CLAIMS

1. An isolated antibody, or antigen-binding portion thereof, that binds to human 4-1BB, wherein said antibody, or antigen-binding portion comprises:

(a) an H-CDR1 as set forth in SEQ ID NO:29;
(b) an H-CDR2 as set forth in SEQ ID NO:30;
(c) an H-CDR3 as set forth in SEQ ID NO:31;
(d) an L-CDR1 as set forth in SEQ ID NO:34;
(e) an L-CDR2 as set forth in SEQ ID NO:35; and
(f) an L-CDR3 as set forth in SEQ ID NO:36.

2. The antibody, or antigen-binding portion according to claim 1, wherein said antibody, or antigen-binding portion comprises a V_H region amino acid sequence as set forth in SEQ ID NO:43.

3. The antibody, or antigen-binding portion according to claim 1, wherein said antibody, or antigen-binding portion comprises a V_L region amino acid sequence as set forth in SEQ ID NO:45.

4. The antibody, or antigen-binding portion according to claim 1, comprising a V_H region amino acid sequence as set forth in SEQ ID NO:43 and a V_L region amino acid sequence as set forth in SEQ ID NO:45.

5. The antibody, or antigen-binding portion according to any one of claims 1 to 4, wherein the antibody isotype is IgG2.

6. The isolated antibody, or antigen-binding portion according to any one of claims 1 to 5, wherein said antibody comprises a heavy chain amino acid sequence as set forth in SEQ ID NO:44 and further comprises a light chain amino acid sequence set forth in

SEQ ID NO:46, with the proviso that the C-terminal lysine residue of SEQ ID NO:44 is optionally absent.

7. The antibody, or antigen-binding portion according to any one of claims 1 to 4, wherein the antibody isotype is IgG1.

8. The antibody, or antigen-binding portion according to claim 7, wherein said antibody comprises the human IgG1 constant domain amino acid sequence comprising the amino acid sequence set forth in SEQ ID NO: 69, with the proviso that the C-terminal lysine residue of SEQ ID NO:69 is optionally absent.

9. A pharmaceutical composition comprising an antibody or antigen-binding portion thereof according to any one of claims 1 to 8, and a pharmaceutically acceptable carrier.

10. An effective amount of an antibody or antigen-binding portion thereof according to any one of claims 1 to 8, or the pharmaceutical composition according to claim 9 for use in reducing tumor growth in a subject in need thereof.

11. The use of an effective amount of an antibody or antigen-binding portion thereof according to any one of claims 1 to 8, or the pharmaceutical composition according to claim 9 in the manufacture of a medicament for reducing tumor growth a subject in need thereof.

12. A therapeutically effective amount of an antibody or antigen-binding portion thereof according to any one of claims 1 to 8, or the pharmaceutical composition according to claim 9, for use in the treatment of cancer.

13. The use of a therapeutically effective amount of an antibody or antigen-binding portion thereof according to any one of claims 1 to 8, or the pharmaceutical composition

according to claim 9 in the manufacture of a medicament for the treatment of cancer in a subject.

14. The antibody or antigen-binding portion thereof or the pharmaceutical composition according to claim 12or the use according to claim 13, wherein said cancer is selected from the group consisting of colorectal cancer, non-Hodgkin's lymphoma, prostate cancer, and melanoma.

15. The antibody or antigen-binding portion thereof or the pharmaceutical composition according to claim 12 or the use according to claim 13, in combination with an immunotherapeutic agent.

16. The antibody or antigen-binding portion or the pharmaceutical composition, or the use according to claim 15, wherein said immunotherapeutic agent is rituximab.

17. An isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide that comprises one or more amino acid sequences selected from SEQ ID NO: 43, 44, 45 or 46.

18. An isolated nucleic acid comprising one or more nucleotide sequences selected from SEQ ID NO: 47, 48, 49, or 50.

19. A vector comprising an isolated nucleic acid according to claim 17 or claim 18.

20. A host cell comprising a vector according to claim 19.

21. A method of producing an antibody comprising expressing the antibody in the host cell according to claim 20.

22. An isolated antibody or antigen-binding portion thereof , that binds to human 4-1BB, wherein said antibody, or antigen binding portion comprises:

(a) a CDR1 domain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 15, and SEQ ID NO: 29;
(b) a CDR2 domain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 2, SEQ ID NO: 16, and SEQ ID NO: 30; and
(c) a CDR3 domain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 3, SEQ ID NO: 17, and SEQ ID NO: 31;

and a V_L region comprising

(d) a CDR1 domain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 6, SEQ ID NO: 20, and SEQ ID NO: 34;
(e) a CDR2 domain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 7, SEQ ID NO: 21, and SEQ ID NO: 35; and
(f) a CDR3 domain comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 8, SEQ ID NO: 22, SEQ ID NO: 36, and SEQ ID NO: 55.

23. The antibody or antigen-binding portion thereof according to claim 22, comprising a V_H chain amino acid sequence selected from the group consisting of SEQ ID NO: 4, SEQ ID NO: 18, SEQ ID NO: 32, and SEQ ID NO: 43 and a V_L region amino acid sequence selected from the group consisting of SEQ ID NO: 9, SEQ ID NO: 23, SEQ ID NO: 37, SEQ ID NO: 45, SEQ ID NO: 51, SEQ ID NO: 56, SEQ ID NO: 60, and SEQ ID NO: 64.

24. A pharmaceutical composition comprising an antibody or antigen-binding portion thereof according to claim 22 or claim 23, and a pharmaceutically acceptable carrier.

25. An effective amount of an antibody or antigen-binding portion thereof according to claim 22 or claim 23, or the pharmaceutical composition according to claim 24 for use in reducing tumor growth in a subject in need thereof.

26. The use of an effective amount of an antibody or antigen-binding portion thereof according to claim 22 or claim 23, or the pharmaceutical composition according to claim 24, in the manufacture of a medicament for reducing tumor growth in a subject in need thereof.

27. An effective amount of an antibody or antigen-binding portion thereof according to claim 22 or claim 23, or the pharmaceutical composition according to claim 24 for use in reducing tumor cell metastasis in a subject in need thereof.

28. The use of an effective amount of an antibody or antigen-binding portion thereof according to claim 22 or claim 23, or the pharmaceutical composition according to claim 24, in the manufacture of a medicament for reducing tumor cell metastasis in a subject.

29. An effective amount of an antibody or antigen-binding portion thereof according to claim 22 or claim 23, or the pharmaceutical composition according to claim 24 for use in treating cancer in a subject in need thereof.

30. The use of an effective amount of an antibody or antigen-binding portion thereof according to claim 22 or claim 23, or the pharmaceutical composition according to claim 24, in the manufacture of a medicament for treating cancer in a subject in need thereof.

31. The antibody or antigen-binding portion thereof according to claim 29 or use according to claim 30, wherein said cancer is selected from the group consisting of colorectal cancer, non-Hodgkin's lymphoma, prostate cancer, or melanoma.

32. A combination therapy comprising an antibody or antigen-binding portion thereof according to claim 22 or claim 23, and a pharmaceutically acceptable carrier in combination with an immunotherapeutic agent.

33. The combination therapy according to claim 32, wherein said immunotherapeutic agent is rituximab.

34. The use according to claim 30, in combination with an immuno-therapeutic agent.

35. The use according to claim 34, wherein said immunotherapeutic agent is rituximab