CLAIMS

1. An anti-C-KIT antibody or an antigen-binding portion thereof, wherein the antibody comprises a heavy chain variable (VH) region and a light chain variable (VL) region, wherein

(a) the VH region amino acid sequence comprises HCDR1 of GYTFTDYYMN (SEQ ID NO: 13), HCDR2 of MGRIYPGSGNTYYAQKFQG (SEQ ID NO: 14) and HCDR3 of GVYYYDY (SEQ ID NO: 15); and the VL region amino acid sequence comprises LCDR1 of RASQGIRTNLA (SEQ ID NO: 16), LCDR2 of AASSLQS (SEQ ID NO: 24) and LCDR3 of QQYNSYPRT (SEQ ID NO: 12);

(b) the VH region amino acid sequence comprises HCDR1 of GYTFTDYYMN (SEQ ID NO: 13), HCDR2 of MGRIYPGSGNTYYAQKFQG (SEQ ID NO: 14) and HCDR3 of GVYYYDY (SEQ ID NO: 15); and the VL region amino acid sequence comprises LCDR1 of RASQGIRTNLA (SEQ ID NO: 16), LCDR2 of AASSLQS (SEQ ID NO: 24) and LCDR3 of QQYANYPRT (SEQ ID NO: 25);

(c) the VH region amino acid sequence comprises HCDR1 of GYTFTDYYMN (SEQ ID NO: 13), HCDR2 of MGRIYPGSGNTYYAQKFQG (SEQ ID NO: 14) and HCDR3 of GVYYYDY (SEQ ID NO: 15); and the VL region amino acid sequence comprises LCDR1 of RASQGIRTNLA (SEQ ID NO: 16), LCDR2 of SASSLQS (SEQ ID NO: 17) and LCDR3 of QQYANYPRT (SEQ ID NO: 25);

(d) the VH region amino acid sequence comprises HCDR1 of GYTFTDYYMN (SEQ ID NO: 13), HCDR2 of MGRIYPGSGNTYYAQKFQG (SEQ ID NO: 14) and HCDR3 of GVYYYDY (SEQ ID NO: 15); and the VL region amino acid sequence comprises LCDR1 of RASQGIRTNLA (SEQ ID NO: 16), LCDR2 of SASSLQS (SEQ ID NO: 17) and LCDR3 of QQYNSYPRT (SEQ ID NO: 12);

(e) the VH region amino acid sequence comprises HCDR1 of GYTFTDYYMN (SEQ ID NO: 13), HCDR2 of MGRIYPGSGNTYYAQKFQG (SEQ ID NO: 14) and HCDR3 of GVYYLDY (SEQ ID NO: 18); and the VL region amino acid sequence comprises LCDR1 of RASQGIRTNVA (SEQ ID NO: 19), LCDR2 of SASYRQS (SEQ ID NO: 20) and LCDR3 of QQYNSYPRT (SEQ ID NO: 12);

(f) the VH region amino acid sequence comprises HCDR1 of GYTFTDYYMN (SEQ ID NO: 13), HCDR2 of MGRIYPGSGNTYYAQKFQG (SEQ ID NO: 14) and HCDR3 of GVYYFDE (SEQ ID NO: 21); and the VL region amino acid sequence comprises LCDR1 of RASQGVRTNLA (SEQ ID NO: 22), LCDR2 of AASSRQS (SEQ ID NO: 23) and LCDR3 of QQYNSYPRT (SEQ ID NO: 12); or

(g) the VH region amino acid sequence comprises HCDR1 of GYTFTDFYMN (SEQ ID NO: 180), HCDR2 of MGRIYPASGNTYYAQKFQG (SEQ ID NO: 26) and HCDR3 of GVWYYDY (SEQ ID NO: 27); and the VL region amino acid sequence comprises LCDR1 of RASQGIRTNLA

(SEQ ID NO: 16), LCDR2 of AASSLQS (SEQ ID NO: 24) and LCDR3 of QQYANYPRT (SEQ ID NO: 25).

2. The antibody or antigen-binding portion of claim 1, wherein

(a) the VH region amino acid sequence comprises SEQ ID NO:185 and the VL region amino acid sequence comprises SEQ ID NO:186;

(b) the VH region amino acid sequence comprises SEQ ID NO:187 and the VL region amino acid sequence comprises SEQ ID NO:188;

(c) the VH region amino acid sequence comprises SEQ ID NO:189 and the VL region amino acid sequence comprises SEQ ID NO:190;

(d) the VH region amino acid sequence comprises SEQ ID NO:191 and the VL region amino acid sequence comprises SEQ ID NO:192;

(e) the VH region amino acid sequence comprises SEQ ID NO:193 and the VL region amino acid sequence comprises SEQ ID NO:194; or

(f) the VH region amino acid sequence comprises SEQ ID NO:195 and the VL region amino acid sequence comprises SEQ ID NO:196.

3. The antibody or antigen-binding portion of claim 1 or 2, wherein the antibody is humanized or chimeric.

4. The antibody or antigen-binding portion of any one of claims 1-3, wherein the VH region, the VL region, or both the VH and the VL region comprise one or more human framework region amino acid sequences.

5. The antibody or antigen-binding portion of any one of claims 1-4, wherein the VH region, the VL region, or both the VH and the VL region comprise a human variable region framework scaffold amino acid sequence into which the CDRs have been inserted.

6. The antibody or antigen-binding portion of claim 1, wherein the VH region comprises an IGHV1-46 human germline scaffold amino acid sequence into which the HCDR1, HCDR2 and HCDR3 amino acid sequences have been inserted.

7. The antibody or antigen-binding portion of claim 1 or 6, wherein the VL region comprises an IGKV1-16 human germline scaffold amino acid sequence into which the LCDR1, LCDR2 and LCDR3 amino acid sequences have been inserted.

8. The antibody or antigen-binding portion of any one of claims 1-7, wherein the antibody comprises an immunoglobulin constant region.

9. The antibody or antigen-binding portion of claim 8, wherein the immunoglobulin constant region is IgG, IgE, IgM, IgD, IgA or IgY.

10. The antibody or antigen-binding portion of claim 9, wherein the immunoglobulin constant region is IgG1, IgG2, IgG3, IgG4, IgA1 or IgA2.

11. The antibody or antigen-binding portion of claim 8, wherein the immunoglobulin constant region is immunologically inert.

12. The antibody or antigen-binding portion of claim 8, wherein the immunoglobulin constant region is a wild-type human IgG1 constant region, a human IgG1 constant region comprising the amino acid substitutions L234A, L235A and G237A or a human IgG1 constant region comprising the amino acid substitutions L234A, L235A, G237A and P331S, wherein numbering is according to the EU index as in Kabat.

13. The antibody or antigen-binding portion of claim 8, wherein the immunoglobulin constant region comprises SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201 or SEQ ID NO:202.

14. The antigen-binding portion of any one of claims 1-13, wherein the antibody or antigen-binding portion is an Fab, an Fab', an $F(ab')_2$, an Fv, an scFv, a maxibody, a minibody, a diabody, a triabody, a tetrabody, or a bis-scFv.

15. The antibody or antigen-binding portion of any one of claims 1-14, wherein the antibody is monoclonal.

16. The antibody or antigen-binding portion of any one of claims 1-15, wherein the antibody is a tetrameric antibody, a tetravalent antibody or a multispecific antibody.

17. The antibody or antigen-binding portion of any one of claims 1-16, wherein the antibody is a bispecific antibody that binds specifically to a first antigen and a second antigen, wherein the first antigen is C-KIT and the second antigen is not C-KIT.

18. The antibody or antigen-binding portion of any one of claims 1-17, wherein the antibody or antigen-binding portion binds specifically to (a) human C-KIT or (b) human C-KIT and cynomolgus C-KIT.

19. An immunoconjugate comprising the antibody or antigen-binding portion of any one of claims 1-18 linked to a therapeutic agent.

20. The immunoconjugate of claim 19, wherein the therapeutic agent is a cytotoxin, a radioisotope, a chemotherapeutic agent, an immunomodulatory agent, a cytostatic enzyme, a cytolytic enzyme, a therapeutic nucleic acid, an anti-angiogenic agent, an anti-proliferative agent, or a pro-apoptotic agent.

21. A pharmaceutical composition comprising the antibody or antigen-binding portion of any one of claims 1-18 or the immunoconjugate of claim 19 or 20, and a pharmaceutically acceptable carrier, diluent or excipient.

22. An isolated nucleic acid molecule encoding
(a) the VH region amino acid sequence;
(b) the VL region amino acid sequence; or
(c) both the VH and the VL region amino acid sequences
of the antibody or antigen-binding portion of any one of claims 1-18.

23. An expression vector comprising the nucleic acid molecule of claim 22.

24. A recombinant host cell comprising the nucleic acid molecule of claim 22 or the expression vector of claim 23.

25. A method of producing an anti-C-KIT antibody or an antigen-binding portion thereof, the method comprising:
culturing a recombinant host cell comprising the expression vector of claim 23 under conditions whereby the nucleic acid molecule is expressed, thereby producing the antibody or antigen-binding portion; and
isolating the antibody or antigen-binding portion from the host cell or culture.

26. Use of the antibody or antigen-binding portion of any one of claims 1-18, the immunoconjugate of claim 19 or 20 or the pharmaceutical composition of claim 21 in the

manufacture of a medicament for enhancing an immune response in a subject, wherein the medicament is to be administered to the subject at a therapeutically effective amount.

27. Use of the antibody or antigen-binding portion of any one of claims 1-18, the immunoconjugate of claim 19 or 20 or the pharmaceutical composition of claim 21 in the manufacture of a medicament for treating cancer, an autoimmune disease, an inflammatory disease, a cardiovascular disease or a fibrotic disease in a subject, wherein the medicament is to be administered to the subject at a therapeutically effective amount.

28. The use of claim 27, wherein the cancer is Gastrointestinal Stromal cancer (GIST), pancreatic cancer, melanoma, breast cancer, lung cancer, bronchial cancer, colorectal cancer, prostate cancer, stomach cancer, ovarian cancer, urinary bladder cancer, brain or central nervous system cancer, peripheral nervous system cancer, esophageal cancer, cervical cancer, uterine or endometrial cancer, cancer of the oral cavity or pharynx, liver cancer, kidney cancer, testicular cancer, biliary tract cancer, small bowel or appendix cancer, salivary gland cancer, thyroid gland cancer, adrenal gland cancer, osteosarcoma, chondrosarcoma or cancer of hematological tissues.

29. The use of claim 27, wherein the autoimmune disease or the inflammatory disease is arthritis, asthma, multiple sclerosis, psoriasis, Crohn's disease, inflammatory bowel disease, lupus, Grave's disease, Hashimoto’s thyroiditis or ankylosing spondylitis.

30. The use of claim 27, wherein the cardiovascular disease is coronary heart disease or atherosclerosis.

31. The method use of claim 27, wherein the fibrotic disease is myocardial infarction, angina, osteoarthritis, pulmonary fibrosis, cystic fibrosis, bronchitis or asthma.

32. The antibody or antigen-binding portion of any one of claims 1-18, the immunoconjugate of claim 19 or 20 or the pharmaceutical composition of claim 21, for use as a medicament.

33. The antibody or antigen-binding portion of any one of claims 1-18, the immunoconjugate of claim 19 or 20 or the pharmaceutical composition of claim 21 for use in the treatment of cancer, an autoimmune disease, an inflammatory disease, a cardiovascular disease or a fibrotic disease.

34. The antibody or antigen-binding portion, the immunoconjugate or the pharmaceutical composition for use according to claim 33, wherein the cancer is Gastrointestinal Stromal cancer (GIST), pancreatic cancer, melanoma, breast cancer, lung cancer, bronchial cancer, colorectal cancer, prostate cancer, stomach cancer, ovarian cancer, urinary bladder cancer, brain or central nervous system cancer, peripheral nervous system cancer, esophageal cancer, cervical cancer, uterine or endometrial cancer, cancer of the oral cavity or pharynx, liver cancer, kidney cancer, testicular cancer, biliary tract cancer, small bowel or appendix cancer, salivary gland cancer, thyroid gland cancer, adrenal gland cancer, osteosarcoma, chondrosarcoma or cancer of hematological tissues.

35. The antibody or antigen-binding portion, the immunoconjugate or the pharmaceutical composition for use according to claim 33, wherein the autoimmune disease or the inflammatory disease is arthritis, asthma, multiple sclerosis, psoriasis, Crohn's disease, inflammatory bowel disease, lupus, Grave's disease, Hashimoto’s thyroiditis or ankylosing spondylitis.

36. The antibody or antigen-binding portion, the immunoconjugate or the pharmaceutical composition for use according to claim 33, wherein the cardiovascular disease is coronary heart disease or atherosclerosis.

37. The antibody or antigen-binding portion, the immunoconjugate or the pharmaceutical composition for use according to claim 33, wherein the fibrotic disease is myocardial infarction, angina, osteoarthritis, pulmonary fibrosis, cystic fibrosis, bronchitis or asthma.