

WHAT IS CLAIMED IS:

1. An antibody, wherein the antibody comprises:
 - (a) a heavy chain variable domain and a light chain variable domain selected from the group of:
 - (i) a heavy chain variable domain that is at least 90% identical to SEQ ID NO: 1 and wherein the heavy chain variable domain includes a histidine at one or more positions in SEQ ID NO: 1 selected from the group consisting of: 33, 34, 50, 52, 57, 59, 100, 102, 103, 107, 108, and 109; and/or a light chain variable domain that is at least 90% identical to SEQ ID NO: 2, wherein the light chain variable domain includes a histidine at one or more positions in SEQ ID NO: 2 selected from the group consisting of: 32, 34, 50, 51, 89, 90, 92, 93, 94, and 96;
 - (ii) a heavy chain variable domain that is at least 90% identical to SEQ ID NO: 84, wherein the heavy chain variable domain includes a histidine at one or more positions in SEQ ID NO: 84 selected from the group consisting of: 27, 29, 32, 50, 54, 58, 99, 100, 102, 104, and 105; and/or a light chain variable domain that is at least 90% identical to SEQ ID NO: 85, wherein the light chain variable domain includes a histidine at one or more positions in SEQ ID NO: 85 selected from the group consisting of: 29, 31, 32, 34, 36, 37, 38, 40, 56, 60, 61, 95, 96, 97, and 100;
 - (iii) a heavy chain variable domain that is at least 90% identical to SEQ ID NO: 178, wherein the heavy chain variable domain includes a histidine at one or more positions in SEQ ID NO: 178 selected from the group consisting of: 33, 52, 56, 57, or 106; and/or a light chain variable domain that is at least 90% identical to SEQ ID NO: 179, wherein the light chain variable domain includes a histidine at one or more positions in SEQ ID NO: 179 selected from the group consisting of 25, 26, 28, 29, 31, 36, 37, 57, 59, 94, 95, 96, and 100; and
 - (iv) a heavy chain variable domain that is at least 90% identical to SEQ ID NO: 272, wherein the heavy chain variable domain includes a histidine at one or

more positions in SEQ ID NO: 272 selected from the group consisting of: 24, 27, 29, 62, 63, 98, and 108; and/or

a light chain variable domain that is at least 90% identical to SEQ ID NO: 273, wherein the light chain variable domain includes a histidine at one or more positions in SEQ ID NO: 273 selected from the group consisting of 27, 28, 29, 31, 32, 89, 92, and 93;

(b) a heavy chain CH1-CH2-CH3 sequence of SEQ ID NO: 351 or SEQ ID NO: 352 comprising one or more of the following:

(i) a methionine to tyrosine substitution at amino acid position 135, a serine to threonine substitution at amino acid position 137, and a threonine to glutamic acid substitution at amino acid position 139;

(ii) a methionine to leucine substitution at amino acid position 311 and an asparagine to serine substitution at amino acid position 317; and

(iii) an alanine to a cysteine substitution at amino acid position 1;
and/or

a light chain C_L sequence of SEQ ID NO: 353 comprising a valine to cysteine substitution at amino acid position 98.

2. The antibody of claim 1, wherein the heavy chain CH1-CH2-CH3 sequence of SEQ ID NO: 351 or SEQ ID NO: 352 comprises:

a methionine to leucine substitution at amino acid position 311 and an asparagine to serine substitution at amino acid position 317.

3. The antibody of claim 2, wherein the antibody comprises heavy chain and light chain sequences selected from the group of:

(i) SEQ ID NO: 354 and SEQ ID NO: 2, respectively;

(ii) SEQ ID NO: 360 and SEQ ID NO: 85, respectively;

(iii) SEQ ID NO: 366 and SEQ ID NO: 179, respectively; and

(iv) SEQ ID NO: 372 and SEQ ID NO: 273, respectively.

4. The antibody of claim 1, wherein the heavy chain CH1-CH2-CH3 sequence of SEQ ID NO: 351 or SEQ ID NO: 352 comprises:

a methionine to tyrosine substitution at amino acid position 135, a serine to threonine substitution at amino acid position 137, and a threonine to glutamic acid substitution at amino acid position 139.

5. The antibody of claim 4, wherein the antibody comprises heavy chain and light chain sequences selected from the group of:

- (i) SEQ ID NO: 355 and SEQ ID NO: 2, respectively;
- (ii) SEQ ID NO: 361 and SEQ ID NO: 85, respectively;
- (iii) SEQ ID NO: 367 and SEQ ID NO: 179, respectively; and
- (iv) SEQ ID NO: 373 and SEQ ID NO: 273, respectively.

6. The antibody of claim 1, wherein the antibody wherein:

the light chain C_L sequence of SEQ ID NO: 353 comprises a valine to cysteine substitution at amino acid position 98.

7. The antibody of claim 6, wherein the antibody comprises heavy chain and light chain sequences selected from the group of:

- (i) SEQ ID NO: 1 and SEQ ID NO: 359, respectively;
- (ii) SEQ ID NO: 84 and SEQ ID NO: 365, respectively;
- (iii) SEQ ID NO: 178 and SEQ ID NO: 371, respectively; and
- (iv) SEQ ID NO: 272 and SEQ ID NO: 377, respectively.

8. The antibody of claim 1, wherein:

the heavy chain CH1-CH2-CH3 sequence of SEQ ID NO: 351 or SEQ ID NO: 352 comprises:

a methionine to leucine substitution at amino acid position 311 and an asparagine to serine substitution at amino acid position 317; and

the light chain C_L sequence of SEQ ID NO: 353 comprises a valine to cysteine substitution at amino acid position 98.

9. The antibody of claim 8, wherein the antibody comprises heavy chain and light chain sequences selected from the group of:

- (i) SEQ ID NO: 354 and SEQ ID NO: 359, respectively;
- (ii) SEQ ID NO: 360 and SEQ ID NO: 365, respectively;
- (iii) SEQ ID NO: 366 and SEQ ID NO: 371, respectively; and
- (iv) SEQ ID NO: 372 and SEQ ID NO: 377, respectively.

10. The antibody of claim 1, wherein:

the heavy chain CH1-CH2-CH3 sequence of SEQ ID NO: 351 or SEQ ID NO: 352 comprises:

a methionine to tyrosine substitution at amino acid position 135, a serine to threonine substitution at amino acid position 137, and a threonine to glutamic acid substitution at amino acid position 139; and

the light chain C_L sequence of SEQ ID NO: 353 comprises a valine to cysteine substitution at amino acid position 98.

11. The antibody of claim 10, wherein the antibody comprises heavy chain and light chain sequences selected from the group of:

- (i) SEQ ID NO: 355 and SEQ ID NO: 359, respectively;
- (ii) SEQ ID NO: 361 and SEQ ID NO: 365, respectively;
- (iii) SEQ ID NO: 367 and SEQ ID NO: 371, respectively; and
- (iv) SEQ ID NO: 373 and SEQ ID NO: 377, respectively.

12. The antibody of claim 1, wherein the heavy chain CH1-CH2-CH3 sequence of SEQ ID NO: 351 or SEQ ID NO: 352 comprises:

an alanine to a cysteine substitution at amino acid position 1.

13. The antibody of claim 12, wherein the antibody comprises heavy chain and light chain sequences selected from the group of:

- (i) SEQ ID NO: 356 and SEQ ID NO: 2, respectively;
- (ii) SEQ ID NO: 362 and SEQ ID NO: 85, respectively;

- (iii) SEQ ID NO: 368 and SEQ ID NO: 179, respectively; and
- (iv) SEQ ID NO: 374 and SEQ ID NO: 273, respectively.

14. The antibody of claim 1, wherein the heavy chain CH1-CH2-CH3 sequence of SEQ ID NO: 351 or SEQ ID NO: 352 comprises:

a methionine to leucine substitution at amino acid position 311 and an asparagine to serine substitution at amino acid position 317; and
an alanine to a cysteine substitution at amino acid position 1.

15. The antibody of claim 16, wherein the antibody comprises a heavy chain and a light chain sequence selected from the group of:

- (i) SEQ ID NO: 357 and SEQ ID NO: 2, respectively;
- (ii) SEQ ID NO: 363 and SEQ ID NO: 85, respectively;
- (iii) SEQ ID NO: 369 and SEQ ID NO: 179, respectively; and
- (iv) SEQ ID NO: 375 and SEQ ID NO: 273, respectively.

16. The antibody of claim 1, wherein the heavy chain CH1-CH2-CH3 sequence of SEQ ID NO: 351 or SEQ ID NO: 352 comprises:

a methionine to tyrosine substitution at amino acid position 135, a serine to threonine substitution at amino acid position 137, and a threonine to glutamic acid substitution at amino acid position 139; and
an alanine to a cysteine substitution at amino acid position 1.

17. The antibody of claim 18, wherein the antibody comprises a heavy chain and a light chain sequence selected from the group of:

- (i) SEQ ID NO: 358 and SEQ ID NO: 2, respectively;
- (ii) SEQ ID NO: 364 and SEQ ID NO: 85, respectively;
- (iii) SEQ ID NO: 370 and SEQ ID NO: 179, respectively; and
- (iv) SEQ ID NO: 376 and SEQ ID NO: 273, respectively.

18. The antibody of any one of claims 1-17, wherein the antibody further comprises a cytotoxic drug conjugated to one or more of the following:

(a) a heavy chain CH1-CH2-CH3 of SEQ ID NO: 351 or SEQ ID NO: 352 comprising one or more of the following:

- (i) the cysteine at amino acid position 103;
- (ii) the cysteine at amino acid position 109;
- (iii) the cysteine at amino acid position 112; and/or

(b) the cysteine at amino acid position 107 of SEQ ID NO: 353.

19. The antibody of any one of claims 6-11 and 18, wherein the antibody further comprises a cytotoxic or cytostatic agent is conjugated to the cysteine at position 98 of SEQ ID NO: 353.

20. The antibody of any one of claims 12-18, wherein the antibody further comprises a cytotoxic or cytostatic agent is conjugated to the cysteine at position 1 of SEQ ID NO: 351 or SEQ ID NO: 352.

21. The antibody of any one of claims 1-20, wherein the first antigen-binding domain comprises one of (a) through (d):

(a) a light chain variable domain of SEQ ID NO: 2, SEQ ID NO: 61, SEQ ID NO: 63, SEQ ID NO: 64, SEQ ID NO: 65, SEQ ID NO: 71, SEQ ID NO: 72, SEQ ID NO: 74, SEQ ID NO: 75, SEQ ID NO: 76, or SEQ ID NO: 78 and/or

a heavy chain variable domain of SEQ ID NO: 1, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 23, SEQ ID NO: 25, SEQ ID NO: 30, SEQ ID NO: 32, SEQ ID NO: 43, SEQ ID NO: 45, SEQ ID NO: 46, SEQ ID NO: 50, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 80, SEQ ID NO: 81, SEQ ID NO: 82, or SEQ ID NO: 83,

wherein the first antigen-binding domain does not comprise (i) a light chain variable domain of SEQ ID NO: 2 and a heavy chain variable domain of SEQ ID NO: 1; (ii) a light chain variable domain of SEQ ID NO: 2 and heavy chain variable domain that is not one of SEQ ID NOs: 20, 21, 23, 25, 30, 32, 43, 45, 46, 50-52, or 80-83; or (iii) a heavy chain variable domain of

SEQ ID NO: 1 and a light chain variable domain that is not one of SEQ ID NOs: 61, 63-65, 71, 72, 74-76, or 78;

(b) a light chain variable domain of SEQ ID NO: 85, SEQ ID NO: 137, SEQ ID NO: 139, SEQ ID NO: 140, SEQ ID NO: 142, SEQ ID NO: 144, SEQ ID NO: 145, SEQ ID NO: 146, SEQ ID NO: 148, SEQ ID NO: 149, SEQ ID NO: 153, SEQ ID NO: 154, SEQ ID NO: 156, SEQ ID NO: 157, SEQ ID NO: 158, SEQ ID NO: 161, SEQ ID NO: 169, SEQ ID NO: 170, SEQ ID NO: 171, SEQ ID NO: 172, SEQ ID NO: 173, SEQ ID NO: 174, SEQ ID NO: 175, SEQ ID NO: 176, or SEQ ID NO: 177, and/or

a heavy chain variable domain of SEQ ID NO: 84, SEQ ID NO: 93, SEQ ID NO: 95, SEQ ID NO: 98, SEQ ID NO: 101, SEQ ID NO: 102, SEQ ID NO: 106, SEQ ID NO: 110, SEQ ID NO: 120, SEQ ID NO: 121, SEQ ID NO: 122, SEQ ID NO: 124, SEQ ID NO: 126, SEQ ID NO: 127, or SEQ ID NO: 166,

wherein the first antigen-binding domain does not comprise (i) a light chain variable domain of SEQ ID NO: 85 and a heavy chain variable domain of SEQ ID NO: 84; (ii) a light chain variable domain of SEQ ID NO: 85 and heavy chain variable domain that is not one of SEQ ID NOs: 93, 95, 98, 101, 102, 106, 110, 120-122, 124, 126, 127, or 166; or (iii) a heavy chain variable domain of SEQ ID NO: 84 and a light chain variable domain that is not one of SEQ ID NOs: 137, 139, 140, 142, 144-146, 148, 149, 153, 154, 156-158, 161, or 169-177;

(c) a light chain variable domain of SEQ ID NO: 179, SEQ ID NO: 229, SEQ ID NO: 230, SEQ ID NO: 232, SEQ ID NO: 233, SEQ ID NO: 235, SEQ ID NO: 240, SEQ ID NO: 241, SEQ ID NO: 246, SEQ ID NO: 248, SEQ ID NO: 251, SEQ ID NO: 252, SEQ ID NO: 253, SEQ ID NO: 257, SEQ ID NO: 263, SEQ ID NO: 264, SEQ ID NO: 268, SEQ ID NO: 269, SEQ ID NO: 270, or SEQ ID NO: 271, and/or

a heavy chain variable domain of SEQ ID NO: 178, SEQ ID NO: 196, SEQ ID NO: 201, SEQ ID NO: 205, SEQ ID NO: 206, SEQ ID NO: 225, SEQ ID NO: 258, SEQ ID NO: 259, SEQ ID NO: 260, or SEQ ID NO: 261,

wherein the first antigen-binding domain does not comprise (i) a light chain variable domain of SEQ ID NO: 179 and a heavy chain variable domain of SEQ ID NO: 178; (ii) a light chain variable domain of SEQ ID NO: 179 and heavy chain variable domain that is not one of SEQ ID NOs: 196, 201, 205, 206, 225, or 258-261; or (iii) a heavy chain variable domain of

SEQ ID NO: 178 and a light chain variable domain that is not one of SEQ ID NOs: 229, 230, 232, 233, 235, 240, 241, 246, 248, 251-253, 257, 263, 264, or 268-271; and

(d) a light chain variable domain of SEQ ID NO: 273, SEQ ID NO: 327, SEQ ID NO: 328, SEQ ID NO: 329, SEQ ID NO: 331, SEQ ID NO: 332, SEQ ID NO: 342, SEQ ID NO: 345, or SEQ ID NO: 346 and/or

a heavy chain variable domain of SEQ ID NO: 272, SEQ ID NO: 281, SEQ ID NO: 284, SEQ ID NO: 286, SEQ ID NO: 305, SEQ ID NO: 306, SEQ ID NO: 311, or SEQ ID NO: 321,

wherein the first antigen-binding domain does not comprise (i) a light chain variable domain of SEQ ID NO: 273 and a heavy chain variable domain of SEQ ID NO: 272; (ii) a light chain variable domain of SEQ ID NO: 273 and heavy chain variable domain that is not one of SEQ ID NOs: 281, 284, 286, 305, 306, 311, or 321; or (iii) a heavy chain variable domain of SEQ ID NO: 272 and a light chain variable domain that is not one of SEQ ID NOs: 327-329, 331, 332, 342, 345, or 346.

22. A pharmaceutical composition comprising the antibody of any one of claims 1-21.

23. A kit comprising at least one dose of the antibody of any one of claims 1-2 or the pharmaceutical composition of claim 22.

24. Use of the antibody of any one of claims 1-21 or the pharmaceutical composition of claim 22 in the manufacture of a medicament for treating cancer in a subject; wherein the cancer is characterized by having a population of cancer cells that have LRRC15 or an epitope of LRRC15 presented on their surface.