

indefinitely self-renew and produce plenty of daughter blast cells with a specific phenotype of CD371, acting as one of most important reasons of leukemia relapse (Siveen et al., *Mol Cancer* (2017);16:13; Yoshida et al., *Cancer Sci* (2016);107:5–11). Given the significant role for CD371 in diseases, antibodies that bind to CD371 and methods of using such agents, are desired.

### 3. SUMMARY

In another aspect, provided herein is an anti-CD371 antibody or an antigen-binding fragment thereof, comprising:

a heavy chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 28; a heavy chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 29; a heavy chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 30; a light chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 31; a light chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 32; and a light chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 33

In another aspect, provided herein is an antibody or an antigen-binding fragment thereof, comprising a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 1, and a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 2.

In another aspect, provided herein is an antibody or an antigen-binding fragment thereof, comprising the amino acid sequence set forth in SEQ ID NO: 8.

In another aspect, provided herein is a bispecific molecule comprising the antibody or antigen-binding fragment thereof as described herein, linked to a second functional moiety.

In another aspect, provided herein is a composition comprising the antibody or antigen-binding fragment thereof, the immunoconjugate, or the bispecific molecule as described herein.

In another aspect, provided herein is a nucleic acid that encodes an antibody or antigen-binding fragment thereof as described herein.

In another aspect, provided herein is an expression vector comprising the nucleic acid molecule as described herein.

In another aspect, provided herein is a host cell comprising the expression vector as described herein.

In another aspect, provided herein is a method for detecting CD371 in a whole cell or tissue, comprising:

contacting a cell or tissue with the antibody or antigen-binding fragment thereof as described herein, wherein said antibody or antigen-binding fragment thereof comprises a detectable label; and

determining the amount of the labeled antibody or antigen-binding fragment thereof bound to said cell or tissue by measuring the amount of detectable label associated with said cell or tissue, wherein the amount of bound antibody or antigen-binding fragment thereof indicates the amount of CD371 in said cell or tissue.

5           In another aspect, provided herein is use of an antibody or antigen-binding fragment thereof as described herein, the immunoconjugate as described herein, the bispecific molecule as described herein, or the composition as described herein in the manufacture of a medicament for reducing tumor burden in a subject, wherein the antibody or antigen-binding fragment thereof as described herein, the immunoconjugate as described herein, the bispecific molecule as described  
10   herein, or the composition as described herein is to be administered to the subject.

          In another aspect, provided herein is use of an antibody or antigen-binding fragment thereof as described herein, the immunoconjugate as described herein, the bispecific molecule as described herein, or the composition of as described herein in the manufacture of a medicament for treating a tumor or neoplasm in a subject, wherein the antibody or antigen-binding fragment  
15   thereof as described herein, the immunoconjugate as described herein, the bispecific molecule as described herein, or the composition as described herein is to be administered to the subject.

          In another aspect, provided herein is use of an antibody or antigen-binding fragment thereof as described herein, the immunoconjugate as described herein, the bispecific molecule as described herein, or the composition as described herein in the manufacture of a medicament for  
20   increasing or lengthening survival of a subject having a tumor or neoplasm, wherein an antibody or antigen-binding fragment thereof as described herein, the immunoconjugate as described herein, the bispecific molecule as described herein, or the composition as described herein is to be administered to the subject.

          In yet another aspect, provided herein is a kit for reducing tumor burden in a subject, treating and/or preventing a tumor or neoplasm in a subject, and/or increasing or lengthening  
25   survival of a subject having a tumor or neoplasm, comprising the antibody or antigen-binding fragment thereof, the immunoconjugate, the bispecific molecule, or the composition as described herein.

          In yet another aspect, provided herein is an antibody or antigen-binding fragment thereof, the immunoconjugate, the bispecific molecule, or the composition as described herein,  
30   for use in therapy.

          The presently disclosed subject matter provides antibodies or antigen-binding fragments thereof that specifically bind to CD371, and methods of using the antibodies or antigen-binding fragments thereof.

35           In certain examples, the anti-CD371 antibody or an antigen-binding fragment thereof comprises a heavy chain variable region comprising an amino acid sequence that is at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 96%, at least about

97%, at least about 98%, at least about 99%, at least about 100% homologous or identical to the amino acid sequence set forth in SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, or SEQ ID NO: 11.

5 In certain examples, the anti-CD371 antibody or an antigen-binding fragment thereof comprises a light chain variable region comprising an amino acid sequence that is at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, at least about 99%, at least about 100% homologous or identical to the amino acid sequence set forth in SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, or SEQ ID NO: 12.

10 In certain examples, the anti-CD371 antibody or an antigen-binding fragment thereof comprises (a) a heavy chain variable region comprising an amino acid sequence that is at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, at least about 99%, at least about 100% homologous or identical to the amino acid sequence set forth in SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID  
15 NO: 7, SEQ ID NO: 9, or SEQ ID NO: 11; and (b) a light chain variable region comprising an amino acid sequence that is at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, at least about 99% at least about 100% homologous or identical to the amino acid sequence set forth in SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, or SEQ ID NO: 12.

## **WHAT IS CLAIMED IS:**

1. An anti-CD371 antibody or an antigen-binding fragment thereof, comprising:  
a heavy chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 28; a heavy chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 29; a heavy chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 30; a light chain variable region CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 31; a light chain variable region CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 32; and a light chain variable region CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 33.
2. The antibody or antigen-binding fragment thereof of claim 1, comprising a heavy chain variable region comprising an amino acid sequence that is at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, at least about 99%, at least about 100% identical to the amino acid sequence set forth in SEQ ID NO: 1.
3. The antibody or antigen-binding fragment thereof of claim 1, comprising a light chain variable region comprising an amino acid sequence that is at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, at least about 99%, at least about 100% identical to the amino acid sequence set forth in SEQ ID NO: 2.
4. The antibody or antigen-binding fragment thereof of claim 1, comprising a heavy chain variable region comprising an amino acid sequence that is at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, at least about 99%, at least about 100% identical to the amino acid sequence set forth in SEQ ID NO: 1, and a light chain variable region comprising an amino acid sequence that is at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, at least about 99%, at least about 100% identical to the amino acid sequence set forth in SEQ ID NO: 2.
5. The antibody or antigen-binding fragment thereof of any one of claims 1-4, comprising a heavy chain variable region comprising the amino acid sequence set forth

in SEQ ID NO: 1, and a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 2.

6. The antibody or antigen-binding fragment thereof of any one of claims 1-5, wherein the antibody or antigen-binding fragment thereof binds to a CD371 comprising the amino acid sequence set forth in SEQ ID NO: 15.

7. The antibody or antigen-binding fragment thereof of any one of claims 1-5, wherein the antibody or antigen-binding fragment thereof binds to human CD371 with a dissociation constant ( $K_D$ ) of between about  $1 \times 10^{-7}$  M and about  $1 \times 10^{-8}$  M or between about  $1 \times 10^{-9}$  M and about  $1 \times 10^{-8}$  M.

8. An antibody or an antigen-binding fragment thereof, comprising a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 1, and a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 2.

9. An antibody or an antigen-binding fragment thereof, comprising the amino acid sequence set forth in SEQ ID NO: 68.

10. The antibody or antigen-binding fragment thereof of any one of claims 1-9, wherein the antibody comprises a human variable region framework region.

11. The antibody or antigen-binding fragment thereof of any one of claims 1-10, which is a chimeric antibody or an antigen-binding fragment thereof.

12. The antibody or antigen-binding portion thereof of any one of claims 1-10, which is a humanized antibody or an antigen-binding fragment thereof.

13. The antibody or antigen-binding fragment thereof of any one of claims 1-12, wherein the antigen-binding fragment of the antibody is a Fab, Fab', F(ab')<sub>2</sub>, variable fragment (Fv), or single chain variable region (scFv).

14. An immunoconjugate comprising the antibody or antigen-binding fragment thereof of any one of claims 1-13, linked to a therapeutic agent.

15. The immunoconjugate of claim 14, wherein said therapeutic agent is a drug, a cytotoxin, or a radioactive isotope.

16. A bispecific molecule comprising the antibody or antigen-binding fragment thereof of any one of claims 1-13, linked to a second functional moiety.
17. The bispecific molecule of claim 16, wherein the second functional moiety has a different binding specificity than said antibody or antigen binding fragment thereof.
18. A composition comprising the antibody or antigen-binding fragment thereof of any one of claims 1-13, the immunoconjugate of claim 14 or 15, or the bispecific molecule of claim 16 or 17.
19. The composition of claim 18, which is a pharmaceutical composition that further comprises a pharmaceutically acceptable carrier.
20. A nucleic acid that encodes an antibody or antigen-binding fragment thereof of any one of claims 1-13.
21. An expression vector comprising the nucleic acid molecule of claim 20.
22. A host cell comprising the expression vector of claim 21.
23. A method for detecting CD371 in a whole cell or tissue, comprising:  
contacting a cell or tissue with the antibody or antigen-binding fragment thereof of any one of claims 1-13, wherein said antibody or antigen-binding fragment thereof comprises a detectable label; and  
determining the amount of the labeled antibody or antigen-binding fragment thereof bound to said cell or tissue by measuring the amount of detectable label associated with said cell or tissue, wherein the amount of bound antibody or antigen-binding fragment thereof indicates the amount of CD371 in said cell or tissue.
24. Use of an antibody or antigen-binding fragment thereof of any one of claims 1-13, the immunoconjugate of claim 14 or 15, the bispecific molecule of claim 16 or 17, or the composition of any one of claims 18 or 19 in the manufacture of a medicament for reducing tumor burden in a subject, wherein the antibody or antigen-binding fragment thereof of any one of claims 1-13, the immunoconjugate of claim 14 or 15, the bispecific molecule of claim 16 or 17, or the composition of any one of claims 18 or 19 is to be administered to the subject .

25. The use of claim 24, wherein the medicament reduces the number of the tumor cells and/or reduces the tumor size in the subject.
26. Use of an antibody or antigen-binding fragment thereof of any one of claims 1-13, the immunoconjugate of claim 14 or 15, the bispecific molecule of claim 16 or 17, or the composition of any one of claims 18 or 19 in the manufacture of a medicament for treating a tumor or neoplasm in a subject, wherein the antibody or antigen-binding fragment thereof of any one of claims 1-13, the immunoconjugate of claim 14 or 15, the bispecific molecule of claim 16 or 17, or the composition of any one of claims 18 or 19 is to be administered to the subject.
27. Use of an antibody or antigen-binding fragment thereof of any one of claims 1-13, the immunoconjugate of claim 14 or 15, the bispecific molecule of claim 16 or 17, or the composition of any one of claims 18 or 19 in the manufacture of a medicament for increasing or lengthening survival of a subject having a tumor or neoplasm, wherein an antibody or antigen-binding fragment thereof of any one of claims 1-13, the immunoconjugate of claim 14 or 15, the bispecific molecule of claim 16 or 17, or the composition of any one of claims 18 or 19 is to be administered to the subject.
28. The use of claim 27, wherein the medicament can reduce tumor burden in the subject.
29. The use of any one of claims 24-28, wherein the tumor or neoplasm is selected from acute myeloid leukemia (AML), multiple myeloma, Non-Hodgkin Lymphoma, Hodgkin Lymphoma, Chronic Lymphocytic Leukemia (CLL), glioblastoma, myelodysplastic syndrome (MDS), and chronic myelogenous leukemia (CML).
30. The use of any one of claims 24-29, wherein the tumor or neoplasm is AML.
31. The use of any one of claims 24-30, wherein the subject is a human.
32. A kit for reducing tumor burden in a subject, treating and/or preventing a tumor or neoplasm in a subject, and/or increasing or lengthening survival of a subject having a tumor or neoplasm, comprising the antibody or antigen-binding fragment thereof of any one of claims 1-13, the immunoconjugate of claim 14 or 15, the bispecific molecule of claim 16 or 17, or the composition of any one of claims 18 or 19.

33. The kit of claim 32, wherein the kit further comprises written instructions for using the antibody or antigen-binding fragment thereof for treating and/or preventing a tumor or neoplasm in a subject, and/or increasing or lengthening survival of a subject having a tumor or neoplasm.

34. An antibody or antigen-binding fragment thereof of any one of claims 1-13, the immunoconjugate of claim 14 or 15, the bispecific molecule of claim 16 or 17, or the composition of any one of claims 18 or 19 for use in therapy.