and RET) and inhibits downstream Raf serine/theorine kinase (ARAF, BRAF, mutant BRAF V600E and CRAF) activity to prevent tumor growth by anti-angiogenic, antiproliferative and pro-apoptotic effects. (**Figure 11**).

**[0011]** Although targeted anti-cancer agents have been effective in the treatment of some human cancers, these agents are generally exhibit unpredictable efficacy, especially. in canines. Therefore, there is a need for improved methods and compositions for predicting efficacy and treating cancers in canine subjects with targeted anti-cancer agents.

**SUMMARY**

**[0011a]** In a first aspect, the present disclosure refers to a use of a histone deacetylase complex (HDAC) inhibitor in the manufacture of a medicament for treating a subject with a cancer harboring at least one mutation in ataxia-telangiectasia mutated (ATM) kinase in a biological sample derived from the cancer; wherein the medicament is to be administered to the subject if there is at least one mutation in ATM kinase,

optionally further comprising identifying or having identified the at least one mutation in ATM kinase.

**[0011b]** In another aspect, the present disclosure refers to a use of a pharmaceutical composition comprising Rapamycin, Dasatinib, Lapatinib, Trametinib, Vorinostat, Imatinib, Crizotinib or Sorafenib, in the manufacture of a medicament for treating a cancer in a canine subject.

**[0011c]** In yet another aspect, the present disclosure refers to a pharmaceutical composition formulated for oral administration, comprising:

Rapamycin, wherein the Rapamycin is present at a concentration of 0.001 mg/mL-10.0 mg/mL; or

Dasatinib, wherein the Dasatinib is present at a concentration of 0.001 mg/mL-10.0 mg/mL; or

Lapatinib, wherein the Lapatinib is present within the composition at a concentration of .001 mg/mL -100.0 mg/mL; or

Trametinib, wherein the Trametinib is present within the composition at a concentration of .001 mg/mL -100.0 mg/mL; or

Vorinostat, wherein the Vorinostat is present within the composition at a concentration of 0.01 mg/mL -500.0 mg/mL;

Imatinib, wherein the Imatinib is present within the composition at a concentration of 0.01 mg/mL -100.0 mg/mL; or

Crizotinib, wherein the Crizotinib is present within the composition at a concentration of 0.01 mg/mL -100.0 mg/mL;

Sorafenib, wherein the Sorafenib is present at a concentration of 0.001 mg/mL- 100.0 mg/mL.

**[0012]** In certain ~~aspects~~examples, described herein is a method of treating a subject with cancer comprising the step of administering a therapeutically effective amount of a histone deacetylase complex (HDAC) inhibitor to a subject having a cancer harboring at least one mutation in ataxia-telangiectasia mutated (ATM) kinase. In certain ~~embodiment~~example, the method includes the step of identifying the mutation in a sample derived from the subject. In certain ~~embodiment~~example, the HDAC inhibitor is selected from the group consisting of: romidepsin, belinostat, panobinostat, vorinostat, givinostat, entinostat, tacedinaline, and mocetinostat. In certain ~~embodiment~~example, the HDAC inhibitor is vorinostat. In certain ~~embodiment~~example, the method, further comprises administering an effective amount of a DNA damaging chemotherapeutic agent. In certain ~~embodiment~~example, the DNA damaging chemotherapeutic agent is selected from the group consisting of: a DNA-alkylating agent, DNA crosslinking agent, antimetabolite, topoisomerase inhibitor and a DNA intercalating agent. In certain ~~embodiment~~example, the DNA-alkylating agent is selected from the group consisting of: a nitrosourea, a triazene and a platinum agent. In certain ~~embodiment~~example, the DNA-alkylating agent is a nitrosourea. In certain ~~embodiment~~example, the nitrosourea is lomustine. In certain ~~embodiment~~example, the method, further comprises performing surgery on the subject. In certain ~~embodiment~~example, the method further comprises administering an effective amount of at least one additional anti-cancer therapeutic agent. In certain ~~embodiment~~example, the method further comprises administering to the subject ionizing radiation. In certain ~~embodiment~~example, the cancer harbors more than one mutant allele of ATM kinase. In certain ~~embodiment~~example, the biological sample is a nucleic acid sample. In certain ~~embodiment~~example, the biological sample is a purified nucleic acid sample. In certain ~~embodiment~~example, the sample is DNA. In certain ~~embodiment~~example, the sample is RNA. In certain ~~embodiment~~example, the identifying is performed by sequencing a nucleic acid sample. In certain ~~embodiment~~example, the cancer is cancer in a canine subject. In certain ~~embodiment~~example, the cancer is selected from the group consisting of: solid tumor, lymphoma, cutaneous T-cell lymphoma,

peripheral T-cell lymphoma, sarcoma, histiocytic sarcoma, multiple myeloma, hemangiosarcoma, lymphosarcoma, osteosarcoma, mammary carcinoma, melanoma, mast cell tumors, lipoma, anal gland adenocarcinoma, lung cancer and thyroid cancer. In certain ~~embodiment~~examples, the cancer is histiocytic sarcoma.

In certain examples~~aspects~~, described herein is a method of treating a subjectwith a cancer harboring at least one mutation in ATM kinase. In certain ~~embodiment~~examples, the method further comprises determining or having determined at least one mutation in ATM kinase in a in a sample derived from the cancer. In certain ~~embodiment~~examples, the method comprises administering to the subject a therapeutically effective amount of a histone deacetylase complex (HDAC) inhibitor. In certain ~~embodiment~~examples, the HDAC inhibitor is vorinostat. In certain ~~embodiment~~examples, the methods further comprise administering a DNA damaging chemotherapeutic agent. In certain ~~embodiment~~examples, the DNA damaging chemotherapeutic agent is lomustine. In certain ~~embodiment~~examples, at least one mutation in ATM kinase is selected from: a missense mutation, a splice site mutation and a frameshift variant. In certain ~~embodiment~~examples, at least one mutation in ATM kinase inhibits ATM kinase activity.

**[0013]** In certain ~~embodiment~~examples, described herein are methods of treating cancer in a canine subject comprising, administering to a subject in need thereof a therapeutically effective amount of a pharmaceutical composition comprising Rapamycin. In certain ~~aspect~~examples, the Rapamycin is administered at a dose equal to or less than 1 mg/kg. In certain ~~aspect~~examples, the Rapamycin is administered at a dose of 0.05-0.1 mg/kg. In certain ~~aspect~~examples, the pharmaceutical composition is administered at a frequency selected from the group consisting of twice daily, once daily, once every other day, once every third day, once every fourth day, once every $5^{th}$ day, or weekly. In certain ~~aspect~~examples, the Rapamycin is administered orally. In certain ~~aspect~~examples, the methods described herein further comprise administering a therapeutically effective amount of at least one additional anti-cancer agent. In certain ~~aspect~~examples, at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent. In certain ~~aspect~~examples, the DNA damaging chemotherapeutic agent is selected from the group consisting of a DNA-alkylating agent, DNA crosslinking agent, antimetabolite, topoisomerase inhibitor and a DNA intercalating agent. In certain ~~aspect~~examples, at least one additional anti-cancer agent is a targeted anti-cancer agent. In certain ~~aspect~~examples, the targeted anti-cancer agent is selected from the group consisting of: Crizotinib, Dasatinib Erlotinib, Gefinitib, Imatinib, Lapatinib, Sorafenib, Trametinib, and Vorinostat. In certain ~~aspect~~examples, the targeted anti-cancer agent is Dasatinib. In certain ~~aspect~~examples, the methods described herein further comprise performing

surgery on the subject. In certain ~~aspect~~examples, the methods described herein further comprise administering to the subject ionizing radiation. In certain ~~aspect~~examples, the cancer harbors at least one mutation in at least one gene selected from the group consisting of mTOR, PI3K, AKT and Ras. In certain ~~aspect~~examples, the methods described herein further comprise having determined from a biological sample derived from the cancer, that the cancer harbors a mutation in at least one gene selected from the group consisting of mTOR, PI3K, AKT and Ras. In certain ~~aspect~~examples, the biological sample is a nucleic acid sample. In certain ~~aspect~~examples, the biological sample is a purified nucleic acid sample. In certain ~~aspect~~examples, the sample is DNA. In certain ~~aspect~~examples, the sample is RNA. In certain ~~aspect~~examples, the determining of the mutation in at least one gene is performed by sequencing the nucleic acid sample. In certain ~~aspect~~examples, the cancer in the canine subject is selected from the group consisting of: solid tumor, leukemia, lymphocytic leukemia, lymphoma, sarcoma, multiple myeloma, hemangiosarcoma, histiocytic sarcoma, lymphosarcoma, osteosarcoma, transitional cell carcinoma, squamous cell carcinoma, mammary carcinoma, melanoma, mast cell tumors, lipoma, anal gland adenocarcinoma, lung cancer, pancreatic cancer, stomach cancer, prostate cancer, nasal cancer, liver cancer, brain cancer, bladder cancer and thyroid cancer. In certain ~~aspect~~examples, the cancer is hemangiosarcoma. In certain ~~embodiment~~examples, described herein are pharmaceutical compositions formulated for oral administration, comprising Rapamycin, wherein the Rapamycin is present at a concentration of 0.001 mg/mL- 10.0 mg/mL.

**[0014]** In certain ~~embodiment~~examples, described herein are methods of treating cancer in a canine subject comprising, administering to a subject in need thereof a therapeutically effective amount of a pharmaceutical composition comprising Dasatinib. In certain ~~aspect~~examples, the Dasatinib is administered at a dose equal to or less than 2 mg/kg. In certain ~~aspect~~examples, the Dasatinib is administered at a dose of 0.5-0.7 mg/kg. In certain ~~aspect~~examples, the pharmaceutical composition is administered at a frequency selected from the group consisting of twice daily, once daily, once every other day, once every third day, once every fourth day, once every $5^{th}$ day, or weekly. In certain ~~aspect~~examples, the Dasatinib is administered orally. In certain ~~aspect~~examples, the methods described herein further comprise administering a therapeutically effective amount of at least one additional anti-cancer agent. In certain ~~aspect~~examples, at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent. In certain ~~aspect~~examples, the DNA damaging chemotherapeutic agent is selected from the group consisting of a DNA-alkylating agent, DNA crosslinking agent, antimetabolite, topoisomerase inhibitor and a DNA intercalating agent. In certain ~~aspect~~examples, at least one additional anti-cancer agent is a targeted

anti-cancer agent. In certain ~~aspect~~examples, the targeted anti-cancer agent is selected from the group consisting of: Crizotinib, Rapamycin, Erlotinib, Gefinitib, Imatinib, Lapatinib, Sorafenib, Trametinib, and Vorinostat. In certain ~~aspect~~examples, the targeted anti-cancer agent is Rapamycin. In certain ~~aspect~~examples, the methods described herein further comprise performing surgery on the subject. In certain ~~aspect~~examples, the methods described herein further comprise administering to the subject ionizing radiation. In certain ~~aspect~~examples, the cancer harbors at least one mutation in at least one gene selected from the group consisting of ABL, BCR-ABL, c-KIT, EPHA2, PDGFR and a Src Family Kinase. In certain ~~aspect~~examples, the methods described herein further comprise having determined from a biological sample derived from the cancer, that the cancer harbors a mutation in at least one gene selected from the group consisting of ABL, BCR-ABL, c-KIT, EPHA2, PDGFR and a Src Family Kinase. In certain ~~aspect~~examples, the biological sample is a nucleic acid sample. In certain ~~aspect~~examples, the biological sample is a purified nucleic acid sample. In certain ~~aspect~~examples, the sample is DNA. In certain ~~aspect~~examples, the sample is RNA. In certain ~~aspect~~examples, the determining of the mutation in at least one gene is performed by sequencing the nucleic acid sample. In certain ~~aspect~~examples, the cancer in the canine subject is selected from the group consisting of: solid tumor, leukemia, lymphocytic leukemia, lymphoma, sarcoma, multiple myeloma, hemangiosarcoma, histiocytic sarcoma, lymphosarcoma, osteosarcoma, transitional cell carcinoma, squamous cell carcinoma, mammary carcinoma, melanoma, mast cell tumors, lipoma, anal gland adenocarcinoma, lung cancer, pancreatic cancer, stomach cancer, prostate cancer, nasal cancer, liver cancer, brain cancer, bladder cancer and thyroid cancer. In certain ~~aspect~~examples, the cancer is osteosarcoma. In certain ~~embodiment~~examples, described herein are pharmaceutical compositions formulated for oral administration, comprising Dasatinib, wherein the Dasatinib is present at a concentration of 0.001 mg/mL - 10.0 mg/mL.

**[0015]** In certain ~~embodiment~~examples, described herein are methods of treating cancer in a canine subject comprising, administering to a subject in need thereof a therapeutically effective amount of a pharmaceutical composition comprising Lapatinib. In certain ~~aspect~~examples, the Lapatinib is administered at a dose equal to or less than 50 mg/kg. In certain ~~aspect~~examples, the Lapatinib is administered at a dose of 5 mg/kg-10 mg/kg. In certain ~~aspect~~examples, the pharmaceutical composition is administered at a frequency selected from the group consisting of twice daily, once daily, once every other day, once every third day, once every fourth day, once every $5^{th}$ day, or weekly. In certain ~~aspect~~examples, the Lapatinib is administered orally. In certain ~~aspect~~examples, the methods described herein further comprise administering a therapeutically

effective amount of at least one additional anti-cancer agent. In certain ~~aspect~~examples, at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent. In certain ~~aspect~~examples, the DNA damaging chemotherapeutic agent is selected from the group consisting of a DNA-alkylating agent, DNA crosslinking agent, antimetabolite, topoisomerase inhibitor and a DNA intercalating agent. In certain ~~aspect~~examples, at least one additional anti-cancer agent is a targeted anti-cancer agent. In certain ~~aspect~~examples, the targeted anti-cancer agent is selected from the group consisting of: Crizotinib, Rapamycin, Erlotinib, Gefinitib, Imatinib, Dasatinib, Sorafenib, Trametinib, and Vorinostat. In certain ~~aspect~~examples, the targeted anti-cancer agent is Trametinib. In certain ~~aspect~~examples, the methods described herein further comprise performing surgery on the subject. In certain ~~aspect~~examples, the methods described herein further comprise administering to the subject ionizing radiation. In certain ~~aspect~~examples, the cancer harbors at least one mutation in at least one gene selected from the group consisting of ERBB1 and ERBB2. In certain ~~aspect~~examples, the methods described herein further comprise having determined from a biological sample derived from the cancer, that the cancer harbors a mutation in at least one gene selected from the group consisting of ERBB1 and ERBB2. In certain ~~aspect~~examples, the biological sample is a nucleic acid sample. In certain ~~aspect~~examples, the biological sample is a purified nucleic acid sample. In certain ~~aspect~~examples, the sample is DNA. In certain ~~aspect~~examples, the sample is RNA. In certain ~~aspect~~examples, the determining of the mutation in at least one gene is performed by sequencing the nucleic acid sample. In certain ~~aspect~~examples, the cancer in the canine subject is selected from the group consisting of: solid tumor, leukemia, lymphocytic leukemia, lymphoma, sarcoma, multiple myeloma, hemangiosarcoma, histiocytic sarcoma, lymphosarcoma, osteosarcoma, transitional cell carcinoma, squamous cell carcinoma, mammary carcinoma, melanoma, mast cell tumors, lipoma, anal gland adenocarcinoma, lung cancer, pancreatic cancer, stomach cancer, prostate cancer, nasal cancer, liver cancer, brain cancer, bladder cancer, thyroid cancer and transitional cell carcinoma. In certain ~~aspect~~examples, the cancer is transitional cell carcinoma. In certain ~~embodiment~~examples, described herein are pharmaceutical compositions formulated for oral administration, comprising Lapatinib, wherein the Lapatinib is present at a concentration of 0.001 mg/mL - 100.0 mg/mL.

**[0016]** In certain ~~embodiment~~examples, described herein are methods of treating cancer in a canine subject comprising, administering to a subject in need thereof a therapeutically effective amount of a pharmaceutical composition comprising Trametinib. In certain ~~aspect~~examples, the Trametinib is administered at a dose equal to or less than 0.05 mg/kg/day. In certain ~~aspect~~examples, the Trametinib is administered at a dose of 0.02 mg/kg/day. In certain ~~aspect~~examples, the

pharmaceutical composition is administered at a frequency selected from the group consisting of twice daily, once daily, once every other day, once every third day, once every fourth day, once every 5th day, or weekly. In certain ~~aspect~~examples, the Trametinib is administered orally. In certain ~~aspect~~examples, the methods described herein further comprise administering a therapeutically effective amount of at least one additional anti-cancer agent. In certain ~~aspect~~examples, at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent. In certain ~~aspect~~examples, the DNA damaging chemotherapeutic agent is selected from the group consisting of a DNA-alkylating agent, DNA crosslinking agent, antimetbolite, topoisomerase inhibitor and a DNA intercalating agent. In certain ~~aspect~~examples, at least one additional anti-cancer agent is a targeted anti-cancer agent. In certain ~~aspect~~examples, the targeted anti-cancer agent is selected from the group consisting of: Crizotinib, Rapamycin, Erlotinib, Gefinitib, Imatinib, Dasatinib, Sorafenib, Lapatinib, and Vorinostat. In certain ~~aspect~~examples, the targeted anti-cancer agent is Rapamycin. In certain ~~aspect~~examples, the targeted anti-cancer agent is Dasatinib. In certain ~~aspect~~examples, the targeted anti-cancer agent is Lapatinib. In certain ~~aspect~~examples, the methods described herein further comprise performing surgery on the subject. In certain ~~aspect~~examples, the methods described herein further comprise administering to the subject ionizing radiation. In certain ~~aspect~~examples, the cancer harbors at least one mutation in at least one gene selected from the group consisting of MEK1 and MEK2. In certain ~~aspect~~examples, the methods described herein further comprise having determined from a biological sample derived from the cancer, that the cancer harbors a mutation in at least one gene selected from the group consisting of MEK1 and MEK2. In certain ~~aspect~~examples, the biological sample is a nucleic acid sample. In certain ~~aspect~~examples, the biological sample is a purified nucleic acid sample. In certain ~~aspect~~examples, the sample is DNA. In certain ~~aspect~~examples, the sample is RNA. In certain ~~aspect~~examples, the determining of the mutation in the at least one gene is performed by sequencing the nucleic acid sample. In certain ~~aspect~~examples, the cancer in the canine subject is selected from the group consisting of: solid tumor, leukemia, lymphocytic leukemia, lymphoma, multiple myeloma, transitional cell carcinoma, squamous cell carcinoma, mammary carcinoma, melanoma, mast cell tumors, lipoma, anal gland adenocarcinoma, lung cancer, pancreatic cancer, stomach cancer, prostate cancer, nasal cancer, liver cancer, brain cancer, bladder cancer, thyroid cancer, gingiva carcinoma, and sarcoma (including: soft tissue sarcoma, splenic stromal sarcoma and spindle cell sarcoma, hemangiosarcoma, histiocytic sarcoma, leiomyosarcoma, lymphosarcoma and osteosarcoma). In certain ~~embodiment~~examples, described herein are pharmaceutical compositions formulated for

oral administration, comprising Trametinib, wherein the Trametinib is present at a concentration of 0.001 mg/mL - 100.0 mg/mL.

**[0017]** In certain ~~embodiment~~examples, described herein are methods of treating cancer in a canine subject comprising, administering to a subject in need thereof a therapeutically effective amount of a pharmaceutical composition comprising Vorinostat. In certain ~~aspect~~examples, the Vorinostat is administered at a dose equal to or less than 100 mg/kg. In certain ~~aspect~~examples, the Vorinostat is administered at a dose of 30-60 mg/kg. In certain ~~aspect~~examples, the pharmaceutical composition is administered at a frequency selected from the group consisting of twice daily, once daily, once every other day, once every third day, once every fourth day, once every 5$^{th}$ day, or weekly. In certain ~~aspect~~examples, the Vorinostat is administered orally. In certain ~~aspect~~examples, the methods described herein further comprise administering a therapeutically effective amount of at least one additional anti-cancer agent. In certain ~~aspect~~examples, at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent. In certain ~~aspect~~examples, the DNA damaging chemotherapeutic agent is selected from the group consisting of a DNA-alkylating agent, DNA crosslinking agent, antimetabolite, topoisomerase inhibitor and a DNA intercalating agent. In certain ~~aspect~~examples, at least one additional anti-cancer agent is a targeted anti-cancer agent. In certain ~~aspect~~examples, the targeted anti-cancer agent is selected from the group consisting of: Crizotinib, Rapamycin, Erlotinib, Gefinitib, Imatinib, Dasatinib, Sorafenib, Lapatinib, and Trametinib. In certain ~~aspect~~examples, the targeted anti-cancer agent is Rapamycin. In certain ~~aspect~~examples, the targeted anti-cancer agent is Trametinib. In certain ~~aspect~~examples, the targeted anti-cancer agent is Lapatinib. In certain ~~aspect~~examples, the methods described herein further comprise performing surgery on the subject. In certain ~~aspect~~examples, the methods described herein further comprise administering to the subject ionizing radiation. In certain ~~aspect~~examples, the cancer harbors at least one mutation in at least one gene selected from the group consisting of p300, CBP, TIF-2, RAR, BCL-6, AML1, STAT5 and HDAC1. In certain ~~aspect~~examples, the methods described herein further comprise having determined from a biological sample derived from the cancer, that the cancer harbors a mutation in at least one gene selected from the group consisting of p300, CBP, TIF-2, RAR, BCL-6, AML1, STAT5 and HDAC1. In certain ~~aspect~~examples, the methods described herein further comprise having determined from a biological sample derived from the cancer, that the cancer overexpresses MYC. In certain ~~aspect~~examples, the biological sample is a nucleic acid sample. In certain ~~aspect~~examples, the biological sample is a purified nucleic acid sample. In certain ~~aspect~~examples, the sample is DNA. In certain ~~aspect~~examples, the sample is RNA. In certain ~~aspect~~examples, the determining of the mutation in at least one gene is

performed by sequencing the nucleic acid sample. In certain ~~aspect~~example**s**, the cancer in the canine subject is selected from the group consisting of: solid tumor, leukemia, lymphocytic leukemia, lymphoma, multiple myeloma, transitional cell carcinoma, squamous cell carcinoma, mammary carcinoma, melanoma, mast cell tumors, lipoma, anal gland adenocarcinoma, lung cancer, pancreatic cancer, stomach cancer, prostate cancer, nasal cancer, liver cancer, brain cancer, bladder cancer, thyroid cancer, gingiva carcinoma, and sarcoma (including: soft tissue sarcoma, splenic stromal sarcoma and spindle cell sarcoma, hemangiosarcoma, histiocytic sarcoma, leiomyosarcoma, lymphosarcoma and osteosarcoma). In certain ~~aspect~~example**s**, the cancer is hemangiosarcoma. In certain ~~aspect~~example**s**, the cancer is histiocytic sarcoma. In certain ~~embodiment~~example**s**, described herein are pharmaceutical compositions formulated for oral administration, comprising Vorinostat, wherein the Vorinostat is present at a concentration of 0.01 mg/mL - 500.0 mg/mL.

**[0018]** In certain ~~embodiment~~example**s**, described herein are methods of treating cancer in a canine subject comprising, administering to a subject in need thereof a therapeutically effective amount of a pharmaceutical composition comprising Imatinib. In certain ~~aspect~~example**s**, the Imatinib is administered at a dose equal to or less than 50 mg/kg. In certain ~~aspect~~example**s**, the Imatinib is administered at a dose of 10 mg/kg. In certain ~~aspect~~example**s**, the pharmaceutical composition is administered at a frequency selected from the group consisting of twice daily, once daily, once every other day, once every third day, once every fourth day, once every $5^{th}$ day, or weekly. In certain ~~aspect~~example**s**, the Imatinib is administered orally. In certain ~~aspect~~example**s**, the methods described herein further comprise administering a therapeutically effective amount of at least one additional anti-cancer agent. In certain ~~aspect~~example**s**, at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent. In certain ~~aspect~~example**s**, the DNA damaging chemotherapeutic agent is selected from the group consisting of a DNA-alkylating agent, DNA crosslinking agent, antimetabolite, topoisomerase inhibitor and a DNA intercalating agent. In certain ~~aspect~~example**s**, the at least one additional anti-cancer agent is a targeted anti-cancer agent. In certain ~~aspect~~example**s**, the targeted anti-cancer agent is selected from the group consisting of: Crizotinib, Rapamycin, Erlotinib, Gefinitib, Lapatinib, Dasatinib, Sorafenib, Trametinib, and Vorinostat. In certain ~~aspect~~example**s**, the targeted anti-cancer agent is Trametinib. In certain ~~aspect~~example**s**, the targeted anti-cancer agent is Rapamycin. In certain ~~aspect~~example**s**, the methods described herein further comprise performing surgery on the subject. In certain ~~aspect~~example**s**, the methods described herein further comprise administering to the subject ionizing radiation. In certain ~~aspect~~example**s**, the cancer harbors at least one mutation in at least one

gene selected from the group consisting of ABL, BCR-ABL, PDGFR, and C-KIT. In certain ~~aspect~~examples, the methods described herein further comprise having determined from a biological sample derived from the cancer, that the cancer harbors a mutation in at least one gene selected from the group consisting of ABL, BCR-ABL, PDGFR, and C-KIT. In certain ~~aspect~~examples, the biological sample is a nucleic acid sample. In certain ~~aspect~~examples, the biological sample is a purified nucleic acid sample. In certain ~~aspect~~examples, the sample is DNA. In certain ~~aspect~~examples, the sample is RNA. In certain ~~aspect~~examples, the determining of the mutation in at least one gene is performed by sequencing the nucleic acid sample. In certain ~~aspect~~examples, the cancer in the canine subject is selected from the group consisting of: solid tumor, leukemia, lymphocytic leukemia, lymphoma, sarcoma, multiple myeloma, hemangiosarcoma, histiocytic sarcoma, lymphosarcoma, osteosarcoma, transitional cell carcinoma, squamous cell carcinoma, mammary carcinoma, melanoma, mast cell tumors, lipoma, anal gland adenocarcinoma, lung cancer, pancreatic cancer, stomach cancer, prostate cancer, nasal cancer, liver cancer, brain cancer, bladder cancer, thyroid cancer and transitional cell carcinoma. In certain ~~aspect~~examples, the cancer is hemangiosarcoma. In certain ~~aspect~~examples, the cancer is mast cell tumors. In certain ~~embodiment~~examples, described herein are pharmaceutical compositions formulated for oral administration, comprising Imatinib, wherein the Imatinib is present at a concentration of 0.01 mg/mL - 100.0 mg/mL.

**[0019]** In certain ~~embodiment~~examples, described herein are methods of treating cancer in a canine subject comprising, administering to a subject in need thereof a therapeutically effective amount of a pharmaceutical composition comprising Crizotinib. In certain ~~aspect~~examples, Crizotinib is administered at a dose equal to or less than 10 mg/kg. In certain ~~aspect~~examples, Crizotinib is administered at a dose of 1 mg/kg- 2 mg/kg. In certain ~~aspect~~examples, the pharmaceutical composition is administered at a frequency selected from the group consisting of twice daily, once daily, once every other day, once every third day, once every fourth day, once every $5^{th}$ day, or weekly. In certain ~~aspect~~examples, Crizotinib is administered orally. In certain ~~aspect~~examples, the methods described herein further comprise administering a therapeutically effective amount of at least one additional anti-cancer agent. In certain ~~aspect~~examples, at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent. In certain ~~aspect~~examples, the DNA damaging chemotherapeutic agent is selected from the group consisting of a DNA-alkylating agent, DNA crosslinking agent, antimetabolite, topoisomerase inhibitor and a DNA intercalating agent. In certain ~~aspect~~examples, at least one additional anti-cancer agent is a targeted anti-cancer agent. In certain ~~aspect~~examples, the targeted anti-cancer agent is selected from

the group consisting of: Imatinib, Rapamycin, Erlotinib, Gefinitib, Lapatinib, Dasatinib, Sorafenib, Trametinib, and Vorinostat. In certain ~~aspect~~examples, the targeted anti-cancer agent is Trametinib. In certain ~~aspect~~examples, the targeted anti-cancer agent is Imatinib. In certain ~~aspect~~examples, the methods described herein further comprise performing surgery on the subject. In certain ~~aspect~~examples, the methods described herein further comprise administering to the subject ionizing radiation. In certain ~~aspect~~examples, the cancer harbors at least one mutation in at least one gene selected from the group consisting of ALK, c-MET and ROS1. In certain ~~aspect~~examples, the methods described herein further comprise having determined from a biological sample derived from the cancer, that the cancer harbors a mutation in at least one gene selected from the group consisting of ALK, c-MET and ROS1. In certain ~~aspect~~examples, the biological sample is a nucleic acid sample. In certain ~~aspect~~examples, the biological sample is a purified nucleic acid sample. In certain ~~aspect~~examples, the sample is DNA. In certain ~~aspect~~examples, the sample is RNA. In certain ~~aspect~~examples, the determining of the mutation in at least one gene is performed by sequencing the nucleic acid sample. In certain ~~aspect~~examples, the cancer in the canine subject is selected from the group consisting of: solid tumor, leukemia, lymphocytic leukemia, lymphoma, sarcoma, multiple myeloma, hemangiosarcoma, histiocytic sarcoma, lymphosarcoma, osteosarcoma, transitional cell carcinoma, squamous cell carcinoma, mammary carcinoma, melanoma, mast cell tumors, lipoma, anal gland adenocarcinoma, lung cancer, pancreatic cancer, stomach cancer, prostate cancer, nasal cancer, liver cancer, brain cancer, bladder cancer, thyroid cancer and transitional cell carcinoma. In certain ~~aspect~~examples, the cancer is hemangiosarcoma. In certain ~~aspect~~examples, the cancer is osteosarcoma. In certain ~~embodiment~~examples, described herein are pharmaceutical compositions formulated for oral administration, comprising Crizotinib, wherein Crizotinib is present at a concentration of 0.01 mg/mL - 100.0 mg/mL.

**[0020]** In certain ~~embodiment~~examples, described herein are methods of treating cancer in a canine subject comprising, administering to a subject in need thereof a therapeutically effective amount of a pharmaceutical composition comprising Sorafenib. In certain ~~aspect~~examples, the Sorafenib is administered at a dose of less than 10 mg/kg. In certain ~~aspect~~examples, the Sorafenib is administered at a dose of 1 mg/kg- 3 mg/kg. In certain ~~aspect~~examples, the pharmaceutical composition is administered at a frequency selected from the group consisting of twice daily, once daily, once every other day, once every third day, once every fourth day, once every $5^{th}$ day, or weekly. In certain ~~aspect~~examples, the Sorafenib is administered orally. In certain ~~aspect~~examples, the methods described herein further comprise administering a therapeutically effective

amount of at least one additional anti-cancer agent. In certain ~~aspect~~examples, at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent. In certain ~~aspect~~examples, the DNA damaging chemotherapeutic agent is selected from the group consisting of a DNA-alkylating agent, DNA crosslinking agent, antimetabolite, topoisomerase inhibitor and a DNA intercalating agent. In certain ~~aspect~~examples, at least one additional anti-cancer agent is a targeted anti-cancer agent. In certain ~~aspect~~examples, the targeted anti-cancer agent is selected from the group consisting of: Imatinib, Rapamycin, Erlotinib, Gefinitib, Lapatinib, Dasatinib, Crizontinib, Trametinib, and Vorinostat. In certain ~~aspect~~examples, the targeted anti-cancer agent is Imatinib. In certain ~~aspect~~examples, the methods described herein further comprise performing surgery on the subject. In certain ~~aspect~~examples, the methods described herein further comprise administering to the subject ionizing radiation. In certain ~~aspect~~examples, the cancer harbors at least one mutation in at least one gene selected from the group consisting of RAF, c-Kit, FLT-3, RET, VEGFRs and PDGFRB. In certain ~~aspect~~examples, the methods described herein further comprise having determined from a biological sample derived from the cancer, that the cancer harbors a mutation in at least one gene selected from the group consisting of RAF, c-Kit, FLT-3, RET, VEGFRs and PDGFRB. In certain ~~aspect~~examples, the biological sample is a nucleic acid sample. In certain ~~aspect~~examples, the biological sample is a purified nucleic acid sample. In certain ~~aspect~~examples, the sample is DNA. In certain ~~aspect~~examples, the sample is RNA. In certain ~~aspect~~examples, the determining of the mutation in at least one gene is performed by sequencing the nucleic acid sample. In certain ~~aspect~~examples, the cancer in the canine subject is selected from the group consisting of: solid tumor, leukemia, lymphocytic leukemia, lymphoma, sarcoma, multiple myeloma, hemangiosarcoma, histiocytic sarcoma, lymphosarcoma, osteosarcoma, transitional cell carcinoma, squamous cell carcinoma, mammary carcinoma, melanoma, mast cell tumors, lipoma, anal gland adenocarcinoma, lung cancer, pancreatic cancer, stomach cancer, prostate cancer, nasal cancer, liver cancer, brain cancer, bladder cancer, thyroid cancer and transitional cell carcinoma. In certain ~~aspect~~examples, the cancer is mast cell tumor. In certain ~~aspect~~examples, the cancer is osteosarcoma. In certain ~~embodiment~~examples, described herein are pharmaceutical compositions formulated for oral administration, comprising Sorafenib, wherein the Sorafenib is present at a concentration of 0.01 mg/mL - 100.0 mg/mL.

**[0021]** In certain ~~aspect~~examples of the methods described herein, the cancer harbors at least one mutation in at least one gene shown in Tables 1, 2 and 12-26. In certain ~~embodiment~~examples, the methods further comprise determining or having determined from a biological sample

derived from the cancer, at least one mutation in at least one gene shown in Tables 1, 2, and 12-26.

**[0022]** In certain ~~aspect~~examples of the methods described herein, the cancer has increased or decreased expression in at least one gene shown in Tables 1, 2 and 12-26 compared to non-cancerous tissue. In certain ~~embodiment~~examples, the methods further comprise determining or having determined from a biological sample derived from the cancer, increased or decreased expression in at least one gene shown in Tables 1, 2, and 12-26 compared to non-cancerous tissue.

## BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWINGS

**[0023]** These and other features, aspects, and advantages of the present invention will become better understood with regard to the following description, and accompanying drawings, where:

**[0024] Figure 1**: is a graph showing the median survival of subjects treated with targeted therapies comprising, HDAC inhibitors, Rapamycin, Dasatinib, Lapatinib, Trametinib, Vorinostat, Imatinib, Crizotinib, Sorafenib, and combinations thereof according to the present disclosure versus subjects treated with traditional non-targeted therapies.

**[0025] Figure 2** is a graph showing Kaplan-Meier survival of canine subjects with splenic hemangiosarcoma that have been either treated with chemotherapy and splenectomy alone ("control") or treated with targeted therapy and chemotherapy and splenectomy ("treated").

**[0026] Figure 3** is a graph showing Kaplan-Meier survival of canine subjects with Transitional Cell Carcinoma (TCC) and/or Urinary Cancer (UC) harboring a BRAF mutation. Dogs treated with targeted drugs (Trametinib, Lapatinib or Lapatinib and Trametinib) with or without standard chemotherapy and a COX2 inhibitor exceeded published median survival times (MST) for either Cox inhibitor treatment alone (195 days) or chemotherapy and Cox2 inhibitor treatment (291 days).

**[0027] Figure 4** is an illustration of mechanisms of Rapamycin action in cancer cell signaling. Rapamycin binds to mTORC1 and acts both upstream and downstream of AKT. S6K1 and 4E-BP1 are two well characterized substrates phosphorylated by mTORC1 implicated in transcription, translation, protein, lipids synthesis and is found to be critical for cell growth and metabolism.

**[0028] Figure 5**: is an illustration of mechanisms of Dasatinib action in cancer cell signaling. Dasatinib has binding activity to a highly conserved ATP binding site to lock the tyrosine kinase in an inactive state. Dasatinib inhibits SRC family kinases, BCR-ABL, KIT, and

**CLAIMS**

**1.** Use of a histone deacetylase complex (HDAC) inhibitor in the manufacture of a medicament for ~~A method of~~ treating a subject with a cancer~~, comprising:~~

~~treating the subject with a cancer~~ harboring at least one mutation in ataxia-telangiectasia mutated (ATM) kinase in a biological sample derived from the cancer; wherein the medicament is to be administered to the subject ~~and~~ if there is at least one mutation in ATM kinase~~, administering to the subject a therapeutically effective amount of a histone deacetylase complex (HDAC) inhibitor~~, optionally~~.~~

~~**2.** The method of claim 1,~~ further comprising identifying or having identified the at least one mutation in ATM kinase.

~~**3.**~~**2.** The ~~method~~use of claim 1 ~~or 2~~, wherein: the HDAC inhibitor is selected from the group consisting of: romidepsin, belinostat, panobinostat, vorinostat, givinostat, entinostat, tacedinaline, and mocetinostat; and/or~~.~~

~~**4.** The method of any one of the above claims, further comprising administering~~ an effective amount of a DNA damaging chemotherapeutic agent is to be further administered, ~~.~~

~~**5.** The method of claim 4 ,~~ optionally wherein the DNA damaging chemotherapeutic agent is selected from the group consisting of: a DNA-alkylating agent, DNA crosslinking agent, antimetabolite, topoisomerase inhibitor and a DNA intercalating agent; ~~.~~

~~**6.**~~ optionally~~The method of claim 5,~~ wherein the DNA-alkylating agent is selected from the group consisting of: a nitrosourea, a triazene and a platinum agent~~.~~.

~~**7.** optionally The method of claim 6, wherein the DNA-alkylating agent is a nitrosourea.~~

~~**8.** The method of claim 7,~~ wherein the nitrosourea is lomustine; and/or~~.~~

~~**9.** The method of any one of the above claims,~~ wherein surgery is to be performed on the subject; and/or~~.~~

~~**10.** The method of any one of the above claims, further comprising administering~~wherein an effective amount of at least one additional anti-cancer therapeutic agent is to be further administered; and/or~~.~~

**11.** The method of any one of the above claims, further comprising administering to the subject wherein ionizing radiation is to be further administered to the subject; and/or.

**12.** The method of any one of the above claims, wherein the cancer harbors more than one mutant allele of ATM kinase; and/or.

**13.** The method of any one of the above claims, wherein the biological sample is a nucleic acid sample,.

**14.** The method of claim 13, wherein optionally the biological sample is a purified nucleic acid sample,.

**15.** The method of claim 14, optionally wherein the purified sample is DNA.

**16.** The method of claim 14, wherein the sample is or RNA; and/or.

**17.** The method of claim 12, wherein the identifying is performed by sequencing a nucleic acid sample; and/or.

**18.** The method of any one of the above claims, wherein the subject is a canine; and/or.

**19.** The method of any one of the above claims, wherein the cancer is selected from the group consisting of: solid tumor, lymphoma, cutaneous T-cell lymphoma, peripheral T-cell lymphoma, sarcoma, histiocytic sarcoma, multiple myeloma, hemangiosarcoma, lymphosarcoma, osteosarcoma, mammary carcinoma, melanoma, mast cell tumors, lipoma, anal gland adenocarcinoma, lung cancer and thyroid cancer; and/or.

**20.** The method of any one of the above claims, wherein the cancer is histiocytic sarcoma.

**21.** A method of treating a subject with cancer, comprising having determined at least one mutation in ATM kinase; and

administering to the subject a therapeutically effective amount of a histone deacetylase complex (HDAC) inhibitor.

**22.** The method of claim 21, wherein the HDAC inhibitor is vorinostat.

**23.** The method of claim 21, further comprising administering a DNA damaging chemotherapeutic agent.

**24.** The method of claim 23; wherein the DNA damaging chemotherapeutic agent is lomustine.

~~25.~~ ~~The method of any one of the above claims, wherein~~ the at least one mutation in ATM kinase is selected from: a missense mutation, a splice site mutation and a frameshift variant~~,~~ .

~~26.~~ ~~The method of claim 25,~~ optionally wherein the at least one mutation in ATM kinase inhibits ATM kinase activity.

**3.** Use of a pharmaceutical composition comprising Rapamycin, Dasatinib, Lapatinib, Trametinib, Vorinostat, Imatinib, Crizotinib or Sorafenib, in the manufacture of a medicament for treating a cancer in a canine subject.

~~27. A method of treating a cancer in a canine subject, comprising: administering to the canine subject in need thereof a therapeutically effective amount of a pharmaceutical composition comprising Rapamycin~~

~~28.~~**4.** The ~~method~~use of claim 3~~27~~, wherein the composition comprises Rapamycin, wherein: the Rapamycin is to be administered at a dose equal to or less than 1 mg/kg~~.~~.

~~29.~~ ~~The method of claim 28, wherein the Rapamycin is administered~~ optionally at a dose of 0.05-0.1 mg/kg; and/or~~.~~

~~30.~~ ~~The method of any one of claims 27-29, wherein~~ the pharmaceutical composition is to be administered at a frequency selected from the group consisting of, twice daily, once daily, once every other day, once every third day, once every fourth day, once every 5$^{th}$ day, or weekly; and/or~~.~~

~~31.~~ ~~The method of any one of claims 27-30, wherein~~ the Rapamycin is to be administered orally; and/or~~.~~

~~32.~~ ~~The method of any one of claims 27-31, further comprising administering~~wherein a therapeutically effective amount of at least one additional anti-cancer agent is to be further administered,~~.~~

~~33.~~ ~~The method of claim 32,~~ optionally wherein the at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent~~,~~ .

~~34.~~ ~~The method of claim 33,~~ optionally wherein the DNA damaging chemotherapeutic agent is selected from the group consisting of: a DNA-alkylating agent, DNA crosslinking agent, antimetabolite, topoisomerase inhibitor and a DNA intercalating agent; or~~.~~

**35.** The method of claim 33, wherein the at least one additional anti-cancer agent is a targeted anti-cancer agent, optionally.

**36.** The method of claim 33 wherein the targeted anti-cancer agent is selected from the group consisting of Crizotinib, Dasatinib Erlotinib, Gefinitib, Imatinib, Lapatinib, Sorafenib, Trametinib, and Vorinostat; and/or.

**37.** The method of claim 36, wherein the targeted anti-cancer agent is Dasatinib.

**38.** The method of any one of claims 27-36, wherein surgery is to be performed further comprising performing surgery on the subject; and/or.

**39.** The method of any one of claims 27-37, further comprising administering to the subject wherein ionizing radiation is to be further administered to the subject; and/or.

**40.** The method of any one of claims 27-38, wherein the cancer harbors at least one mutation in at least one gene selected from the group consisting of mTOR, PI3K, AKT and Ras; and/or.

**41.** The method of any one of claims 27-39, further comprising having determined from a biological sample derived from the cancer, that the cancer harbors a mutation in at least one gene selected from the group consisting of mTOR, PI3K, AKT and Ras, .

**42.** The method of claim 41 optionally wherein the biological sample is a nucleic acid sample,.

**43.** The method of claim 42, wherein the biological sample is optionally a purified nucleic acid sample,.

**44.** The method of claim 43, optionally wherein the purified sample is DNA.

**45.** The method of claim 43, wherein the sample is or RNA; and/or.

further comprising having determined by sequencing the nucleic acid sample derived from the cancer, that the cancer harbors a mutation in at least one gene selected from the group consisting of mTOR, PI3K, AKT and Ras; and/or

**46.** The method of claim 41, wherein the determining of the mutation in the at least one gene is performed by sequencing the nucleic acid sample.

~~47.~~ ~~The method of any one of claims 27-46, wherein~~ the cancer is selected from the group consisting of: solid tumor, leukemia, lymphocytic leukemia, lymphoma, sarcoma, multiple myeloma, ~~-~~hemangiosarcoma, histiocytic sarcoma, lymphosarcoma, osteosarcoma, transitional cell carcinoma, squamous cell carcinoma, mammary carcinoma, melanoma, mast cell tumors, lipoma, anal gland adenocarcinoma, lung cancer, pancreatic cancer, stomach cancer, prostate cancer, nasal cancer, liver cancer, brain cancer, bladder cancer and thyroid cancer.

~~48. The method of claim 47, wherein the cancer is hemangiosarcoma.~~

~~49.~~5. A pharmaceutical composition formulated for oral administration, comprising:

Rapamycin, wherein the Rapamycin is present at a concentration of 0.001 mg/mL-10.0 mg/mL; or

Dasatinib, wherein the Dasatinib is present at a concentration of 0.001 mg/mL-10.0 mg/mL; or

Lapatinib, wherein the Lapatinib is present within the composition at a concentration of .001 mg/mL -100.0 mg/mL; or

Trametinib, wherein the Trametinib is present within the composition at a concentration of .001 mg/mL -100.0 mg/mL; or

Vorinostat, wherein the Vorinostat is present within the composition at a concentration of 0.01 mg/mL -500.0 mg/mL;

Imatinib, wherein the Imatinib is present within the composition at a concentration of 0.01 mg/mL -100.0 mg/mL; or

Crizotinib, wherein the Crizotinib is present within the composition at a concentration of 0.01 mg/mL -100.0 mg/mL;

Sorafenib, wherein the Sorafenib is present at a concentration of 0.001 mg/mL- 100.0 mg/mL.

~~50. A method of treating a cancer in a canine subject, comprising: administering to the canine subject in need thereof a therapeutically effective amount of a pharmaceutical composition comprising Dasatinib.~~

~~51.~~6. The ~~method~~use of claim ~~50~~3, wherein the composition comprises Dasatinib, wherein: the Dasatinib is to be administered at a dose equal to or less than 2 mg/kg, ~~.~~

~~52. The method of claim 51, wherein the Dasatinib is administered~~ optionally at a dose of 0.5-0.7 mg/kg; and/or~~.~~

~~53. The method of any one of claims 50-52, wherein~~ the Dasatinib is to be administered at a frequency selected from the group consisting of twice daily, once daily, once every other day, once every third day, once every fourth day, once every 5$^{th}$ day, or weekly; and/or~~.~~

~~54. The method of any one of claims 50-53, wherein~~ the Dasatinib is to be administered orally; and/or~~.~~

~~55. The method of any one of claims 50-54, further comprising administering~~ a therapeutically effective amount of at least one additional anti-cancer agent is to be further administered, ~~.~~

~~56. The method of claim 55,~~ optionally wherein the at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent, ~~.~~

~~57. The method of claim 56,~~ optionally wherein the DNA damaging chemotherapeutic agent is selected from the group consisting of a DNA-alkylating agent, DNA crosslinking agent, antimetabolite, topoisomerase inhibitor and a DNA intercalating agent; or~~.~~

~~58. The method of claim 55, wherein~~ the at least one additional anti-cancer agent is a targeted anti-cancer agent~~,~~.

~~59. The method of claim 58, wherein the targeted anti-cancer agent is~~ optionally selected from the group consisting of Crizotinib, Erlotinib, Gefinitib, Imatinib, Lapatinib, Rapamycin, Sorafenib, Trametinib, and Vorinostat; and/or~~.~~

~~60. The method of claim 59, wherein the targeted anti-cancer agent is Rapamycin.~~

~~61. The method of any one of claims 50-60,~~ wherein surgery is to be performed ~~further comprising performing surgery~~ on the subject; and/or.

~~62. The method of any one of claims 50-61, further comprising administering~~ionizing radiation is to be further administered to the subject ~~ionizing radiation~~; and/or~~.~~

**63.** The method of any one of claims 50-62, wherein the cancer harbors at least one mutation in at least one gene selected from the group consisting of ABL, BCR-ABL, c-KIT, EPHA2, PDGFR and a Src Family Kinase; and/or.

**64.** The method of any one claims 50-63, further comprising having determined from a biological sample derived from the cancer, that the cancer harbors a mutation in at least one gene selected from the group consisting of ABL, BCR-ABL, c-KIT, EPHA2, PDGFR and a Src Family Kinase,.

**65.** The method of claim 64, optionally wherein the biological sample is a nucleic acid sample, .

**66.** The method of claim 65, wherein the biological sample is optionally a purified nucleic acid sample,.

**67.** The method of claim 66, optionally wherein the purified sample is DNA.

**68.** The method of claim 66, wherein the sample is or RNA; and/or.

**69.** The method of claim 64, wherein further comprising the determining of the mutation in the at least one gene is performed by sequencing a the nucleic acid sample that the cancer harbors a mutation in at least one gene selected from the group consisting of ABL, BCR-ABL, c-KIT, EPHA2, PDGFR and a Src Family Kinase; and/or.

**70.** The method of any one of claims 50-69, wherein the cancer is selected from the group consisting of solid tumor, leukemia, lymphocytic leukemia, lymphoma, sarcoma, multiple myeloma, hemangiosarcoma, histiocytic sarcoma, lymphosarcoma, osteosarcoma, transitional cell carcinoma, squamous cell carcinoma, mammary carcinoma, melanoma, mast cell tumors, lipoma, anal gland adenocarcinoma, lung cancer, pancreatic cancer, stomach cancer, prostate cancer, nasal cancer, liver cancer, brain cancer, bladder cancer and thyroid cancer.

**71.** The method of claim 70, wherein the cancer is osteosarcoma.

**72.** A pharmaceutical composition formulated for oral administration, comprising Dasatinib, wherein the Dasatinib is present at a concentration of 0.001 mg/mL-10.0 mg/mL.

~~**73.** A method of treating a cancer in a canine subject, comprising: administering to the canine subject in need thereof a therapeutically effective amount of a pharmaceutical composition comprising Lapatinib.~~

~~**74.**~~**7.** The ~~method~~use of claim ~~7~~3, wherein the composition comprises Lapatinib, wherein: the Lapatinib is to be administered at a dose equal to or less than 50 mg/kg.~~.~~

~~**75.** The method of claim 74, wherein the Lapatinib is administered~~ optionally at a dose of 5 mg/kg - 10 mg/kg; and/or~~.~~

~~**76.** The method of any one claims 73-75, wherein~~ the Lapatinib is to be administered at a frequency selected from the group consisting of, twice daily, once daily, once every other day, once every third day, once every fourth day, once every 5$^{th}$ day, or weekly; and/or~~.~~

~~**77.** The method of any one of claims 73-76, wherein~~ the Lapatinib is to be administered orally; and/or~~.~~

~~**78.** The method of any one of claims 73-77, further comprising administering~~ a therapeutically effective amount of at least one additional anti-cancer agent is to be further administered,~~.~~

~~**79.** The method of claim 78,~~ optionally wherein the at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent,~~.~~

~~**80.** The method of claim 79,~~ optionally wherein the DNA damaging chemotherapeutic agent is selected from the group consisting of: a DNA-alkylating agent, DNA crosslinking agent, antimetabolite, topoisomerase inhibitor and a DNA intercalating agent; or ~~.~~

~~**81.** The method of claim 78, wherein~~ the at least one additional anti-cancer agent is a targeted anti-cancer agent,~~.~~

~~**82.** The method of claim 81,~~ optionally wherein the targeted anti-cancer agent is selected from the group consisting of: Crizotinib, Erlotinib, Gefinitib, Imatinib, Dasatinib, Rapamycin, Sorafenib, Trametinib, and Vorinostat; and/or~~.~~

~~**83.** The method of claim 82, wherein the targeted anti-cancer agent is Trametinib.~~

~~**84.** The method of any one of claims 73-82,~~ wherein surgery is to be performed ~~further comprising performing surgery~~ on the subject; and/or~~.~~

**85.** The method of any one of claims 73-84, further comprising administeringwherein ionizing radiation is to be further administered to the subject ionizing radiation; and/or.

**86.** The method of any one of the above claims, wherein the cancer harbors at least one mutation in at least one gene selected from the group consisting of ERBB1 and ERBB2.

**87.** The method of any one of claims 73-86, further comprising having determined from a biological sample derived from the cancer, that the cancer harbors a mutation in at least one gene selected from the group consisting ERBB1 and ERBB2,.

**88.** The method of claim 87, optionally wherein the biological sample is a nucleic acid sample,.

**89.** The method of claim 88, wherein the biological sample is optionally a purified nucleic acid sample,.

**90.** The method of claim 89, optionally wherein the purified sample is DNA.

**91.** The method of claim 89, wherein the sample is or RNA; and/or .

**92.** The method of claim 87, further comprising having determined from a biological sample derived from the cancer, that the cancer harbors a mutation in at least one gene selected from the group consisting ERBB1 and ERBB2 wherein the determining of the mutation in the at least one gene is performed by sequencing the nucleic acid sample; and/or.

**93.** The method of any one of claims 73-92, wherein the cancer is selected from the group consisting of: solid tumor, leukemia, lymphocytic leukemia, lymphoma, sarcoma, multiple myeloma, hemangiosarcoma, histiocytic sarcoma, lymphosarcoma, osteosarcoma, transitional cell carcinoma, squamous cell carcinoma, mammary carcinoma, melanoma, mast cell tumors, lipoma, anal gland adenocarcinoma, lung cancer, pancreatic cancer, stomach cancer, prostate cancer, nasal cancer, liver cancer, brain cancer, bladder cancer, thyroid cancer and transitional cell carcinoma.

**94.** The method of claim 93, wherein the cancer is transitional cell carcinoma.

**95.** A pharmaceutical composition formulated for oral administration, comprising

Lapatinib, wherein the Lapatinib is present within the composition at a concentration of .001 mg/mL -100.0 mg/mL.

**96.** A method of treating a cancer in a canine subject, comprising: administering to the canine subject in need thereof a therapeutically effective amount of a pharmaceutical composition comprising Trametinib.

**97.8.** The methoduse of claim 396, wherein the composition comprises Trametinib, wherein: the Trametinib is to be administered at a dose equal to or less than 0.05 mg/kg/day,.

**98.** The method of claim 97, wherein the Trametinib is administeredoptionally at a dose of 0.02 mg/kg/day; and/or.

**99.** The method of any one of claims 96-98, wherein the Trametinib is to be administered at a frequency selected from the group consisting of, twice daily, once daily, once every other day, once every third day, once every fourth day, once every $5^{th}$ day, or weekly; and/or.

**100.** The method of any one of claims 96-99, wherein the Trametinib is to be administered orally; and/or.

**101.** The method of any one of claims 96-100, further comprising administering a therapeutically effective amount of at least one additional anti-cancer agent is to be further administered,.

**102.** The method of claim 101, optionally wherein the at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent, .

**103.** The method of claim 102, optionally wherein the DNA damaging chemotherapeutic agent is selected from the group consisting of: a DNA-alkylating agent, DNA crosslinking agent, antimetabolite, topoisomerase inhibitor and a DNA intercalating agent, or.

**104.** The method of claim 101, wherein the at least one additional anti-cancer agent is a targeted anti-cancer agent, .

**105.** The method of claim 104, optionally wherein the targeted anti-cancer agent is selected from the group consisting of: Crizotinib, Erlotinib, Gefinitib, Imatinib, Dasatinib, Rapamycin, Sorafenib, Lapatinib, and Vorinostat; and/or.

**106.** The method of claim 105, wherein the targeted anti-cancer agent is Rapamycin.

**107.** The method of claim 105, wherein the targeted anti-cancer agent is Dasatinib

**108.** The method of claim 105, wherein the targeted anti-cancer agent is Lapatinib.

**109.** The method of any one of claims 96-108, wherein surgery is to be performed further comprising performing surgery on the subject; and/or

**110.** The method of any one of claims 96-109, further comprising administeringwherein ionizing radiation is to be further administered to the subject ionizing radiation; and/or .

**111.** The method of any one of claims 96-110, wherein the cancer harbors at least one mutation in at least one gene selected from the group consisting of MEK1 and MEK2; and/or.

**112.** The method of any one of claims 96-111, further comprising having determined from a biological sample derived from the cancer, that the cancer harbors a mutation in at least one gene selected from the group consisting of MEK1 and MEK2,.

**113.** The method of claim 112, optionally wherein the biological sample is a nucleic acid sample,.

**114.** The method of claim 113, optionally wherein the biological sample is a purified nucleic acid sample,.

**115.** The method of claim 113, optionally wherein the purified sample is DNA.

**116.** The method of claim 113, wherein the sample is or RNA; and/or.

**117.** The method of claim 112, further comprising having determined from a biological sample derived from the cancer, that the cancer harbors a mutation in at least one gene selected from the group consisting of MEK1 and MEK2 wherein the determining of the mutation in the at least one gene is performed by sequencing the nucleic acid sample.

**118.** The method of any one of the above claims, wherein the cancer is selected from the group consisting of: solid tumor, leukemia, lymphocytic leukemia, lymphoma, multiple myeloma, transitional cell carcinoma, squamous cell carcinoma, mammary carcinoma, melanoma, mast cell tumors, lipoma, anal gland adenocarcinoma, lung cancer, pancreatic cancer, stomach cancer, prostate cancer, nasal cancer, liver cancer, brain cancer, bladder cancer, thyroid cancer, gingiva carcinoma, and sarcoma (including: soft tissue sarcoma, splenic stromal sarcoma and spindle cell sarcoma, hemangiosarcoma, histiocytic sarcoma, leiomyosarcoma, lymphosarcoma and osteosarcoma).

**119.** The method of claim 118, wherein the cancer is transitional cell carcinoma.

~~**120.** A pharmaceutical composition formulated for oral administration, comprising Trametinib, wherein the Trametinib is present within the composition at a concentration of .001 mg/mL -100.0 mg/mL.~~

~~**121.** A method of treating a cancer in a canine subject, comprising administering to the canine subject in need thereof a therapeutically effective amount of a pharmaceutical composition comprising Vorinostat.~~

~~**122.**~~**9.** The ~~method~~use of claim ~~121~~3, wherein the composition comprises Vorinostat, wherein: the Vorinostat is to be administered at a dose equal to or less than 100 mg/kg~~.~~.

~~**123.** The method of claim 122, wherein the Vorinostat is administered~~ optionally at a dose of 30-60 mg/kg; and/or~~.~~

~~**124.** The method of any one claims 121-123, wherein~~ the Vorinostat is to be administered at a frequency selected from the group consisting of: twice daily, once daily, once every other day, once every third day, once every fourth day, once every 5$^{th}$ day, or weekly; and/or~~.~~

~~**125.** The method of any one of claims 121-124, wherein~~ the Vorinostat is to be administered orally; and/or~~.~~

~~**126.** The method of any one of claims 121-125, further comprising administering~~wherein a therapeutically effective amount of at least one additional anti-cancer agent is to be further administered, ~~.~~

~~**127.** The method of claim 126,~~ optionally wherein the at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent~~.~~.

~~**128.** The method of claim 127, wherein the DNA damaging chemotherapeutic agent is~~ optionally selected from the group consisting of: a DNA-alkylating agent, DNA crosslinking agent, antimetabolite, topoisomerase inhibitor and a DNA intercalating agent, or~~.~~

~~**129.** The method of claim 126, wherein~~ the at least one additional anti-cancer agent is a targeted anti-cancer agent~~.~~.

~~**130.** The method of claim 129, wherein the targeted anti-cancer agent is~~ optionally selected from the group consisting of: Crizotinib, Erlotinib, Gefinitib, Imatinib, Dasatinib, Rapamycin, Sorafenib, Lapatinib, and Trametinib; and/or ~~.~~

**131.** The method of claim 130, wherein the targeted anti-cancer agent is Rapamycin.

**132.** The method of claim 130, wherein the targeted anti-cancer agent is Trametinib.

**133.** The method of claim 130, wherein the targeted anti-cancer agent is Lapatinib.

**134.** The method of any one of claims 121-133, wherein surgery is to be performed further comprising performing surgery on the subject; and/or

**135.** The method of any one of claims 121-134, further comprising administeringwherein ionizing radiation is to be further administered to the subject ionizing radiation; and/or.

**136.** The method of any one of claims 121-135, wherein the cancer harbors at least one mutation in at least one gene selected from the group consisting of p300, CBP, TIF-2, RAR, BCL-6, AML1, STAT5 and HDAC1; and/or.

**137.** The method of any one of claims 121-136, further comprising having determined from a biological sample derived from the cancer, that the cancer harbors a mutation in at least one gene selected from the group consisting of p300, CBP, TIF-2, RAR, BCL-6, AML1, STAT5 and HDAC1,.

**138.** The method of claim 137, optionally wherein the biological sample is a nucleic acid sample,.

**139.** The method of claim 138, wherein the biological sample is optionally a purified nucleic acid sample,.

**140.** The method of claim 139, optionally wherein the purified sample is DNA.

**141.** The method of claim 139, wherein the sample is or RNA; and/or.

**142.** The method of claim 137 further comprising having determined from a biological sample derived from the cancer, that the cancer harbors a mutation in at least one gene selected from the group consisting of p300, CBP, TIF-2, RAR, BCL-6, AML1, STAT5 and HDAC1 wherein the determining of the mutation in the at least one gene is performed by sequencing the nucleic acid sample; and/or .

**143.** The method of any one of claims 121-143, wherein the cancer is selected from the group consisting of: solid tumor, leukemia, lymphocytic leukemia, lymphoma, multiple myeloma, transitional cell carcinoma, squamous cell carcinoma, mammary carcinoma, melanoma, mast cell

tumors, lipoma, anal gland adenocarcinoma, lung cancer, pancreatic cancer, stomach cancer, prostate cancer, nasal cancer, liver cancer, brain cancer, bladder cancer, thyroid cancer, gingiva carcinoma, and sarcoma (including: soft tissue sarcoma, splenic stromal sarcoma and spindle cell sarcoma, hemangiosarcoma, histiocytic sarcoma, leiomyosarcoma, lymphosarcoma and osteosarcoma).

~~**144.** The method of claim 143, wherein the cancer is hemangiosarcoma.~~

~~**145.** The method of claim 143, wherein the cancer is histiocytic sarcoma.~~

~~**146.** A pharmaceutical composition formulated for oral administration, comprising Vorinostat, wherein the Vorinostat is present within the composition at a concentration of 0.01 mg/mL -500.0 mg/mL.~~

~~**147.** A method of treating a cancer in a canine subject, comprising administering to the canine subject in need thereof a therapeutically effective amount of a pharmaceutical composition comprising Imatinib.~~

~~**148.**~~**10.** The ~~method~~use of claim ~~147~~3, wherein the composition comprises Imatinib, wherein: the Imatinib is to be administered at a dose equal to or less than 50 mg/kg, ~~.~~

~~**149.** The method of claim 148, wherein the Imatinib is administered~~ optionally at a dose of 10 mg/kg; and/or~~.~~

~~**150.** The method of any one of claims 147-149, wherein~~ the Imatinib is to be administered at a frequency selected from the group consisting of, twice daily, once daily, once every other day, once every third day, once every fourth day, once every 5$^{th}$ day, or weekly; and/or~~.~~

~~**151.** The method of any one of claims 147-150, wherein~~ the Imatinib is to be administered orally; and/or~~.~~

~~**152.** The method of any one claims 147-151, further comprising administering~~wherein a therapeutically effective amount of at least one additional anti-cancer agent is to be further administered,~~.~~

~~**153.** The method of claim 152,~~ optionally wherein the at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent,~~.~~

**154.** The method of claim 153, optionally wherein the DNA damaging chemotherapeutic agent is selected from the group consisting of: a DNA-alkylating agent, DNA crosslinking agent, antimetabolite, topoisomerase inhibitor and a DNA intercalating agent, or.

**155.** The method of claim 154, wherein the at least one additional anti-cancer agent is a targeted anti-cancer agent, .

**156.** The method of claim 155, optionally wherein the targeted anti-cancer agent is selected from the group consisting of: Crizotinib, Erlotinib, Gefinitib, Lapatinib, Dasatinib, Rapamycin, Sorafenib, Trametinib, and Vorinostat; and/or.

**157.** The method of claim 156, wherein the targeted anti-cancer agent is Trametinib.

**158.** The method of claim 156, wherein the targeted anti-cancer agent is Rapamycin.

**159.** The method of any one of claims 147-158, wherein surgery is to be performed further comprising performing surgery on the subject; and/or

**160.** The method of any one of claims 147-159, further comprising administeringwherein ionizing radiation is to be further administered to the subject ionizing radiation; and/or.

**161.** The method of any one of claims 147-160, wherein the cancer harbors at least one mutation in at least one gene selected from the group consisting of ABL, BCR-ABL, PDGFR, and C-KIT; and/or.

**162.** The method of any one of claims 147-161, further comprising having determined from a biological sample derived from the cancer, that the cancer harbors a mutation in at least one gene selected from the group consisting ABL, BCR-ABL, PDGFR, and C-KIT,.

**163.** The method of claim 162, optionally wherein the biological sample is a nucleic acid sample,.

**164.** The method of claim 163, wherein the biological sample is optionally a purified nucleic acid sample,.

**165.** The method of claim 164, optionally wherein the purified sample is DNA.

**166.** The method of claim 164, wherein the sample is or RNA; and/or.

~~**167.** The method of claim 162,~~ further comprising having determined from a biological sample derived from the cancer, that the cancer harbors a mutation in at least one gene selected from the group consisting ABL, BCR-ABL, PDGFR, and C-KIT, wherein the determining of the mutation in the at least one gene is performed by sequencing the nucleic acid sample; and/or~~.~~

~~**168.** The method of any one of claims 147-167, wherein~~ the cancer is selected from the group consisting of: solid tumor, leukemia, lymphocytic leukemia, lymphoma, sarcoma, multiple myeloma, hemangiosarcoma, histiocytic sarcoma, lymphosarcoma, osteosarcoma, transitional cell carcinoma, squamous cell carcinoma, mammary carcinoma, melanoma, mast cell tumors, lipoma, anal gland adenocarcinoma, lung cancer, pancreatic cancer, stomach cancer, prostate cancer, nasal cancer, liver cancer, brain cancer, bladder cancer, thyroid cancer and transitional cell carcinoma.

~~**169.** The method of claim 168, wherein the cancer is hemangiosarcoma.~~

~~**170.** The method of claim 168, wherein the cancer is mast cell tumor.~~

~~**171.** A pharmaceutical composition formulated for oral administration, comprising Imatinib, wherein the Imatinib is present within the composition at a concentration of 0.01 mg/mL -100.0 mg/mL.~~

~~**172.** A method of treating a cancer in a canine subject, comprising administering to the canine subject in need thereof a therapeutically effective amount of a pharmaceutical composition comprising Crizotinib.~~

~~**173.**~~**11.** The ~~method~~use of claim ~~172~~3, wherein the composition comprises Crizotinib, wherein: the Crizotinib is to be administered at a dose equal to or less than 10 mg/kg. ~~.~~

~~**174.** The method of claim 173, wherein the Crizotinib is administered~~ optionally at a dose of 1 mg/kg-2 mg/kg; and/or~~.~~

~~**175.** The method of any one of claims 172-174, wherein~~ the Crizotinib is to be administered at a frequency selected from the group consisting of, twice daily, once daily, once every other day, once every third day, once every fourth day, once every 5$^{th}$ day, or weekly; and/or~~.~~

~~**176.** The method of any one of claims 172-175, wherein~~ the Crizotinib is to be administered orally; and/or~~.~~

~~177.~~ ~~The method of any one of claims 172-176, further comprising administering~~wherein a therapeutically effective amount of at least one additional anti-cancer agent is to be further administered,~~.~~

~~178.~~ ~~The method of claim 177,~~ optionally wherein the at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent,~~.~~

~~179.~~ ~~The method of claim 178,~~ optionally wherein the DNA damaging chemotherapeutic agent is selected from the group consisting of: a DNA-alkylating agent, DNA crosslinking agent, antimetabolite, topoisomerase inhibitor and a DNA intercalating agent or~~.~~

~~180.~~ ~~The method of claim 177,~~ wherein the at least one additional anti-cancer agent is a targeted anti-cancer agent, ~~.~~

~~181.~~ ~~The method of claim 180,~~ optionally wherein the targeted anti-cancer agent is selected from the group consisting of: Imatinib, Erlotinib, Gefinitib, Lapatinib, Dasatinib, Rapamycin, Sorafenib, Trametinib, and Vorinostat; and/or~~.~~

~~182. The method of claim 181, wherein the targeted anti-cancer agent is Trametinib.~~

~~183. The method of claim 181, wherein the targeted anti-cancer agent is Imatinib.~~

~~184.~~ ~~The method of any one of claims 171-183,~~ wherein surgery is to be performed ~~further comprising performing surgery~~ on the subject; and/or~~.~~

~~185.~~ ~~The method of any one of the claims 171-184, further comprising administering~~wherein ionizing radiation is to be further administered to the subject ~~ionizing radiation~~; and/or~~.~~

~~186.~~ ~~The method of any one of claims 171-185, wherein~~ the cancer harbors at least one mutation in at least one gene selected from the group consisting of ALK, c-MET and ROS1; and/or~~.~~

~~187.~~ ~~The method of any one of claims 171-186,~~ further comprising having determined from a biological sample derived from the cancer, that the cancer harbors a mutation in at least one gene selected from the group consisting ALK, c-MET and ROS1,~~.~~

~~188.~~ ~~The method of claim 187,~~ optionally wherein the biological sample is a nucleic acid sample,~~.~~

~~**189.** The method of claim 188, wherein the biological sample is~~ optionally a purified nucleic acid sample~~.~~.

~~**190.** The method of claim 189,~~ optionally wherein the purified sample is DNA~~.~~

~~**191.** The method of claim 189, wherein the sample is~~ or RNA; and/or~~.~~

~~**192.** The method of claim 187,~~ further comprising having determined from a biological sample derived from the cancer, that the cancer harbors a mutation in at least one gene selected from the group consisting ALK, c-MET and ROS1, wherein the determining of the mutation in the at least one gene is performed by sequencing the nucleic acid sample; and/or~~.~~

~~**193.** The method of any one of claims 172-192,~~ wherein the cancer is selected from the group consisting of: solid tumor, leukemia, lymphocytic leukemia, lymphoma, sarcoma, multiple myeloma, hemangiosarcoma, histiocytic sarcoma, lymphosarcoma, osteosarcoma, transitional cell carcinoma, squamous cell carcinoma, mammary carcinoma, melanoma, mast cell tumors, lipoma, anal gland adenocarcinoma, lung cancer, pancreatic cancer, stomach cancer, prostate cancer, nasal cancer, liver cancer, brain cancer, bladder cancer, thyroid cancer and transitional cell carcinoma.

~~**194.** The method of claim 193, wherein the cancer is hemangiosarcoma.~~

~~**195.** The method of claim 193, wherein the cancer is osteosarcoma.~~

~~**196.** A pharmaceutical composition formulated for oral administration, comprising Crizotinib, wherein the Crizotinib is present within the composition at a concentration of 0.01 mg/mL -100.0 mg/mL.~~

~~**197.** A method of treating a cancer in a canine subject, comprising: administering to the canine subject in need thereof a therapeutically effective amount of a pharmaceutical composition comprising Sorafenib.~~

~~**198.**~~**12.** The ~~method~~use of claim ~~197~~3, wherein the composition comprises Sorafenib, wherein: the Sorafenib is to be administered at a dose of less than 10 mg/kg~~.~~.

~~**199.** The method of claim 198, wherein the Sorafenib is administered~~ optionally at a dose of 1 mg/kg – 3 mg/kg; and/or~~.~~

**200.** The method of any one claims 197-199, wherein the Sorafenib is to be administered at a frequency selected from the group consisting of twice daily, once daily, once every other day, once every third day, once every fourth day, once every 5th day, or weekly; and/or.

**201.** The method of any one of claims 197-200, wherein the Sorafenib is to be administered orally; and/or.

**202.** The method of any one of claims 197-201, further comprising administering a therapeutically effective amount of at least one additional anti-cancer agent is to be further administered, .

**203.** The method of claim 202, optionally wherein the at least one additional cancer agent is a DNA damaging chemotherapeutic agent,.

**204.** The method of claim 203, optionally wherein the DNA damaging chemotherapeutic agent is selected from the group consisting of: a DNA-alkylating agent, DNA crosslinking agent, antimetabolite, topoisomerase inhibitor and a DNA intercalating agent, or.

**205.** The method of claim 202, wherein the at least one additional anti-cancer agent is a targeted anti-cancer agent,.

**206.** The method of claim 205, optionally wherein the targeted anti-cancer agent is selected from the group consisting of: Crizotinib, Dasatinib Erlotinib, Gefinitib, Imatinib, Lapatinib, Rapamycin, Trametinib, and Vorinostat; and/or.

**207.** The method of claim 206, wherein the targeted anti-cancer agent is Imatinib.

**208.** The method of any one of claims 197-207, wherein surgery is to be performed further comprising performing surgery on the subject; and/or.

**209.** The method of any one of claims 197-208, further comprising administering wherein ionizing radiation is to be further administered to the subject ionizing radiation; and/or.

**210.** The method of any one claims 197-209, wherein the cancer harbors at least one mutation in at least one gene selected from the group consisting of RAF, c-Kit, FLT-3, RET, VEGFRs and PDGFRB; and/or.

~~**211.** The method of any one of claims 197-210,~~ further comprising having determined from a biological sample derived from the cancer, that the cancer harbors a mutation in at least one gene selected from the group consisting of RAF, c-Kit, FLT-3, RET, VEGFRs and PDGFRB~~.~~.

~~**212.** The method of claim 211,~~ optionally wherein the biological sample is a nucleic acid sample~~.~~.

~~**213.** The method of claim 212, wherein the biological sample is~~ optionally a purified nucleic acid sample~~.~~.

~~**214.** The method of claim 213,~~ optionally wherein the purified sample is DNA~~.~~

~~**215.** The method of claim 213, wherein the sample is~~ or RNA; and/or~~.~~

~~**216.** The method of claim 211,~~ further comprising having determined from a biological sample derived from the cancer, that the cancer harbors a mutation in at least one gene selected from the group consisting of RAF, c-Kit, FLT-3, RET, VEGFRs and PDGFRB, wherein the determining of the mutation in the at least one gene is performed by sequencing the nucleic acid sample; and/or~~.~~

~~**217.** The method of any one of claims 197-216, wherein~~ the canine cancer is selected from the group consisting of: solid tumor, leukemia, lymphocytic leukemia, lymphoma, sarcoma, multiple myeloma, hemangiosarcoma, histiocytic sarcoma, lymphosarcoma, osteosarcoma, transitional cell carcinoma, squamous cell carcinoma, mammary carcinoma, melanoma, mast cell tumors, lipoma, anal gland adenocarcinoma, lung cancer, pancreatic cancer, stomach cancer, prostate cancer, nasal cancer, liver cancer, brain cancer, bladder cancer and thyroid cancer.

~~**218.** The method of claim 217, wherein the cancer is mast cell tumor.~~

~~**219.** The method of claim 217, wherein the cancer is osteosarcoma.~~

~~**220.** A pharmaceutical composition formulated for oral administration, comprising Sorafenib, wherein the Sorafenib is present at a concentration of 0.001 mg/mL - 100.0 mg/mL.~~

~~**221.**~~**13.** The ~~method~~use of any one of claims of 1-4 or 6-12,~~1-48, 50-71, 73-94, 96-119, 121-145, 147-170, 172-195 and 197-219,~~ wherein: the cancer harbors at least one mutation in at least one gene shown in Tables 1, 2 and 12-26; or~~.~~

**~~222.~~** ~~The method of any one of claims 1-48, 50-71, 73-94, 96-119, 121-145, 147-170, 172-195 and 197-219,~~ further comprising determining or having determined from a biological sample derived from the cancer, at least one mutation in at least one gene shown in Tables 1, 2, and 12-26; or~~.~~

**~~223.~~** ~~The method of any one of claims 1-48, 50-71, 73-94, 96-119, 121-145, 147-170, 172-195 and 197-219, wherein~~ the cancer has increased or decreased expression in at least one gene shown in Tables 1, 2 and 12-26 compared to non-cancerous tissue; or~~.~~

**~~224.~~** ~~The method of any one of claims 1-48, 50-71, 73-94, 96-119, 121-145, 147-170, 172-195 and 197-219,~~ further comprising determining or having determined from a biological sample derived from the cancer, increased or decreased expression in at least one gene shown in Tables 1, 2, and 12-26 compared to non-cancerous tissue.