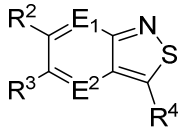
[0002n] In one aspect, the present disclosure provides a process for preparing a compound of the disclosure, comprising providing a compound according to the disclosure and converting it into a compound of the disclosure.

[0003] Provided herein are compound having a structure of formula (I)



(I)

wherein

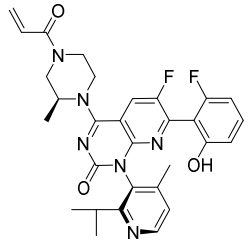
E^1 and E^2 are each independently N or CR^1;

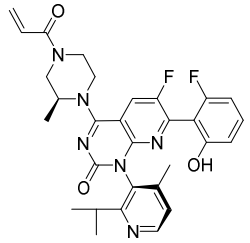
R^1 is independently H, hydroxy, $C_{1–6}$alkyl, $C_{1–6}$haloalkyl, $C_{1\text{-}6}$alkoxy, NH-$C_{1\text{-}6}$alkyl, N($C_{1\text{-}6}$alkyl)$_2$, cyano, or halo;

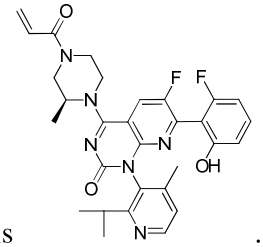
R^2 is halo, $C_{1–6}$alkyl, $C_{1–6}$haloalkyl, OR', N(R')$_2$, $C_{2–3}$alkenyl, $C_{2–3}$alkynyl, $C_{0–3}$ alkylene-$C_{3–14}$cycloalkyl, $C_{0–3}$alkylene-$C_{2–14}$heterocycloalkyl, aryl, heteroaryl, $C_{0–3}$ alkylenearyl, or $C_{0–3}$ alkyleneheteroaryl, and each R' is independently H, $C_{1\text{-}6}$ alkyl, $C_{1\text{-}6}$haloalkyl, $C_{3\text{-}14}$cycloalkyl, $C_{2–14}$heterocycloalkyl, $C_{2\text{-}3}$alkenyl, $C_{2\text{-}3}$alkynyl, aryl, or heteroaryl, or two R' substituents, together with the nitrogen atom to which they are attached, form a 3-7-membered ring;

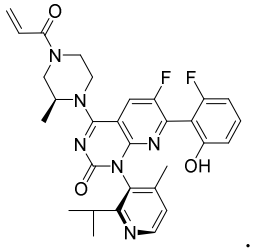
CLAIMS

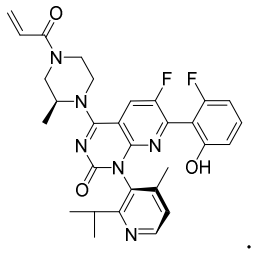
What is claimed is:

1. A compound, wherein the compound is  or a pharmaceutically acceptable salt thereof.

2. A compound, wherein the compound is  or a pharmaceutically acceptable salt thereof.

3. A compound wherein the compound is .

4. A compound, wherein the compound is .

5. A compound, wherein the compound is .

6. Atropisomer 1 of the compound of claim 3, corresponding to the 1st-eluting isomer obtainable by separating the atropoisomers with supercritical fluid chromatography applying Chiralpak IC, 30x250 mm, 5 µm, 55%MeOH/CO_2, 120 g/min, 10.3 MPa (103 bar).

7. Atropisomer 2 of the compound of claim 3, corresponding to the 2nd-eluting isomer obtainable by separating the atropoisomers with supercritical fluid chromatography applying Chiralpak IC, 30x250 mm, 5 µm, 55%MeOH/CO_2, 120 g/min, 10.3 MPa (103 bar).

8. A pharmaceutical composition comprising the compound according to any one of claims 1-5 and a pharmaceutically acceptable excipient.

9. An *in vitro* method of inhibiting KRAS G12C in a cell, comprising contacting the cell with the compound of any one of claims 1-5 or the composition of claim 8.

10. Use of the compound of any one of Claims 1-5 in the manufacture of a medicament for treating cancer in a subject.

11. The use of claim 10, wherein the cancer is non-small cell lung cancer, small intestine cancer, appendix cancer, colorectal cancer, endometrial cancer, pancreatic cancer, liver cancer, small cell lung cancer, cervical cancer, a germ cell tumor, ovarian cancer, a pancreatic neuroendocrine tumor, bladder cancer, myelodysplastic or myeloproliferative neoplasms, head and neck cancer, esophageal cancer, soft tissue sarcoma, malignant mesothelioma, thyroid cancer, leukemia, skin cancer, gastric cancer, nasal cavity cancer, or bile duct cancer.

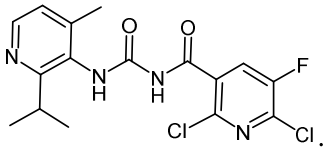
12. The use of claim 10, wherein the cancer is non-small cell lung cancer, small intestine cancer, appendix cancer, colorectal cancer, endometrial cancer, pancreatic cancer, skin cancer, gastric cancer, nasal cavity cancer, or bile duct cancer.

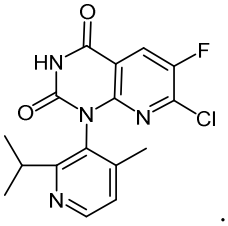
13. The use of claim 12, wherein cancer is non-small cell lung cancer.

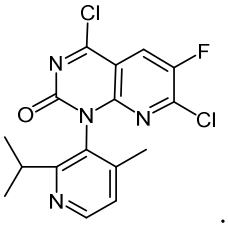
14. The use of claim 12, wherein the cancer is colorectal cancer.

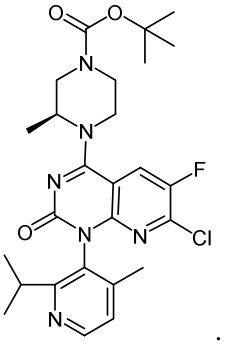
15. The use of claim 12, wherein the cancer is pancreatic cancer.

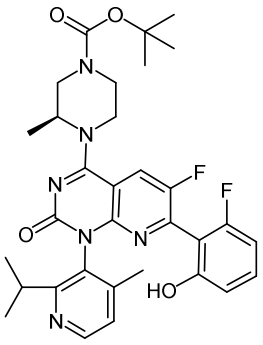
16. The use of any one of claims 12-15, wherein the cancer is mediated by a KRAS G12C mutation.

17. A compound, wherein the compound is .

18. A compound, wherein the compound is .

19. A compound, wherein the compound is .

20. A compound, wherein the compound is .

21. A compound, wherein the compound is .

22. A process for preparing a compound of any one of claims 1-5, comprising providing a compound according to any one claims 17-21 and converting it into a compound of any one of claims 1-5.