

SUMMARY

[0007] According to certain examples, the present disclosure provides methods for treating, ameliorating at least one symptom or indication, or inhibiting the growth of cancer in a subject. The methods according to this example of the disclosure
5 comprise administering a therapeutically effective amount of an antibody or antigen-binding fragment thereof that specifically binds to programmed death 1 (PD-1) in combination with a therapeutically effective amount of a bispecific antibody that specifically binds to CD20 and CD3 to a subject in need thereof.

[0008] In certain examples of the present disclosure, methods are provided for
10 treating, ameliorating at least one symptom or indication, or inhibiting the growth of cancer in a subject. In certain examples of the present disclosure, methods are provided for delaying the growth of a tumor or preventing tumor recurrence. The methods, according to this example of the disclosure, comprise sequentially administering one or more doses of a therapeutically effective amount of an
15 antibody or antigen-binding fragment thereof that specifically binds to PD-1 in combination with one or more doses of a therapeutically effective amount of a bispecific antibody that specifically binds to CD20 and CD3 to a subject in need thereof.

[0009] In certain examples, the cancer or tumor is a heme cell tumor or
20 malignancy. In certain examples, the cancer or tumor is a B-cell tumor. In certain examples, the B-cell tumor is selected from the group consisting of Hodgkin's lymphoma, non-Hodgkin's lymphoma, follicular lymphoma, small lymphocytic lymphoma, lymphoplasmacytoid lymphoma, marginal zone lymphoma, mantle cell lymphoma, diffuse large B-cell lymphoma, B-cell lymphomas, lymphomatoid
25 granulomatosis, Burkitt's lymphoma, acute lymphoblastic leukemia, hairy cell leukemia, and B cell chronic lymphocytic leukemia.

[0010] In certain examples, each dose of anti-PD-1 antibody comprises 0.1 – 20 mg/kg of the subject's body weight. In certain examples, each dose of anti-PD-1 antibody comprises 0.3, 1 or 3 mg/kg of the subject's body weight. In certain
30 examples, each dose of the anti-PD-1 antibody comprises 50 – 600 mg.

[0011] In certain examples, each dose of the bispecific antibody against CD20 and CD3 comprises 0.1 – 10 mg/kg of the subject's body weight. In certain

examples, each dose of the bispecific antibody comprises 10 – 8000 micrograms.

[0012] In certain examples, each dose of the anti-PD-1 antibody comprises 0.3, 1, 3, or 10 mg/kg of the subject's body weight and each dose of the bispecific antibody comprises 10 – 3000 micrograms. In certain examples, each dose of the anti-PD-1 antibody comprises 1, 3, or 10 mg/kg of the subject's body weight and each dose of the bispecific antibody comprises 100, 300, 1000 or 3000 micrograms. In certain examples, each dose of the anti-PD-1 antibody comprises 50 – 300 mg and each dose of the bispecific antibody comprises 100, 300, 1000 or 3000 micrograms.

[0013] In certain examples, the methods of the present disclosure comprise administering a therapeutically effective amount of an anti-PD-1 antibody prior to, concurrent with, or subsequent to a bispecific antibody that specifically binds to CD20 and CD3. In one example, the methods of the present disclosure comprise administering an anti-PD-1 antibody prior to a bispecific anti-CD20/anti-CD3 antibody.

[0014] In certain examples, the methods of the present disclosure comprise administering 0 – 50 therapeutic doses each of an anti-PD-1 antibody and a bispecific antibody against CD20 and CD3, wherein each dose is administered 0.5 – 12 weeks after the immediately preceding dose. In certain examples, each dose of the anti-PD-1 antibody is administered once a week, once in 2 weeks or once in 4 weeks and each dose of the bispecific antibody is administered once a week, once in 2 weeks or once in 4 weeks. In one example, each dose of the anti-PD-1 antibody is administered once in 2 weeks and each dose of the bispecific antibody is administered once a week.

[0015] In certain examples, each dose of the bispecific antibody is administered (as split doses) in more than 1 fractions, e.g., as 2 or more fractions within the dosing period.

[0016] In certain examples, the anti-PD-1 antibody and the bispecific antibody are administered in combination with a third therapeutic agent or therapy.

[0017] According to certain examples, the anti-PD-1 antibody or antigen-binding protein comprises the heavy chain complementarity determining regions (HCDRs) of a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 1 and the light chain CDRs of a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 2. One such type of

antigen-binding protein that can be used in the context of the methods of the present disclosure is an anti-PD-1 antibody such as REGN2810.

[0018] According to certain examples, the bispecific antibody that binds to CD20 and CD3 comprises: (i) a first antigen-binding arm comprising the heavy chain CDRs (A-HCDR1, A-HCDR2 and A-HCDR3) of a HCVR (A-HCVR) of SEQ ID NO: 11 and the light chain CDRs (LCDR1, LCDR2 and LCDR3) of a LCVR of SEQ ID NO: 12; and (ii) a second antigen-binding arm comprising the heavy chain CDRs (B-HCDR1, B-HCDR2 and B-HCDR3) of a HCVR (B-HCVR) of SEQ ID NO: 13 and the light chain CDRs (LCDR1, LCDR2 and LCDR3) of a LCVR of SEQ ID NO: 12.

[0019] In certain examples, the present disclosure provides use of an anti-PD-1 antibody or antigen-binding fragment thereof alone or in combination with a bispecific antibody against CD20 and CD3 in the manufacture of a medicament to treat or inhibit the growth of cancer in a subject, including humans. In certain examples, the cancer is a B-cell cancer. In one example, the cancer is non-Hodgkin's lymphoma. In one example, the cancer is Hodgkin's lymphoma. In one example, the cancer is acute lymphoblastic leukemia.

[0020] Other examples of the present disclosure will become apparent from a review of the ensuing detailed description.

[0020a] In one aspect, the present disclosure relates to use of an antibody or antigen-binding fragment thereof that specifically binds programmed death 1 (PD-1), and a bispecific antibody comprising a first antigen-binding arm that specifically binds CD20 and a second antigen-binding arm that specifically binds CD3, in the manufacture of a medicament for combination therapy to treat B-cell non-Hodgkin's lymphoma, wherein: the anti-PD-1 antibody or antigen-binding fragment thereof comprises three heavy chain complementarity determining regions (CDRs) (HCDR1, HCDR2 and HCDR3) and three light chain CDRs (LCDR1, LCDR2 and LCDR3), wherein HCDR1 comprises the amino acid sequence of SEQ ID NO: 3; HCDR2 comprises the amino acid sequence of SEQ ID NO: 4; HCDR3 comprises the amino acid sequence of SEQ ID NO: 5; LCDR1 comprises the amino acid sequence of SEQ ID NO: 6; LCDR2 comprises the amino acid sequence of SEQ ID NO: 7; and LCDR3 comprises the amino acid sequence of SEQ ID NO: 8; the first antigen-binding arm of the bispecific antibody comprises three heavy chain complementarity determining regions (CDRs) (A-HCDR1, A-HCDR2 and A-HCDR3) and three light chain CDRs (LCDR1, LCDR2 and LCDR3), wherein A-HCDR1 comprises the amino acid sequence of SEQ ID NO: 14; A-HCDR2 comprises the

amino acid sequence of SEQ ID NO: 15; A-HCDR3 comprises the amino acid sequence of SEQ ID NO: 16; LCDR1 comprises the amino acid sequence of SEQ ID NO: 17; LCDR2 comprises the amino acid sequence of SEQ ID NO: 18; and LCDR3 comprises the amino acid sequence of SEQ ID NO: 19; the second antigen-binding arm of the bispecific antibody comprises three heavy chain CDRs (B-HCDR1, B-HCDR2 and B-HCDR3) and three light chain CDRs (LCDR1, LCDR2 and LCDR3), wherein B-HCDR1 comprises the amino acid sequence of SEQ ID NO: 20; B-HCDR2 comprises the amino acid sequence of SEQ ID NO: 21; B-HCDR3 comprises the amino acid sequence of SEQ ID NO: 22; LCDR1 comprises the amino acid sequence of SEQ ID NO: 17; LCDR2 comprises the amino acid sequence of SEQ ID NO: 18; and LCDR3 comprises the amino acid sequence of SEQ ID NO: 19; and each dose of the anti-PD-1 antibody comprises 0.1 to 20 mg/kg of the subject's body weight.

[0020b] In another aspect, the present disclosure relates to use of an antibody or antigen-binding fragment thereof that specifically binds programmed death 1 (PD-1) in the manufacture of a first medicament, and use of a bispecific antibody comprising a first antigen-binding arm that specifically binds CD20 and a second antigen-binding arm that specifically binds CD3 in the manufacture of a second medicament, wherein the first and second medicaments are to be used in combination therapy to treat B-cell non-Hodgkin's lymphoma, wherein the anti-PD-1 antibody or antigen-binding fragment thereof comprises three heavy chain complementarity determining regions (CDRs) (HCDR1, HCDR2 and HCDR3) and three light chain CDRs (LCDR1, LCDR2 and LCDR3), wherein HCDR1 comprises the amino acid sequence of SEQ ID NO: 3; HCDR2 comprises the amino acid sequence of SEQ ID NO: 4; HCDR3 comprises the amino acid sequence of SEQ ID NO: 5; LCDR1 comprises the amino acid sequence of SEQ ID NO: 6; LCDR2 comprises the amino acid sequence of SEQ ID NO: 7; and LCDR3 comprises the amino acid sequence of SEQ ID NO: 8; the first antigen-binding arm of the bispecific antibody comprises three heavy chain complementarity determining regions (CDRs) (A-HCDR1, A-HCDR2 and A-HCDR3) and three light chain CDRs (LCDR1, LCDR2 and LCDR3), wherein A-HCDR1 comprises the amino acid sequence of SEQ ID NO: 14; A-HCDR2 comprises the amino acid sequence of SEQ ID NO: 15; A-HCDR3 comprises the amino acid sequence of SEQ ID NO: 16;

LCCR1 comprises the amino acid sequence of SEQ ID NO: 17; LCCR2 comprises the amino acid sequence of SEQ ID NO: 18; and LCCR3 comprises the amino acid sequence of SEQ ID NO: 19; the second antigen-binding arm of the bispecific antibody comprises three heavy chain CDRs (B-HCCR1, B-HCCR2 and B-HCCR3) and three light chain CDRs (LCCR1, LCCR2 and LCCR3), wherein B-HCCR1 comprises the amino acid sequence of SEQ ID NO: 20; B-HCCR2 comprises the amino acid sequence of SEQ ID NO: 21; B-HCCR3 comprises the amino acid sequence of SEQ ID NO: 22; LCCR1 comprises the amino acid sequence of SEQ ID NO: 17; LCCR2 comprises the amino acid sequence of SEQ ID NO: 18; and LCCR3 comprises the amino acid sequence of SEQ ID NO: 19; and each dose of the anti-PD-1 antibody comprises 0.1 to 20 mg/kg of the subject's body weight.

[0020c] In another aspect, the present disclosure refers to use of an antibody or antigen-binding fragment thereof that specifically binds programmed death 1 (PD-1) in the manufacture of a medicament for use in combinatorial therapy for treating B-cell non-Hodgkin's lymphoma, wherein said medicament is to be administered in combination with a bispecific antibody comprising a first antigen-binding arm that specifically binds CD20 and a second antigen-binding arm that specifically binds CD3, wherein: the anti-PD-1 antibody or antigen-binding fragment thereof comprises three heavy chain complementarity determining regions (CDRs) (HCCR1, HCCR2 and HCCR3) and three light chain CDRs (LCCR1, LCCR2 and LCCR3), wherein HCCR1 comprises the amino acid sequence of SEQ ID NO: 3; HCCR2 comprises the amino acid sequence of SEQ ID NO: 4; HCCR3 comprises the amino acid sequence of SEQ ID NO: 5; LCCR1 comprises the amino acid sequence of SEQ ID NO: 6; LCCR2 comprises the amino acid sequence of SEQ ID NO: 7; and LCCR3 comprises the amino acid sequence of SEQ ID NO: 8; the first antigen-binding arm of the bispecific antibody comprises three heavy chain CDRs (A-HCCR1, A-HCCR2 and A-HCCR3) and three light chain CDRs (LCCR1, LCCR2 and LCCR3), wherein A-HCCR1 comprises the amino acid sequence of SEQ ID NO: 14; A-HCCR2 comprises the amino acid sequence of SEQ ID NO: 15; A-HCCR3 comprises the amino acid sequence of SEQ ID NO: 16; LCCR1 comprises the amino acid sequence of SEQ ID NO: 17; LCCR2 comprises the amino acid sequence of SEQ ID NO: 18; and LCCR3 comprises the amino acid sequence of SEQ ID NO: 19; the second antigen-binding arm of the bispecific antibody comprises three heavy chain CDRs (B-HCCR1, B-HCCR2 and B-HCCR3) and three light chain CDRs (LCCR1, LCCR2 and LCCR3), wherein B-HCCR1

comprises the amino acid sequence of SEQ ID NO: 20; B-HCDR2 comprises the amino acid sequence of SEQ ID NO: 21; B-HCDR3 comprises the amino acid sequence of SEQ ID NO: 22; LCDR1 comprises the amino acid sequence of SEQ ID NO: 17; LCDR2 comprises the amino acid sequence of SEQ ID NO: 18; and
5 LCDR3 comprises the amino acid sequence of SEQ ID NO: 19; and each dose of the anti-PD-1 antibody comprises 0.1 to 20 mg/kg of the subject's body weight.

[0020d] In yet another aspect, the present disclosure refers to use of a bispecific antibody comprising a first antigen-binding arm that specifically binds CD20 and a second antigen-binding arm that specifically binds CD3 in the manufacture of a
10 medicament for use in combinatorial therapy for treating B-cell non-Hodgkin's lymphoma, wherein said medicament is to be administered in combination with an antibody or antigen-binding fragment thereof that specifically binds programmed death 1 (PD-1), wherein: the anti-PD-1 antibody or antigen-binding fragment thereof comprises three heavy chain complementarity determining regions (CDRs)
15 (HCDR1, HCDR2 and HCDR3) and three light chain CDRs (LCDR1, LCDR2 and LCDR3), wherein HCDR1 comprises the amino acid sequence of SEQ ID NO: 3; HCDR2 comprises the amino acid sequence of SEQ ID NO: 4; HCDR3 comprises the amino acid sequence of SEQ ID NO: 5; LCDR1 comprises the amino acid sequence of SEQ ID NO: 6; LCDR2 comprises the amino acid sequence of SEQ ID
20 NO: 7; and LCDR3 comprises the amino acid sequence of SEQ ID NO: 8; the first antigen-binding arm of the bispecific antibody comprises three heavy chain CDRs (A-HCDR1, A-HCDR2 and A-HCDR3) and three light chain CDRs (LCDR1, LCDR2 and LCDR3), wherein A-HCDR1 comprises the amino acid sequence of SEQ ID NO: 14; A-HCDR2 comprises the amino acid sequence of SEQ ID NO: 15;
25 A-HCDR3 comprises the amino acid sequence of SEQ ID NO: 16; LCDR1 comprises the amino acid sequence of SEQ ID NO: 17; LCDR2 comprises the amino acid sequence of SEQ ID NO: 18; and LCDR3 comprises the amino acid sequence of SEQ ID NO: 19; the second antigen-binding arm of the bispecific antibody comprises three heavy chain CDRs (B-HCDR1, B-HCDR2 and B-HCDR3)
30 and three light chain CDRs (LCDR1, LCDR2 and LCDR3), wherein B-HCDR1 comprises the amino acid sequence of SEQ ID NO: 20; B-HCDR2 comprises the amino acid sequence of SEQ ID NO: 21; B-HCDR3 comprises the amino acid sequence of SEQ ID NO: 22; LCDR1 comprises the amino acid sequence of SEQ ID NO: 17; LCDR2 comprises the amino acid sequence of SEQ ID NO: 18; and

LCDR3 comprises the amino acid sequence of SEQ ID NO: 19; and each dose of the anti-PD-1 antibody comprises 0.1 to 20 mg/kg of the subject's body weight.

[0020e] In yet another aspect, the present disclosure refers to use of a pharmaceutical composition in the manufacture of a medicament for treating B-cell non-Hodgkin's lymphoma, said composition comprising an antibody or antigen-binding fragment thereof that specifically binds programmed death 1 (PD-1) and a bispecific antibody comprising a first antigen-binding arm that specifically binds CD20 and a second antigen-binding arm that specifically binds CD3, wherein: the anti-PD-1 antibody or antigen-binding fragment thereof comprises three heavy chain complementarity determining regions (CDRs) (HCDR1, HCDR2 and HCDR3) and three light chain CDRs (LCDR1, LCDR2 and LCDR3), wherein HCDR1 comprises the amino acid sequence of SEQ ID NO: 3; HCDR2 comprises the amino acid sequence of SEQ ID NO: 4; HCDR3 comprises the amino acid sequence of SEQ ID NO: 5; LCDR1 comprises the amino acid sequence of SEQ ID NO: 6; LCDR2 comprises the amino acid sequence of SEQ ID NO: 7; and LCDR3 comprises the amino acid sequence of SEQ ID NO: 8; the first antigen-binding arm of the bispecific antibody comprises three heavy chain CDRs (A-HCDR1, A-HCDR2 and A-HCDR3) and three light chain CDRs (LCDR1, LCDR2 and LCDR3), wherein A-HCDR1 comprises the amino acid sequence of SEQ ID NO: 14; A-HCDR2 comprises the amino acid sequence of SEQ ID NO: 15; A-HCDR3 comprises the amino acid sequence of SEQ ID NO: 16; LCDR1 comprises the amino acid sequence of SEQ ID NO: 17; LCDR2 comprises the amino acid sequence of SEQ ID NO: 18; and LCDR3 comprises the amino acid sequence of SEQ ID NO: 19; the second antigen-binding arm of the bispecific antibody comprises three heavy chain CDRs (B-HCDR1, B-HCDR2 and B-HCDR3) and three light chain CDRs (LCDR1, LCDR2 and LCDR3), wherein B-HCDR1 comprises the amino acid sequence of SEQ ID NO: 20; B-HCDR2 comprises the amino acid sequence of SEQ ID NO: 21; B-HCDR3 comprises the amino acid sequence of SEQ ID NO: 22; LCDR1 comprises the amino acid sequence of SEQ ID NO: 17; LCDR2 comprises the amino acid sequence of SEQ ID NO: 18; and LCDR3 comprises the amino acid sequence of SEQ ID NO: 19; and the composition comprises 0.05 to 600 mg of the anti-PD-1 antibody.

BRIEF DESCRIPTION OF THE FIGURES

[0021] **Figure 1** summarizes the results of in vivo efficacy of anti-mouse PD-1 antibody alone and in combination with bispecific anti-CD20/anti-CD3 antibody against established B16_CD20+ tumors (described in Example 1 herein).

5 [0022] **Figure 2** shows mice randomized into cohorts based on tumor size (as described in Example 2 herein).

[0023] **Figure 3** summarizes the results of in vivo efficacy of anti-mouse PD-1 antibody alone and in combination with bispecific anti-CD20/anti-CD3 antibody against established B16_CD20+ tumors (described in Example 2 herein).

10 [0024] **Figure 4** shows a schematic representation of the treatment arms and dose cohorts for patients with lymphoma (B-cell non-Hodgkin's lymphoma and Hodgkin's lymphoma) (described in Example 3 herein).

[0025] **Figure 5** shows a schematic representation of the treatment arms and dose cohorts for patients with acute lymphoblastic leukemia (described in Example

15 3 herein).

What is claimed is:

1. Use of an antibody or antigen-binding fragment thereof that specifically binds programmed death 1 (PD-1), and a bispecific antibody comprising a first antigen-binding arm that specifically binds CD20 and a second antigen-binding arm that specifically binds CD3, in the manufacture of a medicament for combination therapy to treat B-cell non-Hodgkin's lymphoma, wherein:

the anti-PD-1 antibody or antigen-binding fragment thereof comprises three heavy chain complementarity determining regions (CDRs) (HCDR1, HCDR2 and HCDR3) and three light chain CDRs (LCDR1, LCDR2 and LCDR3), wherein HCDR1 comprises the amino acid sequence of SEQ ID NO: 3; HCDR2 comprises the amino acid sequence of SEQ ID NO: 4; HCDR3 comprises the amino acid sequence of SEQ ID NO: 5; LCDR1 comprises the amino acid sequence of SEQ ID NO: 6; LCDR2 comprises the amino acid sequence of SEQ ID NO: 7; and LCDR3 comprises the amino acid sequence of SEQ ID NO: 8;

the first antigen-binding arm of the bispecific antibody comprises three heavy chain complementarity determining regions (CDRs) (A-HCDR1, A-HCDR2 and A-HCDR3) and three light chain CDRs (LCDR1, LCDR2 and LCDR3), wherein A-HCDR1 comprises the amino acid sequence of SEQ ID NO: 14; A-HCDR2 comprises the amino acid sequence of SEQ ID NO: 15; A-HCDR3 comprises the amino acid sequence of SEQ ID NO: 16; LCDR1 comprises the amino acid sequence of SEQ ID NO: 17; LCDR2 comprises the amino acid sequence of SEQ ID NO: 18; and LCDR3 comprises the amino acid sequence of SEQ ID NO: 19;

the second antigen-binding arm of the bispecific antibody comprises three heavy chain CDRs (B-HCDR1, B-HCDR2 and B-HCDR3) and three light chain CDRs (LCDR1, LCDR2 and LCDR3), wherein B-HCDR1 comprises the amino acid sequence of SEQ ID NO: 20; B-HCDR2 comprises the amino acid sequence of SEQ ID NO: 21; B-HCDR3 comprises the amino acid sequence of SEQ ID NO: 22; LCDR1 comprises the amino acid sequence of SEQ ID NO: 17; LCDR2 comprises the amino acid sequence of SEQ ID NO: 18; and LCDR3 comprises the amino acid sequence of SEQ ID NO: 19; and

each dose of the anti-PD-1 antibody comprises 0.1 to 20 mg/kg of a subject's body weight.

2. Use of an antibody or antigen-binding fragment thereof that
5 specifically binds programmed death 1 (PD-1) in the manufacture of a first medicament, and use of a bispecific antibody comprising a first antigen-binding arm that specifically binds CD20 and a second antigen-binding arm that specifically binds CD3, in the manufacture of a second medicament, wherein the first and second medicaments are to be used in combination
10 therapy to treat B-cell non-Hodgkin's lymphoma, wherein:

the anti-PD-1 antibody or antigen-binding fragment thereof comprises three heavy chain complementarity determining regions (CDRs) (HCDR1, HCDR2 and HCDR3) and three light chain CDRs (LCDR1, LCDR2 and LCDR3), wherein HCDR1 comprises the amino acid sequence of SEQ
15 ID NO: 3; HCDR2 comprises the amino acid sequence of SEQ ID NO: 4; HCDR3 comprises the amino acid sequence of SEQ ID NO: 5; LCDR1 comprises the amino acid sequence of SEQ ID NO: 6; LCDR2 comprises the amino acid sequence of SEQ ID NO: 7; and LCDR3 comprises the amino acid sequence of SEQ ID NO: 8;

20 the first antigen-binding arm of the bispecific antibody comprises three heavy chain complementarity determining regions (CDRs) (A-HCDR1, A-HCDR2 and A-HCDR3) and three light chain CDRs (LCDR1, LCDR2 and LCDR3), wherein A-HCDR1 comprises the amino acid sequence of SEQ ID NO: 14; A-HCDR2 comprises the amino acid
25 sequence of SEQ ID NO: 15; A-HCDR3 comprises the amino acid sequence of SEQ ID NO: 16; LCDR1 comprises the amino acid sequence of SEQ ID NO: 17; LCDR2 comprises the amino acid sequence of SEQ ID NO: 18; and LCDR3 comprises the amino acid sequence of SEQ ID NO: 19;

30 the second antigen-binding arm of the bispecific antibody comprises three heavy chain CDRs (B-HCDR1, B-HCDR2 and B-HCDR3) and three light chain CDRs (LCDR1, LCDR2 and LCDR3), wherein B-HCDR1 comprises the amino acid sequence of SEQ ID NO: 20; B-HCDR2 comprises the amino acid sequence of SEQ ID NO: 21; B-HCDR3 comprises the amino

acid sequence of SEQ ID NO: 22; LCDR1 comprises the amino acid sequence of SEQ ID NO: 17; LCDR2 comprises the amino acid sequence of SEQ ID NO: 18; and LCDR3 comprises the amino acid sequence of SEQ ID NO: 19; and

5 each dose of the anti-PD-1 antibody comprises 0.1 to 20 mg/kg of a subject's body weight.

3. Use of an antibody or antigen-binding fragment thereof that specifically binds programmed death 1 (PD-1) in the manufacture of a medicament for use in
10 combinatorial therapy for treating B-cell non-Hodgkin's lymphoma, wherein said medicament is to be administered in combination with a bispecific antibody comprising a first antigen-binding arm that specifically binds CD20 and a second antigen-binding arm that specifically binds CD3, wherein:

the anti-PD-1 antibody or antigen-binding fragment thereof comprises three
15 heavy chain complementarity determining regions (CDRs) (HCDR1, HCDR2 and HCDR3) and three light chain CDRs (LCDR1, LCDR2 and LCDR3) , wherein HCDR1 comprises the amino acid sequence of SEQ ID NO: 3; HCDR2 comprises the amino acid sequence of SEQ ID NO: 4; HCDR3 comprises the amino acid sequence of SEQ ID NO: 5; LCDR1 comprises the amino acid sequence of SEQ ID
20 NO: 6; LCDR2 comprises the amino acid sequence of SEQ ID NO: 7; and LCDR3 comprises the amino acid sequence of SEQ ID NO: 8;

the first antigen-binding arm of the bispecific antibody comprises three heavy chain CDRs (A-HCDR1, A-HCDR2 and A-HCDR3) and three light chain CDRs (LCDR1, LCDR2 and LCDR3), wherein A-HCDR1 comprises the amino acid
25 sequence of SEQ ID NO: 14; A-HCDR2 comprises the amino acid sequence of SEQ ID NO: 15; A-HCDR3 comprises the amino acid sequence of SEQ ID NO: 16; LCDR1 comprises the amino acid sequence of SEQ ID NO: 17; LCDR2 comprises the amino acid sequence of SEQ ID NO: 18; and LCDR3 comprises the amino acid sequence of SEQ ID NO: 19;

30 the second antigen-binding arm of the bispecific antibody comprises three heavy chain CDRs (B-HCDR1, B-HCDR2 and B-HCDR3) and three light chain CDRs (LCDR1, LCDR2 and LCDR3), wherein B-HCDR1 comprises the amino acid sequence of SEQ ID NO: 20; B-HCDR2 comprises the amino acid sequence of SEQ ID NO: 21; B-HCDR3 comprises the amino acid sequence of SEQ ID NO: 22;

LCDR1 comprises the amino acid sequence of SEQ ID NO: 17; LCDR2 comprises the amino acid sequence of SEQ ID NO: 18; and LCDR3 comprises the amino acid sequence of SEQ ID NO: 19; and

5 each dose of the anti-PD-1 antibody comprises 0.1 to 20 mg/kg of a subject's body weight.

4. Use of a bispecific antibody comprising a first antigen-binding arm that specifically binds CD20 and a second antigen-binding arm that specifically binds CD3 in the manufacture of a medicament for use in combinatorial therapy for
10 treating B-cell non-Hodgkin's lymphoma, wherein said medicament is to be administered in combination with an antibody or antigen-binding fragment thereof that specifically binds programmed death 1 (PD-1), wherein:

the anti-PD-1 antibody or antigen-binding fragment thereof comprises three heavy chain complementarity determining regions (CDRs) (HCDR1, HCDR2 and
15 HCDR3) and three light chain CDRs (LCDR1, LCDR2 and LCDR3) , wherein HCDR1 comprises the amino acid sequence of SEQ ID NO: 3; HCDR2 comprises the amino acid sequence of SEQ ID NO: 4; HCDR3 comprises the amino acid sequence of SEQ ID NO: 5; LCDR1 comprises the amino acid sequence of SEQ ID NO: 6; LCDR2 comprises the amino acid sequence of SEQ ID NO: 7; and LCDR3
20 comprises the amino acid sequence of SEQ ID NO: 8;

the first antigen-binding arm of the bispecific antibody comprises three heavy chain CDRs (A-HCDR1, A-HCDR2 and A-HCDR3) and three light chain CDRs (LCDR1, LCDR2 and LCDR3), wherein A-HCDR1 comprises the amino acid sequence of SEQ ID NO: 14; A-HCDR2 comprises the amino acid sequence of
25 SEQ ID NO: 15; A-HCDR3 comprises the amino acid sequence of SEQ ID NO: 16; LCDR1 comprises the amino acid sequence of SEQ ID NO: 17; LCDR2 comprises the amino acid sequence of SEQ ID NO: 18; and LCDR3 comprises the amino acid sequence of SEQ ID NO: 19;

the second antigen-binding arm of the bispecific antibody comprises three
30 heavy chain CDRs (B-HCDR1, B-HCDR2 and B-HCDR3) and three light chain CDRs (LCDR1, LCDR2 and LCDR3), wherein B-HCDR1 comprises the amino acid sequence of SEQ ID NO: 20; B-HCDR2 comprises the amino acid sequence of SEQ ID NO: 21; B-HCDR3 comprises the amino acid sequence of SEQ ID NO: 22; LCDR1 comprises the amino acid sequence of SEQ ID NO: 17; LCDR2 comprises

the amino acid sequence of SEQ ID NO: 18; and LCDR3 comprises the amino acid sequence of SEQ ID NO: 19; and

each dose of the anti-PD-1 antibody comprises 0.1 to 20 mg/kg of a subject's body weight.

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5. Use of a pharmaceutical composition in the manufacture of a medicament for treating B-cell non-Hodgkin's lymphoma, said composition comprising an antibody or antigen-binding fragment thereof that specifically binds programmed death 1 (PD-1) and a bispecific antibody comprising a first antigen-binding arm that specifically binds CD20 and a second antigen-binding arm that specifically binds CD3, wherein:

the anti-PD-1 antibody or antigen-binding fragment thereof comprises three heavy chain complementarity determining regions (CDRs) (HCDR1, HCDR2 and HCDR3) and three light chain CDRs (LCDR1, LCDR2 and LCDR3), wherein HCDR1 comprises the amino acid sequence of SEQ ID NO: 3; HCDR2 comprises the amino acid sequence of SEQ ID NO: 4; HCDR3 comprises the amino acid sequence of SEQ ID NO: 5; LCDR1 comprises the amino acid sequence of SEQ ID NO: 6; LCDR2 comprises the amino acid sequence of SEQ ID NO: 7; and LCDR3 comprises the amino acid sequence of SEQ ID NO: 8;

the first antigen-binding arm of the bispecific antibody comprises three heavy chain CDRs (A-HCDR1, A-HCDR2 and A-HCDR3) and three light chain CDRs (LCDR1, LCDR2 and LCDR3), wherein A-HCDR1 comprises the amino acid sequence of SEQ ID NO: 14; A-HCDR2 comprises the amino acid sequence of SEQ ID NO: 15; A-HCDR3 comprises the amino acid sequence of SEQ ID NO: 16; LCDR1 comprises the amino acid sequence of SEQ ID NO: 17; LCDR2 comprises the amino acid sequence of SEQ ID NO: 18; and LCDR3 comprises the amino acid sequence of SEQ ID NO: 19;

the second antigen-binding arm of the bispecific antibody comprises three heavy chain CDRs (B-HCDR1, B-HCDR2 and B-HCDR3) and three light chain CDRs (LCDR1, LCDR2 and LCDR3), wherein B-HCDR1 comprises the amino acid sequence of SEQ ID NO: 20; B-HCDR2 comprises the amino acid sequence of SEQ ID NO: 21; B-HCDR3 comprises the amino acid sequence of SEQ ID NO: 22; LCDR1 comprises the amino acid sequence of SEQ ID NO: 17; LCDR2 comprises

the amino acid sequence of SEQ ID NO: 18; and LCDR3 comprises the amino acid sequence of SEQ ID NO: 19; and

the composition comprises 0.05 to 600 mg of the anti-PD-1 antibody.

- 5 6. The use according to anyone of claims 1-4, wherein:
- (a) each dose of the anti-PD-1 antibody comprises 0.3, 1, 3 or 10 mg/kg of the subject's body weight; or
 - (b) each dose of the anti-PD-1 antibody comprises 0.05 to 600 mg.

- 10 7. The use according to any one of claims 1-4 or 6, wherein:
- (a) each dose of the bispecific antibody comprises 0.1 – 10 mg/kg of the subject's body weight; or
 - (b) each dose of the bispecific antibody comprises 10 – 8000 micrograms.

- 15 8. The use according to claim 7, wherein each dose of the anti-PD-1 antibody comprises 1, 3 or 10 mg/kg and each dose of the bispecific antibody comprises 30, 100, 300, 1000 or 2000 micrograms.

- 20 9. The use according to any one of claims 1-4 or 6-8, wherein:
- (a) each dose of the anti-PD-1 antibody is to be administered 0.5 – 12 weeks after the immediately preceding dose;
 - (b) each dose of the bispecific antibody is to be administered 0.5 – 12 weeks after the immediately preceding dose; and/or
 - (c) each dose of the bispecific antibody is split into 2 – 5 fractions within a dosing period.

- 25 10. The use according to claim 9, wherein each dose of the anti-PD1 antibody is to be administered once in two weeks and each dose of the bispecific antibody is to be administered once a week.

- 30 11. The use according to any one of claims 1-4 or 6-10, wherein the anti-PD-1 antibody is to be administered prior to, concurrent with or after the bispecific antibody.

12. The use according to claim 11, wherein the anti-PD-1 antibody is to be administered prior to the bispecific antibody such as wherein the anti-PD-1 antibody is to be administered 1 week prior to the bispecific antibody.

5 13. The use according to any one of claims 1-12, wherein the antibodies are formulated for intravenous, subcutaneous, or intraperitoneal administration.

14. The use according to any one of claims 1-13, wherein:

10 (a) the subject is resistant or inadequately responsive to, or relapsed after prior therapy;

 (b) the administration of the medicament produces a therapeutic effect selected from the group consisting of delay in tumor growth, reduction in tumor cell number, tumor regression, increase in survival, partial response, and complete response; and/or

15 (c) the tumor growth is inhibited by at least 10% as compared to a subject not administered with the medicament, or wherein the tumor growth is inhibited by at least 10% as compared to a subject administered with either antibody as monotherapy.

20 15. The use according to claim 14, wherein tumor growth is delayed by at least 10 days as compared to a subject not administered with the medicament.

25 16. The use according to any one of claims 1-4, or 6-10, wherein the anti-PD-1 antibody is to be administered prior to the bispecific antibody and the tumor growth is inhibited by at least 20% as compared to a subject administered a bispecific anti-CD20/anti-CD3 antibody prior to an anti-PD-1 antibody.

30 17. The use according to any one of claims 1-16, further comprises a third therapeutic agent or therapy to be administered to the subject, wherein the third therapeutic agent or therapy is selected from the group consisting of radiation, surgery, a chemotherapeutic agent, a cancer vaccine, a PD-L1 inhibitor, a LAG-3 inhibitor, a CTLA-4 inhibitor, a TIM3 inhibitor, a BTLA inhibitor, a TIGIT inhibitor, a CD47 inhibitor, an indoleamine-2,3-dioxygenase (IDO) inhibitor, a vascular endothelial growth factor (VEGF) antagonist, an angiopoietin-2 (Ang2) inhibitor, a

transforming growth factor beta (TGFβ) inhibitor, an epidermal growth factor receptor (EGFR) inhibitor, an antibody to a tumor-specific antigen, Bacillus Calmette-Guerin vaccine, granulocyte-macrophage colony-stimulating factor, a cytotoxin, an interleukin 6 receptor (IL-6R) inhibitor, an interleukin 4 receptor (IL-4R) inhibitor, an IL-10 inhibitor, IL-2, IL-7, IL-21, IL-15, an antibody-drug conjugate, an anti-inflammatory drug, and a dietary supplement.

18. The use according to any one of claims 1-17, wherein the anti-PD-1 antibody or antigen binding fragment thereof comprises:

10 (a) a heavy variable chain region (HCVR) comprising the amino acid sequence of SEQ ID NO: 1 and a light variable chain region (LCVR) comprising the amino acid sequence of SEQ ID NO: 2; or

(b) a heavy chain comprising the amino acid sequence of SEQ ID NO: 9 and a light chain comprising the amino acid sequence of SEQ ID NO: 10.

15 19. The use according to any one of claims 1-18, wherein the first antigen-binding arm of the bispecific antibody comprises a A-HCVR comprising the amino acid sequence of SEQ ID NO: 11 and a LCVR comprising the amino acid sequence of SEQ ID NO: 12.

20 20. The use according to anyone of claims 1-19, wherein the second antigen-binding arm of the bispecific antibody comprises a B-HCVR comprising the amino acid sequence of SEQ ID NO: 13 and a LCVR comprising the amino acid sequence of SEQ ID NO: 12.

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