

CLAIMS

WHAT IS CLAIMED IS:

1. ~~A method of treating an individual with a cancer, comprising administering to the individual with the cancer an effective amount of:~~
 - ~~a) a Leukemia Inhibitory Factor (LIF) binding polypeptide; and~~
 - ~~b) a platinum-based antineoplastic agent for use in a combination therapy for treating an individual with a cancer, wherein an effective amount of the Leukemia Inhibitory Factor (LIF) binding polypeptide; and the platinum-based antineoplastic agent is to be administered to the individual with cancer.~~
2. Use of a Leukemia Inhibitory Factor (LIF) binding polypeptide; and a platinum-based antineoplastic agent in the manufacture of a medicament for a combination therapy for the treatment of cancer in an individual, wherein an effective amount of the Leukemia Inhibitory Factor (LIF) binding polypeptide; and the platinum-based antineoplastic agent is to be administered to the individual with cancer.
32. The Leukemia Inhibitory Factor (LIF) binding polypeptide; and the platinum-based antineoplastic agent for use ~~method of claim 04~~ or the use of claim 2, comprising administering wherein an effective amount of the LIF-binding polypeptide is to be further administered to the individual with cancer.
43. The Leukemia Inhibitory Factor (LIF) binding polypeptide; and the platinum-based antineoplastic agent for use ~~method of claim 04~~ or the use of claim 2, further comprising administering wherein an effective amount of the platinum-based antineoplastic agent is to be further administered to the individual with cancer.
54. The Leukemia Inhibitory Factor (LIF) binding polypeptide; and the platinum-based antineoplastic agent for use ~~method of claim 04~~ or the use of claim 2, wherein the LIF-binding polypeptide comprises a fragment of an immunoglobulin variable region, or an immunoglobulin heavy chain constant region.
65. The Leukemia Inhibitory Factor (LIF) binding polypeptide; and the platinum-based antineoplastic agent for use ~~method of claim 04~~ or the use of claim 2, wherein the LIF-binding polypeptide comprises an antibody that specifically binds to LIF.
76. The Leukemia Inhibitory Factor (LIF) binding polypeptide; and the platinum-based antineoplastic agent for use ~~or the use method of claim 56~~, wherein the antibody that specifically binds to LIF comprises at least one framework region derived from a human antibody framework region.

87. The Leukemia Inhibitory Factor (LIF) binding polypeptide; and the platinum-based antineoplastic agent for use or the use method of claim 56, wherein the antibody that specifically binds to LIF is humanized.

98. The Leukemia Inhibitory Factor (LIF) binding polypeptide; and the platinum-based antineoplastic agent for use or the use method of claim 56, wherein the antibody that specifically binds to LIF is deimmunized.

109. The Leukemia Inhibitory Factor (LIF) binding polypeptide; and the platinum-based antineoplastic agent for use or the use method of claim 56, wherein the antibody that specifically binds to LIF comprises two immunoglobulin heavy chains and two immunoglobulin light chains.

1140. The Leukemia Inhibitory Factor (LIF) binding polypeptide; and the platinum-based antineoplastic agent for use or the use method of claim 56, wherein the antibody that specifically binds to LIF is an IgG antibody.

1244. The Leukemia Inhibitory Factor (LIF) binding polypeptide; and the platinum-based antineoplastic agent for use or the use method of claim 56, wherein the antibody that specifically binds to LIF is a Fab, F(ab)₂, single-domain antibody, a single chain variable fragment (scFv), or a nanobody.

1312. The Leukemia Inhibitory Factor (LIF) binding polypeptide; and the platinum-based antineoplastic agent for use or the use method of claim 56, wherein the antibody that specifically binds to LIF comprises:

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

1413. The Leukemia Inhibitory Factor (LIF) binding polypeptide; and the platinum-based antineoplastic agent for use or the use method of claim 56, wherein the antibody that specifically binds to LIF comprises:

- a) an immunoglobulin heavy chain variable region (VH) sequence with the amino acid sequence at least about 80%, 90%, 95%, 97%, 98%, 99%, or 100% 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 the amino acid sequence at least about 80%, 90%, 95%, 97%, 98%, 99%, or 100% identical to the amino acid sequence set forth in any one of SEQ ID NOs: 45-48.

1514. The Leukemia Inhibitory Factor (LIF) binding polypeptide; and the platinum-based antineoplastic agent for use or the use method of claim 1314, wherein the VH sequence is at least about 80%, 90%, 95%, 97%, 98%, 99%, or 100% identical to the amino acid sequence set forth in SEQ ID NO: 42; and the VL sequence is at least about 80%, 90%, 95%, 97%, 98%, 99%, or 100% identical to the amino acid sequence set forth in SEQ ID NO: 46.

1615. The Leukemia Inhibitory Factor (LIF) binding polypeptide; and the platinum-based antineoplastic agent for use or the use method of claim 1415, 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.

1716. The Leukemia Inhibitory Factor (LIF) binding polypeptide; and the platinum-based antineoplastic agent for use or the use method of claim 56, wherein the antibody that specifically binds to LIF comprises:

- a) an immunoglobulin heavy chain sequence with the amino acid sequence at least about 80%, 90%, 95%, 97%, 98%, or 99% 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 the amino acid sequence at least about 80%, 90%, 95%, 97%, 98%, or 99% identical to the amino acid sequence set forth in any one of SEQ ID NOs: 61-64.

1817. The Leukemia Inhibitory Factor (LIF) binding polypeptide; and the platinum-based antineoplastic agent for use or the use method of claim 56, wherein the antibody that specifically binds to LIF binds with a K_D of less than about 200 picomolar.

1918. The Leukemia Inhibitory Factor (LIF) binding polypeptide; and the platinum-based antineoplastic agent for use or the use method of claim 56, wherein the antibody that specifically binds to LIF binds with a K_D of less than about 100 picomolar.

2019. The Leukemia Inhibitory Factor (LIF) binding polypeptide; and the platinum-based antineoplastic agent for use method of claim 01 or the use of claim 2, wherein the platinum-

based antineoplastic agent comprises cisplatin, carboplatin, oxaliplatin, nedaplatin, triplatin tetranitrate, phenathriplatin, picoplatin, satraplatin, or combinations thereof.

2120. The Leukemia Inhibitory Factor (LIF) binding polypeptide; and the platinum-based antineoplastic agent for use or the use method of claim 1920, wherein the platinum-based antineoplastic agent is cisplatin.

2221. The Leukemia Inhibitory Factor (LIF) binding polypeptide; and the platinum-based antineoplastic agent for use method of claim 01 or the use of claim 2, wherein the cancer comprises 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.

2322. The Leukemia Inhibitory Factor (LIF) binding polypeptide; and the platinum-based antineoplastic agent for use or the use method of claim 2422, wherein the cancer comprises non-small cell lung cancer, epithelial ovarian carcinoma, or pancreatic adenocarcinoma.

2423. The Leukemia Inhibitory Factor (LIF) binding polypeptide; and the platinum-based antineoplastic agent for use method of claim 01 or the use of claim 2, wherein the cancer is refractory to treatment with a therapeutic amount of an inhibitor of a LIF-binding polypeptide.

2524. The Leukemia Inhibitory Factor (LIF) binding polypeptide; and the platinum-based antineoplastic agent for use method of claim 01 or the use of claim 2, wherein the cancer is refractory to treatment with a therapeutic amount of a platinum-based antineoplastic agent.

2625. The Leukemia Inhibitory Factor (LIF) binding polypeptide; and the platinum-based antineoplastic agent for use method of claim 01 or the use of claim 2, wherein the Leukemia Inhibitory Factor (LIF) binding polypeptide and the platinum-based antineoplastic agent are to be administered separately.

2726. The Leukemia Inhibitory Factor (LIF) binding polypeptide; and the platinum-based antineoplastic agent for use method of claim 01 or the use of claim 2, wherein the LIF-binding polypeptide and the platinum-based antineoplastic agent are to be administered on different schedules.

2827. The Leukemia Inhibitory Factor (LIF) binding polypeptide; and the platinum-based antineoplastic agent for use method of claim 01 or the use of claim 2, wherein the LIF-binding polypeptide and the platinum-based antineoplastic agent are to be administered in a single composition.

2928. A ~~method of treating an individual with a cancer comprising administering to the individual with cancer an effective amount of a combination of:~~

a) ~~of~~ an antibody that specifically binds Leukemia Inhibitory Factor (LIF) comprising:

- i. an immunoglobulin heavy chain complementarity determining region 1 (VH-CDR1) comprising the amino acid sequence set forth in any one of SEQ ID NOs: 1-3;
- ii. an immunoglobulin heavy chain complementarity determining region 2 (VH-CDR2) comprising the amino acid sequence set forth in any one of SEQ ID NOs: 4 or 5;
- iii. an immunoglobulin heavy chain complementarity determining region 3 (VH-CDR3) comprising the amino acid sequence set forth in any one of SEQ ID NOs: 6-8;
- iv. an immunoglobulin light chain complementarity determining region 1 (VL-CDR1) comprising the amino acid sequence set forth in any one of SEQ ID NOs: 9 or 10;
- v. an immunoglobulin light chain complementarity determining region 2 (VL-CDR2) comprising the amino acid sequence set forth in any one of SEQ ID NOs: 11 or 12; and
- vi. an immunoglobulin light chain complementarity determining region 3 (VL-CDR3) comprising the amino acid sequence set forth in SEQ ID NO: 13; and

b) a platinum-based antineoplastic agent,

for use in treating an individual with a cancer, wherein an effective amount of the combination is to be administered to the individual with cancer.

30. Use of a combination of:

a) an antibody that specifically binds Leukemia Inhibitory Factor (LIF) comprising:

- i. an immunoglobulin heavy chain complementarity determining region 1 (VH-CDR1) comprising the amino acid sequence set forth in any one of SEQ ID NOs: 1-3;
- ii. an immunoglobulin heavy chain complementarity determining region 2 (VH-CDR2) comprising the amino acid sequence set forth in any one of SEQ ID NOs: 4 or 5;
- iii. an immunoglobulin heavy chain complementarity determining region 3 (VH-CDR3) comprising the amino acid sequence set forth in any one of SEQ ID NOs: 6-8;
- iv. an immunoglobulin light chain complementarity determining region 1 (VL-CDR1) comprising the amino acid sequence set forth in any one of SEQ ID NOs: 9 or 10;

v. an immunoglobulin light chain complementarity determining region 2 (VL-CDR2) comprising the amino acid sequence set forth in any one of SEQ ID NOs: 11 or 12; and

vi. an immunoglobulin light chain complementarity determining region 3 (VL-CDR3) comprising the amino acid sequence set forth in SEQ ID NO: 13; and

b) a platinum-based antineoplastic agent,

in the manufacture of a medicament for the treatment of cancer in an individual, wherein an effective amount of the combination is to be administered to the individual with cancer.

3129. The combination for use method of claim 2829 or the use of claim 30, further comprising administering wherein an effective amount of the LIF-binding polypeptide is to be further administered to the individual with cancer.

3230. The combination for use method of claim 2829 or the use of claim 30, further comprising administering wherein an effective amount of the platinum-based antineoplastic agent is to be further administered to the individual with cancer.