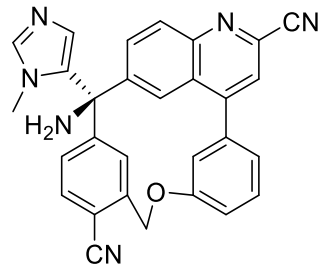
What is claimed is:

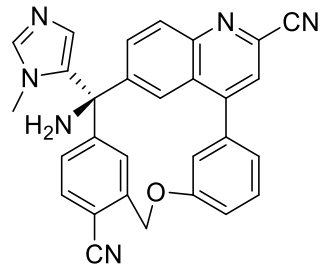
1. Use of Compound (I)



(Compound (I)),

or a pharmaceutically acceptable form thereof, in the manufacture of a medicament for treating a *KRAS*-dependent cancer in a subject in combination with a KRAS inhibitor.

2. Use of Compound (I)



(Compound (I)),

or a pharmaceutically acceptable form thereof, in the manufacture of a medicament for delaying emergence of resistance to a KRAS inhibitor for a cancer in a subject or overcoming resistance to a KRAS inhibitor for a cancer in a subject previously treated with a KRAS inhibitor.

3. The use of claim 1 or claim 2, wherein the cancer is lung cancer, pancreatic cancer, gynecologic cancer, gastrointestinal cancer, breast cancer, neoplasm (metastatic neoplasm, germ cell cancer, plasma cell neoplasm, or myelodysplastic/myeloproliferative neoplasm), carcinoma of unknown primary (CUP), or leukemia.

4. The use of claim 3, wherein:

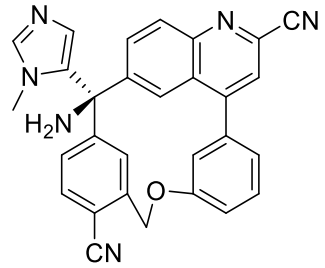
i) the lung cancer is non-small cell lung cancer (NSCLC), non-squamous NSCLC, squamous NSCLC, or lung adenocarcinoma;

ii) the gastrointestinal cancer is colorectal cancer (CRC), colon cancer, pancreatic cancer, pancreatic ductal adenocarcinoma (PDAC), biliary tract cancer, appendiceal cancer, small bowel cancer, stomach cancer, cholangiocarcinoma, ampullary cancer, gallbladder cancer, gastric cancer, gastric adenocarcinoma, esophageal cancer, esophageal adenocarcinoma, urinary tract cancer, GI-neuroendocrine tumor, or gastroesophageal junction adenocarcinoma; or

iii) the gynecological cancer is ovarian cancer, endometrial cancer, peritoneal cancer, or cervical cancer.

5. The use of claim 3, wherein the cancer is lung cancer, colorectal cancer, or pancreatic cancer; optionally wherein the cancer is non-small cell lung cancer, colorectal cancer, or pancreatic ductal adenocarcinoma.

6. Use of Compound (I)



(Compound (I)),

or a pharmaceutically acceptable form thereof, in the manufacture of a medicament for treating pancreatic cancer, pancreatic ductal adenocarcinoma, lung cancer, non-small cell lung cancer, or colorectal cancer in a subject in combination with a KRAS inhibitor.

7 The use of any one of claims 1-6, wherein the KRAS inhibitor is a KRAS G12C inhibitor, a KRAS G12D inhibitor, a KRAS G12S inhibitor, a KRAS G12V inhibitor, a KRAS G12R inhibitor, a KRAS G13D inhibitor, a pan-KRAS inhibitor, or a pan-RAS inhibitor.

8. The use of any one of claims 1-7, wherein the cancer comprises a *KRAS* mutation or a *KRAS* amplification, or a combination thereof.

9. The use of claim 8, wherein the cancer comprises a *KRAS* mutation.

10. The use of claim 9, wherein:

i) the *KRAS* mutation is a *KRAS* G12C mutation and the KRAS inhibitor is a KRAS G12C inhibitor; optionally wherein the KRAS G12C inhibitor is adagrasib (KRAZATI®, MRTX849, Amgen), sotorasib (LUMAKRAS™, AMG-510, Amgen), divarasib (GDC-6036, Genentech), linperlisib (YL-15293), RM007, D-1553 (InvestisBio), JDQ443 (Novartis), LY3537982 (Eli Lilly), LY3499446, ERAS-601, ERAS-007, BI 1823911 (Boehringer Ingelheim), JAB-21822, MK-1084, MK-1086, MK-1087, L-15293, D3S-001, RMC-6291 (Revolution), HBI-2438, FMC-376 (Frontier), BBO-8520 (BridgeBio), ZG19018 (Suzhou Zelgen), UCT-001024 (1200 Pharma), TEB-17231 (280Bio unit of Yingli Pharma), HYP-2A (Sichuan Huiyu), ABSK071 (Abbisko), IBI351 (GFH925; Innovent/Genfleet), ARS-853, ARS-1620, or JNJ-74699157 (ARS-3248); optionally wherein the KRAS G12C inhibitor is adagrasib or sotorasib;

ii) the *KRAS* mutation is a *KRAS* G12D mutation and the KRAS inhibitor is a KRAS G12D inhibitor or a pan-KRAS inhibitor or a pan-RAS inhibitor; optionally wherein the KRAS G12D inhibitor is MRTX1133 (Mirati), TH-Z827, TH-Z835, KD-8, BI-KRAS12D1-3, BI-KRASG12D3, RMC-9805 (Revolution), ASP3082, ASP4396, LY3962673, INCB161734, HRS-4642, or QTX3046 (Quanta); optionally wherein the KRAS G12D inhibitor is MRTX1133;

iii) the *KRAS* mutation is a *KRAS* G12V mutation and the KRAS inhibitor is a KRAS G12V inhibitor;

iv) the *KRAS* mutation is a *KRAS* G12R mutation and the KRAS inhibitor is a KRAS G12R inhibitor;

v) the *KRAS* mutation is a *KRAS* G12S mutation, and the KRAS inhibitor is a KRAS G12S inhibitor; or

vi) the *KRAS* mutation is a *KRAS* G13D mutation and the KRAS inhibitor is a KRAS G13D inhibitor.

11. The use of claim 9, wherein the *KRAS* mutation is a *KRAS* G12C mutation and the KRAS inhibitor is a KRAS G12C inhibitor or a pan-KRAS inhibitor or a pan-RAS inhibitor;

i) optionally wherein the KRAS G12C inhibitor is adagrasib (KRAZATI®, MRTX849, Amgen), sotorasib (LUMAKRAS™, AMG-510, Amgen), divarasib (GDC-6036, Genentech), linperlisib (YL-15293), RM007, D-1553 (InvestisBio), JDQ443 (Novartis), LY3537982 (Eli Lilly), LY3499446, ERAS-601, ERAS-007, BI 1823911 (Boehringer Ingelheim), JAB-21822, MK-1084, MK-1086, MK-1087, L-15293, D3S-001, RMC-6291 (Revolution), HBI-2438, FMC-376 (Frontier), BBO-8520 (BridgeBio), ZG19018 (Suzhou Zelgen), UCT-001024 (1200 Pharma), TEB-17231 (280Bio unit of Yingli Pharma), HYP-2A (Sichuan Huiyu), ABSK071 (Abbisko), IBI351 (GFH925; Innovent/Genfleet), ARS-853, ARS-1620, or JNJ-74699157 (ARS-3248); optionally wherein the KRAS G12C inhibitor is adagrasib or sotorasib;

ii) optionally wherein the pan-KRAS inhibitor is BI-2852, BI-pan-KRAS1-4 (BI1701963), RSC-1255, RMC-6236, RSC-1255, QTX3034 (Quanta), JAB-23425 (Beijing Jacobio), BI-2493, LY4066434, or VRTX-153 (VRise), optionally wherein the KRAS inhibitor is RMC-6236, or optionally wherein the KRAS inhibitor is RSC-1255; or

iii) optionally wherein the KRAS inhibitor is a pan-RAS inhibitor, optionally wherein the pan-RAS inhibitor is a RAS(ON) inhibitor, optionally wherein the pan-RAS inhibitor is a KRAS G12C RAS(ON) inhibitor or a KRAS G12C RAS(OFF) inhibitor, optionally

wherein the KRAS inhibitor is RMC-6236, or optionally wherein the KRAS inhibitor is RSC-1255.

12. The use of any one of claims 1-11, wherein the cancer is non-small cell lung cancer or colorectal cancer.

13. The use of claim 9, wherein the *KRAS* mutation is a *KRAS* G12D mutation and the KRAS inhibitor is a KRAS G12D inhibitor or a pan-KRAS inhibitor or a pan-RAS inhibitor;

i) optionally wherein the KRAS G12D inhibitor is MRTX1133 (Mirati), TH-Z827, TH-Z835, KD-8, BI-KRAS12D1-3, BI-KRASG12D3, RMC-9805 (Revolution), ASP3082, ASP4396, LY3962673, INCB161734, HRS-4642, or QTX3046 (Quanta); optionally wherein the KRAS G12D inhibitor is MRTX1133;

ii) optionally wherein the pan-KRAS inhibitor is BI-2852, BI-pan-KRAS1-4 (BI1701963), RSC-1255, RMC-6236, RSC-1255, QTX3034 (Quanta), JAB-23425 (Beijing Jacobio), BI-2493, LY4066434, or VRTX-153 (VRise), optionally wherein the KRAS inhibitor is RMC-6236, or optionally wherein the KRAS inhibitor is RSC-1255; or

iii) optionally wherein the KRAS inhibitor is a pan-RAS inhibitor, optionally wherein the pan-RAS inhibitor is a RAS(ON) inhibitor, optionally wherein the KRAS inhibitor is RMC-6236, or optionally wherein the KRAS inhibitor is RSC-1255.

14. The use of any one of claims 1-10 or claim 13, wherein the cancer is pancreatic ductal adenocarcinoma, non-small cell lung cancer, colorectal cancer, or gastric cancer.

15. The use of claim 9, wherein the *KRAS* mutation comprises at least two *KRAS* mutations selected from *KRAS* G12C, G12D, G12V, G12R, and G13D mutations, and the KRAS inhibitor is a pan-KRAS inhibitor; optionally wherein the pan-KRAS inhibitor is BI-2852, BI-pan-KRAS1-4 (BI1701963), RSC-1255, RMC-6236, RSC-1255, QTX3034 (Quanta), JAB-23425 (Beijing Jacobio), BI-2493, LY4066434, or VRTX-153 (VRise), or wherein the pan-KRAS

inhibitor is a pan-RAS inhibitor, optionally wherein the KRAS inhibitor is RMC-6236, or optionally wherein the KRAS inhibitor is RSC-1255.

16. The use of claim 15, wherein the cancer comprises a *KRAS* G12C mutation or a *KRAS* G12D mutation.

17. The use of claim 8, wherein the cancer comprises a *KRAS* amplification.

18. The use of any one of claims 1-17, wherein the use is in combination with an additional anticancer agent, optionally selected from an immunotherapy agent, an anti-EGFR monoclonal antibody, an inhibitor of the EGFR signaling pathway, cetuximab, panitumumab, chemotherapy, a platinum-based anticancer agent (e.g., cisplatin or carboplatin), leucovorin, fluorouracil, a topoisomerase inhibitor (e.g., irinotecan or topotecan), a taxane (e.g., paclitaxel, docetaxel, or nab-paclitaxel), gemcitabine, etoposide, pemetrexed, vinorelbine, a VEGF inhibitor (e.g., bevacizumab or ramucirumab), an EGFR inhibitor (e.g., osimertinib, afatinib, erlotinib, dacomitinib, gefitinib, or amivantamab), an ALK inhibitor (e.g., alectinib, brigatinib, lorlatinib, ceritinib, or crizotinib), a ROS1 inhibitor, and a BRAF inhibitor (e.g., dabrafenib, trametinib, or vemurafenib), and combinations thereof, each optionally in combination with radiation.

19. The use of any one of claims 1-18, wherein the Compound (I), or the pharmaceutically acceptable form thereof, is to be administered orally; optionally .wherein the Compound (I), or the pharmaceutically acceptable form thereof, is to be administered at a dose of 0.1-2400 mg per day (free base equivalent), optionally wherein the Compound (I), or the pharmaceutically acceptable form thereof, is to be administered at a dose selected from 0.1-2.5 mg, 0.5-5 mg, 0.5-10 mg, 0.5-25 mg, 0.5-50 mg, 0.5-75 mg, 0.5-100 mg, 0.5-300 mg, 0.5-600 mg, 0.5-1200 mg, 1-5 mg, 1-10 mg, 1-25 mg, 1-50 mg, 1-75 mg, 1-100 mg, 1-300 mg, 1-600 mg, 1-1200 mg, 1-2400 mg, 20-100 mg, 40-75 mg, 50-75 mg, 50-100 mg, 50-150 mg, 75-100 mg, 100-200 mg, 125-200 mg, 150-300 mg, 200-250 mg, 200-400 mg, 300-600 mg, 250-500 mg, 400-600 mg, 500-750

mg, 600-900 mg, 700-100 mg, 650-1000 mg, 800-1200 mg, 900-1500 mg, 1000-1600 mg, 1000-2000 mg, 1200-1600 mg, 1500-2000 mg, 1500-2400 mg, 1800-2400 mg and 2000-2400 mg per day (free base equivalent), or at a dose selected from about 0.5 mg, about 1.5 mg, about 1.6 mg, about 1.7 mg, about 1.8 mg, about 1.9 mg, about 1 mg, about 2 mg, about 2.5 mg, about 3 mg, about 4 mg, about 5 mg, about 6 mg, about 7 mg, about 8 mg, about 9 mg, about 10 mg, about 15 mg, about 20 mg, about 25 mg, about 30 mg, about 35 mg, about 40 mg, about 45 mg, about 50 mg, about 55 mg, about 60 mg, about 65 mg, about 70 mg, about 75 mg, about 80 mg, about 85 mg, about 90 mg, about 95 mg about 100 mg, about 125 mg, about 150 mg, about 175 mg, about 200 mg, about 225 mg, about 250 mg, about 275 mg, about 300 mg, about 325 mg, about 350 mg, about 375 mg, about 400 mg, about 425 mg, about 450 mg, about 475 mg, about 500 mg, about 525 mg, about 550 mg, about 575 mg, about 600 mg, about 650 mg, about 700 mg, about 750 mg, about 800 mg, about 850 mg, about 900 mg, about 950 mg, about 1000 mg, about 1050 mg, about 1100 mg, about 1150 mg, about 1200 mg, about 1250 mg, about 1300 mg, about 1350 mg, about 1400 mg, about 1450 mg, about 1500 mg, about 1550 mg, about 1600 mg, about 1650 mg, about 1700 mg, about 1750 mg, about 1800 mg, about 1850 mg, about 1900 mg, about 1950 mg, about 2000 mg, about 2050 mg, about 2100 mg, about 2150 mg, about 2200 mg, about 2250 mg, about 2300 mg, about 2350 mg, and about 2400 mg per day (free base equivalent); and/or optionally wherein the Compound (I), or the pharmaceutically acceptable form thereof, is to be administered across 1, 2, 3, or 4 doses per day, or is administered once per day, or is to be administered twice per day.

20. The use of any one of claims 1-19, wherein the Compound (I), or the pharmaceutically acceptable form thereof, is to be administered on an interval dosing schedule, optionally wherein the interval dosing schedule is a one week on and one week off dosing schedule, and, where the KRAS inhibitor is to be administered, the KRAS inhibitor is to be administered once per day.

21. A pharmaceutical composition comprising (a) Compound (I) or a pharmaceutically acceptable form thereof, (b) a KRAS inhibitor, and (c) a pharmaceutically acceptable excipient.

22. A pharmaceutical kit or packaging comprising: (i) (a) a pharmaceutical composition comprising Compound (I) or a pharmaceutically acceptable form thereof, and a pharmaceutically acceptable excipient, and (b) a pharmaceutical composition comprising a KRAS inhibitor and a pharmaceutically acceptable excipient, or (ii) the pharmaceutical composition of claim 21.