

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 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].
4. The isolated anti-Ryk antibody or antibody derivative of 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].
5. The isolated anti-Ryk antibody or antibody derivative of 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].
6. 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.

7. The isolated anti-Ryk antibody or antibody derivative of 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].

8. The isolated anti-Ryk antibody or antibody derivative of claim 1, wherein the antibody or antibody derivative is a humanized antibody, *e.g.*, a humanized monoclonal antibody.

9. The isolated anti-Ryk antibody or antibody derivative of 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.

10. The isolated anti-Ryk antibody or antibody derivative of 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].
11. The isolated anti-Ryk antibody or antibody derivative of claim 1, which has lower immunogenicity than Ab5.5 disclosed and/or claimed in WO 2017/172733 A1 in a human.
12. The isolated anti-Ryk antibody or antibody derivative of claim 1, which has a K_D value for binding to a Ryk polypeptide ranging from about 0.01 pM to about 500 pM.
13. A nucleic acid sequence encoding the isolated antibody or antibody derivative of claim 1.
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 claim 1, thereby interfering with the interaction of Wnt and Ryk.
15. The isolated antibody or antibody derivative of claim 1, for use in inhibiting degeneration of a neuron.
16. Use of the isolated antibody or antibody derivative of claim 1 in the preparation 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.
17. The use of claim 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.

18. The isolated antibody or antibody derivative of claim 1, for use in modulating the directional growth of a neuron comprising contacting the neuron with the isolated antibody or antibody derivative.
19. Use of the isolated antibody or antibody derivative of claim 1 in the preparation 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.
20. 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 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.
21. The use of claim 16, wherein the neurological disease, disorder or injury is neuropathic pain.