

CLAIMS

WHAT IS CLAIMED IS:

1. ~~Use of a~~A recombinant antibody that specifically binds Leukemia Inhibitory Factor (LIF) ~~for use in the manufacture of a medicament for treating a cancer, wherein the recombinant antibody comprises:~~

- a) an immunoglobulin heavy chain complementarity determining region 1 (VH-CDR1) comprising an amino acid sequence set forth in ~~any one of SEQ ID NOs: 1-3~~SEQ ID NO: 2 (GFTFSHAW);
- b) an immunoglobulin heavy chain complementarity determining region 2 (VH-CDR2) comprising an amino acid sequence set forth in ~~any one of SEQ ID NOs: 4 or 5~~SEQ ID NO: 5 (IKAKSDDYAT);
- c) an immunoglobulin heavy chain complementarity determining region 3 (VH-CDR3) comprising an amino acid sequence set forth in ~~any one of SEQ ID NOs: 6-8~~SEQ ID NO: 6 (TCWEWDLDF);
- d) an immunoglobulin light chain complementarity determining region 1 (VL-CDR1) comprising an amino acid sequence set forth in ~~any one of SEQ ID NOs: 9 or 10~~SEQ ID NO: 10 (QSLDSDGHTY);
- e) an immunoglobulin light chain complementarity determining region 2 (VL-CDR2) comprising an amino acid sequence set forth in ~~any one of SEQ ID NOs: 11 or 12~~SEQ ID NO: 12 (SVS); and
- f) an immunoglobulin light chain complementarity determining region 3 (VL-CDR3) comprising an amino acid sequence set forth in SEQ ID NO: 13 (MQATHAPPYT);

wherein the recombinant antibody is to be administered to ~~the an~~an individual at a dose ~~from about 75 to about 2000 milligrams~~of about 1500 milligrams.

~~2. The use of claim 1, wherein the recombinant antibody binds to glycosylated LIF.~~

~~3.2. The antibody for use of claim 1 or 2, wherein the recombinant antibody is humanized.~~

~~4. The use of any one of claims 1 to 3, wherein the recombinant antibody is deimmunized.~~

~~5.3. The antibody for use of any one of claims 1 to 4~~claim 1 or claim 2, wherein the recombinant antibody comprises two immunoglobulin heavy chains and two immunoglobulin light chains.

~~6.4. The antibody for use of claim 53, wherein the recombinant antibody is an IgG antibody.~~

~~7.5.~~ The antibody for use of any one of claims 1 to 4 claim 1 or claim 2, wherein the recombinant antibody is a Fab, F(ab)₂, ~~single domain antibody, or~~ a single chain variable fragment (scFv), ~~or a nanobody.~~

~~8.6.~~ The antibody for use of any one of claims 1 to 75, wherein the recombinant antibody specifically binds LIF with a dissociation constant (K_D) of less than about 200 picomolar, preferably less than about 100 picomolar.

~~9.~~ The use of any one of claims 1 to 7, wherein the recombinant antibody specifically binds LIF with a dissociation constant (K_D) of less than about 100 picomolar.

7. The antibody for use of any one of claims 1 to 96, wherein the VH-CDR1 comprises an amino acid sequence set forth in SEQ ID NO: 1 (GFTFSHAWMH), wherein the VH-CDR2 comprises an amino acid sequence set forth in SEQ ID NO: 4 (QIKAKSDDYATYYAESVKG), wherein the VH-CDR3 comprises an amino acid sequence set forth in SEQ ID NO: 6 (TCWEWDLDF), wherein the VL-CDR1 comprises an amino acid sequence set forth in SEQ ID NO: 9 (RSSQSLLDSDGHTYLN), wherein the VL-CDR2 comprises an amino acid sequence set forth in SEQ ID NO: 11 (SVSNLES), and wherein the VL-CDR3 comprises an amino acid sequence set forth in SEQ ID NO: 13 (MQATHAPPYT).

8. The antibody for use in any one of claims 1-7, wherein the recombinant antibody comprises a VH sequence at least 90% identical to the amino acid sequence set forth in SEQ ID NO: 42; and wherein the recombinant antibody comprises a VL sequence at least 90% identical to the amino acid sequence set forth in SEQ ID NO: 46.

~~10.9.~~ The antibody for use in claim 8, wherein the VH sequence is identical to the amino acid sequence set forth in SEQ ID NO: 42; and the VL sequence is identical to the amino acid sequence set forth in SEQ ID NO: 46.

~~11.~~ The use of any one of claims 1 to 9, wherein the VH-CDR1 comprises an amino acid sequence set forth in SEQ ID NO: 2 (GFTFSHAW), wherein the VH-CDR2 comprises an amino acid sequence set forth in SEQ ID NO: 5 (IKAKSDDYAT), wherein the VH-CDR3 comprises an amino acid sequence set forth in SEQ ID NO: 6 (TCWEWDLDF), wherein the VL-CDR1 comprises an amino acid sequence set forth in SEQ ID NO: 10 (QSLLDSDGHTYLN), wherein the VL-CDR2 comprises an amino acid sequence set forth in SEQ ID NO: 12 (SVS), and wherein the VL-CDR3 comprises an amino acid sequence set forth in SEQ ID NO: 13 (MQATHAPPYT).

~~12.~~ The use of any one of claims 1 to 9, wherein the VH-CDR1 comprises an amino acid sequence set forth in SEQ ID NO: 3 (HAWMH), wherein the VH-CDR2 comprises an amino acid sequence set forth in SEQ ID NO: 4 (QIKAKSDDYATYYAESVKG), wherein the VH-CDR3 comprises an amino acid sequence set forth in SEQ ID NO: 7 (WEWDLDF), wherein the

VL-CDR1 comprises an amino acid sequence set forth in SEQ ID NO: 9 (RSSQSLLDSDGHTYLN), wherein the VL-CDR2 comprises an amino acid sequence set forth in SEQ ID NO: 11 (SVSNLES), and wherein the VL-CDR3 comprises an amino acid sequence set forth in SEQ ID NO: 13 (MQATHAPPYT).

13. — The use according to any one of claims 1 to 12, wherein the recombinant antibody comprises:

- a) an immunoglobulin heavy chain variable region (VH) sequence with an amino acid sequence at least about 90% identical to the amino acid sequence set forth in any one of SEQ ID NOs: 41, 42, 44, or 66; and
- b) an immunoglobulin light chain variable region (VL) sequence with an amino acid sequence at least about 90% identical to the amino acid sequence set forth in any one of SEQ ID NOs: 45-48.

14. — The use of claim 13, wherein the VH sequence is at least about 90% identical to the amino acid sequence set forth in SEQ ID NO: 42; and the VL sequence is at least about 90% identical to the amino acid sequence set forth in SEQ ID NO: 46.

15. — The use of claim 14, wherein the VH sequence is identical to the amino acid sequence set forth in SEQ ID NO: 42; and the VL sequence is identical to the amino acid sequence set forth in SEQ ID NO: 46.

16. — The use according to any one of claims 1 to 15, wherein the recombinant antibody comprises:

- a) an immunoglobulin heavy chain sequence with an amino acid sequence at least about 90% identical to the amino acid sequence set forth in any one of SEQ ID NOs: 57-60 or 67; and
- b) an immunoglobulin light chain sequence with an amino acid sequence at least about 90% identical to the amino acid sequence set forth in any one of SEQ ID NOs: 61-64.

17. — The use of claim 16, wherein the immunoglobulin heavy chain sequence is at least about 90% identical to the amino acid sequence set forth in SEQ ID NO: 58; and the immunoglobulin light chain sequence is at least about 90% identical to the amino acid sequence set forth in SEQ ID NO: 62.

18. — The use of claim 17, wherein the immunoglobulin heavy chain sequence is identical to the amino acid sequence set forth in SEQ ID NO: 58; and the immunoglobulin light chain sequence is identical to the amino acid sequence set forth in SEQ ID NO: 62.

19-10. — The antibody use of any one of claims 1 to 18, wherein the cancer is an advanced solid tumor, glioblastoma, stomach cancer, skin cancer, prostate cancer, pancreatic cancer, breast cancer, testicular cancer, thyroid cancer, head and neck cancer, liver cancer, kidney

cancer, esophageal cancer, ovarian cancer, colon cancer, lung cancer, lymphoma, or soft tissue cancer.

~~20.11.~~ The antibody for use of claim ~~19~~10, wherein the cancer is non-small cell lung cancer, epithelial ovarian carcinoma, or pancreatic adenocarcinoma.

~~21.12.~~ The antibody for use of any one of claims 1 to ~~20~~11, wherein the recombinant antibody is to be administered as a component of a pharmaceutical formulation, wherein the pharmaceutical formulation comprising the recombinant antibody and a pharmaceutically acceptable excipient, carrier, or diluent.

~~22.13.~~ The antibody for use of claim ~~12~~21, wherein the pharmaceutical formulation has a pH of about 6.0 and comprises about 25mM histidine, about 6% sucrose, and about 0.01% polysorbate 80, and wherein the recombinant antibody is included at a concentration of about 20 mg/mL.

~~23.~~ The use of claim 21 or claim 22, wherein the pharmaceutical formulation comprises about 25mM histidine, about 6% sucrose, and about 0.01% polysorbate 80, wherein the recombinant antibody is included at a concentration of about 20 mg/mL.

~~24.14.~~ The antibody for use of any one of claims 1 to ~~23~~13, wherein the recombinant antibody is to be administered intravenously about once a week-, about once every two weeks, or about once every three weeks.

~~25.~~ The use of any one of claims 1 to 24, wherein the recombinant antibody is to be administered about once a week.

~~26.~~ The use of any one of claims 1 to 24, wherein the recombinant antibody is to be administered about once every two weeks.

~~27.15.~~ The antibody for use of ~~any one of claims 1 to 24~~claim 14, wherein the recombinant antibody is to be administered about once every three weeks.

~~28.~~ The use of any one of claims 1 to 27, wherein the recombinant antibody is to be administered at a dose of about 750 milligrams.

~~29.~~ The use of any one of claims 1 to 27, wherein the recombinant antibody is to be administered at a dose of about 1125 milligrams.

~~30.~~ The use of any one of claims 1 to 27, wherein the recombinant antibody is to be administered at a dose of about 1500 milligrams.

~~31.~~ The use of any one of claims 1 to 27, wherein the recombinant antibody is to be administered at a dose of about 2000 milligrams.