

Claims

1. An antibody which binds to uPARAP comprising:
 - a. an immunoglobulin light chain variable region comprising or consisting of the amino acid sequence of SEQ ID NO: 3; and
 - b. an immunoglobulin heavy chain variable region comprising or consisting of the amino acid sequence of SEQ ID NO: 6.
2. The antibody according to claim 1, wherein said antibody comprises:
 - a. an immunoglobulin light chain comprising or consisting of the amino acid sequence of SEQ ID NO: 1; and
 - b. an immunoglobulin heavy chain comprising or consisting of the amino acid sequence of SEQ ID NO: 4.
3. An antibody-drug conjugate (ADC) comprising:
 - a. the antibody as defined in any one of the preceding claims,
 - b. an active agent, and
 - c. optionally a linker which links a) to b).
4. The antibody-drug conjugate according to claim 3, wherein the active agent is selected from a therapeutic agent, a radioisotope, and a detectable label.
5. The antibody-drug conjugate according to any one of claims 3 to 4, wherein the active agent is a therapeutic agent, such as a therapeutic agent selected from the group consisting of anti-microtubule/anti-mitotic agents, DNA crosslinking agents, DNA alkylating agents, DNA strand scission agents, anthracyclines, antimetabolites, histone deacetylase inhibitors, kinase inhibitors, metabolism inhibitors, peptide antibiotics, immune checkpoint inhibitors, platinum-based antineoplastics, topoisomerase inhibitors, DNA or RNA polymerase inhibitors, nucleotide based agents, and cytotoxic antibiotics.
6. The antibody-drug conjugate according to any one of claims 3 to 5, wherein the active agent is selected from the group consisting of monomethyl auristatin E (MMAE), monomethyl auristatin F (MMAF), Paclitaxel, Docetaxel, Vinblastine, Vincristine, Vindesine, Vinorelbine, a maytansinoid, Colchicine, Podophyllotoxin, cisplatin, carboplatin, oxaliplatin, mitomycin C (MMC), pyrrolobenzodiazepine, dimeric

- pyrrolobenzodiazepine derivatives, SGD-1882, nitrogen mustards, tris(2-chloroethyl)amine, pyridinobenzodiazepines, indolinobenzodiazepine dimers, Duocarmycin SA, calicheamicin, hamiltroline, Daunorubicin, doxorubicin, epirubicin, idarubicin, PNU-159682, methotrexate, 6-mercaptopurine, 6-thioguanine, fludarabine phosphate, pentostatin, cladribine, 5-fluorouracil, 5-fluorodeoxyuridine, cytarabine, gemcitabine, trichostatin A, vorinostat, belinostat, panabioestat, givinostat, resminostat, abexinostat, quisinostat, rocilinostat, practinostat, CHR-3996, valproic acid, butyric acid, phenylbutyric acid, entinostat, tacedinaline, 4SC202, mocetinostat, romidepsin, nicotinamide, sirtinol, cambinol, EX-527, genistein, lavendustin C, PP1-AG1872, PP2-AG1879, SU6656, CGP77675, PD166285, imatinib, erlotinib, gefitinib, lavendustin A, cetuximab, UCS15A, herbimycin A, radicicol, APO866, GMX-1777, GMX-1778 ATG-019, and OT-82, Pembrolizumab, Nivolumab, Cemiplimab, JTX-4014, Spartalizumab, Camrelizumab, Sintilimab, Tislelizumab, Toripalimab, Dostarlimab, AMP-224, AMP-514; Atezolizumab, Avelumab, Durvalumab, KN035, CK-301, AUNP12, CA-170, BMS-986189, lipoplatin, nedaplatin, picoplatin, phenanthriplatin, satraplatin, triplatin tetranitrate, camptothecin, topotecan, belotecan, lurtotecan, irinotecan, SN-38, exatecan, Dxd, amanitin, alpha-amanitin, actinomycin D, aphidicolin, and derivatives thereof.
7. The antibody-drug conjugate according to any one of claims 3 to 6, wherein the active agent is a derivative of exatecan.
8. The antibody-drug conjugate according to any one of claims 3 to 7, wherein the active agent comprises a radioisotope selected from ^{60}Co , ^{89}Sr , ^{90}Y , $^{99\text{m}}\text{Tc}$, ^{131}I , ^{137}Cs , ^{153}Sm , and ^{223}Rn .
9. The antibody-drug conjugate according to any one of claims 3 to 8, wherein the drug-to-antibody ratio (DAR) is between 1 and 10, such as between 2 and 8, for example between 2 and 6, such as 2 or 4.
10. The antibody-drug conjugate according to any one of claims 3 to 9, wherein the antibody-drug conjugate comprises a linker selected from a cleavable and a non-cleavable linker, optionally wherein the linker is a peptide linker, such as wherein the linker comprises or consists of a dipeptide, such as valine-citrulline (VC) or valine-alanine (VA).

11. The antibody-drug conjugate according to any one of claims 3 to 10, wherein the antibody-drug conjugate further comprises a spacer, such as a spacer comprising p-aminobenzoic acid (PAB), p-aminobenzylcarbamate (PABC), p-aminobenzoyloxycabonyl, or polyethylenglycol (PEG).
12. The antibody-drug conjugate according to any one of claims 3 to 11, wherein the antibody-drug conjugate further comprises an attachment group, such as an attachment group comprising or consisting of maleimide and caproic acid (MC), N-hydroxysuccinimide, reactive attachment groups directed to modified or unmodified protein-bound carbohydrate, peptide sequences that are required for enzymatic reactions, azides or alkynes or being derived from these by reaction with the antibody or a chemically or enzymatically generated derivative thereof.
13. A polypeptide comprising or consisting of the amino acid sequence of SEQ ID NO: 2, further comprising the amino acid sequence of SEQ ID NO: 5.
14. An isolated polynucleotide which encodes the amino acid sequence of any one of SEQ ID NOs: 1, 2, or 3, wherein the polynucleotide further encodes the amino acid sequence of any one of SEQ ID NOs: 4, 5 or 6, such as wherein the polynucleotide comprises SEQ ID NO: 11 and SEQ ID NO: 12.
15. A vector comprising the polynucleotide as defined in claim 14.
16. A host cell comprising the polynucleotide as defined in claim 14 and/or the vector as defined in claim 15.
17. The antibody according to any one of claims 1 to 2 or the antibody-drug conjugate according to any one of claims 3 to 12 for use as a medicament.
18. A pharmaceutical composition comprising the antibody according to any one of claims 1 to 2 or the antibody-drug conjugate according to any one of claims 3 to 12 and a pharmaceutically acceptable buffer, diluent, carrier, adjuvant or excipient.

19. Use of the antibody according to any one of claims 1 to 2, the antibody-drug conjugate according to any one of claims 3 to 12 or the pharmaceutical composition according to claim 18 for the manufacture of a medicament for the treatment of a disease characterised by cells expressing uPARAP, such as wherein the disease
5 characterised by cells expressing uPARAP is selected from cancer, a bone degradation disease such as osteoporosis, fibrosis, and macrophage associated diseases or disorders such as atherosclerosis, arthritis or chronic inflammation.
20. The use according to claim 19, wherein the disease is arthritis and said arthritis is
10 selected from osteoarthritis, inflammatory arthritis, rheumatoid arthritis, psoriatic arthritis, lupus, Lyme disease-induced arthritis such as Lyme arthritis, gout or pseudogout, and ankylosing spondylitis.
21. The use according to claim 19, wherein the disease is cancer, such as wherein the
15 cancer is selected from sarcoma, glioblastoma, mesothelioma, colon cancer, prostate cancer, bone metastases from prostate cancer, breast cancer, head- and neck cancer and leukaemia.
22. The use according to claim 21, wherein the cancer is a solid tumour.
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23. The use according to claim 21, wherein cancer is leukaemia, such as acute lymphoblastic leukaemia (ALL), acute myeloid leukaemia (AML), chronic lymphocytic leukaemia (CLL), and chronic myeloid leukaemia (CML).
24. The use according to claim 21, wherein the cancer is glioblastoma.
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25. The use according to claim 21, wherein the cancer is sarcoma, such as osteosarcoma, or soft tissue sarcoma (STS).
26. The use according to claim 25, wherein the sarcoma is soft tissue sarcoma (STS)
30 selected from epithelioid sarcoma, clear cell sarcoma, alveolar soft part sarcoma, extraskeletal myxoid chondrosarcoma, epithelioid hemangioendothelioma, inflammatory myofibroblastic tumor, undifferentiated embryonal sarcoma, alveolar soft part sarcoma (ASPS), angiosarcoma, chondrosarcoma, dermatofibrosarcoma
35 protuberans (DFSP), desmoid sarcoma, Ewing's sarcoma, fibrosarcoma,

myxofibrosarcome, gastrointestinal stromal tumor (GIST), non-uterine leiomyosarcoma, uterine leiomyosarcoma, liposarcoma, malignant fibro histiocytoma (MFH), malignant peripheral nerve sheath tumor (MPNST), rhabdomyosarcoma, synovial sarcoma, and/or leiomyosarcoma (LMS).

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27. The use according to any one of claims 21 to 26, wherein the cancer is metastatic cancer.

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28. The use according to any one of claims 19 to 27, wherein administration is parenteral, for example, intravenously, intracerebroventricularly, intraarticularly, intra-arterially, intraperitoneally, intrathecally, intraventricularly, intrasternally, intracranially, intramuscularly or subcutaneously, or by infusion techniques.

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29. The use according to any one of claims 19 to 28, wherein the antibody, antibody-drug conjugate or pharmaceutical composition is administered in combination with one or more further agents, such as one or more further therapeutic agents.

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30. The use according to any one of claims 19 to 29, wherein the cells expressing uPARAP display uPARAP overexpression, optionally wherein the cells expressing uPARAP are tumour cells and/or tumour associated cells.

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31. The use according to any one of claims 19 to 30, wherein the antibody, antibody-drug conjugate or composition induces cell death and/or inhibits the growth and/or proliferation of the uPARAP expressing cells.

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32. A kit comprising the antibody according to any one of claims 1 to 2, the antibody-drug conjugate according to any one of claims 3 to 12, or the pharmaceutical composition according to claim 18, optionally further comprising means for administering the antibody or antibody-drug conjugate to a subject and/or instructions for use.