of any of the preceding claims, wherein the intracellular signaling domain comprises a functional signaling domain of 4-1BB and/or a functional signaling domain of CD3 zeta.

39. The method or composition for use of any of the preceding claims, wherein the intracellular signaling domain comprises the amino acid sequence of SEQ ID NO: 7 and/or the amino acid sequence of SEQ ID NO:9 or SEQ ID NO:10; or an amino acid sequence having at least one, two or three modifications but not more than 20, 10 or 5 modifications of the amino acid sequence of SEQ ID NO:7 and/or the amino acid sequence of SEQ ID NO:9 or SEQ ID NO:10; or an amino acid sequence with at least 95% identity to the amino acid sequence of SEQ ID NO:7 and/or the amino acid sequence of SEQ ID NO:9 or SEQ ID NO:10.

40. The method or composition for use of any of the preceding claims, wherein the intracellular signaling domain comprises the amino acid sequence of SEQ ID NO:7 and the amino acid sequence of SEQ ID NO:9 or SEQ ID NO:10, wherein the amino acid sequences comprising the intracellular signaling domain are expressed in the same frame and as a single polypeptide chain.

~~41. The method or composition for use of any of the preceding claims, wherein the CAR further comprises a leader sequence comprising the amino acid sequence of SEQ ID NO:1.~~

~~42. The method or composition for use of any of the preceding claims, wherein the CAR comprises:~~

~~(i) the amino acid sequence of any of SEQ ID NOs: 99, 100, 101, or 98;~~

~~(ii) an amino acid sequence having at least one, two or three modifications but not more than 30, 20 or 10 modifications to any of SEQ ID NOs: 99, 100, 101, or 98; or~~

~~(iii) an amino acid sequence with at least 95% identity to any of SEQ ID NOs: 99, 100, 101, or 98.~~

~~43. The method or composition for use of any of the preceding claims, wherein the cell comprising a CAR comprises a nucleic acid encoding the CAR.~~

~~44. The method or composition of use of claim 43, wherein the nucleic acid encoding the CAR is a lentiviral vector.~~

~~45. The method or composition for use of claim 43 or 44, wherein the nucleic acid encoding the CAR is introduced into the cells by lentiviral transduction.~~

~~46. The method or composition for use of any of claims 43-45, wherein the nucleic acid encoding the CAR is an RNA, e.g., an in vitro transcribed RNA.~~

~~47. The method or composition for use of any of claims 43-46, wherein the nucleic acid encoding the CAR is introduced into the cells by electroporation.~~

~~48. The method or composition for use of any of the preceding claims, wherein the cell is a T cell or an NK cell.~~

~~49. The method or composition for use of claim 48, wherein the T cell is an autologous or allogeneic T cell.~~

50. The method or composition for use of any of the preceding claims, wherein the CRS is a severe CRS, e.g., grade 4 or 5 CRS.

51. The method or composition for use of any of claims 1-49, wherein the CRS is a less than severe CRS, e.g., grade 1, 2, or 3 CRS.

52. The method or composition for use of any of the preceding claims, wherein the subject is a mammal, e.g., a human.

53. The method or composition for use of any of the preceding claims, wherein the subject has or is diagnosed with, a disease associated with a B cell antigen, e.g., CD123, e.g., a hematological cancer, e.g., a lymphoma or a leukemia, e.g., acute myeloid leukemia (AML).

54. The method or composition for use of any of the preceding claims, wherein the dose of the CAR therapy (e.g., CD123 CAR therapy) comprises at least about 1 x 10^5, 5 x 10^6, 1 x 10^7, 1.5 x 10^7, 2 x 10^7, 2.5 x 10^7, 3 x 10^7, 3.5 x 10^7, 4 x 10^7, 5 x 10^7, 1 x 10^8, 1.5 x 10^8, 2 x 10^8, 2.5 x 10^8, 3 x 10^8, 3.5 x 10^8, 4 x 10^8, 5 x 10^8, 1 x 10^9, 2 x 10^9, or 5 x 10^9 cells (e.g., CD123 CAR expressing cells).

55. The method or composition for use of any of the preceding claims, wherein the dose (e.g., each dose) of the JAK-STAT inhibitor (e.g., ruxolitinib) comprises 2.5 mg to 50 mg (e.g., 2.5-5 mg, 5-10 mg, 10-15 mg, 15-20 mg, 20-25 mg, 25-30 mg, 30-35 mg, 35-40 mg, 40-45 mg, or 45-50 mg) of the JAK-STAT inhibitor.

56. A composition comprising a BTK inhibitor (e.g., ibrutinib), alone or in combination with a CAR therapy (e.g., a CD19 CAR therapy, e.g., a CTL019 therapy), for use in preventing cytokine release syndrome (CRS) associated with the CAR therapy, in a subject in need thereof, wherein the subject is identified or has previously been identified as at risk for CRS, thereby preventing CRS in the subject.

57. A method of preventing cytokine release syndrome (CRS), e.g., CRS associated with a CAR therapy (e.g., a CD19 CAR therapy, e.g., a CTL019 therapy) in a subject in need thereof, comprising administering to the subject a BTK inhibitor (e.g., ibrutinib), alone or in combination with the CAR therapy,

wherein the subject is identified or has previously been identified as at risk for CRS, thereby preventing CRS in the subject.

58. The composition for use of claim 56 or the method of claim 57, wherein the subject has been, is being, or will be administered a CAR therapy, e.g., a CD19 CAR therapy, e.g., CTL019.

59. The composition for use of claim 56 or 58, or the method of claims 57-58, further comprising selecting the subject for administration of the BTK inhibitor, e.g., ibrutinib.

60. The composition for use or method of claim 59, wherein the subject is selected based on

(i) his or her risk of developing CRS,

(ii) his or her diagnosis of CRS, and/or

(iii) whether he or she has been, is being, or will be administered a CAR therapy (e.g., a CAR19 therapy, e.g., a CTL019 therapy).

61. The composition for use or method of claim 59 or 60, wherein:

(i) the subject is selected for administration of the BTK inhibitor (e.g., ibrutinib) if the subject is diagnosed with CRS, e.g., severe or non-severe CRS;

(ii) the subject is selected for administration of the BTK inhibitor (e.g., ibrutinib) if the subject is at risk of (e.g., identified as at risk of) developing CRS; or

(iii) the subject is selected for administration of the BTK inhibitor (e.g., ibrutinib) if the subject has been, is being, or will be administered a CAR therapy (e.g., a CAR19 therapy, e.g., a CTL019 therapy).

~~62. The composition for use or method of any of claims 57-61, wherein the BTK inhibitor is chosen from ibrutinib, GDC-0834, RN-486, CGI-560, CGI-1764, HM-71224, CC-292, ONO-4059, CNX-774, or LFM-A13, or a pharmaceutically acceptable salt thereof, e.g., wherein the BTK inhibitor is ibrutinib or a pharmaceutically acceptable salt thereof.~~

~~63. The composition for use or method of any of claims 57-62, wherein CAR therapy is a CAR19 therapy, e.g., a CTL019 therapy.~~

~~64. The composition for use or method of any of claims 57-63, wherein the CAR therapy (e.g., CAR19 therapy) and the BTK inhibitor (e.g., ibrutinib) are administered for a treatment interval, and wherein the treatment interval comprises a single dose of the CAR therapy and multiple doses (e.g., a first and second, and optionally a subsequent dose) of the BTK inhibitor.~~

~~65. The composition for use or method of any of claims 57-64, wherein the dose of the CAR therapy is administered after (e.g., at least 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 7 days, 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, or more, after) administration of the first dose of the BTK inhibitor, e.g., but before administration of the second dose of the inhibitor.~~

~~66. The composition for use or method of any of claims 57-64, wherein the dose of the CAR therapy is administered concurrently with (e.g., within 2 days (e.g., within 2 days, 1 day, 24 hours, 12 hours, 6 hours, 4 hours, 2 hours, or less) of), the administration of the first dose of the BTK inhibitor.~~

~~67. The composition for use or method of any of claims 62-66, wherein one or more subsequent doses of the BTK inhibitor are administered after the second dose of the BTK inhibitor.~~

~~68. The composition for use or method of any of claims 57-67, wherein the doses of the BTK inhibitor are administered once a day (QD).~~

~~69. The composition for use or method of claim 64-68, wherein the treatment interval comprises a duration of at least 7 days, e.g., at least 7 days, 8 days, 9 days, 10 days, 1 week, 2~~

weeks, 3 weeks, 4 weeks, 5 weeks, 6 weeks, 1 month, 2 months, 3 months, 4 months, 5 months, 6 months, 7 months, 8 months, or more.

70. The composition for use or method of any of claims 64-69, wherein the treatment interval is repeated, e.g., one or more times, e.g., 1, 2, 3, 4, or 5 more times.

71. The composition for use or method of any of claims 64-70, wherein the treatment interval is followed by one or more, e.g., 1, 2, 3, 4, or 5, subsequent treatment intervals.

72. The composition for use or method of any of claims 64-71, wherein the dose of the CAR therapy (e.g., the CAR19 therapy) comprises at least about 1×10^5, 5×10^6, 1×10^7, 1.5×10^7, 2×10^7, 2.5×10^7, 3×10^7, 3.5×10^7, 4×10^7, 5×10^7, 1×10^8, 1.5×10^8, 2×10^8, 2.5×10^8, 3×10^8, 3.5×10^8, 4×10^8, 5×10^8, 1×10^9, 2×10^9, or 5×10^9 cells (e.g., CD19 CAR-expressing cells).

73. The composition for use or method of any of claims 64-72, wherein the dose (e.g., each dose) of the BTK inhibitor, e.g., ibrutinib (PCI-32765), comprises about 250 mg, 300 mg, 350 mg, 400 mg, 420 mg, 440 mg, 460 mg, 480 mg, 500 mg, 520 mg, 540 mg, 560 mg, 580 mg, 600 mg (e.g., 250 mg, 420 mg or 560 mg) of ibrutinib.

74. The composition for use or method of any of claims 57-73, wherein the CD19 binding domain comprises a heavy chain complementary determining region 1 (HC CDR1), a heavy chain complementary determining region 2 (HC CDR2), and a heavy chain complementary determining region 3 (HC CDR3) of any CD19 heavy chain binding domain amino acid sequence listed in Table 13A or 14A; and a light chain complementary determining region 1 (LC CDR1), a light chain complementary determining region 2 (LC CDR2), and a light chain complementary determining region 3 (LC CDR3) of any CD19 light chain binding domain amino acid sequence listed in Table 13A or 14A.

75. The composition for use or method of any of claims 57-73, wherein the CD19 binding domain comprises a HC CDR1, a HC CDR2, and a HC CDR3 according to the HC CDR amino

~~acid sequences in Table 15A, and a LC CDR1, a LC CDR2, and a LC CDR3 according to the LC CDR amino acid sequences in Table 16A.~~

~~76. The composition for use or method of any of claims 57-75, wherein the CD19 binding domain comprises:~~

~~(i) the amino acid sequence of any heavy chain variable region of a CD19 binding domain listed in Table 13A or 14A;~~

~~(ii) an amino acid sequence having at least one, two or three modifications but not more than 30, 20 or 10 modifications to the amino acid sequence of any heavy chain variable region of a CD19 binding domain provided in Table 13A or 14A; or~~

~~(iii) an amino acid sequence with at least 95% identity to the amino acid sequence of any heavy chain variable region of a CD19 binding domain provided in Table 13A or 14A.~~

~~77. The composition for use or method of any of claims 57-76, wherein the CD19 binding domain comprises:~~

~~(i) the amino acid sequence of any heavy chain of a CD19 binding domain provided in Table 13A or 14A;~~

~~(ii) an amino acid sequence having at least one, two or three modifications but not more than 30, 20 or 10 modifications to any heavy chain of a CD19 binding domain provided in Table 13A or 14A; or~~

~~(iii) an amino acid sequence with at least 95% identity to the amino acid sequence to any heavy chain of a CD19 binding domain provided in Table 13A or 14A.~~

~~78. The composition for use or method of any of claims 57-77, wherein the CD19 binding domain comprises:~~

~~(i) the amino acid sequence of any light chain variable region of a CD19 binding domain provided in Table 13A or 14A;~~

~~(ii) an amino acid sequence having at least one, two or three modifications but not more than 30, 20 or 10 modifications to the amino acid sequence of any light chain variable region of a CD19 binding domain provided in Table 13A or 14A; or~~

(iii) an amino acid sequence with at least 95% identity to the amino acid sequence of any light chain variable region of a CD19 binding domain provided in Table 13A or 14A.

79. The composition for use or method of any of claims 57-78, wherein the CD19 binding domain comprises:

(i) the amino acid sequence of any light chain of a CD19 binding domain provided in Table 13A or 14A;

(ii) the amino acid sequence having at least one, two or three modifications but not more than 30, 20 or 10 modifications to any light chain of a CD19 binding domain provided in Table 13A or 14A; or

(iii) an amino acid sequence with at least 95% identity to the amino acid sequence to any light chain of a CD19 binding domain provided in Table 13A or 14A.

80. The composition for use or method of any of claims 57-79, wherein the CD19 binding domain comprises the amino acid sequence of any heavy chain variable region listed in Table 13A or 14A, and the amino acid sequence of any light chain variable region listed in Table 13A or 14A.

81. The composition for use or method of any of claims 57-80, wherein the CD19 binding domain comprises:

(i) the amino acid sequence selected from the group consisting of SEQ ID NO: 774, SEQ ID NO: 710, SEQ ID NO: 711, SEQ ID NO: 712, SEQ ID NO:713, SEQ ID NO:714, SEQ ID NO: 715, SEQ ID NO: 716, SEQ ID NO: 717, SEQ ID NO: 718, SEQ ID NO: 719, SEQ ID NO: 720, SEQ ID NO: 721, SEQ ID NO: 775, SEQ ID NO: 777, or SEQ ID NO: 780;

(i) an amino acid sequence having at least one, two or three modifications but not more than 30, 20 or 10 modifications to any of SEQ ID NO: 774, SEQ ID NO: 710, SEQ ID NO: 711, SEQ ID NO: 712, SEQ ID NO:713, SEQ ID NO:714, SEQ ID NO: 715, SEQ ID NO: 716, SEQ ID NO: 717, SEQ ID NO: 718, SEQ ID NO: 719, SEQ ID NO: 720, SEQ ID NO: 721, SEQ ID NO: 775, SEQ ID NO: 777, or SEQ ID NO: 780; or

(iii) an amino acid sequence with at least 95% identity to the amino acid sequence to any of SEQ ID NO: 774, SEQ ID NO: 710, SEQ ID NO: 711, SEQ ID NO: 712, SEQ ID

NO:713, SEQ ID NO:714, SEQ ID NO: 715, SEQ ID NO: 716, SEQ ID NO: 717, SEQ ID NO: 718, SEQ ID NO: 719, SEQ ID NO: 720, SEQ ID NO: 721, SEQ ID NO: 775, SEQ ID NO: 777, or SEQ ID NO: 780.

82. The composition for use or method of any of claims 57-81, wherein the transmembrane domain comprises a transmembrane domain from a protein selected from the group consisting of the alpha, beta or zeta chain of the T-cell receptor, CD28, CD3 epsilon, CD45, CD4, CD5, CD8, CD9, CD16, CD22, CD33, CD37, CD64, CD80, CD86, CD134, CD137 and CD154.

83. The composition for use or method of any of claims 57-82, wherein the transmembrane domain comprises

(i) the amino acid sequence of SEQ ID NO: 6,

(ii) an amino acid sequence comprises at least one, two or three modifications but not more than 20, 10 or 5 modifications of the amino acid sequence of SEQ ID NO:6, or

(iii) a sequence with at least 95% identity to the amino acid sequence of SEQ ID NO:6.

84. The composition for use or method of any of claims 57-83, wherein the CD19 binding domain is connected to the transmembrane domain by a hinge region.

85. The composition for use or method of any of claims 57-84, wherein the hinge region comprises SEQ ID NO:2, or a sequence with at least 95% identity thereof.

86. The composition for use or method of any of claims 57-85, wherein the intracellular signaling domain comprises a costimulatory signaling domain comprising a functional signaling domain obtained from a protein selected from the group consisting of a MHC class I molecule, a TNF receptor protein, an Immunoglobulin-like protein, a cytokine receptor, an integrin, a signaling lymphocytic activation molecule (SLAM protein), an activating NK cell receptor, BTLA, a Toll ligand receptor, OX40, CD2, CD7, CD27, CD28, CD30, CD40, CDS, ICAM-1, LFA-1 (CD11a/CD18), 4-1BB (CD137), B7-H3, CDS, ICAM-1, ICOS (CD278), GITR, BAFFR, LIGHT, HVEM (LIGHTR), KIRDS2, SLAMF7, NKp80 (KLRF1), NKp44,

~~NKp30, NKp46, CD19, CD4, CD8alpha, CD8beta, IL2R beta, IL2R gamma, IL7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, NKG2C, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRTAM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Ly108), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, and a ligand that specifically binds with CD83.~~

~~87. The composition for use or method of claim 86, wherein the costimulatory domain comprises the amino acid sequence of SEQ ID NO:7, or an amino acid sequence having at least one, two or three modifications but not more than 20, 10 or 5 modifications of the amino acid sequence of SEQ ID NO:7, or an amino acid sequence with at least 95% identity to the amino acid sequence of SEQ ID NO:7.~~

~~88. The composition for use or method of claim 86, wherein the intracellular signaling domain comprises a functional signaling domain of 4-1BB and/or a functional signaling domain of CD3 zeta.~~

~~89. The composition for use or method of any of claims 86-88, wherein the intracellular signaling domain comprises the amino acid sequence of SEQ ID NO: 7 and/or the amino acid sequence of SEQ ID NO:9 or SEQ ID NO:10; or an amino acid sequence having at least one, two or three modifications but not more than 20, 10 or 5 modifications of the amino acid sequence of SEQ ID NO:7 and/or the amino acid sequence of SEQ ID NO:9 or SEQ ID NO:10; or an amino acid sequence with at least 95% identity to the amino acid sequence of SEQ ID NO:7 and/or the amino acid sequence of SEQ ID NO:9 or SEQ ID NO:10.~~

~~90. The composition for use or method of any of claims 86-89, wherein the intracellular signaling domain comprises the amino acid sequence of SEQ ID NO:7 and the amino acid sequence of SEQ ID NO:9 or SEQ ID NO:10, wherein the amino acid sequences comprising~~

the intracellular signaling domain are expressed in the same frame and as a single polypeptide chain.

91. The composition for use or method of any of claims 57-90, wherein the CAR further comprises a leader sequence comprising the amino acid sequence of SEQ ID NO:1.

92. The composition for use or method of any of claims 57-91, wherein the CAR comprises:
(i) the amino acid sequence of any of SEQ ID NO: 773; SEQ ID NO: 758; SEQ ID NO: 759, SEQ ID NO: 760, SEQ ID NO: 761, SEQ ID NO: 762, SEQ ID NO: 763, SEQ ID NO: 764, SEQ ID NO: 765, SEQ ID NO: 766, SEQ ID NO: 767, SEQ ID NO: 768, SEQ ID NO: 769, SEQ ID NO: 776, SEQ ID NO: 779, or SEQ ID NO: 781;
(ii) an amino acid sequence having at least one, two or three modifications but not more than 30, 20 or 10 modifications to any of SEQ ID NO: 773; SEQ ID NO: 758; SEQ ID NO: 759, SEQ ID NO: 760, SEQ ID NO: 761, SEQ ID NO: 762, SEQ ID NO: 763, SEQ ID NO: 764, SEQ ID NO: 765, SEQ ID NO: 766, SEQ ID NO: 767, SEQ ID NO: 768, SEQ ID NO: 769, SEQ ID NO: 776, SEQ ID NO: 779, or SEQ ID NO: 781; or
(iii) an amino acid sequence with at least 95% identity to any of SEQ ID NO: 773; SEQ ID NO: 758; SEQ ID NO: 759, SEQ ID NO: 760, SEQ ID NO: 761, SEQ ID NO: 762, SEQ ID NO: 763, SEQ ID NO: 764, SEQ ID NO: 765, SEQ ID NO: 766, SEQ ID NO: 767, SEQ ID NO: 768, SEQ ID NO: 769, SEQ ID NO: 776, SEQ ID NO: 779, or SEQ ID NO: 781.

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93. The composition for use or method of any of claims 57-92, wherein the cell comprising a CAR comprises a nucleic acid encoding the CAR.

94. The composition for use or method of claim 93, wherein the nucleic acid encoding the CAR is a lentiviral vector.

95. The composition for use or method of claim 93 or 94, wherein the nucleic acid encoding the CAR is introduced into the cells by lentiviral transduction.

~~96. The composition for use or method of any of claims 93-95, wherein the nucleic acid encoding the CAR is an RNA, e.g., an in vitro transcribed RNA.~~

~~97. The composition for use or method of any of claims 93-96, wherein the nucleic acid encoding the CAR is introduced into the cells by electroporation.~~

~~98. The composition for use or method of claims 57-97, wherein the cell is a T cell or an NK cell.~~

~~99. The composition for use or method of claim 98, wherein the T cell is an autologous or allogeneic T cell.~~

~~100. The composition for use or method of any of claims 57-99, wherein the CD19 binding domain is the amino acid sequence of SEQ ID NO: 774; or wherein the CAR comprises the amino acid sequence of SEQ ID NO: 773.~~

~~101. The composition for use or method of any of claims 57-100, wherein the CRS is a severe CRS, e.g., grade 4 or 5 CRS.~~

~~102. The composition for use or method of any of claims 57-100, wherein the CRS is a less than severe CRS, e.g., grade 1, 2, or 3 CRS.~~

~~103. The composition for use or method of any of claims 57-102, wherein the subject has a disease associated with expression of a B cell antigen, e.g., CD19, e.g., a cancer, e.g., a hematological cancer, e.g., a lymphoma or a leukemia, e.g., acute lymphoid leukemia (ALL).~~

~~104. The composition for use or method of any of claims 57-103, wherein the subject is a mammal, e.g., a human.~~

105. The composition for use or method of any of the preceding claims, further comprising administering an IL-6 inhibitor (e.g., an anti-IL6 receptor inhibitor, e.g., an anti-IL6 receptor inhibitor, e.g., tocilizumab), to the subject.

106. The composition for use or method of claim 105, wherein the IL-6 inhibitor is administered prior to, concurrently with, or subsequent to, a dose (e.g., a first dose) of the CAR therapy.

107. The composition for use or method of any of claims 105-106, wherein the IL-6 inhibitor is administered prior to or within 2 weeks (e.g., 2 weeks, 1.5 weeks, 1 week, 14 days, 13 days, 12 days, 11 days, 10 days, 9 days, 8 days, 7 days, 6 days, 5 days, 4 days, 3 days, 2 days, 1 day, 24 hours, 20 hours, 15 hours, 10 hours, 5 hours, 2 hours, 1 hour or less) of a first sign of a symptom of CRS (e.g., a fever, e.g., characterized by a temperature of at least 38°C (e.g., at least 38.5 °C), e.g., for two successive measurements in 24 hours (e.g., at least 4, 5, 6, 7, 8 hours, or more, apart)) in the subject.

108. The composition for use or method of claim 107, wherein the IL-6 inhibitor is administered after administration of a dose (e.g., a first dose) of the CAR therapy.

109. The composition for use or method of claim 108, wherein the IL-6 inhibitor is administered 1 hour to 10 days (e.g., 1-24 hours, 1-2 hours, 2-4 hours, 4-8 hours, 8-12 hours, 12-24 hours, 1-2 days, 2-3 days, 3-4 days, 4-5 days, 5-7 days, or 7-10 days) after administration of the dose of the CAR therapy.

110. The composition for use or method of any of claims 105-109, comprising administering a dose of tocilizumab of about 5-15 mg/kg, e.g., 8-12 mg/kg (e.g., about 8 mg/kg, about 9 mg/kg, about 10 mg/kg, about 11 mg/kg, or about 12 mg/kg).

111. The composition for use or method of any of claims 105-110, wherein the subject has (e.g., is diagnosed with or identified as having) a high tumor burden prior to treatment with the CAR-therapy, e.g., wherein the high tumor burden is characterized by at least 40% blasts (e.g.,

at least 40%, 45%, 50%, 60%, 70%, 80%, 90%, 95%, or more, blasts) in a bone marrow of the subject prior to administration of the CAR therapy (e.g., about 1-5 days prior to administration of the CAR therapy).

112. The composition for use or method of any of claims 105-111, wherein the CAR therapy comprises a CD19 CAR-expressing cell, e.g., a CTL-019-expressing cell.

113. An IL-6 inhibitor (e.g., an anti-IL6 receptor inhibitor, e.g., tocilizumab), for use in treating or preventing cytokine release syndrome (CRS) associated with use of a chimeric antigen receptor (CAR) therapy (e.g., a population of cells expressing a CAR in a subject), wherein the IL-6 inhibitor is used prior to, simultaneously with, or within 1 day (e.g., within 24 hours, 12 hours, 6 hours, 5, hours, 4 hours, 3 hours, 2 hours, 1 hour or less) of, use of a dose (e.g., a first dose) of said CAR therapy.

114. A method of treating or preventing cytokine release syndrome (CRS) associated with administration of a chimeric antigen receptor (CAR) therapy (e.g., a population of cells, expressing a CAR) in a subject, comprising administering to the subject an IL-6 inhibitor (e.g., an anti-IL6 receptor inhibitor, e.g., tocilizumab) prior to, simultaneously with, or within 1 day (e.g., within 24 hours, 12 hours, 6 hours, 5, hours, 4 hours, 3 hours, 2 hours, 1 hour or less) of, administration of a dose (e.g., a first dose) of said CAR therapy.

115. The composition for use of claim 113 or the method of claim 114, wherein the IL-6 inhibitor (e.g., tocilizumab) is administered upon (e.g., within 1 hour, 30 minutes, 20 minutes, 15 minutes or less) a first sign of a symptom of CRS (e.g., a fever, e.g., characterized by a temperature of at least 38°C, e.g., for two successive measurements in 24 hours (e.g., at least 4, 5, 6, 7, 8 hours, or more, apart)) in the subject.

116. The composition for use or method,of any of claims 113-115, wherein the CAR comprises an antigen binding domain that binds one or more of the following: CD19; CD123; CD22;

CD30; CD171; CS-1 (also referred to as CD2 subset 1, CRACC, SLAMF7, CD319, and 19A24); C-type lectin-like molecule-1 (CLL-1 or CLECL1); CD33; epidermal growth factor receptor variant III (EGFRvIII); ganglioside G2 (GD2); ganglioside GD3 (aNeu5Ac(2-8)aNeu5Ac(2-3)bDGalp(1-4)bDGlcp(1-1)Cer); TNF receptor family member B-cell maturation (BCMA); Tn antigen ((Tn-Ag) or (GalNAcα-Ser/Thr)); prostate-specific membrane antigen (PSMA); Receptor tyrosine kinase-like orphan receptor 1 (ROR1); Fms-Like Tyrosine Kinase-3 (FLT3); Tumor-associated glycoprotein 72 (TAG72); CD38; CD44v6; Carcinoembryonic antigen (CEA); Epithelial cell adhesion molecule (EPCAM); B7H3 (CD276); KIT (CD117); Interleukin-13 receptor subunit alpha-2 (IL-13Ra2 or CD213A2); Mesothelin; Interleukin 11 receptor alpha (IL-11Ra); prostate stem cell antigen (PSCA); Protease Serine 21 (Testisin or PRSS21); vascular endothelial growth factor receptor 2 (VEGFR2); Lewis(Y) antigen; CD24; Platelet-derived growth factor receptor beta (PDGFR-beta); Stage-specific embryonic antigen-4 (SSEA-4); CD20; Folate receptor alpha; Receptor tyrosine-protein kinase ERBB2 (Her2/neu); Mucin 1, cell surface associated (MUC1); epidermal growth factor receptor (EGFR); neural cell adhesion molecule (NCAM); Prostase; prostatic acid phosphatase (PAP); elongation factor 2 mutated (ELF2M); Ephrin B2; fibroblast activation protein alpha (FAP); insulin-like growth factor 1 receptor (IGF-I receptor), carbonic anhydrase IX (CAIX); Proteasome (Prosome, Macropain) Subunit, Beta Type, 9 (LMP2); glycoprotein 100 (gp100); oncogene fusion protein consisting of breakpoint cluster region (BCR) and Abelson murine leukemia viral oncogene homolog 1 (Abl) (bcr-abl); tyrosinase; ephrin type-A receptor 2 (EphA2); Fucosyl GM1; sialyl Lewis adhesion molecule (sLe); ganglioside GM3 (aNeu5Ac(2-3)bDGalp(1-4)bDGlcp(1-1)Cer); transglutaminase 5 (TGS5); high molecular weight-melanoma-associated antigen (HMWMAA); o-acetyl-GD2 ganglioside (OAcGD2); Folate receptor beta; tumor endothelial marker 1 (TEM1/CD248); tumor endothelial marker 7-related (TEM7R); claudin 6 (CLDN6); thyroid stimulating hormone receptor (TSHR); G protein-coupled receptor class C group 5, member D (GPRC5D); chromosome X open reading frame 61 (CXORF61); CD97; CD179a; anaplastic lymphoma kinase (ALK); Polysialic acid; placenta-specific 1 (PLAC1); hexasaccharide portion of globoH glycoceramide (GloboH); mammary gland differentiation antigen (NY-BR-1); uroplakin 2 (UPK2); Hepatitis A virus cellular receptor 1 (HAVCR1); adrenoceptor beta 3 (ADRB3); pannexin 3 (PANX3); G protein-coupled receptor 20 (GPR20); lymphocyte antigen 6 complex,

locus K 9 (LY6K); Olfactory receptor 51E2 (OR51E2); TCR Gamma Alternate Reading Frame Protein (TARP); Wilms tumor protein (WT1); Cancer/testis antigen 1 (NY-ESO-1); Cancer/testis antigen 2 (LAGE-1a); Melanoma-associated antigen 1 (MAGE-A1); ETS translocation-variant gene 6, located on chromosome 12p (ETV6-AML); sperm protein 17 (SPA17); X Antigen Family, Member 1A (XAGE1); angiopoietin-binding cell surface receptor 2 (Tie 2); melanoma cancer testis antigen-1 (MAD-CT-1); melanoma cancer testis antigen-2 (MAD-CT-2); Fos-related antigen 1; tumor protein p53 (p53); p53 mutant; prostein; surviving; telomerase; prostate carcinoma tumor antigen-1 (PCTA-1 or Galectin 8), melanoma antigen recognized by T cells 1 (MelanA or MART1); Rat sarcoma (Ras) mutant; human Telomerase reverse transcriptase (hTERT); sarcoma translocation breakpoints; melanoma inhibitor of apoptosis (ML-IAP); ERG (transmembrane protease, serine 2 (TMPRSS2) ETS fusion gene); N-Acetyl glucosaminyl-transferase V (NA17); paired box protein Pax-3 (PAX3); Androgen receptor; Cyclin B1; v-myc avian myelocytomatosis viral oncogene neuroblastoma derived homolog (MYCN); Ras Homolog Family Member C (RhoC); Tyrosinase-related protein 2 (TRP-2); Cytochrome P450 1B1 (CYP1B1); CCCTC-Binding Factor (Zinc Finger Protein)-Like (BORIS or Brother of the Regulator of Imprinted Sites), Squamous Cell Carcinoma Antigen Recognized By T Cells 3 (SART3); Paired box protein Pax-5 (PAX5); proacrosin binding protein sp32 (OY-TES1); lymphocyte-specific protein tyrosine kinase (LCK); A kinase anchor protein 4 (AKAP-4); synovial sarcoma, X breakpoint 2 (SSX2); Receptor for Advanced Glycation Endproducts (RAGE-1); renal ubiquitous 1 (RU1); renal ubiquitous 2 (RU2); legumain; human papilloma virus E6 (HPV E6); human papilloma virus E7 (HPV E7); intestinal carboxyl esterase; heat shock protein 70-2 mutated (mut hsp70-2); CD79a; CD79b; CD72; Leukocyte-associated immunoglobulin-like receptor 1 (LAIR1); Fc fragment of IgA receptor (FCAR or CD89); Leukocyte immunoglobulin-like receptor subfamily A member 2 (LILRA2); CD300 molecule-like family member f (CD300LF); C-type lectin domain family 12 member A (CLEC12A); bone marrow stromal cell antigen 2 (BST2); EGF-like module-containing mucin-like hormone receptor-like 2 (EMR2); lymphocyte antigen 75 (LY75); Glypican-3 (GPC3); Fc receptor-like 5 (FCRL5); or immunoglobulin lambda-like polypeptide 1 (IGLL1).

117. The composition for use or method of any of claims 113-115, wherein the antigen recognition domain binds CD19.

118. The composition for use or method of claim 116, wherein the CAR comprises the amino acid sequence of SEQ ID NO: 773.

119. The composition for use or method of any of the preceding claims, wherein the CAR-expressing cell is administered at a dose (e.g., total dose) of 1.5×10^7 to 5×10^9 cells per kg (e.g., 0.3×10^6 to 1×10^8 cells per kg), e.g., wherein the total dose is administered over multiple doses (e.g., a first dose, a second dose, and optionally a third dose).

120. The composition for use or method of claim 119, wherein the first dose comprises 10% of the total dose (e.g., about 1×10^7 cells/kg), e.g., administered on a first day.

121. The composition for use or method of claim 120, wherein the second dose comprises 30% of the total dose (e.g., about 3×10^7 cells/kg), e.g., administered on a subsequent day (e.g., 1, 2, 3, 4, 5, 6, or 7 days after the first dose).

122. The composition for use or method of any of claims 113-121, wherein the IL-6 inhibitor (e.g., tocilizumab) is administered at a dose of about 5-15 mg/kg, e.g., 8-12 mg/kg (e.g., about 8 mg/kg, about 9 mg/kg, about 10 mg/kg, about 11 mg/kg, or about 12 mg/kg).

123. A pharmaceutical composition comprising (i) a population of immune effector cells, expressing a chimeric antigen receptor (CAR), wherein the CAR comprises a CD123 binding domain, a transmembrane domain, and an intracellular signaling domain; and (ii) a JAK-STAT inhibitor, e.g., ruxolitinib.

124. The pharmaceutical composition of claim 123, wherein the composition further comprises an IL-6 inhibitor (e.g., an anti-IL6 receptor inhibitor, e.g., tocilizumab).

~~125. A pharmaceutical composition comprising (i) a CD123 chimeric antigen receptor (CAR) therapy (e.g., a population of immune effector cells expressing a CAR, wherein the CAR comprises a CD123 binding domain, a transmembrane domain, and an intracellular signaling domain); and (ii) a JAK-STAT inhibitor, e.g., ruxolitinib, for use in treating a cancer or for use in preventing cytokine release syndrome (CRS).~~

~~126. The pharmaceutical composition of claim 125, wherein the composition for use further comprises an IL-6 inhibitor (e.g., an anti-IL6 receptor inhibitor, e.g., tocilizumab).~~

~~127. A pharmaceutical composition comprising (i) a BTK inhibitor (e.g., ibrutinib); and (ii) a chimeric antigen receptor (CAR) therapy (e.g., a CD19 CAR-therapy, e.g., a CTL019 therapy); for use in preventing cytokine release syndrome (CRS), e.g., in a subject that is identified or has previously been identified as at risk for CRS.~~

~~128. The pharmaceutical composition of claim 127, wherein the composition further comprises an IL-6 inhibitor (e.g., an anti-IL6 receptor inhibitor, e.g., tocilizumab).~~