

SUMMARY

The present disclosure is based, at least in part, on the development of treatment regimen for solid tumors (*e.g.*, metastatic solid tumors) such as pancreatic ductal adenocarcinoma (PDAC), colorectal cancer (CRC), hepatocellular carcinoma (HCC), cholangiocarcinoma (CAA), renal cell carcinoma (RCC), urothelial, head and neck, breast cancer, lung cancer, or other GI solid tumors, 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. Alternatively or in addition, the present disclosure is based, at least in part, on the unexpectedly discovery that an anti-Galectin 9 antibody G9.2-17 (IgG4) has a quicker clearance rate in human subjects as compared with other antibody therapeutics. Accordingly, a treatment regimen comprising a dosing schedule of once every week was developed to ensure a suitable plasma concentration, *e.g.*, a therapeutic systemic exposure level, of the anti-Galectin 9 antibody for achieving therapeutic effects.

In one aspect, the present disclosure provides a use of an antibody that binds human Galectin-9 (anti-Galectin-9 antibody) in the manufacture of a medicament for treating a solid tumor in a subject, wherein the anti-Galectin-9 antibody comprises: (a) a light chain comprising a light chain variable region (VL), which comprises a light chain (LC) complementarity determining region 1 (CDR1) comprising the amino acid sequence of SEQ ID NO: 1, a LC complementarity determining region 2 (CDR2) comprising the amino acid sequence of SEQ ID NO: 2, and a LC complementarity determining region 3 (CDR3) comprising the amino acid sequence of SEQ ID NO: 3 and (b) a heavy chain comprising a heavy chain variable region (VH), which comprises a heavy chain (HC) complementarity determining region 1 (CDR1) comprising the amino acid sequence of SEQ ID NO: 4, a HC complementarity determining region 2 (CDR2) comprising the amino acid sequence of SEQ ID NO: 5, and a HC complementarity determining region 3 (CDR3) comprising the amino acid sequence of SEQ ID NO: 6; wherein the anti-Galectin-9 antibody is at a dose of 0.2 mg/kg to 32 mg/kg once every week.

In another aspect, the present disclosure provides a use of an antibody that binds human Galectin-9 (anti-Galectin-9 antibody) in the manufacture of a medicament for treating a solid tumor in a subject, 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 complementarity determining region 2 (CDR2) set forth as SEQ ID NO: 2, and a light chain complementarity 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 complementarity determining region 2 (CDR2) set forth as SEQ ID NO: 5, and a heavy chain complementarity determining region 3 (CDR3) set forth as SEQ ID NO: 6 wherein the subject has one or more of the following features: (i) has no infection by SARS-CoV-2; (ii) has no active brain or leptomeningeal metastasis; and (iii) has unresectable metastatic cancer, which is adenocarcinoma, optionally squamous cell carcinoma; and wherein the anti-Galectin-9 antibody is at a dose of 0.2 mg/kg to 32 mg/kg once every two weeks to once every six weeks.

Accordingly, provided herein is a method for treating a solid tumor, the method comprising administering to a subject in need thereof (*e.g.*, a human patient having the target solid tumor) an effective amount of an antibody that binds human Galectin-9 (anti-Galectin-9 antibody). The anti-Galectin-9 antibody may be administered to the subject at a dose of about 0.2 mg/kg to about 32 mg/kg once every week to once every six weeks, *e.g.*, 0.2 mg/kg, 0.63 mg/kg, 2 mg/kg, 6.3 mg/kg, 10 mg/kg, or 16 mg/kg once every week to once every six weeks. In some examples, any of the anti-Galectin-9 antibodies disclosed herein may be administered to the subject by intravenous infusion.

In some examples, the anti-Galectin-9 antibody (*e.g.*, G9.2-17 (IgG4)) may be administered to the subject at a dose of 0.2 mg/kg, 0.63 mg/kg, 2 mg/kg, 6.3 mg/kg, 10 mg/kg, or 16 mg/kg once every two weeks to once every four weeks. In some examples, the anti-Galectin-9 antibody may be administered to the subject once every two weeks. In specific examples, the anti-Galectin-9 antibody (*e.g.*, G9.2-17 (IgG4)) is administered to the subject at a dose of 10 mg/kg or 16 mg/kg once every two weeks to once every four weeks (*e.g.*, once every two weeks).

Alternatively, the anti-Gal-9 antibody such as G9.2-17 (IgG4) may be administered to a subject at a dose of about 650 mg to about 1120 mg once every 2-6 weeks, for example, once every 2 weeks, once every 3 weeks, or once every 4 weeks. In some examples, the anti-Gal-9 antibody is administered to a subject at a dose of about 650 mg to about 700 mg once every 2-6 weeks, for example, once every 2 weeks, once every 3 weeks, or once every 4 weeks. In other examples, the anti-Gal-9 antibody is administered to a subject at a dose of about 1040 mg to about

1120 mg once every 2-6 weeks, for example, once every 2 weeks, once every 3 weeks, or once every 4 weeks.

In some examples, the anti-Galectin-9 antibody (*e.g.*, G9.2-17 (IgG4)) is administered to the subject at a dose of 0.2 mg/kg, 0.63 mg/kg, 2 mg/kg, 6.3 mg/kg, 10 mg/kg, or 16 mg/kg once every week. In specific examples, the anti-Galectin-9 antibody (*e.g.*, G9.2-17 (IgG4)) is administered to the subject at a dose of 10 mg/kg or 16 mg/kg once every week. Alternatively, the anti-Gal-9 antibody disclosed herein, such as G9.2-17 (IgG4), may be administered to the subject at a dose of about 650 mg to about 1120 mg once every week. For example, the anti-Gal-9 antibody can be administered to the subject at a dose of 10 mg/kg once every week or at a flat dose of about 650-700 mg once every week. Alternatively, the anti-Galectin-9 antibody can be administered to the subject at a dose of 16 mg/kg once every week or at a flat dose of about 1040-1120 mg once every week.

In some examples, the anti-Galectin-9 antibody may comprise:

(a) a light chain comprising a light chain variable region (V_L), which comprises a light chain (LC) complementarity determining region 1 (CDR1) comprising the amino acid sequence of SEQ ID NO: 1, a LC complementarity determining region 2 (CDR2) comprising the amino acid sequence of SEQ ID NO: 2, and a LC complementarity determining region 3 (CDR3) comprising the amino acid sequence of SEQ ID NO: 3 and

(b) a heavy chain comprising a heavy chain variable region (V_H), which comprises a heavy chain (HC) complementarity determining region 1 (CDR1) comprising the amino acid sequence of SEQ ID NO: 4, a HC complementarity determining region 2 (CDR2) comprising the amino acid sequence of SEQ ID NO: 5, and a HC complementarity determining region 3 (CDR3) comprising the amino acid sequence of SEQ ID NO: 6.

In some examples, the V_L of the anti-Galectin-9 antibody comprises the amino acid sequence of SEQ ID NO: 8. Alternatively or in addition, the V_H of the anti-Galectin-9 antibody comprises the amino acid sequence of SEQ ID NO: 7.

In some instances, the anti-Galectin-9 antibody is a full-length antibody, for example, an IgG1 or IgG4 molecule. In some examples, the anti-Galectin-9 antibody is a human IgG4 molecule. Such an IgG4 molecule may have a modified Fc region relative to the wildtype human IgG4 counterpart. In some examples, the modified Fc region comprises the amino acid sequence of SEQ ID NO: 14. In specific examples, 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. Such an anti-Galectin-9 antibody may be G9.2-17 (IgG4) as disclosed herein.

In some examples, the solid tumor to be treated by any of the methods disclosed herein may be pancreatic ductal adenocarcinoma (PDAC), colorectal cancer (CRC), hepatocellular carcinoma (HCC), cholangiocarcinoma (CAA), renal cell carcinoma (RCC), urothelial, head and neck, breast cancer, lung cancer, or other GI solid tumors. In some instances, the solid tumor is a metastatic tumor. In some examples, the method comprises administering to a subject having a solid tumor, *e.g.*, PDAC, 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 instances, the subject has one or more of the following features: (i) has no resectable cancer; (ii) has no infection by SARS-CoV-2; (iii) has no active brain or leptomeningeal metastasis; and (iv) has unresectable metastatic cancer, which is adenocarcinoma, optionally squamous cell carcinoma.

In some examples, the subject is free of other anti-cancer therapy concurrently with the anti-Galectin-9 antibody. Alternatively, the method may further comprise administering to the subject an immune checkpoint inhibitor. In some examples, the immune checkpoint inhibitor is an antibody that binds PD-1. Examples include pembrolizumab, nivolumab, tislelizumab, dostarlimab, or cemiplimab. In some instances, the subject is free of exposure to any anti-PD-1 or anti-PD-L1 agent in any prior lines of therapy, free of microsatellite instability (MSI-H) and/or deficient mismatch repair (dMMR), or a combination thereof.

In one example, the antibody that binds PD-1 is nivolumab. In some instances, nivolumab is administered to the subject at a dose of 240 mg once every two weeks. In another example, the antibody that binds PD-1 is tislelizumab. In some instances, tislelizumab is administered intravenously at a dose of about 200 mg once every 3 weeks or at a dose of about 400 mg every six weeks.

In some examples, the anti-Galectin-9 antibody is administered to the subject at a dose of about 0.2 mg/kg to about 32 mg/kg (*e.g.*, about 3 mg/kg to about 15 mg/kg or about 2 mg/kg to about 16 mg/kg or a higher dose level, or about 0.2 mg/kg to about 15 mg/kg, or about 0.2 to about 16 mg/kg or a higher dose level) once every 2-3 weeks. In some examples, the anti-Galectin-9 antibody is administered to the subject at a dose selected from 0.2 mg/kg, 0.63 mg/kg, 2 mg/kg, 4 mg/kg, 6 mg/kg, 6.3 mg/kg, 8 mg/kg, 10 mg/kg, 12 mg/kg, or 16 mg/kg or higher dose level. In some examples, the anti-Galectin-9 antibody is administered to the subject at a dose selected from 2 mg/kg, 4 mg/kg, 8 mg/kg, 12 mg/kg, or 16 mg/kg or a higher dose level. In some examples, the anti-Galectin-9 antibody is administered to the subject at a dose selected from 0.2 mg/kg, 0.63 mg/kg, 2 mg/kg, 4 mg/kg, 6 mg/kg, 6.3 mg/kg, 10 mg/kg, or 16 mg/kg or a higher dose level. In some examples, the antibody is administered once every 2 weeks. In some

examples, the anti-Galectin-9 antibody is administered to the subject at a dose selected from 2 mg/kg, 4 mg/kg, 8 mg/kg, 12 mg/kg, or 16 mg/kg or a higher dose level once every 2 weeks. In some examples, the anti-Galectin-9 antibody is administered to the subject at a dose selected from 0.2 mg/kg, 0.63 mg/kg, 2 mg/kg, 4 mg/kg, 6 mg/kg, 6.3 mg/kg, 10 mg/kg, or 16 mg/kg or a higher dose level once every 2 weeks. In some examples, the anti-Galectin-9 antibody is administered once every 2 weeks for one cycle, once every 2 weeks for two cycles, once every 2 weeks for 3 cycles, once every 2 weeks for 4 cycles, or once every 2 weeks for more than 4 cycles. In some examples, the duration of treatment is 0-3 months, 3-6 months, 12-24 months or longer. In some examples, the duration of treatment is 12-24 months or longer. In some examples, the cycles extend for a duration of 3 months to 6 months, or 6 months to 12 months or 12 months to 24 months or longer. In some examples, the cycle length is modified, e.g., temporarily or permanently to a longer duration, e.g., 3 weeks or 4 weeks. In some examples, the anti-Galectin-9 antibody is administered to the subject by intravenous infusion. In some examples, the cancer is metastatic cancer, including a metastatic cancer of any of the above-mentioned cancers. In some examples, the method of treatment comprising administering the anti-Galectin-9 antibody does not include any other concurrent anti-cancer therapy.

In some examples, the method of treatment employing the anti-Galectin-9 antibody includes another concurrent anti-cancer therapy. Thus, in some examples, the method of treatment employing the anti-Galectin-9 antibody further comprises administering to the subject an immune checkpoint inhibitor. In some examples, the immune checkpoint inhibitor is an antibody that binds PD-1, for example, pembrolizumab, nivolumab, tislelizumab, dostarlimab or cemiplimab. In some examples, the antibody that binds PD-1 is nivolumab, which is administered to the subject at a dose of 240 mg once every two weeks. In some examples, the antibody that binds PD-1 is nivolumab, which is administered to the subject at a dose of about 240 mg every two weeks or about 480 mg once every 4 weeks. In some examples, the antibody that binds PD-1 is pembrolizumab, which is administered at a dose of 200 mg once every 3 weeks. In some examples, the antibody that binds PD-1 is cemiplimab, which is administered at a dose of about 350 mg once every 3 weeks. In some examples, the antibody that binds PD-1 is tislelizumab, which is administered at a dose of about 200 mg once every 3 weeks or about 400 mg every six weeks. In some examples, the antibody that binds PD-1 is dostarlimab, which is administered at a dose of about 500 mg once every 3 weeks or at a dose of about 1000 mg every six weeks. In some examples, the immune checkpoint inhibitor is administered by intravenous infusion.

In some instances, the subject is (v) free of exposure to any anti-PD-1 or anti-PD-L1 agent in any prior lines of therapy, free of microsatellite instability (MSI-H) and/or deficient mismatch repair (dMMR), or a combination thereof. In some instances, the subject has microsatellite instability (MSI-H) and/or deficient mismatch repair (dMMR), or a combination thereof.

5 In some examples, the checkpoint inhibitor is administered to the subject on a day when the subject receives the anti-Galectin 9 antibody. Alternatively, the checkpoint inhibitor and the anti-Galectin 9 antibody are administered to the subject on two consecutive days. For example, the administration of the checkpoint inhibitor is performed prior to the administration of the anti-Galectin 9 antibody or vice versa.

10 In some examples, the subject has undergone one or more prior anti-cancer therapies. In some examples, the one or more prior anti-cancer therapies comprise chemotherapy, immunotherapy, radiation therapy, a therapy involving a biologic agent, or a combination thereof. In some instances, the subject has progressed disease through the one or more prior anti-cancer therapies or is resistant to the one or more prior therapies.

15 In some instances, the subject is a human patient having an elevated level of Galectin-9 relative to a control value. For example, the human patient has an elevated serum or plasma level of Galectin-9 relative to the control value. In some examples, the human patient has cancer cells expressing Galectin-9. Alternatively, or in addition, the human patient has immune cells expressing Galectin-9. In some examples, the cancer cells are in tumor organoids derived from
20 the human patient. In some examples, the control value is based on a value obtained from a healthy human subject.

Any of the methods disclosed herein may further comprise monitoring occurrence of adverse effects in the subject. In some examples, the method may further comprise reducing the dose of the anti-Galectin-9 antibody, the dose of the checkpoint inhibitor, or both when an
25 adverse effect is observed.

In some examples, the subject is administered multiple doses of the anti-Galectin 9 antibody and a later dose is higher than an earlier dose.

Also within the scope of the present disclosure are pharmaceutical compositions for use in treating a solid tumor (*e.g.*, those described herein and including metastatic solid tumors), and
30 uses of any of the anti-Galectin-9 antibodies for manufacturing a medicament for treating the solid tumor, either taken alone or in combination with a checkpoint inhibitor such as any of the anti-PD-1 antibodies disclosed herein.

The details of one or more examples of the disclosure are set forth in the description below. Other features or advantages of the present disclosure are to be apparent from the

following drawing and detailed description of several examples, and also from the appended claims.

BRIEF DESCRIPTION OF DRAWINGS

The following drawings form part of the present specification and are included to further demonstrate certain aspects of the present disclosure, which can be better understood by reference to the drawing in combination with the detailed description of specific embodiments presented herein.

FIG. 1 is a schematic depicting an exemplary study scheme. CRM: reassessment method; RP2D: recommended Phase 2 dose; PK: pharmacokinetics; PD: pharmacodynamics; PDAC: pancreatic ductal adenocarcinoma; CRC: colorectal cancer; CCA: cholangiocarcinoma; TBD: to be decided.

FIG. 2 is a graph showing a representative size exclusion chromatography (SEC) profile for the anti-Galectin-9 antibody. The high molecular weight peaks are labeled.

FIGS. 3A-3F include bar graphs showing levels of Galectin-9 expression as measured in T cells (CD3⁺), macrophages (CD11b⁺,) and tumor cells (Epcam⁺) in S2 and S3 organoid fractions derived from a pancreatic adenocarcinoma biopsy using anti-Galectin-9 G9.2-17 Fab fragment and a commercially available anti-Galectin-9 antibody (9M1-3). S2 fraction: organoids. S3 fraction: single cells. Corresponding isotype for G9.2-17 Fab ("Fab isotype") and "fluorescence minus one" (FMO) 9M1-3 ("Gal9 FMO") were used as controls for specificity, background staining and fluorescence bleed through from other channels. **FIG. 3A** shows levels of Galectin-9 in CD3⁺ cells as measured in the S3 fraction. **FIG. 3B** shows levels of Galectin-9 in CD11b⁺ cells as measured in the S3 fraction. **FIG. 3C** shows levels of Galectin-9 in Epcam⁺ cells as measured in the S3 fraction. **FIG. 3D** shows levels of Galectin-9 in CD3⁺ cells as measured in the S2 fraction. **FIG. 3E** shows levels of Galectin-9 in CD11b⁺ cells as measured in the S2 fraction. **FIG. 3F** shows levels of Galectin-9 in Epcam⁺ cells as measured in the S2 fraction.

FIGS. 4A-4F include bar graphs showing levels of Galectin-9 expression as measured in T cells (CD3⁺), macrophages (CD11b⁺,) and tumor cells (Epcam⁺) in S2 and S3 organoid fractions derived from a colorectal carcinoma biopsy using anti-Galectin-9 G9.2-17 Fab fragment and a commercially available anti-Galectin-9 antibody (9M1-3). S2 fraction: organoids. S3 fraction: single cells. Corresponding isotype for G9.2-17 Fab ("Fab isotype") and FMO 9M1-3 ("Gal9 FMO") were used controls for specificity, background staining and fluorescence bleed through from other channels. **FIG. 4A** shows levels of Galectin-9 in CD3⁺ cells as measured in

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 a solid tumor in a subject, wherein the anti-Galectin-

9 antibody comprises:

(a) a light chain comprising a light chain variable region (VL), which comprises a light chain (LC) complementarity determining region 1 (CDR1) comprising the amino acid sequence of SEQ ID NO: 1, a LC complementarity determining region 2 (CDR2) comprising the amino acid sequence of SEQ ID NO: 2, and a LC complementarity determining region 3 (CDR3) comprising the amino acid sequence of SEQ ID NO: 3 and

(b) a heavy chain comprising a heavy chain variable region (VH), which comprises a heavy chain (HC) complementarity determining region 1 (CDR1) comprising the amino acid sequence of SEQ ID NO: 4, a HC complementarity determining region 2 (CDR2) comprising the amino acid sequence of SEQ ID NO: 5, and a HC complementarity determining region 3 (CDR3) comprising the amino acid sequence of SEQ ID NO: 6;

wherein the anti-Galectin-9 antibody is at a dose of 0.2 mg/kg to 32 mg/kg once every week.

2. The use of claim 1, wherein the anti-Galectin-9 antibody is at a dose of 10 mg/kg to 16 mg/kg once every week; or

wherein the anti-Galectin-9 antibody is at a dose of 10 mg/kg or 16 mg/kg once every week.

3. The use of claim 1, wherein the anti-Galectin-9 antibody is at a dose of 650 mg to 1120 mg once every week; or

wherein the anti-Galectin-9 antibody is at a dose of 650 mg to 700 mg once every week, or 1040 to 1120 mg once every week.

4. Use of an antibody that binds human Galectin-9 (anti-Galectin-9 antibody) in the manufacture of a medicament for treating a solid tumor in a subject, 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 complementarity determining region 2 (CDR2) set forth as SEQ ID NO: 2, and a light chain complementarity 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 complementarity determining region 2 (CDR2) set forth as SEQ ID NO: 5, and a heavy chain complementarity determining region 3 (CDR3) set forth as SEQ ID NO: 6

5 wherein the subject has one or more of the following features:

- (i) has no infection by SARS-CoV-2;
- (ii) has no active brain or leptomeningeal metastasis; and
- (iii) has unresectable metastatic cancer, which is adenocarcinoma, optionally squamous cell carcinoma; and

10 wherein the anti-Galectin-9 antibody is at a dose of 0.2 mg/kg to 32 mg/kg once every two weeks to once every six weeks.

5. The use of claim 4, wherein the anti-Galectin-9 antibody is at a dose of 3 mg/kg to 15 mg/kg or 0.2 mg/kg to 16 mg/kg once every two weeks to once every six weeks, optionally once every two weeks; or

15 wherein the anti-Galectin-9 antibody is at a dose of about 0.2 mg/kg, about 0.6 mg/kg, about 0.63 mg/kg, about 2 mg/kg, about 4 mg/kg, about 6 mg/kg, about 6.3 mg/kg, about 8 mg/kg, about 10 mg/kg, about 12 mg/kg, or about 16 mg/kg once every two weeks to once every six weeks, optionally once every two weeks.

20 6. The use of claim 4, wherein the anti-Galectin-9 antibody is to be administered to the subject at a dose of 650 mg to 1120 mg once every two weeks to once every six weeks, optionally once every two weeks; or

25 wherein the anti-Galectin-9 antibody is at a dose of 650 mg to 700 mg once every two weeks to once every six weeks, optionally once every two weeks, or at a dose of 1040 mg to 1120 mg once every two weeks to once every six weeks, optionally once every two weeks.

30 7. The use of claim 1 or claim 4, wherein the solid tumor is a metastatic solid tumor.

8. The use of claim 1 or claim 4, wherein the solid tumor is pancreatic ductal adenocarcinoma (PDAC), colorectal cancer (CRC), hepatocellular carcinoma (HCC),

cholangiocarcinoma (CAA), renal cell carcinoma (RCC), urothelial cancer, head and neck cancer, breast cancer, lung cancer, or a gastrointestinal (GI) solid tumor.

9. The use of claim 1 or claim 4, wherein the anti-Galectin-9 antibody is formulated
5 for intravenous infusion.

10. The use of claim 1 or claim 4, wherein the V_L of the anti-Galectin-9 antibody
comprises the amino acid sequence of SEQ ID NO: 8; and/or
wherein the V_H of the anti-Galectin-9 antibody comprises the amino acid sequence of
10 SEQ ID NO: 7.

11. The use of claim 1 or claim 4, wherein the anti-Galectin-9 antibody is a full-
length antibody, which is an IgG1 or IgG4 molecule.

12. The use of claim 11, wherein the anti-Galectin-9 antibody is a human IgG4
15 molecule having a modified Fc region relative to the wildtype human IgG4 counterpart; and
wherein the modified Fc region comprises the amino acid sequence of SEQ ID NO: 14.

13. The use of claim 1 or claim 4, wherein the anti-Galectin-9 antibody comprises a
20 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.

14. The use of claim 1 or claim 4, wherein the use further comprises that an immune
checkpoint inhibitor is to be administered to the subject.

15. The use of claim 14, wherein the immune checkpoint inhibitor is an antibody that
25 binds PD-1.

16. The use of claim 15, wherein the antibody that binds PD-1 is pembrolizumab,
30 nivolumab, tislelizumab, dostarlimab, or cemiplimab.

17. The use of claim 14, wherein the checkpoint inhibitor is to be administered to the subject on a day when the subject receives the anti-Galectin 9 antibody;

wherein the checkpoint inhibitor and the anti-Galectin 9 antibody are to be administered to the subject on two consecutive days; or

5 wherein the checkpoint inhibitor is to be administered to the subject prior to the anti-Galectin 9 antibody.

18. The use of claim 1 or claim 4, wherein the subject has undergone one or more prior anti-cancer therapies; or wherein the subject has progressed disease through the one or
10 more prior anti-cancer therapies or is resistant to the one or more prior therapies.

19. The use of claim 18, wherein the one or more prior anti-cancer therapies comprise chemotherapy, immunotherapy, radiation therapy, a therapy involving a biologic agent, or a combination thereof.
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20. The use of claim 1 or claim 4, wherein the subject is a human patient having an elevated serum or plasma level of Galectin-9 relative to a control value.

21. The use of claim 1 or claim 4, wherein the dose of the anti-Galectin-9 antibody is
20 reduced when an adverse effect is observed.

22. The use of claim 14, wherein the dose of the anti-Galectin-9 antibody, the dose of the checkpoint inhibitor, or both are reduced when an adverse effect is observed.

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