CLAIMS

1. A protein comprising an antigen binding site of an antibody, in which:

(i) (a) the protein competitively inhibits binding of C1.2G (comprising a V_H comprising a sequence set forth in SEQ ID NO: 4 and a V_L comprising a sequence set forth in SEQ ID NO: 5) or C1.2 (comprising a heavy chain variable region (V_H) comprising a sequence set forth in SEQ ID NO: 2 and a light chain variable region (V_L) comprising a sequence set forth in SEQ ID NO: 3) to human granulocyte-colony stimulating factor receptor (hG-CSFR); (b) the protein neutralizes granulocyte colony stimulating factor (G-CSF) signaling; and (c) the level of binding of the protein to a polypeptide of SEQ ID NO: 1 in which an alanine is substituted for any one of:

(a) the arginine at position 287 of SEQ ID NO:1;

(b) the histidine at position 237 of SEQ ID NO:1;

(c) the methionine at position 198 of SEQ ID NO:1;

(d) the tyrosine at position 172 of SEQ ID NO:1;

(e) the leucine at position 171 of SEQ ID NO:1; or

(f) the leucine at position 111 of SEQ ID NO:1

is lower than the level of binding of the protein to a polypeptide of SEQ ID NO: 1; and/or

(ii) (a) the protein binds to human granulocyte colony stimulating factor receptor (hG-CSFR); (b) the protein neutralizes granulocyte colony stimulating factor (G-CSF) signaling; and (c) the level of binding of the protein to a polypeptide of SEQ ID NO: 1 in which an alanine is substituted for any one of:

(a) the arginine at position 287 of SEQ ID NO:1;

(b) the histidine at position 237 of SEQ ID NO:1;

(c) the methionine at position 198 of SEQ ID NO:1;

(d) the tyrosine at position 172 of SEQ ID NO:1;

(e) the leucine at position 171 of SEQ ID NO:1; or

(f) the leucine at position 111 of SEQ ID NO:1

is lower than the level of binding of the protein to a polypeptide of SEQ ID NO: 1; and/or

(iii) the protein competitively inhibits the binding of C1.2 (comprising a V_H comprising a sequence set forth in SEQ ID NO: 2 and a V_L comprising a sequence set forth in SEQ ID NO: 3) or C1.2G (comprising a V_H comprising a sequence set forth in SEQ ID NO: 4 and a V_L comprising a sequence set forth in SEQ ID NO: 5) to one or more of (a) a polypeptide of SEQ ID NO: 1 in which an alanine is substituted for the lysine at a position 167 of SEQ ID NO: 1; and/or a polypeptide of SEQ ID NO: 1 in which an alanine is substituted for the histidine at position 168 of SEQ ID NO: 1; and/or

(iv) the antigen binding site binds to human granulocyte-colony stimulating factor receptor (hG-CSFR) and neutralizes granulocyte-colony stimulating factor (G-CSF) signaling, and in which the protein inhibits growth of colony forming units – granulocytes (CFU-G) from $CD34^+$ bone marrow cells grown in the presence of G-CSF with an IC_{50} of at least about 0.2nM; and/or

(v) the antigen binding site binds to both human and cynomolgus monkey granulocyte-colony stimulating factor receptor (G-CSFR) with a similar affinity and neutralizes granulocyte-colony stimulating factor (G-CSF) signaling; and/or

(vi) the antigen binding site binds specifically to the same epitope in human granulocyte-colony stimulating factor receptor (hG-CSFR) as that bound by C1.2 (comprising a heavy chain variable region (V_H) comprising a sequence set forth in SEQ ID NO: 2 and a light chain variable region (V_L) comprising a sequence set forth in SEQ ID NO: 3) or C1.2G (comprising a V_H comprising a sequence set forth in SEQ ID NO: 4 and a V_L comprising a sequence set forth in SEQ ID NO: 5).

2. A protein according to Claim 1 (i), in which the antigen binding site does not detectably bind to the polypeptide comprising the alanine substitution position 287 of SEQ ID NO: 1.

3. A protein according to Claim 1 (i) or (ii), in which the polypeptide to which the protein binds at a reduced level additionally comprises one or more of the following:

(i) an alanine at a position 111 of SEQ ID NO: 1;

(ii) an alanine at a position 171 of SEQ ID NO: 1;

(iii) an alanine at a position 172 of SEQ ID NO: 1; and

(iv) an alanine at a position 198 of SEQ ID NO: 1.

4. A protein according to any of Claims 1 to 3, in which the antigen binding site cross-reacts with:

(i) a polypeptide of SEQ ID NO: 1 in which an alanine is substituted for the lysine at position 167 of SEQ ID NO: 1; and/or

(ii) a polypeptide of SEQ ID NO: 1 in which an alanine is substituted for the histidine at position 168 of SEQ ID NO: 1.

5. A protein according to any of Claims 1 to 4, which competitively inhibits the binding of C1.2 (comprising a heavy chain variable region (V_H) comprising a sequence set forth in SEQ ID NO: 2 and a light chain variable region (V_L) comprising a sequence set forth in SEQ ID NO: 3) or C1.2G (comprising a V_H comprising a sequence set forth in SEQ ID NO: 4 and a V_L comprising a sequence set forth in SEQ ID NO: 5) to one or more of:

(i) a polypeptide of SEQ ID NO: 1 in which an alanine is substituted for the lysine at position 167 of SEQ ID NO: 1; and/or

(ii) a polypeptide of SEQ ID NO: 1 in which an alanine is substituted for the histidine at position 168 of SEQ ID NO: 1.

6. A protein that binds to human granulocyte-colony stimulating factor receptor (hG-CSFR) and neutralizes granulocyte-colony stimulating factor (G-CSF) signaling, the protein comprising at least one of:

(i) a V_H comprising a complementarity determining region (CDR) 1 comprising a sequence set forth in SEQ ID NO: 6, a CDR2 comprising a sequence set forth in SEQ ID NO: 7 and a CDR3 comprising a sequence at least about 55% identity to the sequence set forth in SEQ ID NO: 8;

(ii) a V_H comprising a sequence at least about 80% identical to a sequence set forth in SEQ ID NO: 2 and/or 4;

(iii) a V_L comprising a CDR1 comprising a sequence set forth in SEQ ID NO: 9, a CDR2 comprising a sequence set forth in SEQ ID NO: 10 and a CDR3 comprising a sequence at least about 33% identity to the sequence set forth in SEQ ID NO: 11; and

(iv) a V_L comprising a sequence at least about 80% identical to a sequence set forth in SEQ ID NO: 3 and/or 5.

7. A protein according to Claim 6 comprising at least one variable region of an antibody selected from the group consisting of:

(i) a heavy chain variable region (V_H) comprising an amino acid sequence set forth in SEQ ID NO: 4;

(ii) a light chain variable region (V_L) comprising an amino acid sequence set forth in SEQ ID NO: 5;

(iii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 2;

(iv) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 3;

(v) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 14;

(vi) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 15;

(vii) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 16;

(viii) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 17;

(ix) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 18;

(x) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 19;

(xi) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 20;

(xii) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 21;

(xiii) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 22;

(xiv) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 23;

(xv) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 24;

(xvi) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 25;

(xvii) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 26;

(xviii) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 27;

(xix) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 28;

(xx) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 29;

(xxi) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 30;

(xxii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 31;

(xxiii) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 32;

(xxiv) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 33;

(xxv) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 34;

(xxvi) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 35;

(xxvii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 36;

(xxviii) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 37;

(xxix) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 38;

(xxx) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 39;

(xxxi) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 40;

(xxxii) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 41;

(xxxiii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 42;

(xxxiv) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 43;

(xxxv) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 44;

(xxxvi) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 45;

(xxxvii) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 46;

(xxxviii) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 47;

(xxix) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 48;

(xl) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 49;

(xli) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 50;

(xlii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 51;

(xliii) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 52;

(xliv) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 53;

(xlv) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 54;

(xlvi) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 55;

(xlvii) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 56;

(xlviii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 57;

(xlix) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 58;

(l) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 59;

(li) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 60;

(lii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 61;

(liii) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 62; and

(liv) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 63.

8. A protein according to any of Claims 1 to 7 comprising at least a heavy chain variable region (V_H) and a light chain variable region (V_L), in which the V_H and V_L bind to form a Fv comprising an antigen binding domain, for example, in which

(i) the V_H and the V_L are in a single polypeptide chain, for example, the protein is:

(a) a single chain Fv fragment (scFv);

(b) a dimeric scFv (di-scFv); or

(c) at least one of (i) and/or (ii) linked to a constant region of an antibody, a Fc or a heavy chain constant domain (C_H) 2 and/or C_H3; or

(ii) the V_L and V_H are in separate polypeptide chains, for example, the protein is:

(a) a diabody;

(b) a triabody;

(c) a tetrabody;

(d) a Fab;

(e) a F(ab')$_2$;

(f) a Fv;

(g) one of (i) to (vi) linked to a constant region of an antibody, a Fc or a heavy chain constant domain (C_H) 2 and/or C_H3; or

(h) an antibody.

9. A protein according to any of Claims 1 to 8 which is chimeric, de-immunized, humanized, human or primatized.

10. An antibody according to Claim 8 that binds to human granulocyte-colony stimulating factor receptor (hG-CSFR) and neutralizes granulocyte-colony stimulating factor (G-CSF) signaling, the antibody comprising:

(i) a heavy chain variable region (V_H) comprising an amino acid sequence set forth in SEQ ID NO: 4 and a light chain variable region (V_L) comprising an amino acid sequence set forth in SEQ ID NO: 5;

(ii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 2 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 3;

(iii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 15 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 14;

(iv) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 4 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 16;

(v) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 4 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 17;

(vi) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 4 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 18;

(vii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 20 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 19;

(viii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 4 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 21;

(ix) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 4 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 22;

(x) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 24 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 23;

(ix) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 4 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 25;

(x) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 4 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 26;

(xi) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 28 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 27;

(xii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 4 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 29;

(xiii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 31 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 30;

(xiv) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 33 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 32;

(xv) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 4 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 34;

(xvi) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 36 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 35;

(xvii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 38 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 37;

(xviii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 40 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 39;

(xix) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 42 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 41;

(xx) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 4 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 43;

(xxi) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 45 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 44;

(xxii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 4 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 46;

(xxiii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 4 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 47;

(xxiv) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 49 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 48;

(xxv) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 51 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 50;

(xxvi) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 53 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 52;

(xxvii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 4 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 54;

(xxviii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 55 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 5;

(xxix) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 57 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 56;

(xxx) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 59 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 58;

(xxxi) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 61 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 60;

(xxxii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 4 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 62;

(xxxiii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 4 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 63; and

(xxxix) a V_H comprising three CDRs of a V_H set forth in any one or more of (i) to (xxxiii) and a V_L comprising three CDRs of a V_L set forth in any one or more of (i) to (xxxiii).

11. An antibody according to Claim 8 that binds to human granulocyte-colony stimulating factor receptor (hG-CSFR) and neutralizes granulocyte-colony stimulating factor (G-CSF) signaling, the antibody comprising:

(i) a heavy chain variable region (V_H) comprising an amino acid sequence set forth in SEQ ID NO: 4 and a light chain variable region (V_L) comprising an amino acid sequence set forth in SEQ ID NO: 5; or

(ii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 2 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 3.

12. An antibody comprising:

(i) a heavy chain comprising an amino acid sequence set forth in SEQ ID NO: 64 or 68 and a light chain comprising an amino acid sequence set forth in SEQ ID NO: 65; or

(ii) one heavy chain comprising an amino acid sequence set forth in SEQ ID NO: 64 and one heavy chain comprising an amino acid sequence set forth in SEQ ID NO: 68 and two light chains comprising an amino acid sequence set forth in SEQ ID NO: 65.

13. A composition comprising a protein or antibody according to any of Claims 1 to 12 and a pharmaceutically acceptable carrier or comprising:

(i) an antibody comprising a heavy chain comprising an amino acid sequence set forth in SEQ ID NO: 64 and a light chain comprising an amino acid sequence set forth in SEQ ID NO: 65; and

(ii) (a) an antibody comprising a heavy chain comprising an amino acid sequence set forth in SEQ ID NO: 64 and a light chain comprising an amino acid sequence set forth in SEQ ID NO: 65 and/or (b) an antibody comprising one heavy chain comprising an amino acid sequence set forth in SEQ ID NO: 64 and one heavy chain comprising an amino acid sequence set forth in SEQ ID NO: 68 and two light chains comprising an amino acid sequence set forth in SEQ ID NO: 65,

and, optionally, a pharmaceutically acceptable carrier.

14. Use of a protein or antibody according to any of Claims 1 to 12 or a composition according to Claim 13 in the manufacture of a medicament for treating or preventing a granulocyte-colony stimulating factor (G-CSF)-mediated condition in a subject.

15. Use according to Claim 14, in which the G-CSF-mediated condition is an autoimmune disease, an inflammatory disease or cancer.

16. Use according to Claim, in which the autoimmune disease or the inflammatory disease is arthritis, multiple sclerosis, pulmonary inflammation or chronic obstructive pulmonary disease.

17. Use according to any of Claims 14 to 16, comprising an amount of the protein or antibody sufficient to reduce the number of neutrophils in a subject without inducing neutropenia.

18. Use according to Claim 17, in which the amount of the protein is between about 0.05mg/kg and 30mg/kg.

CLAIMS

1. A protein comprising an antigen binding site of an antibody, in which the antigen binding site binds to human granulocyte-colony stimulating factor receptor (hG-CSFR) and neutralizes granulocyte-colony stimulating factor (G-CSF) signaling, and in which the protein inhibits growth of colony forming units – granulocytes (CFU-G) from $CD34^+$ bone marrow cells grown in the presence of G-CSF with an IC_{50} of at least about 0.2nM.

2. A protein comprising an antigen binding site of an antibody, in which the antigen binding site binds to both human and cynomolgus monkey granulocyte-colony stimulating factor receptor (G-CSFR) with a similar affinity and neutralizes granulocyte-colony stimulating factor (G-CSF) signaling.

3. A protein comprising an antigen binding site of an antibody in which the antigen binding site binds specifically to the same epitope in human granulocyte-colony stimulating factor receptor (hG-CSFR) as that bound by C1.2 (comprising a heavy chain variable region (V_H) comprising a sequence set forth in SEQ ID NO: 2 and a light chain variable region (V_L) comprising a sequence set forth in SEQ ID NO: 3) or C1.2G (comprising a V_H comprising a sequence set forth in SEQ ID NO: 4 and a V_L comprising a sequence set forth in SEQ ID NO: 5).

4. A protein comprising an antigen binding site of an antibody, in which (i) the protein competitively inhibits binding of C1.2 (comprising a heavy chain variable region (V_H) comprising a sequence set forth in SEQ ID NO: 2 and a light chain variable region (V_L) comprising a sequence set forth in SEQ ID NO: 3) or C1.2G (comprising a V_H comprising a sequence set forth in SEQ ID NO: 4 and a V_L comprising a sequence set forth in SEQ ID NO: 5) to human granulocyte-colony stimulating factor receptor (hG-CSFR); (ii) the protein neutralizes granulocyte colony stimulating factor (G-CSF) signaling; and (iii) the level of binding of the protein to a polypeptide of SEQ ID NO: 1 in which an alanine is substituted for any one of:

the arginine at position 287 of SEQ ID NO:1;

the histidine at position 237 of SEQ ID NO:1;

the methionine at position 198 of SEQ ID NO:1;

the tyrosine at position 172 of SEQ ID NO:1;

the leucine at position 171 of SEQ ID NO:1; or

the leucine at position 111 of SEQ ID NO:1:

is lower than the level of binding of the protein to a polypeptide of SEQ ID NO: 1.

5. A protein according to Claim 4, in which the antigen binding site does not detectably bind to the polypeptide comprising the alanine substitution position 287 of SEQ ID NO: 1.

6. A protein comprising an antigen binding site of an antibody, in which (i) the protein binds to human granulocyte colony stimulating factor receptor (hG-CSFR); (ii) the protein neutralizes granulocyte colony stimulating factor (G-CSF) signaling; and (iii) the level of binding of the protein to a polypeptide of SEQ ID NO: 1 in which an alanine is substituted for any one of:

the arginine at position 287 of SEQ ID NO:1;

the histidine at position 237 of SEQ ID NO:1;

the methionine at position 198 of SEQ ID NO:1;

the tyrosine at position 172 of SEQ ID NO:1;

the leucine at position 171 of SEQ ID NO:1; or

the leucine at position 111 of SEQ ID NO:1:

is lower than the level of binding of the protein to a polypeptide of SEQ ID NO: 1.

7. A protein according to any of Claims 4 to 6, in which the polypeptide to which the protein binds at a reduced level additionally comprises one or more of the following:

(i) an alanine at a position 111 of SEQ ID NO: 1;

(ii) an alanine at a position 171 of SEQ ID NO: 1;

(iii) an alanine at a position 172 of SEQ ID NO: 1; and

(iv) an alanine at a position 198 of SEQ ID NO: 1.

8. A protein according to any preceding claim, in which the antigen binding site cross-reacts with:

(i) a polypeptide of SEQ ID NO: 1 in which an alanine is substituted for the lysine at position 167 of SEQ ID NO: 1; and/or

(ii) a polypeptide of SEQ ID NO: 1 in which an alanine is substituted for the histidine at position 168 of SEQ ID NO: 1.

9. A protein according to any preceding claim, which competitively inhibits the binding of C1.2 (comprising a heavy chain variable region (V_H) comprising a sequence set forth in SEQ ID NO: 2 and a light chain variable region (V_L) comprising a sequence set forth in SEQ ID NO: 3) or C1.2G (comprising a V_H comprising a sequence set forth in SEQ ID NO: 4 and a V_L comprising a sequence set forth in SEQ ID NO: 5) to one or more of:

(i) a polypeptide of SEQ ID NO: 1 in which an alanine is substituted for the lysine at position 167 of SEQ ID NO: 1; and/or

(ii) a polypeptide of SEQ ID NO: 1 in which an alanine is substituted for the histidine at position 168 of SEQ ID NO: 1.

10. A protein that binds to human granulocyte-colony stimulating factor receptor (hG-CSFR) and neutralizes granulocyte-colony stimulating factor (G-CSF) signaling, the protein comprising at least one of:

(i) a V_H comprising a complementarity determining region (CDR) 1 comprising a sequence set forth in SEQ ID NO: 6, a CDR2 comprising a sequence set forth in SEQ ID NO: 7 and a CDR3 comprising a sequence at least about 55% identical to the sequence set forth in SEQ ID NO: 8;

(ii) a V_H comprising a sequence at least about 80% identical to a sequence set forth in SEQ ID NO: 2 and/or 4;

(iii) a V_L comprising a CDR1 comprising a sequence set forth in SEQ ID NO: 9, a CDR2 comprising a sequence set forth in SEQ ID NO: 10 and a CDR3 comprising a sequence at least about 33% identical to the sequence set forth in SEQ ID NO: 11; and

(iv) a V_L comprising a sequence at least about 80% identical to a sequence set forth in SEQ ID NO: 3 and/or 5.

11. A protein according to Claim 10, in which the V_H comprises a CDR3 comprising a sequence $LGELGX_1X_2X_3X_4$ (SEQ ID NO: 12), in which:

X_1 is an amino acid selected from the group consisting of tryptophan, glutamine, methionine, serine, phenylalanine, glutamic acid and histidine;

X_2 is an amino acid selected from the group consisting of phenylalanine, tyrosine, methionine, serine, glycine and isoleucine;

X_3 is an amino acid selected from the group consisting of aspartic acid, methionine, glutamine, serine, leucine, valine, arginine and histidine; and

X_4 is an amino acid selected from the group consisting of proline, glutamic acid, alanine, leucine, phenylalanine, tyrosine, threonine, asparagine, aspartic acid, serine, glycine, arginine, and lysine,

or in which:

X_1 is a neutral amino acid;

X_2 is phenylalanine, tyrosine, methionine or serine;

X_3 is aspartic acid, methionine, glutamine, serine or leucine; and

X_4 is proline, glutamic acid, alanine, leucine, phenylalanine or tyrosine.

12. A protein according to Claim 10, in which the V_L comprises a CDR3 comprising a sequence $X_1X_2X_3X_4X_5X_6X_7X_8X_9$ (SEQ ID NO: 13), in which:

X_1 is an amino acid selected from the group consisting of glutamine, glutamic acid, histidine, alanine and serine;

X_2 is an amino acid selected from the group consisting of glutamine, valine, phenylalanine, asparagine and glutamic acid;

X_3 is an amino acid selected from the group consisting of serine and glycine;

X_4 is an amino acid selected from the group consisting of tryptophan, methionine, phenylalanine, tyrosine, isoleucine and leucine;

X_5 is an amino acid selected from the group consisting of glutamic acid, methionine, glutamine, tryptophan, serine, valine, asparagine, glycine, alanine, arganine, histidine, tyrosine, lysine and threonine;

X_6 is an amino acid selected from the group consisting of tyrosine, methionine, isoleucine and threonine;

X_7 is an amino acid selected from the group consisting of proline, alanine, histidine, glycine and lysine;

X_8 is an amino acid selected from the group consisting of leucine, glutamine, methionine, alanine, phenylalanine, isoleucine, lysine, histidine and glycine;

X_9 is an amino acid selected from the group consisting of threonine, phenylalanine, tyrosine, methionine, lysine, serine, histidine, proline, tryptophan, isoleucine, glutamine, glycine and valine,

or in which:

X_1 is as glutamine or glutamic acid;

X_2 is glutamine;

X_3 is an amino acid selected from the group consisting of serine and glycine;

X_4 is an amino acid selected from the group consisting of tryptophan, methionine, phenylalanine and tyrosine;

X_5 is an amino acid selected from the group consisting of glutamic acid, methionine, glutamine, tryptophan, serine, valine, asparagine, glycine and alanine;

X_6 is an amino acid selected from the group consisting of tyrosine, threonine and methionine;

X_7 is an amino acid selected from the group consisting of proline, alanine, histidine and glycine;

X_8 is an amino acid selected from the group consisting of leucine, glutamine, methionine, alanine, phenylalanine and isoleucine;

X_9 is an amino acid selected from the group consisting of threonine, phenylalanine, tyrosine, methionine, lysine, serine, histidine and phenylalanine.

13. A protein that binds to human granulocyte-colony stimulating factor receptor (hG-CSFR) and neutralizes granulocyte-colony stimulating factor (G-CSF) signaling, the protein comprising at least one variable region of an antibody selected from the group consisting of:

(i) a heavy chain variable region (V_H) comprising an amino acid sequence set forth in SEQ ID NO: 2;

(ii) a light chain variable region (V_L) comprising an amino acid sequence set forth in SEQ ID NO: 3;

(iii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 4;

(iv) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 5;

(v) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 14;

(vi) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 15;

(vii) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 16;

(viii) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 17;

(ix) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 18;

(x) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 19;

(xi) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 20;

(xii) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 21;

(xiii) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 22;

(xiv) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 23;

(xv) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 24;

(xvi) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 25;

(xvii) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 26;

(xviii) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 27;

(xix) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 28;

(xx) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 29;

(xxi) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 30;

(xxii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 31;

(xxiii) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 32;

(xxiv) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 33;

(xxv) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 34;

(xxvi) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 35;

(xxvii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 36;

(xxviii) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 37;

(xxix) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 38;

(xxx) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 39;

(xxxi) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 40;

(xxxii) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 41;

(xxxiii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 42;

(xxxiv) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 43;

(xxxv) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 44;

(xxxvi) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 45;

(xxxvii) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 46;

(xxxviii) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 47;

(xxxix) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 48;

(xl) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 49;

(xli) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 50;

(xlii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 51;

(xliii) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 52;

(xliv) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 53;

(xlv) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 54;

(xlvi) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 55;

(xlvii) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 56;

(xlviii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 57;

(xlix) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 58;

(l) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 59;

(li) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 60;

(lii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 61;

(liii) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 62; and

(liv) a V_L comprising an amino acid sequence set forth in SEQ ID NO: 63.

14. A protein according to any preceding claim comprising at least a heavy chain variable region (V_H) and a light chain variable region (V_L), in which the V_H and V_L bind to form a Fv comprising an antigen binding domain, and in which the V_H and the V_L are in a single polypeptide chain or in which the V_L and V_H are in separate polypeptide chains.

15. A protein according to Claim 14, in which if the V_H and the V_L are in a single polypeptide chain the protein is:

(i) a single chain Fv fragment (scFv);

(ii) a dimeric scFv (di-scFv); or

(iii) at least one of (i) and/or (ii) linked to a constant region of an antibody, a Fc or a heavy chain constant domain (C_H) 2 and/or C_H3, or

if the V_L and V_H are in separate polypeptide chains, the protein is:

(i) a diabody;

(ii) a triabody;

(iii) a tetrabody;

(iv) a Fab;

(v) a $F(ab')_2$;

(vi) a Fv;

(vii) one of (i) to (vi) linked to a constant region of an antibody, a Fc or a heavy chain constant domain (C_H) 2 and/or C_H3; or

(viii) an antibody.

16. A protein according to any preceding claim which is chimeric, de-immunized, humanized, human or primatized.

17. An antibody to that binds to human granulocyte-colony stimulating factor receptor (hG-CSFR) and neutralizes granulocyte-colony stimulating factor (G-CSF) signaling, the antibody comprising:

(i) a heavy chain variable region (V_H) comprising an amino acid sequence set forth in SEQ ID NO: 2 and a light chain variable region (V_L) comprising an amino acid sequence set forth in SEQ ID NO: 3;

(ii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 4 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 5;

(iii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 15 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 14;

(iv) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 4 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 16;

(v) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 4 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 17;

(vi) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 4 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 18;

(vii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 20 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 19;

(viii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 4 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 21;

(ix) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 4 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 22;

(x) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 24 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 23;

(ix) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 4 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 25;

(x) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 4 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 26;

(xi) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 28 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 27;

(xii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 4 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 29;

(xiii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 31 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 30;

(xiv) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 33 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 32;

(xv) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 4 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 34;

(xvi) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 36 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 35;

(xvii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 38 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 37;

(xviii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 40 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 39;

(xix) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 42 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 41;

(xx) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 4 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 43;

(xxi) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 45 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 44;

(xxii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 4 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 46;

(xxiii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 4 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 47;

(xxiv) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 49 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 48;

(xxv) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 51 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 50;

(xxvi) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 53 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 52;

(xxvii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 4 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 54;

(xxviii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 55 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 5;

(xxix) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 57 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 56;

(xxx) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 59 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 58;

(xxxi) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 61 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 60;

(xxxii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 4 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 62;

(xxxiii) a V_H comprising an amino acid sequence set forth in SEQ ID NO: 4 and a V_L comprising an amino acid sequence set forth in SEQ ID NO: 63; or

(xxxiv) a V_H comprising three CDRs of a V_H set forth in any one or more of (i) to (xxxiii) and a V_L comprising three CDRs of a V_L set forth in any one or more of (i) to (xxxiii).

18. An antibody to that binds to human granulocyte-colony stimulating factor receptor (hG-CSFR) and neutralizes granulocyte-colony stimulating factor (G-CSF) signaling, the antibody comprising a heavy chain variable region (V_H) comprising an amino acid sequence set forth in SEQ ID NO: 2 and a light chain variable region (V_L) comprising an amino acid sequence set forth in SEQ ID NO: 3.

19. An antibody to that binds to human granulocyte-colony stimulating factor receptor (hG-CSFR) and neutralizes granulocyte-colony stimulating factor (G-CSF) signaling, the antibody comprising a heavy chain variable region (V_H) comprising an amino acid sequence set forth in SEQ ID NO: 4 and a light chain variable region (V_L) comprising an amino acid sequence set forth in SEQ ID NO: 5.

20. An antibody comprising:

(i) a heavy chain comprising an amino acid sequence set forth in SEQ ID NO: 64 or 68 and a light chain comprising an amino acid sequence set forth in SEQ ID NO: 65; or

(ii) one heavy chain comprising an amino acid sequence set forth in SEQ ID NO: 64 and one heavy chain comprising an amino acid sequence set forth in SEQ ID NO: 68 and two light chains comprising an amino acid sequence set forth in SEQ ID NO: 65.

21. The protein or antibody according to any preceding claim, which:

(i) inhibits G-CSF-induced proliferation of a BaF3 cell expressing hG-CSFR with an IC_{50} of at least about 0.5nM;

(ii) binds to a polypeptide comprising amino acids 1 to 311 of SEQ ID NO: 1 expressed as a fusion with an antibody Fc region with an affinity of at least about 0.5nM, in which affinity is determined in an assay in which the polypeptide immobilized and the protein or antibody contacted to the immobilized polypeptide; and/or

(iii) binds to hG-CSFR expressed on the surface of a cell at an affinity of at least about 1nM.

22. A protein or antibody according to any preceding claim conjugated to another compound.

23. A nucleic acid encoding a protein or antibody according to any preceding claim.

24. An isolated genetically-modified cell comprising a nucleic acid according to Claim 23.

25. An isolated protein or antibody encoded by a nucleic acid according to Claim 23 or expressed by a cell according to Claim 24.

26. A composition comprising a protein or antibody according to any of Claims 1 to 22 and 25 and a pharmaceutically acceptable carrier or comprising:

(i) an antibody comprising a heavy chain comprising an amino acid sequence set forth in SEQ ID NO: 64 and a light chain comprising an amino acid sequence set forth in SEQ ID NO: 65; and

(ii) (a) an antibody comprising a heavy chain comprising an amino acid sequence set forth in SEQ ID NO: 64 and a light chain comprising an amino acid sequence set forth in SEQ ID NO: 65 and/or

(b) an antibody comprising one heavy chain comprising an amino acid sequence set forth in SEQ ID NO: 64 and one heavy chain comprising an amino acid sequence set

forth in SEQ ID NO: 68 and two light chains comprising an amino acid sequence set forth in SEQ ID NO: 65,

and, optionally, a pharmaceutically acceptable carrier.