CLAIMS

1. A pharmaceutical composition comprising or consisting of:
    a. 0.5 to 120 mg/mL of a bispecific antibody binding to human CD3 and human CD20,
    b. 20 to 40 mM acetate,
    c. 140 to 260 mM sorbitol,
    d. a surfactant,

    where the pH of the composition is from 5 to 6 and where the bispecific antibody comprises a first binding region binding to human CD3 which comprises the CDR sequences:

    VH-CDR1: SEQ ID NO: 1
    VH-CDR2: SEQ ID NO: 2
    VH-CDR3: SEQ ID NO: 3
    VL-CDR1: SEQ ID NO: 4
    VL-CDR2: GTN, and
    VL-CDR3: SEQ ID NO: 5

    and a second binding region binding to human CD20 which comprises the CDR sequences:

    VH-CDR1: SEQ ID NO: 8
    VH-CDR2: SEQ ID NO: 9
    VH-CDR3: SEQ ID NO: 10
    VL-CDR1: SEQ ID NO: 11
    VL-CDR2: DAS, and
    VL-CDR3: SEQ ID NO: 12.

2. The pharmaceutical composition of claim 1, wherein c. is in the range from 140 to 160 mM sorbitol.

3. The pharmaceutical composition of claim 1 or 2 wherein the first binding region of the bispecific antibody binding to CD3 comprises a VH and a VL sequence having at least 90% sequence identity to the VH and VL sequences of SEQ ID: 6 and 7, such as at least 95%, 96%, 97%, 98%, 99% or 100% sequence identity to the VH and VL sequences of SEQ ID: 6 and 7.

4. The pharmaceutical composition of any of claims 1-3 wherein the second binding region of the bispecific antibody binding to CD20 comprises a VH and a VL sequence having at least 90% sequence identity to the VH and VL sequences of SEQ ID: 13 and 14, such as at least 95%, 96%, 97%, 98%, 99% or 100% sequence identity to the VH and VL sequences of SEQ ID: 13 and 14.

5. The pharmaceutical composition of any of claims 1-4 wherein the bispecific antibody is an IgG1 antibody.

6. The pharmaceutical composition of any one of claims 1-5 wherein the bispecific antibody comprises a first and a second light chain which comprises a first and a second light chain constant region which is selected between a lambda light chain constant region and a kappa light chain constant region such as the light chain constant regions of SEQ ID Nos 22 and 23.

7. The pharmaceutical composition of any one of the above claims wherein the bispecific antibody comprises an Fc region which comprises a first and second heavy chain, wherein said Fc region has been modified so that it has reduced effector functions compared to the bispecific antibody comprising a wild-type IgG1 Fc region.

8. The pharmaceutical composition of any one of the above claims wherein the bispecific antibody comprises an Fc region which has been modified so that binding of C1q to said antibody is reduced compared to the bispecific antibody having a wild-type IgG1 Fc region by at least 70%, at least 80%, at least 90%, at least 95%, at least 97%, or 100%, wherein C1q binding is determined by ELISA.

9. The pharmaceutical composition of any one of the above claims wherein the bispecific antibody comprises a first and second heavy chain each comprising at least a hinge region, a CH2 and CH3 region, wherein in said first heavy chain at least one of the amino acids in the positions corresponding to a positions selected from the group consisting of T366, L368, K370, D399, F405, Y407, and K409 in a human IgG1 heavy chain has been substituted, and in said second heavy chain at least one of the amino acids in the positions corresponding to a position selected from the group consisting of T366, L368, K370, D399, F405, Y407, and K409 in a human IgG1 heavy chain has been substituted, and wherein said first and said second heavy chains are not substituted in the same positions.

10. The pharmaceutical composition of any one of the above claims wherein (i) the amino acid in the position corresponding to F405 in a human IgG1 heavy chain is L in said first heavy chain, and the amino acid in the position corresponding to K409 in a human IgG1 heavy chain is R in said second heavy chain, or (ii) the amino acid in the position corresponding to K409 in a human IgG1 heavy chain is R in said first heavy chain, and the amino acid in the position corresponding to F405 in a human IgG1 heavy chain is L in said second heavy chain.

11. The pharmaceutical composition of any one of the above claims wherein the positions corresponding to positions L234 and L235 in the human IgG1 heavy chain of both the first heavy chain and the second heavy chain of the bispecific antibody are F and E, respectively.

12. The pharmaceutical composition of any one of the above claims wherein the positions corresponding to positions L234, L235, and D265 in the human IgG1 heavy chain of both the first heavy chain and the second heavy chain of the bispecific antibody are F, E, and A, respectively.

13. The pharmaceutical composition of any one of the above claims wherein the positions corresponding to positions L234, L235, and D265 in the human IgG1 heavy chain of both the first constant heavy chain and the second constant heavy chain of the bispecific antibody are F, E, and A, respectively, and wherein the position corresponding to F405 in the human IgG1 heavy chain of the first constant heavy chain is L, and the position corresponding to K409 in the human IgG1 heavy chain of the second constant heavy chain is R.

14. The pharmaceutical composition of any one of the above claims wherein the first and second constant heavy chains comprises an amino acid sequence having at least 90% identity to the amino acid sequence of SEQ ID NO:16.

15. The pharmaceutical composition of any one of the above claims wherein the first and second constant heavy chains comprise the amino acid sequence of SEQ ID Nos: 19 and 20, respectively.

16. The pharmaceutical composition of any one of claims 1-14, wherein the bispecific antibody comprises a CD3 binding arm having a heavy chain and a light chain as defined in SEQ ID NOs. 26 and 24, respectively, and a CD20 binding arm having a heavy chain and a light chain as defined in SEQ ID NOs. 27 and 25, respectively.

17. The pharmaceutical composition if any one of claims 1-14, wherein the bispecific antibody is epcoritamab, or a biosimilar thereof.

18. The pharmaceutical composition of any one of the above claims wherein a. is 0.5 to 120 mg/mL such as 1.0 to 60 mg/mL, or such as 5 to 30 mg/mL, such as 5 mg/mL, or 6 mg/mL, or 7 mg/ml, or 8 mg/ml, or 9 mg/ml, or 10 mg/ml, or 11 mg/ml, or 12 mg/ml, or 13 mg/ml, or 14 mg/ml, or 15 mg/ml, or 16 mg/ml, or 17 mg/ml, or 18 mg/ml, or 19 mg/ml, or 20 mg/ml, or 21 mg/ml, or 22 mg/ml, or 23 mg/ml, or 24 mg/ml, or 25 mg/ml, or 26 mg/ml, or 27 mg/ml, or 28 mg/ml, or 29 mg/ml, 30 mg/ml, 31 mg/ml, 32 mg/ml, 33 mg/ml, 34 mg/ml, 35 mg/ml, 36 mg/ml, 37 mg/ml, 38 mg/ml, 39 mg/ml, 40 mg/ml, 41 mg/ml, 42 mg/ml, 43 mg/ml, 44 mg/ml, 45 mg/ml, 46 mg/ml, 47 mg/ml, 48 mg/ml, 49 mg/ml, 50 mg/ml, 51 mg/ml, 52 mg/ml, 53 mg/ml, 54 mg/ml, 55 mg/ml, 56 mg/ml, 57 mg/ml, 58 mg/ml, 59 mg/ml, or such as 60 mg/ml.

19. The pharmaceutical composition of any one of the above claims wherein b. is 25 to 35 mM, such as 25 mM, 26 mM, 27 mM, 28 mM, 29 mM, 30 mM, 31 mM, 32 mM, 33mM, 34 mM or 35 mM, preferably 30 mM.

20. The pharmaceutical composition of any one of the above claims wherein c. is 145 to 155 mM, such as 145 mM, 146 mM, 147 mM, 148 mM, 149 mM, 150 mM, 151 mM, 152 mM, 153 mM, 154 mM, 155 mM, preferably 150 mM.

21. The pharmaceutical composition of any one of the above claims wherein pH is 5.3 to 5.6, such as 5.4 to 5.6 such as about 5.5.

22. The pharmaceutical composition of any one of the above claims wherein the surfactant is selected from the group comprising glycerol monooleate, benzethonium chloride, sodium docusate, phospholipids, polyethylene alkyl ethers, sodium lauryl sulfate and tricaprylin, benzalkonium chloride, citrimide, cetylpyridinium chloride and phospholipids, alpha tocopherol, glycerol monooleate, myristyl alcohol, phospholipids, poloxamers, polyoxyethylene alkyl ethers, polyoxyethylene castor oil derivatives, polyoxyethylene

sorbintan fatty acid esters, polyoxyethylene sterarates, polyoxyl hydroxystearate, polyoxylglycerides, polysorbates, propylene glycol dilaurate, propylene glycol monolaurate, sorbitan esters sucrose palmitate, sucrose stearate, tricaprylin and TPGS .

23. The pharmaceutical composition of any one of the above claims wherein the surfactant is a polysorbate.

24. The pharmaceutical composition of any one of the above claims wherein the surfactant is polysorbate 20 or 80, such as polysorbate 80.

25. The pharmaceutical composition of any one of the above claims wherein the surfactant is comprised at a concentration from about 0.005% to 0.4% w/v, such as from about 0.01 to 0.1 % w/v, such as from about 0.01 to 0.09 % w/v such as from about 0.01 to 0.06 % w/v such as from about 0.01 to 0.05% w/v such as 0.02% w/v or 0.03% w/v or 0.04% w/v or 0.05% w/v, preferably 0.04% w/v.

26. The pharmaceutical composition of any one of the above claims wherein the composition has a pH of 5.3 to 5.8, or 5.4 to 5.7, such as about 5.5 and comprises or consists of:
    a. 0.5 to 120 mg/mL of the bispecific antibody
    b. 20 to 40 mM acetate
    c. 140 to 260 mM sorbitol
    d. 0.005% to 0.4 % w/v of a surfactant, preferable polysorbate, such as polysorbate 20 or polysorbate 80, such as polysorbate 80.

27. The pharmaceutical composition of claim 26, wherein c. is 140 to 160 mM sorbitol.

28. The pharmaceutical composition of any one of the above claims wherein the composition has a pH of 5.4 to 5.6, such as about 5.5 and comprises or consists of:
    a. 0.5 to 120 mg/mL of the bispecific antibody
    b. 28 to 32 mM acetate
    c. 145 to 155 mM sorbitol
    d. 0.02 to 0.05 % w/v surfactant, preferable polysorbate, such as polysorbate 20 or polysorbate 80, such as polysorbate 80.

29. The pharmaceutical composition according to any of claims 26 to 28 wherein a. is 5 to 60 mg/mL.

30. The pharmaceutical composition according to claim 29 wherein a. is 12 to 24 mg/mL, such as 12mg/mL or 24 mg/mL.

31. The pharmaceutical composition in accordance with any one of claims 1-28, wherein a. is 2 to 8 mg/mL.

32. The pharmaceutical composition in accordance with any one of claims 1-28, wherein a. is 30 to 90 mg/mL.

33. The pharmaceutical composition in accordance with any one of claims 1-28, wherein a. is 5 mg/mL.

34. The pharmaceutical composition in accordance with any one of claims 1-28, wherein a. is 60 mg/mL.

35. The pharmaceutical composition of any one of the above claims wherein the composition has a pH of about 5.5 and comprises or consists of:
    a. 0.5 to 120 mg/mL of the bispecific antibody
    b. 30 mM acetate
    c. 150 mM sorbitol
    d. 0.04 % w/v surfactant, preferable polysorbate, such as polysorbate 20 or polysorbate 80, such as polysorbate 80.

36. The pharmaceutical composition of any one of the above claims wherein the composition has a pH of about 5.5 and comprises or consists of:
    e. 0.5 to 120 mg/mL of the bispecific antibody
    f. 30 mM acetate
    g. 250 mM sorbitol
    h. 0.04 % w/v surfactant, preferable polysorbate, such as polysorbate 20 or polysorbate 80, such as polysorbate 80.

37. The pharmaceutical composition in accordance with claim 35 or claim 36, wherein a. is 2 to 8 mg/mL.

38. The pharmaceutical composition in accordance with claim 35 or claim 36, wherein a. is 30 to 90 mg/mL.

39. The pharmaceutical composition in accordance with claim 35 or claim 36, wherein a. is 10 to 50 mg/mL.

40. The pharmaceutical composition in accordance with claim 35 or claim 36, wherein a. is 12 to 24 mg/mL, such as 12mg/mL or 24 mg/mL.

41. The pharmaceutical composition in accordance with claim 35 or claim 36, wherein a. is 5 mg/mL.

42. The pharmaceutical composition in in accordance with claim 35 or claim 36, wherein a. is 60 mg/mL.

43. The pharmaceutical composition of any one of the above claims wherein the composition does not comprise a hyaluronidase.

44. The pharmaceutical composition of any one of the above claims wherein the composition comprises less than 20 mM Nacl.

45. The pharmaceutical composition of any one of the above claims wherein the composition comprises less than 60 mM Arginine.

46. The pharmaceutical composition of any one of the above claims wherein the composition is a subcutaneous composition.

47. The pharmaceutical composition of any one of the above claims wherein the composition is an intravenous composition.

48. Use of the pharmaceutical composition of any one of the above claims in the manufacture of a medicament for the treatment of cancer.

49. The pharmaceutical composition of any one of the above claims wherein the composition is to be used in subcutaneous administration.

50. The pharmaceutical composition of any one of the above claims 1-45 wherein the composition is to be used in intravenous administration.

51. The pharmaceutical composition of any one of the above claims 1-50 which is in a dosage unit form.

52. The pharmaceutical composition of any one of the above claims which composition is stable for pharmaceutical use for at least 6 months, such as at least 9 month or at least 12 months at a storage temperature of 2-8°C, such as 5°C.

53. Use of the pharmaceutical composition of any one of claims 1-46 for subcutaneous administration.

54. Use of the pharmaceutical composition of any one of claims 1-45 for intravenous administration.

55. The use of any one of claims 53 or 54 wherein the use is for the treatment of cancer.

56. Use of the pharmaceutical composition of any one of claims 1 to 52 in the manufacture of a medicament for the treatment of cancer in a subject, wherein the said medicament is to be administered to a subject in need thereof for a time sufficient to treat the cancer.

57. The use of claim 56 wherein the composition is to be administered subcutaneously or intravenously.

58. The use of any one of claims 56 or 57, wherein the cancer is a B-cell malignancy.

59. A unit dosage form, comprising or consisting of

a. a bispecific antibody comprising a first binding region binding to human CD3 which comprises the CDR sequences:
VH-CDR1: SEQ ID NO: 1
VH-CDR2: SEQ ID NO: 2
VH-CDR3: SEQ ID NO: 3
VL-CDR1: SEQ ID NO: 4

VL-CDR2: GTN, and
VL-CDR3: SEQ ID NO: 5,
and a second binding region binding to human CD20 which comprises the CDR sequences:
VH-CDR1: SEQ ID NO: 8
VH-CDR2: SEQ ID NO: 9
VH-CDR3: SEQ ID NO: 10
VL-CDR1: SEQ ID NO: 11
VL-CDR2: DAS, and
VL-CDR3: SEQ ID NO: 12
in an amount of from 5 µg to 120 mg,

b. acetate buffer and sorbitol in a ratio of between 1:5 and 1:10 wherein the osmolality of the unit dosage form is from 200 to 600 and the pH is from 5.4 to 5.6, and

c. a surfactant.

60. A unit dosage form according to claim 59, comprising or consisting of:

a. a bispecific antibody comprising a first binding region binding to human CD3 which comprises the CDR sequences:
VH-CDR1: SEQ ID NO: 1
VH-CDR2: SEQ ID NO: 2
VH-CDR3: SEQ ID NO: 3
VL-CDR1: SEQ ID NO: 4
VL-CDR2: GTN, and
VL-CDR3: SEQ ID NO: 5,
and a second binding region binding to human CD20 which comprises the CDR sequences:
VH-CDR1: SEQ ID NO: 8
VH-CDR2: SEQ ID NO: 9
VH-CDR3: SEQ ID NO: 10
VL-CDR1: SEQ ID NO: 11
VL-CDR2: DAS, and
VL-CDR3: SEQ ID NO: 12
in an amount of from 5 µg to 120 mg,

b. acetate at a concentration of about 30 mM at pH of about 5.5

c. sorbitol at a concentration of about 150 mM, and

d. about 0.04% w/v polysorbate 80.

61. A unit dosage form according to claim 59, comprising or consisting of:

a. a bispecific antibody comprising a first binding region binding to human CD3 which comprises the CDR sequences:
VH-CDR1: SEQ ID NO: 1
VH-CDR2: SEQ ID NO: 2
VH-CDR3: SEQ ID NO: 3
VL-CDR1: SEQ ID NO: 4
VL-CDR2: GTN, and
VL-CDR3: SEQ ID NO: 5,
and a second binding region binding to human CD20 which comprises the CDR sequences:
VH-CDR1: SEQ ID NO: 8
VH-CDR2: SEQ ID NO: 9
VH-CDR3: SEQ ID NO: 10
VL-CDR1: SEQ ID NO: 11
VL-CDR2: DAS, and
VL-CDR3: SEQ ID NO: 12
in an amount of from 5 µg to 120 mg,

b. acetate at a concentration of about 30 mM at pH of about 5.5

c. sorbitol at a concentration of about 250 mM, and

d. about 0.04% w/v polysorbate 80.

62. The unit dosage form of any one of claims 59 to 61 wherein the first binding region of the bispecific antibody binding to human CD3 comprises the VH and VL sequences of SEQ ID: 6 and 7 and the second binding region of the bispecific antibody binding to human CD20 comprises the VH and VL sequences of SEQ ID: 13 and 14.

63. The unit dosage form of claim 62 wherein the bispecific antibody comprises the first and second constant region heavy chains of SEQ ID NOs: 19 and 20 respectively.

64. The unit dosage form of claim 62 wherein the bispecific antibody comprises a CD3 binding arm having a heavy chain and a light chain as defined in SEQ ID NOs. 26 and 24, respectively, and a CD20 binding arm having a heavy chain and a light chain as defined in SEQ ID NOs. 27 and 25, respectively.

65. The unit dosage form of claim 62, wherein the bispecific antibody is epcoritamab, or a biosimilar thereof.

66. The unit dosage form of any one of claims 59 to 65 wherein the amount of the bispecific antibody is from 40 µg to 80 mg.

67. The unit dosage form of any one of claims 59 to 66 wherein the amount of the bispecific antibody is from 40 µg to 60 mg, such as 40 µg, 50 µg, 100 µg, 150, 160 µg, 170 µg, 180 µg, 190 µg, 200 µg, 250 µg, 300 µg, 350 µg, 400 µg, 450 µg, 500 µg, 600 µg, 700 µg, 800 µg, 900 µg, 1 mg, 2 mg, 3 mg, 4 mg, 5 mg, 6 mg, 7 mg, 8 mg, 9 mg, 10 mg, 11 mg, 12 mg, 13 mg, 14 mg, 15 mg, 16 mg, 17 mg, 18 mg, 19 mg, 20 mg, 21 mg, 22 mg, 23 mg, 24 mg, 25 mg, 26 mg, 27 mg, 28 mg, 29 mg, 30 mg, 31 mg, 32 mg, 33 mg, 34 mg, 35 mg, 36 mg, 37 mg, 38 mg, 39 mg, 40 mg, 41 mg, 42 mg, 43 mg, 44 mg, 45 mg, 46 mg, 47 mg, 48 mg, 49 mg, 50 mg, 51 mg, 52 mg, 53 mg, 54 mg, 55 mg, 56 mg, 57 mg, 58 mg, 59 mg, or such as 60 mg.

68. The unit dosage form of any one of claims 59 to 67 wherein the total volume is from 0.5 mL to 2 mL, such as 1 mL.

69. The unit dosage form of claim 68 which unit dosage form is for subcutaneous administration.

70. The unit dosage form of claim 69, wherein the unit dosage form volume to be administered is about 1.0 ml or 0.8 mL.

71. The unit dosage form of any one of claims 59 to 68 wherein the total volume is from 20 mL to 200 mL wherein the dosage form is for I.V. administration.

72. Use of the unit dosage form of any one of claims 59 to 71 in the manufacture of a medicament for the treatment of cancer in a subject, wherein the said medicament is to be administered to a subject in need thereof for a time sufficient to treat the cancer.

73. Use of the unit dosage form of any one of claims 59 to 71 in the manufacture of a medicament for the treatment of cancer.

74. A container comprising the unit dosage form of any one of claims 59 to 72.

75. A kit-of-parts comprising:
    a. the pharmaceutical composition of any one of claims 1 to 52
    b. a receptacle for the unit dosage form
    c. directions for dilution and/or for use.

76. A kit-of-parts comprising:
    a. the pharmaceutical composition of any one of claims 1 to 52
    b. a diluent
    c. a receptacle for the unit dosage form
    d. directions for dilution and/or for use.

77. A kit-of-parts comprising:
    a. the pharmaceutical composition of any one of claims 1 to 52
    b. a diluent comprising acetate, sorbitol and polysorbate 80
    c. a receptacle for the unit dosage form
    d. directions for dilution and/or for use.

78. The kit-of-parts of claim 77 wherein the ratio of the concentrations of acetate, sorbitol and polysorbate 80 is identical in the diluent and the pharmaceutical composition.

79. The kit-of-parts of any one of claims 75 to 78 wherein
    a. the pharmaceutical composition comprises:
        i. 5 to 60 mg/mL of the bispecific antibody
        ii. 30 mM acetate buffer
        iii. 150 mM sorbitol
        iv. 0.04 % w/v polysorbate 80
        v. pH is 5.5
    b. a receptacle for the unit dosage form, and
    c. directions for dilution and/or for use.

80. A method of preparing a pharmaceutical composition as defined in any one of claims 1 to 47, comprising the steps of mixing in water for injection:

    a. 0.5 to 120 mg/mL of a bispecific antibody comprising a first binding region binding to human CD3 which comprises the CDR sequences:

VH-CDR1: SEQ ID NO: 1
VH-CDR2: SEQ ID NO: 2
VH-CDR3: SEQ ID NO: 3
VL-CDR1: SEQ ID NO: 4
VL-CDR2: GTN, and
VL-CDR3: SEQ ID NO: 5,
and a second binding region binding to human CD20 which comprises the CDR sequences:
VH-CDR1: SEQ ID NO: 8
VH-CDR2: SEQ ID NO: 9
VH-CDR3: SEQ ID NO: 10
VL-CDR1: SEQ ID NO: 11
VL-CDR2: DAS, and
VL-CDR3: SEQ ID NO: 12

b. 3.53 mg/mL of sodium acetate trihydrate
c. 0.24 mg/mL of acetic acid
d. 27.3 mg/mL of sorbitol
e. 0.4 mg polysorbate 80

and adjusting the pH to 5.5 by adding sodium hydroxide.

81. The method of claim 80 wherein a. is 5 mg/mL.

82. The method of claim 80 wherein a. is 12 mg/mL.

83. The method of claim 80 wherein a. is 24 mg/mL.

84. The method of claim 80 wherein a. is 48 mg/mL.

85. The method of claim 80 wherein a. is 60 mg/mL.

86. A method of preparing a unit dosage form as defined in any one of claims 59 to 71, comprising the steps of:
    a. preparing the pharmaceutical composition by the steps of the method of any of claims 80 – 85, or providing a pharmaceutical composition as defined in any one of claims 1 -45;
    b. providing a diluent

c. mixing the pharmaceutical composition and the diluent to a desired bispecific antibody concentration.

87. A method of preparing a unit dosage form as defined in any one of claims 59 to 71, comprising the steps of:
    a. preparing the pharmaceutical composition by the steps of the method of any of claims 80 – 85, or providing a pharmaceutical composition as defined in any one of claims 1 -45;
    b. providing a diluent having the same, or similar, concentrations with regard to substituents as the pharmaceutical composition prepared or provided in step a.
    c. mixing the pharmaceutical composition and the diluent to a desired bispecific antibody concentration.

88. A pharmaceutical composition or a unit dosage form, which is obtainable by any of the methods as defined in any one of claims 80 to 87.