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 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 examples, the method includes the step of identifying the mutation in a sample derived from the subject. In certain examples, the HDAC inhibitor is selected from the group consisting of: romidepsin, belinostat, panobinostat, vorinostat, givinostat, entinostat, tacedinaline, and mocetinostat. In certain examples, the HDAC inhibitor is vorinostat. In certain examples, the method, further comprises administering an effective amount of a DNA damaging chemotherapeutic agent. In certain 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 examples, the DNA-alkylating agent is selected from the group consisting of: a nitrosourea, a triazene and a platinum agent. In certain examples, the DNA-alkylating agent is a nitrosourea. In certain examples, the nitrosourea is lomustine. In certain examples, the method, further comprises performing surgery on the subject. In certain examples, the method further comprises administering an effective amount of at least one additional anti-cancer therapeutic agent. In certain examples, the method further comprises administering to the subject ionizing radiation. In certain examples, the cancer harbors more than one mutant allele of ATM kinase. In certain examples, the biological sample is a nucleic acid sample. In certain examples, the biological sample is a purified nucleic acid sample. In certain examples, the sample is DNA. In certain examples, the sample is RNA. In certain examples, the identifying is performed by sequencing a nucleic acid sample. In certain examples, the cancer is cancer in a canine subject. In certain examples, 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 examples, the cancer is histiocytic sarcoma.

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

[0013] In certain 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 examples, the Rapamycin is administered at a dose equal to or less than 1 mg/kg. In certain examples, the Rapamycin is administered at a dose of 0.05-0.1 mg/kg. In certain 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 examples, the Rapamycin is administered orally. In certain examples, the methods described herein further comprise administering a therapeutically effective amount of at least one additional anti-cancer agent. In certain examples, at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent. In certain 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 examples, at least one additional anti-cancer agent is a targeted anti-cancer agent. In certain 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 examples, the targeted anti-cancer agent is Dasatinib. In certain examples, the methods described herein further comprise performing

surgery on the subject. In certain examples, the methods described herein further comprise administering to the subject ionizing radiation. In certain 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 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 examples, the biological sample is a nucleic acid sample. In certain examples, the biological sample is a purified nucleic acid sample. In certain examples, the sample is DNA. In certain examples, the sample is RNA. In certain examples, the determining of the mutation in at least one gene is performed by sequencing the nucleic acid sample. In certain 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 examples, the cancer is hemangiosarcoma. In certain 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 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 examples, the Dasatinib is administered at a dose equal to or less than 2 mg/kg. In certain examples, the Dasatinib is administered at a dose of 0.5-0.7 mg/kg. In certain 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 examples, the Dasatinib is administered orally. In certain examples, the methods described herein further comprise administering a therapeutically effective amount of at least one additional anti-cancer agent. In certain examples, at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent. In certain 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 examples, at least one additional anti-cancer agent is a targeted

anti-cancer agent. In certain 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 examples, the targeted anti-cancer agent is Rapamycin. In certain examples, the methods described herein further comprise performing surgery on the subject. In certain examples, the methods described herein further comprise administering to the subject ionizing radiation. In certain 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 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 examples, the biological sample is a nucleic acid sample. In certain examples, the biological sample is a purified nucleic acid sample. In certain examples, the sample is DNA. In certain examples, the sample is RNA. In certain examples, the determining of the mutation in at least one gene is performed by sequencing the nucleic acid sample. In certain 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 examples, the cancer is osteosarcoma. In certain 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 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 examples, the Lapatinib is administered at a dose equal to or less than 50 mg/kg. In certain examples, the Lapatinib is administered at a dose of 5 mg/kg-10 mg/kg. In certain 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 examples, the Lapatinib is administered orally. In certain examples, the methods described herein further comprise administering a therapeutically

effective amount of at least one additional anti-cancer agent. In certain examples, at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent. In certain 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 examples, at least one additional anti-cancer agent is a targeted anti-cancer agent. In certain 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 examples, the targeted anti-cancer agent is Trametinib. In certain examples, the methods described herein further comprise performing surgery on the subject. In certain examples, the methods described herein further comprise administering to the subject ionizing radiation. In certain examples, the cancer harbors at least one mutation in at least one gene selected from the group consisting of ERBB1 and ERBB2. In certain 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 examples, the biological sample is a nucleic acid sample. In certain examples, the biological sample is a purified nucleic acid sample. In certain examples, the sample is DNA. In certain examples, the sample is RNA. In certain examples, the determining of the mutation in at least one gene is performed by sequencing the nucleic acid sample. In certain 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 examples, the cancer is transitional cell carcinoma. In certain 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 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 examples, the Trametinib is administered at a dose equal to or less than 0.05 mg/kg/day. In certain examples, the Trametinib is administered at a dose of 0.02 mg/kg/day. In certain 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 examples, the Trametinib is administered orally. In certain examples, the methods described herein further comprise administering a therapeutically effective amount of at least one additional anti-cancer agent. In certain examples, at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent. In certain 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 examples, at least one additional anti-cancer agent is a targeted anti-cancer agent. In certain 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 examples, the targeted anti-cancer agent is Rapamycin. In certain examples, the targeted anti-cancer agent is Dasatinib. In certain examples, the targeted anti-cancer agent is Lapatinib. In certain examples, the methods described herein further comprise performing surgery on the subject. In certain examples, the methods described herein further comprise administering to the subject ionizing radiation. In certain examples, the cancer harbors at least one mutation in at least one gene selected from the group consisting of MEK1 and MEK2. In certain 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 examples, the biological sample is a nucleic acid sample. In certain examples, the biological sample is a purified nucleic acid sample. In certain examples, the sample is DNA. In certain examples, the sample is RNA. In certain examples, the determining of the mutation in the at least one gene is performed by sequencing the nucleic acid sample. In certain 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 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 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 examples, the Vorinostat is administered at a dose equal to or less than 100 mg/kg. In certain examples, the Vorinostat is administered at a dose of 30-60 mg/kg. In certain 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 examples, the Vorinostat is administered orally. In certain examples, the methods described herein further comprise administering a therapeutically effective amount of at least one additional anti-cancer agent. In certain examples, at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent. In certain 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 examples, at least one additional anti-cancer agent is a targeted anti-cancer agent. In certain 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 examples, the targeted anti-cancer agent is Rapamycin. In certain examples, the targeted anti-cancer agent is Trametinib. In certain examples, the targeted anti-cancer agent is Lapatinib. In certain examples, the methods described herein further comprise performing surgery on the subject. In certain examples, the methods described herein further comprise administering to the subject ionizing radiation. In certain 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 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 examples, the methods described herein further comprise having determined from a biological sample derived from the cancer, that the cancer overexpresses MYC. In certain examples, the biological sample is a nucleic acid sample. In certain examples, the biological sample is a purified nucleic acid sample. In certain examples, the sample is DNA. In certain examples, the sample is RNA. In certain examples, the determining of the mutation in at least one gene is

performed by sequencing the nucleic acid sample. In certain 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 examples, the cancer is hemangiosarcoma. In certain examples, the cancer is histiocytic sarcoma. In certain examples, 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 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 Imatinib. In certain examples, the Imatinib is administered at a dose equal to or less than 50 mg/kg. In certain examples, the Imatinib is administered at a dose of 10 mg/kg. In certain 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 examples, the Imatinib is administered orally. In certain examples, the methods described herein further comprise administering a therapeutically effective amount of at least one additional anti-cancer agent. In certain examples, at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent. In certain 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 examples, the at least one additional anti-cancer agent is a targeted anti-cancer agent. In certain examples, the targeted anti-cancer agent is selected from the group consisting of: Crizotinib, Rapamycin, Erlotinib, Gefinitib, Lapatinib, Dasatinib, Sorafenib, Trametinib, and Vorinostat. In certain examples, the targeted anti-cancer agent is Trametinib. In certain examples, the targeted anti-cancer agent is Rapamycin. In certain examples, the methods described herein further comprise performing surgery on the subject. In certain examples, the methods described herein further comprise administering to the subject ionizing radiation. In certain examples, 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 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 examples, the biological sample is a nucleic acid sample. In certain examples, the biological sample is a purified nucleic acid sample. In certain examples, the sample is DNA. In certain examples, the sample is RNA. In certain examples, the determining of the mutation in at least one gene is performed by sequencing the nucleic acid sample. In certain 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 examples, the cancer is hemangiosarcoma. In certain examples, the cancer is mast cell tumors. In certain 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 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 examples, Crizotinib is administered at a dose equal to or less than 10 mg/kg. In certain examples, Crizotinib is administered at a dose of 1 mg/kg- 2 mg/kg. In certain 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 examples, Crizotinib is administered orally. In certain examples, the methods described herein further comprise administering a therapeutically effective amount of at least one additional anti-cancer agent. In certain examples, at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent. In certain 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 examples, at least one additional anti-cancer agent is a targeted anti-cancer agent. In certain 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 examples, the targeted anti-cancer agent is Trametinib. In certain examples, the targeted anti-cancer agent is Imatinib. In certain examples, the methods described herein further comprise performing surgery on the subject. In certain examples, the methods described herein further comprise administering to the subject ionizing radiation. In certain 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 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 examples, the biological sample is a nucleic acid sample. In certain examples, the biological sample is a purified nucleic acid sample. In certain examples, the sample is DNA. In certain examples, the sample is RNA. In certain examples, the determining of the mutation in at least one gene is performed by sequencing the nucleic acid sample. In certain 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 examples, the cancer is hemangiosarcoma. In certain examples, the cancer is osteosarcoma. In certain 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 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 examples, the Sorafenib is administered at a dose of less than 10 mg/kg. In certain examples, the Sorafenib is administered at a dose of 1 mg/kg- 3 mg/kg. In certain 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 examples, the Sorafenib is administered orally. In certain examples, the methods described herein further comprise administering a therapeutically effective

amount of at least one additional anti-cancer agent. In certain examples, at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent. In certain 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 examples, at least one additional anti-cancer agent is a targeted anti-cancer agent. In certain 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 examples, the targeted anti-cancer agent is Imatinib. In certain examples, the methods described herein further comprise performing surgery on the subject. In certain examples, the methods described herein further comprise administering to the subject ionizing radiation. In certain 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 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 examples, the biological sample is a nucleic acid sample. In certain examples, the biological sample is a purified nucleic acid sample. In certain examples, the sample is DNA. In certain examples, the sample is RNA. In certain examples, the determining of the mutation in at least one gene is performed by sequencing the nucleic acid sample. In certain 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 examples, the cancer is mast cell tumor. In certain examples, the cancer is osteosarcoma. In certain 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 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 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 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 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 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.

2. The use of claim 1, wherein:

the HDAC inhibitor is selected from the group consisting of: romidepsin, belinostat, panobinostat, vorinostat, givinostat, entinostat, tacedinaline, and mocetinostat; and/or

an effective amount of a DNA damaging chemotherapeutic agent is to be further administered, 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; optionally wherein the DNA-alkylating agent is selected from the group consisting of: a nitrosourea, a triazene and a platinum agent, optionally wherein the nitrosourea is lomustine; and/or

wherein surgery is to be performed on the subject; and/or

wherein an effective amount of at least one additional anti-cancer therapeutic agent is to be further administered; and/or

wherein ionizing radiation is to be further administered to the subject; and/or

the cancer harbors more than one mutant allele of ATM kinase; and/or

the biological sample is a nucleic acid sample, optionally a purified nucleic acid sample, optionally wherein the purified sample is DNA or RNA; and/or

the identifying is performed by sequencing a nucleic acid sample; and/or.

the subject is a canine; and/or

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

the at least one mutation in ATM kinase is selected from: a missense mutation, a splice site mutation and a frameshift variant, 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.

4. The use of claim 3, wherein the composition comprises Rapamycin, wherein:

the Rapamycin is to be administered at a dose equal to or less than 1 mg/kg, optionally at a dose of 0.05-0.1 mg/kg; and/or

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

the Rapamycin is to be administered orally; and/or

wherein a therapeutically effective amount of at least one additional anti-cancer agent is to be further administered, optionally wherein

the at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent, 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

the at least one additional anti-cancer agent is a targeted anti-cancer agent, optionally selected from the group consisting of Crizotinib, Dasatinib Erlotinib, Gefinitib, Imatinib, Lapatinib, Sorafenib, Trametinib, and Vorinostat;

and/or

wherein surgery is to be performed on the subject; and/or.

wherein ionizing radiation is to be further administered to the subject; and/or

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

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, optionally wherein the biological sample is a nucleic acid sample, optionally a purified nucleic acid sample, optionally wherein the purified sample is DNA 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

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.

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.

6. The use of claim 3, wherein the composition comprises Dasatinib, wherein:

the Dasatinib is to be administered at a dose equal to or less than 2 mg/kg, optionally at a dose of 0.5-0.7 mg/kg; and/or

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

the Dasatinib is to be administered orally; and/or

a therapeutically effective amount of at least one additional anti-cancer agent is to be further administered, optionally wherein

the at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent, 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

the at least one additional anti-cancer agent is a targeted anti-cancer agent, optionally selected from the group consisting of Crizotinib, Erlotinib, Gefinitib, Imatinib, Lapatinib, Rapamycin, Sorafenib, Trametinib, and Vorinostat;

and/or

wherein surgery is to be performed on the subject; and/or.

ionizing radiation is to be further administered to the subject; and/or

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

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, optionally wherein the biological sample is a nucleic acid sample, optionally a purified nucleic acid sample, optionally wherein the purified sample is DNA or RNA; and/or

further comprising determining by sequencing a 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

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.

7. The use of claim 3, wherein the composition comprises Lapatinib, wherein:

the Lapatinib is to be administered at a dose equal to or less than 50 mg/kg, optionally at a dose of 5 mg/kg - 10 mg/kg; and/or

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

the Lapatinib is to be administered orally; and/or

a therapeutically effective amount of at least one additional anti-cancer agent is to be further administered, optionally wherein

the at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent, 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

the at least one additional anti-cancer agent is a targeted anti-cancer agent, 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

wherein surgery is to be performed on the subject; and/or

wherein ionizing radiation is to be further administered to the subject; and/or

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, optionally wherein the biological sample is a nucleic acid sample, optionally a purified nucleic acid sample, optionally wherein the purified sample is DNA or RNA; and/or

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

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.

8. The use of claim 3, 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, optionally at a dose of 0.02 mg/kg/day; and/or

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

the Trametinib is to be administered orally; and/or

a therapeutically effective amount of at least one additional anti-cancer agent is to be further administered, optionally wherein

the at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent, 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

the at least one additional anti-cancer agent is a targeted anti-cancer agent, 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

wherein surgery is to be performed on the subject; and/or

wherein ionizing radiation is to be further administered to the subject; and/or

the cancer harbors at least one mutation in at least one gene selected from the group consisting of MEK1 and MEK2; and/or

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, optionally wherein the biological sample is a nucleic acid sample, optionally a purified nucleic acid sample, optionally wherein the purified sample is DNA or RNA; and/or

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.

9. The use of claim 3, wherein the composition comprises Vorinostat, wherein:

the Vorinostat is to be administered at a dose equal to or less than 100 mg/kg, optionally at a dose of 30-60 mg/kg; and/or

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

the Vorinostat is to be administered orally; and/or

wherein a therapeutically effective amount of at least one additional anti-cancer agent is to be further administered, optionally wherein

the at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent, optionally selected from the group consisting of: a DNA-alkylating agent, DNA crosslinking agent, antimetabolite, topoisomerase inhibitor and a DNA intercalating agent, or

the at least one additional anti-cancer agent is a targeted anti-cancer agent, optionally selected from the group consisting of: Crizotinib, Erlotinib, Gefinitib, Imatinib, Dasatinib, Rapamycin, Sorafenib, Lapatinib, and Trametinib;

and/or

wherein surgery is to be performed on the subject; and/or

wherein ionizing radiation is to be further administered to the subject; and/or

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

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, optionally wherein the biological

sample is a nucleic acid sample, optionally a purified nucleic acid sample, optionally wherein the purified sample is DNA or RNA; and/or

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

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).

10. The use of claim 3, wherein the composition comprises Imatinib, wherein:

the Imatinib is to be administered at a dose equal to or less than 50 mg/kg, optionally at a dose of 10 mg/kg; and/or

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

the Imatinib is to be administered orally; and/or

wherein a therapeutically effective amount of at least one additional anti-cancer agent is to be further administered, optionally wherein

the at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent, 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

the at least one additional anti-cancer agent is a targeted anti-cancer agent, 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

wherein surgery is to be performed on the subject; and/or

wherein ionizing radiation is to be further administered to the subject; and/or

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

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, optionally wherein the biological sample is a nucleic acid sample, optionally a purified nucleic acid sample, optionally wherein the purified sample is DNA or RNA; and/or

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

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.

11. The use of claim 3, wherein the composition comprises Crizotinib, wherein:

the Crizotinib is to be administered at a dose equal to or less than 10 mg/kg, optionally at a dose of 1 mg/kg-2 mg/kg; and/or

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

the Crizotinib is to be administered orally; and/or

wherein a therapeutically effective amount of at least one additional anti-cancer agent is to be further administered, optionally wherein

the at least one additional anti-cancer agent is a DNA damaging chemotherapeutic agent, 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

wherein the at least one additional anti-cancer agent is a targeted anti-cancer agent, 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

wherein surgery is to be performed on the subject; and/or

wherein ionizing radiation is to be further administered to the subject; and/or

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

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, optionally wherein the biological sample is a nucleic acid sample, optionally a purified nucleic acid sample, optionally wherein the purified sample is DNA or RNA; and/or

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

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.

12. The use of claim 3, wherein the composition comprises Sorafenib, wherein:

the Sorafenib is to be administered at a dose of less than 10 mg/kg, optionally at a dose of 1 mg/kg – 3 mg/kg; and/or

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 5^{th} day, or weekly; and/or

the Sorafenib is to be administered orally; and/or

a therapeutically effective amount of at least one additional anti-cancer agent is to be further administered, optionally wherein

the at least one additional cancer agent is a DNA damaging chemotherapeutic agent, 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

the at least one additional anti-cancer agent is a targeted anti-cancer agent, 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

wherein surgery is to be performed on the subject; and/or

wherein ionizing radiation is to be further administered to the subject; and/or

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

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, optionally wherein the biological sample is a nucleic acid sample, optionally a purified nucleic acid sample, optionally wherein the purified sample is DNA or RNA; and/or

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

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.

13. The use of any one of claims of 1-4 or 6-12, wherein:

the cancer harbors at least one mutation in at least one gene shown in Tables 1, 2 and 12-26; or

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

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

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.