

Claims:

[Claim 1]. Use of An-an antigen-binding molecule which is capable of binding to HER3 in the manufacture of a medicament for use in a method of 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:4341

HC-CDR2 having the amino acid sequence of SEQ ID NO:4645

HC-CDR3 having the amino acid sequence of SEQ ID NO:5148; and

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

LC-CDR1 having the amino acid sequence of SEQ ID NO:9188

LC-CDR2 having the amino acid sequence of SEQ ID NO:9492

LC-CDR3 having the amino acid sequence of SEQ ID NO:9995.

~~2. Use of an antigen-binding molecule which is capable of binding to HER3 in the manufacture of a medicament for use in a method of treating or preventing a cancer in a subject, wherein the cancer comprises cells having a 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:43~~

~~HC-CDR2 having the amino acid sequence of SEQ ID NO:46~~

~~HC-CDR3 having the amino acid sequence of SEQ ID NO:51; and~~

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

~~LC-CDR1 having the amino acid sequence of SEQ ID NO:91~~

~~LC-CDR2 having the amino acid sequence of SEQ ID NO:94~~

~~LC-CDR3 having the amino acid sequence of SEQ ID NO:99.~~

~~3. A method of treating or preventing a cancer in a subject, wherein the cancer comprises cells having a mutation resulting in increased expression of a ligand for HER3, wherein the method comprises administering a therapeutically or prophylactically effective amount of an antigen-binding molecule which is capable of binding to HER3 to the subject, 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:43~~

~~HC-CDR2 having the amino acid sequence of SEQ ID NO:46~~

~~HC-CDR3 having the amino acid sequence of SEQ ID NO:51; and~~

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

~~LC-CDR1 having the amino acid sequence of SEQ ID NO:91~~

~~LC-CDR2 having the amino acid sequence of SEQ ID NO:94~~

~~LC-CDR3 having the amino acid sequence of SEQ ID NO:99.~~

[Claim 42]. The ~~antigen-binding molecule for use according to claim 1, the use according to claim 2, or the method according to claim 3,~~ wherein the ligand for HER3 comprises an amino acid sequence having at least 60% sequence identity to the EGF-like domain of an NRG.

5 ~~5. The antigen-binding molecule for use, the use, or the method according to any one of claims 1 to 4, wherein the cancer comprising cells having an NRG gene fusion.~~

[Claim 63]. The ~~antigen-binding molecule for use, the use, or the method~~ according to claim ~~51 or claim 2,~~ wherein the NRG gene fusion is selected from *CLU-NRG1*, *CD74-NRG1*, *DOC4-NRG1*, *SLC3A2-NRG1*,
10 *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*.

15 [Claim 74]. The ~~antigen-binding molecule for use, the use, or the method~~ according to any one of claims 5 or claim 61 to 3, wherein the NRG gene fusion is selected from *CLU-NRG1*, *CD74-NRG1*, *SLC3A2-NRG1* or *VAMP2-NRG1*.

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

[Claim 86]. The ~~antigen-binding molecule for use, the use, or the method~~ according to any one of claims 1 to ~~75,~~ wherein the cancer derives from the lung, breast, head, neck, kidney, ovary, pancreas, prostate,
25 uterus, gallbladder, colon, rectum, bladder, soft tissue or nasopharynx.

[Claim 97]. The ~~antigen-binding molecule for use, the use, or the method~~ according to any one of claims 1 to ~~86,~~ 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
30 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,
35 neuroendocrine tumor and neuroendocrine tumor of the nasopharynx.

[Claim 108]. The ~~antigen-binding molecule for use, the use, or the method~~ according to any one of claims 1 to ~~97,~~ wherein the cancer is selected from lung cancer, non-small cell lung cancer, lung adenocarcinoma, invasive mucinous lung adenocarcinoma and lung squamous cell carcinoma.

~~11. The antigen-binding molecule for use, the use, or the method according to any one of claims 1 to 10, wherein the antigen-binding molecule comprises:~~

~~(i) a 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~~

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(ii) a 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.

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[Claim 129]. The antigen-binding molecule for use, the use, or the method according to any one of claims 1 to 118, 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

10 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 1310]. The antigen-binding molecule for use, the use, or the method according to any one of claims 1 to 129, wherein the antigen-binding molecule comprises:

15 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.

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[Claim 1411]. The antigen-binding molecule for use, the use, or the method according to any one of claims 1 to 1310, 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

25 LC-FR2 having the amino acid sequence of SEQ ID NO:110

LC-FR3 having the amino acid sequence of SEQ ID NO:120

LC-FR4 having the amino acid sequence of SEQ ID NO:125.

30 [Claim 1512]. The antigen-binding molecule for use, the use, or the method according to any one of claims 1 to 1411, wherein the antigen-binding molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:171.

35 [Claim 1613]. The antigen-binding molecule for use, the use, or the method according to any one of claims 1 to 1512, wherein the antigen-binding molecule comprises a light chain comprising the amino acid sequence of SEQ ID NO:177.

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