

Claims:

[Claim 1]. Use of an antigen-binding molecule which is capable of binding to HER3 in the manufacture of a medicament for treating or preventing a cancer in a subject, wherein the cancer comprises cells having an NRG gene fusion mutation resulting in increased expression of a ligand for HER3, and wherein the antigen-binding molecule comprises:

(i) a heavy chain variable (VH) region incorporating the following CDRs:

HC-CDR1 having the amino acid sequence of SEQ ID NO:41

HC-CDR2 having the amino acid sequence of SEQ ID NO:45

HC-CDR3 having the amino acid sequence of SEQ ID NO:48; and

(ii) a light chain variable (VL) region incorporating the following CDRs:

LC-CDR1 having the amino acid sequence of SEQ ID NO:88

LC-CDR2 having the amino acid sequence of SEQ ID NO:92

LC-CDR3 having the amino acid sequence of SEQ ID NO:95.

[Claim 2]. The use according to claim 1, wherein the ligand for HER3 comprises an amino acid sequence having at least 60% sequence identity to the EGF-like domain of an NRG.

[Claim 3]. The use according to claim 1 or claim 2, wherein the NRG gene fusion is selected from *CLU-NRG1*, *CD74-NRG1*, *DOC4-NRG1*, *SLC3A2-NRG1*, *RBPMS-NRG1*, *WRN-NRG1*, *SDC4-NRG1*, *RAB2IL1-NRG1*, *VAMP2-NRG1*, *KIF13B-NRG1*, *THAP7-NRG1*, *SMAD4-NRG1*, *MDK-NRG1*, *TNC-NRG1*, *DIP2B-NRG1*, *MRPL13-NRG1*, *PARP8-NRG1*, *ROCK1-NRG1*, *DPYSL2-NRG1*, *ATP1B1-NRG1*, *CDH6-NRG1*, *APP-NRG1*, *AKAP13-NRG1*, *THBS1-NRG1*, *FOXA1-NRG1*, *PDE7A-NRG1*, *RAB3IL1-NRG1*, *CDK1-NRG1*, *BMPRII-NRG1*, *TNFRSF10B-NRG1*, *MCPH1-NRG1* and *SLC12A2-NRG2*.

[Claim 4]. The use according to any one of claims 1 to 3, wherein the NRG gene fusion is selected from *CLU-NRG1*, *CD74-NRG1*, *SLC3A2-NRG1* or *VAMP2-NRG1*.

[Claim 5]. The use according to any one of claims 1 to 4, wherein the cancer comprises cells expressing HER3.

[Claim 6]. The use according to any one of claims 1 to 5, wherein the cancer derives from the lung, breast, head, neck, kidney, ovary, pancreas, prostate, uterus, gallbladder, colon, rectum, bladder, soft tissue or nasopharynx.

[Claim 7]. The use according to any one of claims 1 to 6, wherein the cancer is selected from lung cancer, non-small cell lung cancer, lung adenocarcinoma, invasive mucinous lung adenocarcinoma, lung squamous cell carcinoma, breast cancer, breast carcinoma, breast invasive carcinoma, head and neck cancer, head and neck squamous cell carcinoma, renal cancer, renal clear cell carcinoma, ovarian cancer, ovarian serous cystadenocarcinoma, pancreatic cancer, pancreatic adenocarcinoma, pancreatic

ductal adenocarcinoma, prostate cancer, prostate adenocarcinoma, endometrial cancer, uterine carcinosarcoma, gallbladder cancer, cholangiocarcinoma, colorectal cancer, bladder cancer, urothelial bladder cancer, sarcoma, soft tissue sarcoma, neuroendocrine tumor and neuroendocrine tumor of the nasopharynx.

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[Claim 8]. The use according to any one of claims 1 to 7, wherein the cancer is selected from lung cancer, non-small cell lung cancer, lung adenocarcinoma, invasive mucinous lung adenocarcinoma and lung squamous cell carcinoma.

10 [Claim 9]. The use according to any one of claims 1 to 8, wherein the antigen-binding molecule comprises:

a VH region comprising an amino acid sequence having at least 70% sequence identity to the amino acid sequence of SEQ ID NO:36; and

15 a VL region comprising an amino acid sequence having at least 70% sequence identity to the amino acid sequence of SEQ ID NO:83.

[Claim 10]. The use according to any one of claims 1 to 9, wherein the antigen-binding molecule comprises:

20 a VH region incorporating the following framework regions (FRs):
HC-FR1 having the amino acid sequence of SEQ ID NO:53
HC-FR2 having the amino acid sequence of SEQ ID NO:59
HC-FR3 having the amino acid sequence of SEQ ID NO:66
HC-FR4 having the amino acid sequence of SEQ ID NO:71.

25 [Claim 11]. The use according to any one of claims 1 to 10, wherein the antigen-binding molecule comprises:

a VL region incorporating the following framework regions (FRs):
LC-FR1 having the amino acid sequence of SEQ ID NO:104
LC-FR2 having the amino acid sequence of SEQ ID NO:110
30 LC-FR3 having the amino acid sequence of SEQ ID NO:120
LC-FR4 having the amino acid sequence of SEQ ID NO:125.

[Claim 12]. The use according to any one of claims 1 to 11, wherein the antigen-binding molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:171.

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[Claim 13]. The use according to any one of claims 1 to 12, wherein the antigen-binding molecule comprises a light chain comprising the amino acid sequence of SEQ ID NO:177.