

Claims:

1. A bispecific antibody of IgG1 1+1 heterodimer format comprising at least one Fab portion that binds CD47 and at least one Fab portion that binds CD20; wherein the Fab portion that binds CD47 exhibits low affinity K_d for CD47, from 0.1 μM to 5.0 μM ; and, wherein the Fab portion that binds CD20 comprises VL CDRs: SEQ ID NO:353 (CDRL1), SEQ ID NO:354 (CDRL2), and SEQ ID NO:355 (CDRL3); and, VH CDRs: SEQ ID NO:356 (CDRH1), SEQ ID NO:357 (CDRH2), and SEQ ID NO:358 (CDRH3); and

wherein the Fab portion that binds CD47 comprises:

(a) a light chain variable region (VL) region comprising VL CDRs SEQ ID NO:359 (CDRL1), SEQ ID NO:360 (CDRL2), and SEQ ID NO:361 (CDRL3); and a heavy chain variable region (VH) region comprising VH CDRs SEQ ID NO:362 (CDRH1), SEQ ID NO:363 (CDRH2), SEQ ID NO:364 (CDRH3);

(b) a light chain variable region (VL) region comprising VL CDRs SEQ ID NO:365 (CDRL1), SEQ ID NO:366 (CDRL2), SEQ ID NO:367 (CDRL3); and a heavy chain variable region (VH) region comprising VH CDRs SEQ ID NO:368 (CDRH1), SEQ ID NO:369 (CDRH2), SEQ ID NO:370 (CDRH3); or

(c) a light chain variable region (VL) region comprising VL CDRs SEQ ID NO:371 (CDRL1), SEQ ID NO:372 (CDRL2), SEQ ID NO:373 (CDRL3); and a heavy chain variable region (VH) region comprising VH CDRs SEQ ID NO:374 (CDRH1), SEQ ID NO:375 (CDRH2), SEQ ID NO:376 (CDRH3);

and, wherein the bispecific antibody selectively binds CD47 in tumor cells and binds less than 5% of CD47 on CD20-/CD47+ cells.

2. The bispecific antibody according to claim 1 that selectively binds B cells.

3. The bispecific antibody according to claim 2 wherein the bispecific antibody comprises an anti-CD47 light chain (LC) constant region comprising SEQ ID NO:340.

4. The bispecific antibody according to claim 3 wherein the bispecific antibody comprises an anti-CD47 heavy chain (HC) constant region comprising SEQ ID NO:342.

5. The bispecific antibody according to claim 2 that selectively binds malignant B cells.

6. The bispecific antibody according to claim 4 that selectively binds malignant B cells.
7. The bispecific antibody according to claim 6 wherein the bispecific antibody comprises an anti-CD20 light chain (LC) constant region comprising SEQ ID NO:344.
8. The bispecific antibody according to claim 7 wherein the bispecific antibody comprises an anti-CD20 heavy chain (HC) constant region comprising SEQ ID NO: 346.
9. The bispecific antibody according to claim 2 wherein the Fab portion that binds CD47 comprises:
 - (i) a light chain variable region (VL) region selected from the group consisting of SEQ ID NO:317, SEQ ID NO:319, and SEQ ID NO:321; and
 - (ii) a heavy chain variable region (VH) region, selected from the group consisting of SEQ ID NO:318, SEQ ID NO:320, and SEQ ID NO:322.
10. The bispecific antibody according to claim 8 wherein the Fab portion that binds CD47 comprises:
 - (i) a light chain variable region (VL) region selected from the group consisting of SEQ ID NO:317, SEQ ID NO:319, and SEQ ID NO:321; and
 - (ii) a heavy chain variable region (VH) region, selected from the group consisting of SEQ ID NO:318, SEQ ID NO:320, and SEQ ID NO:322.
11. The bispecific antibody according to claim 1 comprising a VL region comprising SEQ ID NO:317; and, a VH region comprising SEQ ID NO:318.
12. The bispecific antibody according to claim 1 comprising a VL region comprising SEQ ID NO:319; and, a VH region comprising SEQ ID NO:320.
13. The bispecific antibody according to claim 1 comprising a VL region comprising SEQ ID NO:321; and, a VH region comprising SEQ ID NO:322.
14. The bispecific antibody according to claim 12 comprising an anti-CD47 LC region comprising SEQ ID NO:335 and an anti-CD47 HC region comprising SEQ ID NO:336.

15. The bispecific antibody according to claim 8 comprising an anti-CD20 VL region comprising SEQ ID NO: 323 and a VH region comprising SEQ ID NO: 324.

16. The bispecific antibody according to claim 15 comprising an anti-CD20 LC region comprising SEQ ID NO:331 and an anti-CD20 HC region comprising SEQ ID NO:332.

17. The bispecific antibody according to claim 10 comprising an anti-CD20 VL region comprising SEQ ID NO: 323 and a VH region comprising SEQ ID NO: 324.

18. The bispecific antibody according to claim 17 comprising an anti-CD20 LC region comprising SEQ ID NO:331 and an anti-CD20 HC region comprising SEQ ID NO:332.

19. The bispecific antibody according to claim 18 comprising an anti-CD47 LC region comprising:

(a) SEQ ID NO:333 and an anti-CD47 HC region comprising SEQ ID NO:334;

(b) an anti-CD47 LC region comprising SEQ ID NO:335 and an anti-CD47 HC region comprising SEQ ID NO:336; or

(c) an anti-CD47 LC region comprising SEQ ID NO:337 and an anti-CD47 HC region comprising SEQ ID NO:338.

20. Use of a pharmaceutical composition in the manufacture of a medicament for treating tumors, tumor cells or cancer in a patient wherein the pharmaceutical composition comprises:

i) the bispecific antibody of claim 1; and

ii) at least one pharmaceutically acceptable carrier.

21. The use according to claim 20 wherein the cancer is a hematological malignancy, a B-cell disorder or a B-cell malignancy.