

CLAIMS**WHAT IS CLAIMED IS:**

1. An FLT3 binding domain comprising at least three complementarity determining regions (a CDR1, a CDR2, and a CDR3), wherein
 - the CDR1 comprises a sequence selected from the group consisting of SEQ ID Nos. 77-108, or a sequence comprising one or more amino acid substitutions in a sequence selected from the group consisting of SEQ ID Nos. 77-108;
 - the CDR2 comprises a sequence selected from the group consisting of SEQ ID Nos. 109-154, and 393-394, or a sequence comprising one or more amino acid substitutions in a sequence selected from the group consisting of SEQ ID Nos. 109-154, and 393-394;
 - the CDR3 comprises a sequence selected from the group consisting of SEQ ID Nos. 155-195, or a sequence comprising one or more amino acid substitutions in a sequence selected from the group consisting of SEQ ID Nos. 155-195.
2. The FLT3 binding domain of claim 1, comprising at least one of the following set of sequences (the CDR1, the CDR2, and the CDR3):
 - SEQ ID Nos. 77, 109, and 155;
 - SEQ ID Nos. 78, 109, and 155;
 - SEQ ID Nos. 79, 110, and 156;
 - SEQ ID Nos. 80, 111, and 155;
 - SEQ ID Nos. 81, 112, and 155;
 - SEQ ID Nos. 77, 113, and 157;
 - SEQ ID Nos. 82, 110, and 156;
 - SEQ ID Nos. 77, 114, and 158;
 - SEQ ID Nos. 80, 111, and 155;
 - SEQ ID Nos. 83, 115, and 155;
 - SEQ ID Nos. 84, 111, and 155;
 - SEQ ID Nos. 79, 116, and 156;
 - SEQ ID Nos. 85, 111, and 155;
 - SEQ ID Nos. 86, 110, and 156;
 - SEQ ID Nos. 87, 110, and 156;
 - SEQ ID Nos. 88, 117, and 159;
 - SEQ ID Nos. 88, 118, and 160;
 - SEQ ID Nos. 88, 119, and 161;
 - SEQ ID Nos. 88, 120, and 162;
 - SEQ ID Nos. 88, 121, and 163;
 - SEQ ID Nos. 88, 122, and 164;
 - SEQ ID Nos. 88, 121, and 165;
 - SEQ ID Nos. 88, 121, and 166;
 - SEQ ID Nos. 88, 122, and 167;
 - SEQ ID Nos. 88, 122, and 168;
 - SEQ ID Nos. 88, 121, and 169;
 - SEQ ID Nos. 88, 118, and 165;
 - SEQ ID Nos. 88, 123, and 170;

SEQ ID Nos. 88, 124, and 171;
SEQ ID Nos. 88, 117, and 172;
SEQ ID Nos. 89, 125, and 173;
SEQ ID Nos. 90, 126, and 174;
SEQ ID Nos. 90, 127, and 175;
SEQ ID Nos. 90, 125, and 176;
SEQ ID Nos. 90, 128, and 175;
SEQ ID Nos. 90, 128, and 177;
SEQ ID Nos. 91, 129, and 178;
SEQ ID Nos. 91, 130, and 178;
SEQ ID Nos. 92, 131, and 178;
SEQ ID Nos. 93, 132, and 178;
SEQ ID Nos. 94, 133, and 179;
SEQ ID Nos. 91, 134, and 178;
SEQ ID Nos. 95, 135, and 180;
SEQ ID Nos. 96, 136, and 181;
SEQ ID Nos. 97, 137, and 182;
SEQ ID Nos. 97, 138, and 183;
SEQ ID Nos. 98, 139, and 184;
SEQ ID Nos. 99, 139, and 185;
SEQ ID Nos. 100, 140, and 186;
SEQ ID Nos. 101, 141, and 187;
SEQ ID Nos. 102, 142, and 188;
SEQ ID Nos. 103, 143, and 189;
SEQ ID Nos. 104, 144, and 190;
SEQ ID Nos. 105, 145, and 191;
SEQ ID Nos. 106, 146, and 192;
SEQ ID Nos. 107, 147, and 193;
SEQ ID Nos. 108, 148, and 194;
SEQ ID Nos. 91, 149, and 195;
SEQ ID Nos. 91, 150, and 195;
SEQ ID Nos. 100, 151, and 186;
SEQ ID Nos. 92, 152, and 195;
SEQ ID Nos. 93, 153, and 195;
SEQ ID Nos. 91, 154, and 195;
SEQ ID Nos. 89, 393, and 173; and
SEQ ID Nos. 89, 394, and 173.

3. The FLT3 binding domain of claim 1 or 2, comprising at least one of the following set of sequences (the CDR1, the CDR2, and the CDR3):

SEQ ID Nos. 89, 393, and 173;
SEQ ID Nos. 89, 394, and 173;
SEQ ID Nos. 100, 151, and 186; and
SEQ ID Nos. 91, 149, and 195.

4. The FLT3 binding domain of any one of claims 1-3, wherein the binding domain further comprises a framework region 1, a framework region 2, a framework region 3, and a framework region 4, wherein the framework region 1 comprises a sequence selected from the group consisting of SEQ ID Nos. 273-301, the framework region 2 comprises a sequence

selected from the group consisting of SEQ ID Nos. 302-322, 395, and 406-407, the framework region 3 comprises a sequence selected from the group consisting of SEQ ID Nos. 323-365, and 396, and the framework region 4 comprises a sequence selected from the group consisting of SEQ ID Nos. 366-371.

5. The FLT3 binding domain of any one of claims 1-4, comprising a sequence that is at least about 60% identical to a sequence selected from the group consisting of SEQ ID Nos. 1-76, and 389-390.

6. The FLT3 binding domain of claim 5, comprising a sequence that is at least about 70% identical to a sequence selected from the group consisting of SEQ ID Nos. 71-76, and 389-390.

7. The FLT3 binding domain of any one of claims 1-6, wherein the FLT3 binding domain is an antibody or an antigen binding fragment thereof.

8. The FLT3 binding domain of claim 7, wherein the antibody or an antigen binding fragment thereof comprises at least one of: a monoclonal antibody (mAb), a bispecific antibody, a trispecific antibody, a monovalent antibody, a multivalent antibody, an hIgG, an Fv, an Fd, an Fab, an F(ab')₂, an F(ab'), an Fab2, an Fab3, an scFab, an scFv, an scFvFc, an scFv-zipper, a di-scFv, a tandem scFv, an sdFv, an sdAb, a VH domain, a VL domain, a VHH domain, a half-antibody, a diabody, a single chain diabody, a tandem diabody, a tandem di-scFv, or a tandem tri-scFv.

9. The FLT3 binding domain of claim 8, wherein the FLT3 binding domain is the sdAb.

10. The FLT3 binding domain of any one of claims 1-6, wherein the FLT3 binding domain is part of an antibody or an antigen binding fragment thereof.

11. The FLT3 binding domain of claim 10, wherein the antibody or an antigen binding fragment thereof comprises at least one of: a monoclonal antibody (mAb), a bispecific antibody, a multispecific antibody, a monovalent antibody, a multivalent antibody, an hIgG, an Fv, an Fd, an Fab, an F(ab')₂, an F(ab'), an Fab2, an Fab3, an scFab, an scFv, an scFvFc, an scFv-zipper, a di-scFv, a tandem scFv, a half-antibody, a diabody, a single chain diabody, a tandem diabody, a tandem di-scFv, or a tandem tri-scFv.

12. The FLT3 binding domain of claim 11, wherein the FLT3 binding domain is part of the antibody or an antigen binding fragment thereof and wherein the antibody or an antigen binding fragment thereof comprises the bispecific antibody.

13. The FLT3 binding domain of claim 12, wherein the bispecific antibody comprises (i) the FLT3 binding domain (anti-FLT3) and (ii) a CD3 binding domain.

14. The FLT3 binding domain of claim 13, wherein the CD3 comprises a human CD3.

15. The FLT3 binding domain of claim 13 or 14, wherein the anti-FLT3 domain is an sdAb.
16. The FLT3 binding domain of any one of claims 13-15, wherein the anti-CD3 domain is an scFv.
17. The FLT3 binding domain of claim 11, wherein the FLT3 binding domain is part of the antibody or an antigen binding fragment thereof and wherein the antibody or an antigen binding fragment thereof comprises the multispecific antibody.
18. The FLT3 binding domain of claim 17, wherein the multispecific antibody comprises (i) the FLT3 binding domain (anti-FLT3); (ii) a CD3 binding domain (anti-CD3); and (iii) an albumin binding domain (anti-ALB).
19. The FLT3 binding domain of claim 18, wherein the CD3 comprises a human CD3.
20. The FLT3 binding domain of claim 18 or 19, wherein the albumin comprises a serum albumin.
21. The FLT3 binding domain of claim 20, wherein the serum albumin is a human serum albumin.
22. The FLT3 binding domain of any one of claims 18-21, wherein the FLT3 binding domain (anti-FLT3), the CD3 binding domain (anti-CD3), and the albumin binding domain (anti-ALB) are in at least one of the following formats, from N-terminus to C-terminus:
 - anti-ALB: anti-FLT3: anti-CD3;
 - anti-CD3: anti-FLT3: anti-ALB;
 - anti-FLT3: anti-CD3: anti-ALB;
 - anti-ALB: anti-CD3: anti-FLT3;
 - anti-FLT3: anti-ALB: anti-CD3; and
 - anti-CD3: anti-ALB: anti-FLT3.
23. The FLT3 binding domain of any one of claims 18-22, wherein the anti-FLT3 domain is an sdAb.
24. The FLT3 binding domain of any one of claims 18-23, wherein the anti-CD3 domain is an scFv.
25. The FLT3 binding domain of any one of claims 18-24, wherein the anti-ALB domain is an sdAb.
26. The FLT3 binding domain of any one of claims 18-25, wherein the anti-CD3 domain comprises an amino acid sequence that is at least about 90% identical to the sequence set forth in SEQ ID No. 373.

27. The FLT3 binding domain of any one of claims 18-26, wherein the anti-ALB domain comprises an amino acid sequence that is at least about 90% identical to the sequence set forth in SEQ ID No. 372.
28. The FLT3 binding domain of any one of claims 1-27, wherein the FLT3 binding domain binds to human FLT3 and cynomolgus FLT3.
29. An FLT3 binding domain that has an half-maximal effective concentration (EC_{50}) of at least about 0.5 pM to about 6000 pM in a T-cell dependent cellular cytotoxicity assay, wherein the assay measures the EC_{50} of the FLT3 binding domain in T cells mediated killing of FLT-3 expressing cells.
30. The FLT3 binding domain of claim 29, wherein the FLT-3 expressing cells are leukemia cells.
31. The FLT3 binding domain of claim 30, wherein the leukemia cells are from a cell line, wherein the cell line is MV-4-11, EOL1, THP1, MOLM3, or HL60.
32. The FLT3 binding domain of any one of claims 29-31, comprising at least three complementarity determining regions (a CDR1, a CDR2, and a CDR3), wherein
- the CDR1 comprises a sequence selected from the group consisting of SEQ ID Nos. 89, 91, 92, 93, and 100, or a sequence comprising one or more amino acid substitutions in a sequence selected from the group consisting of SEQ ID Nos. 89, 91, 92, 93, and 100;
 - the CDR2 comprises a sequence selected from the group consisting of SEQ ID Nos. 149, 150, 151, 152, 153, 154, 393, and 394, or a sequence comprising one or more amino acid substitutions in a sequence selected from the group consisting of SEQ ID Nos. 149, 150, 151, 152, 153, 154, 393, and 394;
 - the CDR3 comprises a sequence selected from the group consisting of SEQ ID Nos. 173, 186, and 195, or a sequence comprising one or more amino acid substitutions in a sequence selected from the group consisting of SEQ ID Nos. 173, 186, and 195.
33. The FLT3 binding domain of claim 32, comprising at least one of the following set of sequences (the CDR1, the CDR2, and the CDR3):
- SEQ ID Nos. 91, 149, and 195;
 - SEQ ID Nos. 91, 150, and 195;
 - SEQ ID Nos. 100, 151, and 186;
 - SEQ ID Nos. 92, 152, and 195;
 - SEQ ID Nos. 93, 153, and 195;
 - SEQ ID Nos. 91, 154, and 195;
 - SEQ ID Nos. 89, 393, and 173; and
 - SEQ ID Nos. 89, 394, and 173.

34. The FLT3 binding domain of any one of claims 29-33, comprising a sequence that is at least about 70% identical to a sequence selected from the group consisting of SEQ ID Nos. 71-76, and 389-390.
35. The FLT3 binding domain of claim any one of claims 29-34, wherein the FLT3 binding domain is part of a multispecific antibody.
36. The FLT3 binding domain of claim 35, wherein the multispecific antibody comprises (i) the FLT3 binding domain (anti-FLT3); (ii) a CD3 binding domain (anti-CD3); and (iii) an albumin binding domain (anti-ALB).
37. The FLT3 binding domain of claim 36, wherein the CD3 comprises a human CD3.
38. The FLT3 binding domain of claim 36 or 37, wherein the albumin comprises a serum albumin.
39. The FLT3 binding domain of claim 38, wherein the serum albumin is a human serum albumin.
40. The FLT3 binding domain of any one of claims 36-39, wherein the FLT3 binding domain (anti-FLT3), the CD3 binding domain (anti-CD3), and the albumin binding domain (anti-ALB) are in at least one of the following formats, from N-terminus to C-terminus:
anti-ALB: anti-FLT3: anti-CD3;
anti-CD3: anti-FLT3: anti-ALB;
anti-FLT3: anti-CD3: anti-ALB;
anti-ALB: anti-CD3: anti-FLT3;
anti-FLT3: anti-ALB: anti-CD3; and
anti-CD3: anti-ALB: anti-FLT3.
41. The FLT3 binding domain of any one of claims 29-40, wherein the anti-FLT3 domain is an sdAb.
42. The FLT3 binding domain of any one of claims 36-41, wherein the anti-CD3 domain is an scFv.
43. The FLT3 binding domain of any one of claims 36-42, wherein the anti-ALB domain is an sdAb.
44. The FLT3 binding domain of any one of claims 36-43, wherein the anti-CD3 domain comprises an amino acid sequence that is at least about 90% identical to the sequence set forth in SEQ ID No. 373.
45. The FLT3 binding domain of any one of claims 36-44, wherein the anti-ALB domain comprises an amino acid sequence that is at least about 90% identical to the sequence set forth in SEQ ID No. 372.

46. The FLT3 binding domain of any one of claims 36-45, wherein the FLT3 binding domain binds to a human FLT3, a cynomolgus FLT3, or both.
47. An FLT3 binding domain that binds to a human FLT3 and to a cynomolgus FLT3 with identical affinities or affinities that differ by up to about 58-fold.
48. An FLT3 targeting trispecific protein comprising
(A) a first domain that binds a human CD3;
(B) a second domain that binds a human serum albumin protein; and
(C) a third domain that binds a human FLT3 or a cynomolgus FLT3,
wherein the domains are linked according to any one of the following orientations, from N-terminus to C-terminus: H₂N-(A)-(C)-(B)-COOH, H₂N-(B)-(A)-(C)-COOH, H₂N-(C)-(B)-(A)-COOH, H₂N-(C)-(A)-(B)-COOH, H₂N-(A)-(B)-(C)-COOH, or H₂N-(B)-(C)-(A)-COOH, or *via* linkers L1 and L2, from N-terminus to C-terminus: H₂N-(A)-L1-(C)-L2-(B)-COOH, H₂N-(B)-L1-(A)-L2-(C)-COOH, H₂N-(C)-L1-(B)-L2-(A)-COOH, H₂N-(C)-L1-(A)-L2-(B)-COOH, H₂N-(A)-L1-(B)-L2-(C)-COOH, or H₂N-(B)-L1-(C)-L2-(A)-COOH.
49. The FLT3 targeting trispecific protein of claim 48, wherein the first domain is an scFv that comprises a heavy chain comprising HC CDR1, HC CDR2, HC CDR3, and a light chain comprising LC CDR1, LC CDR2, or LC CDR3, wherein the HC CDR1 comprises the amino acid sequence of SEQ ID NO: 397 or an amino acid sequence comprising one or more substitutions in the sequence of SEQ ID NO: 397; the HC CDR2 comprises the amino acid sequence of SEQ ID NO: 398 or an amino acid sequence comprising one or more substitutions in the sequence of SEQ ID NO: 398; the HC CDR3 comprises the amino acid sequence of SEQ ID NO: 399 or an amino acid sequence comprising one or more substitutions in the sequence of SEQ ID NO: 399; the LC CDR1 comprises the amino acid sequence of SEQ ID NO: 400 or an amino acid sequence comprising one or more substitutions in the sequence of SEQ ID NO: 400; the LC CDR2 comprises the amino acid sequence of SEQ ID NO: 401 or an amino acid sequence comprising one or more substitutions in the sequence of SEQ ID NO: 401; and the LC CDR3 comprises the amino acid sequence of SEQ ID NO: 402 or an amino acid sequence comprising one or more substitutions in the sequence of SEQ ID NO: 402.
50. The FLT3 targeting trispecific protein of claim 48 or 49, wherein the first domain is an scFv that comprises an amino acid sequence that is at least about 90% identical to the sequence set forth in SEQ ID No. 373.
51. The FLT3 targeting trispecific protein of any one of claims 48-50, wherein the second domain is an sdAb that comprises a CDR1, a CDR2, and a CDR3, wherein the CDR1 comprises the amino acid sequence of SEQ ID NO: 403 or an amino acid sequence comprising one or more substitutions in the sequence of SEQ ID NO: 403; the CDR2 comprises the amino acid sequence

of SEQ ID NO: 404 or an amino acid sequence comprising one or more substitutions in the sequence of SEQ ID NO: 404; and the CDR3 comprises the amino acid sequence of SEQ ID NO: 405 or an amino acid sequence comprising one or more substitutions in the sequence of SEQ ID NO: 405.

52. The FLT3 targeting trispecific protein of any one of claims 48-51, wherein the second domain is an sdAb that comprises an amino acid sequence that is at least about 90% identical to the sequence set forth in SEQ ID No. 372.

53. The FLT3 targeting trispecific protein of any one of claims 48-52, wherein the third domain is an sdAb comprising at least three complementarity determining regions (a CDR1, a CDR2, and a CDR3), wherein

- the CDR1 comprises a sequence selected from the group consisting of SEQ ID Nos. 77-108, or a sequence comprising one or more amino acid substitutions in a sequence selected from the group consisting of SEQ ID Nos. 77-108;

- the CDR2 comprises a sequence selected from the group consisting of SEQ ID Nos. 109-154, and 393-394, or a sequence comprising one or more amino acid substitutions in a sequence selected from the group consisting of SEQ ID Nos. 109-154, and 393-394;

- the CDR3 comprises a sequence selected from the group consisting of SEQ ID Nos. 155-195, or a sequence comprising one or more amino acid substitutions in a sequence selected from the group consisting of SEQ ID Nos. 155-195.

54. The FLT3 targeting trispecific protein of any one of claims 48-53, wherein the third domain comprises at least one of the following set of sequences (the CDR1, the CDR2, and the CDR3):

- SEQ ID Nos. 77, 109, and 155;
- SEQ ID Nos. 78, 109, and 155;
- SEQ ID Nos. 79, 110, and 156;
- SEQ ID Nos. 80, 111, and 155;
- SEQ ID Nos. 81, 112, and 155;
- SEQ ID Nos. 77, 113, and 157;
- SEQ ID Nos. 82, 110, and 156;
- SEQ ID Nos. 77, 114, and 158;
- SEQ ID Nos. 80, 111, and 155;
- SEQ ID Nos. 83, 115, and 155;
- SEQ ID Nos. 84, 111, and 155;
- SEQ ID Nos. 79, 116, and 156;
- SEQ ID Nos. 85, 111, and 155;
- SEQ ID Nos. 86, 110, and 156;
- SEQ ID Nos. 87, 110, and 156;
- SEQ ID Nos. 88, 117, and 159;
- SEQ ID Nos. 88, 118, and 160;
- SEQ ID Nos. 88, 119, and 161;
- SEQ ID Nos. 88, 120, and 162;

SEQ ID Nos. 88, 121, and 163;
SEQ ID Nos. 88, 122, and 164;
SEQ ID Nos. 88, 121, and 165;
SEQ ID Nos. 88, 121, and 166;
SEQ ID Nos. 88, 122, and 167;
SEQ ID Nos. 88, 122, and 168;
SEQ ID Nos. 88, 121, and 169;
SEQ ID Nos. 88, 118, and 165;
SEQ ID Nos. 88, 123, and 170;
SEQ ID Nos. 88, 124, and 171;
SEQ ID Nos. 88, 117, and 172;
SEQ ID Nos. 89, 125, and 173;
SEQ ID Nos. 90, 126, and 174;
SEQ ID Nos. 90, 127, and 175;
SEQ ID Nos. 90, 125, and 176;
SEQ ID Nos. 90, 128, and 175;
SEQ ID Nos. 90, 128, and 177;
SEQ ID Nos. 91, 129, and 178;
SEQ ID Nos. 91, 130, and 178;
SEQ ID Nos. 92, 131, and 178;
SEQ ID Nos. 93, 132, and 178;
SEQ ID Nos. 94, 133, and 179;
SEQ ID Nos. 91, 134, and 178;
SEQ ID Nos. 95, 135, and 180;
SEQ ID Nos. 96, 136, and 181;
SEQ ID Nos. 97, 137, and 182;
SEQ ID Nos. 97, 138, and 183;
SEQ ID Nos. 98, 139, and 184;
SEQ ID Nos. 99, 139, and 185;
SEQ ID Nos. 100, 140, and 186;
SEQ ID Nos. 101, 141, and 187;
SEQ ID Nos. 102, 142, and 188;
SEQ ID Nos. 103, 143, and 189;
SEQ ID Nos. 104, 144, and 190;
SEQ ID Nos. 105, 145, and 191;
SEQ ID Nos. 106, 146, and 192;
SEQ ID Nos. 107, 147, and 193;
SEQ ID Nos. 108, 148, and 194;
SEQ ID Nos. 91, 149, and 195;
SEQ ID Nos. 91, 150, and 195;
SEQ ID Nos. 100, 151, and 186;
SEQ ID Nos. 92, 152, and 195;
SEQ ID Nos. 93, 153, and 195;
SEQ ID Nos. 91, 154, and 195;
SEQ ID Nos. 89, 393, and 173; and
SEQ ID Nos. 89, 394, and 173.

55. The FLT3 targeting trispecific protein of any one of claims 48-54, comprising a sequence selected from the group consisting of SEQ ID Nos. 196-272, and 391-392, or a

sequence that is at least about 80% identical to a sequence selected from the group consisting of SEQ ID NOs: 196-272, and 391-392.

56. An FLT3 targeting conditionally active binding protein comprising a binding moiety which comprises a non-CDR loop, a cleavable linker, an FLT3 binding domain, and a CD3 binding domain, wherein the non-CDR loop is capable of binding to the FLT3 binding domain, and wherein the binding moiety is capable of masking the binding of the FLT3 binding domain to its target.

57. The FLT3 targeting trispecific protein of claim 56, wherein the CD3 binding domain is an scFv that comprises a heavy chain comprising HC CDR1, HC CDR2, HC CDR3, and a light chain comprising LC CDR1, LC CDR2, or LC CDR3, wherein the HC CDR1 comprises the amino acid sequence of SEQ ID NO: 397 or an amino acid sequence comprising one or more substitutions in the sequence of SEQ ID NO: 397; the HC CDR2 comprises the amino acid sequence of SEQ ID NO: 398 or an amino acid sequence comprising one or more substitutions in the sequence of SEQ ID NO: 398; the HC CDR3 comprises the amino acid sequence of SEQ ID NO: 399 or an amino acid sequence comprising one or more substitutions in the sequence of SEQ ID NO: 399; the LC CDR1 comprises the amino acid sequence of SEQ ID NO: 400 or an amino acid sequence comprising one or more substitutions in the sequence of SEQ ID NO: 400; the LC CDR2 comprises the amino acid sequence of SEQ ID NO: 401 or an amino acid sequence comprising one or more substitutions in the sequence of SEQ ID NO: 401; and the LC CDR3 comprises the amino acid sequence of SEQ ID NO: 402 or an amino acid sequence comprising one or more substitutions in the sequence of SEQ ID NO: 402.

58. The FLT3 targeting conditionally active binding protein of claim 56 or 57, wherein the CD3 binding domain is an scFv that comprises an amino acid sequence that is at least about 90% identical to the sequence set forth in SEQ ID No. 373.

59. The FLT3 targeting conditionally active binding protein of any claim 56-58, wherein the FLT3 binding domain is an sdAb comprising at least three complementarity determining regions (a CDR1, a CDR2, and a CDR3), wherein

- the CDR1 comprises a sequence selected from the group consisting of SEQ ID Nos. 77-108, or a sequence comprising one or more amino acid substitutions in a sequence selected from the group consisting of SEQ ID Nos. 77-108;

- the CDR2 comprises a sequence selected from the group consisting of SEQ ID Nos. 109-154, and 393-394, or a sequence comprising one or more amino acid substitutions in a sequence selected from the group consisting of SEQ ID Nos. 109-154, and 393-394;

– the CDR3 comprises a sequence selected from the group consisting of SEQ ID Nos. 155-195, or a sequence comprising one or more amino acid substitutions in a sequence selected from the group consisting of SEQ ID Nos. 155-195.

60. The FLT3 targeting conditionally active binding protein of any one of claims 56-59, wherein the FLT3 binding domain comprises at least one of the following set of sequences (the CDR1, the CDR2, and the CDR3):

SEQ ID Nos. 77, 109, and 155;
SEQ ID Nos. 78, 109, and 155;
SEQ ID Nos. 79, 110, and 156;
SEQ ID Nos. 80, 111, and 155;
SEQ ID Nos. 81, 112, and 155;
SEQ ID Nos. 77, 113, and 157;
SEQ ID Nos. 82, 110, and 156;
SEQ ID Nos. 77, 114, and 158;
SEQ ID Nos. 80, 111, and 155;
SEQ ID Nos. 83, 115, and 155;
SEQ ID Nos. 84, 111, and 155;
SEQ ID Nos. 79, 116, and 156;
SEQ ID Nos. 85, 111, and 155;
SEQ ID Nos. 86, 110, and 156;
SEQ ID Nos. 87, 110, and 156;
SEQ ID Nos. 88, 117, and 159;
SEQ ID Nos. 88, 118, and 160;
SEQ ID Nos. 88, 119, and 161;
SEQ ID Nos. 88, 120, and 162;
SEQ ID Nos. 88, 121, and 163;
SEQ ID Nos. 88, 122, and 164;
SEQ ID Nos. 88, 121, and 165;
SEQ ID Nos. 88, 121, and 166;
SEQ ID Nos. 88, 122, and 167;
SEQ ID Nos. 88, 122, and 168;
SEQ ID Nos. 88, 121, and 169;
SEQ ID Nos. 88, 118, and 165;
SEQ ID Nos. 88, 123, and 170;
SEQ ID Nos. 88, 124, and 171;
SEQ ID Nos. 88, 117, and 172;
SEQ ID Nos. 89, 125, and 173;
SEQ ID Nos. 90, 126, and 174;
SEQ ID Nos. 90, 127, and 175;
SEQ ID Nos. 90, 125, and 176;
SEQ ID Nos. 90, 128, and 175;
SEQ ID Nos. 90, 128, and 177;
SEQ ID Nos. 91, 129, and 178;
SEQ ID Nos. 91, 130, and 178;
SEQ ID Nos. 92, 131, and 178;
SEQ ID Nos. 93, 132, and 178;
SEQ ID Nos. 94, 133, and 179;
SEQ ID Nos. 91, 134, and 178;
SEQ ID Nos. 95, 135, and 180;

SEQ ID Nos. 96, 136, and 181;
SEQ ID Nos. 97, 137, and 182;
SEQ ID Nos. 97, 138, and 183;
SEQ ID Nos. 98, 139, and 184;
SEQ ID Nos. 99, 139, and 185;
SEQ ID Nos. 100, 140, and 186;
SEQ ID Nos. 101, 141, and 187;
SEQ ID Nos. 102, 142, and 188;
SEQ ID Nos. 103, 143, and 189;
SEQ ID Nos. 104, 144, and 190;
SEQ ID Nos. 105, 145, and 191;
SEQ ID Nos. 106, 146, and 192;
SEQ ID Nos. 107, 147, and 193;
SEQ ID Nos. 108, 148, and 194;
SEQ ID Nos. 91, 149, and 195;
SEQ ID Nos. 91, 150, and 195;
SEQ ID Nos. 100, 151, and 186;
SEQ ID Nos. 92, 152, and 195;
SEQ ID Nos. 93, 153, and 195;
SEQ ID Nos. 91, 154, and 195;
SEQ ID Nos. 89, 393, and 173; and
SEQ ID Nos. 89, 394, and 173.

61. A pharmaceutical composition comprising an FLT3 binding domain according to any one of claims 1-47, and a pharmaceutically acceptable carrier.
62. A pharmaceutical composition comprising an FLT3 targeting trispecific protein according to any one of claims 48-55, and a pharmaceutically acceptable carrier.
63. A pharmaceutical composition comprising an FLT3 targeting conditionally active binding protein according to any one of claims 56-60, and a pharmaceutically acceptable carrier.
64. A process for the production of an FLT3 binding domain according to any one of claims 1-47, said process comprising culturing a host transformed or transfected with a vector comprising a nucleic acid sequence encoding the FLT3 binding domain according to any one of claims 1-47 under conditions allowing the expression of the FLT3 binding domain and recovering and purifying the produced protein from the culture.
65. A process for the production of an FLT3 targeting trispecific protein according to any one of claims 48-55, said process comprising culturing a host transformed or transfected with a vector comprising a nucleic acid sequence encoding the FLT3 targeting trispecific protein according to any one of claims 48-55 under conditions allowing the expression of the FLT3 targeting trispecific protein and recovering and purifying the produced protein from the culture.
66. A process for the production of an FLT3 targeting conditionally active binding protein according to any one of claims 56-60, said process comprising culturing a host transformed or transfected with a vector comprising a nucleic acid sequence encoding the FLT3 targeting

conditionally active binding protein according to any one of claims 56-60 under conditions allowing the expression of the FLT3 targeting conditionally active binding protein and recovering and purifying the produced protein from the culture.

67. A method for the treatment or amelioration of a proliferative disease, or a tumorous disease, comprising the administration of an FLT3 binding domain according to any one of claims 1-47, or a pharmaceutical composition according to claim 61, to a subject in need thereof.

68. A method for the treatment or amelioration of a proliferative disease, or a tumorous disease, comprising the administration of an FLT3 targeting trispecific protein according to any one of claims 48-55, or a pharmaceutical composition according to claim 62, to a subject in need thereof.

69. A method for the treatment or amelioration of a proliferative disease, or a tumorous disease, comprising the administration of an FLT3 targeting conditionally active binding protein according to any one of claims 56-60, or a pharmaceutical composition according to claim 63, to a subject in need thereof.

70. The method of any one of claims 67-69, wherein the subject is human.

71. The method of claim 69, wherein the method further comprises administration of an agent in combination with an FLT3 binding domain according to any one of claims 1-47, an FLT3 targeting trispecific protein according to any one of claims 48-55, an FLT3 targeting conditionally active binding protein according to any one of claims 56-60, or a pharmaceutical composition according to any one of claims 61-63.

72. The method of any one of claims 67-71, wherein the tumorous disease comprises a hematologic malignancy.

73. The method of claim 72, wherein hematologic malignancy comprises an acute myeloid leukemia (AML), myelodysplastic syndrome, or chronic myelomonocytic leukemia.

74. The method of any one of claims 67-71, wherein the tumorous disease is selected from the group consisting of: acute leukemia (ALL), acute myelogenous leukemia (AML), myeloid leukemia, chronic lymphocytic leukemia (CLL), and chronic myelogenous leukemia (CML), chronic myelomonocytic leukemia, undifferentiated AML (MO), myeloblastic leukemia (M1), myeloblastic leukemia (M2; with cell maturation), promyelocytic leukemia (M3 or M3 variant [M3V]), myelomonocytic leukemia (M4 or M4 variant with eosinophilia [M4E]), monocytic leukemia (M5), erythroleukemia (M6), megakaryoblastic leukemia (M7), isolated granulocytic sarcoma, and chloroma; lymphomas, such as Hodgkin's lymphoma (HL), non-Hodgkin's lymphoma (NEIL), B-cell lymphomas, T-cell lymphomas, lymphoplasmacytoid lymphoma, monocytoid B-cell lymphoma, mucosa-associated lymphoid tissue (MALT) lymphoma, anaplastic (*e.g.*, Ki 1+) large-cell lymphoma, adult T-cell lymphoma/leukemia, mantle cell

lymphoma, angio immunoblastic T-cell lymphoma, angiocentric lymphoma, intestinal T-cell lymphoma, primary mediastinal B-cell lymphoma, precursor T-lymphoblastic lymphoma, T-lymphoblastic; and lymphoma/leukemia (T-Lbly/T-ALL), peripheral T-cell lymphoma, lymphoblastic lymphoma, post-transplantation lymphoproliferative disorder, true histiocytic lymphoma, primary central nervous system lymphoma, primary effusion lymphoma, lymphoblastic lymphoma (LBL), hematopoietic tumors of lymphoid lineage, acute lymphoblastic leukemia, diffuse large B-cell lymphoma, Burkitt's lymphoma, marginal zone lymphoma, nodal marginal zone B cell lymphoma, splenic marginal zone lymphoma, follicular lymphoma, diffuse histiocytic lymphoma (DHL), mucosa-associated lymphatic tissue lymphoma, small cell lymphocytic lymphoma, immunoblastic large cell lymphoma, precursor B-lymphoblastic lymphoma, cutaneous T-cell lymphoma (CTLC) (also called mycosis fungoides or Sezary syndrome), intravascular large B-cell lymphoma, lymphomatoid granulomatosis, T cell/histiocyte-rich large B-cell lymphoma, primary cutaneous diffuse large B-cell lymphoma (leg type), EBV positive diffuse large B-cell lymphoma of the elderly, diffuse large B-cell lymphoma associated with inflammation, intravascular large B-cell lymphoma, ALK-positive large B-cell lymphoma, plasmablastic lymphoma, large B-cell lymphoma arising in HHV8-associated multicentric Castleman disease, B-cell lymphoma unclassified with features intermediate between diffuse large B-cell lymphoma and Burkitt lymphoma, B-cell lymphoma unclassified with features intermediate between diffuse large B-cell lymphoma and classical Hodgkin lymphomalymphoplasmacytic lymphoma, and lymphoplasmacytoid lymphoma (LPL) with Waldenstrom's macroglobulinemia; myelomas, such as IgG myeloma, light chain myeloma, nonsecretory myeloma, smoldering myeloma (also called indolent myeloma), solitary plasmacytoma, and multiple myelomas, chronic lymphocytic leukemia (CLL), hairy cell lymphoma; hematopoietic tumors of myeloid lineage, tumors of mesenchymal origin, including fibrosarcoma and rhabdomyosarcoma; seminoma, teratocarcinoma, tumors of the central and peripheral nervous, including astrocytoma, schwannomas; tumors of mesenchymal origin, including fibrosarcoma, rhabdomyosarcoma, and osteosarcoma; and other tumors, including melanoma, xeroderma pigmentosum, keratoacanthoma, seminoma, thyroid follicular cancer and teratocarcinoma, hematopoietic tumors of lymphoid lineage, for example T-cell and B-cell tumors, including but not limited to T-cell disorders such as T-prolymphocytic leukemia (T-PLL), including of the small cell and cerebriform cell type; large granular lymphocyte leukemia (LGL) preferably of the T-cell type; a/d T-NHL hepatosplenic lymphoma; peripheral/post-thymic T cell lymphoma (pleomorphic and immunoblastic subtypes); angiocentric (nasal) T-cell lymphoma; cancer of the head or neck, renal cancer, rectal cancer, cancer of the thyroid gland; acute myeloid lymphoma, as well as any combinations thereof.