

## METHODS OF TREATING CANCER

### BACKGROUND

[0001] Soluble forms of Fibroblast Growth Factor Receptor 1 (FGFR1) have been shown to inhibit tumor cell growth *in vitro* and *in vivo*. See, e.g., U.S. Patent No. 7,678,890. The efficacy of anti-cancer therapies is, in some instances, dependent on the genetic makeup of the cancer being targeted.

### SUMMARY

[0002] In one aspect, there is provided the use of a fibroblast growth factor receptor 1 (FGFR1) extracellular domain (ECD) or an FGFR1 ECD fusion molecule for preparation of a medicament for treating cancer in a subject, wherein the cancer is characterized by a higher level of FGF2 compared to the level of VEGF, wherein said higher level of FGF2 compared to the level of VEGF indicates therapeutic responsiveness by the cancer to a fibroblast growth factor receptor 1 (FGFR1) extracellular domain (ECD) or an FGFR1 ECD fusion molecule. In another aspect, there is provided the use of an FGFR1 ECD or an FGFR1 ECD fusion molecule for preparation of a medicament for treating cancer in a subject, wherein the cancer is characterized by a lower level of FGF2 compared to the level of VEGF, wherein the medicament comprises an FGFR1 ECD or an FGFR1 ECD fusion molecule, FGFR1 ECD or an FGFR1 ECD fusion molecule and a therapeutically effective amount of at least one anti-angiogenic agent, and wherein said lower level of FGF2 compared to the level of VEGF indicates therapeutic responsiveness by the cancer to an FGFR1 ECD or an FGFR1 ECD fusion molecule, FGFR1 ECD or an FGFR1 ECD fusion molecule and a therapeutically effective amount of at least one anti-angiogenic agent. In a further aspect, there is provided the use of an FGFR1 ECD or FGFR1 ECD fusion molecule for preparation of a medicament for reducing blood vessel density in a solid cancer. In yet another aspect, there is provided the use of an FGFR1 ECD or FGFR1 ECD fusion molecule for preparation of a medicament for treating mesothelioma in a subject, wherein the medicament comprises the FGFR1 ECD or FGFR1 ECD fusion molecule and at least one therapeutic agent selected from paclitaxel, carboplatin, docetaxel, pemetrexed, and cisplatin. In one aspect, there is provided a method of identifying a subject who may benefit from treatment with an FGFR1 ECD or an FGFR1 ECD fusion molecule, the method comprising determining the levels of FGF2 and VEGF in a sample obtained from the subject, wherein a higher level of FGF2 compared to the level of VEGF in the sample indicates that the subject may benefit from treatment with the fibroblast growth factor receptor 1 (FGFR1) extracellular domain (ECD) or an FGFR1 ECD fusion molecule. In another aspect, there is provided a method of

identifying a subject who may benefit from treatment with an FGFR1 ECD or an FGFR1 ECD fusion molecule and at least one anti-angiogenic agent, the method comprising determining the levels of FGF2 and VEGF in a sample obtained from the subject, wherein a lower level of FGF2 compared to the level of VEGF in the sample indicates that the subject may benefit from treatment with the FGFR1 ECD or FGFR1 ECD fusion molecule and the at least one anti-angiogenic agent. In some ~~embodiment~~examples, methods of treating cancer having a higher level of FGF2 compared to the level of VEGF in a subject are provided. In some ~~embodiment~~examples, a higher level of FGF2 compared to the level of VEGF is indicative of therapeutic responsiveness by the cancer to a fibroblast growth factor receptor 1 (FGFR1) extracellular domain (ECD) or an FGFR1 ECD fusion molecule. In some ~~embodiment~~examples, the method comprises administering a therapeutically effective amount of an FGFR1 ECD or an FGFR1 ECD fusion molecule to the subject. In another ~~embodiment~~example is provided a FGFR1 ECD or FGFR1 ECD fusion molecule for use in a method of treating cancer, characterised in that said cancer has a higher level of FGF2 compared to the level of VEGF in a subject. In a further ~~embodiment~~example is provided the use of an FGFR1 ECD or FDFR1 ECD fusion molecule in the manufacture of a medicament for use in a method of treating cancer, characterised in that said cancer has a higher level of FGF 2 compared to the level of VEGF in a subject. In some ~~embodiment~~examples, a method comprises administering a therapeutically effective amount of an FGFR1 ECD or an FGFR1 ECD fusion molecule and a therapeutically effective amount of at least one anti-angiogenic agent to the subject. In some ~~embodiment~~examples, the anti-angiogenic agent is a VEGF antagonist. In some ~~embodiment~~examples, the VEGF antagonist is selected from pazopanib, bevacizumab, axitinib, aflibercept, sorafenib, or sunitinib.

**[0003]** In some ~~embodiment~~examples, methods of treating cancer in a subject are provided, comprising administering a therapeutically effective amount of a fibroblast growth factor receptor 1 (FGFR1) extracellular domain (ECD) or an FGFR1 ECD fusion molecule to the subject. In some ~~embodiment~~examples, a method comprises administering a therapeutically effective amount of an FGFR1 ECD or an FGFR1 ECD fusion molecule and a therapeutically effective amount of at least one anti-angiogenic agent to the subject. In some ~~embodiment~~examples, prior to administration of the FGFR1 ECD or FGFR1 ECD fusion molecule, at least a portion of the cells of the cancer have been determined to have a higher level of FGF2 compared to the level of VEGF. In some ~~embodiment~~examples, at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, or at least 90% of the cells of a cancer

sample have been determined to have a higher level of FGF2 compared to the level of VEGF. In some embodimentsexamples, a higher level of FGF2 compared to the level of VEGF in a cancer is indicative of therapeutic responsiveness by the cancer to an FGFR1 ECD or FGFR1 ECD fusion molecule.

**[0004]** In some embodimentsexamples, methods of identifying a subject who may benefit from treatment with a fibroblast growth factor receptor 1 (FGFR1) extracellular domain (ECD) or an FGFR1 ECD fusion molecule are provided. In some embodimentsexamples, the method comprises determining the levels of FGF2 and VEGF in a sample obtained from the subject, wherein a higher level of FGF2 compared to the level of VEGF in the sample indicates that the subject may benefit from treatment with the fibroblast growth factor receptor 1 (FGFR1) extracellular domain (ECD) or an FGFR1 ECD fusion molecule.

**[0005]** In some embodimentsexamples, methods of predicting responsiveness of a subject with cancer to a fibroblast growth factor receptor 1 (FGFR1) extracellular domain (ECD) or an FGFR1 ECD fusion molecule are provided. In some embodimentsexamples, the method comprises determining the levels of FGF2 and VEGF in a sample obtained from the subject, wherein a higher level of FGF2 compared to the level of VEGF in the sample indicates that the cancer is predicted to respond to the fibroblast growth factor receptor 1 (FGFR1) extracellular domain (ECD) or an FGFR1 ECD fusion molecule.

**[0006]** In some embodimentsexamples, the FGF2 level is FGF2 mRNA level. In some embodimentsexamples, the VEGF level is VEGF mRNA level. In some embodimentsexamples, the mRNA level is determined by quantitative RT-PCR. In some embodimentsexamples, the mRNA level is determined by a method selected from quantitative RT-PCR, microarray, digital PCT, RNA-Seq, RNase Protection Assay (RPA), Northern blot, and in situ hybridization (ISH).

**[0007]** In some embodimentsexamples, the FGF2 level is FGF2 protein level. In some embodimentsexamples, the VEGF level is VEGF protein level. In some embodimentsexamples, the protein level is determined by immunohistochemistry. In some embodimentsexamples, the protein level is determined by a method selected from immunohistochemistry, ELISA, mass spectrometry, reverse phase protein array (RPPA), antibody array, nano-immuno assay, Western blot, and capillary protein analysis assay.

**[0008]** In some embodimentsexamples, the ratio of FGF2 level to VEGF level is greater than 1. In some embodimentsexamples, the ratio of FGF2 level to VEGF level is greater than 1.1. In some embodimentsexamples, the ratio of FGF2 level to VEGF level is greater than 1.2. In some embodimentsexamples, the ratio of FGF2 level to VEGF level is greater than 1.3. In some embodimentsexamples, the ratio of FGF2 level to VEGF level is greater than 1.4. In some embodimentsexamples, the ratio of FGF2 level to VEGF level is greater than 1.5.

**[0009]** In some ~~embodiments~~examples, the cancer is responsive to a FGFR1 ECD or a FGFR1 ECD fusion molecule as a monotherapy. In some ~~embodiments~~examples, the subject is administered a FGFR1 ECD or a FGFR1 ECD fusion molecule as a monotherapy.

**[0010]** In some ~~embodiments~~examples, the cancer is selected from kidney cancer (such as renal cell carcinoma), liver cancer (such as hepatocellular carcinoma), lung cancer, colon cancer, liver cancer, breast cancer, stomach cancer, ovarian cancer, endometrial cancer, esophageal cancer, head and neck cancer, glioblastoma, mesothelioma, and prostate cancer. In some ~~embodiments~~examples, the cancer is gastrointestinal stromal tumor.

**[0011]** In some ~~embodiments~~examples, methods of treating cancer having a lower level of FGF2 compared to the level of VEGF in a subject are provided. In some ~~embodiments~~examples, the method comprises administering to a subject with the cancer an FGFR1 ECD or FGFR1 ECD fusion molecule and at least one anti-angiogenic agent. In some ~~embodiments~~examples, a method comprises administering a therapeutically effective amount of an FGFR1 ECD or an FGFR1 ECD fusion molecule and a therapeutically effective amount of at least one anti-angiogenic agent to the subject. In some ~~embodiments~~examples, the anti-angiogenic agent is a VEGF antagonist. In some ~~embodiments~~examples, the VEGF antagonist is selected from pazopanib, bevacizumab, axitinib, aflibercept, sorafenib, or sunitinib.

**[0012]** In some ~~embodiments~~examples, methods of treating cancer in a subject are provided, comprising administering a therapeutically effective amount of a fibroblast growth factor receptor 1 (FGFR1) extracellular domain (ECD) or an FGFR1 ECD fusion molecule and a therapeutically effective amount of at least one anti-angiogenic agent to the subject. In some ~~embodiments~~examples, prior to administration of the FGFR1 ECD or FGFR1 ECD fusion molecule and at least one anti-angiogenic agent, at least a portion of the cells of the cancer have been determined to have a lower level of FGF2 compared to the level of VEGF. In some ~~embodiments~~examples, at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, or at least 90% of the cells of a cancer sample have been determined to have a lower level of FGF2 compared to the level of VEGF. In some ~~embodiments~~examples, methods of treating a cancer with a lower level of FGF2 compared to the level of VEGF are provided, comprising administering to a subject with the cancer an FGFR1 ECD or FGFR1 ECD fusion molecule and at least one anti-angiogenic agent.

**[0013]** In some ~~embodiments~~examples, methods of identifying a subject who may benefit from treatment with a fibroblast growth factor receptor 1 (FGFR1) extracellular domain (ECD) or an FGFR1 ECD fusion molecule and at least one anti-angiogenic agent are provided. In some ~~embodiments~~examples, the method comprises determining the levels of FGF2 and VEGF in a sample obtained from the subject, wherein the lower level of FGF2 compared to the level of

VEGF in the sample indicates that the subject may benefit from treatment with the fibroblast growth factor receptor 1 (FGFR1) extracellular domain (ECD) or an FGFR1 ECD fusion molecule and at least one anti-angiogenic agent.

**[0014]** In some embodimentsexamples, methods of predicting responsiveness of a subject with cancer to a fibroblast growth factor receptor 1 (FGFR1) extracellular domain (ECD) or an FGFR1 ECD fusion molecule and at least one anti-angiogenic agent are provided. In some embodimentsexamples, the method comprises determining the levels of FGF2 and VEGF in a sample obtained from the subject, wherein a lower level of FGF2 compared to the level of VEGF in the sample indicates that the cancer is predicted to respond to treatment with the fibroblast growth factor receptor 1 (FGFR1) extracellular domain (ECD) or an FGFR1 ECD fusion molecule and at least one anti-angiogenic agent.

**[0015]** In some embodimentsexamples, the FGF2 level is FGF2 mRNA level. In some embodimentsexamples, the VEGF level is VEGF mRNA level. In some embodimentsexamples, the mRNA level is determined by quantitative RT-PCR. In some embodimentsexamples, the mRNA level is determined by a method selected from quantitative RT-PCR, microarray, digital PCT, RNA-Seq, RNase Protection Assay (RPA), Northern blot, and in situ hybridization (ISH).

**[0016]** In some embodimentsexamples, the FGF2 level is FGF2 protein level. In some embodimentsexamples, the VEGF level is VEGF protein level. In some embodimentsexamples, the protein level is determined by immunohistochemistry. In some embodimentsexamples, the protein level is determined by a method selected from immunohistochemistry, ELISA, mass spectrometry, reverse phase protein array (RPPA), antibody array, nano-immuno assay, Western blot, and capillary protein analysis assay.

**[0017]** In some embodimentsexamples, the ratio of FGF2 level to VEGF level is less than 1. In some embodimentsexamples, the ratio of FGF2 level to VEGF level is less than 0.9. In some embodimentsexamples, the ratio of FGF2 level to VEGF level is less than 0.8. In some embodimentsexamples, the ratio of FGF2 level to VEGF level is less than 0.7. In some embodimentsexamples, the ratio of FGF2 level to VEGF level is less than 0.6.

**[0018]** In some embodimentsexamples, the cancer is selected from kidney cancer (such as renal cell carcinoma), liver cancer (such as hepatocellular carcinoma), lung cancer, colon cancer, liver cancer, breast cancer, stomach cancer, ovarian cancer, endometrial cancer, esophageal cancer, head and neck cancer, glioblastoma, mesothelioma, and prostate cancer. In some embodimentsexamples, the cancer is gastrointestinal stromal tumor. In some embodimentsexamples, the cancer is selected from kidney cancer (such as renal cell carcinoma), liver cancer (such as hepatocellular carcinoma), and mesothelioma. In some embodimentsexamples, the cancer is renal cell

carcinoma. In some ~~embodiments~~examples, the cancer is hepatocellular carcinoma. In some ~~embodiments~~examples, the cancer is mesothelioma.

**[0019]** In some ~~embodiments~~examples, methods of treating renal cell carcinoma (RCC) are provided. In some ~~embodiments~~examples, the method comprises administering to a subject with RCC a fibroblast growth factor receptor 1 (FGFR1) extracellular domain (ECD) or an FGFR1 ECD fusion molecule and a VEGF antagonist. In some ~~embodiments~~examples, the method comprises administering to a subject with RCC an FGFR1 ECD or FGFR1 ECD fusion molecule and a VEGF antagonist selected from axitinib, pazopanib, and sorafenib.

**[0020]** In some ~~embodiments~~examples, methods of treating cancer are provided, comprising administering to a subject with cancer an FGFR1 ECD or FGFR1 ECD fusion molecule wherein the subject has previously been treated with at least one therapeutic agent selected from pazopanib, bevacizumab, axitinib, aflibercept, sorafenib, and sunitinib. In some ~~embodiments~~examples, the subject has previously been treated with pazopanib. In some ~~embodiments~~examples, the subject's cancer has become pazopanib-resistant during or following pazopanib treatment. In some ~~embodiments~~examples, methods of treating pazopanib-resistant cancer are provided, comprising administering to a subject with pazopanib-resistant cancer an FGFR1 ECD or FGFR1 ECD fusion molecule. In some ~~embodiments~~examples, the method comprises administering pazopanib and an FGFR1 ECD or FGFR1 ECD fusion molecule.

**[0021]** In some ~~embodiments~~examples, methods of treating cancer are provided, comprising administering to a subject with cancer an FGFR1 ECD or FGFR1 ECD fusion molecule and axitinib, wherein the subject has previously been treated with at least one therapeutic agent selected from pazopanib, bevacizumab, axitinib, aflibercept, sorafenib, and sunitinib. In some such ~~embodiments~~examples, at least one therapeutic agent is selected from pazopanib, axitinib, and sorafenib. In some such ~~embodiments~~examples, at least one therapeutic agent is pazopanib. In some ~~embodiments~~examples, the cancer is selected from kidney cancer (such as renal cell carcinoma), liver cancer (such as hepatocellular carcinoma), glioblastoma, and mesothelioma.

**[0022]** In some ~~embodiments~~examples, methods of treating VEGF-resistant cancers are provided. In some ~~embodiments~~examples, methods comprise administering to a subject with a VEGF-resistant cancer an FGFR1 ECD or FGFR1 ECD fusion molecule. In some ~~embodiments~~examples, a VEGF-resistant cancer is a cancer with high FGF2 expression and/or with an FGF2/VEGF ratio of greater than 1. In some ~~embodiments~~examples, the VEGF-resistant cancer is selected from kidney cancer (such as renal cell carcinoma), liver cancer (such as hepatocellular carcinoma), glioblastoma, and mesothelioma.

**[0023]** In some ~~embodiments~~examples, methods of reducing blood vessel density in a solid cancer are provided. In some ~~embodiments~~examples, methods of reducing blood vessel density in a solid

cancer are provided, wherein the cancer has a higher level of FGF2 compared to the level of VEGF. In some embodimentsexamples, methods of reducing blood vessel density in a VEGF-resistant solid cancer are provided. In some embodimentsexamples, a method of reducing blood vessel density in a solid cancer comprises administering to a subject with cancer an FGFR1 ECD or FGFR1 ECD fusion molecule. In some embodimentsexamples, blood vessel density is measured in the whole tumor sample. In some embodimentsexamples, the cancer is selected from kidney cancer (such as renal cell carcinoma), liver cancer (such as hepatocellular carcinoma), lung cancer, colon cancer, liver cancer, breast cancer, stomach cancer, ovarian cancer, endometrial cancer, esophageal cancer, head and neck cancer, glioblastoma, mesothelioma, and prostate cancer. In some embodimentsexamples, the cancer is selected from kidney cancer (such as renal cell carcinoma), liver cancer (such as hepatocellular carcinoma), glioblastoma, and mesothelioma. In some embodimentsexamples, the cancer is renal cell carcinoma. In some embodimentsexamples, the cancer is hepatocellular carcinoma. In some embodimentsexamples, the cancer is mesothelioma.

**[0024]** In some embodimentsexamples, methods of treating mesothelioma are provided, comprising administering to a subject with mesothelioma an FGFR1 ECD or FGFR1 ECD fusion molecule and at least one therapeutic agent selected from paclitaxel, carboplatin, docetaxel, pemetrexed, and cisplatin. In some embodimentsexamples, the method comprises administering an FGFR1 ECD or FGFR1 ECD fusion molecule, paclitaxel and carboplatin. In some embodimentsexamples, the method comprises administering an FGFR1 ECD or FGFR1 ECD fusion molecule and docetaxel. In some embodimentsexamples, the method comprises administering an FGFR1 ECD or FGFR1 ECD fusion molecule, pemetrexed, and cisplatin. In some embodimentsexamples, administration of the FGFR1 ECD or FGFR1 ECD fusion molecule and at least one therapeutic agent reduces blood vessel density in the mesothelioma. In some embodimentsexamples, the mesothelioma has a high level of FGF2. In some embodimentsexamples, the mesothelioma has a higher level of FGF2 compared to the level of VEGF. In some embodimentsexamples, the ratio of FGF2 level to VEGF level is greater than 1.

**[0025]** In any of the methods described herein, the method may comprise administering an FGFR1 ECD. In some embodimentsexamples, the FGFR1 ECD comprises an amino acid sequence selected from SEQ ID NOs: 1 to 4.

**[0026]** In any of the methods described herein, the method may comprise administering an FGFR1 ECD fusion molecule. In some embodimentsexamples, the FGFR1 ECD fusion molecule comprises an FGFR1 ECD and a fusion partner, and wherein the fusion partner is Fc. In some embodimentsexamples, the FGFR1 ECD fusion molecule comprises a sequence selected from SEQ ID NO: 5 and SEQ ID NO: 6.

[0027] In one ~~embodiment~~example the present ~~invention~~disclosure provides the use of a therapeutically effective amount of an FGFR1 ECD or an FGFR1 ECD fusion molecule for the treatment of cancer in a subject wherein said cancer has a higher level of FGF2 compared to the level of VEGF wherein a higher level of FGF2 compared to the level of VEGF is indicative of therapeutic responsiveness by the cancer to a fibroblast growth factor receptor 1 (FGFR1) extracellular domain (ECD) or an FGFR1 ECD fusion molecule.

[0028] In another ~~embodiment~~examples, the present ~~invention~~disclosure provides the use of a therapeutically effective amount of a fibroblast growth factor receptor 1 (FGFR1) extracellular domain (ECD) or an FGFR1 ECD fusion molecule for the treatment of cancer in a subject, wherein, prior to administration of the FGFR1 ECD or FGFR1 ECD fusion molecule, at least a portion of the cells of the cancer have been determined to have a higher level of FGF2 compared to the level of VEGF, and wherein a higher level of FGF2 compared to the level of VEGF in a cancer is indicative of therapeutic responsiveness by the cancer to an FGFR1 ECD or FGFR1 ECD fusion molecule.

[0029] In another ~~embodiment~~example, the present ~~invention~~disclosure provides the use of a fibroblast growth factor receptor 1 (FGFR1) extracellular domain (ECD) or an FGFR1 ECD fusion molecule in the manufacture of a medicament for the treatment of cancer in a subject wherein said cancer has a higher level of FGF2 compared to the level of VEGF, wherein a higher level of FGF2 compared to the level of VEGF is indicative of therapeutic responsiveness by the cancer to a fibroblast growth factor receptor 1 (FGFR1) extracellular domain (ECD) or an FGFR1 ECD fusion molecule

[0030] In another ~~embodiment~~example, the present ~~invention~~disclosure provides the use of a fibroblast growth factor receptor 1 (FGFR1) extracellular domain (ECD) or an FGFR1 ECD fusion molecule in the manufacture of a medicament for the treatment of cancer in a subject wherein, prior to administration of the FGFR1 ECD or FGFR1 ECD fusion molecule, at least a portion of the cells of the cancer have been determined to have a higher level of FGF2 compared to the level of VEGF, and wherein a higher level of FGF2 compared to the level of VEGF in a cancer is indicative of therapeutic responsiveness by the cancer to an FGFR1 ECD or FGFR1 ECD fusion molecule.

[0031] In one ~~embodiment~~example the present ~~invention~~disclosure provides the use of a therapeutically effective amount of an FGFR1 ECD or an FGFR1 ECD fusion molecule and a therapeutically effective amount of at least one anti-angiogenic agent for the treatment of cancer in a subject wherein said cancer has a lower level of FGF2 compared to the level of VEGF wherein a lower level of FGF2 compared to the level of VEGF is indicative of therapeutic

responsiveness by the cancer to an FGFR1 ECD or FGFR1 ECD fusion molecule and at least one anti-angiogenic agent.

[0032] In another ~~embodiment~~example, the present ~~invention~~disclosure provides the use of a therapeutically effective amount of a fibroblast growth factor receptor 1 (FGFR1) extracellular domain (ECD) or an FGFR1 ECD fusion molecule and at least one anti-angiogenic agent for the treatment of cancer in a subject, wherein, prior to administration of the FGFR1 ECD or FGFR1 ECD fusion molecule and at least one anti-angiogenic agent at least a portion of the cells of the cancer have been determined to have a lower level of FGF2 compared to the level of VEGF, and wherein a lower level of FGF2 compared to the level of VEGF in a cancer is indicative of therapeutic responsiveness by the cancer to an FGFR1 ECD or FGFR1 ECD fusion molecule and at least one anti-angiogenic agent.

[0033] In another ~~embodiment~~example, the present ~~invention~~disclosure provides the use of a fibroblast growth factor receptor 1 (FGFR1) extracellular domain (ECD) or an FGFR1 ECD fusion molecule and an anti-angiogenic agent in the manufacture of a medicament for the treatment of cancer in a subject wherein said cancer has a lower level of FGF2 compared to the level of VEGF, wherein a lower level of FGF2 compared to the level of VEGF is indicative of therapeutic responsiveness by the cancer to a fibroblast growth factor receptor 1 (FGFR1) extracellular domain (ECD) or an FGFR1 ECD fusion molecule and an anti-angiogenic agent.

[0034] In another ~~embodiment~~example, the present ~~invention~~disclosure provides the use of a fibroblast growth factor receptor 1 (FGFR1) extracellular domain (ECD) or an FGFR1 ECD fusion molecule and an anti-angiogenic agent in the manufacture of a medicament for the treatment of cancer in a subject wherein, prior to administration of the FGFR1 ECD or FGFR1 ECD fusion molecule and an anti-angiogenic agent, at least a portion of the cells of the cancer have been determined to have a lower level of FGF2 compared to the level of VEGF, and wherein a lower level of FGF2 compared to the level of VEGF in a cancer is indicative of therapeutic responsiveness by the cancer to an FGFR1 ECD or FGFR1 ECD fusion molecule and an anti-angiogenic agent.

[0035] In one ~~embodiment~~example of the ~~invention~~disclosure is provided an FGFR1 ECD or FGFR1 ECD fusion protein for use in a method of reducing blood vessel density in a solid cancer. In one ~~aspect of this embodiment~~example, said solid cancer has a higher level of FGF2 compared to the level of VEGF.

[0036] In one ~~embodiment~~example of the ~~invention~~disclosure is provided the use of an FGFR1 ECD or FGFR1 ECD fusion protein in the manufacture of a medicament for use in a method of

reducing blood vessel density in a solid cancer. In one ~~aspect of this embodiment~~example, said solid cancer has a higher level of FGF2 compared to the level of VEGF.

**[0037]** In a further ~~embodiment~~example of the ~~invention~~disclosure is provided an FGFR1 ECD or FGFR1 ECD fusion molecule and at least one therapeutic agent selected from paclitaxel, carboplatin, docetaxel, pemetrexed and cisplatin for use in the treatment of mesothelioma. In one ~~aspect of this embodiment~~example, said treatment involves the use of an FGFR1 ECD or FGFR1 ECD fusion molecule, paclitaxel and carboplatin. In one ~~aspect of this embodiment~~example said treatment involves the use of an FGFR1 ECD or FGFR1 ECD fusion molecule and docetaxel. In one ~~aspect of this embodiment~~example, said treatment involves the use of an FGFR1 ECD or FGFR1 ECD fusion molecule, pemetrexed, and cisplatin. In any of these ~~aspects~~examples, administration of the FGFR1 or FGFR1 ECD fusion molecule and at least one therapeutic agent reduces the blood vessel density in said mesothelioma.

**[0038]** In a further ~~embodiment~~example of the ~~invention~~disclosure is provided the use of FGFR1 ECD or FGFR1 ECD fusion molecule and at least one therapeutic agent selected from paclitaxel, carboplatin, docetaxel, pemetrexed and cisplatin in the manufacture of a medicament for use in the treatment of mesothelioma. In one ~~aspect of this embodiment~~example, said medicament comprises an FGFR1 ECD or FGFR1 ECD fusion molecule, paclitaxel and carboplatin. In one ~~aspect of this embodiment~~example said medicament comprises an FGFR1 ECD or FGFR1 ECD fusion molecule and docetaxel. In one ~~aspect of this embodiment~~example, said medicament comprises an FGFR1 ECD or FGFR1 ECD fusion molecule, pemetrexed, and cisplatin. In any of these ~~aspects~~examples, administration of said medicament reduces the blood vessel density in said mesothelioma.

**[0039]** In any ~~aspect of these embodiments~~examples, the FGF2 level or VEGF level may be mRNA levels. In one ~~feature of this aspect~~example, the mRNA level may be determined by quantitative RT-PCR.

**[0040]** Further, in any ~~aspect of these embodiments~~examples, the FGF2 level or VEGF level may be protein levels. In one ~~feature of this aspect~~example, the protein level may be determined by immunohistochemistry.

**[0041]** In any ~~aspect of these embodiments~~examples, the anti-angiogenic agent is a VEGF antagonist. In a further ~~feature of this aspect~~example, the VEGF antagonist is selected from pazopanib, bevacizumab, axitinib, aflibercept, sorafenib, or sunitinib.

**[0042]** In any ~~aspect of these embodiments~~examples, the cancer is selected from kidney cancer (such as renal cell carcinoma), liver cancer (such as hepatocellular carcinoma), lung cancer, colon cancer, liver cancer, breast cancer, stomach cancer, ovarian cancer, endometrial cancer, esophageal cancer, head and neck cancer, glioblastoma, and prostate cancer.

**[0043]** In any ~~aspect of these embodiments~~examples, the composition used in the treatment of cancer or the medicament used in the treatment of cancer comprises an FGFR1 ECD. In one ~~feature of this aspect~~example the FGFR1 ECD comprises an amino acid sequence selected from SEQ ID NOs: 1 to 4.

**[0044]** In any ~~aspect of these embodiments~~examples, the composition used in the treatment of cancer or the medicament used in the treatment of cancer comprises an FGFR1 ECD fusion molecule. In one ~~feature of this aspect~~examples, the FGFR1 ECD fusion molecule comprises an FGFR1 ECD and a fusion partner, and wherein the fusion partner is Fc. In one further ~~feature of this aspect~~example, the FGFR1 ECD fusion molecule comprises a sequence selected from SEQ ID NO: 5 and SEQ ID NO: 6.

**[0045]** In any ~~examples~~aspect of these some embodiments, “at least a portion of the cells” is at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, or at least 90% of the cells of a cancer sample.

**[0046]** In some ~~embodiments~~examples, the FGFR1 ECD or FGFR1 ECD fusion molecule is an amount in the range of about 0.5 mg/kg body weight to about 30 mg/kg body weight, such as an amount in the range of about 8 to about 16 mg/kg body weight, calculated using an extinction coefficient of 1.42 mL/mg\*cm. *See* Table 1. In some ~~embodiments~~examples, the therapeutically effective amount of the FGFR1 ECD or FGFR1 ECD fusion molecule is a dose of about 8 mg/kg body weight. In some ~~embodiments~~examples, the therapeutically effective amount of the FGFR1 ECD or FGFR1 ECD fusion molecule is a dose of about 16 mg/kg body weight. In some ~~embodiments~~examples, the therapeutically effective amount of the FGFR1 ECD or FGFR1 ECD fusion molecule is a dose of about 20 mg/kg body weight. In some ~~embodiments~~examples, dosages may be administered twice a week, weekly, every other week, at a frequency between weekly and every other week, every three weeks, every four weeks, or every month.

**[0047]** In certain ~~embodiments~~examples, the cancer is prostate cancer, breast cancer, colorectal cancer, stomach cancer, lung cancer, brain cancer, ovarian cancer, endometrial cancer, esophageal cancer, head and neck cancer, laryngeal cancer, liver cancer, renal cancer (kidney cancer), glioblastoma, or pancreatic cancer. In certain ~~embodiments~~examples, the cancer is breast cancer, esophageal cancer, renal cancer, head and neck cancer, or lung cancer. In certain ~~embodiments~~examples, the cancer is lung cancer. In some ~~embodiments~~examples, the lung cancer is non-small cell lung cancer. In some ~~embodiments~~examples, the lung cancer is small cell lung cancer. In some ~~embodiments~~examples, the lung cancer is squamous cell carcinoma. In some ~~embodiments~~examples, the cancer is head and neck cancer. In some ~~embodiments~~examples, the head and neck cancer is squamous cell carcinoma of the head and neck. In some ~~examples~~embodiments, the cancer is selected from kidney

cancer (such as renal cell carcinoma), liver cancer (such as hepatocellular carcinoma), and mesothelioma. In some embodimentsexamples, the cancer is renal cell carcinoma. In some embodimentsexamples, the cancer is hepatocellular carcinoma. In some embodimentsexamples, the cancer is mesothelioma.

[0048] Any embodimentexample described herein or any combination thereof applies to any and all methods of the invention described herein.

#### BRIEF DESCRIPTION OF THE DRAWINGS

[0049] FIG. 1A-C show mean tumor volume at various time points in mice implanted with ACHN cells and treated with FGFR1-ECD.339-Fc ("FP-1039"), FGFR1-ECD.339-Fc ("FP-1039") and pazopanib, or albumin, as described in Example 2.

[0050] FIG. 2A-C show mean tumor volume at various time points in mice implanted with 786-0 cells and treated with FGFR1-ECD.339-Fc ("FP-1039"), pazopanib, FGFR1-ECD.339-Fc ("FP-1039") and pazopanib, or albumin, as described in Example 3.

[0051] FIG. 3A-C show mean tumor volume at various time points in mice implanted with A498 cells and treated with FGFR1-ECD.339-Fc ("FP-1039"), pazopanib, FGFR1-ECD.339-Fc ("FP-1039") and pazopanib, or albumin, as described in Example 4.

[0052] FIG. 4A-B show mean tumor volume at various time points in mice implanted with Caki-2 cells and treated with FGFR1-ECD.339-Fc ("FP-1039"), pazopanib, FGFR1-ECD.339-Fc ("FP-1039") and pazopanib, or albumin, as described in Example 5.

[0053] FIG. 5A-C show mean tumor volume at various time points in mice implanted with SK-Hep-1 cells and treated with FGFR1-ECD.339-Fc ("FP-1039"), pazopanib, FGFR1-ECD.339-Fc ("FP-1039") and pazopanib, or albumin, as described in Example 6.

[0054] FIG. 6A-C show mean tumor volume at various time points in mice implanted with (A) HepG2 cells, (B) Huh7 cells, and (C) Hep3B cells and treated with FGFR1-ECD.339-Fc ("FP-1039") or albumin or vehicle, as described in Example 7.

[0055] FIG. 7A-C show (A) mean tumor volume at various time points, and (B) final tumor volume and (C) final tumor weight, in mice implanted with SK-Hep-1 cells and treated with FGFR1-ECD.339-Fc ("FP-1039"), sorafenib, FGFR1-ECD.339-Fc ("FP-1039") and sorafenib, or albumin, as described in Example 8.

[0056] FIG. 8A-B show (A) FGF2 mRNA (normalized to GUSB) and (B) FGF2 protein expression (normalized to total protein) in FGFR1-ECD.339-Fc responder and non-responder xenografts, as described in Example 9.

## CLAIMS

1. A method of treating cancer having a higher level of FGF2 compared to the level of VEGF in a subject, wherein a higher level of FGF2 compared to the level of VEGF is indicative of therapeutic responsiveness by the cancer to a fibroblast growth factor receptor 1 (FGFR1) extracellular domain (ECD) or an FGFR1 ECD fusion molecule, comprising administering a therapeutically effective amount of an FGFR1 ECD or an FGFR1 ECD fusion molecule to the subject.
2. A method of treating cancer in a subject, comprising:  
administering a therapeutically effective amount of a fibroblast growth factor receptor 1 (FGFR1) extracellular domain (ECD) or an FGFR1 ECD fusion molecule to the subject,  
wherein, prior to administration of the FGFR1 ECD or FGFR1 ECD fusion molecule, at least a portion of the cells of the cancer have been determined to have a higher level of FGF2 compared to the level of VEGF, and  
wherein a higher level of FGF2 compared to the level of VEGF in a cancer is indicative of therapeutic responsiveness by the cancer to an FGFR1 ECD or FGFR1 ECD fusion molecule.
3. A method of identifying a subject who may benefit from treatment with a fibroblast growth factor receptor 1 (FGFR1) extracellular domain (ECD) or an FGFR1 ECD fusion molecule, the method comprising determining the levels of FGF2 and VEGF in a sample obtained from the subject, wherein a higher level of FGF2 compared to the level of VEGF in the sample indicates that the subject may benefit from treatment with the fibroblast growth factor receptor 1 (FGFR1) extracellular domain (ECD) or an FGFR1 ECD fusion molecule.
4. The method of any one of the preceding claims, wherein the FGF2 level is FGF2 mRNA level.
5. The method of any one of the preceding claims, wherein the VEGF level is VEGF mRNA level.
6. The method of claim 4 or claim 5, wherein the mRNA level is determined by quantitative RT-PCR.
7. The method of any one of claims 1 to 3, wherein the FGF2 level is FGF2 protein level.
8. The method of any one of claims 1 to 3 and 7, wherein the VEGF level is VEGF protein level.
9. The method of claim 7 or claim 8, wherein the protein level is determined by immunohistochemistry.

10. The method of any one of the preceding claims, wherein the ratio of FGF2 level to VEGF level is greater than 1.
11. The method of any one of the preceding claims, wherein the cancer is responsive to a FGFR1 ECD or a FGFR1 ECD fusion molecule as a monotherapy.
12. The method of any one of the preceding claims, wherein the subject is administered a FGFR1 ECD or a FGFR1 ECD fusion molecule as a monotherapy.
13. The method of any one of the preceding claims, wherein the cancer is selected from kidney cancer (such as renal cell carcinoma), liver cancer (such as hepatocellular carcinoma), lung cancer, colon cancer, liver cancer, breast cancer, stomach cancer, ovarian cancer, endometrial cancer, esophageal cancer, head and neck cancer, glioblastoma, mesothelioma, and prostate cancer.
14. A method of treating cancer having a lower level of FGF2 compared to the level of VEGF in a subject, comprising administering a therapeutically effective amount of an FGFR1 ECD or an FGFR1 ECD fusion molecule and a therapeutically effective amount of at least one anti-angiogenic agent to the subject.
15. A method of treating cancer in a subject, comprising:  
administering a therapeutically effective amount of a fibroblast growth factor receptor 1 (FGFR1) extracellular domain (ECD) or an FGFR1 ECD fusion molecule and at least one anti-angiogenic agent to the subject,  
wherein, prior to administration of the FGFR1 ECD or FGFR1 ECD fusion molecule and at least one anti-angiogenic agent, at least a portion of the cells of the cancer have been determined to have a lower level of FGF2 compared to the level of VEGF.
16. A method of identifying a subject who may benefit from treatment with a fibroblast growth factor receptor 1 (FGFR1) extracellular domain (ECD) or an FGFR1 ECD fusion molecule and at least one anti-angiogenic agent, the method comprising determining the levels of FGF2 and VEGF in a sample obtained from the subject, wherein the lower level of FGF2 compared to the level of VEGF in the sample indicates that the subject may benefit from treatment with the fibroblast growth factor receptor 1 (FGFR1) extracellular domain (ECD) or an FGFR1 ECD fusion molecule and at least one anti-angiogenic agent.
17. The method of any one of claims 14 to 16, wherein the FGF2 level is FGF2 mRNA level.
18. The method of any one of claims 14 to 17, wherein the VEGF level is VEGF mRNA level.
19. The method of any one of claims 17 to 18, wherein the mRNA level is determined by quantitative RT-PCR.

20. The method of any one of claims 14 to 16, wherein the FGF2 level is FGF2 protein level.
21. The method of any one of claims 14 to 16 and 20, wherein the VEGF level is VEGF protein level.
22. The method of claim 20 or claim 21, wherein the protein level is determined by immunohistochemistry.
23. The method of any one of claims 14 to 22, wherein the ratio of FGF2 level to VEGF level is less than 1.
24. The method of any one of claims 14 to 23, wherein the anti-angiogenic agent is a VEGF antagonist.
25. The method of claim 24, wherein the VEGF antagonist is selected from pazopanib, bevacizumab, axitinib, aflibercept, sorafenib, or sunitinib.
26. A method of reducing blood vessel density in a solid cancer, comprising administering to a subject with the solid cancer an FGFR1 ECD or FGFR1 ECD fusion molecule.
27. The method of claim 26, wherein the solid cancer has a higher level of FGF2 compared to the level of VEGF.
28. The method of claim 27, wherein the FGF2 level is FGF2 mRNA level.
29. The method of claim 27 or claim 28, wherein the VEGF level is VEGF mRNA level.
30. The method of claim 28 or claim 29, wherein the mRNA level is determined by quantitative RT-PCR.
31. The method of claim 27, wherein the FGF2 level is FGF2 protein level.
32. The method of claim 27 or claim 31, wherein the VEGF level is VEGF protein level.
33. The method of claim 31 or claim 32, wherein the protein level is determined by immunohistochemistry.
34. The method of any one of claims 27 to 33, wherein the ratio of FGF2 level to VEGF level is greater than 1.
35. The method of any one of claims 14 to 34, wherein the cancer is selected from kidney cancer (such as renal cell carcinoma), liver cancer (such as hepatocellular carcinoma), lung cancer, colon cancer, liver cancer, breast cancer, stomach cancer, ovarian cancer, endometrial cancer, esophageal cancer, head and neck cancer, glioblastoma, mesothelioma, and prostate cancer.
36. A method of treating mesothelioma comprising administering to a subject with

mesothelioma an FGFR1 ECD or FGFR1 ECD fusion molecule and at least one therapeutic agent selected from paclitaxel, carboplatin, docetaxel, pemetrexed, and cisplatin.

37. The method of claim 36, wherein the method comprises administering an FGFR1 ECD or FGFR1 ECD fusion molecule, paclitaxel and carboplatin.

38. The method of claim 36, wherein the method comprises administering an FGFR1 ECD or FGFR1 ECD fusion molecule and docetaxel.

39. The method of claim 36, wherein the method comprises administering an FGFR1 ECD or FGFR1 ECD fusion molecule, pemetrexed, and cisplatin.

40. The method of any one of claim 36 to 39, wherein administration of the FGFR1 ECD or FGFR1 ECD fusion molecule and at least one therapeutic agent reduces blood vessel density in the mesothelioma.

41. The method of any one of claims 36 to 40, wherein the mesothelioma has a higher level of FGF2 compared to a level of FGF2 in a reference sample or cell.

42. The method of any one of claims 36 to 41, wherein the mesothelioma has a higher level of FGF2 compared to the level of VEGF.

43. The method of claim 41 or claim 42, wherein the FGF2 level is FGF2 mRNA level.

44. The method of claim 42 or claim 43, wherein the VEGF level is VEGF mRNA level.

45. The method of claim 43 or claim 44, wherein the mRNA level is determined by quantitative RT-PCR.

46. The method of claim 41 or claim 42, wherein the FGF2 level is FGF2 protein level.

47. The method of claim 42 or claim 46, wherein the VEGF level is VEGF protein level.

48. The method of claim 46 or claim 47, wherein the protein level is determined by immunohistochemistry.

49. The method of any one of claims 42 to 48, wherein the ratio of FGF2 level to VEGF level is greater than 1.

50. The method of any one of the preceding claims, wherein the subject has previously been treated with at least one therapeutic agent selected from pazopanib, bevacizumab, axitinib, aflibercept, sorafenib, and sunitinib.

51. The method of claim 50, wherein the subject has a VEGF-resistant cancer or a pazopanib-resistant cancer.

52. The method of any one of the preceding claims, wherein the method

comprises administering an FGFR1 ECD.

53. The method of claim 52, wherein the FGFR1 ECD comprises an amino acid sequence selected from SEQ ID NOs: 1 to 4.

54. The method of any one of claims 1 to 52, wherein the method comprises administering an FGFR1 ECD fusion molecule.

55. The method of claim 54, wherein the FGFR1 ECD fusion molecule comprises an FGFR1 ECD and a fusion partner, and wherein the fusion partner is Fc.

56. The method of claim 55, wherein the FGFR1 ECD fusion molecule comprises a sequence selected from SEQ ID NO: 5 and SEQ ID NO: 6.

## CLAIMS

1. Use of a fibroblast growth factor receptor 1 (FGFR1) extracellular domain (ECD) or an FGFR1 ECD fusion molecule for preparation of a medicament for treating cancer in a subject, wherein the cancer is characterized by a higher level of FGF2 compared to the level of VEGF, wherein said higher level of FGF2 compared to the level of VEGF indicates therapeutic responsiveness by the cancer to a fibroblast growth factor receptor 1 (FGFR1) extracellular domain (ECD) or an FGFR1 ECD fusion molecule.
2. The use of claim 1, wherein least a portion of the cells of the subject's cancer have been determined to have a higher level of FGF2 compared to the level of VEGF prior to treatment with the FGFR1 ECD or FGFR1 ECD fusion molecule.
3. The use of claim 1 or 2, wherein the FGF2 level is FGF2 mRNA level and the VEGF level is VEGF mRNA level.
4. The use of claim 1 or 2, wherein the FGF2 level is FGF2 protein level and the VEGF level is VEGF protein level.
5. The use of any one of claims 1 to 4, wherein the ratio of FGF2 level to VEGF level is greater than 1.
6. The use of any one of claims 1 to 5, wherein the cancer is responsive to a FGFR1 ECD or a FGFR1 ECD fusion molecule as a monotherapy.
7. The use of any one of claims 1 to 6, wherein the medicament comprises a FGFR1 ECD or a FGFR1 ECD fusion molecule as a monotherapy.
8. The use of any one of claims 1 to 7, wherein the cancer is selected from kidney cancer (such as renal cell carcinoma), liver cancer (such as hepatocellular carcinoma), lung cancer, colon cancer, liver cancer, breast cancer, stomach cancer, ovarian cancer, endometrial cancer, esophageal cancer, head and neck cancer, glioblastoma, mesothelioma, and prostate cancer.
9. Use of an FGFR1 ECD or an FGFR1 ECD fusion molecule for preparation of a medicament for treating cancer in a subject, wherein the cancer is characterized by a lower level of FGF2 compared to the level of VEGF, wherein the medicament comprises an FGFR1 ECD or an FGFR1 ECD fusion molecule, FGFR1 ECD or an FGFR1 ECD fusion molecule and a therapeutically effective amount of at least one anti-angiogenic agent, and wherein said lower level of FGF2 compared to the level of VEGF indicates therapeutic responsiveness by the cancer to an FGFR1

ECD or an FGFR1 ECD fusion molecule, FGFR1 ECD or an FGFR1 ECD fusion molecule and a therapeutically effective amount of at least one anti-angiogenic agent.

10. The use of claim 9, wherein least a portion of the cells of the subject's cancer have been determined to have a lower level of FGF2 compared to the level of VEGF prior to treatment with the FGFR1 ECD or FGFR1 ECD fusion molecule and the at least one anti-angiogenic agent.

11. The use of claim 9 or 10, wherein the FGF2 level is FGF2 mRNA level and the VEGF level is VEGF mRNA level.

12. The use of claim 9 or 10, wherein the FGF2 level is FGF2 protein level and the VEGF level is VEGF protein level.

13. The use of any one of claims 9 to 12, wherein the ratio of FGF2 level to VEGF level is less than 1.

14. The use of any one of claims 9 to 13, wherein the anti-angiogenic agent is a VEGF antagonist.

15. The use of claim 14, wherein the VEGF antagonist is selected from pazopanib, bevacizumab, axitinib, aflibercept, sorafenib, or sunitinib.

16. Use of an FGFR1 ECD or FGFR1 ECD fusion molecule for preparation of a medicament for reducing blood vessel density in a solid cancer.

17. The use of claim 16, wherein the solid cancer has a higher level of FGF2 compared to the level of VEGF.

18. The use of claim 17, wherein the FGF2 level is FGF2 mRNA level and the VEGF level is VEGF mRNA level.

19. The use of claim 17, wherein the FGF2 level is FGF2 protein level and the VEGF level is VEGF protein level.

20. The use of any one of claims 17 to 19, wherein the ratio of FGF2 level to VEGF level is greater than 1.

21. The use of any one of claims 16 to 20, wherein the solid cancer is selected from kidney cancer (such as renal cell carcinoma), liver cancer (such as hepatocellular carcinoma), lung cancer, colon cancer, liver cancer, breast cancer, stomach cancer, ovarian cancer, endometrial cancer, esophageal cancer, head and neck cancer, glioblastoma, mesothelioma, and prostate cancer.

22. Use of an FGFR1 ECD or FGFR1 ECD fusion molecule for preparation of a medicament for treating mesothelioma in a subject, wherein the medicament comprises the FGFR1 ECD or FGFR1 ECD fusion molecule and at least

one therapeutic agent selected from paclitaxel, carboplatin, docetaxel, pemetrexed, and cisplatin.

23. The use of claim 22, wherein the medicament comprises an FGFR1 ECD or FGFR1 ECD fusion molecule, paclitaxel and carboplatin.

24. The use of claim 22, wherein the medicament comprises an FGFR1 ECD or FGFR1 ECD fusion molecule and docetaxel.

25. The use of claim 22, wherein the medicament comprises an FGFR1 ECD or FGFR1 ECD fusion molecule, pemetrexed, and cisplatin.

26. The use of any one of claims 22 to 25, wherein the medicament comprising the FGFR1 ECD or FGFR1 ECD fusion molecule and at least one therapeutic agent reduces blood vessel density in the mesothelioma.

27. The use of any one of claims 22 to 26, wherein a mesothelioma sample or cell of the subject has a higher level of FGF2 compared to a level of FGF2 in a reference sample or cell.

28. The use any one of claims 22 to 27, wherein the subject's mesothelioma is characterized by a higher level of FGF2 compared to the level of VEGF.

29. The use of claim 27 or 28, wherein the FGF2 level is FGF2 mRNA level and the VEGF level is VEGF mRNA level.

30. The use of claim 27 or 28, wherein the FGF2 level is FGF2 protein level and the VEGF level is VEGF protein level.

31. The use of any one of claims 27 to 30, wherein the ratio of FGF2 level to VEGF level is greater than 1.

32. The use of any one of claims 1 to 31, wherein the subject has previously been treated with at least one therapeutic agent selected from pazopanib, bevacizumab, axitinib, aflibercept, sorafenib, and sunitinib.

33. The use of claim 32, wherein the subject has a VEGF-resistant cancer or a pazopanib-resistant cancer.

34. The use of any one of claims 1 to 33, wherein the FGFR1 ECD or FGFR1 ECD fusion molecule comprises an amino acid sequence selected from SEQ ID NOs: 1 to 4.

35. The use of any one of claims 1 to 34, wherein the FGFR1 ECD fusion molecule comprises an FGFR1 ECD and a fusion partner, wherein the fusion partner is Fc.

36. The use of claim 35, wherein the FGFR1 ECD fusion molecule comprises a sequence selected from SEQ ID NO: 5 and SEQ ID NO: 6.

37. A method of identifying a subject who may benefit from treatment with an FGFR1 ECD or an FGFR1 ECD fusion molecule, the method comprising determining the levels of FGF2 and VEGF in a sample obtained from the subject, wherein a higher level of FGF2 compared to the level of VEGF in the sample indicates that the subject may benefit from treatment with the fibroblast growth factor receptor 1 (FGFR1) extracellular domain (ECD) or an FGFR1 ECD fusion molecule.

38. A method of identifying a subject who may benefit from treatment with an FGFR1 ECD or an FGFR1 ECD fusion molecule and at least one anti-angiogenic agent, the method comprising determining the levels of FGF2 and VEGF in a sample obtained from the subject, wherein a lower level of FGF2 compared to the level of VEGF in the sample indicates that the subject may benefit from treatment with the FGFR1 ECD or FGFR1 ECD fusion molecule and the at least one anti-angiogenic agent.