## CLAIMS

**What is claimed is:**

1. An antibody drug conjugate of the formula

$$Ab\text{-}(L\text{-}(D)_m)_n$$

or a pharmaceutically acceptable salt thereof; wherein
Ab is an antibody or antigen binding fragment thereof that specifically binds to an epitope of human cKIT;
L is a linker;
D is a drug moiety;
m is an integer from 1 to 8; and
n is an integer from 1 to 10.

2. The antibody drug conjugate of claim 1, wherein said n is 3 or 4.

3. The antibody drug conjugate of claim 1 or 2, wherein said antibody or antigen binding fragment thereof specifically binds the extracellular domain of cKIT (SEQ ID NO.160).

4. The antibody drug conjugate of claim 1 or 2, wherein said antibody or antigen binding fragment specifically binds to an epitope of human cKIT at domains 1-3 (SEQ ID NO.155).

5. The antibody drug conjugate of claim 1 or 2, wherein said antibody or antigen binding fragment thereof specifically binds human cKIT at SEQ ID NO. 161 and SEQ ID NO. 162.

6. The antibody drug conjugate of any of claims 1-3, wherein said antibody or antigen binding fragment thereof comprises:

(i) a heavy chain variable region that comprises (a) a HCDR1 (CDR-Complementarity Determining Region) of SEQ ID NO: 76, (b) a HCDR2 of SEQ ID NO: 77, (c) a HCDR3 of SEQ ID NO: 78; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 85, (e) a LCDR2 of SEQ ID NO: 86, and (f) a LCDR3 of SEQ ID NO: 87;

(ii) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 22, (b) a HCDR2 of SEQ ID NO: 23, (c) a HCDR3 of SEQ ID NO: 24; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 31, (e) a LCDR2 of SEQ ID NO: 32, and (f) a LCDR3 of SEQ ID NO: 33;

(iii) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 130, (b) a HCDR2 of SEQ ID NO: 131, (c) a HCDR3 of SEQ ID NO: 132; and a light chain variable region that comprises:

(d) a LCDR1 of SEQ ID NO: 139, (e) a LCDR2 of SEQ ID NO: 140, and (f) a LCDR3 of SEQ ID NO: 141;

(iv) a heavy chain variable region that comprises: (a) a HCDR1 of SEQ ID NO: 58, (b) a HCDR2 of SEQ ID NO: 59, (c) a HCDR3 of SEQ ID NO: 60; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 67, (e) a LCDR2 of SEQ ID NO: 68, and (f) a LCDR3 of SEQ ID NO: 69;

(v) a heavy chain variable region that comprises: (a) a HCDR1 of SEQ ID NO: 40, (b) a HCDR2 of SEQ ID NO: 41, (c) a HCDR3 of SEQ ID NO: 42; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 49, (e) a LCDR2 of SEQ ID NO: 50, and (f) a LCDR3 of SEQ ID NO: 51;

(vi) a heavy chain variable region that comprises: (a) a HCDR1 of SEQ ID NO: 94, (b) a HCDR2 of SEQ ID NO: 95, (c) a HCDR3 of SEQ ID NO: 96; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 103, (d) a LCDR2 of SEQ ID NO: 104, and (f) a LCDR3 of SEQ ID NO: 105;

(vii) a heavy chain variable region that comprises: (a) a HCDR1 of SEQ ID NO: 112, (b) a HCDR2 of SEQ ID NO: 113, (c) a HCDR3 of SEQ ID NO: 114; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 121, (e) a LCDR2 of SEQ ID NO: 122, and (f) a LCDR3 of SEQ ID NO: 123; or

(viii) a heavy chain variable region that comprises: (a) a HCDR1 of SEQ ID NO: 3, (b) a HCDR2 of SEQ ID NO: 4, (c) a HCDR3 of SEQ ID NO: 5; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 12, (e) a LCDR2 of SEQ ID NO: 13, and (f) a LCDR3 of SEQ ID NO: 14.

7. The antibody drug conjugate of any of the preceding claims in which at least one amino acid within a CDR is substituted by a corresponding residue of a corresponding CDR of another anti-cKIT antibody in Table 1.

8. The antibody drug conjugate of any of the preceding claims in which one or two amino acids within a CDR have been modified, deleted or substituted.

9. The antibody drug conjugate of any of the preceding claims that retains at least 90, 91, 92, 93, 94, 95, 96, 97, 98 or 99% identity over either the variable light or variable heavy region.

10. The antibody drug conjugate of any of the preceding claims wherein the antibody is a monoclonal antibody, a chimeric antibody, a humanized antibody, a human engineered antibody, a human antibody, a single chain antibody(scFv) or an antibody fragment.

11. The antibody drug conjugate of any one of claims 1-10, wherein said linker (L) is selected from the group consisting of a cleavable linker, a non-cleavable linker, a hydrophilic linker, a procharged linker and a dicarboxylic acid based linker.

12. The antibody drug conjugate of claim 11, wherein the linker is derived from a cross-linking reagent selected from the group consisting of N-succinimidyl-3-(2-pyridyldithio)propionate (SPDP), N-succinimidyl 4-(2-pyridyldithio)pentanoate (SPP), N-succinimidyl 4-(2-pyridyldithio)butanoate (SPDB), N-succinimidyl-4-(2-pyridyldithio)2-sulfo-butanoate (sulfo-SPDB), N-succinimidyl iodoacetate (SIA), N-succinimidyl(4-iodoacetyl)aminobenzoate (SIAB), maleimide PEG NHS, N-succinimidyl 4-(maleimidomethyl) cyclohexanecarboxylate (SMCC), N- sulfosuccinimidyl 4-(maleimidomethyl) cyclohexanecarboxylate (sulfo-SMCC) or 2,5-dioxopyrrolidin-1-yl 17-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)-5,8,11,14-tetraoxo-4,7,10,13-tetraazaheptadecan-1-oate (CX1-1).

13. The antibody drug conjugate of claim 12, wherein said linker is derived from the cross-linking reagent N-succinimidyl 4-(maleimidomethyl) cyclohexanecarboxylate (SMCC).

14. The antibody drug conjugate of any one of claims 1-13, wherein said drug moiety (D) is selected from a group consisting of a V-ATPase inhibitor, a pro-apoptotic agent, a Bcl2 inhibitor, an MCL1 inhibitor, a HSP90 inhibitor, an IAP inhibitor, an mTor inhibitor, a microtubule stabilizer, a microtubule destabilizer, an auristatin, a dolastatin, a maytansinoid, a MetAP (methionine aminopeptidase), an inhibitor of nuclear export of proteins CRM1, a DPPIV inhibitor, proteasome inhibitors, inhibitors of phosphoryl transfer reactions in mitochondria, a protein synthesis inhibitor, a kinase inhibitor, a CDK2 inhibitor, a CDK9 inhibitor, a kinesin inhibitor, an HDAC inhibitor, a DNA damaging agent, a DNA alkylating agent, a DNA intercalator, a DNA minor groove binder and a DHFR inhibitor.

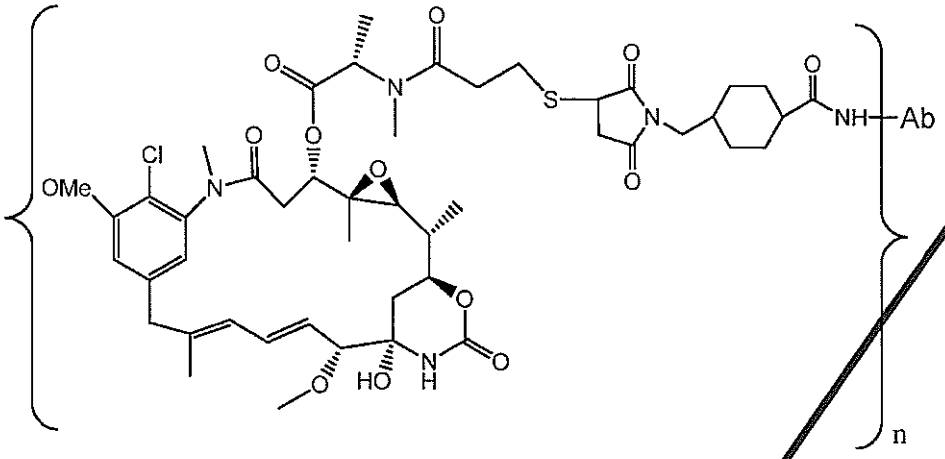
15. The antibody drug conjugate of claim 14, wherein the drug moiety is a maytansinoid.

16. The antibody drug conjugate of claim 15, wherein the maytansinoid is N(2')- deacetyl-N(2')-(3-mercapto-1-oxopropyl)-maytansine (DM1) or N(2')-deacetyl-N2-(4- mercapto-4-methyl- 1 -oxopentyl)-maytansine (DM4).

17. The antibody drug conjugate of any of the preceding claims in combination with another therapeutic agent.

18. The antibody drug conjugate of any of the preceding claims in combination with a therapeutic agent listed in Table 16.

19. An antibody drug conjugate of the formula




or a pharmaceutically acceptable salt thereof; wherein;
Ab is an antibody or antigen binding fragment thereof that specifically binds to human cKIT, and at least n number of primary amines; and n is an integer from 1 to 10.

20. The antibody drug conjugate of claim 19, wherein said antibody or antigen binding fragment specifically binds to an epitope of human cKIT at domains 1-3 (SEQ ID NO.155).

21. The antibody drug conjugate of claim 19, wherein said antibody or antigen binding fragment thereof specifically binds human cKIT at SEQ ID NO. 161 and SEQ ID NO. 162.

22. The antibody drug conjugate of claim 19, wherein said Ab is an antibody or antigen binding fragment thereof comprises:

(i) a heavy chain variable region that comprises (a) a HCDR1 (CDR-Complementarity Determining Region) of SEQ ID NO: 76, (b) a HCDR2 of SEQ ID NO: 77, (c) a HCDR3 of SEQ ID NO: 78; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 85, (e) a LCDR2 of SEQ ID NO: 86, and (f) a LCDR3 of SEQ ID NO: 87;

(ii) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 22, (b) a HCDR2 of SEQ ID NO: 23, (c) a HCDR3 of SEQ ID NO: 24; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 31, (e) a LCDR2 of SEQ ID NO: 32, and (f) a LCDR3 of SEQ ID NO: 33;

(iii) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 130, (b) a HCDR2 of SEQ ID NO: 131, (c) a HCDR3 of SEQ ID NO: 132; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 139, (e) a LCDR2 of SEQ ID NO: 140, and (f) a LCDR3 of SEQ ID NO: 141;

(iv) a heavy chain variable region that comprises: (a) a HCDR1 of SEQ ID NO: 58, (b) a HCDR2 of SEQ ID NO: 59, (c) a HCDR3 of SEQ ID NO: 60; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 67, (e) a LCDR2 of SEQ ID NO: 68, and (f) a LCDR3 of SEQ ID NO: 69;

(v) a heavy chain variable region that comprises: (a) a HCDR1 of SEQ ID NO: 40, (b) a HCDR2 of SEQ ID NO: 41, (c) a HCDR3 of SEQ ID NO: 42; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 49, (e) a LCDR2 of SEQ ID NO: 50, and (f) a LCDR3 of SEQ ID NO: 51;

(vi) a heavy chain variable region that comprises: (a) a HCDR1 of SEQ ID NO: 94, (b) a HCDR2 of SEQ ID NO: 95, (c) a HCDR3 of SEQ ID NO: 96; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 103, (d) a LCDR2 of SEQ ID NO: 104, and (f) a LCDR3 of SEQ ID NO: 105;

(vii) a heavy chain variable region that comprises: (a) a HCDR1 of SEQ ID NO: 112, (b) a HCDR2 of SEQ ID NO: 113, (c) a HCDR3 of SEQ ID NO: 114; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 121, (e) a LCDR2 of SEQ ID NO: 122, and (f) a LCDR3 of SEQ ID NO: 123; or

(viii) a heavy chain variable region that comprises: (a) a HCDR1 of SEQ ID NO: 3, (b) a HCDR2 of SEQ ID NO: 4, (c) a HCDR3 of SEQ ID NO: 5; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 12, (e) a LCDR2 of SEQ ID NO: 13, and (f) a LCDR3 of SEQ ID NO: 14.

23. The antibody drug conjugate of any of the preceding claims in which at least one amino acid within a CDR is substituted by a corresponding residue of a corresponding CDR of another anti-cKIT antibody of Table 1.

24. The antibody drug conjugate of any of the preceding claims in which one or two amino acids within a CDR have been modified deleted or substituted.

25. The antibody drug conjugate of any of the preceding claims that retains at least 90, 91, 92, 93, 94, 95, 96, 97, 98 or 99% identity over either the variable light or variable heavy region.

26. The antibody drug conjugate of any of claims 19-25, wherein the antibody is a monoclonal antibody, a chimeric antibody, a humanized antibody, a human engineered antibody, a human antibody, a single chain antibody(scFv) or an antibody fragment.

27. The antibody drug conjugate of any of claims 19-25, wherein said n is an integer from 2 to 8.

28. The antibody drug conjugate of any of claims 19-25, wherein said n is an integer from 3 to 4.

29. The antibody drug conjugate of any of claims 19-28 in combination with another therapeutic agent.

30. The antibody drug conjugate of any of claims 19-28 in combination with a therapeutic agent listed in Table 16.

31. A pharmaceutical composition comprising the antibody drug conjugate of any one of claims 1-28 and a pharmaceutically acceptable carrier.

32. The pharmaceutical composition of claim 31 wherein said composition is prepared as a lyophilisate.

33. The pharmaceutical composition of claim 32, wherein said lyophilisate comprises the antibody drug conjugate of any one of claims 1 to 28, sodium succinate, and polysorbate 20.

34. A method of treating an cKIT positive cancer in a patient in need thereof, comprising administering to said patient the antibody drug conjugate of any of claims 1-28, or the pharmaceutical composition of claims 31-33.

35. The method of claim 34, wherein said cancer is selected from the group consisting of gastrointestinal stromal tumors (GIST), small cell lung cancer (SCLC), acute myeloid leukemia (AML), melanoma, mast cell leukemia (MCL), mastocytosis, neurofibromatosis, breast cancer, non-small cell lung cancer (NSCLC) and pancreatic cancer.

36. The method of claim 35, wherein the antibody drug conjugate or the pharmaceutical composition is administered in combination with another therapeutic agent.

37. The method of claim 36, wherein the antibody drug conjugate or the pharmaceutical composition is administered in combination with a therapeutic listed in Table 16.

38. The antibody drug conjugate of any of claims 1-28 for use as a medicament.

39. The antibody drug conjugate of any of claims 1-28, or the pharmaceutical composition of any of claims 31-33, for use in the treatment of a cKIT positive cancer.

40. The antibody drug conjugate of claim 39 administered in combination with another therapeutic agent.

41. The antibody drug conjugate of claim 40 administered in combination with a therapeutic agent listed in Table 16.

42. A nucleic acid that encodes the antibody or antigen binding fragment of any of claims 1-28.

43. A vector comprising the nucleic acid of claim 42.

44. A host cell comprising the vector according to claim 43.

45. A process for producing an antibody or antigen binding fragment comprising cultivating the host cell of claim 44 and recovering the antibody from the culture.

46. A process for producing an anti-cKIT antibody drug conjugate, the process comprising:
(a) chemically linking SMCC to a drug moiety DM-1;
(b) conjugating said linker-drug to the antibody recovered from the cell culture of claim 45; and
(c) purifying the antibody drug conjugate.

47. The antibody drug conjugate made according to claim 46 having an average maytansinoid to antibody ratio (MAR), measured with a UV spectrophotometer, about 3.5.

48. An antibody or antigen binding fragment thereof that comprises:

(i) a heavy chain variable region that comprises (a) a HCDR1 (CDR-Complementarity Determining Region) of SEQ ID NO: 76, (b) a HCDR2 of SEQ ID NO: 77, (c) a HCDR3 of SEQ ID NO: 78; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 85, (e) a LCDR2 of SEQ ID NO: 86, and (f) a LCDR3 of SEQ ID NO: 87;

(ii) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 22, (b) a HCDR2 of SEQ ID NO: 23, (c) a HCDR3 of SEQ ID NO: 24; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 31, (e) a LCDR2 of SEQ ID NO: 32, and (f) a LCDR3 of SEQ ID NO: 33;

(iii) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 130, (b) a HCDR2 of SEQ ID NO: 131, (c) a HCDR3 of SEQ ID NO: 132; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 139, (e) a LCDR2 of SEQ ID NO: 140, and (f) a LCDR3 of SEQ ID NO: 141;

(iv) a heavy chain variable region that comprises: (a) a HCDR1 of SEQ ID NO: 58, (b) a HCDR2 of SEQ ID NO: 59, (c) a HCDR3 of SEQ ID NO: 60; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 67, (e) a LCDR2 of SEQ ID NO: 68, and (f) a LCDR3 of SEQ ID NO: 69;

(v) a heavy chain variable region that comprises: (a) a HCDR1 of SEQ ID NO: 40, (b) a HCDR2 of SEQ ID NO: 41, (c) a HCDR3 of SEQ ID NO: 42; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 49, (e) a LCDR2 of SEQ ID NO: 50, and (f) a LCDR3 of SEQ ID NO: 51;

(vi) a heavy chain variable region that comprises: (a) a HCDR1 of SEQ ID NO: 94, (b) a HCDR2 of SEQ ID NO: 95, (c) a HCDR3 of SEQ ID NO: 96; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 103, (d) a LCDR2 of SEQ ID NO: 104, and (f) a LCDR3 of SEQ ID NO: 105;

(vii) a heavy chain variable region that comprises: (a) a HCDR1 of SEQ ID NO: 112, (b) a HCDR2 of SEQ ID NO: 113, (c) a HCDR3 of SEQ ID NO: 114; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 121, (c) a LCDR2 of SEQ ID NO: 122, and (f) a LCDR3 of SEQ ID NO: 123; or

(viii) a heavy chain variable region that comprises: (a) a HCDR1 of SEQ ID NO: 3, (b) a HCDR2 of SEQ ID NO: 4, (c) a HCDR3 of SEQ ID NO: 5; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 12, (e) a LCDR2 of SEQ ID NO: 13, and (f) a LCDR3 of SEQ ID NO: 14.

49. A diagnostic reagent comprising the antibody or antigen binding fragment thereof of claim 48 which is labeled.

50. The diagnostic reagent of claim 49, wherein the label is selected from the group consisting of a radiolabel, a fluorophore, a chromophore, an imaging agent and a metal ion.

## CLAIMS

**What is claimed is:**

1. An antibody drug conjugate of the formula

$$Ab\text{-}(L\text{-}(D)_m)_n$$

or a pharmaceutically acceptable salt thereof; wherein

Ab is an antibody or antigen binding fragment thereof that specifically binds to an epitope of human cKIT;

L is a linker;

D is a drug moiety;

m is an integer from 1 to 8; and

n is an integer from 1 to 10.

2. The antibody drug conjugate of claim 1, wherein said n is 3 or 4.

3. The antibody drug conjugate of claim 1 or 2, wherein said antibody or antigen binding fragment thereof specifically binds the extracellular domain of cKIT (SEQ ID NO.160).

4. The antibody drug conjugate of claim 1 or 2, wherein said antibody or antigen binding fragment specifically binds to an epitope of human cKIT at domains 1-3 (SEQ ID NO.155).

5. The antibody drug conjugate of claim 1 or 2, wherein said antibody or antigen binding fragment thereof specifically binds human cKIT at SEQ ID NO. 161 and SEQ ID NO. 162.

6. The antibody drug conjugate of any of claims 1-3, wherein said antibody or antigen binding fragment thereof comprises:

(i) a heavy chain variable region that comprises (a) a HCDR1 (CDR-Complementarity Determining Region) of SEQ ID NO: 76, (b) a HCDR2 of SEQ ID NO: 77, (c) a HCDR3 of SEQ ID NO: 78; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 85, (e) a LCDR2 of SEQ ID NO: 86, and (f) a LCDR3 of SEQ ID NO: 87;

(ii) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 22, (b) a HCDR2 of SEQ ID NO: 23, (c) a HCDR3 of SEQ ID NO: 24; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 31, (e) a LCDR2 of SEQ ID NO: 32, and (f) a LCDR3 of SEQ ID NO: 33;

(iii) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 130, (b) a HCDR2 of SEQ ID NO: 131, (c) a HCDR3 of SEQ ID NO: 132; and a light chain variable region that comprises:

(d) a LCDR1 of SEQ ID NO: 139, (e) a LCDR2 of SEQ ID NO: 140, and (f) a LCDR3 of SEQ ID NO: 141;

(iv) a heavy chain variable region that comprises: (a) a HCDR1 of SEQ ID NO: 58, (b) a HCDR2 of SEQ ID NO: 59, (c) a HCDR3 of SEQ ID NO: 60; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 67, (e) a LCDR2 of SEQ ID NO: 68, and (f) a LCDR3 of SEQ ID NO: 69;

(v) a heavy chain variable region that comprises: (a) a HCDR1 of SEQ ID NO: 40, (b) a HCDR2 of SEQ ID NO: 41, (c) a HCDR3 of SEQ ID NO: 42; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 49, (e) a LCDR2 of SEQ ID NO: 50, and (f) a LCDR3 of SEQ ID NO: 51;

(vi) a heavy chain variable region that comprises: (a) a HCDR1 of SEQ ID NO: 94, (b) a HCDR2 of SEQ ID NO: 95, (c) a HCDR3 of SEQ ID NO: 96; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 103, (d) a LCDR2 of SEQ ID NO: 104, and (f) a LCDR3 of SEQ ID NO: 105;

(vii) a heavy chain variable region that comprises: (a) a HCDR1 of SEQ ID NO: 112, (b) a HCDR2 of SEQ ID NO: 113, (c) a HCDR3 of SEQ ID NO: 114; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 121, (e) a LCDR2 of SEQ ID NO: 122, and (f) a LCDR3 of SEQ ID NO: 123; or

(viii) a heavy chain variable region that comprises: (a) a HCDR1 of SEQ ID NO: 3, (b) a HCDR2 of SEQ ID NO: 4, (c) a HCDR3 of SEQ ID NO: 5; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 12, (e) a LCDR2 of SEQ ID NO: 13, and (f) a LCDR3 of SEQ ID NO: 14.

7. The antibody drug conjugate of any of the preceding claims in which at least one amino acid within a CDR is substituted by a corresponding residue of a corresponding CDR of another anti-cKIT antibody in Table 1.

8. The antibody drug conjugate of any of the preceding claims in which one or two amino acids within a CDR have been modified, deleted or substituted.

9. The antibody drug conjugate of any of the preceding claims that retains at least 90, 91, 92, 93, 94, 95, 96, 97, 98 or 99% identity over either the variable light or variable heavy region.

10. The antibody drug conjugate of any of the preceding claims wherein the antibody is a monoclonal antibody, a chimeric antibody, a humanized antibody, a human engineered antibody, a human antibody, a single chain antibody(scFv) or an antibody fragment.

11. The antibody drug conjugate of any one of claims 1-10, wherein said linker (L) is selected from the group consisting of a cleavable linker, a non-cleavable linker, a hydrophilic linker, a procharged linker and a dicarboxylic acid based linker.

12. The antibody drug conjugate of claim 11, wherein the linker is derived from a cross-linking reagent selected from the group consisting of N-succinimidyl-3-(2-pyridyldithio)propionate (SPDP), N-succinimidyl 4-(2-pyridyldithio)pentanoate (SPP), N-succinimidyl 4-(2-pyridyldithio)butanoate (SPDB), N-succinimidyl-4-(2-pyridyldithio)2-sulfo-butanoate (sulfo-SPDB), N-succinimidyl iodoacetate (SIA), N-succinimidyl(4-iodoacetyl)aminobenzoate (SIAB), maleimide PEG NHS, N-succinimidyl 4-(maleimidomethyl) cyclohexanecarboxylate (SMCC), N- sulfosuccinimidyl 4-(maleimidomethyl) cyclohexanecarboxylate (sulfo-SMCC) or 2,5-dioxopyrrolidin-1-yl 17-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)-5,8,11,14-tetraoxo-4,7,10,13-tetraazaheptadecan-1-oate (CX1-1).

13. The antibody drug conjugate of claim 12, wherein said linker is derived from the cross-linking reagent N-succinimidyl 4-(maleimidomethyl) cyclohexanecarboxylate (SMCC).

14. The antibody drug conjugate of any one of claims 1-13, wherein said drug moiety (D) is selected from a group consisting of a V-ATPase inhibitor, a pro-apoptotic agent, a Bcl2 inhibitor, an MCL1 inhibitor, a HSP90 inhibitor, an IAP inhibitor, an mTor inhibitor, a microtubule stabilizer, a microtubule destabilizer, an auristatin, a dolastatin, a maytansinoid, a MetAP (methionine aminopeptidase), an inhibitor of nuclear export of proteins CRM1, a DPPIV inhibitor, proteasome inhibitors, inhibitors of phosphoryl transfer reactions in mitochondria, a protein synthesis inhibitor, a kinase inhibitor, a CDK2 inhibitor, a CDK9 inhibitor, a kinesin inhibitor, an HDAC inhibitor, a DNA damaging agent, a DNA alkylating agent, a DNA intercalator, a DNA minor groove binder and a DHFR inhibitor.

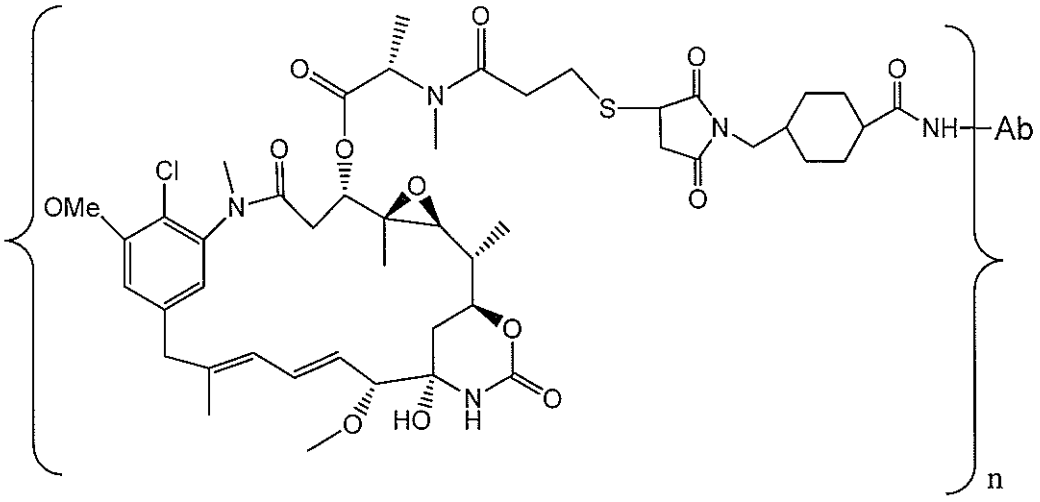
15. The antibody drug conjugate of claim 14, wherein the drug moiety is a maytansinoid.

16. The antibody drug conjugate of claim 15, wherein the maytansinoid is N(2')- deacetyl-N(2')-(3-mercapto-l-oxopropyl)-maytansine (DM1) or N(2')-deacetyl-N2-(4- mercapto-4-methyl- 1 -oxopentyl)-maytansine (DM4).

17. The antibody drug conjugate of any of the preceding claims in combination with another therapeutic agent.

18. The antibody drug conjugate of any of the preceding claims in combination with a therapeutic agent listed in Table 16.

19. An antibody drug conjugate of the formula




or a pharmaceutically acceptable salt thereof; wherein;
Ab is an antibody or antigen binding fragment thereof that specifically binds to human cKIT, and at least n number of primary amines; and n is an integer from 1 to 10.

20. The antibody drug conjugate of claim 19, wherein said antibody or antigen binding fragment specifically binds to an epitope of human cKIT at domains 1-3 (SEQ ID NO.155).

21. The antibody drug conjugate of claim 19, wherein said antibody or antigen binding fragment thereof specifically binds human cKIT at SEQ ID NO. 161 and SEQ ID NO. 162.

22. The antibody drug conjugate of claim 19, wherein said Ab is an antibody or antigen binding fragment thereof comprises:

(i) a heavy chain variable region that comprises (a) a HCDR1 (CDR-Complementarity Determining Region) of SEQ ID NO: 76, (b) a HCDR2 of SEQ ID NO: 77, (c) a HCDR3 of SEQ ID NO: 78; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 85, (e) a LCDR2 of SEQ ID NO: 86, and (f) a LCDR3 of SEQ ID NO: 87;

(ii) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 22, (b) a HCDR2 of SEQ ID NO: 23, (c) a HCDR3 of SEQ ID NO: 24; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 31, (e) a LCDR2 of SEQ ID NO: 32, and (f) a LCDR3 of SEQ ID NO: 33;

(iii) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 130, (b) a HCDR2 of SEQ ID NO: 131, (c) a HCDR3 of SEQ ID NO: 132; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 139, (e) a LCDR2 of SEQ ID NO: 140, and (f) a LCDR3 of SEQ ID NO: 141;

(iv) a heavy chain variable region that comprises: (a) a HCDR1 of SEQ ID NO: 58, (b) a HCDR2 of SEQ ID NO: 59, (c) a HCDR3 of SEQ ID NO: 60; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 67, (e) a LCDR2 of SEQ ID NO: 68, and (f) a LCDR3 of SEQ ID NO: 69;

(v) a heavy chain variable region that comprises: (a) a HCDR1 of SEQ ID NO: 40, (b) a HCDR2 of SEQ ID NO: 41, (c) a HCDR3 of SEQ ID NO: 42; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 49, (e) a LCDR2 of SEQ ID NO: 50, and (f) a LCDR3 of SEQ ID NO: 51;

(vi) a heavy chain variable region that comprises: (a) a HCDR1 of SEQ ID NO: 94, (b) a HCDR2 of SEQ ID NO: 95, (c) a HCDR3 of SEQ ID NO: 96; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 103, (d) a LCDR2 of SEQ ID NO: 104, and (f) a LCDR3 of SEQ ID NO: 105;

(vii) a heavy chain variable region that comprises: (a) a HCDR1 of SEQ ID NO: 112, (b) a HCDR2 of SEQ ID NO: 113, (c) a HCDR3 of SEQ ID NO: 114; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 121, (e) a LCDR2 of SEQ ID NO: 122, and (f) a LCDR3 of SEQ ID NO: 123; or

(viii) a heavy chain variable region that comprises: (a) a HCDR1 of SEQ ID NO: 3, (b) a HCDR2 of SEQ ID NO: 4, (c) a HCDR3 of SEQ ID NO: 5; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 12, (e) a LCDR2 of SEQ ID NO: 13, and (f) a LCDR3 of SEQ ID NO: 14.

23. The antibody drug conjugate of any of the preceding claims in which at least one amino acid within a CDR is substituted by a corresponding residue of a corresponding CDR of another anti-cKIT antibody of Table 1.

24. The antibody drug conjugate of any of the preceding claims in which one or two amino acids within a CDR have been modified, deleted or substituted.

25. The antibody drug conjugate of any of the preceding claims that retains at least 90, 91, 92, 93, 94, 95, 96, 97, 98 or 99% identity over either the variable light or variable heavy region.

26. The antibody drug conjugate of any of claims 19-25, wherein the antibody is a monoclonal antibody, a chimeric antibody, a humanized antibody, a human engineered antibody, a human antibody, a single chain antibody(scFv) or an antibody fragment.

27. The antibody drug conjugate of any of claims 19-25, wherein said n is an integer from 2 to 8.

28. The antibody drug conjugate of any of claims 19-25, wherein said n is an integer from 3 to 4.

29. The antibody drug conjugate of any of claims 19-28 in combination with another therapeutic agent.

30. The antibody drug conjugate of any of claims 19-28 in combination with a therapeutic agent listed in Table 16.

31. A pharmaceutical composition comprising the antibody drug conjugate of any one of claims 1-28 and a pharmaceutically acceptable carrier.

32. The pharmaceutical composition of claim 31 wherein said composition is prepared as a lyophilisate.

33. The pharmaceutical composition of claim 32, wherein said lyophilisate comprises the antibody drug conjugate of any one of claims 1 to 28, sodium succinate, and polysorbate 20.

34. The antibody drug conjugate of any of claims 1-28 for use as a medicament.

35. The antibody drug conjugate of any of claims 1-28, or the pharmaceutical composition of any of claims 31-33, for use in the treatment of a cKIT positive cancer.

36. The antibody drug conjugate of claim 35 administered in combination with another therapeutic agent.

37. The antibody drug conjugate of claim 36 administered in combination with a therapeutic agent listed in Table 16.

38. A nucleic acid that encodes the antibody or antigen binding fragment of any of claims 1-28.

39. A vector comprising the nucleic acid of claim 38.

40. A host cell comprising the vector according to claim 39.

41. A process for producing an antibody or antigen binding fragment comprising cultivating the host cell of claim 40 and recovering the antibody from the culture.

42. A process for producing an anti-cKIT antibody drug conjugate, the process comprising:
(a) chemically linking SMCC to a drug moiety DM-1;
(b) conjugating said linker-drug to the antibody recovered from the cell culture of claim 41; and
(c) purifying the antibody drug conjugate.

43. The antibody drug conjugate made according to claim 42 having an average maytansinoid to antibody ratio (MAR), measured with a UV spectrophotometer, about 3.5.

44. An antibody or antigen binding fragment thereof that comprises:

(i) a heavy chain variable region that comprises (a) a HCDR1 (CDR-Complementarity Determining Region) of SEQ ID NO: 76, (b) a HCDR2 of SEQ ID NO: 77, (c) a HCDR3 of SEQ ID NO: 78; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 85, (e) a LCDR2 of SEQ ID NO: 86, and (f) a LCDR3 of SEQ ID NO: 87;

(ii) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 22, (b) a HCDR2 of SEQ ID NO: 23, (c) a HCDR3 of SEQ ID NO: 24; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 31, (e) a LCDR2 of SEQ ID NO: 32, and (f) a LCDR3 of SEQ ID NO: 33;

(iii) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 130, (b) a HCDR2 of SEQ ID NO: 131, (c) a HCDR3 of SEQ ID NO: 132; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 139, (e) a LCDR2 of SEQ ID NO: 140, and (f) a LCDR3 of SEQ ID NO: 141;

(iv) a heavy chain variable region that comprises: (a) a HCDR1 of SEQ ID NO: 58, (b) a HCDR2 of SEQ ID NO: 59, (c) a HCDR3 of SEQ ID NO: 60; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 67, (e) a LCDR2 of SEQ ID NO: 68, and (f) a LCDR3 of SEQ ID NO: 69;

(v) a heavy chain variable region that comprises: (a) a HCDR1 of SEQ ID NO: 40, (b) a HCDR2 of SEQ ID NO: 41, (c) a HCDR3 of SEQ ID NO: 42; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 49, (e) a LCDR2 of SEQ ID NO: 50, and (f) a LCDR3 of SEQ ID NO: 51;

(vi) a heavy chain variable region that comprises: (a) a HCDR1 of SEQ ID NO: 94, (b) a HCDR2 of SEQ ID NO: 95, (c) a HCDR3 of SEQ ID NO: 96; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 103, (d) a LCDR2 of SEQ ID NO: 104, and (f) a LCDR3 of SEQ ID NO: 105;

(vii) a heavy chain variable region that comprises: (a) a HCDR1 of SEQ ID NO: 112, (b) a HCDR2 of SEQ ID NO: 113, (c) a HCDR3 of SEQ ID NO: 114; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 121, (e) a LCDR2 of SEQ ID NO: 122, and (f) a LCDR3 of SEQ ID NO: 123; or

(viii) a heavy chain variable region that comprises: (a) a HCDR1 of SEQ ID NO: 3, (b) a HCDR2 of SEQ ID NO: 4, (c) a HCDR3 of SEQ ID NO: 5; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO: 12, (e) a LCDR2 of SEQ ID NO: 13, and (f) a LCDR3 of SEQ ID NO: 14.

45. A diagnostic reagent comprising the antibody or antigen binding fragment thereof of claim 44 which is labeled.

46. The diagnostic reagent of claim 45, wherein the label is selected from the group consisting of a radiolabel, a fluorophore, a chromophore, an imaging agent, and a metal ion.