In a further embodiment an antibody that specifically binds to DR5 is provided, comprising a variable heavy chain and a variable light chain comprising an amino acid sequence selected from the group of: SEQ ID NO.:7 and SEQ ID NO.:8; SEQ ID NO.:23 and SEQ ID NO.:24; SEQ ID NO.:26 and SEQ ID NO.:24; SEQ ID NO.:23 and SEQ ID NO.:29; SEQ ID NO.:23 and SEQ ID NO.:30; SEQ ID NO.:26 and SEQ ID NO.:31; SEQ ID NO.:26 and SEQ ID NO.:32; SEQ ID NO.:26 and SEQ ID NO.:30; SEQ ID NO.:23 and SEQ ID NO.:31; SEQ ID NO.:82 and SEQ ID NO.:85; SEQ ID NO.:100 and SEQ ID NO.:101; SEQ ID NO.:102 and SEQ ID NO.:103; SEQ ID NO.:106 and SEQ ID NO.:107; SEQ ID NO.:94 and SEQ ID NO.:95;

In a further embodiment an antibody that specifically binds to DR5 is provided comprising a variable heavy chain comprising an amino acid sequence of SEQ ID NO.:7 and a variable light chain comprising an amino acid sequence of SEQ ID NO.:8.

In another aspect, the present application relates to a pharmaceutical composition comprising a bispecific antibody or the antibody that specifically binds to DR5 of the present application.

In another aspect, the present application relates to a bispecific antibody targeting DR5 and FAP or an antibody that specifically binds to DR5 of the present application for the treatment of cancer. In one preferred embodiment said cancer is pancreatic cancer or colorectal carcinoma. In another embodiment, use of the bispecific antibody or an antibody that specifically binds to DR5 as a medicament is provided. Preferably said use is for the treatment of cancer, preferably pancreatic cancer or colorectal carcinoma. In another aspect, the present application relates to use of the bispecific antibody targeting DR5 and FAP or an antibody that specifically binds to DR5 of the present application in the manufacture of a medicament for the treatment of cancer.

The present application also relates to a nucleic acid sequence comprising a sequence encoding a heavy chain of a bispecific antibody or an antibody that specifically binds to DR5 of the present application. In another aspect, the present application relates to isolated polynucleotides encoding a heavy chain and a light chain of an antibody that specifically binds to DR5 of the present application. The present application also relates toa nucleic acid sequence comprising a sequence encoding a light chain of a bispecific antibody or an antibody that specifically binds to DR5 of the present application. In another aspect, the present application relates to an expression vector comprising a nucleic acid sequence of the present application. In another aspect, the present application relates to a prokaryotic or eukaryotic host cell comprising a vector of the present application. In another aspect, the present application relates to a

and wherein the antigen binding site specific for FAP comprises a variable heavy chain comprising an amino acid sequence selected from the group of: SEQ ID NO.:15 and SEQ ID NO.:39 ; and a variable light chain comprising an amino acid sequence selected from the group of SEQ ID NO.:16 and SEQ ID NO.:40.

3. The bispecific antibody of claim 1 or 2, wherein the antigen binding site specific for DR5 comprises

(a) a heavy chain CDR1 of SEQ ID NO.:1;

(b) a heavy chain CDR2 of SEQ ID NO.:2;

(c) a heavy chain CDR3 of SEQ ID NO.:3;

(d) a light chain CDR1 of SEQ ID NO.:4;

(e) a light chain CDR2 of SEQ ID NO.:5;

(f) a light chain CDR3 of SEQ ID NO.:6

and the antigen binding site specific for FAP comprises

(a) a heavy chain CDR1 of SEQ ID NO.:9;

(b) a heavy chain CDR2 of SEQ ID NO.:10;

(c) a heavy chain CDR3 of SEQ ID NO.:11;

(d) a light chain CDR1 of SEQ ID NO.:12;

(e) a light chain CDR2 of SEQ ID NO.:13;

(f) a light chain CDR3 of SEQ ID NO.:14.

4. The bispecific antibody of any of claims 1 to 3, wherein the antigen binding site specific for DR5

comprises a variable heavy chain comprising an amino acid sequence of SEQ ID NO.:7 and a variable light chain comprising an amino acid sequence of SEQ ID NO.:8; and the antigen binding site specific for FAP comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO.:15 and a light chain variable region comprising an amino acid sequence of SEQ ID NO.:16.

5. The bispecific antibody of any of claims 1 to 4, comprising an Fc domain, at least one Fab fragment comprising the antigen binding site specific for DR5, and at least one Fab fragment comprising the antigen binding site specific for FAP.

6. The bispecific antibody of claim 5, wherein at least one of the Fab fragments is connected to the first or second subunit of the Fc domain via the light chain (VLCL) and at least one Fab fragment is connected to the first or second subunit of the Fc domain via the heavy chain (VHCH1).

7. The bispecific antibody of any of claims 1 to 6, comprising an Fc domain, at least one Fab fragment comprising the antigen binding site specific for DR5, and at least one Fab fragment comprising the antigen binding site specific for FAP wherein either the variable regions or the constant regions of the heavy and light chain of at least one Fab fragment are exchanged with each other.

8. The bispecific antibody of claim 7, comprising two Fab fragments comprising each an antigen binding site specific for DR5, and two Fab fragments comprising each an antigen binding site specific for FAP.

9. The bispecific antibody of claim 8, wherein the bispecific antibody is bivalent both for DR5 and FAP.

10. The bispecific antibody of claim 7, comprising two Fab fragments comprising each an antigen binding site specific for DR5, and one Fab fragment comprising an antigen binding site specific for FAP.

11. The bispecific antibody of claim 10, wherein the bispecific antibody is bivalent for DR5 and monovalent for FAP.

12. The bispecific antibody of claim 10, comprising one additional Fab fragment comprising an antigen binding site specific for DR5.

13. The bispecific antibody of claim 12, wherein the bispecific antibody is trivalent for DR5 and monovalent for FAP.

14. The bispecific antibody of claim 7, comprising one Fab fragment comprising an antigen binding site specific for DR5, and one Fab fragment comprising an antigen binding site specific for FAP.

15. The bispecific antibody of claim 14, wherein the bispecific antibody is monovalent for DR5 and monovalent for FAP.

16. The bispecific antibody of any of claims 7 to 15, wherein either the variable regions or the constant regions of the heavy and light chain of the Fab fragment(s) comprising an antigen binding site specific for FAP are exchanged with each other.

17. The bispecific antibody of any of claims 5 to 16, wherein at least one of the Fab fragments are connected to the Fc domain via a peptide linker.

18. The bispecific antibody of any of claims 5 to 17, wherein the Fc domain comprises one or more amino acid substitution that reduces binding to an Fc receptor and/or effector function.

19. The bispecific antibody of claim 18, wherein said one or more amino acid substitution is at one or more position selected from the group of L234, L235, and P329 in the human IgG1 Fc domain.

20. The bispecific antibody of claim 19, wherein each subunit of the Fc domain comprises three amino acid substitutions that reduce binding to an activating or inhibitory Fc receptor and/or effector function wherein said amino acid substitutions are L234A, L235A and P329G in the human IgG1 Fc domain.

21. The bispecific antibody of any of claims 5 to 20, wherein the Fc domain comprises a first heavy chain and a second heavy chain, wherein the first heavy chain comprises a first dimerization module and the second heavy chain comprises a second dimerization module allowing a heterodimerization of the two heavy chains.

22. The bispecific antibody of claim 21, wherein the first dimerization module comprises knobs and the second dimerization module comprises holes according to the knobs into holes strategy.

23. An antibody that specifically binds to DR5, comprising
(a) a heavy chain complementarity determining region 1 (CDR1) of SEQ ID NO.:1;
(b) a heavy chain complementarity determining region 2(CDR2) of SEQ ID NO.:2;
(c) a heavy chain complementarity determining region 3 (CDR3) selected from the group of SEQ ID NO.:3, SEQ ID NO.:96, SEQ ID NO.:98, SEQ ID NO.:104 and SEQ ID NO.:108;
(d) a light chain CDR1 of SEQ ID NO.:4;

(e) a light chain CDR2 of SEQ ID NO.:5; and

(f) a light chain CDR3 selected from the group of SEQ ID NO.:6, SEQ ID NO.:99, SEQ ID NO.:105, SEQ ID NO.:109 and SEQ ID NO.:97.

24. The antibody of claim 23, comprising

(a) a heavy chain CDR1 of SEQ ID NO.:1;

(b) a heavy chain CDR2 of SEQ ID NO.:2;

(c) a heavy chain CDR3 of SEQ ID NO.:3;

(d) a light chain CDR1 of SEQ ID NO.:4;

(e) a light chain CDR2 of SEQ ID NO.:5;

(f) a light chain CDR3 of SEQ ID NO.:6.

25. The antibody of claim 23, comprising a variable heavy chain and a variable light chain comprising an amino acid sequence selected from the group of: SEQ ID NO.:7 and SEQ ID NO.:8; SEQ ID NO.:100 and SEQ ID NO.:101; SEQ ID NO.:102 and SEQ ID NO.:103; SEQ ID NO.:106 and SEQ ID NO.:107; SEQ ID NO.:94 and SEQ ID NO.:95.

26. The antibody of any of claims 23 to 25, comprising a variable heavy chain comprising an amino acid sequence of SEQ ID NO.:7 and a variable light chain comprising an amino acid sequence of SEQ ID NO.:8.

27. A pharmaceutical composition comprising a bispecific antibody of claims 1 to 22 or the antibody of claims 23 to 26.

28. The bispecific antibody of claims 1 to 22 or the antibody of claims 23 to 26 for the treatment of cancer.

29. The bispecific antibody of claims 1 to 22 or the antibody of claims 23 to 26 for use as a medicament.

30. Use of the bispecific antibody of claims 1 to 22 or the antibody of claims 23 to 26 in the manufacture of a medicament for the treatment of cancer.

31. The use of claim 30, wherein the medicament is for treatment of pancreatic cancer or colorectal carcinoma.

32. Isolated polynucleotides encoding a heavy chain and a light chain of an antibody of claims 23 to 26.

33. An expression vector comprising a nucleic acid sequence of claim 32.

34. A prokaryotic or eukaryotic host cell comprising a vector according to claim 33.

35. A method of producing an antibody comprising culturing the host cell of claim 34 so that the antibody is produced.