CLAIMS

1. Use of an anti-GREM1 antagonist in the manufacture of a medicament for treating or preventing a cancer.

2. Use according to claim 1, wherein:

(a) the cancer is a solid cancer;

(b) the cancer has stromal GREM1 overexpression;

(c) the cancer is selected from colorectal cancer, multiple myeloma, pancreatic cancer, bladder cancer, breast cancer, lung cancer, stomach cancer, duodenal cancer, oesophageal cancer, head and neck cancer, prostate cancer, glioma, endometrial cancer, liver cancer, spleen cancer, bone-resident cancer, and osteosarcoma; optionally wherein:

(i) the cancer is colorectal cancer; further optionally wherein the colorectal cancer is a mesenchymal subtype colorectal cancer;

(ii) the cancer is multiple myeloma;

(iii) the cancer is breast cancer;

(d) the cancer has epithelial GREM1 overexpression; optionally wherein the cancer is a GREM1-initiated cancer;

(e) the cancer is a disseminated cancer; and/or

(f) the cancer is an established cancer, optionally wherein the established cancer is an established colorectal cancer.

3. Use according to any one of the preceding claims, wherein the antagonist is a peptide, a protein, an antibody, a polynucleotide, an oligonucleotide, an antisense RNA, a small interfering RNA (siRNA), a small molecule inhibitor or a small hairpin RNA (shRNA).

4. Use according to claim 3, wherein:

(a) the antagonist is an antibody which binds to an epitope on Gremlin-1 comprising at least one residue selected from Ile131, Lys147, Lys148, Phe149, Thr150, Thr151, Arg169, Lys174 and Gln175, wherein the residue numbering is according to SEQ ID NO: 1; optionally wherein:

(i) the antibody binds an epitope comprising all of Ile131, Lys147, Lys148, Phe149, Thr150, Thr151, Arg169, Lys174 and Gln175; and/or

(ii) Lys147, Lys148, Phe149, Thr150, Thr151, Arg169, Lys174 and Gln175 are located on the same Gremlin-1 monomer and Ile131 is located on the second Gremlin-1 monomer;

(b) the antagonist is an anti-Gremlin-1 antibody which comprises heavy chain complementarity determining region (HCDR) sequences contained within a heavy chain variable region (HCVR) of SEQ ID NO: 10 or 12 and/or light chain complementarity determining region (LCDR) sequences contained within a light chain variable region (LCVR) of SEQ ID NO: 11 or 13; or

(c) the antagonist is an anti-Gremlin-1 antibody which comprises at least one HCDR sequence selected from SEQ ID NOs: 3, 4, 5 and 6 and/or at least one LCDR sequence selected from SEQ ID NOs: 7, 8 and 9; optionally wherein:

(i) the anti-Gremlin-1 antibody comprises a HCDR3 sequence of SEQ ID NO: 6;

(ii) the anti-Gremlin-1 antibody comprises an HCDR1/HCDR2/HCDR3 sequence combination selected from SEQ ID NOs: 4/5/6 or from SEQ ID NOs:3/5/6 and/or an LCDR1/LCDR2/LCDR3 sequence combination selected from SEQ ID NOs: 7/8/9;

(iii) the anti-Gremlin-1 antibody comprises a HCDR1/HCDR2/HCDR3/LCDR1/LCDR2/LCDR3 sequence combination of SEQ ID NOs: 4/5/6/7/8/9 or SEQ ID NOs: 3/5/6/7/8/9; and/or

(iv) the anti-Gremlin-1 antibody comprises a heavy chain variable region (HCVR) sequence of SEQ ID NO: 10 or 12 and/or a light chain variable region (LCVR) sequence of SEQ ID NO: 11 or 13, or sequences which are at least 95% identical thereto.

5. Use according to claim 4(c)(iv), wherein:

(a) the anti-Gremlin-1 antibody comprises a HCVR and LCVR sequence pair of SEQ ID NOs: 10/11 or 12/13 or sequences which are at least 95% identical thereto; optionally wherein the anti-Gremlin-1 antibody comprises HCDR1/HCDR2/HCDR3/LCDR1/LCDR2/LCDR3 sequences consisting of SEQ ID

NOs: 4/5/6/7/8/9 or SEQ ID NOs: 3/5/6/7/8/9 and the remainder of the HCVR and LCVR comprise at least 95% identity to SEQ ID NOs: 10, 11, 12 and/or 13 respectively; and/or

(b) the anti-Gremlin-1 antibody comprises a heavy chain of SEQ ID NO: 14, 16, 18, 22, 28, 30, 32 or 34 and/or a light chain of SEQ ID NO: 15, 17, 19, 23, 29, 31, 33 or 35, or sequences which are at least 95% identical thereto.

6. Use according to claim 5(b), wherein the anti-Gremlin-1 antibody comprises a heavy and light chain pair of SEQ ID NOs: 14/15, 16/17, 18/19, 22/23, 28/29 or 30/31, 32/33, 34/35, or sequences which are at least 95% identical thereto; optionally wherein the HCDR1/HCDR2/HCDR3/LCDR1/LCDR2/LCDR3 sequences of the antibody consist of SEQ ID NOs: 4/5/6/7/8/9 or SEQ ID NOs: 3/5/6/7/8/9 and the remainder of the heavy and light chains comprise at least 95% identity to SEQ ID NOs: 14, 15, 16 and/or 17 respectively.

7. Use according to claim 3, wherein:

(a) the antagonist is an antibody which competes for binding to Gremlin-1 with an antibody as defined in any one of claims 4-6-; or

(b) the antagonist is an antibody which binds the same epitope on Gremlin-1 as an antibody defined in any one of claims 4-6.

8. Use according to any one of claims 3-7, wherein:

(a) the antagonist antibody is a chimeric, human or humanised antibody; and/or

(b) the antagonist antibody is a Fab, modified Fab, Fab', modified Fab', $F(ab')_2$, Fv, single domain antibody or an scFv.

9. Use according to claim 3, wherein the antagonist is a polynucleotide encoding an antibody as defined in any one of claims 4-8, or an expression vector carrying said polynucleotide.

10. Use according to any one of claims 3-8, wherein the antagonist antibody is comprised in pharmaceutical composition further comprising a pharmaceutically acceptable adjuvant and/or carrier.

11. Use according to any one of the preceding claims, wherein:

(a) the medicament is to be administered with an additional anti-cancer agent separately, sequentially or simultaneously; optionally wherein said additional anti-cancer agent is a chemotherapeutic agent; and/or
(b) the medicament is to be administered separately, sequentially or simultaneously with radiotherapy.

12. Use of an anti-cancer agent in the manufacture of a medicament for treating a cancer wherein the medicament is to be administered separately, sequentially or simultaneously with an anti-GREM1 antagonist.

13. Use according to claim 12, wherein:
(a) said anti-cancer agent is a chemotherapeutic agent; and/or
(b) said cancer, said antagonist and/or said treatment are as defined in any one of claims 1-11(a).

14. A composition or kit comprising an anti-GREM1 antagonist and an additional anti-cancer agent.

15. A composition or kit according to claim 14, wherein:
(a) the anti-GREM1 antagonist is as defined in any one of claims 3-9; and/or
(b) the additional anti-cancer agent is a chemotherapeutic agent.

16. The composition or kit of claim 14 or claim 15, wherein:
(a) said anti-cancer or chemotherapeutic agent is suitable for treatment of colorectal cancer, optionally selected from 5-fluoruracil, oxaliplatin, irinotecan, folinic acid, cetuximab, nivolumab or bevacizumab; or
(b) said anticancer or chemotherapeutic agent is suitable for treatment of multiple myeloma, optionally selected from an anti-CD38 antibody (such as daratumumab), an anti-SLAMF7 antibody (such as elotuzumab), an anti-IL-6 antibody (such as

siltuximab), or bortezumib or iMID (lenalidomide/pomalenomide) or an analogue of either thereof.

17. A method for detecting cancer in a patient, the method comprising measuring stromal expression of GREM1 in a sample obtained from the patient, wherein stromal overexpression of GREM1 indicates that the patient comprises a cancer.

18. A method for prognosing a cancer in a patient, the method comprising determining whether or not a cancer biopsy obtained from the patient comprises stromal overexpression of GREM1, wherein stromal overexpression of GREM1 in the cancer biopsy indicates that the patient has a worse prognosis than in the situation of normal stromal expression of GREM1.

19. A method for determining whether or not a patient having or suspected of having or being at risk of developing cancer is likely to respond to treatment with a chemotherapeutic agent, which method comprises measuring stromal expression of GREM1 in a sample obtained from the patient, and thereby predicting whether or not the patient is likely to respond to treatment with the chemotherapeutic agent.

20. A method for determining whether or not a patient having or suspected of having or being at risk of developing cancer is likely to respond to treatment with a GREM1 antagonist, the method comprising measuring stromal expression of GREM1 in a sample obtained from the patient, and thereby predicting whether or not the patient is likely to respond to treatment with the GREM1 antagonist.