

FLT3 BINDING PROTEINS AND METHODS OF USE**CROSS-REFERENCE**

[0001] This application claims the benefit of U.S. Provisional Application No. 62/980,051 filed on February 21, 2020, which is incorporated by reference herein in its entirety.

SEQUENCE LISTING

[0002] The instant application contains a Sequence Listing which has been submitted electronically in ASCII format and is hereby incorporated by reference in its entirety. Said ASCII copy, created on February 19, 2021, is named 47517-744_601_SL.txt and is 532,727 bytes in size.

INCORPORATION BY REFERENCE

[0003] All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication, patent, or patent application was specifically and individually indicated to be incorporated by reference.

BACKGROUND

[0004] FMS-like tyrosine kinase 3 (FLT3) is a type I transmembrane protein that plays an essential role in normal hematopoiesis and is physiologically expressed on normal hematopoietic stem cells (HSCs), as well as lymphoid, myeloid and granulocyte/macrophage progenitor cells in humans, and are believed to play an important role in early hematopoiesis. In mature hematopoietic cells, FLT3 expression has been reported in subsets of dendritic cells and natural killer cells. Due to its important role in regulating survival, proliferation, and differentiation of hematopoietic cells (B and T cells), aberrant FLT3 activity is involved in the development and progression of cancers of the hematopoietic system. For example, internal tandem duplications of FLT3 are the most common mutations associated with acute myelogenous leukemia (AML). FLT3 is also present on malignant blasts in AML, providing a target for antibody and cellular immunotherapy¹. As such, there is a need for therapies, *e.g.*, antibodies, that can specifically target and destroy cells that overexpress FLT3. Further, there is a need for a greater choice of treatment options which allows physicians to select the therapeutic with the best side effect profile for an individual patient. The present disclosure provides novel polypeptides and protein therapeutics useful in methods of treatment, particularly for treatment of conditions associated with abnormal expression of FLT3.

SUMMARY

[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;

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.

[0006] In some embodiments, the FLT3 binding domain comprises 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.

[0007] In some embodiments, 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. In some embodiments, the FLT3 binding domain comprises 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. In some embodiments, the FLT3 binding domain comprises 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. In some embodiments, the FLT3 binding domain comprises the FLT3 binding domain is an antibody or an antigen binding fragment thereof. In some embodiments, 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. In some embodiments, the FLT3 binding domain is the sdAb. In some embodiments, the FLT3 binding domain is part of an antibody or an antigen binding fragment thereof. In some embodiments, 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. In some embodiments, 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.

[0008] In some embodiments, the FLT3 binding domain comprises the bispecific antibody comprises (i) the FLT3 binding domain (anti-FLT3) and (ii) a CD3 binding domain. In some embodiments, the FLT3 binding domain comprises the CD3 comprises a human CD3. In some embodiments, the anti-FLT3 domain is an sdAb. In some embodiments, the anti-CD3 domain is an scFv. In some embodiments, 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. In some embodiments, 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). In some embodiments, the CD3 comprises a human CD3. In some embodiments, the albumin comprises a serum albumin. In some embodiments, the serum albumin is a human serum albumin. In some embodiments, 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.

[0009] In some embodiments, the anti-FLT3 domain is an sdAb. In some embodiments, the anti-CD3 domain is an scFv. In some embodiments, the anti-ALB domain is an sdAb. In some embodiments, 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. In some embodiments, 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. In some embodiments, the FLT3 binding domain binds to human FLT3 and cynomolgus FLT3.

[0010] One embodiment provides 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. In some embodiments, the FLT-3 expressing cells are leukemia cells. In some embodiments, the leukemia cells are from a cell line, wherein the cell line is MV-4-11, EOL1, THP1, MOLM3, or HL60. In some embodiments, the FLT3 binding domain comprises 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.

[0011] In some embodiments, the FLT3 binding domain comprises 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.

[0012] In some embodiments, the FLT3 binding domain comprises 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.

In some embodiments, the FLT3 binding domain is part of a multispecific antibody. In some embodiments, 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). In some embodiments, the CD3 comprises a human CD3. In some embodiments, the albumin comprises a serum albumin. In some embodiments, the serum albumin is a human serum albumin. In some embodiments, 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.

[0013] In some embodiments, the anti-FLT3 domain is an sdAb. In some embodiments, anti-CD3 domain is an scFv. In some embodiments, the anti-ALB domain is an sdAb. In some embodiments, 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. In some embodiments, 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. In some embodiments, the FLT3 binding domain binds to a human FLT3, a cynomolgus FLT3, or both.

[0014] One embodiment provides 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.

One embodiment provides 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.

[0015] In some embodiments, 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.

[0016] In some embodiments, 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.

In some embodiments, 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.

[0017] In some embodiments, 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.

In some embodiments, 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.

[0018] In some embodiments, 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.

[0019] In some embodiments, the FLT3 targeting trispecific protein comprises 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. One embodiment provides 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.

[0020] In some embodiments, 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.

[0021] In some embodiments, 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.

In some embodiments, 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.

[0022] In some embodiments, 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.

[0023] One embodiment provides a pharmaceutical composition comprising an FLT3 binding domain according to this disclosure, and a pharmaceutically acceptable carrier.

One embodiment provides a pharmaceutical composition comprising an FLT3 targeting trispecific protein according to this disclosure, and a pharmaceutically acceptable carrier.

[0024] One embodiment provides a pharmaceutical composition comprising an FLT3 targeting conditionally active binding protein according to this disclosure, and a pharmaceutically acceptable carrier.

[0025] One embodiment provides a process for the production of an FLT3 binding domain according to any this disclosure, said process comprising culturing a host transformed or transfected with a vector comprising a nucleic acid sequence encoding the FLT3 binding domain according to this disclosure under conditions allowing the expression of the FLT3 binding domain and recovering and purifying the produced protein from the culture.

[0026] One embodiment provides a process for the production of an FLT3 targeting trispecific protein according to this disclosure, 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 this disclosure under conditions allowing the expression of the FLT3 targeting trispecific protein and recovering and purifying the produced protein from the culture.

One embodiment provides a process for the production of an FLT3 targeting conditionally active binding protein according to this disclosure, 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 this disclosure under conditions allowing the expression of the FLT3 targeting conditionally active binding protein and recovering and purifying the produced protein from the culture.

[0027] One embodiment provides 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 this disclosure, or a pharmaceutical composition according to this disclosure, to a subject in need thereof. One embodiment provides 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 this disclosure, or a pharmaceutical composition according to this disclosure, to a subject in need thereof. One embodiment provides 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 this disclosure, or a pharmaceutical composition according to claim this disclosure, to a subject in need thereof. In some embodiments, the subject is human. In some embodiments, the method further comprises administration of an agent in combination with an FLT3 binding domain according to this disclosure, an FLT3 targeting trispecific protein according to this disclosure, an

FLT3 targeting conditionally active binding protein according to this disclosure, or a pharmaceutical composition according to this disclosure. In some embodiments, the tumorous disease comprises a hematologic malignancy. In some embodiments, the hematologic malignancy comprises an acute myeloid leukemia (AML), myelodysplastic syndrome, or chronic myelomonocytic leukemia. In some embodiments, 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 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.

[0028] 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. 89, 91, 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, 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. 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.

[0029] In some embodiments, the FLT3 binding domain comprises 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.

[0030] In some embodiments, the FLT3 binding 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. In some embodiments, the FLT3 binding domain comprises an amino acid sequence selected from the group consisting of SEQ ID Nos. 71, 73, 389, and 390. In some

embodiments, the FLT3 binding domain is a single domain antibody (sdAb). In some embodiments, the FLT3 binding domain is part of an antibody or an antigen binding fragment thereof. In some embodiments, the FLT3 binding domain comprises is part of the antibody or an antigen binding fragment thereof and wherein the antibody or an antigen binding fragment thereof comprises a bispecific antibody. In some embodiments, the bispecific antibody comprises (i) the FLT3 binding domain (anti-FLT3) and (ii) a CD3 binding domain (anti-CD3). In some embodiments, the anti-CD3 domain is a single chain variable fragment (scFv). In some embodiments, the CD3 comprises a human CD3. In some embodiments, 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 a multispecific antibody. In some embodiments, 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). In some embodiments, the anti-CD3 domain is an scFv. In some embodiments, the anti-CD3 domain comprises an amino acid sequence that is at least 90% identical to the sequence of SEQ ID No. 373. In some embodiments, the CD3 comprises a human CD3. In some embodiments, the anti-ALB domain is an sdAb. In some embodiments, the anti-ALB domain comprises an amino acid sequence that is at least 90% identical to the sequence of SEQ ID No. 372. In some embodiments, the albumin comprises a human serum albumin.

[0031] In some embodiments, 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.

[0032] In some embodiments, 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. In some embodiments, the FLT3 binding domain binds to human FLT3.

[0033] One embodiment provides 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,

wherein the CDR1 comprises a sequence selected from the group consisting of SEQ ID Nos. 89, 91, 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, 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; and 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.

[0034] In some embodiments, 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.

[0035] In some embodiments, the first domain is an scFv that comprises an amino acid sequence that is at least 90% identical to the sequence set forth in SEQ ID No. 373. In some embodiments, the FLT3 targeting trispecific protein of claim 22, 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.

[0036] In some embodiments, the FLT3 targeting trispecific protein of claim 25, wherein the second domain is an sdAb that comprises an amino acid sequence that is at least 90% identical to the sequence set forth in SEQ ID No. 372.

[0037] One embodiment provides a method of treating a hematologic malignancy, the method comprising administering to a subject in need thereof 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,

wherein the CDR1 comprises a sequence selected from the group consisting of SEQ ID Nos. 89, 91, 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, 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. 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. In some embodiments, 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. In some embodiments, 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. In some embodiments, the hematologic malignancy comprises an acute myeloid leukemia (AML), a myelodysplastic syndrome, or a chronic myelomonocytic leukemia.

BRIEF DESCRIPTION OF THE DRAWINGS

[0038] The novel features of the invention are set forth with particularity in the appended claims. A better understanding of the features and advantages of the present invention will be obtained by reference to the following detailed description that sets forth illustrative embodiments, in which the principles of the invention are utilized, and the accompanying drawings of which:

[0039] FIG. 1 illustrates the results of a TDCC Assay with MV-4-11 Cells and Anti-CD3/Anti-FLT3 Multispecific Proteins Containing Llama Anti-FLT3 Sequences FLL21, FLL57, FLL62, FLL1, and FLL103, ran in the presence of 15 mg/ml bovine serum albumin (BSA). The y-axis shows the normalized percentage of viability of the cancer cells.

[0040] FIG. 2 illustrates the results of a TDCC Assay with MV-4-11 Cells and Anti-CD3/Anti-FLT3 Multispecific Proteins Containing Llama Anti-FLT3 Sequences FLL107, FLL112, FLL125, FLL129, and FLL137, ran in the presence of 15 mg/ml BSA. The y-axis shows the normalized percentage of viability of the cancer cells.

[0041] FIG. 3 illustrates the results of a TDCC Assay with MV-4-11 Cells and Anti-CD3/Anti-FLT3 Multispecific Proteins Containing Llama Anti-FLT3 Sequences FLL14, FLL141, FLL142, FLL143, and FLL146, ran in the presence of 15 mg/ml BSA. The y-axis shows the normalized percentage of viability of the cancer cells.

[0042] FIG. 4 illustrates the results of a TDCC Assay with MV-4-11 Cells and Anti-CD3/Anti-FLT3 Multispecific Proteins Containing Llama Anti-FLT3 Sequences FLL15, FLL154, FLL158, FLL160, and FLL168, ran in the presence of 15 mg/ml BSA. The y-axis shows the normalized percentage of viability of the cancer cells.

[0043] FIG. 5 illustrates the results of a TDCC Assay with MV-4-11 Cells and Anti-CD3/Anti-FLT3 Multispecific Proteins Containing Llama Anti-FLT3 Sequences FLL173, FLL177, FLL178, FLL179, and FLL190, ran in the presence of 15 mg/ml BSA. The y-axis shows the normalized percentage of viability of the cancer cells.

[0044] FIG. 6 illustrates the results of a TDCC Assay with MV-4-11 Cells and Anti-CD3/Anti-FLT3 Multispecific Proteins Containing Llama Anti-FLT3 Sequences FLL26, FLL32, FLL34, FLL38, and FLL39, ran in the presence of 15 mg/ml BSA. The y-axis shows the normalized percentage of viability of the cancer cells.

[0045] FIG. 7 illustrates the results of a TDCC Assay with MV-4-11 Cells and Anti-CD3/Anti-FLT3 Multispecific Proteins Containing Llama Anti-FLT3 Sequences FLL4, FLL40, FLL43, FLL45, and FLL51, ran in the presence of 15 mg/ml BSA. The y-axis shows the normalized percentage of viability of the cancer cells.

[0046] FIG. 8 illustrates the results of a TDCC Assay with MV-4-11 Cells and Anti-CD3/Anti-FLT3 Multispecific Proteins Containing Llama Anti-FLT3 Sequences FLL53, FLL55, FLL6, FLL61, and FLL75, ran in the presence of 15 mg/ml BSA. The y-axis shows the normalized percentage of viability of the cancer cells.

[0047] FIG. 9 illustrates the results of a TDCC Assay with MV-4-11 Cells and Anti-CD3/Anti-FLT3 Multispecific Proteins Containing Llama Anti-FLT3 Sequences FLL76, FLL77, FLL78, FLL82, and FLL822, ran in the presence of 15 mg/ml BSA. The y-axis shows the normalized percentage of viability of the cancer cells.

[0048] FIG. 10 illustrates the results of a TDCC Assay with MV-4-11 Cells and Anti-CD3/Anti-FLT3 Multispecific Proteins Containing Llama Anti-FLT3 Sequences FLL83,

FLL94, and FLL99 and with a negative control molecule targeting GFP, ran in the presence of 15 mg/ml BSA. The y-axis shows the normalized percentage of viability of the cancer cells.

[0049] FIG. 11 illustrates the results of a TDCC Assay with MV-4-11 Cells and Anti-CD3/Anti-FLT3 Multispecific Proteins Containing Llama Anti-FLT3 Sequences FLL8, FLL41, FLL71, FLL92, FLL134, and FLL153, ran in the presence of 15 mg/ml BSA. The y-axis shows the normalized percentage of viability of the cancer cells.

[0050] FIG. 12 illustrates the results of a TDCC Assay with MV-4-11 Cells and Anti-CD3/Anti-FLT3 Multispecific Proteins Containing Llama Anti-FLT3 Sequences FLL21, FLL57, FLL62, FLL1, and FLL103, ran in the presence of 15 mg/ml HSA. The y-axis shows the normalized percentage of viability of the cancer cells.

[0051] FIG. 13 illustrates the results of a TDCC Assay with MV-4-11 Cells and Anti-CD3/Anti-FLT3 Multispecific Proteins Containing Llama Anti-FLT3 Sequences FLL107, FLL112, FLL125, FLL129, and FLL137, ran in the presence of 15 mg/ml HSA. The y-axis shows the normalized percentage of viability of the cancer cells.

[0052] FIG. 14 illustrates the results of a TDCC Assay with MV-4-11 Cells and Anti-CD3/Anti-FLT3 Multispecific Proteins Containing Llama Anti-FLT3 Sequences FLL14, FLL141, FLL142, FLL143, and FLL146, ran in the presence of 15 mg/ml HSA. The y-axis shows the normalized percentage of viability of the cancer cells.

[0053] FIG. 15 illustrates the results of a TDCC Assay with MV-4-11 Cells and Anti-CD3/Anti-FLT3 Multispecific Proteins Containing Llama Anti-FLT3 Sequences FLL15, FLL154, FLL158, FLL160, FLL168, ran in the presence of 15 mg/ml HSA. The y-axis shows the normalized percentage of viability of the cancer cells.

[0054] FIG. 16 illustrates the results of a TDCC Assay with MV-4-11 Cells and Anti-CD3/Anti-FLT3 Multispecific Proteins Containing Llama Anti-FLT3 Sequences FLL173, FLL177, FLL178, FLL179, and FLL190, ran in the presence of 15 mg/ml HSA. The y-axis shows the normalized percentage of viability of the cancer cells.

[0055] FIG. 17 illustrates the results of a TDCC Assay with MV-4-11 Cells and Anti-CD3/Anti-FLT3 Multispecific Proteins Containing Llama Anti-FLT3 Sequences FLL26, FLL32, FLL34, FLL38, and FLL39, ran the presence of 15 mg/ml HSA. The y-axis shows the normalized percentage of viability of the cancer cells.

[0056] FIG. 18 illustrates the results of a TDCC Assay with MV-4-11 Cells and Anti-CD3/Anti-FLT3 Multispecific Proteins Containing Llama Anti-FLT3 Sequences FLL4, FLL40, FLL43, FLL45, and FLL51, ran in the presence of 15 mg/ml HSA. The y-axis shows the normalized percentage of viability of the cancer cells.

[0057] **FIG. 19** illustrates the results of a TDCC Assay with MV-4-11 Cells and Anti-CD3/Anti-FLT3 Multispecific Proteins Containing Llama Anti-FLT3 Sequences FLL53, FLL55, FLL6, FLL61, and FLL75, ran in the presence of 15 mg/ml HSA. The y-axis shows the normalized percentage of viability of the cancer cells.

[0058] **FIG. 20** illustrates the results of a TDCC Assay with MV-4-11 Cells and Anti-CD3/Anti-FLT3 Multispecific Proteins Containing Llama Anti-FLT3 Sequences FLL76, FLL77, FLL78, FLL82, and FLL822, ran in the presence of 15 mg/ml HSA. The y-axis shows the normalized percentage of viability of the cancer cells.

[0059] **FIG. 21** illustrates the results of a TDCC Assay with MV-4-11 Cells and Anti-CD3/Anti-FLT3 Multispecific Proteins Containing Llama Anti-FLT3 Sequences FLL83, FLL94, and FLL99 and with a negative control molecule targeting GFP, ran in the presence of 15 mg/ml HSA. The y-axis shows the normalized percentage of viability of the cancer cells.

[0060] **FIG. 22** illustrates the results of a TDCC Assay with MV-4-11 Cells and Anti-CD3/Anti-FLT3 Multispecific Proteins Containing Llama Anti-FLT3 Sequences FLL8, FLL41, FLL71, FLL92, FLL134, and FLL153, ran in the presence of 15 mg/ml HSA. The y-axis shows the normalized percentage of viability of the cancer cells.

[0061] **FIG. 23** illustrates an SDS-PAGE of purified humanized anti-FLT3/anti-albumin/anti-CD3 Multispecific Proteins under non-reducing (first and third panels) and reducing (second and fourth panels) conditions. Lanes 1-8 in order: FLH141, FLH107, FLH34, FLH4, FLH78, FLH19C, FLH92a, FLH92b. The migration of molecular weight standards (in kDa) is indicated by the horizontal lines and the numbers to the left of each gel image.

[0062] **FIG. 24** illustrates the results of a TDCC Assay with MV-4-11 Cells and Anti-CD3/Anti-FLT3 Multispecific Proteins Containing Humanized Anti-FLT3 Sequences FLH4, FLH78, FLH19C, FLH141, FLH107, and FLH34 and with a negative control molecule targeting GFP, ran in the presence of 15 mg/ml BSA. The y-axis shows the normalized percentage of viability of the cancer cells.

[0063] **FIG. 25** illustrates the results of a TDCC Assay with MV-4-11 Cells and Anti-CD3/Anti-FLT3 Multispecific Proteins Containing Humanized Anti-FLT3 Sequences FLH4, FLH78, FLH19C, FLH141, FLH107, and FLH34 and with a negative control molecule targeting GFP, ran in the presence of 15 mg/ml HSA.

[0064] **FIG. 26** illustrates the results of a TDCC Assay with EOL1 Cells and Anti-CD3/Anti-FLT3 Multispecific Proteins Containing Humanized Anti-FLT3 Sequences FLH4, FLH78, FLH19C, FLH141, FLH107, and FLH34 and with a negative control molecule targeting GFP, ran in the presence of 15 mg/ml BSA.

[0065] **FIG. 27** illustrates the results of a TDCC Assay with EOL1 Cells and Anti-CD3/Anti-FLT3 Multispecific Proteins Containing Humanized Anti-FLT3 Sequences FLH4, FLH78, FLH19C, FLH141, FLH107, and FLH34 and with a negative control molecule targeting GFP. The assay was run in the presence of 15 mg/ml HSA.

[0066] **FIG. 28** provides exemplary arrangements of various domains of an FLT3 targeting conditionally active binding protein of this disclosure. The aTarget domain depicted in **FIG. 28 Version 1** and **Version 2** corresponds to an FLT3 binding domain as described herein.

[0067] **FIG. 29** illustrates a variable domain of an exemplary immunoglobulin domain, comprising complementarity determining regions (CDR1, CDR2, and CDR3), and non-CDR loops connecting the beta strand (AB, CC', C" D, EF, and DE).

[0068] **FIG. 30** illustrates the results of a TDCC Assay with THP1 Cells and Anti-CD3/Anti-FLT3 Multispecific Proteins Containing Humanized Anti-FLT3 Sequences FLH141, FLH107, FLH34, FLH4, FLH78, FLH19C, FLH92a, FLH92b, without the addition of any type of albumin.

[0069] **FIG. 31** illustrates the results of a TDCC Assay with THP1 Cells and Anti-CD3/Anti-FLT3 Multispecific Proteins Containing Humanized Anti-FLT3 Sequences FLH141, FLH107, FLH34, FLH4, FLH78, FLH19C, FLH92a, FLH92b, ran in the presence of 15 mg/ml HSA.

[0070] **FIG. 32** illustrates the results of a TDCC Assay with MOLM13 Cells and Anti-CD3/Anti-FLT3 Multispecific Proteins Containing Humanized Anti-FLT3 Sequences FLH141, FLH107, FLH34, FLH4, FLH78, FLH19C, FLH92a, FLH92b, and with a negative control molecule targeting GFP, ran in the presence of 15 mg/ml HSA.

[0071] **FIG. 33** illustrates the results of a TDCC Assay with HL60 Cells and Anti-CD3/Anti-FLT3 Multispecific Proteins Containing Humanized Anti-FLT3 Sequences FLH141, FLH107, FLH34, FLH4, FLH78, FLH19C, FLH92a, FLH92b, and with a negative control molecule targeting GFP, ran in the presence of 15 mg/ml HSA.

[0072] **FIG. 34** illustrates the pharmacokinetics of a FLT3 Multispecific Protein Containing Humanized Anti-FLT3 Sequence FLH19C, in cynomolgus monkeys after single i.v. doses of 10 µg/kg, 100 µg/kg, and 1000 µg/kg. Plotted are mean values measured in samples collected from two test subjects per dose group.

[0073] **FIG. 35** illustrates the amount of soluble FLT3L present in serum samples collected from cynomolgus monkeys after single i.v. doses of 10 µg/kg, 100 µg/kg, and 1000 µg/kg of a FLT3 Multispecific Protein Containing Humanized Anti-FLT3 Sequence FLH19C. Plotted are mean values measured in samples collected from two test subjects per dose group.

[0074] **FIG. 36** illustrates the amount of FLT3 transcript present in RNA prepared from whole blood collected from cynomolgus monkeys after single i.v. doses of 100 µg/kg and 1000 µg/kg

of a FLT3 Multispecific Protein Containing Humanized Anti-FLT3 Sequence FLH19C. Plotted are technical replicates. Data are plotted each individual test subject in each dose group.

[0075] **FIG. 37** illustrates the amount of FLT3 transcript present in RNA prepared from bone marrow collected from cynomolgus monkeys after single i.v. doses of 100 µg/kg and 1000 µg/kg of a FLT3 Multispecific Protein Containing Humanized Anti-FLT3 Sequence FLH19C. Plotted are technical replicates. Data are plotted for each individual test subject in each dose group.

[0076] **FIG. 38** illustrates the results of a TDCC Assay with MV-4-11 Cells and Anti-CD3/Anti-FLT3 Multispecific Proteins Containing Humanized Anti-FLT3 Sequences FLH4, FLH78, FLH19C, FLH141, FLH107, FLH34, FLH92a, and FLH92b, ran in the presence of 15 mg/ml BSA. The y-axis shows the normalized percentage of viability of the cancer cells. The T cells in this assay were obtained from a different donor compared to the assay FIG. 24.

[0077] **FIG. 39** illustrates the results of a TDCC Assay with MV-4-11 Cells and Anti-CD3/Anti-FLT3 Multispecific Proteins Containing Humanized Anti-FLT3 Sequences FLH4, FLH78, FLH19C, FLH141, FLH107, FLH34, FLH92a, and FLH92b, ran in the presence of 15 mg/ml HSA. The y-axis shows the normalized percentage of viability of the cancer cells. The T cells in this assay were obtained from a different donor compared to the assay in FIG. 25.

DETAILED DESCRIPTION OF THE INVENTION

Certain definitions

[0078] The terminology used herein is for the purpose of describing particular cases only and is not intended to be limiting. As used herein, the singular forms “a”, “an” and “the” are intended to include the plural forms as well, unless the context clearly indicates otherwise. Furthermore, to the extent that the terms “including”, “includes”, “having”, “has”, “with”, or variants thereof are used in either the detailed description and/or the claims, such terms are intended to be inclusive in a manner similar to the term “comprising.”

[0079] The term “about” or “approximately” means within an acceptable error range for the particular value as determined by one of ordinary skill in the art, which will depend in part on how the value is measured or determined, *e.g.*, the limitations of the measurement system. For example, “about” can mean within 1 or more than 1 standard deviation, per the practice in the given value. Where particular values are described in the application and claims, unless otherwise stated the term “about” should be assumed to mean an acceptable error range for the particular value.

[0080] The terms “individual,” “patient,” or “subject” are used interchangeably. None of the terms require or are limited to situation characterized by the supervision (*e.g.* constant or

intermittent) of a health care worker (*e.g.* a doctor, a registered nurse, a nurse practitioner, a physician's assistant, an orderly, or a hospice worker).

[0081] An "antibody" typically refers to a Y-shaped tetrameric protein comprising two heavy (H) and two light (L) polypeptide chains held together by covalent disulfide bonds and non-covalent interactions. Human light chains comprise a variable domain (VL) and a constant domain (CL) wherein the constant domain may be readily classified as kappa or lambda based on amino acid sequence and gene loci. Each heavy chain comprises one variable domain (VH) and a constant region, which in the case of IgG, IgA, and IgD, comprises three domains termed CH1, CH2, and CH3 (IgM and IgE have a fourth domain, CH4). In IgG, IgA, and IgD classes the CH1 and CH2 domains are separated by a flexible hinge region, which is a proline and cysteine rich segment of variable length (generally from about 10 to about 60 amino acids in IgG). The variable domains in both the light and heavy chains are joined to the constant domains by a "J" region of about 12 or more amino acids and the heavy chain also has a "D" region of about 10 additional amino acids. Each class of antibody further comprises inter-chain and intra-chain disulfide bonds formed by paired cysteine residues. There are two types of native disulfide bridges or bonds in immunoglobulin molecules: interchain and intrachain disulfide bonds. The location and number of interchain disulfide bonds vary according to the immunoglobulin class and species. Interchain disulfide bonds are located on the surface of the immunoglobulin, are accessible to solvent and are usually relatively easily reduced. In the human IgG1 isotype there are four interchain disulfide bonds, one from each heavy chain to the light chain and two between the heavy chains. The interchain disulfide bonds are not required for chain association. As is well known the cysteine rich IgG1 hinge region of the heavy chain has generally been held to consist of three parts: an upper hinge, a core hinge, and a lower hinge. Those skilled in the art will appreciate that that the IgG1 hinge region contain the cysteines in the heavy chain that comprise the interchain disulfide bonds (two heavy/heavy, two heavy/light), which provide structural flexibility that facilitates Fab movements. The interchain disulfide bond between the light and heavy chain of IgG1 are formed between C214 of the kappa or lambda light chain and C220 in the upper hinge region of the heavy chain. The interchain disulfide bonds between the heavy chains are at positions C226 and C229 (all numbered per the EU index according to Kabat, et al., *infra.*)

[0082] As used herein the term "antibody" includes polyclonal antibodies, multiclonal antibodies, monoclonal antibodies, chimeric antibodies, deimmunized, humanized and primatized antibodies, CDR grafted antibodies, human antibodies, recombinantly produced antibodies, intrabodies, multispecific antibodies, bispecific antibodies, monovalent antibodies (*e.g.*, a monovalent IgG), multivalent antibodies, anti-idiotypic antibodies, synthetic antibodies,

including muteins and variants thereof, immunospecific antibody fragments such as: hIgG, a V-NAR, Fv, Fd, Fab, F(ab')₂, F(ab'), Fab2, Fab3 fragments, single-chain fragments (*e.g.*, di-scFv, scFv, scFvFc, scFv-zipper, scFab), disulfide-linked Fvs (sdFv), a Fd fragment consisting of the VH and CH1 domains, linear antibodies, single domain antibodies such as nanobodies or single variable domain antibodies comprising merely one variable domain such as sdAb (VH, VL, or VHH domains), “r IgG” (“half antibody”), diabodies, single chain diabodies, tandem diabodies (Tandab's), tandem di-scFv, tandem tri-scFv, “minibodies” are in some instances exemplified by a structure which is as follows: (VH-VL-CH3)₂, (scFv-CH3)₂, ((scFv)₂-CH3+CH3), ((scFv)₂-CH3) or (scFv-CH3-scFv)₂, multibodies such as triabodies or tetrabodies,; and derivatives thereof including Fc fusions and other modifications, and any other immunoreactive molecule so long as it comprises a domain having a binding site for preferential association or binding with an FLT3 protein. Moreover, unless dictated otherwise by contextual constraints the term further comprises all classes of antibodies (*i.e.* IgA, IgD, IgE, IgG, and IgM) and all subclasses (*i.e.*, IgG1, IgG2, IgG3, IgG4, IgA1, and IgA2). Heavy-chain constant domains that correspond to the different classes of antibodies are typically denoted by the corresponding lower case Greek letter alpha, delta, epsilon, gamma, and mu, respectively. Light chains of the antibodies from any vertebrate species can be assigned to one of two clearly distinct types, called kappa (kappa) and lambda (lambda), based on the amino acid sequences of their constant domains.

[0083] In some embodiments, the FLT3 binding proteins comprise a heavy chain only antibody, such as a VH or a VHH domain. In some cases, the FLT3 binding proteins comprise a heavy chain only antibody that is an engineered human VH domain. In some examples, the engineered human VH domain is produced by panning of phage display libraries. In some embodiments, the FLT3 binding proteins comprise a VHH. The term “VHH,” as used herein, refers to single chain antibody binding domain devoid of light chain. In some cases, a VHH is derived from an antibody of the type that can be found in Camelidae or cartilaginous fish which are naturally devoid of light chains or to a synthetic and non-immunized VHH which can be constructed accordingly. Each heavy chain comprises a variable region encoded by V-, D- and J exons. A VHH, in some cases, is a natural VHH, such as a Camelid-derived VHH, or a recombinant protein comprising a heavy chain variable domain. In some embodiments, the VHH is derived from a species selected from the group consisting of camels, llamas, vicunas, guanacos, and cartilaginous fish (such as, but not limited to, sharks). In another embodiment, the VHH is derived from an alpaca (such as, but not limited to, a Huacaya Alpaca or a Suri alpaca).

[0084] As used herein, “Variable region” or “variable domain” refers to the fact that certain portions of the variable domains differ extensively in sequence among antibodies and are used in

the binding and specificity of each particular antibody for its particular antigen. However, the variability is not evenly distributed throughout the variable domains of antibodies. It is concentrated in three segments called complementarity-determining regions (CDRs) or hypervariable regions both in the light-chain and the heavy-chain variable domains. The more highly conserved portions of variable domains are called the framework (FR). The variable domains of native heavy and light chains each comprise four FR regions, largely adopting a β -sheet configuration, connected by three CDRs, which form loops connecting, and in some cases forming part of, the β sheet structure. The CDRs in each chain are held together in close proximity by the FR regions and, with the CDRs from the other chain, contribute to the formation of the antigen-binding site of antibodies (see Kabat et al., Sequences of Proteins of Immunological Interest, Fifth Edition, National Institute of Health, Bethesda, Md. (1991)). The constant domains are not involved directly in binding an antibody to an antigen, but exhibit various effector functions, such as participation of the antibody in antibody-dependent cellular toxicity. The assignment of amino acids to each domain, framework region and CDR is, in some embodiments, in accordance with one of the numbering schemes provided by Kabat et al. (1991) Sequences of Proteins of Immunological Interest (5th Ed.), US Dept. of Health and Human Services, PHS, NIH, NIH Publication no. 91-3242; Chothia et al., 1987, PMID: 3681981; Chothia et al., 1989, PMID: 2687698; MacCallum et al., 1996, PMID: 8876650; or Dubel, Ed. (2007) Handbook of Therapeutic Antibodies, 3rd Ed., Wiley-VCH Verlag GmbH and Co or AbM (Oxford Molecular/MSI Pharmacopeia) unless otherwise noted. In some embodiments of this disclosure, the FLT3 binding proteins comprise heavy chain only antibodies, such as VH or VHH domains, and comprise three CDRs. Such heavy chain only antibodies, in some embodiments, bind FLT3 as a monomer with no dependency on dimerisation with a VL (light chain variable) region for optimal binding affinity.

[0085] “Variable domain residue numbering as in Kabat” or “amino acid position numbering as in Kabat,” and variations thereof, refers to the numbering system used for heavy chain variable domains or light chain variable domains of the compilation of antibodies in Kabat *et al.*, Sequences of Proteins of Immunological Interest, 5th Ed. Public Health Service, National Institutes of Health, Bethesda, Md. (1991). Using this numbering system, the actual linear amino acid sequence may contain fewer or additional amino acids corresponding to a shortening of, or insertion into, a FR or CDR of the variable domain. For example, a heavy chain variable domain may include a single amino acid insert (residue 52a according to Kabat) after residue 52 of H2 and inserted residues (*e.g.*, residues 82a, 82b, and 82c, etc. according to Kabat) after heavy chain FR residue 82. The Kabat numbering of residues may be determined for a given antibody by alignment at regions of homology of the sequence of the antibody with a “standard”

Kabat numbered sequence. It is not intended that CDRs of the present disclosure necessarily correspond to the Kabat numbering convention.

[0086] The term “Framework” or “FR” residues (or regions) refer to variable domain residues other than the CDR or hypervariable region residues as herein defined. A “human consensus framework” is a framework which represents the most commonly occurring amino acid residue in a selection of human immunoglobulin VL or VH framework sequences.

[0087] The term “epitope,” as used herein, refers to an antigenic determinant that interacts with a specific antigen binding site in the variable region of an antibody molecule known as a paratope. A single antigen may have more than one epitope. Thus, different antibodies may bind to different areas on an antigen and may have different biological effects. Epitopes may be either conformational or linear. A conformational epitope is produced by spatially juxtaposed amino acids from different segments of the linear polypeptide chain. A linear epitope is one produced by adjacent amino acid residues in a polypeptide chain. In certain circumstance, an epitope may include moieties of saccharides, phosphoryl groups, or sulfonyl groups on the antigen.

[0088] As used herein, the term “Percent (%) amino acid sequence identity” with respect to a sequence is defined as the percentage of amino acid residues in a candidate sequence that are identical with the amino acid residues in the specific sequence, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity, and not considering any conservative substitutions as part of the sequence identity. Alignment for purposes of determining percent amino acid sequence identity can be achieved in various ways that are within the skill in the art, for instance, using publicly available computer softwares such as EMBOSS MATCHER, EMBOSS WATER, EMBOSS STRETCHER, EMBOSS NEEDLE, EMBOSS LALIGN, BLAST, BLAST-2, ALIGN or Megalign (DNASTAR) software. Those skilled in the art can determine appropriate parameters for measuring alignment, including any algorithms needed to achieve maximal alignment over the full length of the sequences being compared. Alignment for purposes of determining percent amino acid sequence identity can for example be achieved using publicly available sequence comparison computer program ALIGN-2. The source code for the ALIGN-2 sequence comparison computer program is available with user documentation in the U.S. Copyright Office, Washington D.C., 20559, where it is registered under U.S. Copyright Registration No. TXU510087. The ALIGN-2 program can be compiled for use on a UNIX operating system, such as a digital UNIX V4.0D. All sequence comparison parameters are set by the ALIGN-2 program and do not vary.

[0089] As used herein, “elimination half-time” is used in its ordinary sense, as is described in Goodman and Gillman's The Pharmaceutical Basis of Therapeutics 21-25 (Alfred Goodman

Gilman, Louis S. Goodman, and Alfred Gilman, eds., 6th ed. 1980). Briefly, the term is meant to encompass a quantitative measure of the time course of drug elimination. The elimination of most drugs is exponential (*i.e.*, follows first-order kinetics), since drug concentrations usually do not approach those required for saturation of the elimination process. The rate of an exponential process may be expressed by its rate constant, k , which expresses the fractional change per unit of time, or by its half-time, $t_{1/2}$ the time required for 50% completion of the process. The units of these two constants are time^{-1} and time, respectively. A first-order rate constant and the half-time of the reaction are simply related ($k \times t_{1/2} = 0.693$) and may be interchanged accordingly. Since first-order elimination kinetics dictates that a constant fraction of drug is lost per unit time, a plot of the log of drug concentration versus time is linear at all times following the initial distribution phase (*i.e.*, after drug absorption and distribution are complete). The half-time for drug elimination can be accurately determined from such a graph.

[0090] As used herein, the term “binding affinity” refers to the affinity of the proteins described in the disclosure to their binding targets, and is expressed numerically using “ K_d ” values. If two or more proteins are indicated to have comparable binding affinities towards their binding targets, then the K_d values for binding of the respective proteins towards their binding targets, are within ± 2 -fold of each other. If two or more proteins are indicated to have comparable binding affinities towards single binding target, then the K_d values for binding of the respective proteins towards said single binding target, are within ± 2 -fold of each other. If a protein is indicated to bind two or more targets with comparable binding affinities, then the K_d values for binding of said protein to the two or more targets are within ± 2 -fold of each other. In general, a higher K_d value corresponds to a weaker binding. In some embodiments, the “ K_d ” is measured by a radiolabeled antigen binding assay (RIA) or surface plasmon resonance assays using a BIAcore™-2000 or a BIAcore™-3000 (BIAcore, Inc., Piscataway, N.J.). In certain embodiments, an “on-rate” or “rate of association” or “association rate” or “ k_{on} ” and an “off-rate” or “rate of dissociation” or “dissociation rate” or “ k_{off} ” are also determined with the surface plasmon resonance technique using a BIAcore™-2000 or a BIAcore™-3000 (BIAcore, Inc., Piscataway, N.J.). In additional embodiments, the “ K_d ”, “ k_{on} ”, and “ k_{off} ” are measured using the OCTET® Systems (Pall Life Sciences). In an exemplary method for measuring binding affinity using the OCTET® Systems, the ligand, *e.g.*, biotinylated human or cynomolgus FLT3, is immobilized on the OCTET® streptavidin capillary sensor tip surface which streptavidin tips are then activated according to manufacturer's instructions using about 20-50 $\mu\text{g/ml}$ human or cynomolgus FLT3 protein. A solution of PBS/Casein is also introduced as a blocking agent. For association kinetic measurements, FLT3 binding protein variants are introduced at a concentration ranging from about 10 ng/mL to about 100 $\mu\text{g/mL}$, about 50

ng/mL to about 5 µg/mL, or about 2 ng/mL to about 20 µg/mL. In some embodiments, the FLT3 binding single domain proteins are used at a concentration ranging from about 2 ng/mL to about 20 µg/mL. Complete dissociation is observed in case of the negative control, assay buffer without the binding proteins. The kinetic parameters of the binding reactions are then determined using an appropriate tool, *e.g.*, ForteBio software.

[0091] As used herein, in some embodiments, “treatment” or “treating” or “treated” refers to therapeutic treatment wherein the object is to slow (lessen) an undesired physiological condition, disorder or disease, or to obtain beneficial or desired clinical results. For the purposes described herein, beneficial or desired clinical results include, but are not limited to, alleviation of symptoms; diminishment of the extent of the condition, disorder or disease; stabilization (*i.e.*, not worsening) of the state of the condition, disorder or disease; delay in onset or slowing of the progression of the condition, disorder or disease; amelioration of the condition, disorder or disease state; and remission (whether partial or total), whether detectable or undetectable, or enhancement or improvement of the condition, disorder or disease. Treatment includes eliciting a clinically significant response without excessive levels of side effects. Treatment also includes prolonging survival as compared to expected survival if not receiving treatment. In other embodiments, “treatment” or “treating” or “treated” refers to prophylactic measures, wherein the object is to delay onset of or reduce severity of an undesired physiological condition, disorder or disease, such as, for example is a person who is predisposed to a disease (*e.g.*, an individual who carries a genetic marker for a disease such as breast cancer).

[0092] An “FLT3 targeting TriTAC,” or an “FLT3 targeting trispecific protein,” as used herein refers to a trispecific binding protein that comprises a binding moiety that is specific for a bulk serum protein, a first target antigen binding domain, and a second target antigen binding domain, wherein at least one of the first target antigen binding domain and the second target antigen binding domain comprises an FLT3 binding protein as described herein, and at least one of the first target antigen binding domain and the second target antigen binding domain comprises a domain that binds a CD3.

[0093] A “ProTriTAC,” or an “FLT3 targeting protrispecific protein,” as used herein refers to a trispecific binding protein that is conditionally activated, and comprises (i) a cleavable linker; (ii) a dual binding moiety that is specific for a bulk serum protein and also comprises a masking moiety which prohibits the binding of a first target antigen binding domain or a second target antigen binding domain to its target, wherein at least one of the first target antigen binding domain and the second target antigen binding domain comprises an FLT3 binding domain as described herein. The ProTriTAC proteins of this disclosure are, in some cases, activated from a

masked state to an active state by cleavage of the cleavable linker, for example, in a protease rich environment, such as in a tumor microenvironment.

FLT3 binding proteins

[0094] FLT3, also known as fetal liver kinase 2 (FLK-2), stem cell tyrosine kinase 1 (STK-1) and CD135, is a member of the class III receptor tyrosine kinases. Normally, FLT3 is expressed on immature myeloid-lymphocytic precursor cells and dendritic cell precursors, but rarely on mature adult cells. FLT3 is overexpressed in approximately 90% of acute myeloid leukemia (AML), a majority of acute lymphocytic leukemia (ALL) and the blast-crisis phase of chronic myeloid leukemia (BC-CML). Stimulation by FLT3 ligand (FL) enhances the proliferation and survival of leukemia cells. Inhibition of FLT3 signaling leads to apoptosis in dendritic cells and inhibition of immune responses. The MAPK, PI3K and Stat5 pathways have been identified to be involved in the downstream signaling of activated FLT3 (*See e.g.*, Stirewalt D L and J P, Radich, J P. Nat Rev Cancer 3:650-665 (2003)).

[0095] Described herein are proteins that comprise an FLT3 binding domain, pharmaceutical compositions thereof, as well as nucleic acids, recombinant expression vectors and host cells for making such proteins thereof. Also provided are methods of using the disclosed proteins comprising an FLT3 binding domain of this disclosure, in the prevention, and/or treatment of diseases, conditions and disorders. In some embodiments, an FLT3 binding domain of this disclosure inhibits FL-induced phosphorylation of wild-type FLT3 and downstream kinases of MPK, PI3K, and STAT5 pathways in a disease such as leukemia. In some embodiments, an FLT3 binding domain of this disclosure has an improved ability to activate downstream immune effector functions such as antibody dependent cellular cytotoxicity (ADCC).

[0096] In some embodiments, the FLT3 binding domain binds to a human FLT3 protein comprising a sequence as set forth in SEQ ID No. 388 (UniProt ID: P36888). In some embodiments, the FLT3 binding domain binds to a protein comprising a truncated sequence compared to SEQ ID No. 388 (UniProt ID: P36888).

[0097] In some embodiments, the FLT3 binding domains disclosed herein recognize full-length FLT3 (*e.g.*, an FLT3 protein comprising the sequence of SEQ ID No. 388 (UniProt ID: P36888)). In certain instances, the FLT3 binding domains disclosed herein recognize an epitope within FLT3, such as, in some cases the FLT3 binding proteins interact with one or more amino acids found within a domain of human FLT3. The epitope to which the antibodies bind may consist of a single contiguous sequence of 3 or more (*e.g.*, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or more) amino acids located within a domain of FLT3 (*e.g.*, an FLT3 protein comprising the sequence of SEQ ID No. 388 (UniProt ID: P36888)). Alternatively, the epitope may consist of a plurality of non-contiguous amino acids (or amino acid sequences)

located within a domain of FLT3 (*e.g.*, an FLT3 protein comprising the sequence of SEQ ID No. 388 (UniProt ID: P36888)).

[0098] In some embodiments, the FLT3 binding proteins of this disclosure binds to the full length of an FLT3 protein or to a fragment thereof, such as epitope containing fragments within the full length FLT3 protein, as described above. In some cases, the epitope containing fragment comprises antigenic or immunogenic fragments and derivatives thereof of the FLT3 protein. Epitope containing fragments, including antigenic or immunogenic fragments, are, in some embodiments, 12 amino acids or more, *e.g.*, 20 amino acids or more, 50 or 100 amino acids or more. The FLT3 fragments, in some embodiments, comprises 95% or more of the length of the full protein, 90% or more, 75% or 50% or 25% or 10% or more of the length of the full protein. In some embodiments, the epitope-containing fragments of FLT3 including antigenic or immunogenic fragments are capable of eliciting a relevant immune response in a patient. Derivatives of FLT3 include, in some embodiments, variants on the sequence in which one or more (*e.g.*, 1-20 such as 15 amino acids, or up to 20% such as up to 10% or 5% or 1% by number of amino acids based on the total length of the protein) deletions, insertions or substitutions have been made to the FLT3 sequence (*e.g.*, an FLT3 protein comprising the sequence of SEQ ID No. 388 (UniProt ID: P36888)).

[0099] In some embodiments, substitutions comprise conservative substitutions. Derivatives and variants of, in some examples, have essentially the same biological function as the protein from which they are derived. For instance, derivatives and variants of FLT3 are, in some cases, comparably antigenic or immunogenic to the protein from which they are derived, have either the ligand-binding activity, or the active receptor-complex forming ability, or preferably both, of the protein from which they are derived, and have the same tissue distribution as FLT3.

[00100] In some embodiments, the FLT3 binding protein specifically binds FLT3 with equivalent or better affinity as that of a reference FLT3 binding protein, and the FLT3 binding protein in such embodiments comprises an affinity matured FLT3 binding molecule, and is derived from the FLT3 binding parental molecule, comprising one or more amino acid mutations (*e.g.*, a stabilizing mutation, a destabilizing mutation) with respect to the FLT3 binding parental molecule. In some embodiments, the affinity matured FLT3 binding molecule has superior stability with respect to selected destabilizing agents, as that of a reference FLT3 binding parental molecule. In some embodiments, the affinity matured FLT3 binding molecule is identified in a process comprising panning of one or more pre-candidate FLT3 binding molecules derived from one or more FLT3 binding parental molecule, expressed in a phage display library, against an FLT3 protein, such as a human FLT3 protein. The pre-candidate

FLT3 binding molecule comprises, in some embodiments, amino acid substitutions in the variable regions, CDRs, or framework residues, relative to a parental molecule.

[00101] As used herein, “Phage display,” refers to a technique by which variant polypeptides are displayed as fusion proteins to at least a portion of a coat protein on the surface of phage, *e.g.*, filamentous phage, particles. A utility of phage display lies in the fact that large libraries of randomized protein variants can be rapidly and efficiently selected for those sequences that bind to a target molecule with high affinity. Display of peptide and protein libraries on phage has been used for screening millions of polypeptides for ones with specific binding properties. Polyvalent phage display methods have been used for displaying small random peptides and small proteins through fusions to either gene III or gene VIII of filamentous phage. *See e.g.*, Wells and Lowman, *Curr. Opin. Struct. Biol.*, 3:355-362 (1992), and references cited therein. In monovalent phage display, a protein or peptide library is fused to a gene III or a portion thereof, and expressed at low levels in the presence of wild type gene III protein so that phage particles display one copy or none of the fusion proteins. Avidity effects are reduced relative to polyvalent phage so that selection is on the basis of intrinsic ligand affinity, and phagemid vectors are used, which simplify DNA manipulations. *See e.g.*, Lowman and Wells, *Methods: A companion to Methods in Enzymology*, 3:205-0216 (1991).

[00102] In some embodiments, the panning comprises using varying binding times and concentrations to identify FLT3 binding molecules with increased or decreased on-rates, from pre-candidate FLT3 binding molecules. In some embodiments, the panning comprises using varying wash times to identify FLT3 binding molecules with increased or decreased off-rates, from pre-candidate FLT3 molecules. In some embodiments, the panning comprises using both varying binding times and varying wash times. In some embodiments, one or more stabilizing mutations are combined to increase the stability of the affinity matured FLT3 binding molecule, for example, by shuffling to create a second-stage combinatorial library from such mutants and conducting a second round of panning followed by a binding selection.

[00103] In some embodiments, the affinity matured FLT3 binding molecule comprises an equivalent or better affinity to a FLT3 protein (such as human FLT3 protein) as that of a FLT3 binding parental molecule, but that has reduced cross reactivity, or in some embodiments, increased cross reactivity, with selected substances, such as ligands, proteins, antigens, or the like, other than the FLT3 epitope for which the FLT3 binding parental molecule is specific, or is designed to be specific for. In regard to the latter, an affinity matured FLT3 binding molecule, in some embodiments, is more successfully tested in animal models if the affinity matured FLT3 binding molecule is reacted with both human FLT3 and the corresponding target of the animal model, *e.g.* mouse FLT3 or cynomolgus FLT3.

[00104] In some embodiments, the FLT3 binding protein comprises an antigen-specific binding domain polypeptide that specifically bind to targets, such as targets on diseased cells, or targets on other cells that support the diseased state, such as targets on stromal cells that support tumor growth or targets on immune cells that support disease-mediated immunosuppression. In some examples, the antigen-specific binding domain includes antibodies, single chain antibodies, Fabs, Fv, T-cell receptor binding domains, ligand binding domains, receptor binding domains, domain antibodies, single domain antibodies, minibodies, nanobodies, peptibodies, or various other antibody mimics (such as affimers, affitins, alphabodies, atrimers, CTLA4-based molecules, adnectins, anticalins, Kunitz domain-based proteins, avimers, knottins, fynomers, darpins, affibodies, affilins, monobodies and armadillo repeat protein-based proteins).

[00105] In some embodiments, the FLT3 binding domain is an anti-FLT3 antibody or an antigen binding fragment thereof, or a variant of the anti-FLT3 or an antigen binding fragment thereof. As used herein, the term “variant” refers to variants and derivatives of an antibody or an antigen binding fragment thereof, as described herein. In certain embodiments, amino acid sequence variants of the anti-FLT3 antibodies or antigen binding fragments thereof described herein are contemplated. For example, in certain embodiments amino acid sequence variants of anti-FLT3 antibodies or antigen binding fragments thereof described herein are contemplated to improve the binding affinity and/or other biological properties of the same. Exemplary method for preparing amino acid variants include, but are not limited to, introducing appropriate modifications into the nucleotide sequence encoding the antibody or antigen binding fragments thereof, or by peptide synthesis. Such modifications include, for example, deletions from, and/or insertions into and/or substitutions of residues within the amino acid sequences of the antibody or antigen binding fragments thereof.

[00106] Any combination of deletion, insertion, and substitution can be made to arrive at the final construct, provided that the final construct possesses the desired characteristics, *e.g.*, antigen- binding. In certain embodiments, variants having one or more amino acid substitutions are provided. Sites of interest for substitution mutagenesis include the CDRs and framework regions. Examples of such substitutions are described below. Amino acid substitutions may be introduced into an antibody or antigen binding fragments thereof of interest and the products screened for a desired activity, *e.g.*, retained/improved antigen binding, decreased immunogenicity, altered Antibody dependent cellular cytotoxicity (ADCC), or improved T-cell mediated cytotoxicity (TDCC). Both conservative and non-conservative amino acid substitutions are contemplated for preparing the variants.

[00107] In another example of a substitution to create a variant anti-FLT3 antibody or antigen binding fragments thereof, one or more hypervariable region residues of a parent antibody or

antigen binding fragments thereof are substituted. In general, variants are then selected based on improvements in desired properties compared to a parent antibody, for example, increased affinity, reduced affinity, reduced immunogenicity, increased pH dependence of binding.

[00108] In some embodiments, the FLT3 binding domain is a single domain antibody (sdAb), such as a heavy chain variable domain (VH), a variable domain (VHH) of a llama derived sdAb, a peptide, a ligand or a small molecule entity specific for FLT3. In some embodiments, the FLT3 binding domain described herein is any domain that binds to FLT3 including but not limited to domains from a monoclonal antibody, a polyclonal antibody, a recombinant antibody, a human antibody, a humanized antibody. In certain embodiments, the FLT3 binding domain is a single-domain antibody. In other embodiments, the FLT3 binding domain is a peptide. In further embodiments, the FLT3 binding domain is a small molecule.

[00109] Generally, it should be noted that the term single domain antibody as used herein in its broadest sense is not limited to a specific biological source or to a specific method of preparation. Single domain antibodies are antibodies whose complementary determining regions are part of a single domain polypeptide. Examples include, but are not limited to, heavy chain antibodies, antibodies naturally devoid of light chains, single domain antibodies derived from conventional 4-chain antibodies, engineered antibodies and single domain scaffolds other than those derived from antibodies. Single domain antibodies may be any of the art, or any future single domain antibodies. Single domain antibodies may be derived from any species including, but not limited to mouse, human, camel, llama, goat, rabbit, bovine. For example, in some embodiments, the single domain antibodies of the disclosure are obtained: (1) by isolating the VHH domain of a naturally occurring heavy chain antibody; (2) by expression of a nucleotide sequence encoding a naturally occurring VHH domain; (3) by “humanization” of a naturally occurring VHH domain or by expression of a nucleic acid encoding a such humanized VHH domain; (4) by “camelization” of a naturally occurring VH domain from any animal species, and in particular from a species of mammal, such as from a human being, or by expression of a nucleic acid encoding such a camelized VH domain; (5) by “camelization” of a “domain antibody” or “Dab,” or by expression of a nucleic acid encoding such a camelized VH domain; (6) by using synthetic or semi-synthetic techniques for preparing proteins, polypeptides or other amino acid sequences; (7) by preparing a nucleic acid encoding a single domain antibody using techniques for nucleic acid synthesis known in the field, followed by expression of the nucleic acid thus obtained; and/or (8) by any combination of one or more of the foregoing.

[00110] In one embodiment, a single domain antibody corresponds to the VHH domains of naturally occurring heavy chain antibodies directed against FLT3. As further described herein, such VHH sequences can generally be generated or obtained by suitably immunizing a species

of Llama with FLT3, (*i.e.*, so as to raise an immune response and/or heavy chain antibodies directed against FLT3), by obtaining a suitable biological sample from said Llama (such as a blood sample, serum sample or sample of B-cells), and by generating VHH sequences directed against FLT3, starting from said sample, using any suitable technique.

[00111] In another embodiment, such naturally occurring VHH domains against FLT3, are obtained from naïve libraries of Camelid VHH sequences, for example by screening such a library using FLT3, or at least one part, fragment, antigenic determinant or epitope thereof using one or more screening techniques known in the field. Such libraries and techniques are for example described in WO 99/37681, WO 01/90190, WO 03/025020 and WO 03/035694. Alternatively, improved synthetic or semi-synthetic libraries derived from naïve VHH libraries are used, such as VHH libraries obtained from naïve VHH libraries by techniques such as random mutagenesis and/or CDR shuffling, as for example described in WO 00/43507.

[00112] In a further embodiment, yet another technique for obtaining VHH sequences directed against FLT3, involves suitably immunizing a transgenic mammal that is capable of expressing heavy chain antibodies (*i.e.*, so as to raise an immune response and/or heavy chain antibodies directed against FLT3), obtaining a suitable biological sample from said transgenic mammal (such as a blood sample, serum sample or sample of B-cells), and then generating VHH sequences directed against FLT3, starting from said sample, using any suitable technique known in the field. For example, for this purpose, the heavy chain antibody-expressing rats or mice and the further methods and techniques described in WO 02/085945 and in WO 04/049794 can be used.

[00113] In some embodiments, an anti-FLT3 single domain antibody of this disclosure comprises a single domain antibody with an amino acid sequence that corresponds to the amino acid sequence of a non-human antibody and/or a naturally occurring VHH domain, *e.g.*, a llama anti-FLT3 antibody, but that has been “humanized,” *i.e.*, by replacing one or more amino acid residues in the amino acid sequence of said non-human anti-FLT3 and/or the naturally occurring VHH sequence (and in particular in the framework sequences) by one or more of the amino acid residues that occur at the corresponding position(s) in a VH domain from a conventional 4-chain antibody from a human being (*e.g.*, as indicated above). This can be performed in a manner known in the field, which will be clear to the skilled person, for example on the basis of the further description herein. Again, it should be noted that such humanized anti-FLT3 single domain antibodies of the disclosure are obtained in any suitable manner known per se (*i.e.*, as indicated under points (1)-(8) above) and thus are not strictly limited to polypeptides that have been obtained using a polypeptide that comprises a non-human anti-FLT3 antibody and/or the naturally occurring VHH sequence as a starting material. In some additional embodiments, a

single domain anti-FLT3 antibody, as described herein, comprises a single domain antibody with an amino acid sequence that corresponds to the amino acid sequence of a naturally occurring VH domain, but that has been “camelized” i.e., by replacing one or more amino acid residues in the amino acid sequence of a naturally occurring VH domain from a conventional 4-chain antibody by one or more of the amino acid residues that occur at the corresponding position(s) in a VHH domain of a heavy chain antibody. Such “camelizing” substitutions are preferably inserted at amino acid positions that form and/or are present at the VH-VL interface, and/or at the so-called Camelidae hallmark residues. *See e.g.*, WO 94/04678 and Davies and Riechmann (1994 and 1996)). Preferably, the VH sequence that is used as a starting material or starting point for generating or designing the camelized single domain is preferably a VH sequence from a mammal, more preferably the VH sequence of a human being, such as a VH3 sequence. However, it should be noted that such camelized anti-FLT3 single domain antibodies of the disclosure, in certain embodiments, are obtained in any suitable manner known in the field (i.e., as indicated under points (1)-(8) above) and thus are not strictly limited to polypeptides that have been obtained using a polypeptide that comprises a naturally occurring VH domain as a starting material. For example, as further described herein, both “humanization” and “camelization” is performed by providing a nucleotide sequence that encodes a naturally occurring VHH domain or VH domain, respectively, and then changing, one or more codons in said nucleotide sequence in such a way that the new nucleotide sequence encodes a “humanized” or “camelized” single domain antibody, respectively. This nucleic acid can then be expressed, so as to provide a desired anti-FLT3 single domain antibody of the disclosure. Alternatively, in other embodiments, based on the amino acid sequence of a naturally occurring VHH domain or VH domain, respectively, the amino acid sequence of the desired humanized or camelized anti-FLT3 single domain antibody of the disclosure, respectively, are designed and then synthesized de novo using known techniques for peptide synthesis. In some embodiments, based on the amino acid sequence or nucleotide sequence of a naturally occurring VHH domain or VH domain, respectively, a nucleotide sequence encoding the desired humanized or camelized anti-FLT3 single domain antibody of the disclosure, respectively, is designed and then synthesized de novo using known techniques for nucleic acid synthesis, after which the nucleic acid thus obtained is expressed in using known expression techniques, so as to provide the desired anti-FLT3 single domain antibody of the disclosure.

[00114] Other suitable methods and techniques for obtaining the anti-FLT3 single domain antibody of the disclosure and/or nucleic acids encoding the same, starting from naturally occurring VH sequences or VHH sequences for example comprises combining one or more parts of one or more naturally occurring VH sequences (such as one or more framework (FR)

sequences and/or complementarity determining region (CDR) sequences), one or more parts of one or more naturally occurring VHH sequences (such as one or more FR sequences or CDR sequences), and/or one or more synthetic or semi-synthetic sequences, in a suitable manner, so as to provide an anti-FLT3 single domain antibody of the disclosure or a nucleotide sequence or nucleic acid encoding the same.

[00115] In some embodiments, the FLT3 binding domain is an anti-FLT3 specific antibody comprising a heavy chain variable complementarity determining region CDR1, a heavy chain variable CDR2, a heavy chain variable CDR3, a light chain variable CDR1, a light chain variable CDR2, and a light chain variable CDR3. In some embodiments, the FLT3 binding domain comprises any domain that binds to FLT3 including but not limited to domains from a monoclonal antibody, a polyclonal antibody, a recombinant antibody, a human antibody, a humanized antibody, or antigen binding fragments such as single domain antibodies (sdAb), Fab, Fab', F(ab)2, and Fv fragments, fragments comprised of one or more CDRs, single-chain antibodies (*e.g.*, single chain Fv fragments (scFv)), disulfide stabilized (dsFv) Fv fragments, heteroconjugate antibodies (*e.g.*, bispecific antibodies), pFv fragments, heavy chain monomers or dimers, light chain monomers or dimers, and dimers consisting of one heavy chain and one light chain. In some embodiments, the FLT3 binding domain is a single domain antibody. In some embodiments, the anti-FLT3 single domain antibody comprises heavy chain variable complementarity determining regions (CDR), CDR1, CDR2, and CDR3.

[00116] In some embodiments, the FLT3 binding domain is a polypeptide comprising an amino acid sequence that is comprised of four framework regions/sequences (f1-f4) interrupted by three complementarity determining regions/sequences, as represented by the formula: f1-r1-f2-r2-f3-r3-f4, wherein r1, r2, and r3 are complementarity determining regions CDR1, CDR2, and CDR3, respectively, and f1, f2, f3, and f4 are framework residues. The framework residues of the FLT3 binding protein of the present disclosure comprise, for example, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, or 94 amino acid residues, and the complementarity determining regions comprise, for example, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, or 36 amino acid residues.

[00117] In some embodiments, the binding proteins described herein comprise a polypeptide having a sequence selected from SEQ ID Nos. 1-76, and 389-390, subsequences thereof, and variants thereof. In some embodiments, the FLT3 binding protein comprises at least 60%-95% or more homology to a sequence selected from SEQ ID Nos. 1-76, and 389-390, subsequences thereof, and variants thereof. In some embodiments, the FLT3 binding protein comprises at least 60%, 61%, 62%, 63%, 63%, 65%, 66%, 67%, 68%, 69%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or more homology to a sequence selected from SEQ ID Nos. 1-76, and

389-390, subsequences thereof, and variants thereof. In some embodiments, the FLT3 binding protein comprises at least 60%-95% or more identity to a sequence selected from SEQ ID Nos. 1-76, and 389-390, subsequences thereof, and variants thereof. In some embodiments, the FLT3 binding protein comprises at least 60%, 61%, 62%, 63%, 63%, 65%, 66%, 67%, 68%, 69%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or more identity to a sequence selected from SEQ ID Nos. 1-76, and 389-390, subsequences thereof, and variants thereof.

[00118] In some embodiments, the CDR1 comprises the amino acid 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. In some embodiments, the CDR2 comprises the amino acid 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. In some embodiments, the CDR3 comprises the amino acid 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 CDR1 comprises the amino acid 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. In some embodiments, the CDR2 comprises the amino acid 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. In some embodiments, the CDR3 comprises the amino acid sequence selected from the group consisting of SEQ ID Nos. 173, 186 or 195 or a sequence comprising one or more amino acid substitutions in a sequence selected from the group consisting of SEQ ID Nos. 173, 196 or 195.

[00119] In various embodiments, the FLT3 binding domain of the present disclosure is at least about 60%, about 61%, at least about 62%, about 63%, about 64%, about 65%, about 66%, about 67%, about 68%, about 69%, about 70%, about 71%, about 72%, about 73%, about 74%, about 75%, about 76%, about 77%, about 78%, about 79%, about 80%, about 81%, about 82%, about 83%, about 84%, about 85%, about 86%, about 87%, about 88%, about 89%, about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, about 98%, about 99%, or about 100% identical to an amino acid sequence selected from SEQ ID Nos. 1-76, and 389-390.

[00120] In various embodiments, the FLT3 binding domain of the present disclosure is at least about 75%, about 76%, about 77%, about 78%, about 79%, about 80%, about 81%, about 82%,

about 83%, about 84%, about 85%, about 86%, about 87%, about 88%, about 89%, about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, about 98%, about 99%, or about 100% identical to an amino acid sequence selected from SEQ ID Nos. 1-76, and 389-390.

[00121] In various embodiments, a complementarity determining region of the FLT3 binding domain of the present disclosure is at least about 10%, about 20%, about 30%, about 40%, about 50%, about 60%, about 70%, about 80%, about 81%, about 82%, about 83%, about 84%, about 85%, about 86%, about 87%, about 88%, about 89%, about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, about 98%, about 99%, or about 100% identical to the amino acid sequence set forth in any one of SEQ ID Nos. 77-108.

[00122] In various embodiments, a complementarity determining region of the FLT3 binding domain of the present disclosure is at least about 10%, about 20%, about 30%, about 40%, about 50%, about 60%, about 70%, about 80%, about 81%, about 82%, about 83%, about 84%, about 85%, about 86%, about 87%, about 88%, about 89%, about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, about 98%, about 99%, or about 100% identical to the amino acid sequence set forth in SEQ ID Nos. 109-154, and 393-394.

[00123] In various embodiments, a complementarity determining region of the FLT3 binding domain of the present disclosure is at least about 10%, about 20%, about 30%, about 40%, about 50%, about 60%, about 70%, about 80%, about 81%, about 82%, about 83%, about 84%, about 85%, about 86%, about 87%, about 88%, about 89%, about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, about 98%, about 99%, or about 100% identical to the amino acid sequence set forth in SEQ ID Nos. 155-195.

[00124] In various embodiments, a complementarity determining region of the FLT3 binding domain of the present disclosure is at least about 10%, about 20%, about 30%, about 40%, about 50%, about 60%, about 70%, about 80%, about 81%, about 82%, about 83%, about 84%, about 85%, about 86%, about 87%, about 88%, about 89%, about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, about 98%, about 99%, or about 100% identical to the amino acid sequence set forth in any one of SEQ ID Nos. 89, 91, 92, 93, and 100, and wherein the FLT3 binding domain comprises a humanized FLT3 binding domain.

[00125] In various embodiments, a complementarity determining region of the FLT3 binding domain of the present disclosure is at least about 10%, about 20%, about 30%, about 40%, about 50%, about 60%, about 70%, about 80%, about 81%, about 82%, about 83%, about 84%, about 85%, about 86%, about 87%, about 88%, about 89%, about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, about 98%, about 99%, or about 100% identical to the amino acid sequence set forth in any one of SEQ ID Nos. 149, 150, 151, 152,

153, and 154, and wherein the FLT3 binding domain comprises a humanized FLT3 binding domain.

[00126] In various embodiments, a complementarity determining region of the FLT3 binding domain of the present disclosure is at least about 10%, about 20%, about 30%, about 40%, about 50%, about 60%, about 70%, about 80%, about 81%, about 82%, about 83%, about 84%, about 85%, about 86%, about 87%, about 88%, about 89%, about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, about 98%, about 99%, or about 100% identical to the amino acid sequence set forth in any one of SEQ ID Nos. 173, 186 and 195, and wherein the FLT3 binding domain comprises a humanized FLT3 binding domain.

[00127] In some embodiments, the FLT3 binding domains of this disclosure comprises a set of three CDR sequences, as provided in **Table 1**.

[00128] **Table 1: CDR sequences of exemplary FLT3 binding domains of this disclosure**

FLT3 Binder	CDR1	CDR2	CDR3
FLL101	77	109	155
FLL103	78	109	155
FLL116	77	109	155
FLL125	79	110	156
FLL129	80	111	155
FLL137	81	112	155
FLL14	77	109	155
FLL146	77	113	157
FLL158	82	110	156
FLL179	77	114	158
FLL181	80	111	155
FLL187	77	109	155
FLL32	83	115	155
FLL51	84	111	155
FLL55	79	116	156
FLL77	85	111	155
FLL97	77	109	155
FLL21	79	110	156
FLL57	86	110	156
FLL62	87	110	156
FLL79	79	110	156
FLL86	79	110	156
FLL112	88	117	159
FLL142	88	118	160
FLL143	88	119	161
FLL154	88	120	162
FLL168	88	121	163

FLT3 Binder	CDR1	CDR2	CDR3
FLL170	88	122	164
FLL188	88	121	165
FLL40	88	122	164
FLL6	88	121	166
FLL75	88	122	167
FLL83	88	122	168
FLL94	88	121	169
FLL99	88	118	165
FLL38	88	123	170
FLL53	88	124	171
FLL553	88	122	167
FLL74	88	117	172
FLL102	89	125	173
FLL122	89	125	173
FLL134	90	126	174
FLL153	90	127	175
FLL41	90	125	176
FLL67	90	125	176
FLL92	89	125	173
FLL71	90	128	175
FLL8	90	128	177
FLL84	90	125	176
FLL107	91	129	178
FLL141	91	130	178
FLL34	92	131	178
FLL4	93	132	178
FLL61	94	133	179
FLL78	91	134	178
FLL1	95	135	180
FLL26	96	136	181
FLL160	97	137	182
FLL173	97	138	183
FLL178	98	139	184
FLL27	99	139	185
FLL190	100	140	186
FLL43	101	141	187
FLL15	102	142	188
FLL45	103	143	189
FLL39	104	144	190
FLL177	105	145	191
FLL823	106	146	192
FLL76	107	147	193

FLT3 Binder	CDR1	CDR2	CDR3
FLL822	108	148	194
FLH107	91	149	195
FLH141	91	150	195
FLH19C	100	151	186
FLH34	92	152	195
FLH4	93	153	195
FLH78	91	154	195
FLH92a	89	393	173
FLH92b	89	394	173

[00129] In some embodiments, the FLT3 binding domain is cross-reactive with human cynomolgus (cyno) and mouse FLT3. In some embodiments, the FLT3 binding domain is specific for human FLT3. In certain embodiments, the FLT3 binding domains disclosed herein bind to human FLT3 with a human K_d (hK_d). In certain embodiments, the FLT3 binding domains disclosed herein bind to cynomolgus FLT3 with a cyno K_d (cK_d). In certain embodiments, the FLT3 binding domains disclosed herein bind to cynomolgus FLT3 with a mouse K_d (mK_d). In certain embodiments, the FLT3 binding domains disclosed herein bind to both cynomolgus FLT3 and a human FLT3, with a cyno K_d (cK_d) and a human K_d (hK_d), respectively. In certain embodiments, the FLT3 binding domains disclosed herein bind to cynomolgus FLT3, mouse FLT3, and a human FLT3, with a cyno K_d (cK_d), mouse K_d (mK_d), and a human K_d (hK_d), respectively. In some embodiments, the FLT3 binding protein binds to human, mouse and cynomolgus FLT3 with comparable binding affinities (*i.e.*, hK_d, mK_d and cK_d values do not differ by more than $\pm 10\%$). In some embodiments, the hK_d, mK_d and the cK_d range from about 0.1 nM to about 500 nM. In some embodiments, the hK_d, mK_d and the cK_d range from about 0.1 nM to about 450 nM. In some embodiments, the hK_d, mK_d and the cK_d range from about 0.1 nM to about 400 nM. In some embodiments, the hK_d, mK_d and the cK_d range from about 0.1 nM to about 350 nM. In some embodiments, the hK_d, mK_d and the cK_d range from about 0.1 nM to about 300 nM. In some embodiments, the hK_d, mK_d and the cK_d range from about 0.1 nM to about 250 nM. In some embodiments, the hK_d, mK_d and the cK_d range from about 0.1 nM to about 200 nM. In some embodiments, the hK_d, mK_d and the cK_d range from about 0.1 nM to about 150 nM. In some embodiments, the hK_d, mK_d and the cK_d range from about 0.1 nM to about 100 nM. In some embodiments, the hK_d, mK_d and the cK_d range from about 0.1 nM to about 90 nM. In some embodiments, the hK_d, mK_d and the cK_d range from about 0.2 nM to about 80 nM. In some embodiments, the hK_d, mK_d and the cK_d range from about 0.3 nM to about 70 nM. In some embodiments, the hK_d, mK_d and the cK_d range from about 0.4 nM to about 50 nM. In some embodiments, the hK_d, mK_d and the

cKd range from about 0.5 nM to about 30 nM. In some embodiments, the hKd, mKd and the cKd range from about 0.6 nM to about 10 nM. In some embodiments, the hKd, mKd and the cKd range from about 0.7 nM to about 8 nM. In some embodiments, the hKd, mKd and the cKd range from about 0.8 nM to about 6 nM. In some embodiments, the hKd, mKd and the cKd range from about 0.9 nM to about 4 nM. In some embodiments, the hKd, mKd and the cKd range from about 1 nM to about 2 nM.

[00130] In some embodiments, any of the foregoing FLT3 binding domains (*e.g.*, anti-FLT3 single domain antibodies of SEQ ID Nos. 1-76, and 389-390) are affinity peptide tagged for ease of purification. In some embodiments, the affinity peptide tag is six consecutive histidine residues, also referred to as 6X-his (SEQ ID No. 374). In certain embodiments, the FLT3 binding domains of the present disclosure preferentially bind membrane bound FLT3 over soluble FLT3. Membrane bound FLT3 refers to the presence of FLT3 in or on the cell membrane surface of a cell that expresses FLT3. Soluble FLT3 refers to FLT3 that is no longer on in or on the cell membrane surface of a cell that expresses or expressed FLT3. In certain instances, the soluble FLT3 is present in the blood and/or lymphatic circulation in a subject. In one embodiment, the FLT3 binding domains bind membrane-bound FLT3 at least 5 fold, 10 fold, 15 fold, 20 fold, 25 fold, 30 fold, 40 fold, 50 fold, 100 fold, 500 fold, or 1000 fold greater than soluble FLT3. In one embodiment, the FLT3 binding proteins of the present disclosure preferentially bind membrane-bound FLT3 30 fold greater than soluble FLT3. Determining the preferential binding of an antigen binding protein to membrane bound FLT3 over soluble FLT3 can be readily determined using binding assays.

[00131] It is contemplated that in some embodiments the FLT3 binding protein is fairly small and no more than 25 kDa, no more than 20 kDa, no more than 15 kDa, or no more than 10 kDa in some embodiments. In certain instances, the FLT3 binding protein is 5 kDa or less if it is a peptide or small molecule entity.

[00132] In other embodiments, the FLT3 binding proteins described herein comprise small molecule entity (SME) binders for FLT3. SME binders are small molecules averaging about 500 to 2000 Da in size and are attached to the FLT3 binding proteins by known methods, such as sortase ligation or conjugation. In these instances, the FLT3 binding protein comprises a domain comprising a sortase recognition sequence, *e.g.*, LPETG (SEQ ID No. 376). To attach a SME binder to FLT3 binding protein comprising a sortase recognition sequence, the protein is incubated with a sortase and a SME binder whereby the sortase attaches the SME binder to the recognition sequence. In yet other embodiments, the FLT3 binding proteins described herein comprise a knottin peptide for binding FLT3. Knottins are disulfide-stabilized peptides with a cysteine knot scaffold and have average sizes about 3.5 kDa. Knottins have been contemplated

for binding to certain tumor molecules such as FLT3. In further embodiments, the FLT3 binding proteins described herein comprise a natural FLT3 ligand.

[00133] In some embodiments, the FLT3 binding protein comprises more than one domain and are of a single-polypeptide design with flexible linkage of the domains. This allows for facile production and manufacturing of the FLT3 binding proteins as they can be encoded by single cDNA molecule to be easily incorporated into a vector. Further, in some embodiments where the FLT3 binding proteins described herein are a monomeric single polypeptide chain, there are no chain pairing issues or a requirement for dimerization. It is contemplated that, in such embodiments, the FLT3 binding proteins described herein have a reduced tendency to aggregate.

[00134] In the FLT3 binding proteins comprising more than one domain, the domains are linked by one or more internal linker. In certain embodiments, the internal linkers are “short,” i.e., consist of 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12 amino acid residues. Thus, in certain instances, the internal linkers consist of about 12 or less amino acid residues. In the case of 0 amino acid residues, the internal linker is a peptide bond. In certain embodiments, the internal linkers are “long,” i.e., consist of 15, 20 or 25 amino acid residues. In some embodiments, the internal linkers consist of about 3 to about 15, for example 8, 9 or 10 contiguous amino acid residues. Regarding the amino acid composition of the internal linkers, peptides are selected with properties that confer flexibility to the FLT3 binding proteins, do not interfere with the binding domains as well as resist cleavage from proteases. For example, glycine and serine residues generally provide protease resistance. Examples of internal linkers suitable for linking the domains in the FLT3 binding proteins include but are not limited to (GS)_n (SEQ ID No. 377), (GGS)_n (SEQ ID No. 378), (GGGS)_n (SEQ ID No. 379), (GGSG)_n (SEQ ID No. 380), (GGSGG)_n (SEQ ID No. 381), (GGGGS)_n (SEQ ID No. 382), (GGGGG)_n (SEQ ID No. 383), or (GGG)_n (SEQ ID No. 384), wherein n is 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10. In one embodiment, the linker is (GGGGSGGGSGGGSGGGGS) (SEQ ID No. 385), (GGGGSGGGSGGGGS) (SEQ ID No. 386), or (GGGGSGGGS) (SEQ ID No. 387).

[00135] In some cases, where the FLT3 binding protein comprises more than one domain, the domains within the FLT3 binding proteins are conjugated using an enzymatic site-specific conjugation method which involves the use of a mammalian or bacterial transglutaminase enzyme. Microbial transglutaminases (mTGs) are versatile tools in modern research and biotechnology. The availability of large quantities of relatively pure enzymes, ease of use, and lack of regulation by calcium and guanosine-5'-triphosphate (GTP) has propelled mTG to be the main cross-linking enzyme used in both the food industry and biotechnology. Currently, mTGs are used in many applications to attach proteins and peptides to small molecules, polymers,

surfaces, DNA, as well as to other proteins. *See e.g.*, Pavel Strp, Veracity of microbial transglutaminase, Bioconjugate Chem. 25, 5, 855-862.

[00136] In some examples are provided FLT3 binding proteins comprising more than one domain, wherein one of the domains comprises an acceptor glutamine in a constant region, which can then be conjugated to another domain *via* a lysine-based linker (*e.g.*, any primary amine chain which is a substrate for TGase, *e.g.* comprising an alkylamine, oxoamine) wherein the conjugation occurs exclusively on one or more acceptor glutamine residues present in the targeting moiety outside of the antigen combining site (*e.g.*, outside a variable region, in a constant region). Conjugation thus does not occur on a glutamine, *e.g.* an at least partly surface exposed glutamine, within the variable region. The FLT3 binding protein, in some examples, is formed by reacting one of the domains with a lysine-based linker in the presence of a TGase.

[00137] In some embodiments, where one or more domains within the FLT3 binding proteins are directly joined, a hybrid vector is made where the DNA encoding the directly joined domains are themselves directly ligated to each other. In some embodiments, where linkers are used, a hybrid vector is made where the DNA encoding one domain is ligated to the DNA encoding one end of a linker moiety and the DNA encoding another domain is ligated to the other end of the linker moiety.

[00138] In some embodiments, the FLT3 binding protein is a single chain variable fragments (scFv), single-domain antibody such as a heavy chain variable domain (VH), a light chain variable domain (VL) and a variable domain (VHH) of camelid derived single domain antibody. In other embodiments, the FLT3 binding protein is a non-Ig binding domain, i.e., an antibody mimetic, such as anticalins, affilins, affibody molecules, affimers, affitins, alphabodies, avimers, DARPins, fynomers, kunitz domain peptides, and monobodies. In further embodiments, the FLT3 binding protein is a ligand or peptide that binds to or associates with FLT3. In yet further embodiments, the FLT3 binding protein is a knottin. In yet further embodiments, the binding domain to FLT3 is a small molecular entity.

[00139] In certain embodiments, the FLT3 binding proteins according to the present disclosure may be incorporated into FLT3 targeting trispecific proteins. In some embodiments, the trispecific proteins comprise a CD3 binding domain, a half-life extension domain, and an FLT3 binding domain according to this disclosure. In some embodiments, the FLT3 binding trispecific protein comprises a trispecific antibody.

Multispecific FLT3 targeting proteins, such as FLT3 targeting trispecific proteins (also referred to herein as FLT3 targeting TriTAC™ proteins or molecules)

[00140] In one aspect is described herein a multispecific or a multivalent protein comprising an FLT3 binding protein according to the present disclosure. In some embodiments, the

multispecific protein further comprises a domain which specifically binds to a CD3. In some embodiments, the multispecific protein further comprises a domain which specifically binds to human CD3. In some embodiments, the multispecific protein further comprises a domain which specifically binds to CD3-gamma. In some embodiments, the multispecific protein further comprises a domain which specifically binds to CD3-delta. In some embodiments, the multispecific protein further comprises a domain which specifically binds to CD3-epsilon.

[00141] In additional embodiments, the multispecific protein further comprises a domain which specifically binds to the T cell receptor (TCR). In some embodiments, the multispecific protein further comprises a domain which specifically binds the alpha chain of the TCR. In some embodiments, the multispecific protein further comprises a domain which specifically binds the beta chain of the TCR.

[00142] In certain embodiments, the CD3 binding domain of the multispecific proteins exhibits not only potent CD3 binding affinities with human CD3, but shows excellent cross reactivity with the respective cynomolgus monkey CD3 proteins. In some instances, the CD3 binding domain of the multispecific proteins are cross-reactive with CD3 from cynomolgus monkey. In certain instances, human:cynomolgous KD (hKd: cKd) ratios for CD3 binding are between 20:1 and 1:2.

[00143] In some embodiments, the CD3 binding domain of the multispecific protein is any domain that binds to CD3 including but not limited to domains from a monoclonal antibody, a polyclonal antibody, a recombinant antibody, a human antibody, a humanized antibody, or antigen binding fragments of the CD3 binding antibodies, such as single domain antibodies (sdAb), Fab, F(ab')₂, and Fv fragments, fragments comprised of one or more CDRs, single-chain antibodies (*e.g.*, single chain Fv fragments (scFv), disulfide stabilized (dsFv) Fv fragments, heteroconjugate antibodies (*e.g.*, bispecific antibodies), pFv fragments, heavy chain monomers or dimers, light chain monomers or dimers, and dimers consisting of one heavy chain and one light chain. In some instances, it is beneficial for the CD3 binding domain to be derived from the same species in which the multispecific protein comprising a single domain serum albumin binding protein described herein will ultimately be used in. For example, for use in humans, it may be beneficial for the CD3 binding domain of the multispecific protein comprising an FLT3 binding protein described herein to comprise human or humanized residues from the antigen binding domain of an antibody or antibody fragment. Exemplary amino acid sequence for the CD3 binding domain of a multispecific (*e.g.*, trispecific) FLT3 targeting protein of this disclosure is provided as SEQ ID No. 373.

[00144] In some embodiments, the serum albumin binding domain (also referred to herein as the half-life extension domain) of a multispecific protein comprising an FLT3 binding protein as

described herein can be any domain that binds to serum albumin including but not limited to domains from a monoclonal antibody, a polyclonal antibody, a recombinant antibody, a human antibody, a humanized antibody. In some embodiments, the serum albumin binding domain is a single chain variable fragments (scFv), single-domain antibody such as a heavy chain variable domain (VH), a light chain variable domain (VL) and a variable domain (VHH) of camelid derived sdAb, or antigen binding fragments of the HSA binding antibodies, such as Fab, F(ab')₂, and Fv fragments, fragments comprised of one or more CDRs, single-chain antibodies (*e.g.*, single chain Fv fragments (scFv)), disulfide stabilized (dsFv) Fv fragments, heteroconjugate antibodies (*e.g.*, bispecific antibodies), pFv fragments, heavy chain monomers or dimers, light chain monomers or dimers, and dimers consisting of one heavy chain and one light chain, peptide, ligand or small molecule entity specific for serum albumin. In certain embodiments, the HSA binding domain is a single-domain antibody. In other embodiments, the serum albumin binding domain is a peptide. In further embodiments, the serum albumin binding domain is a small molecule. It is contemplated that the serum albumin binding domain of the multispecific binding protein comprising a single chain variable fragment CD3 binding protein is fairly small and no more than 25 kD, no more than 20 kD, no more than 15 kD, or no more than 10 kD in some embodiments. In certain instances, the serum albumin binding is 5 kD or less if it is a peptide or small molecule entity. Exemplary amino acid sequence for a serum albumin binding domain of a multispecific (*e.g.*, trispecific) FLT3 targeting protein of this disclosure is provided as SEQ ID No. 372.

[00145] The half-life extension domain of a multispecific binding protein as described herein, comprising a single chain variable fragment CD3 binding protein provides for altered pharmacodynamics and pharmacokinetics of the single chain variable fragment CD3 binding protein itself. As above, the half-life extension domain extends the elimination half-time. The half-life extension domain also alters pharmacodynamic properties including alteration of tissue distribution, penetration, and diffusion of the single chain variable fragment CD3 binding protein. In some embodiments, the half-life extension domain provides for improved tissue (including tumor) targeting, tissue distribution, tissue penetration, diffusion within the tissue, and enhanced efficacy as compared with a protein without a half-life extension domain. In one embodiment, therapeutic methods effectively and efficiently utilize a reduced amount of the multispecific binding protein comprising a single chain variable fragment CD3 binding protein, resulting in reduced side effects, such as reduced off-target, such as non-tumor cell cytotoxicity.

[00146] The half-life extension domain of a multispecific binding protein as described herein, comprising an FLT3 binding domain provides for altered pharmacodynamics and pharmacokinetics of FLT3 binding domain itself. As above, the half-life extension domain

extends the elimination half-time. The half-life extension domain also alters pharmacodynamic properties including alteration of tissue distribution, penetration, and diffusion of the FLT3 binding domain. In some embodiments, the half-life extension domain provides for improved tissue (including tumor) targeting, tissue distribution, tissue penetration, diffusion within the tissue, and enhanced efficacy as compared with a protein without a half-life extension domain. In one embodiment, therapeutic methods effectively and efficiently utilize a reduced amount of the multispecific binding protein comprising an FLT3 binding domain, resulting in reduced side effects, such as reduced off-target, such as non-tumor cell cytotoxicity.

[00147] Further, the binding affinity of the half-life extension domain, in some embodiments, is selected so as to target a specific elimination half-time in a multispecific binding protein comprising an FLT3 binding protein as described herein. Thus, in some embodiments, the half-life extension domain has a high binding affinity. In other embodiments, the half-life extension domain has a medium binding affinity. In yet other embodiments, the half-life extension domain has a low or marginal binding affinity. Exemplary binding affinities include K_d of 10 nM or less (high), between 10 nM and 100 nM (medium), and greater than 100 nM (low). As above, binding affinities to serum albumin are determined by known methods such as Surface Plasmon Resonance (SPR).

[00148] An FLT3 targeting multispecific protein of this disclosure, in certain embodiments, comprises (A) a first domain which binds to a CD3; (B) a second domain which is an half-life extension domain; and (C) a third domain which is an FLT3 binding protein as described herein. In certain embodiments, the first domain comprises an scFv that specifically binds the CD3. The CD3 protein comprises, for instance, a human CD3 protein. In certain embodiments, the second domain comprises an sdAb that specifically binds a bulk serum protein. In some instances, the bulk serum protein is albumin, such as, a serum albumin, such as, a human serum albumin.

[00149] The domains (A), (B), and (C), are, in some embodiments, linked *via* linkers L1 and L2, in any one of the following orientations: $H_2N-(A)-L1-(C)-L2-(B)-COOH$, $H_2N-(B)-L1-(A)-L2-(C)-COOH$, $H_2N-(C)-L1-(B)-L2-(A)-COOH$, $H_2N-(C)-L1-(A)-L2-(B)-COOH$, $H_2N-(A)-L1-(B)-(C)-L2-COOH$, or $H_2N-(B)-(C)-(A)-COOH$.

[00150] An FLT3 targeting multispecific protein of this disclosure, in some embodiments, comprises an amino acid sequence that is at least about 70% to at least about 100% identical to a sequence selected from the group consisting of SEQ ID Nos. 196-272, and 391-392. In some embodiments, an FLT3 targeting multispecific protein of this disclosure, in some embodiments, comprises an amino acid sequence that is at least about 70%, at least about 75%, at least about 76%, at least about 77%, about 78%, at least about 79%, at least about 80%, at least about 81%, at least about 82%, at least about 83%, at least about 84%, at least about 85%, at least about

86%, at least about 87%, at least about 88%, at least about 89%, at least about 90%, at least about 91%, at least about 92%, at least about 93%, at least about 94%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, at least about 99%, to at least about 100% identical to a sequence selected from the group consisting of SEQ ID Nos. 196-272, and 391-392.

[00151] An FLT3 targeting multispecific protein of this disclosure, in some embodiments, comprises an EC₅₀ of about 0.5 pM to about 6000 pM, such as such as an EC₅₀ from about 0.5 pM to about 1500 pM, about 1 pM to about 4000 pM, about 10 pM to about 2000 pM, about 20 pM to about 1000 pM, about 30 pM to about 40 pM to about 500 pM, or about 50 pM to about 100 pM, in a T cell dependent cellular cytotoxicity (TDCC) assay that measures the potency of the multispecific protein in T cell mediated killing of cells, such as leukemia or lymphoma cells (*see, e.g.*, TDCC EC₅₀ values provided in **Table 5** and **Table 6**). In some embodiments, the EC₅₀ in the TDCC assay is from about 0.5 pM to about 6000 pM, such as from about 0.5 pM to about 35 pM.

Conditionally active multispecific FLT3 targeting proteins, such as conditionally active FLT3 targeting trispecific proteins (also referred to herein as FLT3 targeting ProTriTAC™ or protrispecific proteins or molecules)

[00152] One embodiment of this disclosure provides a conditionally active multispecific protein comprising an FLT3 binding domain as disclosed herein (for example, in some embodiment this disclosure provides an FLT3 targeting protrispecific/ProTriTAC™ protein comprising an FLT3 binding domain of this disclosure). Examples are illustrated in **FIG. 28**. In some embodiments, the conditionally active multispecific protein further comprises a domain which specifically binds to a CD3 and a binding moiety which specifically binds to a bulk serum protein, such as a human serum albumin. In some embodiments, the binding moiety is capable of masking the interaction of the FLT3 binding domain or the CD3 binding domain, to their targets. In some embodiments, a binding moiety of this disclosure comprises a masking moiety and a cleavable linker, such as a protease cleavable linker. In some embodiments, the masking moiety comprises a modified non-CDR loop sequence and a non-cleavable linker. The binding moiety is capable of synergistically expanding a therapeutic window of a conditionally active FLT3 targeting protrispecific protein, by both steric masking and specific masking. In some embodiments, the binding moiety combines both steric masking (for example, *via* binding to a bulk serum albumin) and specific masking (for example, *via* non-CDR loops binding to the CDRs of an anti-FLT3 domain or an anti-CD3 scFv domain). In some cases, modifying the non-CDR loops within the binding moiety does not affect albumin binding. The protease cleavable linker, in some cases, enables activation of an FLT3 targeting protrispecific protein in

a single proteolytic event, thereby allowing more efficient conversion of the protrispecific molecule in tumor microenvironment. Further, tumor-associated proteolytic activation, in some cases, reveals active T cell engager with minimal off-tumor activity after activation. The present disclosure, in some embodiments, provides a half-life extended T cell engager format (ProTriTAC™) comprising an FLT3 binding moiety as described herein, which in some cases represents a new and improved approach to engineer conditionally active T cell engagers.

[00153] The half-life of the FLT3 binding domain in a conditionally active protrispecific format is, in some embodiments, extended in systemic circulation by using the binding moiety as described above which acts as a safety switch that keeps the multispecific protein in the pro format in an inert state until it reaches the tumor microenvironment where it is conditionally activated by cleavage of the linker and is able to bind its target antigen(s). The safety switch, in certain instances, provides several advantages: some examples including (i) expanding the therapeutic window of the conditionally active FLT3 targeting protein; (ii) reducing target-mediated drug disposition by maintaining the conditionally active FLT3 targeting protein in systemic circulation; (iii) reducing the concentration of undesirable activated protein in systemic circulation, thereby minimizing the spread of chemistry, manufacturing, and controls related impurities, *e.g.*, pre-activated drug product, endogenous viruses, host-cell proteins, DNA, leachables, anti-foam, antibiotics, toxins, solvents, heavy metals; (iv) reducing the concentration of undesirable activated proteins in systemic circulation, thereby minimizing the spread of product related impurities, aggregates, breakdown products, product variants due to: oxidation, deamidation, denaturation, loss of C-term Lys in MAbs; (v) preventing aberrant activation in circulation; (vi) reducing the toxicities associated with the leakage of activated species from diseased tissue or other pathophysiological conditions, *e.g.*, tumors, autoimmune diseases, inflammations, viral infections, tissue remodeling events (such as myocardial infarction, skin wound healing), or external injury (such as X-ray, CT scan, UV exposure); and (vii) reducing non-specific binding of the conditionally active FLT3 targeting protein. Furthermore, post-activation, or in other words post breaking of the safety switch, the conditionally active FLT3 targeting protein is separated from the safety switch which provided extended half-life, and thus is cleared from circulation.

[00154] In some embodiments, the conditionally active FLT3 targeting protein format gives the FLT3 binding domain a significantly longer serum half-life and reduces the likelihood of its undesirable activation in circulation, thereby producing a “biobetter” version.

[00155] A binding moiety as described herein comprises at least one non-CDR loop. In some embodiments, a non-CDR loop provides a binding site for binding of the binding moiety to an FLT3 binding domain of this disclosure. In some cases, the binding moiety masks binding of

the FLT3 binding domain to its target antigen, *e.g.*, *via* steric occlusion, *via* specific intermolecular interactions, or a combination of both.

[00156] In some embodiments, a binding moiety as described herein further comprise complementarity determining regions (CDRs), for instance, specific for binding a bulk serum protein (*e.g.*, a human serum albumin). In some instances, a binding moiety of this disclosure is a domain derived from an immunoglobulin molecule (Ig molecule). The Ig may be of any class or subclass (IgG1, IgG2, IgG3, IgG4, IgA, IgE, IgM etc). A polypeptide chain of an Ig molecule folds into a series of parallel beta strands linked by loops. In the variable region, three of the loops constitute the “complementarity determining regions” (CDRs) which determine the antigen binding specificity of the molecule. An IgG molecule comprises at least two heavy (H) chains and two light (L) chains inter-connected by disulfide bonds, or an antigen binding fragment thereof. Each heavy chain is comprised of a heavy chain variable region (abbreviated herein as VH) and a heavy chain constant region. The heavy chain constant region is comprised of three domains, CH1, CH2 and CH3. Each light chain is comprised of a light chain variable region (abbreviated herein as VL) and a light chain constant region. The light chain constant region is comprised of one domain, CL. The VH and VL regions can be further subdivided into regions of hypervariability, termed complementarity determining regions (CDRs) with are hypervariable in sequence and/or involved in antigen recognition and/or usually form structurally defined loops, interspersed with regions that are more conserved, termed framework regions (FR). Each VH and VL is composed of three CDRs and four FRs, arranged from amino-terminus to carboxy-terminus in the following order: FR1, CDR1, FR2, CDR2, FR3, CDR3, FR4. In some embodiments of this disclosure, at least some or all of the amino acid sequences of FR1, FR2, FR3, and FR4 are part of the “non-CDR loop” of the binding moieties described herein. As shown in **FIG. 29**, a variable domain of an immunoglobulin molecule has several beta strands that are arranged in two sheets. The variable domains of both light and heavy immunoglobulin chains contain three hypervariable loops, or complementarity-determining regions (CDRs). The three CDRs of a V domain (CDR1, CDR2, CDR3) cluster at one end of the beta barrel. The CDRs are the loops that connect beta strands B-C, C'-C", and F-G of the immunoglobulin fold, whereas the bottom loops that connect beta strands AB, CC', C" -D and E-F of the immunoglobulin fold, and the top loop that connects the D-E strands of the immunoglobulin fold are the non-CDR loops. In some embodiments of this disclosure, at least some amino acid residues of a constant domain, CH1, CH2, or CH3, are part of the “non-CDR loop” of the binding moieties described herein. Non-CDR loops comprise, in some embodiments, one or more of AB, CD, EF, and DE loops of a C1-set domain of an Ig or an Ig-like molecule; AB, CC', EF, FG, BC, and EC' loops of a C2-set domain of an Ig or an Ig-like

molecule; DE, BD, GF, A(A1A2)B, and EF loops of I(Intermediate)-set domain of an Ig or Ig-like molecule.

[00157] Within the variable domain, the CDRs are believed to be responsible for antigen recognition and binding, while the FR residues are considered a scaffold for the CDRs.

However, in certain cases, some of the FR residues play an important role in antigen recognition and binding. Framework region residues that affect Ag binding are divided into two categories. The first are FR residues that contact the antigen, thus are part of the binding-site, and some of these residues are close in sequence to the CDRs. Other residues are those that are far from the CDRs in sequence, but are in close proximity to it in the 3-D structure of the molecule, *e.g.*, a loop in heavy chain.

[00158] In some embodiments, the non-CDR loop is modified to generate an antigen binding site specific for a bulk serum protein, such as albumin. It is contemplated that various techniques can be used for modifying the non-CDR loop, *e.g.*, site-directed mutagenesis, random mutagenesis, insertion of at least one amino acid that is foreign to the non-CDR loop amino acid sequence, amino acid substitution. An antigen peptide is inserted into a non-CDR loop, in some examples. In some examples, an antigenic peptide is substituted for the non-CDR loop. The modification, to generate an antigen binding site, is in some cases in only one non-CDR loop. In other instances, more than one non-CDR loop are modified. For instance, the modification is in any one of the non-CDR loops shown in **FIG. 29**, *i.e.*, AB, CC', C" D, EF, and D-E. In some cases, the modification is in the DE loop. In other cases the modifications are in all four of AB, CC', C" -D, E-F loops. In certain examples, the binding moieties described herein are bound to the FLT3 binding domain *via* their AB, CC', C" D, or EF loop and are bound to a bulk-serum protein, such as albumin, *via* their B-C, C'-C", or F-G loop. In certain examples, the binding moiety is bound to the FLT3 binding domain *via* its AB, CC', C" D, and EF loop and is bound to a bulk-serum protein, such as albumin, *via* its BC, C'C", and FG loop. In certain examples, the binding moiety is bound to the FLT3 binding domain *via* one or more of AB, CC', C" D, and E-F loop and is bound to a bulk-serum protein, such as albumin, *via* one or more of BC, C'C", and FG loop. In certain examples, the binding moiety is bound to a bulk serum protein, such as albumin, *via* its AB, CC', C" D, or EF loop and is bound to the FLT3 binding domain *via* its BC, C'C", or FG loop. In certain examples, the binding moiety is bound to a bulk serum protein, such as albumin, *via* its AB, CC', C" D, and EF loop and is bound to the FLT3 binding domain *via* its BC, C'C", and FG loop. In certain examples, the binding moiety of the first embodiment is bound to a bulk serum protein, such as albumin, *via* one or more of AB, CC', C" D, and E-F loop and is bound to the FLT3 binding protein, *via* one or more of BC, C'C", and FG loop.

[00159] The bulk serum protein comprises, for example, albumin, fibrinogen, or a globulin. In some embodiments, the binding moieties are engineered scaffolds. Engineered scaffolds comprise, for example, sdAb, a scFv, a Fab, a VHH, a fibronectin type III domain, immunoglobulin-like scaffold (as suggested in Halaby et al., 1999. Prot Eng 12(7):563-571), DARPIn, cystine knot peptide, lipocalin, three-helix bundle scaffold, protein G-related albumin-binding module, or a DNA or RNA aptamer scaffold.

[00160] In some cases, the binding moieties comprise a binding site for the bulk serum protein. In some embodiments, the CDRs within the binding moieties provide a binding site for the bulk serum protein. The bulk serum protein is, in some examples, a globulin, albumin, transferrin, IgG1, IgG2, IgG4, IgG3, IgA monomer, Factor XIII, Fibrinogen, IgE, or pentameric IgM. In some embodiments, the binding moieties comprise a binding site for an immunoglobulin light chain. In some embodiments, the CDRs provide a binding site for the immunoglobulin light chain. The immunoglobulin light chain is, in some examples, an Igk free light chain or an Igλ free light chain.

[00161] The binding moieties are any kinds of polypeptides. For example, in certain instances the binding moieties are natural peptides, synthetic peptides, or fibronectin scaffolds, or engineered bulk serum proteins. In some examples, the binding moieties comprise any type of binding domain, including but not limited to, domains from a monoclonal antibody, a polyclonal antibody, a recombinant antibody, a human antibody, a humanized antibody. In some embodiments, the binding moiety is a single chain variable fragment (scFv), a soluble TCR fragment, a single-domain antibody such as a heavy chain variable domain (VH), a light chain variable domain (VL) and a variable domain (VHH) of camelid derived nanobody. In other embodiments, the binding moieties are non-Ig binding domains, i.e., antibody mimetic, such as anticalins, affilins, affibody molecules, affimers, affitins, alphabodies, avimers, DARPins, fynomers, kunitz domain peptides, and monobodies.

Integration into chimeric antigen receptors (CAR)

[00162] The FLT3 binding proteins of the present disclosure can, in certain examples, be incorporated into a chimeric antigen receptor (CAR). An engineered immune effector cell, *e.g.*, a T cell or NK cell, can be used to express a CAR that includes an FLT3 binding protein containing, for example, an anti-FLT3 single domain antibody as described herein. In one embodiment, the CAR including the FLT3 binding protein as described herein is connected to a transmembrane domain *via* a hinge region, and further a costimulatory domain, *e.g.*, a functional signaling domain obtained from OX40, CD27, CD28, CD5, ICAM-1, LFA-1 (CD11a/CD18), ICOS (CD278), or 4-1BB. In some embodiments, the CAR further comprises a sequence encoding an intracellular signaling domain, such as 4-1BB and/or CD3 zeta.

FLT3 Binding Protein Modifications

[00163] The FLT3 binding proteins described herein, including FLT3 binding domains (*e.g.*, an FLT3 binding sdAb of this disclosure) and FLT3 targeting multispecific proteins (*e.g.*, an FLT3 targeting trispecific protein as described herein) encompass derivatives or analogs in which (i) an amino acid is substituted with an amino acid residue that is not one encoded by the genetic code, (ii) the mature polypeptide is fused with another compound such as polyethylene glycol, or (iii) additional amino acids are fused to the protein, such as a leader or secretory sequence or a sequence for purification of the protein.

[00164] Typical modifications include, but are not limited to, acetylation, acylation, ADP-ribosylation, amidation, covalent attachment of flavin, covalent attachment of a heme moiety, covalent attachment of a nucleotide or nucleotide derivative, covalent attachment of a lipid or lipid derivative, covalent attachment of phosphatidylinositol, cross-linking, cyclization, disulfide bond formation, demethylation, formation of covalent crosslinks, formation of cystine, formation of pyroglutamate, formylation, gamma carboxylation, glycosylation, GPI anchor formation, hydroxylation, iodination, methylation, myristoylation, oxidation, proteolytic processing, phosphorylation, prenylation, racemization, selenoylation, sulfation, transfer-RNA mediated addition of amino acids to proteins such as arginylation, and ubiquitination.

[00165] Modifications are made anywhere in the FLT3 binding proteins described herein, including the peptide backbone, the amino acid side-chains, and the amino or carboxyl termini. Certain common peptide modifications that are useful for modification of the FLT3 binding proteins include glycosylation, lipid attachment, sulfation, gamma-carboxylation of glutamic acid residues, hydroxylation, blockage of the amino or carboxyl group in a polypeptide, or both, by a covalent modification, and ADP-ribosylation.

[00166] In some embodiments, derivatives of the FLT3 binding proteins as described herein comprise immunoreactive modulator derivatives and antigen binding molecules comprising one or more modifications.

[00167] In some embodiments, the FLT3 binding proteins of the disclosure are monovalent or multivalent bivalent, trivalent, etc.). As used herein, the term “valency” refers to the number of potential target binding sites associated with an antibody. Each target binding site specifically binds one target molecule or specific position or locus on a target molecule. When an antibody is monovalent, each binding site of the molecule will specifically bind to a single antigen position or epitope. When an antibody comprises more than one target binding site (multivalent), each target binding site may specifically bind the same or different molecules (*e.g.*, may bind to different ligands or different antigens, or different epitopes or positions on the same antigen).

[00168] In some embodiments, the FLT3 binding proteins as set forth above are fused to an Fc region from any species, including but not limited to, human immunoglobulin, such as human IgG1, a human IgG2, a human IgG3, human IgG4, to generate Fc-fusion FLT3 binding proteins. In some embodiments, the Fc-fusion FLT3 binding proteins of this disclosure have extended half-life compared to an otherwise identical FLT3 binding protein. In some embodiments, the Fc-fusion FLT3 binding proteins of this disclosure contain *inter alia* one or more additional amino acid residue substitutions, mutations and/or modifications, *e.g.*, in the Fc region. which result in a binding protein with preferred characteristics including, but not limited to: altered pharmacokinetics, extended serum half-life.

[00169] In some embodiments, such Fc-fused FLT3 binding proteins provide extended half-lives in a mammal, such as in a human, of greater than 5 days, greater than 10 days, greater than 15 days, greater than 20 days, greater than 25 days, greater than 30 days, greater than 35 days, greater than 40 days, greater than 45 days, greater than 2 months, greater than 3 months, greater than 4 months, or greater than 5 months. The increased half-life, in some cases, results in a higher serum titer which thus reduces the frequency of the administration of the FLT3 binding proteins and/or reduces the concentration of the antibodies to be administered. Binding to human FcRn *in vivo* and serum half-life of human FcRn high affinity binding polypeptides is assayed, in some examples, in transgenic mice or transfected human cell lines expressing human FcRn, or in primates to which the polypeptides with a variant Fc region are administered.

[00170] The FLT3 binding proteins, in some cases, are differentially modified during or after production, *e.g.*, by glycosylation, acetylation, phosphorylation, amidation, derivatization by known protecting/blocking groups, proteolytic cleavage, linkage to an antibody molecule or other cellular ligand, etc. Any of numerous chemical modifications are carried out by techniques, including but not limited, to specific chemical cleavage by cyanogen bromide, trypsin, chymotrypsin, papain, V8 protease, NaBH₄, acetylation, formylation, oxidation, reduction, metabolic synthesis in the presence of tunicamycin, etc.

[00171] Various post-translational modifications of the FLT3 binding proteins also encompassed by the disclosure include, for example, N-linked or O-linked carbohydrate chains, processing of N-terminal or C-terminal ends, attachment of chemical moieties to the amino acid backbone, chemical modifications of N-linked or O-linked carbohydrate chains, and addition or deletion of an N-terminal methionine residue as a result of prokaryotic host cell expression. Moreover, the FLT3 binding proteins are, in some cases, modified with a detectable label, such as an enzymatic, fluorescent, radioisotopic or affinity label to allow for detection and isolation of the modulator.

Polynucleotides Encoding FLT3 Binding Proteins

[00172] Also provided, in some embodiments, are polynucleotide molecules encoding FLT3 binding proteins described herein. In some embodiments, the polynucleotide molecules are provided as a DNA construct. In other embodiments, the polynucleotide molecules are provided as a messenger RNA transcript.

[00173] The polynucleotide molecules are constructed by known methods such as by combining the genes encoding a single domain FLT3 binding protein or gene encoding various domains of FLT3 binding proteins comprising more than one domain. In some embodiments, the gene encoding the domains are either separated by peptide linkers or, in other embodiments, directly linked by a peptide bond, into a single genetic construct operably linked to a suitable promoter, and optionally a suitable transcription terminator, and expressing it in bacteria or other appropriate expression system such as, for example CHO cells. Depending on the vector system and host utilized, any number of suitable transcription and translation elements, including constitutive and inducible promoters, may be used. The promoter is selected such that it drives the expression of the polynucleotide in the respective host cell.

[00174] In some embodiments, the polynucleotide coding for an FLT3 binding protein as described herein is inserted into a vector, preferably an expression vector, which represents a further embodiment. This recombinant vector can be constructed according to known methods. Vectors of particular interest include plasmids, phagemids, phage derivatives, virii (*e.g.*, retroviruses, adenoviruses, adeno-associated viruses, herpes viruses, lentiviruses, and the like), and cosmids.

[00175] A variety of expression vector/host systems may be utilized to contain and express the polynucleotide encoding the polypeptide of the described FLT3 binding protein. Examples of expression vectors for expression in *E.coli* are pSKK (Le Gall et al., J Immunol Methods. (2004) 285(1):111-27) or pcDNA5 (Invitrogen) for expression in mammalian cells.

[00176] Thus, the FLT3 binding proteins as described herein, in some embodiments, are produced by introducing a vector encoding the protein as described above into a host cell and culturing said host cell under conditions whereby the protein domains are expressed, may be isolated and, optionally, further purified.

Pharmaceutical Compositions

[00177] Also provided, in some embodiments, are pharmaceutical compositions comprising an anti-FLT3 binding protein described herein, a vector comprising the polynucleotide encoding the polypeptide of the FLT3 binding proteins or a host cell transformed by this vector and at least one pharmaceutically acceptable carrier. The term “pharmaceutically acceptable carrier” includes, but is not limited to, any carrier that does not interfere with the effectiveness of the

biological activity of the ingredients and that is not toxic to the patient to whom it is administered. Examples of suitable pharmaceutical carriers are well known in the art and include phosphate buffered saline solutions, water, emulsions, such as oil/water emulsions, various types of wetting agents, sterile solutions etc. Such carriers can be formulated by conventional methods and can be administered to the subject at a suitable dose. Preferably, the compositions are sterile. These compositions may also contain adjuvants such as preservative, emulsifying agents and dispersing agents. Prevention of the action of microorganisms may be ensured by the inclusion of various antibacterial and antifungal agents. A further embodiment provides one or more of the above described FLT3 binding proteins packaged in lyophilized form, or packaged in an aqueous medium.

[00178] In some embodiments of the pharmaceutical compositions, the FLT3 binding proteins described herein are encapsulated in nanoparticles. In some embodiments, the nanoparticles are fullerenes, liquid crystals, liposome, quantum dots, superparamagnetic nanoparticles, dendrimers, or nanorods. In other embodiments of the pharmaceutical compositions, the FLT3 binding protein is attached to liposomes. In some instances, the FLT3 binding proteins are conjugated to the surface of liposomes. In some instances, the FLT3 binding proteins are encapsulated within the shell of a liposome. In some instances, the liposome is a cationic liposome.

[00179] The FLT3 binding proteins described herein are contemplated for use as a medicament. Administration is effected by different ways, *e.g.* by intravenous, intraperitoneal, subcutaneous, intramuscular, topical or intradermal administration. In some embodiments, the route of administration depends on the kind of therapy and the kind of compound contained in the pharmaceutical composition. The dosage regimen will be determined by the attending physician and other clinical factors. Dosages for any one patient depends on many factors, including the patient's size, body surface area, age, sex, the particular compound to be administered, time and route of administration, the kind of therapy, general health and other drugs being administered concurrently. An "effective dose" refers to amounts of the active ingredient that are sufficient to affect the course and the severity of the disease, leading to the reduction or remission of such pathology and may be determined using known methods.

[00180] In some embodiments, the FLT3 binding proteins of this disclosure are administered at a dosage of up to 10 mg/kg at a frequency of once a week. In some cases, the dosage ranges from about 1 ng/kg to about 10 mg/kg, for example about 1 ng/kg to about 70 ng/kg, about 1 ng/kg to about 160 ng/kg, about 1 ng/kg to about 200 ng/kg. In some embodiments, the dose is from about 1 ng/kg to about 10 ng/kg, about 5 ng/kg to about 15 ng/kg, about 12 ng/kg to about 20 ng/kg, about 18 ng/kg to about 30 ng/kg, about 25 ng/kg to about 50 ng/kg, about 35 ng/kg to

about 60 ng/kg, about 45 ng/kg to about 70 ng/kg, about 65 ng/kg to about 85 ng/kg, about 80 ng/kg to about 1 µg/kg, about 0.5 µg/kg to about 5 µg/kg, about 2 µg/kg to about 10 µg/kg, about 7 µg/kg to about 15 µg/kg, about 12 µg/kg to about 25 µg/kg, about 20 µg/kg to about 50 µg/kg, about 35 µg/kg to about 70 µg/kg, about 45 µg/kg to about 80 µg/kg, about 65 µg/kg to about 90 µg/kg, about 85 µg/kg to about 0.1 mg/kg, about 0.095 mg/kg to about 10 mg/kg. In some cases, the dosage is about 0.1 mg/kg to about 0.2 mg/kg; about 0.25 mg/kg to about 0.5 mg/kg, about 0.45 mg/kg to about 1 mg/kg, about 0.75 mg/kg to about 3 mg/kg, about 2.5 mg/kg to about 4 mg/kg, about 3.5 mg/kg to about 5 mg/kg, about 4.5 mg/kg to about 6 mg/kg, about 5.5 mg/kg to about 7 mg/kg, about 6.5 mg/kg to about 8 mg/kg, about 7.5 mg/kg to about 9 mg/kg, or about 8.5 mg/kg to about 10 mg/kg. The frequency of administration, in some embodiments, is about less than daily, every other day, less than once a day, twice a week, weekly, once in 7 days, once in two weeks, once in three weeks, once in four weeks, or once a month. In some cases, the frequency of administration is weekly. In some cases, the frequency of administration is weekly and the dosage is up to 10 mg/kg. In some cases, duration of administration is from about 1 day to about 4 weeks or longer.

Methods of treatment

[00181] Also provided in certain embodiments are methods of treating a condition associated with malignant cells expressing FLT3 in a subject comprising administering to a subject in need thereof an effective amount of an FLT3 binding domains or multispecific proteins (including conditionally active multispecific proteins) comprising an FLT3 binding domain of this disclosure, or a CAR comprising an FLT3 binding protein as described herein, or a pharmaceutical composition comprising the same. In some embodiments, the condition is a cancer. In some embodiment the condition is a hematologic malignancy derived from either of the two major blood cell lineages, *i.e.*, the myeloid cell line (which produces granulocytes, erythrocytes, thrombocytes, macrophages and mast cells) or lymphoid cell line (which produces B, T, NK and plasma cells), such as all types of leukemias, lymphomas, and myelomas, *e.g.*, acute, chronic, lymphocytic and/or myelogenous leukemias, such as 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 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 of said cancers.

[00182] In some embodiments, the condition is Myelodysplastic syndrome (“MDS”) which refers to a diverse group of hematopoietic stem cell disorders. MDS is characterized by a cellular marrow with impaired morphology and maturation (dysmyelopoiesis), peripheral blood cytopenias, and a variable risk of progression to acute leukemia, resulting from ineffective blood cell production.

[00183] In another aspect, the disclosure provides a method of inhibiting tumor growth or progression in a subject who has malignant cells expressing FLT3, comprising administering to the subject in need thereof an effective amount of an FLT3 binding domains or multispecific proteins comprising an FLT3 binding domain of this disclosure, or a CAR comprising an FLT3 binding protein as described herein, or a pharmaceutical composition comprising the same. In another aspect, the disclosure provides a method of inhibiting metastasis of malignant cells expressing FLT3 in a subject, comprising administering to the subject in need thereof an effective amount of an FLT3 binding domains or multispecific proteins comprising an FLT3 binding domain of this disclosure, or a pharmaceutical composition comprising the same. In another aspect, the disclosure provides a method of inducing tumor regression in a subject who has malignant cells expressing FLT3, comprising administering to the subject in need thereof an effective amount of an FLT3 binding domains or multispecific proteins comprising an FLT3 binding domain of this disclosure, or a pharmaceutical composition comprising the same. In some embodiments, the methods as described herein further comprise administering an effective amount of a second therapeutic agent. In some embodiments, the second therapeutic agent is a biotherapeutic agent, for example, an antibody. In some embodiments, the second therapeutic agent is a cytokine, TNFa (Tumor Necrosis Factor alpha), a PAP (phosphatidic acid phosphatase) inhibitor, an oncolytic virus, a kinase inhibitor, an IDO (Indoleamine-pyrrole 2,3-dioxygenase) inhibitor, a glutaminase GLS1 inhibitor, a CAR (Chimeric Antigen Receptor)-T cell or T cell therapy, a TLR (Toll-Like Receptor) Agonist (*e.g.*, TLR3, TLR4, TLR5, TLR7, TLR9), or a tumor vaccine.

[00184] In some embodiments, the FLT3 binding protein of this disclosure or a pharmaceutical composition comprising the same, reduces the growth of tumor cells *in vivo* when administered to a subject who has tumor cells that express FLT3. Measurement of the reduction of the growth of tumor cells can be determined by multiple different methodologies well known in the art. Nonlimiting examples include direct measurement of tumor dimension, measurement of excised tumor mass and comparison to control subjects, measurement *via* imaging techniques (*e.g.*, CT or MRI) that may or may not use isotopes or luminescent molecules (*e.g.*, luciferase) for

enhanced analysis, and the like. In specific embodiments, administration of the FLT3 binding proteins of the disclosure or a pharmaceutical composition comprising the same results in a reduction of *in vivo* growth of tumor cells as compared to a control antigen binding agent by at least about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or 100%, with an about 100% reduction in tumor growth indicating a complete response and disappearance of the tumor. In further embodiments, administration of the FLT3 binding proteins of the disclosure or a pharmaceutical composition comprising the same results in a reduction of *in vivo* growth of tumor cells as compared to a control antigen binding agent by about 50-100%, about 75-100% or about 90-100%. In further embodiments, administration of the FLT3 binding proteins of the disclosure or a pharmaceutical composition comprising the same results in a reduction of *in vivo* growth of tumor cells as compared to a control antigen binding agent by about 50-60%, about 60-70%, about 70-80%, about 80-90%, or about 90-100%.

[00185] In some embodiments, the FLT3 binding proteins of the present disclosure are administered to treat a neoplastic condition. Neoplastic conditions, in some embodiments, are benign or malignant; solid tumors or other blood neoplasia; and, in some embodiments, are selected from the group including, but not limited to: adrenal gland tumors, AIDS-associated cancers, alveolar soft part sarcoma, astrocytic tumors, autonomic ganglia tumors, bladder cancer (squamous cell carcinoma and transitional cell carcinoma), blastocoelic disorders, bone cancer (adamantinoma, aneurismal bone cysts, osteochondroma, osteosarcoma), brain and spinal cord cancers, metastatic brain tumors, breast cancer including triple negative breast cancer, carotid body tumors, cervical cancer, chondrosarcoma, chordoma, chromophobe renal cell carcinoma, clear cell carcinoma, colon cancer, colorectal cancer, cutaneous benign fibrous histiocytomas, desmoplastic small round cell tumors, ependymomas, epithelial disorders, Ewing's tumors, extraskeletal myxoid chondrosarcoma, fibrogenesis imperfecta ossium, fibrous dysplasia of the bone, gallbladder and bile duct cancers, gastric cancer, gastrointestinal, gestational trophoblastic disease, germ cell tumors, glandular disorders, head and neck cancers, hypothalamic, intestinal cancer, islet cell tumors, Kaposi's Sarcoma, kidney cancer (nephroblastoma, papillary renal cell carcinoma), leukemias, lipoma/benign lipomatous tumors, liposarcoma/malignant lipomatous tumors, liver cancer (hepatoblastoma, hepatocellular carcinoma), lymphomas, lung cancers (small cell carcinoma, adenocarcinoma, squamous cell carcinoma, large cell carcinoma etc.), macrophagal disorders, medulloblastoma, melanoma, meningiomas, multiple endocrine neoplasia, multiple myeloma, myelodysplastic syndrome, neuroblastoma, neuroendocrine tumors, ovarian cancer, pancreatic cancers, papillary thyroid carcinomas, parathyroid tumors, pediatric cancers, peripheral nerve sheath tumors, phaeochromocytoma, pituitary tumors, prostate cancer, posterior uveal melanoma, rare hematologic disorders, renal metastatic cancer,

rhabdoid tumor, rhabdomyosarcoma, sarcomas, skin cancer, soft-tissue sarcomas, squamous cell cancer, stomach cancer, stromal disorders, synovial sarcoma, testicular cancer, thymic carcinoma, thymoma, thyroid metastatic cancer, and uterine cancers (carcinoma of the cervix, endometrial carcinoma, and leiomyoma).

[00186] In certain embodiments the FLT3 binding proteins of the present disclosure are used as a front line therapy and administered to subjects who have not previously been treated for the cancerous condition. In other embodiments the FLT3 binding proteins of the present disclosure are used to treat subjects that have previously been treated (with an FLT3 binding protein of this disclosure or with other anti-cancer agent) and have relapsed or determined to be refractory to the previous treatment. In some embodiments the FLT3 binding proteins of the present disclosure are used to treat subjects that have recurrent tumors. In some aspects, the FLT3 binding proteins of the present disclosure are administered to treat a proliferative disorder comprising a solid tumor including, but not limited to, adrenal, liver, kidney, bladder, breast, gastric, ovarian, cervical, uterine, esophageal, colorectal, prostate, pancreatic, lung (both small cell and non-small cell), thyroid, carcinomas, sarcomas, glioblastomas and various head and neck tumors. In some embodiments, the FLT3 binding proteins of the present disclosure are administered to a subject suffering from melanoma. In some embodiments, the FLT3 binding proteins of the present disclosure are used to diagnose, monitor, treat or prevent melanoma. The term “melanoma,” as used herein, includes all types of melanoma including, but not limited to, primary melanoma, malignant melanoma, cutaneous melanoma, extracutaneous melanoma, superficial spreading melanoma, polypoid melanoma, melanocarcinomas, melano epitheliomas, melano sarcomas, melanoma in situ, nodular malignant melanoma, lentigo maligna melanoma, lentiginous melanoma, lentiginous malignant melanoma, mucosal lentiginous melanoma, mucosal melanoma, acral lentiginous melanoma, soft tissue melanoma, ocular melanoma, invasive melanoma, familial atypical mole and melanoma (FAM-M) syndrome, desmoplastic malignant melanoma or uveal melanoma. In some embodiments, possible indications for administration of the FLT3 binding proteins of this disclosure or pharmaceutical compositions comprising the same are tumorous diseases especially epithelial cancers/carcinomas such as breast cancer, colon cancer, prostate cancer, head and neck cancer, skin cancer, cancers of the genito-urinary tract, *e.g.*, ovarian cancer, endometrial cancer, cervix cancer and kidney cancer, lung cancer, gastric cancer, cancer of the small intestine, liver cancer, pancreas cancer, gall bladder cancer, cancers of the bile duct, esophagus cancer, cancer of the salivary glands and cancer of the thyroid gland. In some embodiments, the administration of the FLT3 binding proteins of this disclosure or pharmaceutical compositions comprising the same is indicated for minimal residual disease, such as early solid tumor, advanced solid tumor or metastatic solid

tumor, which is characterized by the local and non-local reoccurrence of the tumor caused by the survival of single cells.

[00187] In selected aspects an FLT3 binding proteins of the disclosure is incorporated into a chimeric antigen receptors (CAR) and the FLT3 CAR is administered in a CAR based therapy effective at treating a cancer, such as: a hematologic malignancy derived from either of the two major blood cell lineages, *i.e.*, the myeloid cell line (which produces granulocytes, erythrocytes, thrombocytes, macrophages and mast cells) or lymphoid cell line (which produces B, T, NK and plasma cells), such as all types of leukemias, lymphomas, and myelomas, *e.g.*, AML; epithelial cancers/carcinomas such as breast cancer; colon cancer, prostate cancer; head and neck cancer; skin cancer; cancers of the genito-urinary tract, *e.g.*, ovarian cancer, endometrial cancer, cervix cancer and kidney cancer; lung cancer; gastric cancer; cancer of the small intestine; liver cancer; pancreas cancer; gall bladder cancer; cancers of the bile duct; esophagus cancer; cancer of the salivatory glands and cancer of the thyroid gland; small cell lung cancer; non-small cell lung cancer (*e.g.*, squamous cell non-small cell lung cancer or squamous cell small cell lung cancer) and large cell neuroendocrine carcinoma (LCNEC).

[00188] A chimeric antigen receptor is generally an artificially constructed hybrid protein or polypeptide containing or comprising an antigen binding domain of an antibody linked to a signaling domain (*e.g.*, T-cell signaling or T-cell activation domains). In some embodiments, CARs comprising the FLT3 binding proteins of the present disclosure have the ability to redirect the specificity and reactivity of sensitized lymphocytes (*e.g.*, T-cells) toward FLT3 positive target cells in a non-MHC-restricted manner by exploiting the antigen-binding properties of antibodies or antigen binding fragments thereof. The non-MHC-restricted antigen recognition gives T-cells expressing FLT3 CARs the ability to recognize tumorigenic FLT3 independent of antigen processing, thus bypassing a major mechanism of tumor escape. Moreover, when expressed in T-cells, CARs advantageously do not dimerize with endogenous T cell receptor (TCR) alpha and beta chains. In some embodiments the disclosed FLT3 binding proteins are administered to refractory patients (*i.e.*, those whose disease recurs during or shortly after completing a course of initial therapy); sensitive patients (*i.e.*, those whose relapse is longer than 2-3 months after primary therapy); or patients exhibiting resistance to a platinum based agent (*e.g.*, carboplatin, cisplatin, oxaliplatin) and/or a taxane (*e.g.*, docetaxel, paclitaxel, larotaxel or cabazitaxel). In another embodiment the disclosed FLT3 CAR treatments are effective at treating ovarian cancer, including ovarian-serous carcinoma and ovarian-papillary serous carcinoma.

[00189] In another embodiment the FLT3 binding proteins of the disclosure, the FLT3 CAR, or the FLT3 sensitized lymphocytes, or any combination thereof are used in maintenance therapy

to reduce or eliminate the chance of tumor recurrence following the initial presentation of the disease. In some cases, the disorder has been treated and the initial tumor mass eliminated, reduced or otherwise ameliorated so the patient is asymptomatic or in remission. At such time the subject is administered pharmaceutically effective amounts of the disclosed the FLT3 binding proteins of the disclosure, the FLT3 CAR, or the FLT3 sensitized lymphocytes, or any combination thereof one or more times regardless of if there is little or no indication of disease using standard diagnostic procedures. In some embodiments, the FLT3 binding proteins of the disclosure, the FLT3 CAR, or the FLT3 sensitized lymphocytes, or any combination thereof is administered on a regular schedule over a period of time, such as weekly, every two weeks, monthly, every six weeks, every two months, every three months every six months or annually, for example, to reduce the potential of disease recurrence. Moreover such treatments are in some embodiments continued for a period of weeks, months, years or even indefinitely depending on the patient response and clinical and diagnostic parameters.

[00190] In yet another embodiment, the FLT3 binding proteins of the disclosure, the FLT3 CAR, or the FLT3 sensitized lymphocytes, or any combination thereof are used to prophylactically or as an adjuvant therapy to prevent or reduce the possibility of tumor metastasis following a debulking procedure. As used in the present disclosure a “debulking procedure,” is means any procedure, technique or method that eliminates, reduces, treats or ameliorates a tumor or tumor proliferation. Exemplary debulking procedures include, but are not limited to, surgery, radiation treatments (*i.e.*, beam radiation), chemotherapy, immunotherapy or ablation. In some embodiments, at appropriate times, the FLT3 binding proteins of the disclosure, the FLT3 CAR, or the FLT3 sensitized lymphocytes, or any combination thereof are administered as suggested by clinical, diagnostic or theranostic procedures to reduce tumor metastasis. In some embodiments, the dosing regimen is accompanied by appropriate diagnostic or monitoring techniques that allow it to be modified.

[00191] Yet other embodiments of the disclosure comprise administering the FLT3 binding protein of the disclosure, the FLT3 CAR, or the FLT3 sensitized lymphocytes, or any combination thereof to subjects that are asymptomatic but at risk of developing a proliferative disorder. That is, in some embodiments, the FLT3 binding protein of the disclosure, the FLT3 CAR, or the FLT3 sensitized lymphocytes, or any combination thereof are used in preventative sense and given to patients that have been examined or tested and have one or more noted risk factors (*e.g.*, genomic indications, family history, *in vivo* or *in vitro* test results, etc.) but have not developed neoplasia. In such cases those skilled in the art would be able to determine an effective dosing regimen through empirical observation or through accepted clinical practices.

[00192] In some embodiments of the methods described herein, the FLT3 binding proteins, or compositions as described herein are administered in combination with an agent for treatment of the particular disease, disorder or condition. Agents include but are not limited to, therapies involving antibodies, small molecules (*e.g.*, chemotherapeutics), hormones (steroidal, peptide, and the like), radiotherapies (γ -rays, X-rays, and/or the directed delivery of radioisotopes, microwaves, UV radiation and the like), gene therapies (*e.g.*, antisense, retroviral therapy and the like) and other immunotherapies. In some embodiments, an FLT3 binding protein as described herein is administered in combination with anti-diarrheal agents, anti-emetic agents, analgesics, opioids and/or non-steroidal anti-inflammatory agents. In some embodiments, an FLT3 binding protein as described herein is administered in combination with anti-cancer agents. Nonlimiting examples of anti-cancer agents that can be used in the various embodiments of the disclosure, including pharmaceutical compositions and dosage forms and kits of the disclosure, include: acivicin; aclarubicin; acodazole hydrochloride; acronine; adozelesin; aldesleukin; altretamine; ambomycin; ametantrone acetate; aminoglutethimide; amsacrine; anastrozole; anthramycin; asparaginase; asperlin; azacitidine; azetepa; azotomycin; batimastat; benzodepa; bicalutamide; bisantrene hydrochloride; bisnafide dimesylate; bizelesin; bleomycin sulfate; brequinar sodium; bropiramine; busulfan; cactinomycin; calusterone; caracemide; carbetimer; carboplatin; carmustine; carubicin hydrochloride; carzelesin; cedefingol; chlorambucil; cirolemycin; cisplatin; cladribine; crisnatol mesylate; cyclophosphamide; cytarabine; dacarbazine; dactinomycin; daunorubicin hydrochloride; decitabine; dexormaplatin; dezaguanine; dezaguanine mesylate; diaziquone; docetaxel; doxorubicin; doxorubicin hydrochloride; droloxifene; droloxifene citrate; dromostanolone propionate; duazomycin; edatrexate; eflornithine hydrochloride; elsamitrucin; enloplatin; enpromate; epipropidine; epirubicin hydrochloride; erbulozole; esorubicin hydrochloride; estramustine; estramustine phosphate sodium; etanidazole; etoposide; etoposide phosphate; etoprine; fadrozole hydrochloride; fazarabine; fenretinide; floxuridine; fludarabine phosphate; fluorouracil; flurocitabine; fosquidone; fostriecin sodium; gemcitabine; gemcitabine hydrochloride; hydroxyurea; idarubicin hydrochloride; ifosfamide; ilmofosine; interleukin II (including recombinant interleukin II, or rIL2), interferon alpha-2a; interferon alpha-2b; interferon alpha-n1; interferon alpha-n3; interferon beta-I a; interferon gamma-I b; iproplatin; irinotecan hydrochloride; lanreotide acetate; letrozole; leuprolide acetate; liarozole hydrochloride; lometrexol sodium; lomustine; losoxantrone hydrochloride; masoprocil; maytansine; mechlorethamine hydrochloride; megestrol acetate; melengestrol acetate; melphalan; menogaril; mercaptopurine; methotrexate; methotrexate sodium; metoprine; meturedopa; mitindomide; mitocarcin; mitocromin; mitogillin; mitomalcin; mitomycin; mitosper; mitotane; mitoxantrone

hydrochloride; mycophenolic acid; nocodazole; nogalamycin; ormaplatin; oxisuran; paclitaxel; pegaspargase; peliomycin; pentamustine; peplomycin sulfate; perfosfamide; pipobroman; pipsulfan; piroxantrone hydrochloride; plicamycin; plomestane; porfimer sodium; porfiromycin; prednimustine; procarbazine hydrochloride; puromycin; puromycin hydrochloride; pyrazofurin; riboprime; rogletimide; safingol; safingol hydrochloride; semustine; simtrazene; sparfosate sodium; sparsomycin; spirogermanium hydrochloride; spiromustine; spiroplatin; streptonigrin; streptozocin; sulofenur; talisomycin; tecogalan sodium; tegafur; teloxantrone hydrochloride; temoporfin; teniposide; teroxirone; testolactone; thiamiprine; thioguanine; thiotepa; tiazofurin; tirapazamine; toremifene citrate; trestolone acetate; triciribine phosphate; trimetrexate; trimetrexate glucuronate; triptorelin; tubulozole hydrochloride; uracil mustard; uredepa; vapreotide; verteporfin; vinblastine sulfate; vincristine sulfate; vindesine; vindesine sulfate; vinepidine sulfate; vinglycinat sulfate; vinleurosine sulfate; vinorelbine tartrate; vinzolidine sulfate; vinzolidine sulfate; vorozole; zeniplatin; zinostatin; zorubicin hydrochloride. Other examples of anti-cancer drugs include, but are not limited to: 20-epi-1,25 dihydroxyvitamin D3; 5-ethynyluracil; abiraterone; aclarubicin; acylfulvene; adecypenol; adozelesin; aldesleukin; ALL-TK antagonists; altretamine; ambamustine; amidox; amifostine; aminolevulinic acid; amrubicin; amsacrine; anagrelide; anastrozole; andrographolide; angiogenesis inhibitors; antagonist D; antagonist G; antarelix; anti-dorsalizing morphogenetic protein-1; antiandrogen, prostatic carcinoma; antiestrogen; antineoplaston; antisense oligonucleotides; aphidicolin glycinate; apoptosis gene modulators; apoptosis regulators; apurinic acid; ara-CDP-DL-PTBA; arginine deaminase; asulacrine; atamestane; atrimustine; axinastatin 1; axinastatin 2; axinastatin 3; azasetron; azatoxin; azatyrosine; baccatin III derivatives; balanol; batimastat; BCR/ABL antagonists; benzochlorins; benzoylstauroporine; beta lactam derivatives; beta-alethine; betaclamycin B; betulinic acid; bFGF inhibitor; bicalutamide; bisantrene; bisaziridinylspermine; bisnafide; bistratene A; bizelesin; breflate; bropirimine; budotitane; buthionine sulfoximine; calcipotriol; calphostin C; camptothecin derivatives; canarypox IL-2; capecitabine; carboxamide-amino-triazole; carboxyamidotriazole; CaRest M3; CARN 700; cartilage derived inhibitor; carzelesin; casein kinase inhibitors (ICOS); castanospermine; cecropin B; cetrorelix; chlorins; chloroquinoxaline sulfonamide; cicaprost; cis-porphyrin; cladribine; clomifene analogues; clotrimazole; collismycin A; collismycin B; combretastatin A4; combretastatin analogue; conagenin; crambescidin 816; crisnatol; cryptophycin 8; cryptophycin A derivatives; curacin A; cyclopentantraquinones; cycloplattam; cypemycin; cytarabine ocfosfate; cytolytic factor; cytostatin; dacliximab; decitabine; dehydrodidemnin B; deslorelin; dexamethasone; dexifosfamide; dexrazoxane; dexverapamil; diaziqune; didemnin B; didox; diethylnorspermine; dihydro-5-azacytidine; dihydrotaxol, 9-

dioxamycin; diphenyl spiromustine; docetaxel; docosanol; dolasetron; doxifluridine; droloxifene; dronabinol; duocarmycin SA; ebselen; ecomustine; edelfosine; edrecolomab; eflornithine; elemene; emitefur; epirubicin; epristeride; estramustine analogue; estrogen agonists; estrogen antagonists; etanidazole; etoposide phosphate; exemestane; fadrozole; fazarabine; fenretinide; filgrastim; finasteride; flavopiridol; flezelastine; fluasterone; fludarabine; fluorodaunorubicin hydrochloride; forfenimex; formestane; fostriecin; fotemustine; gadolinium texaphyrin; gallium nitrate; galocitabine; ganirelix; gelatinase inhibitors; gemcitabine; glutathione inhibitors; hepsulfam; heregulin; hexamethylene bisacetamide; hypericin; ibandronic acid; idarubicin; idoxifene; idramantone; ilmofosine; ilomastat; imidazoacridones; imiquimod; immunostimulant peptides; insulin-like growth factor-I receptor inhibitor; interferon agonists; interferons; interleukins; iobenguane; iododoxorubicin; ipomeanol, 4-; iroplact; irsogladine; isobengazole; isohomohalicondrin B; itasetron; jasplakinolide; kahalalide F; lamellarin-N triacetate; lanreotide; leinamycin; lenograstim; lentinan sulfate; leptolstatin; letrozole; leukemia inhibiting factor; leukocyte alpha interferon; leuprolide+estrogen+progesterone; leuprorelin; levamisole; liarozole; linear polyamine analogue; lipophilic disaccharide peptide; lipophilic platinum compounds; lissoclinamide 7; lobaplatin; lombricine; lometrexol; lonidamine; losoxantrone; HMG-CoA reductase inhibitor (such as but not limited to, Lovastatin, Pravastatin, Fluvastatin, Statin, Simvastatin, and Atorvastatin); loxoribine; lurtotecan; lutetium texaphyrin; lysofylline; lytic peptides; maitansine; mannostatin A; marimastat; masoprolol; maspin; matrilysin inhibitors; matrix metalloproteinase inhibitors; menogaril; merbarone; meterelin; methioninase; metoclopramide; MIF inhibitor; mifepristone; miltefosine; mirimostim; mismatched double stranded RNA; mitoguazone; mitolactol; mitomycin analogues; mitonafide; mitotoxin fibroblast growth factor-saporin; mitoxantrone; mofarotene; molgramostim; monoclonal antibody, human chorionic gonadotrophin; monophosphoryl lipid A+myobacterium cell wall sk; mopidamol; multiple drug resistance gene inhibitor; multiple tumor suppressor 1-based therapy; mustard anticancer agent; mycaperoxide B; mycobacterial cell wall extract; myriaporone; N-acetyldinaline; N-substituted benzamides; nafarelin; nagrestip; naloxone+pentazocine; napavin; naphterpin; nartograstim; nedaplatin; nemorubicin; neridronic acid; neutral endopeptidase; nilutamide; nisamycin; nitric oxide modulators; nitroxide antioxidant; nitrullyn; O6-benzylguanine; octreotide; okicenone; oligonucleotides; onapristone; ondansetron; ondansetron; oracin; oral cytokine inducer; ormaplatin; osaterone; oxaliplatin; oxaunomycin; paclitaxel; paclitaxel analogues; paclitaxel derivatives; palauamine; palmitoylrhizoxin; pamidronic acid; panaxytriol; panomifene; parabactin; pazelliptine; pegaspargase; peldesine; pentosan polysulfate sodium; pentostatin; pentrozole; perflubron; perfosfamide; perillyl alcohol; phenazinomycin; phenylacetate;

phosphatase inhibitors; picibanil; pilocarpine hydrochloride; pirarubicin; piritrexim; placetin A; placetin B; plasminogen activator inhibitor; platinum complex; platinum compounds; platinum-triamine complex; porfimer sodium; porfiromycin; prednisone; propyl bis-acridone; prostaglandin J2; proteasome inhibitors; protein A-based immune modulator; protein kinase C inhibitor; protein kinase C inhibitors, microalgal; protein tyrosine phosphatase inhibitors; purine nucleoside phosphorylase inhibitors; purpurins; pyrazoloacridine; pyridoxylated hemoglobin polyoxyethylene conjugate; raf antagonists; raltitrexed; ramosetron; ras farnesyl protein transferase inhibitors; ras inhibitors; ras-GAP inhibitor; retelliptine demethylated; rhenium Re 186 etidronate; rhizoxin; ribozymes; RII retinamide; rogletimide; rohitukine; romurtide; roquinimex; rubiginone B1; ruboxyl; safingol; saintopin; SarCNU; sarcophytol A; sargramostim; Sdi 1 mimetics; semustine; senescence derived inhibitor 1; sense oligonucleotides; signal transduction inhibitors; signal transduction modulators; single chain antigen binding protein; sizofiran; sobuzoxane; sodium borocaptate; sodium phenylacetate; solverol; somatomedin binding protein; sonermin; sparfosic acid; spicamycin D; spiromustine; splenopentin; spongistatin 1; squalamine; stem cell inhibitor; stem-cell division inhibitors; stipiamide; stromelysin inhibitors; sulfinosine; superactive vasoactive intestinal peptide antagonist; suradista; suramin; swainsonine; synthetic glycosaminoglycans; tallimustine; tamoxifen methiodide; tauromustine; tazarotene; tecogalan sodium; tegafur; tellurapyrylium; telomerase inhibitors; temoporfin; temozolomide; teniposide; tetrachlorodecaoxide; tetrazomine; thaliblastine; thiocoraline; thrombopoietin; thrombopoietin mimetic; thymalfasin; thymopoietin receptor agonist; thymotrigan; thyroid stimulating hormone; tin ethyl etiopurpurin; tirapazamine; titanocene bichloride; topsentin; toremifene; totipotent stem cell factor; translation inhibitors; tretinoin; triacetyluridine; triciribine; trimetrexate; triptorelin; tropisetron; turosteride; tyrosine kinase inhibitors; tyrphostins; UBC inhibitors; ubenimex; urogenital sinus-derived growth inhibitory factor; urokinase receptor antagonists; vapreotide; variolin B; vector system, erythrocyte gene therapy; velaresol; veramine; verdins; verteporfin; vinorelbine; vinxaltine; Vitaxin®; vorozole; zanoterone; zeniplatin; zilascorb; and zinostatin stimalamer. Additional anti-cancer drugs are 5-fluorouracil and leucovorin. These two agents are particularly useful when used in methods employing thalidomide and a topoisomerase inhibitor. In some embodiments, the FLT3 binding protein of the present disclosure is used in combination with gemcitabine. In some embodiments, the FLT3 binding protein as described herein is administered before, during, or after surgery.

[00193] The modality of administration of an FLT3 binding protein as described herein (*e.g.*, an FLT3 targeting trispecific protein) or a pharmaceutical composition comprising the same, is, in some embodiment, in accord with known methods, *e.g.*, injection or infusion by

subcutaneous, intravenous, intraperitoneal, intracerebral, intradermic, intramuscular, intraocular, intraarterial, intrathecal, or intralesional routes, or by inhalation or by sustained release systems. In some embodiments the an FLT3 binding protein as described herein (*e.g.*, an FLT3 targeting trispecific protein) or a pharmaceutical composition comprising the same is administered by infusion or by bolus injection. In some embodiments an FLT3 binding protein as described herein (*e.g.*, an FLT3 targeting trispecific protein) or a pharmaceutical composition comprising the same is administered through the nose or lung, *e.g.*, as a liquid or powder aerosol (lyophilized). In some embodiments an FLT3 binding protein as described herein (*e.g.*, an FLT3 targeting trispecific protein) or a pharmaceutical composition comprising the same is administered intravenously, parenterally or subcutaneously as desired. When administered systemically, a pharmaceutical composition comprising an FLT3 binding protein as described herein (*e.g.*, an FLT3 targeting trispecific protein) is for instance sterile, pyrogen-free and in a parenterally acceptable solution having due regard for pH, isotonicity, and stability.

Methods of detection of FLT3 expression and diagnosis of FLT3 associated cancer

[00194] According to another embodiment of the disclosure, kits for detecting expression of FLT3 *in vitro* or *in vivo* are provided. The kits include the foregoing FLT3 binding protein (*e.g.*, an FLT3 binding protein containing a labeled anti-FLT3 single domain antibody or antigen binding fragments thereof), and one or more compounds for detecting the label. In some embodiments, the label is selected from the group consisting of a fluorescent label, an enzyme label, a radioactive label, a nuclear magnetic resonance active label, a luminescent label, and a chromophore label.

[00195] In some cases, FLT3 expression is detected in a biological sample. The sample can be any sample, including, but not limited to, tissue from biopsies, autopsies and pathology specimens. Biological samples also include sections of tissues, for example, frozen sections taken for histological purposes. Biological samples further include body fluids, such as blood, serum, plasma, sputum, spinal fluid or urine. A biological sample is typically obtained from a mammal, such as a human or non-human primate.

[00196] In one embodiment, provided is a method of determining if a subject has cancer by contacting a sample from the subject with an anti-FLT3 single domain antibody as disclosed herein; and detecting binding of the single domain antibody to the sample. An increase in binding of the antibody to the sample as compared to binding of the antibody to a control sample identifies the subject as having cancer.

[00197] In another embodiment, provided is a method of confirming a diagnosis of cancer in a subject by contacting a sample from a subject diagnosed with cancer with an anti-FLT3 single domain antibody as disclosed herein; and detecting binding of the antibody to the sample. An

increase in binding of the antibody to the sample as compared to binding of the antibody to a control sample confirms the diagnosis of cancer in the subject.

[00198] In some examples of the disclosed methods, the FLT3 single domain antibody is directly labeled. In some examples, the methods further include contacting a second antibody that specifically binds the anti-FLT3 single domain antibody with the sample; and detecting the binding of the second antibody. An increase in binding of the second antibody to the sample as compared to binding of the second antibody to a control sample detects a condition in the subject or confirms the diagnosis of cancer in the subject. In some cases, the condition is a hematologic malignancy derived from either of the two major blood cell lineages, *i.e.*, the myeloid cell line (which produces granulocytes, erythrocytes, thrombocytes, macrophages and mast cells) or lymphoid cell line (which produces B, T, NK and plasma cells), such as all types of leukemias, lymphomas, and myelomas, *e.g.*, AML. In some embodiments, the cancer is a neuroendocrine cancer, prostate cancer, lung cancer, stomach cancer, squamous cell carcinoma, pancreatic cancer, cholangiocarcinoma, triple negative breast cancer or ovarian cancer (such as epithelial ovarian carcinoma), or any other type of cancer that expresses FLT3. In some examples, the control sample is a sample from a subject without cancer. In particular examples, the sample is a blood or tissue sample.

[00199] In some cases, the antibody that binds (for example specifically binds) FLT3 is directly labeled with a detectable label. In another embodiment, the antibody that binds (for example, specifically binds) FLT3 (the first antibody) is unlabeled and a second antibody or other molecule that can bind the antibody that specifically binds FLT3 is labeled. A second antibody is chosen such that it is able to specifically bind the specific species and class of the first antibody. For example, if the first antibody is a llama IgG, then the secondary antibody may be an anti-llama-IgG. Other molecules that can bind to antibodies include, without limitation, Protein A and Protein G, both of which are available commercially. Suitable labels for the antibody or secondary antibody are described above, and include various enzymes, prosthetic groups, fluorescent materials, luminescent materials, magnetic agents and radioactive materials. Non-limiting examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase, beta-galactosidase, or acetylcholinesterase. Non-limiting examples of suitable prosthetic group complexes include streptavidin/biotin and avidin/biotin. Non-limiting examples of suitable fluorescent materials include umbelliferon, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin. A non-limiting exemplary luminescent material is luminol; a non-limiting exemplary magnetic agent is gadolinium, and non-limiting exemplary radioactive labels include ¹²⁵I, ¹³¹I, ³⁵S or ³H.

[00200] In an alternative embodiment, FLT3 can be assayed in a biological sample by a competition immunoassay utilizing FLT3 standards labeled with a detectable substance and an unlabeled antibody that specifically binds FLT3. In this assay, the biological sample, the labeled FLT3 standards and the antibody that specifically bind FLT3 are combined and the amount of labeled FLT3 standard bound to the unlabeled antibody is determined. The amount of FLT3 in the biological sample is inversely proportional to the amount of labeled FLT3 standard bound to the antibody that specifically binds FLT3.

[00201] The immunoassays and method disclosed herein can be used for a number of purposes. In one embodiment, the antibody that specifically binds FLT3 may be used to detect the production of FLT3 in cells in cell culture. In another embodiment, the antibody can be used to detect the amount of FLT3 in a biological sample, such as a tissue sample, or a blood or serum sample. In some examples, the FLT3 is cell-surface FLT3. In other examples, the FLT3 is soluble FLT3 (*e.g.*, FLT3 in a cell culture supernatant or soluble FLT3 in a body fluid sample, such as a blood or serum sample).

[00202] In one embodiment, a kit is provided for detecting FLT3 in a biological sample, such as a blood sample or tissue sample. For example, to confirm a cancer diagnosis in a subject, a biopsy can be performed to obtain a tissue sample for histological examination. Alternatively, a blood sample can be obtained to detect the presence of soluble FLT3 protein or fragment. Kits for detecting a polypeptide will typically comprise a single domain antibody, according to the present disclosure, that specifically binds FLT3. In some embodiments, an antibody fragment, such as an scFv fragment, a VH domain, or a Fab is included in the kit. In a further embodiment, the antibody is labeled (for example, with a fluorescent, radioactive, or an enzymatic label).

[00203] In one embodiment, a kit includes instructional materials disclosing means of use of an antibody that binds FLT3. The instructional materials may be written, in an electronic form (such as a computer diskette or compact disk), may be visual (such as video files), or provided through an electronic network, for example, over the internet, World Wide Web, an intranet, or other network. The kits may also include additional components to facilitate the particular application for which the kit is designed. Thus, for example, the kit may additionally contain means of detecting a label (such as enzyme substrates for enzymatic labels, filter sets to detect fluorescent labels, appropriate secondary labels such as a secondary antibody, or the like). The kits may additionally include buffers and other reagents routinely used for the practice of a particular method. Such kits and appropriate contents are well known to those of skill in the art.

[00204] In one embodiment, the diagnostic kit comprises an immunoassay. Although the details of the immunoassays may vary with the particular format employed, the method of detecting FLT3 in a biological sample generally includes the steps of contacting the biological

sample with an antibody which specifically reacts, under immunologically reactive conditions, to an FLT3 polypeptide. The antibody is allowed to specifically bind under immunologically reactive conditions to form an immune complex, and the presence of the immune complex (bound antibody) is detected directly or indirectly.

[00205] Methods of determining the presence or absence of a cell surface marker are well known in the art. For example, the antibodies can be conjugated to other compounds including, but not limited to, enzymes, magnetic beads, colloidal magnetic beads, haptens, fluorochromes, metal compounds, radioactive compounds or drugs. The antibodies can also be utilized in immunoassays such as but not limited to radioimmunoassays (RIAs), ELISA, or immunohistochemical assays. The antibodies can also be used for fluorescence activated cell sorting (FACS). FACS employs a plurality of color channels, low angle and obtuse light-scattering detection channels, and impedance channels, among other more sophisticated levels of detection, to separate or sort cells. *See* U.S. Patent No. 5, 061,620). Any of the single domain antibodies that bind FLT3, as disclosed herein, can be used in these assays. Thus, the antibodies can be used in a conventional immunoassay, including, without limitation, an ELISA, an RIA, FACS, tissue immunohistochemistry, Western blot or immunoprecipitation.

EXAMPLES

Example 1: Screening of Phage Display Library for Identification of FLT3 Binding Domains

[00206] Llamas were immunized with purified FLT3 protein expressed in Expi293 cells. A phage display library for expression of heavy variable antibody domains was constructed from circulating B cells isolated from the immunized llamas (*See* van der Linden , de Geus , Stok , Bos ,van Wassenaar, Verrips, and Frenken. 2000. J Immunol Methods 240:185–195). Phage clones were screened for binding to FLT3 by expressing llama anti-FLT3 proteins in *E. coli*, preparing periplasmic extracts, and performing colorimetric ELISAs. Seventy unique heavy chain only sequences were identified (SEQ ID Nos. 1-70) that produced a signal in the ELISA screening with human FLT3 protein (data provided in Table 2) relative to control wells that lacked FLT3 protein. The CDR1, CDR2, and CDR3 sequences for these heavy variable domains are listed in Table 1, above.

[00207] **Table 2: Binding of Llama Anti-Human FLT3 Antibodies to Human FLT3 in an ELISA Assay** (The numerical values in Table 2 represent the absorbance readings for the colorimetric ELISA)

Sequence name	ELISA FLT3	ELISA control	FLT3 / control
FLL101	1.7	0.5	3
FLL103	3.8	0.1	28
FLL116	1.1	0.2	5
FLL125	2.1	0.1	17
FLL129	2.6	0.3	9
FLL137	1.8	0.2	8
FLL14	1.8	0.4	5
FLL146	0.9	0.2	4
FLL158	2.1	0.1	17
FLL179	3.7	0.2	17
FLL181	3.2	0.6	5
FLL187	1.9	0.1	18
FLL32	1.6	0.3	5
FLL51	2.9	0.2	16
FLL55	2.0	0.3	6
FLL77	4.0	0.2	22
FLL97	1.4	0.2	7
FLL21	3.3	0.2	20
FLL57	1.4	0.2	9
FLL62	0.5	0.1	5
FLL79	0.6	0.1	4
FLL86	1.9	0.1	15
FLL112	3.6	0.1	34
FLL142	4.0	0.3	15
FLL143	4.0	0.1	47
FLL154	4.0	0.5	8
FLL168	4.0	0.1	28
FLL170	4.0	0.1	38
FLL188	4.0	0.1	51
FLL40	4.0	0.2	21
FLL6	3.8	0.2	16
FLL75	4.0	0.2	19
FLL83	3.8	0.1	35
FLL94	4.0	0.8	5
FLL99	3.7	0.3	13
FLL38	4.0	0.1	45
FLL53	3.9	0.2	17
FLL553	3.7	0.1	37
FLL74	3.9	0.7	6
FLL102	3.7	0.1	37
FLL122	4.0	0.2	26
FLL134	1.3	0.1	15
FLL153	1.4	0.1	15
FLL41	0.8	0.2	5
FLL67	2.7	0.2	12

Sequence name	ELISA FLT3	ELISA control	FLT3 / control
FLL92	4.0	0.2	25
FLL71	1.9	0.2	9
FLL8	3.3	0.2	14
FLL84	1.3	0.3	4
FLL107	3.8	0.3	11
FLL141	4.0	0.1	28
FLL34	4.0	0.1	39
FLL4	3.7	0.1	43
FLL61	3.9	0.2	25
FLL78	4.0	0.1	27
FLL1	3.4	0.3	11
FLL26	2.9	0.8	4
FLL160	0.7	0.1	9
FLL173	0.5	0.1	6
FLL178	4.0	0.1	48
FLL27	4.0	0.4	10
FLL190	4.0	0.1	43
FLL43	2.0	0.2	12
FLL15	2.5	0.1	31
FLL45	4.0	0.1	28
FLL39	1.9	0.2	12
FLL177	4.0	0.1	54
FLL823	3.6	0.9	4
FLL76	0.5	0.1	5
FLL822	4.0	0.2	17

Example 2: Incorporation of FLT3 Binding Heavy Chain Only Single Domain Antibodies into FLT3 targeting Multispecific Proteins and T Cell Dependent Cellular Cytotoxicity Assays

[00208] The anti-FLT3 antibody sequences were cloned into DNA constructs for expression of recombinant multispecific proteins (SEQ ID Nos. 196-266). The coding sequences of the multispecific proteins contained a signal peptide for secreted cell expression, one of the anti-FLT3 antibody variable domains (SEQ ID Nos. 1-70), a humanized single domain anti-albumin antibody variable domain (SEQ ID No. 372), a humanized anti-CD3 antibody scFv fragment (SEQ ID No. 373), and a repeat of six histidine sequences (SEQ ID No. 374). A linker sequence was inserted at the junctions between the antibody domains (SEQ ID No. 375). These anti-FLT3/anti-albumin/anti-CD3 multispecific protein constructs were transfected into Expi293 cells (Life Technologies). The amount of multispecific protein in the conditioned media from the transfected Expi293 cells was quantitated using by using an Octet instrument with Protein A

tips using a multispecific protein of similar molecular weight to the anti-FLT3/anti-albumin/anti-CD3 proteins as a standard.

[00209] The conditioned media were tested in a T-cell dependent cellular cytotoxicity assay (See Nazarian AA, Archibeque IL, Nguyen YH, Wang P, Sinclair AM, Powers DA. 2015. J Biomol Screen. 20:519-27). In this assay, luciferase labelled MV-4-11 cells (biphenotypic B myelomonocytic leukemia cell line, ATCC® CRL-9591™), which express FLT3, were combined with purified human T cells and a titration of anti-FLT3/anti-albumin/anti-CD3 multispecific protein. If a multispecific protein directs T cells to kill the MV-4-11 cells, the signal in a luciferase assay performed at 48 hours after starting the experiment should decrease. **Figs. 1-11** show graphs of TDCC viability results. EC₅₀ values from the TDCC assay are listed in Tables 3 and 4. The most potent molecule had an EC₅₀ value of 3 pM. A negative control for the TDCC assays was an anti-GFP/anti-albumin/anti-CD3 protein, and this protein did not direct the T cells to kills the MV-4-11 cells except for slight activity at the highest concentration tested (e.g., **Figs. 10 and 21**). As the multispecific proteins contain an anti-albumin domain, TDCC assay were also performed in the presence of 15 mg/ml human serum albumin (HSA) to measure directed T cell killing while bound to albumin (**Figs. 12-21**). For all of the FLT3-targeting multispecific proteins tested, the EC₅₀ values for directed T cell killing increased in the presence of HSA (Table 3), and also relative to EC₅₀ values for directed T cell killing in the presence of bovine serum albumin (BSA) (**Figs. 1-11** and **Tables 3 and 4**). The anti-albumin domain in the multispecific proteins does not bind to BSA (data not shown).

[00210] Table 3: EC₅₀ Values for Redirected T Cell Killing of MV-4-11 Cells by Anti-FLT3/Anti-Albumin/Anti-CD3 Multispecific Proteins Containing Llama Anti-FLT3 Sequences (n/a indicates insufficient activity to calculate an EC₅₀ using the protein concentrations tested)

FLT3 Binder	EC₅₀ (pM)	EC₅₀ with HSA (pM)
FLL21	169	1182
FLL57	384	3119
FLL62	619	6816
FLL1	56	888
FLL103	141	1355
FLL107	11	85
FLL112	136	1330
FLL125	330	1717
FLL129	1168	n/a
FLL137	705	n/a
FLL14	257	1147
FLL141	16	77

FLT3 Binder	EC₅₀ (pM)	EC₅₀ with HSA (pM)
FLL142	233	984
FLL143	70	345
FLL146	989	5678
FLL15	108	613
FLL154	152	818
FLL158	546	1973
FLL160	n/a	n/a
FLL168	77	383
FLL173	n/a	n/a
FLL177	n/a	n/a
FLL178	n/a	n/a
FLL179	176	1162
FLL190	37	239
FLL26	136	1186
FLL32	175	1172
FLL34	17	170
FLL38	104	814
FLL39	1387	n/a
FLL4	21	181
FLL40	69	601
FLL43	223	1478
FLL45	407	n/a
FLL51	906	4649
FLL53	n/a	n/a
FLL55	192	1077
FLL6	201	1859
FLL61	39	424
FLL75	224	2102
FLL76	n/a	n/a
FLL77	224	1582
FLL78	21	194
FLL82	1185	n/a
FLL822	n/a	n/a
FLL83	134	1274
FLL94	202	2836
FLL99	202	1746

[00211] Table 4: EC₅₀ Values for Redirected T Cell Killing of MV-4-11 Cells by Anti-FLT3/Anti-Albumin/Anti-CD3 Multispecific Proteins Containing Llama Anti-FLT3 Sequences

FLT3 Binder	EC₅₀ with BSA (pM)	EC₅₀ with HSA (pM)
FLL8	26	680
FLL41	380	2200

FLL71	83	1900
FLL92	3	53
FLL134	66	1700
FLL153	150	3000

Example 3: Humanized Anti-FLT3 Binding Heavy Chain Only Single Domain Antibodies and Multispecific Proteins containing the same

[00212] Seven of the llama anti-FLT3 antibody sequences were humanized by grafting their CDR sequences onto human germline sequences, while retaining some llama framework sequences to ensure the antibodies did not lose activity (SEQ ID Nos. 71-76; 389-390). These eight humanized sequences were cloned into expression constructs for expression of anti-FLT3/anti-albumin/anti-CD3 multispecific proteins (SEQ ID Nos. 267-272; 391-392) in CHO cells. The constructs were stably transfected into CHO cells, and pools of stable transfectants were used to express the multispecific proteins. Affinity and multi modal chromatography were used to purify the multispecific proteins from the CHO conditioned media. An SDS-PAGE of the purified proteins (**Fig. 23**) shows the proteins were purified to greater than 95% purity. The purified proteins were also analyzed by analytical size exclusion chromatography and were found to be 99% monomer (data not shown). These purified proteins were tested in a TDCC assay as described in Example 2 using FLT3-expressing MV-4-11 (acute myeloid leukemia cell line) and EOL1 cells (acute myeloid (eosinophilic) leukemia cell line). The assays were run in the presence 15 mg/ml BSA or 15 mg/ml HSA to measure directed cell killing while bound to albumin. Because the anti-albumin domain in these multispecific proteins does not measurably bind to BSA, BSA served as a negative control for the addition of HSA. The results of these TDCC assays are plotted in **Figs. 24-27** and **Figs. 38-39**, and the EC₅₀ values for directed T cell killing are listed in **Table 5** and **Table 6**. The MV-4-11 data in **Figs. 24-25** and **Figs. 38-39** and the corresponding EC₅₀ values in **Tables 5** and **6** represent the results of assays performed using T cells isolated from two different T cell donors. Potent directed T cell killing was observed with both cell lines in the absence of HSA, with EC₅₀ values ranging from 1.6 pM to 22 pM. With addition of HSA, the EC₅₀ values increased, ranging from 10 pM to 408pM. The purified proteins were also tested in a TDCC assay with FLT3-expression THP1 cells (acute monocytic leukemia) in the absence or presence of 15 mg/ml HSA (**Figs. 30** and **31**) with FLT3-expressing MOLM13 (acute myeloid leukemia) and HL60 (human leukemia) cells (**Figs. 32** and **33**) in the presence of 15 mg/ml HSA. The EC₅₀ values calculated from these TDCC assay data are also listed in **Table 5**. With the THP1 cells, EC₅₀ values ranged from 23 pM to 268 pM in the absence of HSA and 46 pM to 856 pM in the presence of HSA. With the MOLM13 cells in the presence of HSA the EC₅₀ values ranged from 30 pM to 229 pM, and with HL60 cells in the

presence of HSA the EC₅₀ values ranged from 551 pM to 5478 pM. Compared to all of the other cell lines, the potency of FLT3 TriTAC directed T cell killing with HL60 cells was less potent. It is expected that if viability of the HL60 cells had been measured at a later time point, for example 72 or 96 hours, that the magnitude of killing would have been greater and that killing would have been more potent. A negative control anti-GFP/anti-albumin/anti-CD3 protein had no activity in these TDCC assays except for a minor amount of killing at the highest concentrations tested (>10 nM).

[00213] Table 5: EC₅₀ Values for Redirected T Cell Killing of MV-4-11, EOL1, THP1, MOLM13, and HL60 Cells by Purified Anti-FLT3/Anti-Albumin/Anti-CD3 Multispecific Proteins Containing Humanized Anti-FLT3 Sequences

FLT3 Binder	EOL1 EC ₅₀ (pM)	EOL1 + HSA EC ₅₀ (pM)	MV-4-11 EC ₅₀ (pM)	MV-4-11 + HSA EC ₅₀ (pM)	THP1 EC ₅₀ (pM)	THP1 + HSA EC ₅₀ (pM)	MOLM-13 + HSA EC ₅₀ (pM)	HL60 + HSA EC ₅₀ (pM)
FLH107	1.6	10	5.9	47	23	46	30	551
FLH141	3.5	24	9.6	119	25	118	54	1634
FLH19C	9.4	47	16	184	155	458	90	1518
FLH34	3	22	8.5	91	28	127	47	1027
FLH4	4.2	27	9.7	90	38	179	69	1828
FLH78	5.2	35	12	101	51	221	97	1702
FLH92a	not tested	not tested	not tested	not tested	268	856	188	3876
FLH92b	not tested	not tested	not tested	not tested	109	461	229	5478

[00214] Table 6: EC₅₀ Values for Redirected T Cell Killing of MV-4-11 Cells by Purified Anti-FLT3/Anti-Albumin/Anti-CD3 Multispecific Proteins Containing Humanized Anti-FLT3 Sequences

FLT3 Binder	MV-4-11 EC ₅₀ (pM)	MV-4-11 + HSA EC ₅₀ (pM)
FLH107	2.4	90
FLH141	1.7	45
FLH19C	6.9	224
FLH34	2	124
FLH4	1.9	92
FLH78	2.2	104
FLH92a	22	408
FLH92b	17	390

Example 4: Affinity Determinations for Anti-FLT3 Multispecific Proteins

[00215] The affinities of the purified multispecific proteins for human and cynomolgus FLT3 were measured with an Octet instrument with streptavidin tips were loaded with biotinylated human or cynomolgus FLT3 protein. The tips were then incubated with solutions containing 50,

16.7, 5.6, or 1.9 nM of the multispecific protein. Affinities (K_D), listed in Table 7, were calculated by measuring the on rate and off rate of binding of anti-FLT3/anti-albumin/anti-CD3 multispecific proteins to the captured biotinylated FLT3 proteins. The multispecific proteins bound to human FLT3 with affinities ranging from 0.7 to 8.1 nM, and they bound to cynomolgus FLT3 with affinities ranging from 2.7 to 214 nM.

[00216] Table 7: Affinities of Purified Anti-FLT3/Anti-Albumin/Anti-CD3 Multispecific Proteins Containing Humanized Anti-FLT3 Sequences for Human or Cynomolgus Monkey FLT3

FLT3 Binder	Human K_D (nM)	Cynomolgus K_D (nM)	Cyno / human (fold change)
FLH107	0.7	10	14.3
FLH19C	1.9	2.7	1.4
FLH141	1.9	35	18.4
FLH34	2.1	19	9.0
FLH4	3.7	214	57.8
FLH78	4.1	161	39.3
FLH92a	8.1	11.8	1.5
FLH92b	4.9	7.8	1.6

[00217] Additional affinity determinations were performed using conditioned media from Example 2 with known concentrations of anti-FLT3/anti-CD3 multispecific proteins. The multispecific proteins tested contain llama anti-FLT3 sequences FLL8, FLL41, FLL71, FLL92, FLL134, or FLL153. An Octet instrument with streptavidin tips were loaded with biotinylated human or cynomolgus FLT3 protein, and K_D values for binding FLT3 were calculated by measuring the on rate and off rate of binding of anti-FLT3/anti-CD3 multispecific proteins to the biotinylated FLT3 proteins. The affinity measurements were made using a single 50 nM concentration of anti-FLT3/anti-CD3 multispecific proteins, which allowed for rank ordering potency. The measured relative affinities are listed in **Table 8**. The multispecific proteins bound to human FLT3 with K_D values ranging from 1.4 to 41 nM to cynomolgus FLT3 with K_D values ranging from 2 to 102 nM.

[00218] Table 8: Relative affinities of Purified Anti-FLT3/Anti-Albumin/Anti-CD3 Multispecific Proteins Containing Llama Anti-FLT3 Sequences for Human or Cynomolgus Monkey FLT3

FLT3 Binder	Human K _D (nM)	Cynomolgus K _D (nM)	Cyno / human (fold change)
FLL8	9.3	18	1.9
FLL41	31	34	1.1
FLL71	18	26	1.4
FLL92	1.4	2	1.4
FLL134	18	24	1.3
FLL153	41	102	2.5

Example 5: Tumor regression and inhibition in an orthotopic EOL1 xenograft model

[00219] *In vivo* efficacy study of an exemplary FLT3 targeted multispecific protein of this disclosure is performed with EOL1, expressing luciferase and GFP, orthotopic model. EOL1 LucGFP cells are injected intravenously through the tail vein into 6-8 weeks old female Nod/Scid/IL2Rg^{-/-} (NSG) animals. Intraperitoneal injection of D-luciferin, followed by anesthesia with isoflurane and subsequent whole body bioluminescence imaging (BLI) is to enable monitoring of tumor burden. Bioluminescent signals emitted by the interaction between luciferase expressed by the tumor cells and luciferin are captured by imaging and quantified as total flux (photons/sec) using. When the total flux reaches an average of 15E6 for all animals, the animals are injected through bolus tail vein with expanded T cells from PBMC. Briefly, pan-T cells are activated with a suitable human T Cell Activation/Expansion Kit. After three days, IL2 is added every two days until day 11. Cells are harvested, activation/expansion beads are magnetically removed, and cells are washed and resuspended in PBS. 2-days post T cell injection, mice are imaged as described above and animals are randomized into groups.

[00220] Three days post T-cell implant, a single dose of an FLT3 targeted multispecific protein of this disclosure and a negative control GFP targeted multispecific protein is administered *via* bolus tail vein injection. Animals are sacrificed when they exhibit hindlimb paralysis, an endpoint for AML orthotopic model. It is expected that the FLT3 targeted multispecific protein will result in tumor regression in a dose-dependent manner.

Example 6: Pharmacokinetics and Pharmacodynamics of FLT3 TriTACs in Cynomolgus Monkeys

[00221] A FLT3 TriTAC (SEQ ID NO: 269, containing the FLT3 binder FLH19C, SEQ ID NO: 73) was administered at doses of 10, 100, and 1000 µg/kg single i.v. bolus doses to cynomolgus monkeys, with two test subjects per dose group. This FLT3 TriTAC binds to cynomolgus FLT3 (*see Table 7*) and binds to cynomolgus CD3 and cynomolgus serum albumin, with affinities of 3.3 nM and 4.4 nM, respectively, as determined using biolayer interferometry (*data not shown*). The amount of FLT3 TriTAC present in serum samples collected at different time points after dosing was measured using an electrochemiluminescent ELISA assay using

labeled antibodies recognizing the anti-ALB and anti-CD3 domains of the FLT3 TriTAC molecule as capture and detection reagents. The measured serum concentrations versus time and dose are plotted in **Fig. 34**. The pharmacokinetic properties calculated from these data are listed in **Table 9**.

[00222] Table 9: Pharmacokinetic Properties of a FLT3 TriTAC Dosed in Cynomolgus Monkeys

Dose	T _{max} (h)	C _{max} (nM)	AUC ₁₆₈ (h*nM)	AUC _{INF} (h*nM)	Half-life (h)	Cl (μg/(h*nM))	V _z (ug/(nM))
10 μg/kg	0.5	5.44	279	373	85.9	0.0805	10.0
100 μg/kg	0.5	94.1	4520	5450	75.4	0.0555	6.06
1,000 μg/kg	2	846	35600	61200	147	0.0493	10.4

[00223] To determine if the FLT3 TriTAC directed cynomolgus T cells to kill endogenous cynomolgus FLT3-expressing cells, soluble FLT3L in serum and FLT3 RNA in whole blood were measured in sample collected from the pharmacokinetic study described above. Depletion of FLT3-expressing cells was expected to result in an increase in soluble FLT3L (*see Brauchle et al. Mol Cancer Ther 2020;19:1875–88*). An electrochemiluminescent ELISA specific for Non-Human Primate FLT3L (Meso Scale Discovery) was used to measure the levels of FLT3L in serum samples collected at different time points (**Fig. 35**). With the 100 and 1,000 μg/kg dose groups, the soluble FLT3L increased over the time course of the study. One of the two subjects in the 10 μg/kg dose group had a slight increase in FLT3L at the 72 and 144 hour times points that returned to pre-dose levels at the 336 hour time point. If FLT3 expressing cells are depleted from whole blood or bone marrow, then FLT3 transcripts were expected to be depleted from RNA purified from whole blood or bone marrow. RNA was purified from whole blood or bone marrow using kits (Qiagen), cDNA was prepared by a reverse transcriptase reaction, and qPCR was used to measure the amount of FLT3 present using a standard curve qPCR method. FNTA was used as a house keeping gene for the qPCR reactions. Plotted in **Fig. 36** are FTL3 RNA levels normalized to FNTA for blood samples isolated from the 100 and 1,000 μg/kg groups. Plotted in **Fig. 37** are FTL3 RNA levels normalized to FNTA for bone marrow samples isolated from the 100 and 1,000 μg/kg groups. Compared to samples collected prior to dosing, FLT3 RNA is greatly reduced at all time points measured. The combined FLT3L and FLT3 RNA data indicate that the FLT3 TriTAC, when dosed at 100 and 1,000 μg/kg, eliminated FLT3 expressing cells in cynomolgus monkeys.

[00224] While preferred embodiments of the present invention have been shown and described herein, it will be obvious to those skilled in the art that such embodiments are provided by way of example only. Numerous variations, changes, and substitutions will now occur to those

skilled in the art without departing from the invention. It should be understood that various alternatives to the embodiments of the invention described herein may be employed in practicing the invention. It is intended that the following claims define the scope of the invention and that methods and structures within the scope of these claims and their equivalents be covered thereby.

SEQUENCES

SEQ ID NO.	Sequence descriptor	Seq. name	Amino acid sequence
1	FLT3 antibody variable domain	FLL101	QVQLQESGGGLVQAGGSLRLSCAASGVTFSINYIDWY RQAPGKQREWVAQITRDSNSFYADSVKGRFAISRDN KNTVYLQMNNLKPEDTAVYYCRVLSYWGQGTQVTVSS
2	FLT3 antibody variable domain	FLL103	QVQLQESGGGLVQAGGSLRLSCEASGPTFSINYIDWY RQAPGKQREWVAQITRDSNSFYADSVKGRFAISRDN KNTVYLQMNSLKPEDTAVYYCRVLSYWGQGTQVTVSS
3	FLT3 antibody variable domain	FLL116	QVQLQESGGGLVQAGGSLRLSCAASGVTFSINYIDWY RQAPGKQREWVAQITRDSNSFYADSVKGRFAISRDN KNTVYLQMNSLKPEDTAVYYCRVLSYWGQGTQVTVSS
4	FLT3 antibody variable domain	FLL125	QVQLQESGGGLVQAGGSLRLSCAASGSTFSRNYIDWY RQAPGKQREWVAQITSGGNTHYEPSLKGRFTISRDN KNTAYLQMNSLKPEDTAVYYCRILDYWGQGTQVTVSS
5	FLT3 antibody variable domain	FLL129	QVQLQESGGGLVQAGGSLRLSCAASGVTFSASYIDWY RQAPGNEREWVAQITRGGDSFYADSVKGRFAISRDN KNTVYLQMNSLKPEDTAVYYCRVLSYWGQGTQVTVSS
6	FLT3 antibody variable domain	FLL137	QVQLQESGGGLVQAGGSLRLSCAASGSTFNNYAMDWF RQAPGKQREWVAQITRDSSSFYADSVKGRFAISRDN KNTVYLQMNSLKPEDTAVYYCRVLSYWGQGTQVTVSS
7	FLT3 antibody variable domain	FLL14	QVQLQESGGGLVQAGGSLRLSCAASGVTFSINYIDWY RQAPGKQREWVAQITRDSNSFYADSVKGRFAISRDN KNTVYLQMNSLKPEDTAVYYCRLLSYWGQGTQVTVSS
8	FLT3 antibody variable domain	FLL146	QVQLQESGGGLVQAGGSLRLSCAASGVTFSINYIDWY RQAPGKQREWVAQITRDDTSFYADSVKGRFAISRDN KNTVYLQMNNLRPEDTAVYYCRLLSFWGQGTQVTVSS
9	FLT3 antibody variable domain	FLL158	QVQLQESGGGLVQPGGSLRLSCAASGSTFGRNYIDWY RQAPGKQREWVAQITSGGNTHYEPSLKGRFTISRDN KNTAYLQMNSLKPEDTAVYYCRILDYWGQGTQVTVSS
10	FLT3 antibody variable domain	FLL179	QVQLQESGGGLVQAGGSLRLSCKASGVTFSINYIDWY RQAPGKQREWVAQITRDGSSFYADSVKGRFAISRDN KNTVYLQMNSLKPEDTAVYYCRILSDWGQGTQVTVSS
11	FLT3 antibody variable domain	FLL181	QVQLQESGGGLVQAGDSLRLSCAASGVTFSASYIDWY RQAPGNEREWVAQITRGGDSFYADSVKGRFAISRDN KNTVYLQMNSLKPEDTAVYYCRVLSYWGQGTQVTVSS
12	FLT3 antibody variable domain	FLL187	QVQLQESGGGLVQPGGSLRLSCAASGVTFSINYIDWY RQAPGKQREWVAQITRDSNSFYADSVKGRFAISRDN KNTVYLQMNSLKPEDTAVYYCRVLSYWGQGTQVTVSS
13	FLT3 antibody variable domain	FLL32	QVQLQESGGGLVQAGGSLRLSCQASGVTFNINYIDWY RQAPGRQREWVAQITRDSTRFYADSVKGRFAISRDN KNMVYQLNSLKPEDTAVYYCRILSYWGQGTQVTVSS
14	FLT3 antibody variable domain	FLL51	QVQLQESGGGLVQPGGSLRLSCAASGFDFSISYIDWY RQAPGNEREWVAQITRGGDSFYADSVKGRFAISRDN KNTVYLQMNSLKPEDTAVYYCRILSYWGQGTQVTVSS
15	FLT3 antibody variable domain	FLL55	QVQLQESGGGLVQAGGSLRLSCAASGSTFSRNYIDWY RQAPGKQREWVAQITSAGNTHYEPSLKGRFTISRDN KNTAYLQMNSLKPEDTAVYYCRILDYWGQGTQVTVSS
16	FLT3 antibody variable domain	FLL77	QVQLQESGGGLVQPGGSLRLSCAASGVTFSISYIDWY RQAPGNEREWVAQITRGGDSFYADSVKGRFAISRDN KNTVYLQMNSLKPEDTAVYYCRILSYWGQGTQVTVSS

17	FLT3 antibody variable domain	FLL97	QVQLQESGGGLVQAGGSLRLSCAASGVTFSSINIDWY RQAPGKQREWVAQITRDSNSFYADSVKGRFAVSRDNA KNTVYLQMNSLKPEDTAVYYCRVLSYWGQGTQVTVSS
18	FLT3 antibody variable domain	FLL21	QVQLQESGGGLVQPGGSLTSLCAASGSTFSRNYIDWY RQAPGKQREWVAQITSGGNTHYEPSLKGRFTISRDN KNTAYLQMNSLKPEDTAVYYCRILDYWGQGTQVTVSS
19	FLT3 antibody variable domain	FLL57	QVQLQESGGGLVQAGGSLRLSCAASGSTFSKNYIDWY RQAPGKQREWVAQITSGGNTHYEPSLKGRFTISRDN KNTAYLQMNSLKPEDTAVYYCRILDYWGQGTQVTVSS
20	FLT3 antibody variable domain	FLL62	QVQLQESGGGLVQAGGSLRLSCAASGSTSSRNYIDWY RQAPGKQREWVAQITSGGNTHYEPSLKGRFTISRDN KNTAYLQMNSLKPEDTAVYYCRILDYWGQGTQVTVSS
21	FLT3 antibody variable domain	FLL79	QVQLQESGGGLVQAGGSLRLSCASGSTFSRNYIDWY RQAPGKQREWVAQITSGGNTHYEPSLKGRFTISRDN KNTAYLQMNSLKPEDTAVYYCRILDYWGQGTQVTVSS
22	FLT3 antibody variable domain	FLL86	QVQLQESGGGLVQPGDPLRLSCAASGSTFSRNYIDWY RQAPGKQREWVAQITSGGNTHYEPSLKGRFTISRDN KNTAYLQMNSLKPEDTAVYYCRILDYWGQGTQVTVSS
23	FLT3 antibody variable domain	FLL112	QVQLQESGGGLVQAGGSLRLSCAVSGRTFSGFGTGWF RQAPGKEREFFVAAISWAGGRTHYEDSVKGRFTIHRDN AKNTVYLQMNSLKPEDTAVYYCAAQVSRAYDGIWYSG GDYWGQGTQVTVSS
24	FLT3 antibody variable domain	FLL142	QVQLQESGGGLVQAGGSLRLSCAVSGRTFSGFGTGWF RQAPGKEREFFVAAISWDGGRTHYADFVKGRFTISRDN AKNTVYLQMNSLKPEDTAVYYCAAQVARAYDSKWYSG GDYWGQGTQVTVSS
25	FLT3 antibody variable domain	FLL143	QVQLQESGGGLVQAGGSLRLSCAVSGRTFSGFGTGWF RQAPGKEREFFVAAISWVGGRTHYADSVKGRFTISRDN AKNTVYLQMNSLKPEDTAVYYCAAQVARAYDGNWYSG GDYWGQGTQVTVSS
26	FLT3 antibody variable domain	FLL154	QVQLQESGGGLVQAGGSLRLSCAVSGRTFSGFGTGWF RQAPGKEREFFVAAISWSGGRTHYADSVKGRFTISRDN AKNTVYLQMNSLKPEDTAVYYCAGQVARAYDGNWYSR GDYWGQGTQVTVSS
27	FLT3 antibody variable domain	FLL168	QVQLQESGGGSVQAGGSLRLSCAFSGRTFSGFGTGWF RQAPEKEREFFVAAISWDGGRTHYADSVKGRFTISRDN AKNTVYLQMDSLKPEDTAIYYCAAQVSRAYDGRWYSA VDYWGRTQVTVSS
28	FLT3 antibody variable domain	FLL170	QVQLQESGGGLVQAGGSLRLSCAVSGRTFSGFGTGWF RQAPGKEREFFVAAISWSGGTTHYADSVKGRFTISRDN AKNTVYLQMNSLKPEDTAVYYCAGQVARAYDSSWYSR GDYWGQGTQVTVSS
29	FLT3 antibody variable domain	FLL188	QVQLQESGGGLVQAGGSLGLSCAVSGRTFSGFGTGWF RQPEKEREFFVAAISWDGGRTHYADSVKGRFTISRDN AKNTVFLQMNSLKPEDTAVYYCAAQVARAYDSRWYSG GDYWGQGTQVTVSS
30	FLT3 antibody variable domain	FLL40	QVQLQESGGGLVQAGGSLRLSCAVSGRTFSGFGTGWF RQAPGKEREFFVAAISWSGGTTHYADSVKGRFTISRDN AKNTVSLVYLQMNSLKPDDTAVYYCAGQVARAYDSSW YSRGDYLQGTQVTVSS
31	FLT3 antibody variable domain	FLL6	QVQLQESGGGLVQAGGSLRLSCAVSGRTFSGFGTGWF RQAPGKEREFFVAAISWDGGRTHYADSVKGRFTISRDN AANTVYLQMNSLKPEDTAVYYCAGQVSRAYDSMWYGR DDYWGQGTQVTVSS
32	FLT3 antibody variable domain	FLL75	QVQLQESGGGLVQAGGSLRLSCAVSGRTFSGFGTGWF RQAPGKEREFFVAAISWSGGTTHYADSVKGRFTISRDN AKNTVNLVYLQMNDLRPEDTAVYYCAGQVARAYDSNW YSRGDYWGQGTQVTVSS
33	FLT3 antibody variable domain	FLL83	QVQLQESGGGLVQAGGSLRLSCAVSGRTFSGFGTGWF RQAPGKEREFFVAAISWSGGTTHYADSVKGRFTISRDN AENTVYLEMNSLKPEDTAVYICAGQVSRAYDSNWYSR DDYWGQGTQVTVSS

34	FLT3 antibody variable domain	FLL94	QVQLQESGGGLVQAGGSLRLSCAVSGRTFSGFGTGWFRQAPGKEREFVAAISWDGGRTHYADSVKGRFTISRDN AKNTVY LQMNSLKPEDTAIYYCAGQVARAYDTRWYSR GDYWGQGTQVTVSS
35	FLT3 antibody variable domain	FLL99	QVQLQESGGGLVQAGGSLRLSCAVSGRTFSGFGTGWFRQAPGKEREFVAAISWDGGRTHYADSVKGRFTISRDN AKNTVY LQMNSLKPEDTAVYYCAAQVARAYDSRWYSG GDYWGQGTQVTVSS
36	FLT3 antibody variable domain	FLL38	QVQLQESGGGLVQAGGSLRLSCAVSGRTFSGFGTGWFRQAPGKEREFVAAVSWSGGTTEIADSVKGRFTISRDN AKNTVY LQMNSLKPEDTAVYYCAGQVARAYDSRWYSR GDYWGQGTQVTVSS
37	FLT3 antibody variable domain	FLL53	QVQLQESGGGLVQAGDSLRLSCAVSGRTFSGFGTGWFRQAPGKEREFVAAVSQSGGTTHYADSVKGRFTISRDN AKNTE TLVY LQMNSLKPEDTAVYYCAGQVARAYDSSW YARGDYWGQGTQVTVSS
38	FLT3 antibody variable domain	FLL553	QVQLQESGGGLVQAGGSLRLSCAVSGRTFSGFGTGWFRQAPGKEREFVAAISWSGGTTHYADSVKGRFTISRDN AKNTVNLVY LQMNSLRPEDTAVYYCAGQVARAYDSNW YSRGDYWGQGTQVTVSS
39	FLT3 antibody variable domain	FLL74	QVQLQESGGGLVQAGGSLRLSCRFSGRTFSGFGTGWFRQAPGKEREFVAAISWAGGRTHYEDSVKGRFTISRDN AKNTVY LQMNSLKPEDTAVYYCAVQVSRAYDGIWYSG GDYWGQGTQVTVSS
40	FLT3 antibody variable domain	FLL102	QVQLQESGGGLVQAGGSLMVSCAASGGTWSSYATGWFRQVP GKERKLIAGISRSGGRYYAESVKGRFTISRDN AKNTVY LQMNTLKPDDTAVYYCAAARYFTSSVYVTS G NDYDYWGQGTQVTVSS
41	FLT3 antibody variable domain	FLL122	QVQLQESGGGLVQAGGSLMVSCAASGGTWSSYATGWFRQVP GKERELIAGISRSGGRYYAESVKGRFTISRDN AKNTVY LQMNTLKPDDTAVYYCAAARYFTSSVYVTS G NDYDYWGQGTQVTVSS
42	FLT3 antibody variable domain	FLL134	QVQLQESGGGLVQPGGSLRLSCAASGGTFSSYATGWFRQVP GKEREFIAGISRNSGRYYAESVKGRFTISRDN AKNTVY LQMNTLRPDDTAVYYCAAARYFTRDAIYTS G D DYDYWGQGTQVTASS
43	FLT3 antibody variable domain	FLL153	QVQLQESGGGLVQVGGSLMVSCAASGGTFSSYATGWFRQVP GKEREFIAGVSRNSGRYYAESVKGRFTISRDN AKNTVY LQMNTLKPDDTGYYCAAARYFTRDAVYTS G DDYDYWGQGTQVTVSS
44	FLT3 antibody variable domain	FLL41	QVQLQESGGGLVQLGDSL MVSCAASGGTFSSYATGWFRQVP GREREFIAGISRSGGRYYAESVKGRFTISRDN AKNTVY LQMNTLKPDDTAVYYCAAARYFTSSVYVTS G DDYDYWGQGTQVTVSS
45	FLT3 antibody variable domain	FLL67	QVQLQESGGGLVQLGDSL MVSCAASGGTFSSYATGWFRQVP GKEREFIAGISRSGGRYYAESVKGRFTISRDN AKNTVY LQMNTLKPDDTAVYYCAAARYFTSSVYVTS G DDYDYWGQGTQVTVSS
46	FLT3 antibody variable domain	FLL92	QVQLQESGGGLVQAGGSLMVSCAASGGTWSSYATGWFRQVP GKERELIAGISRSGGRYYAESVKGRFTISRDN AKNTVY LQMNTLKSDDTAVYYCAAARYFTSSVYVTS G NDYDYWGQGTQVTVSS
47	FLT3 antibody variable domain	FLL71	QVQLQESGGGLVQVGGSLMVSCAASGGTFSSYATGWFRQVP GKEREFIAGISRNSGRYYAESVKGRFTISRDN AKNTVY LQMNTLKPDDTAVYYCAAARYFTRDAVYTS G DDYDYWGQGTQVTVSS
48	FLT3 antibody variable domain	FLL8	QVQLQESGGGLVQVGGSLMVSCAASGGTFSSYATGWFRQVP GKEREFIAGISRNSGRYYAESVKGRFTISRDN AKNTVY LQMNTLKPDDTAVYYCAAARYFTRDVYVTS G DDYDYWGQGTQVTVSS
49	FLT3 antibody variable domain	FLL84	QVQLQESGGGLVQAGGSLMVSCAASGGTFSSYATGWFRQVP GKEREFIAGISRSGGRYYAESVKGRFTISRDN

			AKNTVYLMQNTLKPDDTAVYYCAAARYFTTSVVYTS DDYDWGQGTQVTVSS
50	FLT3 antibody variable domain	FLL107	QVQLQESGGGLVQAGGSLRLSCAASGRFTSSYAMGWF RQAPGKEREFFVAAISWSGSNTYYADSVKGRFTISRDN AKNTVYLMQDSLKPEDTAVYYCAAGGSTRVVVTTTPV VKYWGQGTQVTVSS
51	FLT3 antibody variable domain	FLL141	QVQLQESGGGLVQAGGSLRLSCAASGRFTSSYAMGWF RQAPGMEREFFVAAISWSGYSTYYADSVKGRFTISRDD AKNTVYLMQDSLKPEDTAVYYCAAGGSTRVVVTTTPV VKYWGQGTQVTVSS
52	FLT3 antibody variable domain	FLL34	QVQLQESGGGLVQAGGSLRLSCAASGRFTSSYALGWF RQAPGKEREFFVAAISWSGGNTYYADSVKGRFTISRDD AKNTVYLMQDSLKPEDTAVYYCAAGGSTRVVVTTTPV VKYWGQGTQVTVSS
53	FLT3 antibody variable domain	FLL4	QVQLQESGGGLVQAGGSLRLSCAASERTFSSYTMGWF RQAPGKEREFFVAAMSWSGGSTYYADSVKGRFTISRDN AKNTVYLMQDSLKPEDTAVYYCAAGGSTRVVVTTTPV VKYWGQGTQVTVSS
54	FLT3 antibody variable domain	FLL61	QVQLQESGGGLVQAGGSLRLSCAASERTFSSYAMGWF RQAPGKEREFFVAAISWSGGSTYYADSVKGRFTISRDN AKNTVYLMQDSLKPEDTAVYYCAAGGSTRVVVTTPI VKYWGQGTQVTVSS
55	FLT3 antibody variable domain	FLL78	QVQLQESGGGLVQAGGSLRLSCAASGRFTSSYAMGWF RQAPGKEREFFVAAISWSGSSTYYADSVKGRFTISRDN AKNTVYLLMDSLKPEDTAVYYCAAGGSTRVVVTTTPV VKYWGQGTQVTVSS
56	FLT3 antibody variable domain	FLL1	QVQLQESGGGLVQAGGSLRLSCAASGRFTSTLTVAWF RQAPGKEREFFVASIPSGSNTGYAESVKGRFTISRDI AKNTVYLMQNSLKPEDTAMYFCAARIYFGSSRGYDYW GQGTQVTVSS
57	FLT3 antibody variable domain	FLL26	QVQLQESGGGLVQAGGSLRLSCAASGRFTFTTYTVAWF RQAPGKEREFLVASIPTGSNTAYAESVKGRFTISRGN AKNTVYLMQNSLKPEDTAMYYCAARTYFGSSRGYDYW GQGTQVTVSS
58	FLT3 antibody variable domain	FLL160	QVQLQESGGGLVQAGDSLRLSCATSGRTFNLYRVGWF RQAPGKEREFFVARITWSADITQYADSVKGRFTISRDN AKNTVYLMQNSLKPEDTAIYYCATTLRKSSGIYHVD YDDWGQGTQVTVSS
59	FLT3 antibody variable domain	FLL173	QVQLQESGGGLVQAGGSLRLSCATSGRTFNLYRVGWF RQAPGKEREFFVARITWSADITQYADSVKGRFTISRDN AKNTVYLMQNSLKPEDTAIYYCATTLRKSSGIYHTDD YDYWGQGTQVTVSS
60	FLT3 antibody variable domain	FLL178	QVQLQESGGGLVQPGGSLRLSCAASGFTFSDYAMSWV RQAPGKGLEWVSGISSGGYKIGYTDSTKGRFTISRDN AKNTLYLMQNSLTAEDTAVYYCAKGTQWSWLRDNTS RGQGTQVTVSS
61	FLT3 antibody variable domain	FLL27	QVQLQESGGGLVQPGGSLRLSCKASGFTFSSYAMSWV RQAPGKGLEWVSGISSGGYKIGYTDSTKGRFTISRDN AKNTLYLMQNSLNAEDTAVYYCAKGTQWSWALRDSTS RGQGTQVTVSS
62	FLT3 antibody variable domain	FLL190	QVQLQESGGGLVQAGGSLTLSTASGSTFSINHFWSY RQAPGKQRELVAFISSDGVSIDVESVKGRFTISGDND KNTAYLMQNLKPEDTAVYYCYRGFWGQGTQVTVSS
63	FLT3 antibody variable domain	FLL43	QVQLQESGGGLVQPGGSLTLSTASGSTFSINHFAWY RQAPGKQRELVAFISSDGRSTDVESVKGRFTISGDND KNTAYLMQNLKPEDTAVYYCYRGFSWGQGTQVTVSS
64	FLT3 antibody variable domain	FLL15	QVQLQESGGGLVQAGGSLSLSCAASEGTISHAAMGWF RQAPGKERQFVAYDTWTGGSTNYADSVKDRFTITGDH AKNTVYLMQNSLKPEDTGVIYCAVRGRYSASYTYTNP ASYKYWGQGTQVTVSS
65	FLT3 antibody variable domain	FLL45	QVQLQESGGGLVQAGGSLRLSCAASGGTFSSAMGWF RQAPGKEREFFVATITQNDVPTYTHSVKGRFTISRDN

			AKNTMYLQMNSLKPEDTAVYYCAQRVAQASGWRTTIK DYGWGGGTQVTVSS
66	FLT3 antibody variable domain	FLL39	QVQLQESGGGLVQAGGSLRLSCAASGLTSSTYRMAWF RQAPGKEREFAAGISYSADSGGSTNYADSVKGRFTIS RDNAKNTVYLQMSSLKPEDTAVYYCAAGRYSGTYNSP YSSSYVYWGQGTQVTVSS
67	FLT3 antibody variable domain	FLL177	QVQLQESGGGLVQAGGSLRLSCAASGSTFSRNTMGWF RQAPGKERVFVLGISWSGIRSYLDSAKARFTISRDN AKNTVYLQMNSLRPEDTAVYYCAAQEGSSPGPYKYWG QGTQVTVSS
68	FLT3 antibody variable domain	FLL823	QVQLQESGGGVVQVGGSLRLSCAASGGTFGYAVGW RQAPGKEREFAAFTWNGAYLYSDPVKGRFTISRDN KNTVYLQMNSLKSEDTAVYYCGLDRWSAVVESTPSTR GQGTQVTVSS
69	FLT3 antibody variable domain	FLL76	QVQLQESGGGLVQAGGSLRLSCAASGGAFSSVYMGWF RQAPGKEREFAAIVISWSGRITDYADSVKGRFTISRDN NAKSTVYLQMNNLKPEDTAVYYCAAKTGMIDLRST FDYWGQGTQVTVSS
70	FLT3 antibody variable domain	FLL822	QVQLQESGGGSVQAGGSLRLSCTASGRFTDYTMGW RQAPGKEREFMGLISSNGYRRYTGSMKDRFTISRDN VKKTIVYLQMNDLKPEDTAVYYCAASEDHGAPRYDWG QGTQVTVSS
71	FLT3 antibody variable domain	FLH107	EVQLLESGGGLVQPGGSLTLSCAASGRTFSSYAMGW RQAPGKEREFAAISWSGSNTYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAAGGSTRVVTTTPV VKYWGQGTQVTVSS
72	FLT3 antibody variable domain	FLH141	EVQLLESGGGLVQPGGSLTLSCAASGRTFSSYAMGW RQAPGMEREFAAISWSGYSTYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAAGGSTRVVTTTPV VKYWGQGTQVTVSS
73	FLT3 antibody variable domain	FLH19C	EVQLVESGGGLVQPGGSLTLSCAASGSTFSINHF RQAPGKQRELVAFISSDGVSIDVESVKGRFTISGDN KNTAYLQMNSLRAEDTAVYYCYRGFWGQGTQVTVSS
74	FLT3 antibody variable domain	FLH34	EVQLLESGGGLVQPGGSLTLSCAASGRTFSSYALGW RQAPGKEREFAAISWSGGNTYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAAGGSTRVVTTTPV VKYWGQGTQVTVSS
75	FLT3 antibody variable domain	FLH4	EVQLLESGGGLVQPGGSLTLSCAASERTFSSYTMGW RQAPGKEREFAAMSWSGGSTYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAAGGSTRVVTTTPV VKYWGQGTQVTVSS
76	FLT3 antibody variable domain	FLH78	EVQLLESGGGLVQPGGSLTLSCAASGRTFSSYAMGW RQAPGKEREFAAISWSGSSTYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAAGGSTRVVTTTPV VKYWGQGTQVTVSS
77	CDR1	FLL101	GVTFSINYID
78	CDR1	FLL103	GPTFSINYID
77	CDR1	FLL116	GVTFSINYID
79	CDR1	FLL125	GSTFSRNYID
80	CDR1	FLL129	GVTFSASYID
81	CDR1	FLL137	GSTFNNYAMD

77	CDR1	FLL14	GVTFSINYID
77	CDR1	FLL146	GVTFSINYID
82	CDR1	FLL158	GSTFGRNYID
77	CDR1	FLL179	GVTFSINYID
80	CDR1	FLL181	GVTFSASYID
77	CDR1	FLL187	GVTFSINYID
83	CDR1	FLL32	GVTFNINYID
84	CDR1	FLL51	GFDFSISYID
79	CDR1	FLL55	GSTFSRNYID
85	CDR1	FLL77	GVTFSISYID
77	CDR1	FLL97	GVTFSINYID
79	CDR1	FLL21	GSTFSRNYID
86	CDR1	FLL57	GSTFSKNYID
87	CDR1	FLL62	GSTSSRNYID
79	CDR1	FLL79	GSTFSRNYID
79	CDR1	FLL86	GSTFSRNYID
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89	CDR1	FLL102	GGTWSSYATG
89	CDR1	FLL122	GGTWSSYATG
90	CDR1	FLL134	GGTFSSYATG
90	CDR1	FLL153	GGTFSSYATG
90	CDR1	FLL41	GGTFSSYATG
90	CDR1	FLL67	GGTFSSYATG
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91	CDR1	FLL107	GRTFSSYAMG
91	CDR1	FLL141	GRTFSSYAMG
92	CDR1	FLL34	GRTFSSYALG

93	CDR1	FLL4	ERTFSSYTMG
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91	CDR1	FLL78	GRTFSSYAMG
95	CDR1	FLL1	GRTFSTLTVA
96	CDR1	FLL26	GRTFTTYTVA
97	CDR1	FLL160	GRTFNLYRVG
97	CDR1	FLL173	GRTFNLYRVG
98	CDR1	FLL178	GFTFSDYAMS
99	CDR1	FLL27	GFTFSSYAMS
100	CDR1	FLL190	GSTFSINHFS
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102	CDR1	FLL15	EGTISHAAMG
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105	CDR1	FLL177	GSTFSRNTMG
106	CDR1	FLL823	GGTFGYAVG
107	CDR1	FLL76	GGAFFSSVVG
108	CDR1	FLL822	GRTFTDYTMG
91	CDR1	FLH107	GRTFSSYAMG
91	CDR1	FLH141	GRTFSSYAMG
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111	CDR2	FLL129	QITRGGDSFYADSVKG
112	CDR2	FLL137	QITRDSSSFYADSVKG
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121	CDR2	FLL168	AISWDGGRTHYADSVKG
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153	CDR2	FLH4	MSWSGGSTYYADSVKG
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155	CDR3	FLL103	LSY
155	CDR3	FLL116	LSY
156	CDR3	FLL125	LDY
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155	CDR3	FLL14	LSY
157	CDR3	FLL146	LSF
156	CDR3	FLL158	LDY
158	CDR3	FLL179	LSD
155	CDR3	FLL181	LSY
155	CDR3	FLL187	LSY
155	CDR3	FLL32	LSY
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156	CDR3	FLL55	LDY

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165	CDR3	FLL188	AQVARAYDSRWYSGGDY
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176	CDR3	FLL41	ARYFTTSVVYTSGDDYDY
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173	CDR3	FLL92	ARYFTSSVVYTSGNDYDY
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287	framework 1	FLL92	QVQLQESGGGLVQAGGSLMVSCAAS
288	framework 1	FLL71	QVQLQESGGGLVQVGGSLMVSCAAS
288	framework 1	FLL8	QVQLQESGGGLVQVGGSLMVSCAAS
287	framework 1	FLL84	QVQLQESGGGLVQAGGSLMVSCAAS
273	framework 1	FLL107	QVQLQESGGGLVQAGGSLRLSCAAS
273	framework 1	FLL141	QVQLQESGGGLVQAGGSLRLSCAAS
273	framework 1	FLL34	QVQLQESGGGLVQAGGSLRLSCAAS
273	framework 1	FLL4	QVQLQESGGGLVQAGGSLRLSCAAS
273	framework 1	FLL61	QVQLQESGGGLVQAGGSLRLSCAAS

290	framework 1	FLL78	QVQLQESGGGWVQAGGSLRLSCAAS
273	framework 1	FLL1	QVQLQESGGGLVQAGGSLRLSCAAS
273	framework 1	FLL26	QVQLQESGGGLVQAGGSLRLSCAAS
291	framework 1	FLL160	QVQLQESGGGLVQAGDSLRLSCATS
292	framework 1	FLL173	QVQLQESGGGLVQAGGSLRLSCATS
275	framework 1	FLL178	QVQLQESGGGLVQPGGSLRLSCAAS
293	framework 1	FLL27	QVQLQESGGGLVQPGGSLRLSCKAS
294	framework 1	FLL190	QVQLQESGGGLVQAGGSLTLSCITAS
295	framework 1	FLL43	QVQLQESGGGLVQPGGSLTLSCITAS
296	framework 1	FLL15	QVQLQESGGGLVQAGGSLSLSCAAS
273	framework 1	FLL45	QVQLQESGGGLVQAGGSLRLSCAAS
273	framework 1	FLL39	QVQLQESGGGLVQAGGSLRLSCAAS
297	framework 1	FLL177	QVQLQESGGGLVQTGGSLRLSCAAS
298	framework 1	FLL823	QVQLQESGGGVVQVGGSLRLSCAAS
273	framework 1	FLL76	QVQLQESGGGLVQAGGSLRLSCAAS
299	framework 1	FLL822	QVQLQESGGGSVQAGGSLRLSCTAS
300	framework 1	FLH107	EVQLLES GGGLVQPGGSLTLSCAAS
300	framework 1	FLH141	EVQLLES GGGLVQPGGSLTLSCAAS
301	framework 1	FLH19C	EVQLVES GGGLVQPGGSLTLSCAAS
300	framework 1	FLH34	EVQLLES GGGLVQPGGSLTLSCAAS
300	framework 1	FLH4	EVQLLES GGGLVQPGGSLTLSCAAS
300	framework 1	FLH78	EVQLLES GGGLVQPGGSLTLSCAAS
302	framework 2	FLL101	WYRQAPGKQREWVA

302	framework 2	FLL103	WYRQAPGKQREWVA
302	framework 2	FLL116	WYRQAPGKQREWVA
302	framework 2	FLL125	WYRQAPGKQREWVA
303	framework 2	FLL129	WYRQAPGNEREWVA
304	framework 2	FLL137	WFRQAPGKQREWVA
302	framework 2	FLL14	WYRQAPGKQREWVA
302	framework 2	FLL146	WYRQAPGKQREWVA
302	framework 2	FLL158	WYRQAPGKQREWVA
302	framework 2	FLL179	WYRQAPGKQREWVA
303	framework 2	FLL181	WYRQAPGNEREWVA
302	framework 2	FLL187	WYRQAPGKQREWVA
305	framework 2	FLL32	WYRQAPGRQREWVA
303	framework 2	FLL51	WYRQAPGNEREWVA
302	framework 2	FLL55	WYRQAPGKQREWVA
303	framework 2	FLL77	WYRQAPGNEREWVA
302	framework 2	FLL97	WYRQAPGKQREWVA
302	framework 2	FLL21	WYRQAPGKQREWVA
302	framework 2	FLL57	WYRQAPGKQREWVA
302	framework 2	FLL62	WYRQAPGKQREWVA
302	framework 2	FLL79	WYRQAPGKQREWVA
302	framework 2	FLL86	WYRQAPGKQREWVA
306	framework 2	FLL112	WFRQAPGKEREVVA
306	framework 2	FLL142	WFRQAPGKEREVVA

306	framework 2	FLL143	WFRQAPGKEREFA
306	framework 2	FLL154	WFRQAPGKEREFA
307	framework 2	FLL168	WFRQAPGKEREFA
306	framework 2	FLL170	WFRQAPGKEREFA
308	framework 2	FLL188	WFRQPPGKEREFA
306	framework 2	FLL40	WFRQAPGKEREFA
306	framework 2	FLL6	WFRQAPGKEREFA
306	framework 2	FLL75	WFRQAPGKEREFA
306	framework 2	FLL83	WFRQAPGKEREFA
307	framework 2	FLL94	WFRQAPGKEREFA
306	framework 2	FLL99	WFRQAPGKEREFA
306	framework 2	FLL38	WFRQAPGKEREFA
306	framework 2	FLL53	WFRQAPGKEREFA
306	framework 2	FLL553	WFRQAPGKEREFA
306	framework 2	FLL74	WFRQAPGKEREFA
406	framework 2	FLL102	WFRQVPKEREKLA
309	framework 2	FLL122	WFRQVPKEREKLA
310	framework 2	FLL134	WFRQVPKEREKLA
310	framework 2	FLL153	WFRQVPKEREKLA
311	framework 2	FLL41	WFRQVPKEREKLA
310	framework 2	FLL67	WFRQVPKEREKLA
309	framework 2	FLL92	WFRQVPKEREKLA
310	framework 2	FLL71	WFRQVPKEREKLA

310	framework 2	FLL8	WFRQVPGKEREFA
310	framework 2	FLL84	WFRQVPGKEREFA
306	framework 2	FLL107	WFRQAPGKEREFA
312	framework 2	FLL141	WFRQAPGMEREFA
306	framework 2	FLL34	WFRQAPGKEREFA
306	framework 2	FLL4	WFRQAPGKEREFA
306	framework 2	FLL61	WFRQAPGKEREFA
306	framework 2	FLL78	WFRQAPGKEREFA
313	framework 2	FLL1	WFRQAPGKEREFA
314	framework 2	FLL26	WFRQAPGKEREFLV
306	framework 2	FLL160	WFRQAPGKEREFA
306	framework 2	FLL173	WFRQAPGKEREFA
315	framework 2	FLL178	WVRQAPGKGLEWVS
315	framework 2	FLL27	WVRQAPGKGLEWVS
316	framework 2	FLL190	WYRQAPGKQREFA
316	framework 2	FLL43	WYRQAPGKQREFA
317	framework 2	FLL15	WFRQAPGKERQFA
306	framework 2	FLL45	WFRQAPGKEREFA
318	framework 2	FLL39	WFRQAPGKEREF
319	framework 2	FLL177	WFRQAPGKERVFVL
306	framework 2	FLL823	WFRQAPGKEREFA
306	framework 2	FLL76	WFRQAPGKEREFA
320	framework 2	FLL822	WFRQAPGKEREFML

321	framework 2	FLH107	WFRQAPGKEREVAA
322	framework 2	FLH141	WFRQAPGMEREVAA
407	framework 2	FLH19C	WYRQAPGKQRELVAF
321	framework 2	FLH34	WFRQAPGKEREVAA
321	framework 2	FLH4	WFRQAPGKEREVAA
321	framework 2	FLH78	WFRQAPGKEREVAA
323	framework 3	FLL101	RFAISRDNAKNTVYLMNNLKPEDTAVYYCRV
324	framework 3	FLL103	RFAVSRDNAKNTVYLMNSLKPEDTAVYYCRV
325	framework 3	FLL116	RFAISRDNAKNTVYLMNSLKPEDTAVYYCRV
326	framework 3	FLL125	RFTISRDNAKNTAYLMNSLKPEDTAVYYCRI
325	framework 3	FLL129	RFAISRDNAKNTVYLMNSLKPEDTAVYYCRV
325	framework 3	FLL137	RFAISRDNAKNTVYLMNSLKPEDTAVYYCRV
327	framework 3	FLL14	RFAISRDNAKNTVYLMNSLKPEDTAVYYCRL
328	framework 3	FLL146	RFAISRDNAKNTVYLMNNLRPEDTAVYYCRL
326	framework 3	FLL158	RFTISRDNAKNTAYLMNSLKPEDTAVYYCRI
329	framework 3	FLL179	RFAISRDNAKNTVYLMNSLKPEDTAVYYCRI
325	framework 3	FLL181	RFAISRDNAKNTVYLMNSLKPEDTAVYYCRV
330	framework 3	FLL187	RFAISRENAKNTVYLMNSLKPEDTAVYYCRV
331	framework 3	FLL32	RFAISRDNAKNMVYLQLNSLKPEDTAVYYCRI
329	framework 3	FLL51	RFAISRDNAKNTVYLMNSLKPEDTAVYYCRI
326	framework 3	FLL55	RFTISRDNAKNTAYLMNSLKPEDTAVYYCRI
329	framework 3	FLL77	RFAISRDNAKNTVYLMNSLKPEDTAVYYCRI
324	framework 3	FLL97	RFAVSRDNAKNTVYLMNSLKPEDTAVYYCRV

326	framework 3	FLL21	RFTISRDNAKNTAYLQMNSLKPEDTAVYYCRI
326	framework 3	FLL57	RFTISRDNAKNTAYLQMNSLKPEDTAVYYCRI
326	framework 3	FLL62	RFTISRDNAKNTAYLQMNSLKPEDTAVYYCRI
326	framework 3	FLL79	RFTISRDNAKNTAYLQMNSLKPEDTAVYYCRI
326	framework 3	FLL86	RFTISRDNAKNTAYLQMNSLKPEDTAVYYCRI
332	framework 3	FLL112	RFTIHRDNAKNTVYLQMNSLKPEDTAVYYCA
333	framework 3	FLL142	RFTISRDNAKNTVYLQMNSLKPEDTAVYYCA
333	framework 3	FLL143	RFTISRDNAKNTVYLQMNSLKPEDTAVYYCA
333	framework 3	FLL154	RFTISRDNAKNTVYLQMNSLKPEDTAVYYCA
334	framework 3	FLL168	RFTISRDNAKNTVYLQMDSLKPEDTAIYYCA
333	framework 3	FLL170	RFTISRDNAKNTVYLQMNSLKPEDTAVYYCA
335	framework 3	FLL188	RFTISRDNAKNTVFLQMNSLKPEDTAVYYCA
336	framework 3	FLL40	RFTISRDNAKNTVSLVYLQMNSLKPDDTAVYYCA
337	framework 3	FLL6	RFTISRDNAAANTVYLQMNSLKPEDTAVYYCA
338	framework 3	FLL75	RFTISRDNAKNTVNLVYLQMNDLRPEDTAVYYCA
339	framework 3	FLL83	RFTISRDNAAENTVYLEMNSLKPEDTAVYICA
340	framework 3	FLL94	RFTISRDNAKNTVYLQMNSLKPEDTAIYYCA
333	framework 3	FLL99	RFTISRDNAKNTVYLQMNSLKPEDTAVYYCA
341	framework 3	FLL38	RFTISRDNAKNTVYLQMSSLKPGDTAVYYCA
342	framework 3	FLL53	RFTISRDNAKNTETLVYLQMNSLKPEDTAVYYCA
343	framework 3	FLL553	RFTISRDNAKNTVNLVYLQMNSLRPEDTAVYYCA
333	framework 3	FLL74	RFTISRDNAKNTVYLQMNSLKPEDTAVYYCA
344	framework 3	FLL102	RFTISRDNAKNTVYLQMNTLKPDDTAVYYCAA

344	framework 3	FLL122	RFTISRDNKNTVYLMNTLKPDDTAVYYCAA
345	framework 3	FLL134	RFTISRDNKNTVYLMNTLRPDDTAVYYCAA
346	framework 3	FLL153	RFTISRDNKNTVYLMNTLKPDDTGVYYCAA
344	framework 3	FLL41	RFTISRDNKNTVYLMNTLKPDDTAVYYCAA
344	framework 3	FLL67	RFTISRDNKNTVYLMNTLKPDDTAVYYCAA
347	framework 3	FLL92	RFTISRDNKNTVYLMNTLKSDDTAVYYCAA
344	framework 3	FLL71	RFTISRDNKNTVYLMNTLKPDDTAVYYCAA
344	framework 3	FLL8	RFTISRDNKNTVYLMNTLKPDDTAVYYCAA
344	framework 3	FLL84	RFTISRDNKNTVYLMNTLKPDDTAVYYCAA
348	framework 3	FLL107	RFTISRDNKNTVYLMDSLKPEDTAVYYCA
349	framework 3	FLL141	RFTISRDDAKNTVYLMDSLKPEDTAVYYCA
349	framework 3	FLL34	RFTISRDDAKNTVYLMDSLKPEDTAVYYCA
348	framework 3	FLL4	RFTISRDNKNTVYLMDSLKPEDTAVYYCA
348	framework 3	FLL61	RFTISRDNKNTVYLMDSLKPEDTAVYYCA
350	framework 3	FLL78	RFTISRDNKNTVYLLMDSLKPEDTAVYYCA
351	framework 3	FLL1	RFTISRDIKNTVYLMNSLKPEDTAMYFCAA
352	framework 3	FLL26	RFTISRGNKNTVYLMNSLKPEDTAMYYCAA
353	framework 3	FLL160	RFTISRDNKNTVYLMNSLKPEDTAIYYCAT
353	framework 3	FLL173	RFTISRDNKNTVYLMNSLKPEDTAIYYCAT
354	framework 3	FLL178	RFTISRDNKNTLYLMNSLTAEDTAVYYCAK
355	framework 3	FLL27	RFTISRDNKNTLYLMNSLNAEDTAVYYCAK
356	framework 3	FLL190	RFTISGDNDKNTAYLMNGLKPEDTAVYYCY
356	framework 3	FLL43	RFTISGDNDKNTAYLMNGLKPEDTAVYYCY

357	framework 3	FLL15	RFTITGDHAKNTVYLMNSLKPEDTGVYYCAV
358	framework 3	FLL45	RFTISRDNKNTMYLMNSLKPEDTAVYYCAQ
359	framework 3	FLL39	RFTISRDNKNTVYLMSSSLKPEDTAVYYCAA
360	framework 3	FLL177	RFTISRDNKNTVYLMNSLRPEDTAVYYCA
361	framework 3	FLL823	RFTISRDNKNTVYLMNSLKSEDTAVYYCGL
362	framework 3	FLL76	RFSISRDNKSTVYLMNNLKPEDTAVYYCA
363	framework 3	FLL822	RFTISRDNVKKTVYLMNDLKPEDTAVYYCAA
364	framework 3	FLH107	RFTISRDNKNTLYLMNSLRAEDTAVYYCAA
364	framework 3	FLH141	RFTISRDNKNTLYLMNSLRAEDTAVYYCAA
365	framework 3	FLH19C	RFTISGDNSKNTAYLMNSLRAEDTAVYYCYY
364	framework 3	FLH34	RFTISRDNKNTLYLMNSLRAEDTAVYYCAA
364	framework 3	FLH4	RFTISRDNKNTLYLMNSLRAEDTAVYYCAA
364	framework 3	FLH78	RFTISRDNKNTLYLMNSLRAEDTAVYYCAA
366	framework 4	FLL101	WGQGTQVTVSS
366	framework 4	FLL103	WGQGTQVTVSS
366	framework 4	FLL116	WGQGTQVTVSS
366	framework 4	FLL125	WGQGTQVTVSS
366	framework 4	FLL129	WGQGTQVTVSS
366	framework 4	FLL137	WGQGTQVTVSS
366	framework 4	FLL14	WGQGTQVTVSS
366	framework 4	FLL146	WGQGTQVTVSS
366	framework 4	FLL158	WGQGTQVTVSS
366	framework 4	FLL179	WGQGTQVTVSS

366	framework 4	FLL181	WGQGTQVTVSS
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366	framework 4	FLL32	WGQGTQVTVSS
366	framework 4	FLL51	WGQGTQVTVSS
366	framework 4	FLL55	WGQGTQVTVSS
366	framework 4	FLL77	WGQGTQVTVSS
366	framework 4	FLL97	WGQGTQVTVSS
366	framework 4	FLL21	WGQGTQVTVSS
366	framework 4	FLL57	WGQGTQVTVSS
366	framework 4	FLL62	WGQGTQVTVSS
366	framework 4	FLL79	WGQGTQVTVSS
366	framework 4	FLL86	WGQGTQVTVSS
366	framework 4	FLL112	WGQGTQVTVSS
366	framework 4	FLL142	WGQGTQVTVSS
366	framework 4	FLL143	WGQGTQVTVSS
366	framework 4	FLL154	WGQGTQVTVSS
367	framework 4	FLL168	WGRGTQVTVSS
366	framework 4	FLL170	WGQGTQVTVSS
366	framework 4	FLL188	WGQGTQVTVSS
368	framework 4	FLL40	LGQGTQVTVSS
366	framework 4	FLL6	WGQGTQVTVSS
366	framework 4	FLL75	WGQGTQVTVSS
366	framework 4	FLL83	WGQGTQVTVSS

366	framework 4	FLL94	WGQGTQVTVSS
366	framework 4	FLL99	WGQGTQVTVSS
366	framework 4	FLL38	WGQGTQVTVSS
366	framework 4	FLL53	WGQGTQVTVSS
366	framework 4	FLL553	WGQGTQVTVSS
366	framework 4	FLL74	WGQGTQVTVSS
366	framework 4	FLL102	WGQGTQVTVSS
366	framework 4	FLL122	WGQGTQVTVSS
369	framework 4	FLL134	WGQGTQVTASS
366	framework 4	FLL153	WGQGTQVTVSS
366	framework 4	FLL41	WGQGTQVTVSS
366	framework 4	FLL67	WGQGTQVTVSS
366	framework 4	FLL92	WGQGTQVTVSS
366	framework 4	FLL71	WGQGTQVTVSS
366	framework 4	FLL8	WGQGTQVTVSS
366	framework 4	FLL84	WGQGTQVTVSS
366	framework 4	FLL107	WGQGTQVTVSS
366	framework 4	FLL141	WGQGTQVTVSS
366	framework 4	FLL34	WGQGTQVTVSS
366	framework 4	FLL4	WGQGTQVTVSS
366	framework 4	FLL61	WGQGTQVTVSS
366	framework 4	FLL78	WGQGTQVTVSS
366	framework 4	FLL1	WGQGTQVTVSS

366	framework 4	FLL26	WGQGTQVTVSS
366	framework 4	FLL160	WGQGTQVTVSS
366	framework 4	FLL173	WGQGTQVTVSS
370	framework 4	FLL178	RGQGTQVTVSS
370	framework 4	FLL27	RGQGTQVTVSS
366	framework 4	FLL190	WGQGTQVTVSS
366	framework 4	FLL43	WGQGTQVTVSS
366	framework 4	FLL15	WGQGTQVTVSS
366	framework 4	FLL45	WGQGTQVTVSS
366	framework 4	FLL39	WGQGTQVTVSS
366	framework 4	FLL177	WGQGTQVTVSS
370	framework 4	FLL823	RGQGTQVTVSS
366	framework 4	FLL76	WGQGTQVTVSS
366	framework 4	FLL822	WGQGTQVTVSS
371	framework 4	FLH107	WGQGTLVTVSS
371	framework 4	FLH141	WGQGTLVTVSS
371	framework 4	FLH19C	WGQGTLVTVSS
371	framework 4	FLH34	WGQGTLVTVSS
371	framework 4	FLH4	WGQGTLVTVSS
371	framework 4	FLH78	WGQGTLVTVSS
196	anti-FLT3/anti-HSA/anti-CD3 fusion protein	FLL101	QVQLQESGGGLVQAGGSLRLSCAASGVTFSSINIDWY RQAPGKQREWVAQITRDSNSFYADSVKGRFAISRDN KNTVYLQMNNLKPEDTAVYYCRVLSYWGQGTQVTVSS GGGSGGGSEVQLVESGGGLVQPGNSRLSCAASGFT FSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYADSVK GRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSL SVSSQGTLVTVSSGGGSGGGSEVQLVESGGGLVQPG GSLKLSAASGFTFNKYAINWVRQAPGKGLEWVARIR SKYNNYATYYADQVKDRFTISRDDSKNTAYLQMNNLK TEDTAVYYCVRHANFGNSYISYWAYWGQGTLVTVSSG

			GGGSGGGSGGGSGQT VVTQEP SLTVSPGGT VTLTCA SSTGAVTSGNYPNWVQQKPGQAPRGLIGG TKFLVP GT PARFSGSLLGGKAAL TL SGVQPEDEAEYYCTLWYSNR WVFGGGTKLTVLHHHHHH
197	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL103	QVQLQESGGGLVQAGGSLRLSCEASGPTFSINYIDWY RQAPGKQREWVAQITRDSNSFYADSVKGRFAVSRDNA KNTVYLQMNSLKPEDTAVYYCRVLSYWGQGTQVTVSS GGGSGGGSEVQLVESGGGLVQPGNSLRLS CAASGFT FSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYADSVK GRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSL SVSSQGT LVTVSSGGGSGGGSEVQLVESGGGLVQPG GSLKLS CAASGFTFNKYAINWVRQAPGKGLEWVARIR SKYNNYATYYADQVKDRFTISRDDSKNTAYLQMN NLK TEDTAVYYCVRHANFGNSYISYWAYWGQGT LVTVSSG GGGSGGGSGGGSGQT VVTQEP SLTVSPGGT VTLTCA SSTGAVTSGNYPNWVQQKPGQAPRGLIGG TKFLVP GT PARFSGSLLGGKAAL TL SGVQPEDEAEYYCTLWYSNR WVFGGGTKLTVLHHHHHH
198	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL116	QVQLQESGGGLVQAGGSLRLS CAASGVTFSINYIDWY RQAPGKQREWVAQITRDSNSFYADSVKGRFAISR DNA KNTVYLQMNSLKPEDTAVYYCRVLSYWGQGTQVTVSS GGGSGGGSEVQLVESGGGLVQPGNSLRLS CAASGFT FSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYADSVK GRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSL SVSSQGT LVTVSSGGGSGGGSEVQLVESGGGLVQPG GSLKLS CAASGFTFNKYAINWVRQAPGKGLEWVARIR SKYNNYATYYADQVKDRFTISRDDSKNTAYLQMN NLK TEDTAVYYCVRHANFGNSYISYWAYWGQGT LVTVSSG GGGSGGGSGGGSGQT VVTQEP SLTVSPGGT VTLTCA SSTGAVTSGNYPNWVQQKPGQAPRGLIGG TKFLVP GT PARFSGSLLGGKAAL TL SGVQPEDEAEYYCTLWYSNR WVFGGGTKLTVLHHHHHH
199	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL125	QVQLQESGGGLVQAGGSLRLS CAASGSTFSRNYIDWY RQAPGKQREWVAQITSGGNTHYEPSLKGRTISR DNA KNTAYLQMNSLKPEDTAVYYCRILDYWGQGTQVTVSS GGGSGGGSEVQLVESGGGLVQPGNSLRLS CAASGFT FSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYADSVK GRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSL SVSSQGT LVTVSSGGGSGGGSEVQLVESGGGLVQPG GSLKLS CAASGFTFNKYAINWVRQAPGKGLEWVARIR SKYNNYATYYADQVKDRFTISRDDSKNTAYLQMN NLK TEDTAVYYCVRHANFGNSYISYWAYWGQGT LVTVSSG GGGSGGGSGGGSGQT VVTQEP SLTVSPGGT VTLTCA SSTGAVTSGNYPNWVQQKPGQAPRGLIGG TKFLVP GT PARFSGSLLGGKAAL TL SGVQPEDEAEYYCTLWYSNR WVFGGGTKLTVLHHHHHH
200	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL129	QVQLQESGGGLVQAGGSLRLS CAASGVTFSASYIDWY RQAPGNEREWVAQITRGDSFYADSVKGRFAISR DNA KNTVYLQMNSLKPEDTAVYYCRVLSYWGQGTQVTVSS GGGSGGGSEVQLVESGGGLVQPGNSLRLS CAASGFT FSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYADSVK GRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSL SVSSQGT LVTVSSGGGSGGGSEVQLVESGGGLVQPG GSLKLS CAASGFTFNKYAINWVRQAPGKGLEWVARIR SKYNNYATYYADQVKDRFTISRDDSKNTAYLQMN NLK TEDTAVYYCVRHANFGNSYISYWAYWGQGT LVTVSSG GGGSGGGSGGGSGQT VVTQEP SLTVSPGGT VTLTCA SSTGAVTSGNYPNWVQQKPGQAPRGLIGG TKFLVP GT PARFSGSLLGGKAAL TL SGVQPEDEAEYYCTLWYSNR WVFGGGTKLTVLHHHHHH
201	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL137	QVQLQESGGGLVQAGGSLRLS CAASGSTFNNYAMDWF RQAPGKQREWVAQITRDS SFYADSVKGRFAISR DNA KNTVYLQMNSLKPEDTAVYYCRVLSYWGQGTQVTVSS

			GGGSGGGSEVQLVESGGGLVQPGNSLRSLSCAASGFT FSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYADSVK GRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSL SVSSQGTTLVTVSSGGGSGGGSEVQLVESGGGLVQPG GSLKLSAASGFTFNKYAINWVRQAPGKGLEWVARIR SKYNNYATYYADQVKDRFTISRDDSKNTAYLQMNNLK TEDTAVYYCVRHANFGNSYISYWAYWGQGTTLTVSSG GGGSGGGSGGGGSQTVVTQEPSTLTVSPGGTVTLTCA SSTGAVTSGNYPNWVQQKPGQAPRGLIGGTFKFLVPGT PARFSGSLGGAALTLGSGVQPEDEAEYYCTLWYSNR WVFGGGTKLTVLHHHHHH
202	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL14	QVQLQESGGGLVQAGGSLRLSCAASGVTFSINYIDWY RQAPGKQREWVAQITRDSNSFYADSVKGRFAISRDN KNTVYLQMNSLRPEDTAVYYCRLLSYWGQGTQVTVSS GGGSGGGSEVQLVESGGGLVQPGNSLRSLSCAASGFT FSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYADSVK GRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSL SVSSQGTTLVTVSSGGGSGGGSEVQLVESGGGLVQPG GSLKLSAASGFTFNKYAINWVRQAPGKGLEWVARIR SKYNNYATYYADQVKDRFTISRDDSKNTAYLQMNNLK TEDTAVYYCVRHANFGNSYISYWAYWGQGTTLTVSSG GGGSGGGSGGGGSQTVVTQEPSTLTVSPGGTVTLTCA SSTGAVTSGNYPNWVQQKPGQAPRGLIGGTFKFLVPGT PARFSGSLGGAALTLGSGVQPEDEAEYYCTLWYSNR WVFGGGTKLTVLHHHHHH
203	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL146	QVQLQESGGGLVQAGGSLRLSCAASGVTFSINYIDWY RQAPGKQREWVAQITRDDTSFYADSVKGRFAISRDN KNTVYLQMNSLRPEDTAVYYCRLLSFWGQGTQVTVSS GGGSGGGSEVQLVESGGGLVQPGNSLRSLSCAASGFT FSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYADSVK GRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSL SVSSQGTTLVTVSSGGGSGGGSEVQLVESGGGLVQPG GSLKLSAASGFTFNKYAINWVRQAPGKGLEWVARIR SKYNNYATYYADQVKDRFTISRDDSKNTAYLQMNNLK TEDTAVYYCVRHANFGNSYISYWAYWGQGTTLTVSSG GGGSGGGSGGGGSQTVVTQEPSTLTVSPGGTVTLTCA SSTGAVTSGNYPNWVQQKPGQAPRGLIGGTFKFLVPGT PARFSGSLGGAALTLGSGVQPEDEAEYYCTLWYSNR WVFGGGTKLTVLHHHHHH
204	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL158	QVQLQESGGGLVQPGGSLRLSCAASGSTFGRNYIDWY RQAPGKQREWVAQITSGGNTHYEPSTLGRFTISRDN KNTAYLQMNSLRPEDTAVYYCRILDYWGQGTQVTVSS GGGSGGGSEVQLVESGGGLVQPGNSLRSLSCAASGFT FSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYADSVK GRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSL SVSSQGTTLVTVSSGGGSGGGSEVQLVESGGGLVQPG GSLKLSAASGFTFNKYAINWVRQAPGKGLEWVARIR SKYNNYATYYADQVKDRFTISRDDSKNTAYLQMNNLK TEDTAVYYCVRHANFGNSYISYWAYWGQGTTLTVSSG GGGSGGGSGGGGSQTVVTQEPSTLTVSPGGTVTLTCA SSTGAVTSGNYPNWVQQKPGQAPRGLIGGTFKFLVPGT PARFSGSLGGAALTLGSGVQPEDEAEYYCTLWYSNR WVFGGGTKLTVLHHHHHH
205	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL179	QVQLQESGGGLVQAGGSLRLSCKASGVTFSINYIDWY RQAPGKQREWVAQITRDGSSFYADSVKGRFAISRDN KNTVYLQMNSLRPEDTAVYYCRILSDWGQGTQVTVSS GGGSGGGSEVQLVESGGGLVQPGNSLRSLSCAASGFT FSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYADSVK GRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSL SVSSQGTTLVTVSSGGGSGGGSEVQLVESGGGLVQPG GSLKLSAASGFTFNKYAINWVRQAPGKGLEWVARIR SKYNNYATYYADQVKDRFTISRDDSKNTAYLQMNNLK TEDTAVYYCVRHANFGNSYISYWAYWGQGTTLTVSSG

			GGGSGGGSGGGSGQTVVTTQEPSTVSPGGTVTLTCA SSTGAVTSGNYPNWVQQKPGQAPRGLIGGTFKFLVPGT PARFSGSLLGGKAALTLSGVQPEDEAEYYCTLWYSNR WVFGGGTKLTVLHHHHHH
206	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL181	QVQLQESGGGLVQAGDSRLRLSCAASGVTFSSASYIDWY RQAPGNEREWVAQITRGDSFYADSVKGRFAISRDN KNTVYLQMNSLKPEDTAVYYCRVLSYWGQGTQVTVSS GGGSGGGSEVQLVESGGGLVQPGNSRLRLSCAASGFT FSKFGMSWVRQAPGKLEWVSSISGSGRDTLYADSVK GRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSL SVSSQGTTLVTVSSGGGSGGGSEVQLVESGGGLVQPG GSLKLSCAASGFTFNKYAINWVRQAPGKLEWVARIR SKYNNYATYYADQVKDRFTISRDDSKNTAYLQMNNLK TEDTAVYYCVRHANFGNSYISYWAYWGQGTTLTVSSG GGGSGGGSGGGSGQTVVTTQEPSTVSPGGTVTLTCA SSTGAVTSGNYPNWVQQKPGQAPRGLIGGTFKFLVPGT PARFSGSLLGGKAALTLSGVQPEDEAEYYCTLWYSNR WVFGGGTKLTVLHHHHHH
207	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL187	QVQLQESGGGLVQPGGSLRLSCAASGVTFSSINIDWY RQAPGKQREWVAQITRDSNSFYADSVKGRFAISRDN KNTVYLQMNSLKPEDTAVYYCRVLSYWGQGTQVTVSS GGGSGGGSEVQLVESGGGLVQPGNSRLRLSCAASGFT FSKFGMSWVRQAPGKLEWVSSISGSGRDTLYADSVK GRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSL SVSSQGTTLVTVSSGGGSGGGSEVQLVESGGGLVQPG GSLKLSCAASGFTFNKYAINWVRQAPGKLEWVARIR SKYNNYATYYADQVKDRFTISRDDSKNTAYLQMNNLK TEDTAVYYCVRHANFGNSYISYWAYWGQGTTLTVSSG GGGSGGGSGGGSGQTVVTTQEPSTVSPGGTVTLTCA SSTGAVTSGNYPNWVQQKPGQAPRGLIGGTFKFLVPGT PARFSGSLLGGKAALTLSGVQPEDEAEYYCTLWYSNR WVFGGGTKLTVLHHHHHH
208	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL32	QVQLQESGGGLVQAGGSLRLSCQASGVTFNINIDWY RQAPGRQREWVAQITRDSTRFYADSVKGRFAISRDN KNMVYLQNLNLPEDTAVYYCRILSYWGQGTQVTVSS GGGSGGGSEVQLVESGGGLVQPGNSRLRLSCAASGFT FSKFGMSWVRQAPGKLEWVSSISGSGRDTLYADSVK GRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSL SVSSQGTTLVTVSSGGGSGGGSEVQLVESGGGLVQPG GSLKLSCAASGFTFNKYAINWVRQAPGKLEWVARIR SKYNNYATYYADQVKDRFTISRDDSKNTAYLQMNNLK TEDTAVYYCVRHANFGNSYISYWAYWGQGTTLTVSSG GGGSGGGSGGGSGQTVVTTQEPSTVSPGGTVTLTCA SSTGAVTSGNYPNWVQQKPGQAPRGLIGGTFKFLVPGT PARFSGSLLGGKAALTLSGVQPEDEAEYYCTLWYSNR WVFGGGTKLTVLHHHHHH
209	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL51	QVQLQESGGGLVQPGGSLRLSCAASGFDFSSISYIDWY RQAPGNEREWVAQITRGDSFYADSVKGRFAISRDN KNTVYLQMNSLKPEDTAVYYCRILSYWGQGTQVTVSS GGGSGGGSEVQLVESGGGLVQPGNSRLRLSCAASGFT FSKFGMSWVRQAPGKLEWVSSISGSGRDTLYADSVK GRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSL SVSSQGTTLVTVSSGGGSGGGSEVQLVESGGGLVQPG GSLKLSCAASGFTFNKYAINWVRQAPGKLEWVARIR SKYNNYATYYADQVKDRFTISRDDSKNTAYLQMNNLK TEDTAVYYCVRHANFGNSYISYWAYWGQGTTLTVSSG GGGSGGGSGGGSGQTVVTTQEPSTVSPGGTVTLTCA SSTGAVTSGNYPNWVQQKPGQAPRGLIGGTFKFLVPGT PARFSGSLLGGKAALTLSGVQPEDEAEYYCTLWYSNR WVFGGGTKLTVLHHHHHH
210	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL55	QVQLQESGGGLVQAGGSLRLSCAASGSTFSRNYIDWY RQAPGKQREWVAQITSAGNTHYEPFLKGRFTISRDN KNTAYLQMNSLKPEDTAVYYCRILDYWGQGTQVTVSS

			GGGSGGGSEVQLVESGGGLVQPGNSLRSLSCAASGFT FSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYADSVK GRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSL SVSSQGTSLVTVSSGGGSGGGSEVQLVESGGGLVQPG GSLKLSAASGFTFNKYAINWVRQAPGKGLEWVARIR SKYNNYATYYADQVKDRFTISRDDSKNTAYLQMNNLK TEDTAVYYCVRHANFGNSYISYWAYWGQGTSLVTVSSG GGGSGGGSGGGGSQTVVTQEPSTVSPGGTVTLTCA SSTGAVTSGNYPNWVQQKPGQAPRGLIGGTFKFLVPGT PARFSGSLLGGKAALTLSGVQPEDEAEYYCTLWYSNR WVFGGGTKLTVLHHHHHH
211	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL77	QVQLQESGGGLVQPGGSLRLSCAASGVTFSISYIDWY RQAPGNEREWVAQITRGGDSFYADSVKGRFAISRDN KNTVYLQMNSLRKPEDTAVYYCRILSYWGQGTQVTVSS GGGSGGGSEVQLVESGGGLVQPGNSLRSLSCAASGFT FSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYADSVK GRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSL SVSSQGTSLVTVSSGGGSGGGSEVQLVESGGGLVQPG GSLKLSAASGFTFNKYAINWVRQAPGKGLEWVARIR SKYNNYATYYADQVKDRFTISRDDSKNTAYLQMNNLK TEDTAVYYCVRHANFGNSYISYWAYWGQGTSLVTVSSG GGGSGGGSGGGGSQTVVTQEPSTVSPGGTVTLTCA SSTGAVTSGNYPNWVQQKPGQAPRGLIGGTFKFLVPGT PARFSGSLLGGKAALTLSGVQPEDEAEYYCTLWYSNR WVFGGGTKLTVLHHHHHH
212	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL97	QVQLQESGGGLVQAGGSLRLSCAASGVTFSINYIDWY RQAPGKQREWVAQITRDSNSFYADSVKGRFAVSRDN KNTVYLQMNSLRKPEDTAVYYCRVLSYWGQGTQVTVSS GGGSGGGSEVQLVESGGGLVQPGNSLRSLSCAASGFT FSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYADSVK GRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSL SVSSQGTSLVTVSSGGGSGGGSEVQLVESGGGLVQPG GSLKLSAASGFTFNKYAINWVRQAPGKGLEWVARIR SKYNNYATYYADQVKDRFTISRDDSKNTAYLQMNNLK TEDTAVYYCVRHANFGNSYISYWAYWGQGTSLVTVSSG GGGSGGGSGGGGSQTVVTQEPSTVSPGGTVTLTCA SSTGAVTSGNYPNWVQQKPGQAPRGLIGGTFKFLVPGT PARFSGSLLGGKAALTLSGVQPEDEAEYYCTLWYSNR WVFGGGTKLTVLHHHHHH
213	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL21	QVQLQESGGGLVQPGGSLTLSCAASGSTFSRNYIDWY RQAPGKQREWVAQITSGGNTHYEPSTLGRFTISRDN KNTAYLQMNSLRKPEDTAVYYCRILDYWGQGTQVTVSS GGGSGGGSEVQLVESGGGLVQPGNSLRSLSCAASGFT FSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYADSVK GRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSL SVSSQGTSLVTVSSGGGSGGGSEVQLVESGGGLVQPG GSLKLSAASGFTFNKYAINWVRQAPGKGLEWVARIR SKYNNYATYYADQVKDRFTISRDDSKNTAYLQMNNLK TEDTAVYYCVRHANFGNSYISYWAYWGQGTSLVTVSSG GGGSGGGSGGGGSQTVVTQEPSTVSPGGTVTLTCA SSTGAVTSGNYPNWVQQKPGQAPRGLIGGTFKFLVPGT PARFSGSLLGGKAALTLSGVQPEDEAEYYCTLWYSNR WVFGGGTKLTVLHHHHHH
214	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL57	QVQLQESGGGLVQAGGSLRLSCAASGSTFSKNYIDWY RQAPGKQREWVAQITSGGNTHYEPSTLGRFTISRDN KNTAYLQMNSLRKPEDTAVYYCRILDYWGQGTQVTVSS GGGSGGGSEVQLVESGGGLVQPGNSLRSLSCAASGFT FSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYADSVK GRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSL SVSSQGTSLVTVSSGGGSGGGSEVQLVESGGGLVQPG GSLKLSAASGFTFNKYAINWVRQAPGKGLEWVARIR SKYNNYATYYADQVKDRFTISRDDSKNTAYLQMNNLK TEDTAVYYCVRHANFGNSYISYWAYWGQGTSLVTVSSG

			GGGSGGGSGGGGSQTVVTQEPSTVSPGGTVTLTCA SSTGAVTSGNYPNWVQQKPGQAPRGLIGGTFKFLVPGT PARFSGSLLGGKAALTLSGVQPEDEAEYYCTLWYSNR WVFGGGTKLTVLHHHHHH
215	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL62	QVQLQESGGGLVQAGGSLRLSCAASGSTSSRNYIDWY RQAPGKQREWVAQITSGGNTHYEPSTLKGRTISRDN KNTAYLQMNSLKPEDTAVYYCRILDYWGQGTQVTVSS GGGSGGGSEVQLVESGGGLVQPGNSRLSCAASGFT FSKFGMSWVRQAPGKLEWVSSISGSGRDTLYADSVK GRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSL SVSSQGT LVTVSSGGGSGGGSEVQLVESGGGLVQPG GSLKLSCAASGFTFNKYAINWVRQAPGKLEWVARIR SKYNNYATYYADQVKDRFTISRDDSKNTAYLQMNNLK TEDTAVYYCVRHANFGNSYISYWAYWGQGT LVTVSSG GGGSGGGSGGGGSQTVVTQEPSTVSPGGTVTLTCA SSTGAVTSGNYPNWVQQKPGQAPRGLIGGTFKFLVPGT PARFSGSLLGGKAALTLSGVQPEDEAEYYCTLWYSNR WVFGGGTKLTVLHHHHHH
216	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL79	QVQLQESGGGLVQAGGSLRLSCASGSTFSRNYIDWY RQAPGKQREWVAQITSGGNTHYEPSTLKGRTISRDN KNTAYLQMNSLKPEDTAVYYCRILDYWGQGTQVTVSS GGGSGGGSEVQLVESGGGLVQPGNSRLSCAASGFT FSKFGMSWVRQAPGKLEWVSSISGSGRDTLYADSVK GRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSL SVSSQGT LVTVSSGGGSGGGSEVQLVESGGGLVQPG GSLKLSCAASGFTFNKYAINWVRQAPGKLEWVARIR SKYNNYATYYADQVKDRFTISRDDSKNTAYLQMNNLK TEDTAVYYCVRHANFGNSYISYWAYWGQGT LVTVSSG GGGSGGGSGGGGSQTVVTQEPSTVSPGGTVTLTCA SSTGAVTSGNYPNWVQQKPGQAPRGLIGGTFKFLVPGT PARFSGSLLGGKAALTLSGVQPEDEAEYYCTLWYSNR WVFGGGTKLTVLHHHHHH
217	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL86	QVQLQESGGGLVQPGDPLRLSCAASGSTFSRNYIDWY RQAPGKQREWVAQITSGGNTHYEPSTLKGRTISRDN KNTAYLQMNSLKPEDTAVYYCRILDYWGQGTQVTVSS GGGSGGGSEVQLVESGGGLVQPGNSRLSCAASGFT FSKFGMSWVRQAPGKLEWVSSISGSGRDTLYADSVK GRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSL SVSSQGT LVTVSSGGGSGGGSEVQLVESGGGLVQPG GSLKLSCAASGFTFNKYAINWVRQAPGKLEWVARIR SKYNNYATYYADQVKDRFTISRDDSKNTAYLQMNNLK TEDTAVYYCVRHANFGNSYISYWAYWGQGT LVTVSSG GGGSGGGSGGGGSQTVVTQEPSTVSPGGTVTLTCA SSTGAVTSGNYPNWVQQKPGQAPRGLIGGTFKFLVPGT PARFSGSLLGGKAALTLSGVQPEDEAEYYCTLWYSNR WVFGGGTKLTVLHHHHHH
218	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL112	QVQLQESGGGLVQAGGSLRLSCAVSGRTFSGFGTGWF RQAPGKEREFAAISWAGGRTHYEDSVKGRFTIHRDN AKNTVYLQMNSLKPEDTAVYYCAAQVSRAYDGIWYSG GDYWGQGTQVTVSSGGGSGGGSEVQLVESGGGLVQPG NSRLSCAASGFTFSKFGMSWVRQAPGKLEWVSSI SGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNSLRP EDTAVYYCTIGGSLSVSSQGT LVTVSSGGGSGGGSE VQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINWVR QAPGKLEWVARIRSKYNNYATYYADQVKDRFTISR DSKNTAYLQMNNLKTEDTAVYYCVRHANFGNSYISY AYWGQGT LVTVSSGGGSGGGSGGGGSQTVVTQEP STVSPGGTVTLTCASTGAVTSGNYPNWVQQKPGQAP RGLIGGTFKFLVPGTPARFSGSLLGGKAALTLSGVQPE DEAEYYCTLWYSNRWVFGGGTKLTVLHHHHHH
219	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL142	QVQLQESGGGLVQAGGSLRLSCAVSGRTFSGFGTGWF RQAPGKEREFAAISWDGGRTHYADFVKGRFTISRDN AKNTVYLQMNSLKPEDTAVYYCAAQVARAYDSKWYSG

			GDYWGQGTQVTVSSGGGGSGGGSEVQLVESGGGLVQPGNSLRRLSCAASGFTFSKFGMSWVRQAPGKLEWVSSISGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTTLTVTVSSGGGGSGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINWVRQAPGKLEWVARIRSKYNNYATYYADQVKDRFTISRDSKNTAYLQMNNLKTEDTAVYYCVRHANFGNSYISYWYWGQGTTLTVTVSSGGGGSGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCASSTGAVTSGNYPNWVQQKPGQAPRGLIGGTKFLVPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCTLWYSNRWVFGGGTKLTVLHHHHHH
220	anti-FLT3/anti-HSA/anti-CD3 fusion protein	FLL143	QVQLQESGGGLVQAGGSLRLSCAVSGRTFSGFGTGWRQAPGKEREFAAISWVGGRTHYADSVKGRFTISRDN AKNTVYLQMNSLKPEDTAVYYCAAQVARAYDGNWYSGDYWGQGTQVTVSSGGGGSGGGSEVQLVESGGGLVQPGNSLRRLSCAASGFTFSKFGMSWVRQAPGKLEWVSSISGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTTLTVTVSSGGGGSGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINWVRQAPGKLEWVARIRSKYNNYATYYADQVKDRFTISRDSKNTAYLQMNNLKTEDTAVYYCVRHANFGNSYISYWYWGQGTTLTVTVSSGGGGSGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCASSTGAVTSGNYPNWVQQKPGQAPRGLIGGTKFLVPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCTLWYSNRWVFGGGTKLTVLHHHHHH
221	anti-FLT3/anti-HSA/anti-CD3 fusion protein	FLL154	QVQLQESGGGLVQAGGSLRLSCAVSGRTFSGFGTGWRQAPGKEREFAAISWVGGRTHYADSVKGRFTISRDN AKNTVYLQMNSLKPEDTAVYYCAGQVARAYDGNWYSRGDYWGQGTQVTVSSGGGGSGGGSEVQLVESGGGLVQPGNSLRRLSCAASGFTFSKFGMSWVRQAPGKLEWVSSISGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTTLTVTVSSGGGGSGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINWVRQAPGKLEWVARIRSKYNNYATYYADQVKDRFTISRDSKNTAYLQMNNLKTEDTAVYYCVRHANFGNSYISYWYWGQGTTLTVTVSSGGGGSGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCASSTGAVTSGNYPNWVQQKPGQAPRGLIGGTKFLVPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCTLWYSNRWVFGGGTKLTVLHHHHHH
222	anti-FLT3/anti-HSA/anti-CD3 fusion protein	FLL168	QVQLQESGGGSVQAGGSLRLSCAFSGRTFSGFGTGWRQAPEKEREFAAISWDGGRTHYADSVKGRFTISRDN AKNTVYLQMDSLKPEDTAIYYCAAQVSRAYDGRWYSAVDYWGRTQVTVSSGGGGSGGGSEVQLVESGGGLVQPGNSLRRLSCAASGFTFSKFGMSWVRQAPGKLEWVSSISGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTTLTVTVSSGGGGSGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINWVRQAPGKLEWVARIRSKYNNYATYYADQVKDRFTISRDSKNTAYLQMNNLKTEDTAVYYCVRHANFGNSYISYWYWGQGTTLTVTVSSGGGGSGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCASSTGAVTSGNYPNWVQQKPGQAPRGLIGGTKFLVPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCTLWYSNRWVFGGGTKLTVLHHHHHH
223	anti-FLT3/anti-HSA/anti-CD3 fusion protein	FLL170	QVQLQESGGGLVQAGGSLRLSCAVSGRTFSGFGTGWRQAPGKEREFAAISWVGGRTHYADSVKGRFTISRDN AKNTVYLQMNSLKPEDTAVYYCAGQVARAYDSSWYSRGDYWGQGTQVTVSSGGGGSGGGSEVQLVESGGGLVQPGNSLRRLSCAASGFTFSKFGMSWVRQAPGKLEWVSSISGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTTLTVTVSSGGGGSGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINWVRQAPGKLEWVARIRSKYNNYATYYADQVKDRFTISRDSKNTAYLQMNNLKTEDTAVYYCVRHANFGNSYISYW

			AYWGQGTTLVTVSSGGGGSGGGSGGGGSQTVVTQEPS LTVSPGGTVTLTCASSTGAVTSGNYPNWWQQKPGQAP RGLIGGTKFLVPGTPARFSGSLLGGKAALTLSGVQPE DEAEYYCTLWYSNRWVFGGGTKLTVLHHHHHH
224	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL188	QVQLQESGGGLVQAGGSLGLSCAVSGRTFSFGFTGWF RQPPEKEREFEVAAISWDGGRTHYADSVKGRFTISRDN AKNTVFLQMNSLKPEDTAVYYCAAQVARAYDSRWYSG GDYWGQGTQVTVSSGGGGSGGGSEVQLVESGGGLVQP GNSLRSLSCAASGFTFSKFGMSWVRQAPGKLEWVSSI SGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNSLRP EDTAVYYCTIGGSLSVSSQGTTLVTVSSGGGGSGGGSE VQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINWVR QAPGKLEWVARIRSKYNNYATYYADQVKDRFTISR DSKNTAYLQMNSLKPEDTAVYYCVRHANFGNSYISYW AYWGQGTTLVTVSSGGGGSGGGSGGGGSQTVVTQEPS LTVSPGGTVTLTCASSTGAVTSGNYPNWWQQKPGQAP RGLIGGTKFLVPGTPARFSGSLLGGKAALTLSGVQPE DEAEYYCTLWYSNRWVFGGGTKLTVLHHHHHH
225	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL40	QVQLQESGGGLVQAGGSLRLSCAVSGRTFSFGFTGWF RQAPGKEREFEVAAISWGGTTHYADSVKGRFTISRDN AKNTVSLVYLQMNSLKPDDTAVYYCAGQVARAYDSSW YSRGDYLQGGTQVTVSSGGGGSGGGSEVQLVESGGGL VQPGNSLRSLSCAASGFTFSKFGMSWVRQAPGKLEWV SSISGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNS LRPEDTAVYYCTIGGSLSVSSQGTTLVTVSSGGGGSGG GSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAIN WVRQAPGKLEWVARIRSKYNNYATYYADQVKDRFTI SRDSSKNTAYLQMNSLKPEDTAVYYCVRHANFGNSYI SYWAYWGQGTTLVTVSSGGGGSGGGSGGGGSQTVVTQ EPSTLTVSPGGTVTLTCASSTGAVTSGNYPNWWQQKPG QAPRGLIGGTKFLVPGTPARFSGSLLGGKAALTLSGV QPEDEAEYYCTLWYSNRWVFGGGTKLTVLHHHHHH
226	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL6	QVQLQESGGGLVQAGGSLRLSCAVSGRTFSFGFTGWF RQAPGKEREFEVAAISWDGGRTHYADSVKGRFTISRDN AANTVYLQMNSLKPEDTAVYYCAGQVSRAYDSMWYGR DDYWGQGTQVTVSSGGGGSGGGSEVQLVESGGGLVQP GNSLRSLSCAASGFTFSKFGMSWVRQAPGKLEWVSSI SGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNSLRP EDTAVYYCTIGGSLSVSSQGTTLVTVSSGGGGSGGGSE VQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINWVR QAPGKLEWVARIRSKYNNYATYYADQVKDRFTISR DSKNTAYLQMNSLKPEDTAVYYCVRHANFGNSYISYW AYWGQGTTLVTVSSGGGGSGGGSGGGGSQTVVTQEPS LTVSPGGTVTLTCASSTGAVTSGNYPNWWQQKPGQAP RGLIGGTKFLVPGTPARFSGSLLGGKAALTLSGVQPE DEAEYYCTLWYSNRWVFGGGTKLTVLHHHHHH
227	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL75	QVQLQESGGGLVQAGGSLRLSCAVSGRTFSFGFTGWF RQAPGKEREFEVAAISWGGTTHYADSVKGRFTISRDN AKNTVNLVYLQMNDLRPEDTAVYYCAGQVARAYDSNW YSRGDYWGQGTQVTVSSGGGGSGGGSEVQLVESGGGL VQPGNSLRSLSCAASGFTFSKFGMSWVRQAPGKLEWV SSISGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNS LRPEDTAVYYCTIGGSLSVSSQGTTLVTVSSGGGGSGG GSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAIN WVRQAPGKLEWVARIRSKYNNYATYYADQVKDRFTI SRDSSKNTAYLQMNSLKPEDTAVYYCVRHANFGNSYI SYWAYWGQGTTLVTVSSGGGGSGGGSGGGGSQTVVTQ EPSTLTVSPGGTVTLTCASSTGAVTSGNYPNWWQQKPG QAPRGLIGGTKFLVPGTPARFSGSLLGGKAALTLSGV QPEDEAEYYCTLWYSNRWVFGGGTKLTVLHHHHHH
228	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL83	QVQLQESGGGLVQAGGSLRLSCAVSGRTFSFGFTGWF RQAPGKEREFEVAAISWGGTTHYADSVKGRFTISRDN AENTVYLEMNSLKPEDTAVYICAGQVSRAYDSNWYSR

			DDYWQGTQVTVSSGGGGSGGGSEVQLVESGGGLVQPGNSLRRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTTLTVTVSSGGGGSGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINWVRQAPGKGLEWVARIRSKYNNYATYYADQVKDRFTISRDSKNTAYLQMNNLKTEDTAVYYCVRHANFGNSYISYWYWGQGTTLTVTVSSGGGGSGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCASSTGAVTSGNYPNWVQKPGQAPRGLIGGTKFLVPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCTLWYSNRWVFGGKTCLTVLHHHHHH
229	anti-FLT3/anti-HSA/anti-CD3 fusion protein	FLL94	QVQLQESGGGLVQAGGSLRLSCAVSGRTFSGFGTGWRQAPEKEREFEVAAISWDGGRTHYADSVKGRFTISRDN AKNTVYLQMNSLKPEDTAIYYCAGQVARAYDTRWYSR GDYWGQGTQVTVSSGGGGSGGGSEVQLVESGGGLVQPGNSLRRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTTLTVTVSSGGGGSGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINWVRQAPGKGLEWVARIRSKYNNYATYYADQVKDRFTISRDSKNTAYLQMNNLKTEDTAVYYCVRHANFGNSYISYWYWGQGTTLTVTVSSGGGGSGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCASSTGAVTSGNYPNWVQKPGQAPRGLIGGTKFLVPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCTLWYSNRWVFGGKTCLTVLHHHHHH
230	anti-FLT3/anti-HSA/anti-CD3 fusion protein	FLL99	QVQLQESGGGLVQAGGSLRLSCAVSGRTFSGFGTGWRQAPGKEREFEVAAISWDGGRTHYADSVKGRFTISRDN AKNTVYLQMNSLKPEDTAVYYCAAQVARAYDSRWYSG GDYWGQGTQVTVSSGGGGSGGGSEVQLVESGGGLVQPGNSLRRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTTLTVTVSSGGGGSGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINWVRQAPGKGLEWVARIRSKYNNYATYYADQVKDRFTISRDSKNTAYLQMNNLKTEDTAVYYCVRHANFGNSYISYWYWGQGTTLTVTVSSGGGGSGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCASSTGAVTSGNYPNWVQKPGQAPRGLIGGTKFLVPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCTLWYSNRWVFGGKTCLTVLHHHHHH
231	anti-FLT3/anti-HSA/anti-CD3 fusion protein	FLL38	QVQLQESGGGLVQAGGSLRLSCAVSGRTFSGFGTGWRQAPGKEREFEVAAVSWSGGTTEIADSVKGRFTISRDN AKNTVYLQMSSSLKPGDTAVYYCAGQVARAYDSRWYSR GDYWGQGTQVTVSSGGGGSGGGSEVQLVESGGGLVQPGNSLRRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTTLTVTVSSGGGGSGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINWVRQAPGKGLEWVARIRSKYNNYATYYADQVKDRFTISRDSKNTAYLQMNNLKTEDTAVYYCVRHANFGNSYISYWYWGQGTTLTVTVSSGGGGSGGGSGGGGSQTVVTQEPSLTVSPGGTVTLTCASSTGAVTSGNYPNWVQKPGQAPRGLIGGTKFLVPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCTLWYSNRWVFGGKTCLTVLHHHHHH
232	anti-FLT3/anti-HSA/anti-CD3 fusion protein	FLL53	QVQLQESGGGLVQAGDSLRLSCAVSGRTFSGFGTGWRQAPGKEREFEVAAVSQSGGTTHYADSVKGRFTISRDN AKNTETLVYLQMNSLKPEDTAVYYCAGQVARAYDSSWYARGDYWGQGTQVTVSSGGGGSGGGSEVQLVESGGGLVQPGNSLRRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTTLTVTVSSGGGGSGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINWVRQAPGKGLEWVARIRSKYNNYATYYADQVKDRFTISRDDSNTAYLQMNNLKTEDTAVYYCVRHANFGNSYI

			SYWAYWGQGTTLTVTVSSGGGGSGGGSGGGGSQTVVTQ EPSLTVSPGGTVTLTCASSTGAVTSGNYPNWVQQKPG QAPRGLIGGTFKFLVPGTPARFSGSLGGKAAALTLSGV QPEDEAEYYCTLWYSNRWVFGGGTKLTVLHHHHHH
233	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL553	QVQLQESGGGLVQAGGSLRLSCAVSGRTFSGFGTGW RQAPGKEREFAAISWSGGTTHYADSVKGRFTISRDN AKNTVNLVYLQMNLSRPEDTAVYYCAGQVARAYDSNW YSRGDYWGQGTQVTVSSGGGGSGGGSEVQLVESGGGL VQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKLEWV SSISGSGRDTLYADSVKGRFTISRDNKTTLYLQMN LRPEDTAVYYCTIGGSLSVSSQGTTLTVTVSSGGGGSGG GSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAIN WVRQAPGKLEWVARIRSKYNNYATYYADQVKDRFTI SRDDSKNTAYLQMNLLKTEDTAVYYCVRHANFGNSYI SYWAYWGQGTTLTVTVSSGGGGSGGGSGGGGSQTVVTQ EPSLTVSPGGTVTLTCASSTGAVTSGNYPNWVQQKPG QAPRGLIGGTFKFLVPGTPARFSGSLGGKAAALTLSGV QPEDEAEYYCTLWYSNRWVFGGGTKLTVLHHHHHH
234	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL74	QVQLQESGGGLVQAGGSLRLSCRFSGRTFSGFGTGW RQAPGKEREFAAISWAGGRTHYEDSVKGRFTISRDN AKNTVYLQMNLSKPEDTAVYYCAVQVSRAYDGIWYSG GDYWGQGTQVTVSSGGGGSGGGSEVQLVESGGGLVQ GNSLRLSCAASGFTFSKFGMSWVRQAPGKLEWVSSI SGSGRDTLYADSVKGRFTISRDNKTTLYLQMNLSRP EDTAVYYCTIGGSLSVSSQGTTLTVTVSSGGGGSGGGSE VQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINWVR QAPGKLEWVARIRSKYNNYATYYADQVKDRFTISR DSKNTAYLQMNLLKTEDTAVYYCVRHANFGNSYISY AYWGQGTTLTVTVSSGGGGSGGGSGGGGSQTVVTQEP SLTVSPGGTVTLTCASSTGAVTSGNYPNWVQQKPGQAP RGLIGGTFKFLVPGTPARFSGSLGGKAAALTLSGVQPE DEAEYYCTLWYSNRWVFGGGTKLTVLHHHHHH
235	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL102	QVQLQESGGGLVQAGGSLMVSCAASGGTWSSYATGW RQVPGERKLIAGISRSGGRTYYAESVKGRFTISRDN AKNTVYLQMNLLKPDDETAVYYCAAARYFTSSVYTS NDYDYWGQGTQVTVSSGGGGSGGGSEVQLVESGGGLV QPGNSLRLSCAASGFTFSKFGMSWVRQAPGKLEWVS SISGSGRDTLYADSVKGRFTISRDNKTTLYLQMN RPEDTAVYYCTIGGSLSVSSQGTTLTVTVSSGGGGSGG SEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINW VRQAPGKLEWVARIRSKYNNYATYYADQVKDRFTI SRDDSKNTAYLQMNLLKTEDTAVYYCVRHANFGNSYI SYWAYWGQGTTLTVTVSSGGGGSGGGSGGGGSQTVVTQ EPSLTVSPGGTVTLTCASSTGAVTSGNYPNWVQQKPGQ APRGLIGGTFKFLVPGTPARFSGSLGGKAAALTLSGVQ PEDEAEYYCTLWYSNRWVFGGGTKLTVLHHHHHH
236	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL122	QVQLQESGGGLVQAGGSLMVSCAASGGTWSSYATGW RQVPGERELIAGISRSGGRTYYAESVKGRFTISRDN AKNTVYLQMNLLKPDDETAVYYCAAARYFTSSVYTS NDYDYWGQGTQVTVSSGGGGSGGGSEVQLVESGGGLV QPGNSLRLSCAASGFTFSKFGMSWVRQAPGKLEWVS SISGSGRDTLYADSVKGRFTISRDNKTTLYLQMN RPEDTAVYYCTIGGSLSVSSQGTTLTVTVSSGGGGSGG SEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINW VRQAPGKLEWVARIRSKYNNYATYYADQVKDRFTI SRDDSKNTAYLQMNLLKTEDTAVYYCVRHANFGNSYI SYWAYWGQGTTLTVTVSSGGGGSGGGSGGGGSQTVVTQ EPSLTVSPGGTVTLTCASSTGAVTSGNYPNWVQQKPGQ APRGLIGGTFKFLVPGTPARFSGSLGGKAAALTLSGVQ PEDEAEYYCTLWYSNRWVFGGGTKLTVLHHHHHH
237	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL134	QVQLQESGGGLVQPGGSLRLSCAASGGTFSSYATGW RQVPGEREFIAGISRSNGRTYYAESVKGRFTISRDN AKNTVYLQMNLLRPDDTAVYYCAAARYFTRDAIYTS GSD

			DYDYWGQGTQVTASSGGGGSGGGSEVQLVESGGGLVQPGNSLRSLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTTLVTVSSGGGGSGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINWVRQAPGKGLEWVARIRSKYNNYATYYADQVKDRFTISRDDS KNTAYLQMNNLKTEDTAVYYCVRHANFGNSYISYWAYWGQGTTLVTVSSGGGGSGGGSGGGGSQTVVTQEP SLTVSPGGTVTLTCASSTGAVTSGNYPNWVQQKPGQA PRGLIGGTKFLVPGTPARFSGSLGGKAALTLSGVQPEDEAEYYCTLWYSNRWVFGGGTKLTVLHHHHHH
238	anti-FLT3/anti-HSA/anti-CD3 fusion protein	FLL153	QVQLQESGGGLVQVGGSLMVSCAASGGTFSSYATGWF RQVPGEREFIAIGVSRNSGRTYAESVKGRFTISRDN AKNTVYLQMNNTLKPDDTGVIYCAAARYFTRDAVYTS GDDYDYWGQGTQVTVSSGGGGSGGGSEVQLVESGGGLV QPGNSLRSLSCAASGFTFSKFGMSWVRQAPGKGLEWVS SISGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNSLR PEDTAVYYCTIGGSLSVSSQGTTLVTVSSGGGGSGGG SEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINW VRQAPGKGLEWVARIRSKYNNYATYYADQVKDRFTISR DDS KNTAYLQMNNLKTEDTAVYYCVRHANFGNSYIS YWAYWGQGTTLVTVSSGGGGSGGGSGGGGSQTVVTQE PSLTVSPGGTVTLTCASSTGAVTSGNYPNWVQQKPGQ APRGLIGGTKFLVPGTPARFSGSLGGKAALTLSGVQ PEDEAEYYCTLWYSNRWVFGGGTKLTVLHHHHHH
239	anti-FLT3/anti-HSA/anti-CD3 fusion protein	FLL41	QVQLQESGGGLVQLGDSLMVSCAASGGTFSSYATGWF RQVPGREFIAGISRSGGRTYYAESVKGRFTISRDN AKNTVYLQMNNTLKPDDTAVYYCAAARYFTTSVYTS GDDYDYWGQGTQVTVSSGGGGSGGGSEVQLVESGGGLV QPGNSLRSLSCAASGFTFSKFGMSWVRQAPGKGLEWVS SISGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNSLR PEDTAVYYCTIGGSLSVSSQGTTLVTVSSGGGGSGGG SEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINW VRQAPGKGLEWVARIRSKYNNYATYYADQVKDRFTISR DDS KNTAYLQMNNLKTEDTAVYYCVRHANFGNSYIS YWAYWGQGTTLVTVSSGGGGSGGGSGGGGSQTVVTQE PSLTVSPGGTVTLTCASSTGAVTSGNYPNWVQQKPGQ APRGLIGGTKFLVPGTPARFSGSLGGKAALTLSGVQ PEDEAEYYCTLWYSNRWVFGGGTKLTVLHHHHHH
240	anti-FLT3/anti-HSA/anti-CD3 fusion protein	FLL67	QVQLQESGGGLVQLGDSLMVSCAASGGTFSSYATGWF RQVPGEREFIAIGISRSGGRTYYAESVKGRFTISRDN AKNTVYLQMNNTLKPDDTAVYYCAAARYFTTSVYTS GDDYDYWGQGTQVTVSSGGGGSGGGSEVQLVESGGGLV QPGNSLRSLSCAASGFTFSKFGMSWVRQAPGKGLEWVS SISGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNSLR PEDTAVYYCTIGGSLSVSSQGTTLVTVSSGGGGSGGG SEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINW VRQAPGKGLEWVARIRSKYNNYATYYADQVKDRFTISR DDS KNTAYLQMNNLKTEDTAVYYCVRHANFGNSYIS YWAYWGQGTTLVTVSSGGGGSGGGSGGGGSQTVVTQE PSLTVSPGGTVTLTCASSTGAVTSGNYPNWVQQKPGQ APRGLIGGTKFLVPGTPARFSGSLGGKAALTLSGVQ PEDEAEYYCTLWYSNRWVFGGGTKLTVLHHHHHH
241	anti-FLT3/anti-HSA/anti-CD3 fusion protein	FLL92	QVQLQESGGGLVQAGSLMVSCAASGGTWSSYATGWF RQVPGERELIAGISRSGGRTYYAESVKGRFTISRDN AKNTVYLQMNNTLKSDDTAVYYCAAARYFTSSVYTS GNDYDYWGQGTQVTVSSGGGGSGGGSEVQLVESGGGLV QPGNSLRSLSCAASGFTFSKFGMSWVRQAPGKGLEWVS SISGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNSLR PEDTAVYYCTIGGSLSVSSQGTTLVTVSSGGGGSGGG SEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINW VRQAPGKGLEWVARIRSKYNNYATYYADQVKDRFTISR DDS KNTAYLQMNNLKTEDTAVYYCVRHANFGNSYIS

			YWAYWGQGTTLTVSSGGGSGGGGSGGGGSGTQVVTQE PSLTVSPGGTVTLTCASSTGAVTSGNYPNWVQQKPGQ APRGLIGGTKFLVPGTPARFSGSLLGGKAALTLSGVQ PEDEAEYYCTLWYSNRWVFGGGTKLTVLHHHHHH
243	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL71	QVQLQESGGGLVQVGGSLMVSCAASGGTFSSYATGWF RQVPGEREFIAGISRNSGRYYAESVKGRFTISRDN AKNTVYLQMNLTLPDDTAVYYCAAARYFTRDAVYTS DDYDYGQGTQVTVSSGGGSGGGSEVQLVESGGGLV QPGNSLRSLCAASGFTFSKFGMSWVRQAPGKLEWVS SISGSGRDTLYADSVKGRFTISRDNAKTTLYLQMN SLRPEDTAVYYCTIGGSLSVSSQGTTLTVSSGGGSGGG SEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINW VRQAPGKLEWVARIRSKYNNYATYYADQVKDRFTIS RDDSKNTAYLQMNLTEDTAVYYCVRHANFGNSYIS YWAYWGQGTTLTVSSGGGSGGGGSGGGGSGTQVVTQE PSLTVSPGGTVTLTCASSTGAVTSGNYPNWVQQKPGQ APRGLIGGTKFLVPGTPARFSGSLLGGKAALTLSGVQ PEDEAEYYCTLWYSNRWVFGGGTKLTVLHHHHHH
244	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL8	QVQLQESGGGLVQVGGSLMVSCAASGGTFSSYATGWF RQVPGEREFIAGISRNSGRYYAESVKGRFTISRDN AKNTVYLQMNLTLPDDTAVYYCAAARYFTRDVVYTS DDYDYGQGTQVTVSSGGGSGGGSEVQLVESGGGLV QPGNSLRSLCAASGFTFSKFGMSWVRQAPGKLEWVS SISGSGRDTLYADSVKGRFTISRDNAKTTLYLQMN SLRPEDTAVYYCTIGGSLSVSSQGTTLTVSSGGGSGGG SEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINW VRQAPGKLEWVARIRSKYNNYATYYADQVKDRFTIS RDDSKNTAYLQMNLTEDTAVYYCVRHANFGNSYIS YWAYWGQGTTLTVSSGGGSGGGGSGGGGSGTQVVTQE PSLTVSPGGTVTLTCASSTGAVTSGNYPNWVQQKPGQ APRGLIGGTKFLVPGTPARFSGSLLGGKAALTLSGVQ PEDEAEYYCTLWYSNRWVFGGGTKLTVLHHHHHH
245	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL84	QVQLQESGGGLVQAGGSLMVSCAASGGTFSSYATGWF RQVPGEREFIAGISRSGGRYYAESVKGRFTISRDN AKNTVYLQMNLTLPDDTAVYYCAAARYFTTSVYTS DDYDYGQGTQVTVSSGGGSGGGSEVQLVESGGGLV QPGNSLRSLCAASGFTFSKFGMSWVRQAPGKLEWVS SISGSGRDTLYADSVKGRFTISRDNAKTTLYLQMN SLRPEDTAVYYCTIGGSLSVSSQGTTLTVSSGGGSGGG SEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINW VRQAPGKLEWVARIRSKYNNYATYYADQVKDRFTIS RDDSKNTAYLQMNLTEDTAVYYCVRHANFGNSYIS YWAYWGQGTTLTVSSGGGSGGGGSGGGGSGTQVVTQE PSLTVSPGGTVTLTCASSTGAVTSGNYPNWVQQKPGQ APRGLIGGTKFLVPGTPARFSGSLLGGKAALTLSGVQ PEDEAEYYCTLWYSNRWVFGGGTKLTVLHHHHHH
246	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL107	QVQLQESGGGLVQAGGSLRLSCAASGRTFSSYAMGWF RQAPGKREFVAAISWSGSNTYYADSVKGRFTISRDN AKNTVYLQMDSLKPEDTAVYYCAAGGSTRVVTTTPV VKYWGQGTQVTVSSGGGSGGGSEVQLVESGGGLVQ PNSLRSLCAASGFTFSKFGMSWVRQAPGKLEWVS SISGSGRDTLYADSVKGRFTISRDNAKTTLYLQMN SLRPEDTAVYYCTIGGSLSVSSQGTTLTVSSGGGSGGG SEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINW VRQAPGKLEWVARIRSKYNNYATYYADQVKDRFTIS RDSKNTAYLQMNLTEDTAVYYCVRHANFGNSYISY WAYWGQGTTLTVSSGGGSGGGGSGGGGSGTQVVTQE PSLTVSPGGTVTLTCASSTGAVTSGNYPNWVQQKPGQ APRGLIGGTKFLVPGTPARFSGSLLGGKAALTLSGVQ PEDEAEYYCTLWYSNRWVFGGGTKLTVLHHHHHH
247	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL141	QVQLQESGGGLVQAGGSLRLSCAASGRTFSSYAMGWF RQAPGMEREFVAAISWSGYSTYYADSVKGRFTISR DDAKNTVYLQMDSLKPEDTAVYYCAAGGSTRVVTTTPV

			VKYWGQGTQVTVSSGGGGSGGGSEVQLVESGGGLVQPGNSLRRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTTLTVTVSSGGGGSGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINWVRQAPGKGLEWVARIRSKYNNYATYYADQVKDRFTISRDSKNTAYLQMNNLKTEDTAVYYCVRHANFGNSYISYWVAYWGQGTTLTVTVSSGGGGSGGGSGGGSGQTVVTQEPSLTVSPGGTVTLTCASSTGAVTSGNYPNWVQQKPGQAPRGLIGGTKFLVPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCTLWYSNRWVFGGGTKLTVLHHHHHH
248	anti-FLT3/anti-HSA/anti-CD3 fusion protein	FLL34	QVQLQESGGGLVQAGGSLRLSCAASGRTFSSYALGWFQAPGKEREFFVAAISWSGGNTYYADSVKGRFTISRDDAKNTVYLQMDSLKPEDTAVYYCAAGGSTRVVTTTPVVKYWGQGTQVTVSSGGGGSGGGSEVQLVESGGGLVQPGNSLRRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTTLTVTVSSGGGGSGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINWVRQAPGKGLEWVARIRSKYNNYATYYADQVKDRFTISRDSKNTAYLQMNNLKTEDTAVYYCVRHANFGNSYISYWVAYWGQGTTLTVTVSSGGGGSGGGSGGGSGQTVVTQEPSLTVSPGGTVTLTCASSTGAVTSGNYPNWVQQKPGQAPRGLIGGTKFLVPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCTLWYSNRWVFGGGTKLTVLHHHHHH
249	anti-FLT3/anti-HSA/anti-CD3 fusion protein	FLL4	QVQLQESGGGLVQAGGSLRLSCAASERTFSSYTMGWFQAPGKEREFFVAAMSWSGGSTYYADSVKGRFTISRDN AKNTVYLQMDSLKPEDTAVYYCAAGGSTRVVTTTPVVKYWGQGTQVTVSSGGGGSGGGSEVQLVESGGGLVQPGNSLRRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTTLTVTVSSGGGGSGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINWVRQAPGKGLEWVARIRSKYNNYATYYADQVKDRFTISRDSKNTAYLQMNNLKTEDTAVYYCVRHANFGNSYISYWVAYWGQGTTLTVTVSSGGGGSGGGSGGGSGQTVVTQEPSLTVSPGGTVTLTCASSTGAVTSGNYPNWVQQKPGQAPRGLIGGTKFLVPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCTLWYSNRWVFGGGTKLTVLHHHHHH
250	anti-FLT3/anti-HSA/anti-CD3 fusion protein	FLL61	QVQLQESGGGLVQAGGSLRLSCAASERTFSSYAMGWFQAPGKEREFFVAAISWSGGSTYYADSVKGRFTISRDN AKNTVYLQMDSLKPEDTAVYYCAAGGSTRVVTTTPVVKYWGQGTQVTVSSGGGGSGGGSEVQLVESGGGLVQPGNSLRRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTTLTVTVSSGGGGSGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINWVRQAPGKGLEWVARIRSKYNNYATYYADQVKDRFTISRDSKNTAYLQMNNLKTEDTAVYYCVRHANFGNSYISYWVAYWGQGTTLTVTVSSGGGGSGGGSGGGSGQTVVTQEPSLTVSPGGTVTLTCASSTGAVTSGNYPNWVQQKPGQAPRGLIGGTKFLVPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCTLWYSNRWVFGGGTKLTVLHHHHHH
251	anti-FLT3/anti-HSA/anti-CD3 fusion protein	FLL78	QVQLQESGGGWVQAGGSLRLSCAASGRTFSSYAMGWFQAPGKEREFFVAAISWSGSSTYYADSVKGRFTISRDN AKNTVYLLMDSLKPEDTAVYYCAAGGSTRVVTTTPVVKYWGQGTQVTVSSGGGGSGGGSEVQLVESGGGLVQPGNSLRRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTTLTVTVSSGGGGSGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINWVRQAPGKGLEWVARIRSKYNNYATYYADQVKDRFTISRDSKNTAYLQMNNLKTEDTAVYYCVRHANFGNSYISYW

			AYWGQGTLLVTVSSGGGGSGGGSGGGGSQTVVTQEPS LTVSPGGTVTLTCASSTGAVTSGNYPNWVQQKPGQAP RGLIGGTKFLVPGTPARFSGSLGGKAALTLSGVQPE DEAEYYCTLWYSNRWVFGGGTKLTVLHHHHHH
252	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL1	QVQLQESGGGLVQAGGSLRLSCAASGRTFTSTLVAWF RQAPGKEREFFVASIPSGSNTGYAESVKGRFTISRDI AKNTVYLQMNSLKPEDTAMYFCAARIYFGSSRGYDYW GQGTQVTVSSGGGGSGGGSEVQLVESGGGLVQPGNSL RLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSG RDTLYADSVKGRFTISRDNAKTTLYLQMNSLRPEDTA VYYCTIGGSLSVSSQGTLLVTVSSGGGGSGGGSEVQLV ESGGGLVQPGGSLKLSCAASGFTFNKYAINWVRQAPG KGLEWVARIRSKYNNYATYYADQVKDRFTISRDDSKN TAYLQMNNLKTEDTAVYYCVRHANFGNSYISYWAYWG QGTLLVTVSSGGGGSGGGSGGGGSQTVVTQEPSLTVS PGGTVTTLTCASSTGAVTSGNYPNWVQQKPGQAPRGLI GGTKFLVPGTPARFSGSLGGKAALTLSGVQPEDEAE YYCTLWYSNRWVFGGGTKLTVLHHHHHH
253	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL26	QVQLQESGGGLVQAGGSLRLSCAASGRTFTTYYTVAWF RQAPGKEREFLVASIPTGSNTAYAESVKGRFTISRGN AKNTVYLQMNSLKPEDTAMYYCAARTYFGSSRGYDYW GQGTQVTVSSGGGGSGGGSEVQLVESGGGLVQPGNSL RLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSG RDTLYADSVKGRFTISRDNAKTTLYLQMNSLRPEDTA VYYCTIGGSLSVSSQGTLLVTVSSGGGGSGGGSEVQLV ESGGGLVQPGGSLKLSCAASGFTFNKYAINWVRQAPG KGLEWVARIRSKYNNYATYYADQVKDRFTISRDDSKN TAYLQMNNLKTEDTAVYYCVRHANFGNSYISYWAYWG QGTLLVTVSSGGGGSGGGSGGGGSQTVVTQEPSLTVS PGGTVTTLTCASSTGAVTSGNYPNWVQQKPGQAPRGLI GGTKFLVPGTPARFSGSLGGKAALTLSGVQPEDEAE YYCTLWYSNRWVFGGGTKLTVLHHHHHH
254	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL160	QVQLQESGGGLVQAGDSLRLSCATSGRTFNLYRVGWF RQAPGKEREFFVARITWSADITQYADSVKGRFTISRDN AKNTVYLQMNSLKPEDTAIYYCATTLRKSSGIYHVD YDDWGQGTQVTVSSGGGGSGGGSEVQLVESGGGLVQ GNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSI SGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNSLRP EDTAVYYCTIGGSLSVSSQGTLLVTVSSGGGGSGGGSE VQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINWVR QAPGKGLEWVARIRSKYNNYATYYADQVKDRFTISR DSKNTAYLQMNNLKTEDTAVYYCVRHANFGNSYISY AYWGQGTLLVTVSSGGGGSGGGSGGGGSQTVVTQEPS LTVSPGGTVTLTCASSTGAVTSGNYPNWVQQKPGQAP RGLIGGTKFLVPGTPARFSGSLGGKAALTLSGVQPE DEAEYYCTLWYSNRWVFGGGTKLTVLHHHHHH
255	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL173	QVQLQESGGGLVQAGGSLRLSCATSGRTFNLYRVGWF RQAPGKEREFFVARITWSADITQYTDVSKGRFTISRDN AKNTVYLQMNSLKPEDTAIYYCATTLRKSSGIYHTDD YDYWGQGTQVTVSSGGGGSGGGSEVQLVESGGGLVQ GNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSI SGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNSLRP EDTAVYYCTIGGSLSVSSQGTLLVTVSSGGGGSGGGSE VQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINWVR QAPGKGLEWVARIRSKYNNYATYYADQVKDRFTISR DSKNTAYLQMNNLKTEDTAVYYCVRHANFGNSYISY AYWGQGTLLVTVSSGGGGSGGGSGGGGSQTVVTQEPS LTVSPGGTVTLTCASSTGAVTSGNYPNWVQQKPGQAP RGLIGGTKFLVPGTPARFSGSLGGKAALTLSGVQPE DEAEYYCTLWYSNRWVFGGGTKLTVLHHHHHH
256	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL178	QVQLQESGGGLVQPGGSLRLSCAASGFTFSDYAMSWV RQAPGKGLEWVSGISSGGYKIGYTDSTKGRFTISRDN AKNTLYLQMNSLTAEDTAVYYCAKGTQWSWSLRDNTS

			RGQGTQVTVSSGGGGSGGGSEVQLVESGGGLVQPGNS LRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGS GRDTLYADSVKGRFTISRDNAKTTLYLQMNSLRPEDT AVYYCTIGGSLSVSSQGTTLTVSSGGGGSGGGSEVQL VESGGGLVQPGGSLKLSAASGFTFNKYAINWVRQAP GKGLEWVARIRSKYNNYATYYADQVKDRFTISRDDSK NTAYLQMNNLKTEDTAVYYCVRHANFGNSYISYWAYW GQGTTLTVTVSSGGGGSGGGSGGGGSQTVVTQEPSTLV SPGGTVTLTCASSTGAVTSGNYPNWVQKPGQAPRGL IGGTFKFLVPGTPARFSGSLLGGKAALTLSGVQPEDEA EYYCTLWYSNRWVFGGGTKLTVLHHHHHH
257	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL27	QVQLQESGGGLVQPGGSLRLSCAASGFTFSSYAMSWV RQAPGKGLEWVSGISSGGYKIGYTDSTKGRFTISRDN AKNTLYLQMNSLNAEDTAVYYCAKGTQWSWALRDSTS RGQGTQVTVSSGGGGSGGGSEVQLVESGGGLVQPGNS LRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGS GRDTLYADSVKGRFTISRDNAKTTLYLQMNSLRPEDT AVYYCTIGGSLSVSSQGTTLTVSSGGGGSGGGSEVQL VESGGGLVQPGGSLKLSAASGFTFNKYAINWVRQAP GKGLEWVARIRSKYNNYATYYADQVKDRFTISRDDSK NTAYLQMNNLKTEDTAVYYCVRHANFGNSYISYWAYW GQGTTLTVTVSSGGGGSGGGSGGGGSQTVVTQEPSTLV SPGGTVTLTCASSTGAVTSGNYPNWVQKPGQAPRGL IGGTFKFLVPGTPARFSGSLLGGKAALTLSGVQPEDEA EYYCTLWYSNRWVFGGGTKLTVLHHHHHH
258	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL190	QVQLQESGGGLVQAGGSLTSLCTASGSTFSINHFWSY RQAPGKQRELVAFISSDGVSIDVESVKGRFTISGDND KNTAYLQMNLKPEDTAVYYCYRFGWGQGTQVTVSS GGGGSGGGSEVQLVESGGGLVQPGNSLRLSCAASGFT FSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYADSVK GRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSL SVSSQGTTLTVTVSSGGGGSGGGSEVQLVESGGGLVQPG GSLKLSAASGFTFNKYAINWVRQAPGKGLEWVARIR SKYNNYATYYADQVKDRFTISRDDSKNTAYLQMNNLK TEDTAVYYCVRHANFGNSYISYWAYWGQGTTLTVSSG GGGGSGGGSGGGGSQTVVTQEPSTLVSPGGTVTLTCA SSTGAVTSGNYPNWVQKPGQAPRGLIGGTFKFLVPGT PARFSGSLLGGKAALTLSGVQPEDEAEYYCTLWYSNR WVFGGGTKLTVLHHHHHH
259	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL43	QVQLQESGGGLVQPGGSLTSLCTASGSTFSINHFAYW RQAPGKQRELVAFISSDGRSTDVESVKGRFTISGDND KNTAYLQMNLKPEDTAVYYCYRGSWGQGTQVTVSS GGGGSGGGSEVQLVESGGGLVQPGNSLRLSCAASGFT FSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYADSVK GRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSL SVSSQGTTLTVTVSSGGGGSGGGSEVQLVESGGGLVQPG GSLKLSAASGFTFNKYAINWVRQAPGKGLEWVARIR SKYNNYATYYADQVKDRFTISRDDSKNTAYLQMNNLK TEDTAVYYCVRHANFGNSYISYWAYWGQGTTLTVSSG GGGGSGGGSGGGGSQTVVTQEPSTLVSPGGTVTLTCA SSTGAVTSGNYPNWVQKPGQAPRGLIGGTFKFLVPGT PARFSGSLLGGKAALTLSGVQPEDEAEYYCTLWYSNR WVFGGGTKLTVLHHHHHH
260	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL15	QVQLQESGGGLVQAGGSLSLSCAASEGTISHAAMGWF RQAPGKERQFVAYDTWTGGSTNYADSVKDRFTITGDH AKNTVYLQMNSLKPEDTGVIYCAVRGRYSASYTYTNP ASYKYWGQGTQVTVSSGGGGSGGGSEVQLVESGGGLV QPGNSLRLSCAASGFTFSKFGMSWVRQAPGKGLEWVS SISGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNSL RPEDTAVYYCTIGGSLSVSSQGTTLTVSSGGGGSGGG SEVQLVESGGGLVQPGGSLKLSAASGFTFNKYAINW VRQAPGKGLEWVARIRSKYNNYATYYADQVKDRFTIS RDDSKNTAYLQMNNLKTEDTAVYYCVRHANFGNSYIS

			YWAYWGQGTTLTVSSGGGSGGGGSGGGGSGTQVVTQE PSLTVSPGGTVTLTCASSTGAVTSGNYPNWVQQKPGQ APRGLIGGKFLVPGTTPARFSGSLLGGKAALTLSGVQ PEDEAEYYCTLWYSNRWVFGGGTKLTVLHHHHHH
261	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL45	QVQLQESGGGLVQAGGSLRLSCAASGGTFSSSAMGWF RQAPGKEREFVATITQNDVPTYTHSVKGRFTISRDN AKNTMYLQMNSLKPEDTAVYYCAQRVAQASGWRTTIK DYGWQGTQVTVSSGGGSGGGSEVQLVESGGGLVQ PGNSLRLSCAASGFTFSKFGMSWVRQAPGKLEWVSS ISGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNSLR PEDTAVYYCTIGGSLSVSSQGTTLTVSSGGGSGGGG EVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINWV RQAPGKLEWVARIRSKYNNYATYYADQVKDRFTISR DDSKNTAYLQMNNLKTEDTAVYYCVRHANFGNSYISY WAYWGQGTTLTVSSGGGSGGGGSGGGGSGTQVVTQEP SLTVSPGGTVTLTCASSTGAVTSGNYPNWVQQKPGQA PRGLIGGKFLVPGTTPARFSGSLLGGKAALTLSGVQ PEDEAEYYCTLWYSNRWVFGGGTKLTVLHHHHHH
262	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL39	QVQLQESGGGLVQAGGSLRLSCAASGLTSSTYRMAWF RQAPGKEREFVATITQNDVPTYTHSVKGRFTISRDN AKNTMYLQMNSLKPEDTAVYYCAAGRYSGTYNSP YSSSYVYWGQGTQVTVSSGGGSGGGSEVQLVESGGG LVQPGNSLRLSCAASGFTFSKFGMSWVRQAPGKLEW VSSISGSGRDTLYADSVKGRFTISRDNAKTTLYLQMN SLRPEDTAVYYCTIGGSLSVSSQGTTLTVSSGGGSGG GGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAI NWVRQAPGKLEWVARIRSKYNNYATYYADQVKDRFT ISRDDSKNTAYLQMNNLKTEDTAVYYCVRHANFGNSY ISYWAYWGQGTTLTVSSGGGSGGGGSGGGGSGTQVVT QEPSTVSPGGTVTLTCASSTGAVTSGNYPNWVQQK GQAPRGLIGGKFLVPGTTPARFSGSLLGGKAALTLSG VQPEDEAEYYCTLWYSNRWVFGGGTKLTVLHHHHHH
263	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL177	QVQLQESGGGLVQAGGSLRLSCAASGSTFSRNTMGWF RQAPGKERFVFLGISWSGIRSYLLDSAKARFTISRDN AKNTVYLQMNSLRPEDTAVYYCAAQEGSSPGPYKYWG QGTQVTVSSGGGSGGGSEVQLVESGGGLVQPGNSLR LSCAASGFTFSKFGMSWVRQAPGKLEWVSSISGSGR DTLYADSVKGRFTISRDNAKTTLYLQMNSLRPEDTAV YYCTIGGSLSVSSQGTTLTVSSGGGSGGGSEVQLVE SGGGLVQPGGSLKLSCAASGFTFNKYAINWVRQAPGK GLEWVARIRSKYNNYATYYADQVKDRFTISRDDSKNT AYLQMNNLKTEDTAVYYCVRHANFGNSYISYWAYWGQ GTLTVTVSSGGGSGGGGSGGGGSGTQVVTQEPSTVSP GGTVTLTCASSTGAVTSGNYPNWVQQKPGQAPRGLIG GKFLVPGTTPARFSGSLLGGKAALTLSGVQPEDEAEY YCTLWYSNRWVFGGGTKLTVLHHHHHH
264	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL823	QVQLQESGGGVVQVGGSLRLSCAASGGTFGYAVGW RQAPGKEREFVAAVTWNGAYLYSDPVKGRFTISRDN KNTVYLQMNSLKSSEDVAVYYCGLDRWSAVVESTPSTR GQGTQVTVSSGGGSGGGSEVQLVESGGGLVQPGNSL RLSCAASGFTFSKFGMSWVRQAPGKLEWVSSISGSG RDTLYADSVKGRFTISRDNAKTTLYLQMNSLRPEDTA VYYCTIGGSLSVSSQGTTLTVSSGGGSGGGSEVQLV ESGGGLVQPGGSLKLSCAASGFTFNKYAINWVRQAPG KLEWVARIRSKYNNYATYYADQVKDRFTISRDDSKN TAYLQMNNLKTEDTAVYYCVRHANFGNSYISYWAYWG QGTTLTVTVSSGGGSGGGGSGGGGSGTQVVTQEPSTV PGGTVTLTCASSTGAVTSGNYPNWVQQKPGQAPRGLI GGTKFLVPGTTPARFSGSLLGGKAALTLSGVQPEDEAE YYCTLWYSNRWVFGGGTKLTVLHHHHHH
265	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLL76	QVQLQESGGGLVQAGGSLRLSCAASGGAFSSVYMGWF RQAPGKEREFVAAVISWGRITDYADSVKGRFTISRDN NAKSTVYLQMNNLKPEDTAVYYCAAKTGMIDLRST

			FDYWQQTQVTVSSGGGGSGGGSEVQLVESGGGLVQPGNSLRRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTTLTVTVSSGGGGSGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINWVRQAPGKGLEWVARIRSKYNNYATYYADQVKDRFTISRDSKNTAYLQMNNLKTEDTAVYYCVRHANFGNSYISYWAWGQGTTLTVTVSSGGGGSGGGSGGGSGQTVVTQEPSLTVSPGGTVTLTCASSTGAVTSGNYPNWVQQKPGQAPRGLIGGTKFLVPGTPARFSGSLGGKAALTLSGVQPEDEAEYYCTLWYSNRWVFGGGTKLTVLHHHHHH
266	anti-FLT3/anti-HSA/anti-CD3 fusion protein	FLH822	QVQLQESGGGSVQAGGSLRLSCTASGRTFTDYMGMWFRQAPGKEREFLGISSNGYRRYTGSMKDRFTISRDNVKKTVYLQMNDLKPEDTAVYYCAASEDHGAPRYDWGQGTQVTVSSGGGGSGGGSEVQLVESGGGLVQPGNSLRRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTTLTVTVSSGGGGSGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINWVRQAPGKGLEWVARIRSKYNNYATYYADQVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHANFGNSYISYWAYWGQGTTLTVTVSSGGGGSGGGSGGGSGQTVVTQEPSLTVSPGGTVTLTCASSTGAVTSGNYPNWVQQKPGQAPRGLIGGTKFLVPGTPARFSGSLGGKAALTLSGVQPEDEAEYYCTLWYSNRWVFGGGTKLTVLHHHHHH
267	anti-FLT3/anti-HSA/anti-CD3 fusion protein	FLH107	EVQLLESGGGLVQPGGSLTLSCAASGRTFSSYAMGMWFRQAPGKEREFAAISWSGSNTYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAAGGSTRVVTTPPVVKYWQGTTLTVTVSSGGGGSGGGSEVQLVESGGGLVQPGNSLRRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTTLTVTVSSGGGGSGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINWVRQAPGKGLEWVARIRSKYNNYATYYADQVKDRFTISRDSKNTAYLQMNNLKTEDTAVYYCVRHANFGNSYISYWAWGQGTTLTVTVSSGGGGSGGGSGGGSGQTVVTQEPSLTVSPGGTVTLTCASSTGAVTSGNYPNWVQQKPGQAPRGLIGGTKFLVPGTPARFSGSLGGKAALTLSGVQPEDEAEYYCTLWYSNRWVFGGGTKLTVLHHHHHH
268	anti-FLT3/anti-HSA/anti-CD3 fusion protein	FLH141	EVQLLESGGGLVQPGGSLTLSCAASGRTFSSYAMGMWFRQAPGMEREFAAISWSGYSTYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAAGGSTRVVTTPPVVKYWQGTTLTVTVSSGGGGSGGGSEVQLVESGGGLVQPGNSLRRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTTLTVTVSSGGGGSGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINWVRQAPGKGLEWVARIRSKYNNYATYYADQVKDRFTISRDSKNTAYLQMNNLKTEDTAVYYCVRHANFGNSYISYWAWGQGTTLTVTVSSGGGGSGGGSGGGSGQTVVTQEPSLTVSPGGTVTLTCASSTGAVTSGNYPNWVQQKPGQAPRGLIGGTKFLVPGTPARFSGSLGGKAALTLSGVQPEDEAEYYCTLWYSNRWVFGGGTKLTVLHHHHHH
269	anti-FLT3/anti-HSA/anti-CD3 fusion protein	FLH19C	EVQLVESGGGLVQPGGSLTLSCAASGSTFSINHFWSYRQAPGKQRELVAFISSDGVSIDVESVKGRFTISGDNSKNTAYLQMNSLRAEDTAVYYCYRGFWGQGTTLTVTVSSGGGGSGGGSEVQLVESGGGLVQPGNSLRRLSCAASGFTFSKFGMSWVRQAPGKGLEWVSSISGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTTLTVTVSSGGGGSGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINWVRQAPGKGLEWVARIRSKYNNYATYYADQVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHANFGNSYISYWAYWGQGTTLTVTVSS

			GGGSGGGGSGGGGSGTQVVTQEPSTLTVSPGGTVTLTCA SSTGAVTSGNYPNWVQQKPGQAPRGLIGGKFLVPGT PARFSGSLGGAALTLTSGVQPEDEAEYYCTLWYSNR WVFGGKTLTVLHHHHH
270	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLH34	EVQLLESGGGLVQPGGSLTLSCAASGRTFSSYALGWF RQAPGKEREFAAISWSGGNTYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAAGSTRVVTTPV VKYWGQGTLLTVSSGGGGSGGGSEVQLVESGGGLVQP GNSLRSLCAASGFTFSKFGMSWVRQAPGKLEWVSSI SGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNSLRP EDTAVYYCTIGGSLSVSSQGTLLTVSSGGGGSGGGSE VQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINWVR QAPGKLEWVARIRSKYNNYATYYADQVKDRFTISR DSKNTAYLQMNNLKTEDTAVYYCVRHANFGNSYISY AYWGQGTLLTVSSGGGGSGGGSGGGSGTQVVTQEP LTVSPGGTVTLTCAASSTGAVTSGNYPNWVQQKPGQAP RGLIGGKFLVPGTAPRFGSLGGAALTLTSGVQPE DEAEYYCTLWYSNRWVFGGKTLTVLHHHHH
271	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLH4	EVQLLESGGGLVQPGGSLTLSCAASERTFSSYTMGWF RQAPGKEREFAAMSWSGGSTYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAAGSTRVVTTPV VKYWGQGTLLTVSSGGGGSGGGSEVQLVESGGGLVQP GNSLRSLCAASGFTFSKFGMSWVRQAPGKLEWVSSI SGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNSLRP EDTAVYYCTIGGSLSVSSQGTLLTVSSGGGGSGGGSE VQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINWVR QAPGKLEWVARIRSKYNNYATYYADQVKDRFTISR DSKNTAYLQMNNLKTEDTAVYYCVRHANFGNSYISY AYWGQGTLLTVSSGGGGSGGGSGGGSGTQVVTQEP LTVSPGGTVTLTCAASSTGAVTSGNYPNWVQQKPGQAP RGLIGGKFLVPGTAPRFGSLGGAALTLTSGVQPE DEAEYYCTLWYSNRWVFGGKTLTVLHHHHH
272	anti-FLT3/anti- HSA/anti-CD3 fusion protein	FLH78	EVQLLESGGGLVQPGGSLTLSCAASGRTFSSYAMGWF RQAPGKEREFAAISWSGSSTYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAAGSTRVVTTPV VKYWGQGTLLTVSSGGGGSGGGSEVQLVESGGGLVQP GNSLRSLCAASGFTFSKFGMSWVRQAPGKLEWVSSI SGSGRDTLYADSVKGRFTISRDNAKTTLYLQMNSLRP EDTAVYYCTIGGSLSVSSQGTLLTVSSGGGGSGGGSE VQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINWVR QAPGKLEWVARIRSKYNNYATYYADQVKDRFTISR DSKNTAYLQMNNLKTEDTAVYYCVRHANFGNSYISY AYWGQGTLLTVSSGGGGSGGGSGGGSGTQVVTQEP LTVSPGGTVTLTCAASSTGAVTSGNYPNWVQQKPGQAP RGLIGGKFLVPGTAPRFGSLGGAALTLTSGVQPE DEAEYYCTLWYSNRWVFGGKTLTVLHHHHH
372	sdAb	Anti- albumin	EVQLVESGGGLVQPGNSLRSLCAASGFTFSKFGMSWV RQAPGKLEWVSSISGSGRDTLYADSVKGRFTISRDN AKTTLYLQMNSLRPEDTAVYYCTIGGSLSVSSQGTLLV TVSS
373	scFv	Anti- CD3	EVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAINWV RQAPGKLEWVARIRSKYNNYATYYADQVKDRFTISR DDSKNTAYLQMNNLKTEDTAVYYCVRHANFGNSYISY WAYWGQGTLLTVSSGGGGSGGGSGGGSGTQVVTQEP SLTVSPGGTVTLTCAASSTGAVTSGNYPNWVQQKPGQA PRGLIGGKFLVPGTAPRFGSLGGAALTLTSGVQPE DEAEYYCTLWYSNRWVFGGKTLTVL
374	Tag	6x-His	HHHHH
375	linker	G4SG3S	GGGGSGGG

376	Sortase		LPETG
377	linker	(GS) _n	(GS) _n
378	linker	(GGS) _n	(GGS) _n
379	linker	(GGGS) _n	(GGGS) _n
380	linker	(GGSG) _n	(GGSG) _n
381	linker	(GGSGG) _n	(GGSGG) _n
382	linker	(GGGGS) _n	(GGGGS) _n
383	linker	(GGGGG) _n	(GGGGG) _n
384	linker	(GGG) _n	(GGG) _n
385	linker		GGGSGGGSGGGSGGGGS
386	linker		GGGSGGGSGGGGS
387	linker		GGGSGGGGS
388	P36888		MPALARDGGQLPLLVVFSAMIFGTITNQDLPVIKCVL INHKNNDS SVGKSSSYPMVSESPEDLGALRPQSSGT VYEA AAVEVDVSASITLQVLVDAPGNISCLWVFKHSS LNCQPHFDLQNRGVVSMVILKMTETQAGEYLLFIQSE ATNYTILFTVSI RNTLLYTLRRPYFRKMENQDALVCI SESVPEPIVEWVLCDSQGESCKEESPAVVKKEEKVLH ELFGTDIRCCARNELGRECTRLFTIDLNQTPQTTL PQ LFLKVGEPLWIRCKAVHVNHGFGLTWELENKALEEGN YFEMSTYSTNRTMIRILFAFVSSVARNDTGYYTCSSS KHPSQSALVTIVEKGFINATNSSEIDYEEFCFS VRFKAYPQIRCTWTF SRKSFPCQKGLDNGYSISKFC NHKHQPGEYIFHAENDDAQFTKMFTLNIRRKPVLA E ASASQASCFSDGYPLPSWTWKKCSDKSPNCTEEITE GVWNRKANRKFVQWVSSSTLNMSEAIKGFVLKCCAY NSLGTSCETILLNSPGFPFFIQDNISFYATIGVCLLF IVVLTLLICHKYKKQFRYESQLQMVQVTGSSDNEYFY VDFREYEDLKWEFPRENLEFGKVLGSGAFGKVMNAT AYGISKTGVSIQVAVKMLKEKADSSEREALMSELKMM TQLGSHENIVNLLGACTLSGPIYLI FEYCCYGDLLNY LRSKREKFHRTWTEIFKEHNFSFYPTFQSHPNSSMPG SREVQIHPDSDQISGLHGNSFHSEDEIEYENQKRLEE EEDLNVLTFFEDLLCFAYQVAKGMEFLEFKSCVHRDLA ARNVLVTHGKVVKICDFGLARDIMSDSNYVVRGNARL PVKWMAPESLFEGITYTIKSDVWSYGILLWEIFSLGVN PYPGIPVDANFYKLIQNGFKMDQPFYATEEIIYIMQS CWA FDSRKRPSFPNLT SFLGCQLADAE EAMYQNVDG RVSECPHTYQNRPF SREMDLGLLS PQAQVEDS
389	FLT3 antibody variable domain	FLH92a	EVQLLESGGGLVQPGGSLT LSCAASGGTWSSYA TGWFRQAPGKERELIAGISRSGGRITYYADSVKG RFTISRDN SKNTLYLQMN SLRAEDTAVYYCAAA RYFTSSV VYTS GNDYDYWGQGT LVTVSS

390	FLT3 antibody variable domain	FLH92b	EVQLLESGGGLVQPGGSLTLSCAASGGTWSSYA TGWFRQAPGKERELIAGISRSGGRTYYADSVKG RFTISRDN SKNTVYLQMNSLRAEDTAVYYCAKA RYFTSSVVYTS GNDYDYWGQGT LVT VSS
391	anti-FLT3/anti-HSA/anti-CD3 fusion protein	FLH92a	EVQLLESGGGLVQPGGSLTLSCAASGGTWSSYA TGWFRQAPGKERELIAGISRSGGRTYYADSVKG RFTISRDN SKNTLYLQMNSLRAEDTAVYYCAAA RYFTSSVVYTS GNDYDYWGQGT LVT VSSGGGGS GGGSEVQLVESGGGLVQPGNSLRSLCAASGFTF SKFGMSWVRQAPGKLEWVSSISGSGRDTLYAD SVKGRFTISRDN AKTTLYLQMNSLRPEDTAVYY CTIGGSLSVSSQGT LVT VSSGGGSGGGSEVQL VESGGGLVQPGGSLKLSCAASGFTFNKYAINWV RQAPGKLEWVARIRSKYNNYATYYADQVKDRF TISRDDSKNTAYLQMNNLKTEDTAVYYCVRHAN FGNSYISYWAYWGQGT LVT VSSGGGSGGGGSG GGGSQTVVTQEP SLTVSPGGTVTLTCASSTGAV TSGNYPNWVQQKPGQAPRGLIGGTKFLVPGTPA RFGSLLGGKAALTLSGVQPEDEAEYYCTLWYS NRWVFGGKT LTVLHHHHHH
392	anti-FLT3/anti-HSA/anti-CD3 fusion protein	FLH92b	EVQLLESGGGLVQPGGSLTLSCAASGGTWSSYA TGWFRQAPGKERELIAGISRSGGRTYYADSVKG RFTISRDN SKNTVYLQMNSLRAEDTAVYYCAKA RYFTSSVVYTS GNDYDYWGQGT LVT VSSGGGGS GGGSEVQLVESGGGLVQPGNSLRSLCAASGFTF SKFGMSWVRQAPGKLEWVSSISGSGRDTLYAD SVKGRFTISRDN AKTTLYLQMNSLRPEDTAVYY CTIGGSLSVSSQGT LVT VSSGGGSGGGSEVQL VESGGGLVQPGGSLKLSCAASGFTFNKYAINWV RQAPGKLEWVARIRSKYNNYATYYADQVKDRF TISRDDSKNTAYLQMNNLKTEDTAVYYCVRHAN FGNSYISYWAYWGQGT LVT VSSGGGSGGGGSG GGGSQTVVTQEP SLTVSPGGTVTLTCASSTGAV TSGNYPNWVQQKPGQAPRGLIGGTKFLVPGTPA RFGSLLGGKAALTLSGVQPEDEAEYYCTLWYS NRWVFGGKT LTVLHHHHHH
89	CDR1	FLH92a	GGTWSSYATG
89	CDR1	FLH92b	GGTWSSYATG
393	CDR2	FLH92a	GISRSGGRTYYADSVKG
394	CDR2	FLH92b	GISRSGGRTYYADSVKG
173	CDR3	FLH92a	ARYFTSSVVYTS GNDYDY
173	CDR3	FLH92b	ARYFTSSVVYTS GNDYDY
300	framework 1	FLH92a	EVQLLESGGGLVQPGGSLTLSCAAS
300	framework 1	FLH92b	EVQLLESGGGLVQPGGSLTLSCAAS
395	framework 2	FLH92a	WFRQAPGKERELIA

395	framework 2	FLH92b	WFRQAPGKERELIA
364	framework 3	FLH92a	RFTISRDN SKNTLYLQMNSLRAEDTAVYYCAA
396	framework 3	FLH92b	RFTISRDN SKNTVYLYQMNSLRAEDTAVYYCAK
371	framework 4	FLH92a	WGQGTLVTVSS
371	framework 4	FLH92b	WGQGTLVTVSS
397	CD3 binder exemplary HC CDR1 (heavy chain CDR1)		GFTFNKYAIN
398	CD3 binder exemplary HC CDR2		RIRSKYNNYATYYADQVK
399	CD3 binder exemplary HC CDR3		HANFGNSYISYWAY
400	CD3 binder exemplary LC CDR1 (light chain CDR1)		ASSTGAVTSGNYPN
401	CD3 binder exemplary LC CDR2		GTKFLVP
402	CD3 binder exemplary LC CDR3		TLWYSNRWV
403	HSA binder exemplary CDR1		GFTFSKFGMS
404	HSA binder exemplary CDR2		SISGSGRDTLYADSVK
405	HSA binder exemplary CDR3		GGSLSV