

We Claim:

1. An antibody or an antigen-binding fragment thereof binding to TIE-2 (tyrosine-protein kinase receptor) comprising:

a heavy-chain variable region comprising a heavy-chain CDR1 of SEQ ID NO: 1, a heavy-chain CDR2 of SEQ ID NO: 2 and a heavy-chain CDR3 of SEQ ID NO: 3, and a light-chain variable region comprising a light-chain CDR1 of SEQ ID NO: 4, a light-chain CDR2 of SEQ ID NO: 5 and a light-chain CDR3 of SEQ ID NO: 6;

a heavy-chain variable region comprising a heavy-chain CDR1 of SEQ ID NO: 7, a heavy-chain CDR2 of SEQ ID NO: 8 and a heavy-chain CDR3 of SEQ ID NO: 9, and a light-chain variable region comprising a light-chain CDR1 of SEQ ID NO: 10, a light-chain CDR2 of SEQ ID NO: 11, and a light-chain CDR3 of SEQ ID NO: 12;

a heavy-chain variable region comprising a heavy-chain CDR1 of SEQ ID NO: 13, a heavy-chain CDR2 of SEQ ID NO: 14 and a heavy-chain CDR3 of SEQ ID NO: 15, and a light-chain variable region comprising a light-chain CDR1 of SEQ ID NO: 16, a light-chain CDR2 of SEQ ID NO: 17, and a light-chain CDR3 of SEQ ID NO: 18;

a heavy-chain variable region comprising a heavy-chain CDR1 of SEQ ID NO: 19, a heavy-chain CDR2 of SEQ ID NO: 20 and a heavy-chain CDR3 of SEQ ID NO: 21, and a light-chain variable region comprising a light-chain CDR1 of SEQ ID NO: 22, a light-chain CDR2 of SEQ ID NO: 23, and a light-chain CDR3 of SEQ ID NO: 24;

a heavy-chain variable region comprising a heavy-chain CDR1 of SEQ ID NO: 25, a heavy-chain CDR2 of SEQ ID NO: 26 and a heavy-chain CDR3 of SEQ ID NO: 27, and a light-chain variable region comprising a light-chain CDR1 of SEQ ID NO: 28, a light-chain CDR2 of SEQ ID NO: 29, and a light-chain CDR3 of SEQ ID NO: 30; or

a heavy-chain variable region comprising a heavy-chain CDR1 of SEQ ID NO: 31, a heavy-chain CDR2 of SEQ ID NO: 32 and a heavy-chain CDR3 of SEQ ID NO: 33, and a light-chain variable region comprising a light-chain CDR1 of SEQ ID NO: 34, a light-chain CDR2 of SEQ ID NO: 35, and a light-chain CDR3 of SEQ ID NO: 36

~~a heavy-chain variable region comprising a heavy-chain CDR1 selected from the group consisting of SEQ ID NOS: 1, 7, 13, 19, 25 and 31, a heavy-chain CDR2 selected from the group consisting of SEQ ID NOS: 2, 8, 14, 20, 26 and 32, and a heavy-chain CDR3 selected from the group consisting of SEQ ID NOS: 3, 9, 15, 21, 27 and 33, and~~

~~a light chain variable region comprising a light chain CDR1 selected from the group~~

consisting of SEQ ID NOS: 4, 10, 16, 22, 28 and 34, a light chain CDR2 selected from the group consisting of SEQ ID NOS: 5, 11, 17, 23, 29 and 35, and a light chain CDR3 selected from the group consisting of SEQ ID NOS: 6, 12, 18, 24, 30 and 36.

2. — The antibody or an antigen-binding fragment thereof according to claim 1, wherein the antibody or an antigen-binding fragment thereof comprises:

a heavy-chain variable region comprising a heavy-chain CDR1 of SEQ ID NO: 1, a heavy-chain CDR2 of SEQ ID NO: 2 and a heavy-chain CDR3 of SEQ ID NO: 3, and a light-chain variable region comprising a light-chain CDR1 of SEQ ID NO: 4, a light-chain CDR2 of SEQ ID NO: 5 and a light-chain CDR3 of SEQ ID NO: 6;

a heavy-chain variable region comprising a heavy-chain CDR1 of SEQ ID NO: 7, a heavy-chain CDR2 of SEQ ID NO: 8 and a heavy-chain CDR3 of SEQ ID NO: 9, and a light-chain variable region comprising a light-chain CDR1 of SEQ ID NO: 10, a light-chain CDR2 of SEQ ID NO: 11, and a light-chain CDR3 of SEQ ID NO: 12;

a heavy-chain variable region comprising a heavy-chain CDR1 of SEQ ID NO: 13, a heavy-chain CDR2 of SEQ ID NO: 14 and a heavy-chain CDR3 of SEQ ID NO: 15, and a light-chain variable region comprising a light-chain CDR1 of SEQ ID NO: 16, a light-chain CDR2 of SEQ ID NO: 17, and a light-chain CDR3 of SEQ ID NO: 18;

a heavy-chain variable region comprising a heavy-chain CDR1 of SEQ ID NO: 19, a heavy-chain CDR2 of SEQ ID NO: 20, and a heavy-chain CDR3 of SEQ ID NO: 21, and a light-chain variable region comprising a light-chain CDR1 of SEQ ID NO: 22, a light-chain CDR2 of SEQ ID NO: 23, and a light-chain CDR3 of SEQ ID NO: 24;

a heavy-chain variable region comprising a heavy-chain CDR1 of SEQ ID NO: 25, a heavy-chain CDR2 of SEQ ID NO: 26, and a heavy-chain CDR3 of SEQ ID NO: 27, and a light-chain variable region comprising a light-chain CDR1 of SEQ ID NO: 28, a light-chain CDR2 of SEQ ID NO: 29, and a light-chain CDR3 of SEQ ID NO: 30; or

a heavy-chain variable region comprising a heavy-chain CDR1 of SEQ ID NO: 31, a heavy-chain CDR2 of SEQ ID NO: 32, and a heavy-chain CDR3 of SEQ ID NO: 33, and a light-chain variable region comprising a light-chain CDR1 of SEQ ID NO: 34, a light-chain CDR2 of SEQ ID NO: 35, and a light-chain CDR3 of SEQ ID NO: 36.

32. The antibody or an antigen-binding fragment thereof according to claim 1, wherein the antibody or an antigen-binding fragment thereof comprises a heavy-chain variable

region selected from the group consisting of SEQ ID NOS: 38, 42, 46, 50, 54 and 58.

43. The antibody or an antigen-binding fragment thereof according to claim 1, wherein the antibody or an antigen-binding fragment thereof comprises a light-chain variable region selected from the group consisting of SEQ ID NOS: 40, 44, 48, 52, 56 and 60.

54. A nucleic acid encoding the antibody or an antigen-binding fragment thereof according to any one of claims 1 to 43.

65. The nucleic acid according to claim 54, wherein the nucleic acid encoding the heavy-chain variable region is selected from the group consisting of SEQ ID NOS: 37, 41, 45, 49, 53 and 57 ; and wherein the nucleic acid encoding the light-chain variable region is selected from the group consisting of SEQ ID NOS: 39, 43, 47, 51, 55 and 59.

~~7. The nucleic acid according to claim 5, wherein the nucleic acid encoding the light-chain variable region is selected from the group consisting of SEQ ID NOS: 39, 43, 47, 51, 55 and 59.~~

86. An expression vector comprising the nucleic acid according to claim 54.

97. A cell transformed with the expression vector according to claim 86.

~~108~~. A method of producing an antibody binding to TIE2 or antigen-binding fragment thereof comprising:

(a) culturing the cell according to claim 97; and

(b) recovering an antibody or antigen-binding fragment thereof from the cultured cell.

~~149~~. A composition comprising the antibody or an antigen-binding fragment thereof according to any one of claims 1 to 43 as an active ingredient for preventing or treating an angiogenesis-related disease selected from the group consisting of tumor, cancer, metastasis of tumor or cancer, diabetic retinopathy, retinopathy of prematurity, corneal graft rejection, macular degeneration, neovascular glaucoma, erythrosis, proliferative retinopathy, psoriasis, hemophilic arthritis, capillary formation of atherosclerotic plaques, keloid, wound

granulation, vascular adhesion, rheumatoid arthritis, osteoarthritis, autoimmune diseases, Crohn's disease, restenosis, atherosclerosis, intestinal adhesions, cat scratch disease, ulcers, diabetic foot ulcers, liver cirrhosis, nephritis, diabetic nephropathy, chronic renal failure, diabetes mellitus, inflammatory diseases, idiopathic pulmonary fibrosis, sepsis, acute respiratory distress syndrome, and neurodegenerative diseases.

~~12.—The composition according to claim 11, wherein the angiogenesis-related disease is selected from the group consisting of tumor, cancer, metastasis of tumor or cancer, diabetic retinopathy, retinopathy of prematurity, corneal graft rejection, macular degeneration, neovascular glaucoma, erythrosis, proliferative retinopathy, psoriasis, hemophilic arthritis, capillary formation of atherosclerotic plaques, keloid, wound granulation, vascular adhesion, rheumatoid arthritis, osteoarthritis, autoimmune diseases, Crohn's disease, restenosis, atherosclerosis, intestinal adhesions, cat scratch disease, ulcers, diabetic foot ulcers, liver cirrhosis, nephritis, diabetic nephropathy, chronic renal failure, diabetes mellitus, inflammatory diseases, idiopathic pulmonary fibrosis, sepsis, acute respiratory distress syndrome, and neurodegenerative diseases.~~

~~13~~10. A composition comprising the antibody or an antigen-binding fragment thereof according to any one of claims 1 to ~~4~~3 as an active ingredient for stabilization of a blood vessel.

~~14~~11. A composition comprising the antibody or an antigen-binding fragment thereof according to any one of claims 1 to ~~4~~3 as an active ingredient for diagnosing an angiogenesis-related disease.

~~15~~12. A composition comprising the antibody or an antigen-binding fragment thereof according to any one of claims 1 to ~~4~~3 as an active ingredient for preventing or treating a tumor or a cancer.

~~16~~13. A composition comprising the antibody or an antigen-binding fragment thereof according to any one of claims 1 to ~~4~~3 as an active ingredient for combined administration with other therapeutic drugs.