CLAIMS

1. An isolated antibody which binds to CD74 variants 1 and 2, which comprises:

(a) a V_H region comprising the sequence of SEQ ID NO: 19 and a V_L region comprising the sequence of SEQ ID NO: 26 **[011]**;

(b) a V_H region comprising the sequence of SEQ ID NO: 7 and a V_L region comprising the sequence of SEQ ID NO: 23 **[005]**; or

(c) a V_H region comprising the sequence of SEQ ID NO: 11 and a V_L region comprising the sequence of SEQ ID NO: 26 **[006]**.

2. The antibody of claim 1, which is a human monoclonal antibody.

3. The antibody of any one of the preceding claims, which has an isotype selected from IgG1 and IgG4.

4. An antibody of any one of the preceding claims, which is conjugated to a therapeutic moiety.

5. The antibody of claim 4, which is conjugated to the therapeutic moiety via a linker attached to sulphydryl residues in the antibody, obtained by at least partial reduction of the antibody.

6. The antibody of any one of claims 4 and 5, wherein the therapeutic moiety is a cytotoxic moiety, a radioisotope, a chemotherapeutic agent, a lytic peptide or a cytokine.

7. The antibody of claim 6, which is conjugated to a cytotoxic moiety.

8. The antibody of claim 7, wherein the cytotoxic moiety is selected from the group consisting of taxol; cytochalasin B; gramicidin D; ethidium bromide; emetine; mitomycin; etoposide; tenoposide; vincristine; vinblastine; colchicin; doxorubicin; daunorubicin; dihydroxy anthracin dione; maytansine or an analog or derivative thereof; an auristatin or a functional peptide analog or derivative thereof dolastatin 10 or 15 or an analogue thereof; irinotecan or an analogue thereof; mitoxantrone; mithramycin; actinomycin D; 1–dehydrotestosterone; a glucocorticoid; procaine; tetracaine; lidocaine; propranolol; puromycin; calicheamicin or an analog or derivative thereof; an antimetabolite such as methotrexate, 6 mercaptopurine, 6 thioguanine, cytarabine, fludarabin, 5 fluorouracil, decarbazine, hydroxyurea, asparaginase, gemcitabine, or cladribine; an alkylating agent such as mechlorethamine, thioepa, chlorambucil, melphalan, carmustine (BSNU), lomustine (CCNU), cyclophosphamide, busulfan,

dibromomannitol, streptozotocin, dacarbazine (DTIC), procarbazine, mitomycin C; a platinum derivative such as cisplatin or carboplatin; duocarmycin A, duocarmycin SA, rachelmycin (CC-1065), or an analog or derivative thereof; an antibiotic such as dactinomycin, bleomycin, daunorubicin, doxorubicin, idarubicin, mithramycin, mitomycin, mitoxantrone, plicamycin, anthramycin (AMC)); pyrrolo[2,1-c][1,4]-benzodiazepines (PDB); diphtheria toxin and related molecules such as diphtheria A chain and active fragments thereof and hybrid molecules, ricin toxin such as ricin A or a deglycosylated ricin A chain toxin, cholera toxin, a Shiga-like toxin such as SLT I, SLT II, SLT IIV, LT toxin, C3 toxin, Shiga toxin, pertussis toxin, tetanus toxin, soybean Bowman-Birk protease inhibitor, Pseudomonas exotoxin, alorin, saporin, modeccin, gelanin, abrin A chain, modeccin A chain, alpha-sarcin, Aleurites fordii proteins, dianthin proteins, Phytolacca americana proteins such as PAPI, PAPII, and PAP-S, momordica charantia inhibitor, curcin, crotin, sapaonaria officinalis inhibitor, gelonin, mitogellin, restrictocin, phenomycin, and enomycin toxins; ribonuclease (RNase); DNase I, Staphylococcal enterotoxin A; pokeweed antiviral protein; diphtherin toxin; and Pseudomonas endotoxin.

9. The antibody of claim 7, which is conjugated to a cytotoxic moiety selected from the group consisting of an anthracycline, a pyrrolo[2,1-c][1,4]-benzodiazepine, maytansine, calicheamicin, duocarmycin, rachelmycin (CC-1065), dolastatin 10 or 15, and irinotecan.

10. The antibody of claim 7, wherein the cytotoxic moiety is an auristatin or a functional peptide analog or derivate thereof, optionally conjugated to the antibody via a linker attached to one or more cysteine residues in the antibody.

11. The antibody of claim 6, which is conjugated to a cytokine selected from the group consisting of IL-2, IL-4, IL-6, IL-7, IL-10, IL-12, IL-13, IL-15, IL-18, IL-23, IL-24, IL-27, IL-28a, IL-28b, IL-29, KGF, IFNα, IFNβ, IFNγ, GM-CSF, CD40L, Flt3 ligand, stem cell factor, ancestim, and TNFα.

12. The antibody of any one of the preceding claims, which is a multispecific antibody, comprising a first antigen-binding region of an antibody as defined in any one of the preceding claims, and at least one second antigen-binding region having a different binding specificity.

13. The antibody of claim 12, which is a bispecific antibody, optionally wherein the second antigen-binding region has binding specificity for an antigen on a human effector cell.

14. The antibody of claim 13, wherein the human effector cell is a T cell.

15. The antibody of any one of claims 12 to 14, which is a bispecific antibody wherein

the first antigen-binding region is linked to a first Fc-region having an amino acid substitution at a position selected from the group consisting of 366, 368, 370, 399, 405, 407 and 409, and the second antigen-binding region is linked to a second Fc-region having an amino acid substitution at a position selected from the group consisting of 366, 368, 370, 399, 405, 407 and 409, and

the first and second Fc-regions are not substituted in the same positions.

16. An anti-idiotypic antibody against the antibody of any preceding claim.

17. An expression vector comprising a nucleotide sequence encoding an amino acid sequence of SEQ ID NO: 19 and an amino acid sequence of SEQ ID NO: 26; or an amino acid sequence of SEQ ID NO: 7 and an amino acid sequence of SEQ ID NO: 23; or an amino acid sequence of SEQ ID NO: 11 and an amino acid sequence of SEQ ID NO: 26.

18. An expression vector according to claim 17, further comprising a nucleotide sequence encoding the constant region of a human antibody light chain, of a human antibody heavy chain, or both.

19. A recombinant eukaryotic or prokaryotic host cell which produces the antibody of any one of claims 1 to 3.

20. A pharmaceutical composition comprising the antibody of any one of claims 1 to 15 and a pharmaceutically acceptable carrier.

21. The antibody of any one of claims 1 to 15 for use as a medicament.

22. Use of the antibody of any one of claims 1 to 15 in the manufacture of a medicament for the treatment of cancer.

23. Use of the antibody of any one of claims 1 to 15 in the manufacture of a medicament for cancer prophylaxis.

24. The antibody for the use of claim 23, wherein the cancer prophylaxis comprises one or more of reducing the risk for developing cancer, reducing the risk for cancer progression, and/or reducing the risk of recurrence of a cancer in remission.

25. The antibody for the use of any one of claims 21 to 24, wherein the cancer is selected from the group consisting of breast cancer, colorectal cancer, endometrial/cervical cancer, gastric cancer, head and neck cancer, lung cancer, malignant glioma, malignant melanoma, ovarian cancer, pancreatic cancer, prostate cancer, renal cancer, liver cancer, thymus cancer, malignant fibrous histiosarcoma, acoustic schwannoma, pituitary adenoma, an adenoma, malignant lymphoma, B cell chronic lymphocytic leukemia (B-CLL), chronic myeloid leukemia (CML) in blast phase, non-Hodgkin's lymphoma (NHL), multiple myeloma (MM), monocytiod B cell lymphoma (MBCL), hairy-cell leukemia (HCL), and T cell lymphoma.

26. Use of the antibody of claim 25 in the manufacture of a medicament for the treatment of an autoimmune disease.

27. The antibody for the use of any one of claims 21 to 26 in combination with at least one further therapeutic agent.

28. The antibody for the use of claim 27, wherein at least one further therapeutic agent is selected from a second antibody or ADC; a chemotherapeutic agent; an inhibitor of angiogenesis, neovascularization, and/or other vascularization; an anti-cancer immunogen; a cytokine or chemokine; a cell cycle control or apoptosis regulator; a hormonal regulating agent; an anti-anergic agent; a tumor suppressor gene-containing nucleic acid or vector; an anti-cancer nucleic acid; a virus or viral proteins; immune system cells; a differentiation inducing agent; a CD74 up-regulating agent; and an anti-inflammatory, immunosuppressive and/or immunomodulatory agent; or a combination of any thereof.

29. The antibody for the use of claim 27, wherein at least one therapeutic agent is selected from a CD20-specific antibody, a CD138-specific antibody, a CD38-specific antibody, an anti-VEGF-A antibody, melphalan, lenalidomide, bortezomib, fluorouracil, gemcitabine, irinotecan, or cisplatin.

30. Use of the antibody of any of claims 4 to 14 in the manufacture of a medicament for inducing cell death, inhibiting growth, and/or inhibiting proliferation of a cell expressing CD74.