

SUMMARY

[0004a] One embodiment provides a 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. 91, 89, and 100, or a sequence comprising one or more amino acid substitutions in a sequence selected from the group consisting of SEQ ID NOs. 91, 89, and 100; the CDR2 comprises a sequence selected from the group consisting of SEQ ID NOs. 149, 151, 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, 151, 393, and 394; the CDR3 comprises a sequence selected from the group consisting of SEQ ID NOs. 195, 173, and 186, or a sequence comprising one or more amino acid substitutions in a sequence selected from the group consisting of SEQ ID NOs. 195, 173, and 186.

[0004b] One embodiment provides a 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 CDR1 comprises a sequence selected from the group consisting of SEQ ID NOs. 91, 89, and 100, or a sequence comprising one or more amino acid substitutions in a sequence selected from the group consisting of SEQ ID NOs. 91, 89, and 100; the CDR2 comprises a sequence selected from the group consisting of SEQ ID NOs. 149, 151, 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, 151, 393, and 394; the CDR3 comprises a sequence selected from the group consisting of SEQ ID NOs. 195, 173, and 186, or a sequence comprising one or more amino acid substitutions in a sequence selected from the group consisting of SEQ ID Nos. 195, 173, and 186.

[0004c] One embodiment provides pharmaceutical composition comprising the FLT3 binding domain as described herein or the FLT3 targeting trispecific protein as described herein, and a pharmaceutically acceptable carrier.

[0004d] One embodiment provides a use of an FLT3 binding domain in the manufacture of a medicament for the treatment of cancer, wherein the FLT3 binding domain is to be administered to a subject in need thereof, wherein 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. 91, 89, and 100, or a sequence comprising one or more amino acid substitutions in a sequence selected from the group consisting of SEQ ID NOs. 91, 89, and 100; the CDR2 comprises a sequence selected from the group consisting of SEQ ID NOs. 149, 151, 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, 151, 393, and 394; the CDR3 comprises a sequence selected from the group consisting of SEQ ID NOs. 195, 173, and 186, or a sequence comprising one or more amino acid substitutions in a sequence selected from the group consisting of SEQ ID NOs. 195, 173, and 186.

[0004e] One embodiment provides a use of an FLT3 targeting trispecific protein in the manufacture of a medicament for the treatment of cancer, wherein the FLT3 targeting trispecific protein is to be administered to a subject in need thereof; wherein the FLT3 targeting trispecific protein comprises (A) a first domain that binds to a human CD3; (B) a second domain that binds to a human serum albumin protein; and (C) a third domain that binds to a human FLT3, wherein the CDR1 comprises a sequence selected from the group consisting of SEQ ID NOs. 91, 89, and 100, or a sequence comprising one or more amino acid substitutions in a sequence selected from the group consisting of SEQ ID NOs. 91, 89, and 100; the CDR2 comprises a sequence selected from the group consisting of SEQ ID NOs. 149, 151, 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, 151, 393, and 394; the CDR3 comprises a sequence selected from the group consisting of SEQ ID NOs. 195, 173, and 186, or a sequence comprising one or more amino acid substitutions in a sequence selected from the group consisting of SEQ ID NOs. 195, 173, and 186.

[0004f] One embodiment provides 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. 91, 89, and 100, or a sequence comprising one or more amino acid substitutions in a sequence selected from the group consisting of SEQ ID NOs. 91, 89, and 100; the CDR2 comprises a sequence selected from the group consisting of SEQ ID NOs. 149, 151, 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, 151, 393, and 394; the CDR3 comprises a sequence selected from the group consisting of SEQ ID NOs. 195, 173, and 186, or a sequence comprising one or more amino acid substitutions in a sequence selected from the group consisting of SEQ ID NOs. 195, 173, and 186, or an FLT3 targeting trispecific protein comprising (A) a first domain that binds to a human CD3; (B) a second domain that binds to a human serum albumin protein; and (C) a third domain that binds to a human FLT3, wherein the CDR1 comprises a sequence selected from the group consisting of SEQ ID NOs. 91, 89, and 100, or a sequence comprising one or more amino acid substitutions in a sequence selected from the group consisting of SEQ ID NOs. 91, 89, and 100; the CDR2 comprises a sequence selected from the group consisting of SEQ ID NOs. 149, 151,

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, 151, 393, and 394; the CDR3 comprises a sequence selected from the group consisting of SEQ ID NOs. 195, 173, and 186, or a sequence comprising one or more amino acid substitutions in a sequence selected from the group consisting of SEQ ID NOs. 195, 173, and 186, for use in therapy.

[0005] One embodiment provides 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. In some embodiments, 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;

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. 91, ~~77-108~~89, and 100, or a sequence comprising one or more amino acid substitutions in a sequence selected from the group consisting of SEQ ID Nos. 91, ~~77-108~~89, and 100;

—the CDR2 comprises a sequence selected from the group consisting of SEQ ID Nos. ~~109-154~~149, 151, and 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. ~~109-154~~149, 151, and 393, and -394;

—the CDR3 comprises a sequence selected from the group consisting of SEQ ID Nos. 195, ~~155-173~~, and 186, or a sequence comprising one or more amino acid substitutions in a sequence selected from the group consisting of SEQ ID Nos. 195, ~~155-173~~, and 186.

~~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.~~

~~3.2.~~ 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. 91, 149, and 195
SEQ ID NOs. 89, 393, and 173;
SEQ ID NOs. 89, 394, and 173; and
SEQ ID NOs. 100, 151, and 186.

~~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.~~

~~6.3.~~ 3. The FLT3 binding domain of claim ~~5~~1 or 2, comprising a sequence that is at least about ~~70~~80% identical to a sequence selected from the group consisting of SEQ ID NOs. 71, ~~-73~~6, and 389, ~~and~~ -390.

~~7.4.~~ 4. The FLT3 binding domain of any one of claims 1-~~6~~3, wherein the FLT3 binding domain is an antibody or an antigen binding fragment thereof.

~~8.5.~~ 5. The FLT3 binding domain of claim ~~7~~4, 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 hcIgG, 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.

~~9.6.~~ 6. The FLT3 binding domain of claim ~~8~~5, wherein the FLT3 binding domain is the sdAb.

~~10.7.~~ 7. The FLT3 binding domain of any one of claims 1-~~6~~3, wherein the FLT3 binding domain is part of an antibody or an antigen binding fragment thereof.

~~11.8.~~ 8. The FLT3 binding domain of claim ~~10~~7, 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.

~~12.9.~~ 12.9. The FLT3 binding domain of claim ~~8~~14, 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.

~~13.10.~~ 13.10. The FLT3 binding domain of claim ~~12~~9, wherein the bispecific antibody comprises (i) the FLT3 binding domain (anti-FLT3) and (ii) a CD3 binding domain.

~~14.11.~~ 14.11. The FLT3 binding domain of claim ~~13~~10, wherein the CD3 comprises a human CD3.

~~15.12.~~ 15.12. The FLT3 binding domain of claim ~~13~~10 or ~~14~~11, wherein the anti-FLT3 domain is an sdAb.

~~16.13.~~ 16.13. The FLT3 binding domain of any one of claims ~~13~~10-~~15~~12, wherein the anti-CD3 domain is an scFv.

~~17.14.~~ 17.14. The FLT3 binding domain of claim ~~14~~8, 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.

~~18.15.~~ 18.15. The FLT3 binding domain of claim ~~17~~14, 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.~~ 19. The FLT3 binding domain of any one of claims ~~18~~15-17, wherein the CD3 comprises a human CD3.

~~20.16. The FLT3 binding domain of claim 18 or 19, wherein the albumin comprises a serum albumin.~~

~~21.17.~~ 21.17. The FLT3 binding domain of any one of claims ~~20~~15-20, wherein the ~~serum~~ albumin comprises a human serum albumin.

~~22.18.~~ 22.18. The FLT3 binding domain of any one of claims ~~18~~15-21~~7~~, wherein the FLT3 binding domain (anti-FLT3), the CD3 binding domain (anti-CD3), and the albumin binding domain (anti-ALB) are in an 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.~~19. The FLT3 binding domain of any one of claims ~~18~~15-~~18~~22, wherein the anti-FLT3 domain is an sdAb.

~~24.~~20. The FLT3 binding domain of any one of claims ~~18~~15-~~23~~19, wherein the anti-CD3 domain is an scFv.

~~25.~~21. The FLT3 binding domain of any one of claims ~~18~~15-~~24~~20, wherein the anti-ALB domain is an sdAb.

~~26.~~22. The FLT3 binding domain of any one of claims ~~18~~15-~~25~~21, 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 ~~e~~e. 373.

~~27.~~23. The FLT3 binding domain of any one of claims ~~18~~15-~~26~~22, 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 ~~e~~e. 372.

24. The FLT3 binding domain of any one of claims 15-23, wherein the FLT3 binding domain is part of the multispecific antibody, wherein the multispecific antibody comprises a sequence that is at least 80% identical to a sequence selected from the group consisting of SEQ ID NOs. 267, 269, 391, and 392.

~~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 (EC₅₀) of at least about 0.5 pM to about 6000 pM in a T-cell dependent cellular cytotoxicity assay, wherein the assay measures the EC₅₀ 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 an 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.~~

~~47.25. 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.~~

~~48.26. 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. 91, 77-10889, and 100, or a sequence comprising one or more amino acid substitutions in a sequence selected from the group consisting of SEQ ID Nos. 91, 77-10889, and 100;~~

~~—the CDR2 comprises a sequence selected from the group consisting of SEQ ID Nos. 109-154149, 151, and 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. 109-154149, 151, and 393, and 394;~~

~~—the CDR3 comprises a sequence selected from the group consisting of SEQ ID Nos. 195, 155-173, and 186, or a sequence comprising one or more amino acid substitutions in a sequence selected from the group consisting of SEQ ID Nos. 195, 173, and 18655.~~

~~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.~~

~~57-27.~~ The FLT3 targeting trispecific protein of claim 5626, wherein the CD3-bindingfirst 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.

~~58-28.~~ The FLT3 targeting trispecific protein targeting conditionally active binding protein of claim 56-26 or 5727, 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.

29. The FLT3 targeting trispecific protein of any one of claims 26-28, 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.

30. The FLT3 targeting trispecific protein of any one of claims 26-29, 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.

~~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.~~31. A pharmaceutical composition comprising ~~the~~an FLT3 binding domain according to any one of claims 1-~~47~~25 or the FLT3 targeting trispecific protein according to any one of claims 26-30, 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.~~

32. Use of an FLT3 binding domain in the manufacture of a medicament for the treatment of cancer, wherein the FLT3 binding domain is to be administered to a subject in need thereof,
wherein 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. 91, 89, and 100, or a sequence comprising one or more amino acid substitutions in a sequence selected from the group consisting of SEQ ID NOs. 91, 89, and 100;
the CDR2 comprises a sequence selected from the group consisting of SEQ ID NOs. 149, 151, 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, 151, 393, and 394;
the CDR3 comprises a sequence selected from the group consisting of SEQ ID NOs. 195, 173, and 186, or a sequence comprising one or more amino acid substitutions in a sequence selected from the group consisting of SEQ ID NOs. 195, 173, and 186.

33. The use of claim 32, wherein the FLT3 binding domain comprises a sequence that is at least about 80% identical to a sequence selected from the group consisting of SEQ ID NOs. 71, 73, 389, and 390.

34. Use of ~~A~~an FLT3 targeting trispecific protein in the manufacture of a medicament for ~~method for the treatment or amelioration of a cancer~~proliferative disease, or a tumorous disease,
wherein the ~~comprising the an~~ FLT3 targeting trispecific protein is to be administered ~~binding domain according to any one of claims 1-47, or a pharmaceutical composition according to claim 61,~~
to a subject in need thereof;
wherein the FLT3 targeting trispecific protein comprises
(A) a first domain that binds to a human CD3;
(B) a second domain that binds to a human serum albumin protein; and
(C) a third domain that binds to a human FLT3,
~~67.~~ wherein the CDR1 comprises a sequence selected from the group consisting of SEQ ID NOs. 91, 89, and 100, or a sequence comprising one or more amino acid substitutions in a sequence selected from the group consisting of SEQ ID NOs. 91, 89, and 100; the CDR2 comprises a sequence selected from the group consisting of SEQ ID NOs. 149, 151, 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, 151, 393, and 394; the CDR3 comprises a sequence selected from the group consisting of SEQ ID NOs. 195, 173, and 186, or a sequence comprising one or more amino acid substitutions in a sequence selected from the group consisting of SEQ ID NOs. 195, 173, and 186.

35. The use of any one of claims 32-34, wherein the cancer comprises a hematologic malignancy.

36. The use of claim 34 or 35, wherein the third domain comprises an amino acid sequence that is at least 80% identical to a sequence selected from the group consisting of SEQ ID NOs. 71, 73, 389, and 390.

37. The use of any one of claims 34-36, wherein the trispecific protein comprises an amino acid sequence that is at least 80% identical to a sequence selected from the group consisting of SEQ ID NOs. 267, 269, 391, and 392.

~~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 use of any one of claims 35-37,~~The method of claim 72,~~ wherein hematologic malignancy comprises an acute myeloid leukemia (AML), a myelodysplastic syndrome, or a chronic myelomonocytic leukemia.

38. 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 (M0), 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 (NHL), 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, angioimmunoblastic 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 (CTCL) (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 lymphoma, lymphoplasmacytic 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 plasmocytoma, 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.~~

39. 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. 91, 89, and 100, or a sequence comprising one or more amino acid substitutions in a sequence selected from the group consisting of SEQ ID NOs. 91, 89, and 100;

the CDR2 comprises a sequence selected from the group consisting of SEQ ID NOs. 149, 151, 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, 151, 393, and 394;

the CDR3 comprises a sequence selected from the group consisting of SEQ ID NOs. 195, 173, and 186, or a sequence comprising one or more amino acid substitutions in a sequence selected from the group consisting of SEQ ID NOs. 195, 173, and 186, or

an FLT3 targeting trispecific protein comprising

(A) a first domain that binds to a human CD3;

(B) a second domain that binds to a human serum albumin protein; and

(C) a third domain that binds to a human FLT3,

wherein the CDR1 comprises a sequence selected from the group consisting of SEQ ID NOs. 91, 89, and 100, or a sequence comprising one or more amino acid substitutions in a sequence selected from the group consisting of SEQ ID NOs. 91, 89, and 100; the CDR2 comprises a sequence selected from the group consisting of SEQ ID NOs. 149, 151, 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, 151, 393, and 394; the CDR3 comprises a sequence selected from the group consisting of SEQ ID NOs. 195, 173, and 186, or a sequence comprising one or more amino acid substitutions in a sequence selected from the group consisting of SEQ ID NOs. 195, 173, and 186, for use in therapy.