

CLAIMS

What is claimed is:

1. A method of treating a CD70-expressing cancer in a subject, the method comprising administering to the subject a therapeutically effective amount of a nonfucosylated anti-CD70 antibody, wherein the method results in a depletion of cancer cells in the subject, wherein the method does not result in a depletion of CD70+ T regulatory cells (CD70+ Tregs) in the subject, wherein the anti-CD70 antibody comprises a heavy chain variable region comprising the three CDRs of SEQ ID NO:1, a light chain variable region comprising the three CDRs of SEQ ID NO:2, wherein the CDRs of the anti-CD70 antibody are defined by the Kabat numbering scheme, and an Fc domain, and wherein the cancer is selected from the group consisting of myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML).
2. The method of claim 1, wherein the anti-CD70 antibody comprises a heavy chain variable region comprising an amino acid sequence at least 85% identical to the amino acid sequence of SEQ ID NO:1 and a light chain variable region comprising an amino acid sequence at least 85% identical to the amino acid sequence of SEQ ID NO:2.
3. The method of claim 1, wherein the anti-CD70 antibody a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:1 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:2.
4. The method of any one of claims 1-3, wherein the Fc domain is an antibody effector domain mediating one or more of antibody-dependent cellular cytotoxicity (ADCC), antibody-dependent cellular phagocytosis (ADCP), and complement-dependent cellular cytotoxicity (CDC).
5. The method of any one of claims 1-3, wherein the Fc domain is an antibody effector domain mediating ADCC.
6. The method of any one of claims 1-5, wherein the Fc domain is a human Fc domain.

7. The method of any one of claims 1-6, wherein the anti-CD70 antibody is vorsetuzumab.
8. The method of any one of claims 1-7, wherein the antibody is conjugated to a therapeutic agent.
9. The method of claim 8, wherein the therapeutic agent is a chemotherapeutic agent or an immunomodulatory agent.
10. The method of claim 8, wherein the therapeutic agent is a chemotherapeutic agent.
11. The method of claim 10, wherein the chemotherapeutic agent is monomethyl auristatin E (MMAE) or monomethyl auristatin F (MMAF).
12. The method of claim 8, wherein the therapeutic agent is an immunomodulatory agent.
13. The method of any one of claims 1-12, wherein the method comprises administering a population of anti-CD70 antibodies, wherein each antibody in the population of anti-CD70 antibodies comprises a heavy chain variable region comprising the three CDRs of SEQ ID NO:1, a light chain variable region comprising the three CDRs of SEQ ID NO:2, wherein the CDRs of the anti-CD70 antibody are defined by the Kabat numbering scheme, and an Fc domain, wherein at least 50% of the anti-CD70 antibodies in the population of the anti-CD70 antibodies lack core fucosylation.
14. The method of claim 13, wherein at least 70% of the anti-CD70 antibodies in the population of the anti-CD70 antibodies lack core fucosylation.
15. The method of claim 13, wherein at least 90% of the anti-CD70 antibodies in the population of the anti-CD70 antibodies lack core fucosylation.
16. The method of any one of claims 1-15, wherein the cancer is MDS.

17. The method of claim 16, wherein the MDS is relapsed or refractory MDS.
18. The method of claim 17, wherein the subject experienced treatment failure after prior hypomethylating agent (HMA) therapy for the MDS.
19. The method of any one of claims 1-15, wherein the cancer is AML.
20. The method of claim 19, wherein the AML is relapsed or refractory AML.
21. The method of claim 20, wherein the subject received 2 prior treatment regimens to treat the AML.
22. The method of claim 20, wherein the subject received 3 prior treatment regimens to treat the AML.
23. The method of any one of claims 1-22, wherein at least about 0.1%, at least about 1%, at least about 2%, at least about 3%, at least about 4%, at least about 5%, at least about 6%, at least about 7%, at least about 8%, at least about 9%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 60%, at least about 70%, or at least about 80% of the cancer cells express CD70.
24. The method of any one of claims 1-23, wherein administering the nonfucosylated anti-CD70 antibody to the subject results in a depletion of cancer cells by at least about 5%, at least about 6%, at least about 7%, at least about 8%, at least about 9%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 60%, at least about 70%, at least about 80%, at least about 90%, at least about 95%, or about 100% compared to the amount of cancer cells before administering the nonfucosylated anti-CD70 antibody to the subject.

25. The method of any one of claims 1-24, wherein administering the nonfucosylated anti-CD70 antibody to the subject results in a depletion of CD70+ Tregs of no more than about 20%, about 10%, about 9%, about 8%, about 7%, about 6%, about 5%, about 4%, about 3%, about 2%, about 1%, or about 0.1% compared to the amount of CD70+ Tregs before administering the afucosylated anti-CD70 antibody to the subject.

26. The method of any one of claims 1-25, wherein one or more therapeutic effects in the subject is improved after administration of the nonfucosylated anti-CD70 antibody relative to a baseline.

27. The method of claim 26, wherein the one or more therapeutic effects is selected from the group consisting of: objective response rate, duration of response, time to response, progression free survival and overall survival.

28. The method of any one of claims 1-27, wherein the objective response rate is at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 60%, at least about 70%, or at least about 80%.

29. The method of any one of claims 1-28, wherein the subject exhibits progression-free survival of at least about 1 month, at least about 2 months, at least about 3 months, at least about 4 months, at least about 5 months, at least about 6 months, at least about 7 months, at least about 8 months, at least about 9 months, at least about 10 months, at least about 11 months, at least about 12 months, at least about eighteen months, at least about two years, at least about three years, at least about four years, or at least about five years after administration of the nonfucosylated anti-CD70 antibody.

30. The method of any one of claims 1-29, wherein the subject exhibits overall survival of at least about 1 month, at least about 2 months, at least about 3 months, at least about 4 months, at least about 5 months, at least about 6 months, at least about 7 months, at least about 8 months, at least about 9 months, at least about 10 months, at least about 11 months, at least about 12 months, at least about eighteen months, at least about two years, at least about three years, at

least about four years, or at least about five years after administration of the nonfucosylated anti-CD70 antibody.

31. The method of any one of claims 1-30, wherein the duration of response to the anti-CD70 antibody is at least about 1 month, at least about 2 months, at least about 3 months, at least about 4 months, at least about 5 months, at least about 6 months, at least about 7 months, at least about 8 months, at least about 9 months, at least about 10 months, at least about 11 months, at least about 12 months, at least about eighteen months, at least about two years, at least about three years, at least about four years, or at least about five years after administration of the nonfucosylated anti-CD70 antibody.

32. The method of any one of claims 1-31, wherein the route of administration for the anti-CD70 antibody is intravenous.

33. The method of any one of claims 1-32, wherein the subject is a human.

34. The method of any one of claims 1-33, wherein the anti-CD70 antibody is administered in combination with azacitidine.

35. The method of any one of claims 1-33, wherein the anti-CD70 antibody is administered in combination with venetoclax.

36. The method of any one of claims 1-33, wherein the anti-CD70 antibody is administered in combination with azacitidine and venetoclax.

37. The method of any one of claims 1-35, wherein the anti-CD70 antibody is administered in combination with fluoroquinolone.

38. A pharmaceutical composition for the treatment of a CD70-expressing cancer, the composition comprising a nonfucosylated anti-CD70 antibody, wherein the anti-CD70 antibody comprises a heavy chain variable region comprising the three CDRs of SEQ ID NO:1, a light

chain variable region comprising the three CDRs of SEQ ID NO:2, wherein the CDRs of the anti-CD70 antibody are defined by the Kabat numbering scheme, and an Fc domain, and at least one pharmaceutically compatible ingredient, wherein the composition is for use in the method of any one of claims 1-37.

39. A kit comprising a nonfucosylated anti-CD70 antibody, wherein the anti-CD70 antibody comprises a heavy chain variable region comprising the three CDRs of SEQ ID NO:1, a light chain variable region comprising the three CDRs of SEQ ID NO:2, wherein the CDRs of the anti-CD70 antibody are defined by the Kabat numbering scheme, and an Fc domain, and instructions for using the anti-CD70 antibodies in the method of any one of claims 1-37.