

CLAIMS

1. An isolated anti-Ryk antibody or antibody derivative that:
 - a) specifically binds to a Wnt-binding domain on Ryk or specifically binds to an epitope within a region of the ectodomain of Ryk, *e.g.*, amino-acids 35-211 of mouse Ryk (SEQ ID NO:24) or amino-acids 26-227 of human Ryk (SEQ ID NO:25), the antibody or antibody derivative comprising a light chain variable region comprising the CDR sequence set forth in SEQ ID NO:1 [RANRLVE];
 - b) specifically binds to the same epitope on a Wnt-binding domain on Ryk or the same epitope within a region of the ectodomain of Ryk, amino-acids 35-211 of mouse Ryk (SEQ ID NO:24) or amino-acids 26-227 of human Ryk (SEQ ID NO:25), as does a reference antibody or antibody derivative, or cross-competes for specific binding to the Wnt-binding domain on Ryk or the same epitope within a region of the ectodomain of Ryk, with a reference antibody or antibody derivative, the reference antibody or antibody derivative comprising a light chain variable region comprising the CDR sequence set forth in SEQ ID NO:1 [RANRLVE];
 - c) specifically binds to a Wnt-binding domain on Ryk or specifically binds to an epitope within a region of the ectodomain of Ryk, *e.g.*, amino-acids 35-211 of mouse Ryk (SEQ ID NO:24) or amino-acids 26-227 of human Ryk (SEQ ID NO:25), said antibody or antibody derivative comprising a heavy chain variable region comprising the CDR sequence set forth in SEQ ID NO:2 [STGGGGTY], SEQ ID NO:3 [HGDSGDY] or SEQ ID NO:4 [HGDQGDY]; or
 - d) specifically binds to the same epitope on a Wnt-binding domain on Ryk or the same epitope within a region of the ectodomain of Ryk, *e.g.*, amino-acids 35-211 of mouse Ryk (SEQ ID NO:24) or amino-acids 26-227 of human Ryk (SEQ ID NO:25), as does a reference antibody or antibody derivative, or cross-competes for specific binding to the Wnt-binding domain on Ryk or the same epitope within a region of the ectodomain of Ryk with a reference antibody or antibody derivative, the reference antibody or antibody derivative comprising a heavy chain variable region comprising the CDR sequence set forth in SEQ ID NO:2 [STGGGGTY], SEQ ID NO:3 [HGDSGDY] or SEQ ID NO:4 [HGDQGDY],provided that the antibody or antibody derivative is not an isolated anti-Ryk antibody or antibody derivative disclosed and/or claimed in WO 2017/172733 A1.

2. The isolated anti-Ryk antibody or antibody derivative of claim 1, which comprises a light chain variable region comprising the CDR sequence set forth in SEQ ID NO:1.

3. ~~The isolated anti-Ryk antibody or antibody derivative of claim 2, wherein the light chain variable region further comprises the CDR sequences set forth in SEQ ID NO:5 [KASQDINSYLS] and SEQ ID NO:6 [LQYDEFPLT].~~

43. The isolated anti-Ryk antibody or antibody derivative of ~~any of claims 1-3~~ claim 1, which comprises a heavy chain variable region comprising the CDR sequence set forth in SEQ ID NO:2 [STGGGGTY], SEQ ID NO:3 [HGDSGDY] or SEQ ID NO:4 [HGDQGDY].

5. ~~The isolated anti-Ryk antibody or antibody derivative of claim 4, wherein the heavy chain variable region comprises the CDR sequences set forth in SEQ ID NO:2 [STGGGGTY], SEQ ID NO:7 [GFTFSSY], and one of SEQ ID NO:3 [HGDSGDY], SEQ ID NO:4 [HGDQGDY], or SEQ ID NO:8 [HGDNGDY].~~

6. ~~The isolated anti-Ryk antibody or antibody derivative of any of claims 1-5, wherein the light chain variable region comprises the CDR sequences set forth in SEQ ID NO: 1 [RANRLVE], SEQ ID NO:5 [KASQDINSYLS] and SEQ ID NO:6 [LQYDEFPLT], and the heavy chain variable region comprises the CDR sequences set forth in SEQ ID NO:2 [STGGGGTY], SEQ ID NO:7 [GFTFSSY], and one of SEQ ID NO:3 [HGDSGDY], SEQ ID NO:4 [HGDQGD], or SEQ ID NO:8 [HGDNGDY].~~

74. The isolated anti-Ryk antibody or antibody derivative of ~~any of claims 1-6~~ claim 1, wherein the light chain variable region comprises an amino acid sequence comprising at least about 85% sequence identity to SEQ ID NO:11 [VL1], SEQ ID NO:12 [VL2], or SEQ ID NO:13 [VL3].

8. ~~The isolated anti-Ryk antibody or antibody derivative of claim 7, wherein the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 11 [VL1], SEQ ID NO: 12 [VL2], or SEQ ID NO: 13 [VL3].~~

95. The isolated anti-Ryk antibody or antibody derivative of ~~any of claims 1-8~~ claim 1, wherein the heavy chain variable region comprises an amino acid sequence comprising at least about 85% sequence identity to SEQ ID NO:14 [VH1], SEQ ID NO:15 [VH2], SEQ ID NO:16 [VH3], SEQ ID NO:17 [VH4], or SEQ ID NO:18 [VH5].

~~10. The isolated anti-Ryk antibody or antibody derivative of claim 9, wherein the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 14 [VH1], SEQ ID NO: 15 [VH2], SEQ ID NO: 16 [VH3], SEQ ID NO: 17 [VH4], or SEQ ID NO: 18 [VH5].~~

~~11. The isolated anti-Ryk antibody or antibody derivative of any of claims 1-10, wherein the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 11 [VL1], SEQ ID NO: 12 [VL2], or SEQ ID NO: 13 [VL3], and the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 14 [VH1], SEQ ID NO: 15 [VH2], SEQ ID NO: 16 [VH3], SEQ ID NO: 17 [VH4], or SEQ ID NO: 18 [VH5].~~

126. An isolated anti-Ryk antibody or antibody derivative that:

- a) specifically binds to a Wnt-binding domain on Ryk or specifically binds to an epitope within a region of the ectodomain of Ryk, *e.g.*, amino-acids 35-211 of mouse Ryk (SEQ ID NO:24) or amino-acids 26-227 of human Ryk (SEQ ID NO:25), the antibody or antibody derivative comprises a light chain variable region comprising an amino acid sequence comprising at least about 85% sequence identity to SEQ ID NO:11 [VL1], SEQ ID NO:12 [VL2], or SEQ ID NO:13 [VL3];
- b) specifically binds to the same epitope on a Wnt-binding domain on Ryk or the same epitope within a region of the ectodomain of Ryk, *e.g.*, amino-acids 35-211 of mouse Ryk (SEQ ID NO:24) or amino-acids 26-227 of human Ryk (SEQ ID NO:25), as does a reference antibody or antibody derivative, or cross-competes for specific binding to the Wnt-binding domain on Ryk or the same epitope within a region of the ectodomain of Ryk with a reference antibody or antibody derivative, the reference antibody or antibody derivative comprising a light chain variable region comprising an amino acid sequence comprising at least about 85% sequence identity to SEQ ID NO:11 [VL1], SEQ ID NO:12 [VL2], or SEQ ID NO:13 [VL3];
- c) specifically binds to a Wnt-binding domain on Ryk or specifically binds to an epitope within a region of the ectodomain of Ryk, *e.g.*, amino-acids 35-211 of mouse Ryk (SEQ ID NO:24) or

amino-acids 26-227 of human Ryk (SEQ ID NO:25), the antibody or antibody derivative comprises a heavy chain variable region that comprises an amino acid sequence comprising at least about 85% sequence identity to SEQ ID NO:14 [VH1], SEQ ID NO:15 [VH2], SEQ ID NO:16 [VH3], SEQ ID NO:17 [VH4], or SEQ ID NO:18 [VH5]; or

d) specifically binds to the same epitope on a Wnt-binding domain on Ryk or the same epitope within a region of the ectodomain of Ryk, *e.g.*, amino-acids 35-211 of mouse Ryk (SEQ ID NO:24) or amino-acids 26-227 of human Ryk (SEQ ID NO:25), as does a reference antibody or antibody derivative, or cross-competes for specific binding to the Wnt-binding domain on Ryk or the same epitope within a region of the ectodomain of Ryk with a reference antibody or antibody derivative, the reference antibody or antibody derivative comprising a heavy chain variable region that comprises an amino acid sequence comprising at least about 85% sequence identity to SEQ ID NO:14 [VH1], SEQ ID NO:15 [VH2], SEQ ID NO:16 [VH3], SEQ ID NO:17 [VH4], or SEQ ID NO:18 [VH5],

provided that the antibody or antibody derivative is not an isolated anti-Ryk antibody or antibody derivative disclosed and/or claimed in WO 2017/172733 A1.

~~13. The isolated anti-Ryk antibody or antibody derivative of claim 12, wherein the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 11 [VL1], SEQ ID NO: 12 [VL2], or SEQ ID NO: 13 [VL3].~~

~~14. The isolated anti-Ryk antibody or antibody derivative of claim 12 or 13, wherein the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 14 [VH1], SEQ ID NO: 15 [VH2], SEQ ID NO: 16 [VH3], SEQ ID NO: 17 [VH4], or SEQ ID NO: 18 [VH5].~~

~~157.~~ The isolated anti-Ryk antibody or antibody derivative of ~~any of claims 12-14~~ claim 6, wherein the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:11 [VL1], SEQ ID NO:12 [VL2], or SEQ ID NO:13 [VL3], and the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:14 [VH1], SEQ ID NO:15 [VH2], SEQ ID NO:16 [VH3], SEQ ID NO:17 [VH4], or SEQ ID NO:18 [VH5].

16. — The isolated anti-Ryk antibody or antibody derivative of claim 15, wherein the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 11 [VL1] and the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 14 [VH1].
17. — The isolated anti-Ryk antibody or antibody derivative of claim 15, wherein the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 11 [VL1] and the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 15 [VH2].
18. — The isolated anti-Ryk antibody or antibody derivative of claim 15, wherein the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 11 [VL1] and the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 16 [VH3].
19. — The isolated anti-Ryk antibody or antibody derivative of claim 15, wherein the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 11 [VL1] and the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 17 [VH4].
20. — The isolated anti-Ryk antibody or antibody derivative of claim 15, wherein the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 11 [VL1] and the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 18 [VH5].
21. — The isolated anti-Ryk antibody or antibody derivative of claim 15, wherein the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 12 [VL2] and the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 14 [VH1].
22. — The isolated anti-Ryk antibody or antibody derivative of claim 15, wherein the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 12 [VL2] and the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 15 [VH2].
23. — The isolated anti-Ryk antibody or antibody derivative of claim 15, wherein the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 12 [VL2] and the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 16 [VH3].
24. — The isolated anti-Ryk antibody or antibody derivative of claim 15, wherein the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 12 [VL2] and the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 17 [VH4].

~~25. The isolated anti-Ryk antibody or antibody derivative of claim 15, wherein the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 12 [VL2] and the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 18 [VH5].~~

~~26. The isolated anti-Ryk antibody or antibody derivative of claim 15, wherein the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 13 [VL3] and the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 14 [VH1].~~

~~27. The isolated anti-Ryk antibody or antibody derivative of claim 15, wherein the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 13 [VL3] and the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 15 [VH2].~~

~~28. The isolated anti-Ryk antibody or antibody derivative of claim 15, wherein the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 13 [VL3] and the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 16 [VH3].~~

~~29. The isolated anti-Ryk antibody or antibody derivative of claim 15, wherein the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 13 [VL3] and the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 17 [VH4].~~

~~30. The isolated anti-Ryk antibody or antibody derivative of claim 15, wherein the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 13 [VL3] and the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO: 18 [VH5].~~

318. The isolated anti-Ryk antibody or antibody derivative of ~~any of claims 1-30~~ claim 1, wherein the antibody or antibody derivative is a humanized antibody, *e.g.*, a humanized monoclonal antibody.

~~32. The isolated anti-Ryk antibody or antibody derivative of any of claims 1-30, wherein the antibody or antibody derivative is selected from the group consisting of a polyclonal antibody, a monoclonal antibody, an antibody fragment, a single chain antibody, a single domain antibody, *e.g.*, sdAb, sdFv, or nanobody, an intrabody, a peptibody, a chimeric antibody, a fully human antibody, a humanized antibody, a heteroconjugate antibody, a multispecific antibody, *e.g.*, a bispecific antibody, a diabody, a triabody, a tetrabody, a tandem di-scFv, and a tandem tri-scFv.~~

~~33. The isolated anti-Ryk antibody or antibody derivative of claim 32, wherein the antibody fragment is an antigen binding (Fab) fragment, a F(ab')₂ fragment, a Fab' fragment, a Fv fragment, a recombinant IgG (rlgG) fragment, a single chain antibody fragment, e.g., a single chain variable fragment (scFv), or a single domain antibody fragment.~~

349. The isolated anti-Ryk antibody or antibody derivative of ~~any of claims 1-33~~ claim 1, wherein the antibody or antibody derivative inhibits or reduces Ryk binding to Wnt or the antibody or antibody derivative specifically binds to an epitope within amino acid residues 90-183 of Ryk.

~~35. The isolated anti-Ryk antibody or antibody derivative of any of claims 1-34, wherein the antibody or antibody derivative specifically binds to an epitope within amino acid residues 90-183 of Ryk.~~

~~36~~10. The isolated anti-Ryk antibody or antibody derivative of ~~any of claims 1-35~~ claim 1, wherein the antibody or antibody derivative specifically binds to an epitope within or comprising the amino acid sequence set forth in SEQ ID NO:19 [SRTIYDPV] or an epitope within or comprising an amino acid sequence having at least about 80% sequence identity to the amino acid sequence set forth in SEQ ID NO:19 [SRTIYDPV].

~~37. The isolated anti-Ryk antibody or antibody derivative of claim 36, wherein the antibody or antibody derivative specifically binds to an epitope within or comprising the amino acid sequence set forth in SEQ ID NO:20 [ARTIYDPV], SEQ ID NO:21 [PRTIYDPV] or SEQ ID NO:22 [SRTL~~Y~~DPV].~~

~~38. The isolated anti-Ryk antibody or antibody derivative of claim 36, wherein the antibody or antibody derivative specifically binds to an epitope within or comprising the amino acid sequence set forth in SEQ ID NO:23 [SRXIYDPV], X being a natural amino acid that is not T.~~

3911. The isolated anti-Ryk antibody or antibody derivative of ~~any of claims 1-38~~ claim 1, which has lower immunogenicity than Ab5.5 disclosed and/or claimed in WO 2017/172733 A1 in a human.

40. — ~~The isolated anti-Ryk antibody or antibody derivative of claim 39, which has a DRB1 risk score that is at least about 30% lower than the DRB1 risk score of Ab5.5 disclosed and/or claimed in WO 2017/172733 A1.~~

41. — ~~The isolated anti-Ryk antibody or antibody derivative of claim 39 or 40, which has a DRB1 risk score ranging from about 500 to about 700.~~

4212. The isolated anti-Ryk antibody or antibody derivative of ~~any of claims 1-41~~ claim 1, which has a K_D value for binding to a Ryk polypeptide ranging from about 0.01 pM to about 500 pM.

43. — ~~An immunoconjugate comprising the isolated antibody or antibody derivative of any of claims 1-42, linked to a detecting or therapeutic agent.~~

44. — ~~The immunoconjugate of claim 43, wherein the detecting or therapeutic agent is a cytotoxin or a radioactive isotope.~~

45. — ~~A bispecific molecule comprising the isolated antibody or antibody derivative of any of claims 1-44, linked to a second functional moiety having a different binding specificity than the isolated antibody or antibody derivative of any of claims 1-44.~~

46. — ~~A pharmaceutical composition comprising an effective amount of the antibody or antibody derivative of any of claims 1-42, the immunoconjugate of claim 43 or 44, or the bispecific molecule of claim 45, and a pharmaceutically acceptable carrier or excipient.~~

4713. A nucleic acid sequence encoding the isolated antibody or antibody derivative of ~~any of claims 1-42 or the bispecific molecule of claim 45~~ claim 1.

~~48. — A vector comprising the nucleic acid sequence of claim 47.~~

~~49. — The vector of claim 48, wherein the vector is an expression vector.~~

~~50. — A host cell comprising the vector of claim 48 or 49.~~

~~51. — The host cell of claim 50, wherein the host cell is a mammalian host cell.~~

~~52. — A transgenic non human animal, e.g., a transgenic mouse, comprising the host cell of claim 50 or 51, wherein the non human animal or mouse expresses a polypeptide encoded by the nucleic acid.~~

~~53~~14. A method of interfering with interaction of Wnt and Ryk comprising contacting a sample comprising Wnt and Ryk with the isolated antibody or antibody derivative of any of claims 1-42, the immunoconjugate of claim 43 or 43, or the bispecific molecule of claim 45 claim 1, thereby interfering with the interaction of Wnt and Ryk.

~~54~~15. The isolated antibody or antibody derivative of claim 1, A method for use in inhibiting degeneration of a neuron, ~~the method comprising contacting the neuron with the isolated antibody or antibody derivative of any of claims 1-42, the immunoconjugate of claim 43 or 44, the bispecific molecule of claim 45, the pharmaceutical composition of claim 46, the nucleic acid sequence of claim 47, the vector of claim 48 or 49, or the host cell of claim 50 or 51 , thereby inhibiting degeneration of the neuron.~~

~~55. — The method of claim 54, wherein degeneration of an axon of the neuron is inhibited or wherein degeneration of a cell body of the neuron is inhibited.~~

~~56. — The method of claim 55, wherein the axon is a spinal cord commissural axon, an upper motor neuron axon or a central nervous system axon.~~

~~57. — The method of claim 54, wherein the neuron is a damaged spinal cord neuron.~~

~~58. — The method of claim 54, wherein the neuron is a sensory neuron.~~

~~59. — The method of claim 54, wherein the neuron is a motor neuron.~~

60. — ~~The method of claim 54, wherein the neuron is a cerebellar granule neuron, a dorsal root ganglion neuron, a cortical neuron, a sympathetic neuron, or a hippocampal neuron.~~

61. — ~~The method of claim 54, wherein the neuron forms part of a nerve graft or a nerve transplant.~~

62. — ~~The method of claim 61, wherein the nerve graft or the nerve transplant forms part of an organism.~~

63. — ~~The method of any of claims 54-62, wherein the neuron is contacted with the isolated antibody or antibody derivative, the immunoconjugate, the bispecific molecule, the pharmaceutical composition, the nucleic acid sequence, the vector or the host cell ex vivo or in vitro.~~

64. — ~~The method of claim 63, wherein the organism is a mammal.~~

65. — ~~The method of claim 64, wherein the mammal is a human.~~

6616. Use of the isolated antibody or antibody derivative of claim 1 in the preparation~~A method of a medicament for preventing or treating a neurological disease, disorder or injury in a subject having or being at risk of developing the neurological disease, disorder or injury comprising administering to the subject an effective amount of the isolated antibody or antibody derivative of any of claims 1-42, the immunoconjugate of claim 43 or 44, the bispecific molecule of claim 45, the pharmaceutical composition of claim 46, the nucleic acid sequence of claim 47, the vector of claim 48 or 49, or the host cell of claim 50 or 51, thereby treating the neurological disease, disorder or injury in the subject.~~

6717. The method~~use of claim-66 16, wherein the neurological disease or disorder is a neurodegenerative disease or disorder, e.g., amyotrophic lateral sclerosis, Alzheimer's disease or Parkinson's disease or the neurological injury is a spinal cord injury, a traumatic brain injury, or a peripheral nerve injury.~~

68. — ~~The method of claim 66, wherein the neurological injury is a spinal cord injury, a traumatic brain injury, or a peripheral nerve injury.~~

~~6918. The isolated antibody or antibody derivative of claim 1,A method for use in modulating the directional growth of a neuron comprising contacting the neuron with the isolated antibody or antibody derivative of any of claims 1-42, the immunoconjugate of claim 43 or 44, the bispecific molecule of claim 45, the pharmaceutical composition of claim 46, the nucleic acid sequence of claim 47, the vector of claim 48 or 49, or the host cell of claim 50 or 51, thereby modulating the directional growth of the neuron.~~

~~70. — The method of claim 69, wherein the neuron is a spinal cord commissural axon, an upper motor neuron axon, a central nervous system axon, a peripheral nervous system axon, a damaged spinal cord neuron, a sensory neuron, or a motor neuron.~~

~~71. — The method of claim 70, wherein the directional growth facilitates regeneration of the neuron.~~

~~72. — Use of an effective amount of the isolated antibody or antibody derivative of any of claims 1-42, the immunoconjugate of claim 43 or 44, the bispecific molecule of claim 45, the nucleic acid sequence of claim 47, the vector of claim 48 or 49, or the host cell of claim 50 or 51 for manufacturing a medicament for treating or preventing a neurological disease, disorder or injury in a subject having or being at risk of developing the neurological disease, disorder or injury.~~

~~73. — The use of claim 72, wherein the neurological disease or disorder is a neurodegenerative disease or disorder.~~

~~7419. Use of the isolated antibody or antibody derivative of claim 1 in the preparationA method of a medicament for preventing or treating a cancer or tumor in a subject having or being at risk of developing the cancer or tumor comprising administering to the subject an effective amount of the isolated antibody or antibody derivative of any of claims 1-42, the immunoconjugate of claim 43 or 44, the bispecific molecule of claim 45, the pharmaceutical composition of claim 46, the nucleic acid sequence of claim 47, the vector of claim 48 or 49, or the host cell of claim 50 or 51, thereby treating or treating the cancer or tumor in the subject.~~

75. — The method of claim 74, wherein the cancer or tumor is caused by or associated with overexpression of Ryk and/or Wnt5a in a subject.

76. — The method of claim 74 or 75, wherein the cancer or tumor is glioma, glioblastoma multiforme (GBM), a lymphoma, a leukemia, a brain cancer, a multiple myeloma, a pancreatic cancer, cholangiocarcinoma (a bile duct cancer), a liver cancer, a stomach cancer, a breast cancer, a kidney cancer, a lung cancer, a colorectal cancer, a colon cancer, a prostate cancer, an ovarian cancer, a cervical cancer, a skin cancer, melanoma, an esophagus cancer, a head and neck cancer, a thymic cancer, gastric cancer, melanoma, prostate cancer, ovarian cancer, small cell lung cancer, or an atypical teratoid rhabdoid tumor.

77. — The method of claim 76, wherein the glioma is low grade glioma.

78. — The method of claim 76, wherein the leukemia is T- and B-cell acute lymphoblastic leukemia or acute myeloid leukemia.

79. — The method of claim 76, wherein the lymphoma is diffuse large B-cell lymphoma (DLBC).

80. — The method of claim 76, wherein the thymic cancer is thymoma (THYM).

81. — The method of any of claims 74-80, which is used to treat a cancer or tumor in a subject.

82. — The method of any of claims 74-80, which is used to prevent a cancer or tumor in a subject.

83. — The method of any of claims 74-82, wherein the subject is a human.

84. — Use of an effective amount of the isolated antibody or antibody derivative of any of claims 1-42, the immunoconjugate of claim 43 or 44, the bispecific molecule of claim 45, the nucleic acid sequence of claim 47, the vector of claim 48 or 49, or the host cell of claim 50 or 51 for manufacturing a medicament for preventing or treating a cancer or tumor in a subject having or being at risk of developing the cancer or tumor.

8520. A method for assessing a Ryk polypeptide in a sample, which method comprises:

a) contacting a sample containing or suspected of containing a Ryk polypeptide with the isolated antibody or antibody derivative of any of claims 1-42, the immunoconjugate of claim 43 or 44, or the bispecific molecule of claim 45 claim 1; and

b) assessing binding between the Ryk polypeptide, if present in the sample, and the isolated antibody or antibody derivative, the immunoconjugate or the bispecific molecule to assess the presence, absence, level or amount of the Ryk polypeptide in the sample.

86. — ~~The method of claim 85, wherein the sample is a liquid, a semi-liquid or a solid sample.~~

87. — ~~The method of claim 85 or 86, wherein the sample is a biological sample.~~

88. — ~~The method of claim 87, wherein the biological sample is a blood or a urine sample.~~

89. — ~~The method of claim 88, wherein the blood sample is a serum, a plasma or a whole blood sample.~~

90. — ~~The method of any of claims 85-89, wherein the sample is a clinical sample, e.g., a tissue biopsy sample.~~

91. — ~~The method of any of claims 85-90, wherein the Ryk polypeptide is a natural Ryk polypeptide, protein or a fragment thereof.~~

92. — ~~The method of any of claims 85-91, wherein the Ryk polypeptide is contacted with the isolated antibody or antibody derivative of any of claims 1-42.~~

93. — ~~The method of any of claims 85-91, wherein the Ryk polypeptide is contacted with the immunoconjugate of claim 43 or 44.~~

94. — ~~The method of any of claims 85-91, wherein the Ryk polypeptide is contacted with the bispecific molecule of claim 45.~~

95. — ~~The method of any of claims 85-94, wherein the binding between the Ryk polypeptide, if present in the sample, and the isolated antibody or antibody derivative, the immunoconjugate or the bispecific molecule is assessed by a format selected from the group consisting of an enzyme-linked immunosorbent assay (ELISA), immunoblotting, immunoprecipitation, radioimmunoassay (RIA), immune-staining, latex agglutination, indirect hemagglutination assay (IHA), complement fixation, indirect immunofluorescent assay (IFA), nephelometry, flow cytometry assay, surface plasmon resonance (SPR), chemiluminescence assay, lateral flow immunoassay, u-capture assay, inhibition assay and avidity assay.~~

96. — ~~The method of any of claims 85-95, which is used to assess the presence or absence of the Ryk polypeptide in the sample.~~
97. — ~~The method of any of claims 85-95, which is used to assess the level or amount of the Ryk polypeptide in the sample.~~
98. — ~~The method of any of claims 85-97, wherein the sample is isolated or derived from a subject.~~
99. — ~~The method of claim 98, wherein the subject is a mammal.~~
100. — ~~The method of claim 99, wherein the mammal is a human.~~
101. — ~~The method of any of claims 98-100, which is used for diagnosis, prognosis, stratification, risk assessment, or treatment monitoring of a disease, disorder or injury associated with abnormal level or amount of the Ryk polypeptide in a subject.~~
102. — ~~The method of claim 101, wherein the assessed level or amount of the Ryk polypeptide is compared with a threshold value or range to assess whether a level or amount of the Ryk polypeptide in a subject is normal or abnormal.~~
103. — ~~The method of claim 102, wherein the threshold value or range is obtained or derived from a subject or a population of subjects that have the disease, disorder or injury, a subject or a population of subjects that do not have the disease, disorder or injury, or a subject or a population of subjects that are treated, cured or recovered from the disease, disorder or injury.~~
104. — ~~The method of any of claims 101-103, which is used to for diagnosis, prognosis, stratification, risk assessment, or treatment monitoring of a disease, disorder or injury associated with abnormally low level or amount of the Ryk polypeptide in a subject.~~
105. — ~~The method of any of claims 101-103, which is used to for diagnosis, prognosis, stratification, risk assessment, or treatment monitoring of a disease, disorder or injury associated with abnormally high level or amount of the Ryk polypeptide in a subject.~~
106. — ~~The method of claim 105, wherein the disease, disorder or injury is degeneration of a neuron, a neurological disease, disorder or injury, a tumor or a cancer.~~

~~107. The method of any of claims 101-106, which further comprises treating a subject for the disease, disorder or injury.~~

~~108. The method of claim 107, wherein the treatment comprises modulating or adjusting level or amount of the Ryk polypeptide in the subject.~~

~~109~~21. The method use of claim ~~66~~ 16, wherein the neurological disease, disorder or injury is neuropathic pain.

~~110. The method of claim 109, wherein the neuropathic pain is caused by a lesion or disease of the somatosensory system.~~

~~111. The method of claim 109 or 110, wherein the neuropathic pain is peripheral neuropathic pain, central neuropathic pain, or mixed (peripheral and central) neuropathic pain.~~

~~112. The method of any of claims 109-111, wherein the isolated antibody or antibody derivative, the immunoconjugate, the bispecific molecule, the pharmaceutical composition, the nucleic acid sequence, the vector, or the host cell is administered to the subject via intrathecal administration or infusion.~~