

CLAIMS

What is claimed is:

1. A Galectin-9 (GAL9) antigen binding molecule, comprising: a first antigen binding site (ABS) specific for a first epitope of a first GAL9 antigen, wherein the first antigen binding site comprises all three VH CDRs from any one of the ABS clones selected from P9-28, P9-02B, P9-04, P9-05, P9-08, P9-09, P9-10, P9-15, P9-16, P9-18, P9-19, P9-20, P9-21, P9-22, P9-27, P9-31, P9-32, P9-36, P9-39, P9-49, P9-54, and P9-58.
2. A Galectin-9 (GAL9) antigen binding molecule, comprising a first antigen binding site (ABS) specific for a first epitope of a first GAL9 antigen, wherein the first antigen binding site comprises all three VL CDRs from any one of the ABS clones selected from P9-28, P9-02B, P9-04, P9-05, P9-08, P9-09, P9-10, P9-15, P9-16, P9-18, P9-19, P9-20, P9-21, P9-22, P9-27, P9-31, P9-32, P9-36, P9-39, P9-49, P9-54, and P9-58.
3. A Galectin-9 (GAL9) antigen binding molecule, comprising a first antigen binding site (ABS) specific for a first epitope of a first GAL9 antigen, wherein the first antigen binding site comprises all three VH CDRs and all three VL CDRs from any one of the ABS clones selected from P9-28, P9-02B, P9-04, P9-05, P9-08, P9-09, P9-10, P9-15, P9-16, P9-18, P9-19, P9-20, P9-21, P9-22, P9-27, P9-31, P9-32, P9-36, P9-39, P9-49, P9-54, and P9-58.
4. A Galectin-9 (GAL9) antigen binding molecule, comprising a first antigen binding site (ABS) specific for a first epitope of a first GAL9 antigen, wherein the first antigen binding site comprises the VL sequence and the VH sequence from any one of the ABS clones selected from P9-28, P9-02B, P9-04, P9-05, P9-08, P9-09, P9-10, P9-15, P9-16, P9-18, P9-19, P9-20, P9-21, P9-22, P9-27, P9-31, P9-32, P9-36, P9-39, P9-49, P9-54, and P9-58.
5. The GAL9 antigen binding molecule of claim 4, wherein the first antigen binding site (ABS) further comprises a first IgG heavy chain polypeptide and a first IgG light chain polypeptide.
6. The GAL9 antigen binding molecule of any one of claims 1-5, wherein the GAL9 antigen is a human GAL9 antigen.

7. The GAL9 antigen binding molecule of any of claims 1-6, wherein the GAL9 antigen binding molecule further comprises a second antigen binding site (ABS).
8. The GAL9 antigen binding molecule of claim 7, wherein the second ABS is specific for a GAL9 antigen.
9. The GAL9 antigen binding molecule of claim 7, wherein the second ABS is specific for a second epitope of the first GAL9 antigen.
10. The GAL9 antigen binding molecule of claim 7, wherein the second ABS is specific for the first epitope of the first GAL9 antigen and is identical to the first ABS.
11. The GAL9 antigen binding molecule of any one of claims 7-10, wherein the second ABS comprises all three VH CDRs, all three VL CDRs, or all three VH CDRs and all three VL CDRs from another ABS clone selected from P9-02B, P9-04, P9-05, P9-08, P9-09, P9-10, P9-15, P9-16, P9-18, P9-19, P9-20, P9-21, P9-22, P9-27, P9-28, P9-31, P9-32, P9-36, P9-39, P9-49, P9-54, and P9-58.
12. The GAL9 antigen binding molecule of claim 11, wherein the second antigen binding site comprises the VL sequence and the VH sequence from the other ABS clone.
13. The GAL9 antigen binding molecule of claim 12, wherein the second antigen binding site comprises a full immunoglobulin heavy chain sequence comprising the VH sequence and a full immunoglobulin light chain sequence comprising the VL sequence from the other ABS clone.
14. The GAL9 antigen binding molecule of claim 7, wherein the second antigen binding site is specific for an antigen other than the first GAL9 antigen.
15. The GAL9 antigen binding molecule of any one of the preceding claims, wherein the first antigen binding site comprises all three VH CDRs, all three VL CDRs, or all three VH CDRs and all three VL CDRs from any one of the ABS clones selected from: P9-18, P9-15, P9-21, P9-22, P9-28, and P9-32.
16. The GAL9 antigen binding molecule of any of claims 1-14, wherein the first antigen binding site comprises all three VH CDRs, all three VL CDRs, or all three VH CDRs and all three VL CDRs from any one of the ABS clones selected from: P9-18, P9-15, P9-21, and P9-28.

17. The GAL9 antigen binding molecule of any of claims 1-14, wherein the first antigen binding site comprises all three VH CDRs, all three VL CDRs, or all three VH CDRs and all three VL CDRs from ABS clone P9-15.
18. The GAL9 antigen binding molecule of any of claims 1-14, wherein the first antigen binding site comprises all three VH CDRs, all three VL CDRs, or all three VH CDRs and all three VL CDRs from ABS clone P9-18.
19. The GAL9 antigen binding molecule of any of claims 1-14, wherein the first antigen binding site comprises all three VH CDRs, all three VL CDRs, or all three VH CDRs and all three VL CDRs from ABS clone P9-21.
20. The GAL9 antigen binding molecule of any of claims 1-14, wherein the first antigen binding site comprises all three VH CDRs, all three VL CDRs, or all three VH CDRs and all three VL CDRs from ABS clone P9-28.
21. The GAL9 antigen binding molecule of any of claims 1-20, wherein the GAL9 antigen binding molecule comprises an antibody format selected from the group consisting of: full-length antibodies, Fab fragments, Fvs, scFvs, tandem scFvs, Diabodies, scDiabodies, DARTs, tandAbs, minibodies, and B-bodies.
22. The GAL9 antigen binding molecule of any of claims 1-21, wherein the GAL9 antigen binding molecule increases TNF- α secretion by activated immune cells upon contact, wherein the increase is greater than an 80-fold increase relative to activated immune cells treated with a control agent.
23. The GAL9 antigen binding molecule of any of claims 1-22, wherein the GAL9 antigen binding molecule increases IFN- γ secretion by activated immune cells upon contact, wherein the increase is greater than a 1.2-fold increase relative to activated immune cells treated with a control agent.
24. The GAL9 antigen binding molecule of any of claims 1-23, wherein the GAL9 antigen binding molecule increases CD40L surface expression of activated CD8⁺ T-cells upon contact, wherein the increase is greater than a 2-fold increase relative to activated CD8⁺ T-cells treated with a control agent.

25. The GAL9 antigen binding molecule of any of claims 1-24, wherein the GAL9 antigen binding molecule increases OX40 surface expression of activated CD8⁺ T-cells upon contact, wherein the increase is greater than a 2-fold increase relative to activated CD8⁺ T-cells treated with a control agent.
26. The GAL9 antigen binding molecule of any of claims 1-25, wherein the GAL9 antigen binding molecule increases IL-12 production of activated dendritic cells (DCs) upon contact, wherein the increase is greater than an 20-fold increase relative to activated DCs treated with a control agent.
27. The GAL9 antigen binding molecule of any of claims 1-26, wherein the GAL9 antigen binding molecule increases PD-L2 surface expression on activated dendritic cells (DCs) upon contact, wherein the increase is greater than an 4-fold increase relative to activated DCs treated with a control agent.
28. The GAL9 antigen binding molecule of any of claims 22-27, wherein the control agent is a negative control agent or positive control agent.
29. The GAL9 antigen binding molecule of claim 28, wherein the control agent is a control antibody.
30. The GAL9 antigen binding molecule of claim 29, wherein the control antibody is selected from the group consisting of: an ECA42 clone anti-GAL9 antibody, an RG9.1 clone anti-GAL9 antibody, an RG9.35 clone anti-GAL9 antibody, an anti-PD1 antibody, and a non-GAL9 binding isotype control antibody.
31. The GAL9 antigen binding molecule of any one of claims 22-30, wherein the activated immune cells, activated CD8⁺ T-cells, or activated DCs were activated by peptide stimulation, e.g., by a peptide or plurality of peptides known to induce an immune response.
32. A GAL9 antigen binding molecule, wherein the GAL9 antigen binding molecule increases TNF- α secretion by activated immune cells, wherein the increase is greater than an 80-fold increase relative to activated immune cells treated with a control agent.

33. A GAL9 antigen binding molecule, wherein the GAL9 antigen binding molecule increases IFN γ secretion by activated immune cells, wherein the increase is greater than an 1.2-fold increase relative to activated immune cells treated with a control agent.
34. A GAL9 antigen binding molecule, wherein the GAL9 antigen binding molecule increases CD40L surface expression of Activated CD8 $^{+}$ T-cells, wherein the increase is greater than a 2-fold increase relative to activated CD8 $^{+}$ T-cells treated with a control agent.
35. A GAL9 antigen binding molecule, wherein the GAL9 antigen binding molecule increases OX40 surface expression of Activated CD8 $^{+}$ T-cells, wherein the increase is greater than a 2-fold increase relative to activated CD8 $^{+}$ T-cells treated with a control agent.
36. A GAL9 antigen binding molecule, wherein the GAL9 antigen binding molecule increases IL-12 production of activated dendritic cells (DCs), wherein the increase is greater than an 20-fold increase relative to activated DCs treated with a control agent.
37. A GAL9 antigen binding molecule, wherein the GAL9 antigen binding molecule increases PD-L2 surface expression on activated dendritic cells (DCs), wherein the increase is greater than an 4-fold increase relative to activated DCs treated with a control agent.
38. A GAL9 antigen binding molecule, wherein the GAL9 antigen binding molecule demonstrates one or more of the following properties:
 - A) increases TNF- α secretion by activated immune cells, wherein the increase is greater than an 80-fold increase relative to activated immune cells treated with a control agent,
 - B) increases IFN- γ secretion by activated immune cells, wherein the increase is greater than an 1.2-fold increase relative to activated immune cells treated with a control agent,
 - C) increases CD40L surface expression of activated CD8 $^{+}$ T-cells, wherein the increase is greater than a 2-fold increase relative to activated CD8 $^{+}$ T-cells treated with a control agent,

D) increases OX40 surface expression of activated CD8⁺ T-cells, wherein the increase is greater than a 2-fold increase relative to activated CD8⁺ T-cells treated with a control agent,

E) increases IL-12 production of activated dendritic cells (DCs), wherein the increase is greater than an 20-fold increase relative to activated DCs treated with a control agent,

F) increases PD-L2 surface expression on activated dendritic cells (DCs), wherein the increase is greater than an 4-fold increase relative to activated DCs treated with a control agent.

39. The GAL9 antigen binding molecule of any one of claims 32-38, wherein the control agent is a negative control agent or positive control agent.
40. The GAL9 antigen binding molecule of claim 39, wherein the control agent is a control antibody.
41. The GAL9 antigen binding molecule of claim 40, wherein the control antibody is selected from the group consisting of: an ECA42 clone anti-GAL9 antibody, an RG9.1 clone anti-GAL9 antibody, an RG9.35 clone anti-GAL9 antibody, an anti-PD1 antibody, and an non-GAL9 binding isotype control antibody.
42. The GAL9 antigen binding molecule of any one of claims 32-41, wherein the activated immune cells, activated CD8⁺ T-cells, or activated DCs were activated by peptide stimulation, *e.g.*, by a peptide or plurality of peptides known to induce an immune response.
43. The GAL9 antigen binding molecule of any of claims 32-39, comprising a first antigen binding site specific for a first epitope of a first GAL9 antigen, wherein the first antigen binding site comprises all three VH CDRs and all three VL CDRs from any one of the ABS clones selected from, P9-02B, P9-04, P9-05, P9-08, P9-09, P9-10, P9-15, P9-16, P9-18, P9-19, P9-20, P9-21, P9-22, P9-27, P9-28, P9-31, P9-32, P9-36, P9-39, P9-49, P9-54, and P9-58.
44. The GAL9 antigen binding molecule of claim 43, comprising the VL sequence and the VH sequence from any one of the ABS clones selected from P9-02B, P9-04, P9-05, P9-

08, P9-09, P9-10, P9-15, P9-16, P9-18, P9-19, P9-20, P9-21, P9-22, P9-27, P9-28, P9-31, P9-32, P9-36, P9-39, P9-49, P9-54, and P9-58.

45. The GAL9 antigen binding molecule of claim 44, comprising a full immunoglobulin heavy chain sequence comprising the VH sequence and a full immunoglobulin light chain sequence comprising the VL sequence, wherein the VH sequence and the VL sequence are from any one of the ABS clones selected from, P9-02B, P9-04, P9-05, P9-08, P9-09, P9-10, P9-15, P9-16, P9-18, P9-19, P9-20, P9-21, P9-22, P9-27, P9-28, P9-31, P9-32, P9-36, P9-39, P9-49, P9-54, and P9-58.
46. The GAL9 antigen binding molecule of any one of claims 32-45, wherein the GAL9 antigen is a human GAL9 antigen.
47. The GAL9 antigen binding molecule of any of claims 32-46, wherein the GAL9 antigen binding molecule further comprises a second antigen binding site.
48. The GAL9 antigen binding molecule of claim 47, wherein the second antigen binding site is specific for the GAL9 antigen.
49. The GAL9 antigen binding molecule of claim 48, wherein the second antigen binding site is identical to the first antigen binding site.
50. The GAL9 antigen binding molecule of claim 47, wherein the second antigen binding site is specific for a second epitope of the first GAL9 antigen.
51. The GAL9 antigen binding molecule of claim 50, wherein the second antigen binding site comprises all three VH CDRs and all three VL CDRs from another ABS clone selected from, P9-02B, P9-04, P9-05, P9-08, P9-09, P9-10, P9-15, P9-16, P9-18, P9-19, P9-20, P9-21, P9-22, P9-27, P9-28, P9-31, P9-32, P9-36, P9-39, P9-49, P9-54, and P9-58.
52. The GAL9 antigen binding molecule of claim 51, wherein the second antigen binding site comprises the VL sequence and the VH sequence from the other ABS clone.
53. The GAL9 antigen binding molecule of claim 52, wherein the second antigen binding site comprises a full immunoglobulin heavy chain sequence comprising the VH sequence and a full immunoglobulin light chain sequence comprising the VL sequence from the other ABS clone.

54. The GAL9 antigen binding molecule of claim 47, wherein the second antigen binding site is specific for an antigen other than the first GAL9 antigen.
55. The GAL9 antigen binding molecule of any of claims 43-54, wherein the first antigen binding site comprises all three VH CDRs and all three VL CDRs from any one of the ABS clones selected from: P9-15, P9-18, P9-21, P9-22, P9-28, and P9-32.
56. The GAL9 antigen binding molecule of any of claims 43-54, wherein the first antigen binding site comprises all three VH CDRs and all three VL CDRs from any one of the ABS clones selected from: P9-15, P9-18, P9-21, and P9-28.
57. The GAL9 antigen binding molecule of any of claims 43-54, wherein the first antigen binding site comprises all three VH CDRs and all three VL CDRs from ABS clone P9-15.
58. The GAL9 antigen binding molecule of any of claims 43-54, wherein the first antigen binding site comprises all three VH CDRs and all three VL CDRs from ABS clone P9-18.
59. The GAL9 antigen binding molecule of any of claims 43-54, wherein the first antigen binding site comprises all three VH CDRs and all three VL CDRs from ABS clone P9-21.
60. The GAL9 antigen binding molecule of any of claims 43-54, wherein the first antigen binding site comprises all three VH CDRs and all three VL CDRs from ABS clone P9-28.
61. The GAL9 antigen binding molecule of any of claims 32-60, wherein the GAL9 antigen binding molecule comprises an antibody format selected from the group consisting of: full-length antibodies, Fab fragments, Fvs, scFvs, tandem scFvs, Diabodies, scDiabodies, DARTs, tandAbs, minibodies, and B-bodies.
62. A GAL9 antigen binding molecule which binds to the same epitope as a GAL9 antigen binding molecule of any one of the preceding claims.
63. A GAL9 antigen binding molecule which competes for binding with a GAL9 antigen binding molecule of any one of the preceding claims.

- 64. The GAL9 antigen binding molecule of any one of the preceding claims, which is purified.
- 65. A pharmaceutical composition comprising the GAL9 antigen binding molecule of any one of the preceding claims and a pharmaceutically acceptable diluent.
- 66. A method for treating a subject with cancer, the method comprising administering a therapeutically effective amount of the pharmaceutical composition of claim 65 to the subject.
- 67. The method of claim 66, wherein the cancer is selected from the group consisting of: pancreatic cancer, ovarian cancer, breast cancer, lung cancer, gastric cancer, melanoma, Ewing sarcoma, chronic lymphocytic leukemia, mantle cell lymphoma, B-ALL, hematological cancer, head and neck squamous cell carcinoma, prostate cancer, colon cancer, renal cancer, uterine cancer, and viral-induced cancer.