

CLAIMS

1. ~~A method of treating a cancer in a subject in need thereof, the method comprising:
administering to the subject an effective amount of an anti-Dkk-1 antibody or antigen binding fragment thereof,
wherein the subject is determined to have a constitutively activating mutation of beta-catenin protein (SEQ ID NO:2), and
wherein the cancer is an esophageal cancer, a uterine cancer, a liver cancer, or a cholangiocarcinoma.~~
2. ~~A method of treating a subject suffering from a cancer, comprising the steps of:
obtaining a sample of a cancer cell from the subject;
determining a sequence of a beta-catenin protein in the sample; and
administering to the subject an effective amount of an anti-Dkk-1 antibody or antigen binding fragment thereof if the sequence of a beta-catenin protein (SEQ ID NO: 2) includes a constitutively activating mutation,
wherein the cancer is an esophageal cancer, a uterine cancer, a liver cancer, or a cholangiocarcinoma.~~
3. ~~A method of treating a cancer in a subject in need thereof, the method comprising:
administering to the subject an effective amount of an anti-Dkk-1 antibody or antigen binding fragment thereof,
wherein the subject has a constitutively activating mutation of a beta-catenin protein (SEQ ID NO: 2), and
wherein the cancer is an esophageal cancer, a uterine cancer, a liver cancer, or a cholangiocarcinoma.~~
4. ~~The method of any one of Claims 1 to 3, further including administering an effective amount of a chemotherapeutic agent.~~

5. ~~The method of Claim 4, wherein the chemotherapeutic agent is a taxane, paclitaxel, docetaxel, carbazitaxel, gemcitabine, carboplatin, cisplatin, oxaliplatin, fluorouracil, capecitabine, or tegafur, or any functional analog thereof.~~
6. ~~The method of any one of Claims 1-5, wherein the anti-Dkk-1 antibody, or antigen binding fragment thereof, comprises a light chain variable region (LCVR) and a heavy chain variable region (HCVR), wherein the LCVR comprises complementarity determining regions (CDRs) LCDR1, LCDR2, and LCDR3 and the HCVR comprises CDRs HCDR1, HCDR2 and HCDR3, wherein LCDR1 has the amino sequence of SEQ ID NO: 6, LCDR2 has the amino sequence of SEQ ID NO: 7, LCDR3 has the amino sequence of SEQ ID NO: 8, HCDR1 has the amino sequence of SEQ ID NO: 9, HCDR2 has the amino sequence of SEQ ID NO: 10, and an HCDR3 has the amino sequence of SEQ ID NO: 11.~~
7. ~~The method of Claim 6, wherein the LCVR comprises the amino acid sequence of SEQ ID NO: 12 and the HCVR comprises the amino acid sequence of SEQ ID NO: 13.~~
8. ~~The method of Claim 6 or 7, wherein the LCVR and HCVR comprise amino acid sequences selected from the group consisting of: (i) a LCVR comprising the amino acid sequence of SEQ ID NO: 14 and a HCVR comprising the amino acid sequence of SEQ ID NO: 15; (ii) a LCVR comprising the amino acid sequence of SEQ ID NO: 16 and a HCVR comprising the amino acid sequence of SEQ ID NO: 17; (iii) a LCVR comprising the amino acid sequence of SEQ ID NO: 18 and a HCVR comprising the amino acid sequence of SEQ ID NO: 15; (iv) a LCVR comprising the amino acid sequence of SEQ ID NO: 19 and a HCVR comprising the amino acid sequence of SEQ ID NO: 15.~~
9. ~~The method of Claim 8, wherein the LCVR comprises the amino acid sequence of SEQ ID NO: 16 and the HCVR comprises the amino acid sequence of SEQ ID NO: 17.~~

- ~~10. The method of Claim 9, wherein the anti Dkk 1 antibody comprises a heavy chain and a light chain amino acid sequence selected from the group consisting of a) a heavy chain comprising the amino acid sequence of SEQ ID NO: 24 and light chain comprising the amino acid sequence of SEQ ID NO: 21, b) a heavy chain comprising the amino acid sequence of SEQ ID NO: 22 and a light chain comprising the amino acid sequence of SEQ ID NO: 23, c) a heavy chain comprising the amino acid sequence of SEQ ID NO: 24 and a light chain comprising the amino acid sequence of SEQ ID NO: 25, and d) a heavy chain comprising the amino acid sequence of SEQ ID NO: 24 and a light chain comprising the amino acid sequence of SEQ ID NO: 26.~~
- ~~11. The method of Claim 10, wherein the anti Dkk 1 antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 22 and a light chain comprising the amino acid sequence of SEQ ID NO: 23.~~
- ~~12. The method of any one of Claims 1-11, wherein the subject is a human.~~
- ~~13. The method of any one of Claim 1 to 3, wherein the mutation includes a deletion of exon 3 (SEQ ID NO: 4).~~
- ~~14. The method of Claim 13, wherein the mutation includes a deletion of Exons 2, 3, and 4 (SEQ ID NOs. 3, 4, and 5).~~
- ~~15. The method of any one of Claim 1 to 3, wherein the mutation includes a deletion within exon 3 (SEQ ID NO: 4).~~
- ~~16. The method of any one of Claim 1 to 3, wherein the mutation is a deletion of any subsequence within the amino acid sequence of the protein of SEQ ID NO: 2, wherein said subsequence includes at least one residue selected from Ser33, Ser37, Thr41, and Ser45.~~
- ~~17. The method of any one of Claim 1 to 3, wherein the mutation is a mutation of any one of the amino acid residues selected from Ser33, Ser37, Thr41, and Ser45 of the protein of SEQ ID NO: 2.~~

- ~~18. The method of any one of Claims 1 to 3, wherein the mutation is any one of the mutations of amino acid residues of in the protein of SEQ ID NO:2 listed in Table 1.~~
- ~~19. A method of treating a cancer in a subject in need thereof, the method comprising:
administering to the subject an effective amount of an anti Dkk-1 antibody or antigen binding fragment thereof,
wherein the subject is determined to have a constitutively activating mutation of beta-catenin protein (SEQ ID NO:2), and
wherein the cancer is a stomach cancer.~~
- ~~20. The method of Claim 19, further including administering an effective amount of a chemotherapeutic agent.~~
- ~~21. The method of Claim 20, wherein the chemotherapeutic agent is a taxane, paclitaxel, docetaxel, carbazitaxel, gemcitabine, carboplatin, cisplatin, oxaliplatin, fluorouracil, capecitabine, or tegafur, or any functional analog thereof.~~
- ~~22. The method of any one of Claims 19-21, wherein the anti Dkk-1 antibody, or antigen binding fragment thereof, comprises a light chain variable region (LCVR) and a heavy chain variable region (HCVR), wherein the LCVR comprises complementarity determining regions (CDRs) LCDR1, LCDR2, and LCDR3 and the HCVR comprises CDRs HCDR1, HCDR2 and HCDR3, wherein LCDR1 has the amino sequence of SEQ ID NO: 6, LCDR2 has the amino sequence of SEQ ID NO: 7, LCDR3 has the amino sequence of SEQ ID NO: 8, HCDR1 has the amino sequence of SEQ ID NO: 9, HCDR2 has the amino sequence of SEQ ID NO: 10, and an HCDR3 has the amino sequence of SEQ ID NO: 11.~~
- ~~23. The method of Claim 22, wherein the LCVR comprises the amino acid sequence of SEQ ID NO: 12 and the HCVR comprises the amino acid sequence of SEQ ID NO: 13.~~

24. ~~The method of Claim 22 or Claim 23, wherein the LCVR and HCVR comprise amino acid sequences selected from the group consisting of: (i) a LCVR comprising the amino acid sequence of SEQ ID NO: 14 and a HCVR comprising the amino acid sequence of SEQ ID NO: 15; (ii) a LCVR comprising the amino acid sequence of SEQ ID NO: 16 and a HCVR comprising the amino acid sequence of SEQ ID NO: 17; (iii) a LCVR comprising the amino acid sequence of SEQ ID NO: 18 and a HCVR comprising the amino acid sequence of SEQ ID NO: 15; (iv) a LCVR comprising the amino acid sequence of SEQ ID NO: 19 and a HCVR comprising the amino acid sequence of SEQ ID NO: 15.~~
25. ~~The method of Claim 24, wherein the LCVR comprises the amino acid sequence of SEQ ID NO: 16 and the HCVR comprises the amino acid sequence of SEQ ID NO: 17.~~
26. ~~The method of Claim 25, wherein the anti Dkk 1 antibody comprises a heavy chain and a light chain amino acid sequence selected from the group consisting of a) a heavy chain comprising the amino acid sequence of SEQ ID NO: 24 and light chain comprising the amino acid sequence of SEQ ID NO: 21, b) a heavy chain comprising the amino acid sequence of SEQ ID NO: 22 and a light chain comprising the amino acid sequence of SEQ ID NO: 23, c) a heavy chain comprising the amino acid sequence of SEQ ID NO: 24 and a light chain comprising the amino acid sequence of SEQ ID NO: 25, and d) a heavy chain comprising the amino acid sequence of SEQ ID NO: 24 and a light chain comprising the amino acid sequence of SEQ ID NO: 26.~~
27. ~~The method of Claim 26, wherein the anti Dkk 1 antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 22 and a light chain comprising the amino acid sequence of SEQ ID NO: 23.~~
28. ~~The method of any one of Claims 19-27, wherein the subject is a human.~~
29. ~~The method of Claim 19, wherein the mutation includes a deletion of exon 3 (SEQ ID NO: 4).~~

- ~~30. The method of Claim 29, wherein the mutation includes a deletion of Exons 2, 3, and 4 (SEQ ID NOs. 3, 4, and 5).~~
- ~~31. The method of Claim 19, wherein the mutation includes a deletion within exon 3 (SEQ ID NO: 4).~~
- ~~32. The method of Claim 19, wherein the mutation is a deletion of any subsequence within the amino acid sequence of the protein of SEQ ID NO: 2, wherein said subsequence includes at least one residue selected from Ser33, Ser37, Thr41, and Ser45.~~
- ~~33. The method of Claim 19, wherein the mutation is a mutation of any one of the amino acid residues selected from Ser33, Ser37, Thr41, and Ser45 of the protein of SEQ ID NO: 2.~~
- ~~34. The method of Claim 19, wherein the mutation is any one of the mutations of amino acid residues of in the protein of SEQ ID NO:2 listed in Table 1.~~
1. An invention not claimed in any divisional application.