cholangiocarcinoma (CAA), involving an antibody capable of binding to human Galectin-9, either alone or in combination with a checkpoint inhibitor such as an anti-PD-1 antibody.

In one aspect, the present disclosure describes a use of an antibody that binds human Galectin-9 (anti-Galectin-9 antibody) in the manufacture of a medicament for treating cancer in a subject in need thereof, wherein the anti-Galectin-9 antibody comprises a light chain complementarity determining region 1 (CDR1) set forth as SEQ ID NO: 1, a light chain complementary determining region 2 (CDR2) set forth as SEQ ID NO: 2, and a light chain complementary determining region 3 (CDR3) set forth as SEQ ID NO: 3 and comprises a heavy chain complementarity determining region 1 (CDR1) set forth as SEQ ID NO: 4, a heavy chain complementary determining region 2 (CDR2) set forth as SEQ ID NO: 5, and a heavy chain complementary determining region 3 (CDR3) set forth as SEQ ID NO: 6, wherein the subject is a human patient, who has undergone one or more prior anti-cancer therapies, has relapsed after one or more prior therapies, and/or has an elevated level of Galectin-9 relative to a control value, which is based on a value obtained from a healthy human subject, and wherein the anti-Galectin-9 antibody is to be administered to the subject at a dose of about 1 mg/kg to about 32 mg/kg.

Accordingly, one example of the present disclosure describes a method for treating a solid tumor in a subject by administering an antibody that binds human Galectin-9. In some examples, the solid tumor is pancreatic adenocarcinoma (PDA), colorectal cancer (CRC), or hepatocellular carcinoma (HCC), or cholangiocarcinoma. In some examples, the method comprises administering to a subject having a solid tumor, *e.g.*, PDA, CRC, HCC, or CCA an effective amount of an antibody that binds human Galectin-9 (referred to herein as an anti-Gal 9 antibody or anti-Galectin-9 antibody).

In some examples, the anti-Galectin-9 antibody is antibody G9.2-17, the structure of which is described herein. In some examples, the anti-Galectin-9 antibody comprises the same heavy chain complementary determining regions (CDRs) and/or the same light chain CDRs as reference antibody G9.2-17, the sequences of which are described herein. In some examples, the anti-Galectin-9 antibody comprises the heavy chain variable domain of antibody G9.2-17, and/or a light chain variable domain of antibody G9.2-17.

In some examples, the antibody comprises a light chain complementarity determining region 1 (CDR1) set forth as SEQ ID NO: 1, a light chain complementary determining region 2 (CDR2) set forth as SEQ ID NO: 2, and a light chain complementary determining region 3 (CDR3) set forth as SEQ ID NO: 3 and/or comprises a heavy chain complementarity determining region 1 (CDR1) set forth as SEQ ID NO: 4, a heavy chain complementary determining region 2 (CDR2) set forth as SEQ ID NO: 5, and a heavy chain complementary determining region 3 (CDR3) set forth as SEQ ID NO: 6. In some examples, the antibody comprises a heavy chain variable region comprising SEQ ID NO: 7. In some examples, the antibody comprises a light chain variable region comprising SEQ ID NO: 8.

WHAT IS CLAIMED IS:

1. Use of an antibody that binds human Galectin-9 (anti-Galectin-9 antibody) in the manufacture of a medicament for treating cancer in a subject in need thereof, wherein the anti-Galectin-9 antibody comprises a light chain complementarity determining region 1 (CDR1) set forth as SEQ ID NO: 1, a light chain complementary determining region 2 (CDR2) set forth as SEQ ID NO: 2, and a light chain complementary determining region 3 (CDR3) set forth as SEQ ID NO: 3 and comprises a heavy chain complementarity determining region 1 (CDR1) set forth as SEQ ID NO: 4, a heavy chain complementary determining region 2 (CDR2) set forth as SEQ ID NO: 5, and a heavy chain complementary determining region 3 (CDR3) set forth as SEQ ID NO: 6, wherein the subject is a human patient, who has undergone one or more prior anti-cancer therapies, has relapsed after one or more prior therapies, and/or has an elevated level of Galectin-9 relative to a control value, which is based on a value obtained from a healthy human subject, and

wherein the anti-Galectin-9 antibody is to be administered to the subject at a dose of about 1 mg/kg to about 32 mg/kg.

2. The use of claim 1, wherein the cancer is a solid tumor.

3. The use of claim 2, wherein the solid tumor is pancreatic cancer, colorectal cancer (CRC), hepatocellular carcinoma (HCC), or cholangiocarcinoma (CCA).

4. The use of claim 2 or claim 3, wherein the solid tumor is a metastatic tumor.

5. The use of any one of claims 1-4, wherein the anti-Galectin-9 antibody is to be administered to the subject once every two weeks.

6. The use of claim 4, wherein the anti-Galectin-9 antibody is to be administered to the subject at a dose of about 1 mg/kg to about 16 mg/kg.

7. The use of any one of claims 1-6, wherein the anti-Galectin-9 antibody is to be administered to the subject at a dose of about 1 mg/kg, about 2 mg/kg, about 4 mg/kg, about 6 mg/kg, about 8 mg/kg, about 10 mg/kg, about 12 mg/kg, or about 16 mg/kg.

8. The use of any one of claims 1-7, wherein the anti-Galectin-9 antibody is to be administered to the subject by intravenous infusion.

9. The use of any one of claims 1-8, wherein the subject is free of other anti-cancer therapy concurrently with the treatment involving the anti-Galectin-9 antibody.

10. The use of any one of claims 1-9, wherein the method further comprises that an immune checkpoint inhibitor is to be administered to the subject.

11. The use of claim 10, wherein the immune checkpoint inhibitor is an antibody that binds PD-1.

12. The use of claim 11, wherein the antibody that binds PD-1 is selected from the group consisting of pembrolizumab, nivolumab, tislelizumab or cemiplimab.

13. The use of claim 11 or claim 12, wherein the antibody that binds PD-1 is nivolumab, which is to be administered to the subject at a dose of 240 mg once every two weeks.

14. The use of claim 11 or 12, wherein the antibody that binds PD-1 is tislelizumab, which is to be administered at a dose of 200 mg once every 3 weeks.

15. The use of any one of claims 10-14, wherein the immune checkpoint inhibitor is to be administered by intravenous infusion.

16. The use of any one of claims 1-15, wherein the anti-Galectin-9 antibody comprises a light chain variable domain of SEQ ID NO: 8, and a heavy chain variable domain of SEQ ID NO: 7.

17. The use of any one of claims 1-16, wherein the anti-Galectin-9 antibody is a full-length antibody.

18. The use of any one of claims 1-17, wherein the anti-Galectin-9 antibody is an IgG1 or IgG4 molecule.

19. The use of claim 18, wherein the anti-Galectin-9 antibody is an IgG4 molecule having a modified Fc region of human IgG4.

20. The use of claim 19, wherein the modified Fc region of human IgG4 comprises the amino acid sequence of SEQ ID NO: 14.

21. The use of any one of claims 1-20, wherein the anti-Galectin-9 antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 19 and a light chain comprising the amino acid sequence of SEQ ID NO: 15.

22. The use of any one of claims 1-21, wherein the subject has undergone one or more prior anti-cancer therapies.

23. The use of claim 22, wherein the one or more prior anti-cancer therapies comprise chemotherapy, immunotherapy, radiation therapy, a therapy involving a biologic agent, or a combination thereof.

24. The use of claim 22 or claim 23, wherein the subject has progressed disease through the one or more prior anti-cancer therapies or is resistant to the one or more prior therapies.

25. The use of any one of claims 1-22, wherein the subject is a human patient having an elevated level of Galectin-9 relative to the control value.

26. The use of claim 25, wherein the human patient has an elevated serum or plasma level of Galectin-9 relative to the control value.

27. The use of claim 25, wherein the human patient has cancer cells expressing Galectin-9.

28. The use of claim 25, wherein the human patient has immune cells expressing Galectin-9.

29. The use of claim 27, wherein the cancer cells are in tumor organoids derived from the human patient.

30. The use of claim 28, wherein the immune cells are in tumor organoids derived from the human patient.

31. The use of any one of claims 1-30, wherein the subject is to be monitored for occurrence of adverse effects.

32. The use of claim 31, wherein the subject is to be administered with a reduced dose of the anti-Galectin-9 antibody, a reduced dose of the checkpoint inhibitor, or both, in the presence of one or more adverse effects.