

What is claimed is:

1. A humanized antibody or antigen binding fragment thereof that binds to human FLT3, wherein the antibody or fragment comprises:
 - i. a light chain variable region (VL) comprising an amino acid sequence with at least 95% identity to any one of the sequences selected from the group consisting of: SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, and SEQ ID NO:38; and/or
 - ii. a heavy chain variable region (VH) comprising an amino acid sequence with at least 95% identity to any one of the sequences selected from the group consisting of: SEQ ID NO:3, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, and SEQ ID NO:27.
2. The humanized antibody or fragment of claim 1, wherein:
 - a) (i) the VL comprises complementarity determining regions (CDRs) having at least 97%, 98%, 99% or 100% identity to the amino acid sequences of CDR-L1 of SEQ ID NO:86, CDR-L2 of SEQ ID NO: 87, and CDR-L3 of SEQ ID NO: 88, and (ii) the VH comprises CDRs having at least 97%, 98%, 99% or 100% identity to the amino acid sequences of CDR-H1 of SEQ ID NO: 89, CDR-H2 of SEQ ID NO: 90, and CDR-L3 of SEQ ID NO:91;
 - b) wherein the VL comprises the amino acid sequence of SEQ ID NO:1, and the VH comprises the amino acid sequence of SEQ ID NO:3; or
 - c) wherein the VL comprises the amino acid sequence of SEQ ID NO:2, and the VH comprises the amino acid sequence of SEQ ID NO:3.
3. A single chain variable domain (scFv) comprising an antigen binding fragment of claim 1 or 2.

4. The scFv of claim 3, wherein:
 - a) the scFv comprises a linker between the VL and the VH, wherein the linker has the formula (Gly₃₋₄-Ser)₁₋₄; or
 - b) wherein the scFv has the amino acid sequence selected from the group consisting of: SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, and SEQ ID NO:49, optionally wherein the scFv has the amino acid sequence of SEQ ID NO:4 or SEQ ID NO: 5.
5. A chimeric antigen receptor (CAR), wherein the CAR comprises: (i) an extracellular domain comprising (a) an antibody or fragment of claim 1 or 2, or (b) an scFv of claim 3 or 4; (ii) a transmembrane domain; and (iii) an intracellular domain.
6. The CAR of claim 5, wherein the transmembrane domain is a CD3 transmembrane domain, a CD4 transmembrane domain, a CD8 transmembrane domain, or a CD28 transmembrane domain.
7. The CAR of claim 5 or 6, wherein:
 - a) the intracellular domain comprises an activation domain, wherein, when the CAR is expressed in a T cell, the activation domain transmits an activation signal after the extracellular domain binds FLT3; or
 - b) wherein the intracellular domain comprises an activation domain, wherein the activation domain comprises an intracellular signaling domain of CD3zeta, CD3epsilon, or FcRgamma.
8. The CAR of claim 7, wherein the intracellular domain further comprises one or more co-stimulatory domains.
9. The CAR of claim 8, wherein the one or more co-stimulatory domains are from one or more of: CD28, 4-1BB, CD27, OX40 or ICOS, preferably CD28 and/or 4-1BB.

10. The CAR of any one of claims 5-9, wherein the CAR comprises a spacer or hinge region between the extracellular domain and the transmembrane domain; wherein the spacer or hinge region is preferably from the extracellular domain of CD8; wherein the extracellular domain preferably comprises a cleavable signal peptide.
11. The CAR of claim 5, wherein a) the extracellular domain comprises an scFv comprising the amino acid sequence of SEQ ID NO:4; the transmembrane domain comprises a CD8 transmembrane domain; and the intracellular domain comprises an intracellular signaling domain of CD3zeta and a co-stimulatory domain of CD28 and/or 4-1BB and/or b) where the CAR comprises the amino acid sequence selected from the group consisting of: SEQ ID NO:6, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, and SEQ ID NO:15.
12. The CAR of any one of claims 5-11, which further comprises a safety switch polypeptide, wherein the safety switch polypeptide is bound to the CAR by a self-cleaving peptide, wherein the safety switch polypeptide is preferably iCasp9 or EGFRt, and wherein the self-cleaving peptide is preferably T2A, P2A, E2A, F2A or IRES.
13. The CAR of any one of claims 5-12, wherein a T cell expressing the CAR is activated or stimulated to proliferate when the extracellular domain binds to FLT3.
14. The CAR of any one of claims 5-13, wherein the CAR, when expressed on the surface of a T cell, directs the T cell to kill a cell expressing FLT3.
15. An immune cell expressing a CAR of any one of claims 5-14 or comprising a nucleic acid encoding a CAR of any one of claims 5-14.
16. The immune cell of claim 15, wherein the immune cell is a T cell, a NK cell, a macrophage or a monocyte, preferably a T cell.

17. The immune cell of claim 15 or 16, wherein the immune cell comprises a nucleic acid, wherein the nucleic acid comprises a sequence selected from the group consisting of: SEQ ID NO:60, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, and SEQ ID NO:69.
18. The immune cell of any one of claims 15-17, wherein the immune cell has been derived from a subject before introducing the CAR or the nucleic acid, wherein the subject is preferably a human.
19. The immune cell of any one of claims 15-18, where the immune cell expressing the CAR or comprising the nucleic acid is further expanded to generate a population of cells.
20. A population of immune cells expressing a CAR of any one of claims 5-14 or comprising a nucleic acid encoding a CAR of any one of claims 5-14.
21. A pharmaceutical composition comprising (i) a humanized antibody or fragment of claim 1 or 2, an scFv of claim 3 or 4, an immune cell of any one of claims 15-19, or a population of immune cells of claim 20, and (ii) a pharmaceutically acceptable carrier.
22. Use of a therapeutically effective amount of: (i) an immune cell of any one of claims 15-19, (ii) a population of immune cells of claim 20, or (iii) a pharmaceutical composition of claim 21 in the manufacture of a medicament for treating a hematologic cancer in a subject in need thereof, wherein the medicament is to be administered to the subject.
23. The use of claim 22, where the hematologic cancer is acute myeloid leukemia (AML), acute lymphoblastic leukemia (ALL), chronic myeloid leukemia (CML), chronic lymphocytic leukemia (CLL), blastic plasmacytoid dendritic cell neoplasm (BPDCN), peripheral T cell lymphoma, follicular lymphoma, diffuse large B cell lymphoma, Hodgkin lymphoma, non-Hodgkin lymphoma, neuroblastoma, a non-malignant inherited or acquired marrow disorder, multiple myeloma, or a dendritic cell neoplasm, preferably AML, ALL or dendritic cell neoplasm.

24. Use of a therapeutically effective amount of: (i) an immune cell of any one of claims 15-19, (ii) a population of immune cells of claim 20, or (ii) a pharmaceutical composition of claim 21 in the manufacture of a medicament for preparing or conditioning a subject in need thereof for hematopoietic cell transplantation, wherein the medicament is to be administered to the subject.
25. The use of claim 24, wherein the therapeutically effective amount reduces the cell population expressing FLT3 by at least 90% in the subject.
26. The use of claim 24 or 25, wherein the subject in need thereof has a hematologic cancer.
27. The use of claim 26, wherein the hematologic cancer is acute myeloid leukemia (AML), acute lymphoblastic leukemia (ALL), chronic myeloid leukemia (CML), chronic lymphocytic leukemia (CLL), blastic plasmacytoid dendritic cell neoplasm (BPDCN), peripheral T cell lymphoma, follicular lymphoma, diffuse large B cell lymphoma, Hodgkin lymphoma, non-Hodgkin lymphoma, neuroblastoma, a non-malignant inherited or acquired marrow disorder, multiple myeloma, or a dendritic cell neoplasm, preferably AML, ALL or dendritic cell neoplasm.
28. The use of any one of claims 22-27, wherein a) the medicament reduces circulating myeloid lineages in the subject, optionally wherein the medicament reduces circulating myeloid lineages by at least 60%, at least 65%, at least 70%, at least 75%, at least 80% or at least 85% relative to baseline levels; b) the medicament reduces bone marrow lineage frequencies and numbers in the subject, optionally wherein the medicament reduces bone marrow frequencies and/or numbers by at least 50%, at least 55% or at least 60% relative to baseline levels; c) the medicament specifically targets human CD34⁺ hematopoietic stem cells and/or hematopoietic progenitor cells; and/or d) the medicament reduces human CD34⁺CD38⁺ cell population in bone marrow mononuclear cells of the subject by at least 50%, at least 55%, at least 60% or at least 65% relative to baseline levels, and/or

reduces human CD34⁺CD38⁻ cell population in bone marrow mononuclear cells of the subject by at least 60%, at least 65%, at least 70%, at least 75%, at least 80% or at least 85% relative to baseline levels.

29. The use of any one of claims 22-28, wherein hematopoietic cell transplantation to the subject is to be further performed after administration.
30. The use of claim 29, wherein the hematopoietic cell transplantation comprises transplantation to the subject of hematopoietic stem cells and/or hematopoietic progenitor cells; wherein the hematopoietic cell transplantation preferably occurs 5 days to 6 weeks after the administration, or wherein the hematopoietic cell transplantation preferably occurs about 2 to 3 weeks after the administration.
31. The use of any one of claims 22-30, wherein the therapeutically effective amount of the immune cells or the population of immune cells is a dose from about 50,000,000 to 10,000,000,000 cells, preferably about 100,000,000 to 2,000,000,000 cells.
32. The use of any one of claims 22-31, wherein the administration is intravenous, preferably by infusion into the subject.
33. The use of any one of claims 22-32, wherein the administration occurs once or every 3-7 days for 2 to 3 weeks.
34. The use of any one of claims 22-33, wherein the following steps are to be performed prior to administration of the medicament:
 - (i) isolating immune cells from blood that has been collected from the subject;
 - (ii) introducing a nucleic acid encoding a CAR of any one of claims 5-18 into the isolated immune cells; and
 - (iii) expanding the isolated immune cells obtained in step (ii), wherein the expanding yields the immune cells or the population of immune cells that are to be administered to the subject .

35. The use of any one of claims 22-34, wherein a checkpoint inhibitor is to be further administered, wherein the checkpoint inhibitor is preferably an antagonist of PD1, PD-L1 or CTLA4, wherein the antagonist is preferably an antagonistic antibody.
36. The use of any one of claims 22-35, wherein the subject is a human.