SUMMARY

Provided herein is a method of treating cancer in a subject in need thereof comprising administering to the subject a KRAS G12D inhibitor, or a pharmaceutically acceptable salt thereof, and a PD-1 inhibitor or a PD-L1 inhibitor, or pharmaceutically acceptable salt thereof. Targeting KRAS G12D mutant tumors with a selective and reversible inhibitor in combination with PD-1/PD-L1 disrupting agents may be a promising cancer treatment for patients with KRAS G12D mutations.

In one aspect, provided herein is use of a KRAS G12D inhibitor, or a pharmaceutically acceptable salt thereof, and a PD-1 inhibitor or a PD-L1 inhibitor, or pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating cancer.

In another aspect, provided herein is use of:

a pharmaceutical composition comprising a KRAS G12D inhibitor, or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier or excipient; and

a pharmaceutical composition comprising a PD-1 inhibitor or a PD-L1 inhibitor, or pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier or excipient,

in the manufacture of a medicament for treating cancer.

In another aspect, provided herein is use of a KRAS G12D inhibitor that is 3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile, or a pharmaceutically acceptable salt thereof, and a PD-1 inhibitor that is retifanlimab, in the manufacture of a medicament for treating cancer.

In another aspect, provided herein is a pharmaceutical composition comprising

a) a KRAS G12D inhibitor, or a pharmaceutically acceptable salt thereof;

b) a PD-1 inhibitor or a PD-L1 inhibitor, or a pharmaceutically acceptable salt thereof; and

c) at least one pharmaceutically acceptable carrier or excipient.

In another aspect, provided herein is a pharmaceutical combination comprising a KRAS G12D inhibitor, or a pharmaceutically acceptable salt thereof, and a PD-1 inhibitor or a PD-L1 inhibitor, or pharmaceutically acceptable salt thereof.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 shows antitumor activity of Compound 1 ± retifanlimab in the CT-26 Clone 299 Model.

Figure 2 shows tumor growth delay following cessation of treatment with Compound 1 ± retifanlimab in the CT-26 Clone 299 model.

Figure 3 shows body weight changes of CT-26 Clone 299 tumor-bearing mice administered Compound 1 ± retifanlimab.

Figure 4 shows inhibition of pERK in CT-26 clone 299 tumors by Compound 1 ± retifanlimab after 5 days of treatment.

Figure 5 shows antitumor activity of Compound 1 ± Compound 2 in the CT-26 Clone 299 model.

Figure 6 shows tumor growth delay following cessation of treatment with Compound 1 ± Compound 2 in the CT-26 Clone 299 model.

Figure 7 shows body weight changes of CT-26 Clone 299 tumor-bearing mice administered Compound 1 ± Compound 2.

Figure 8 shows inhibition of pERK in CT-26 Clone 299 tumors by Compound 1 ± Compound 2 after 5 days of treatment.

Figure 9 shows antitumor activity of Compound 1 ± anti-mouse-PD-1 antibody RMP1-14 in the KPCY-013 (2838c3) Model.

Figure 10 shows antitumor activity of Compound 1 ± anti-mouse-PD-L1 antibody 10F.9G2 in the KPCY-013 (2838c3) Model.

Figure 11 shows antitumor activity of Compound 3 ± retifanlimab in the CT-26 Clone 299 Model.

Figure 12 shows antitumor activity of Compound 3 ± Compound 2 in the CT-26 Clone 299 Model.

DETAILED DESCRIPTION

Ras proteins are part of the family of small GTPases that are activated by growth factors and various extracellular stimuli. The Ras family regulates intracellular signaling pathways responsible for growth, migration, survival and differentiation of cells. Activation of

CLAIMS

What is claimed is:

1. Use of a KRAS G12D inhibitor, or a pharmaceutically acceptable salt thereof, and a PD-1 inhibitor or a PD-L1 inhibitor, or pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating cancer.

2. The use of claim 1, wherein the PD-1 inhibitor is a PD-1 immune checkpoint inhibitor.

3. The use of claim 1 or 2, wherein the PD-1 inhibitor is an anti-PD-1 antibody.

4. The use of any one of claims 1 to 3, wherein the PD-1 inhibitor is selected from retifanlimab, nivolumab, pembrolizumab, cemiplimab, and dostarlimab.

5. The use of any one of claims 1 to 4, wherein the PD-1 inhibitor is retifanlimab.

6. The use of claim 1, wherein the PD-1 inhibitor is a small molecule inhibitor.

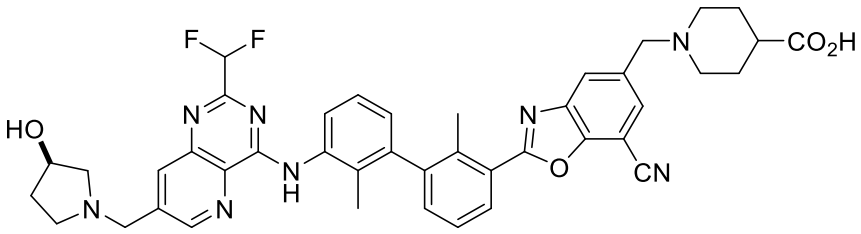
7. The use of claim 1, wherein the KRAS G12D inhibitor, or a pharmaceutically acceptable salt thereof, is to be administered in combination with a PD-L1 inhibitor, or pharmaceutically acceptable salt thereof.

8. The use of claim 1 or 7, wherein the PD-L1 inhibitor is an anti-PD-L1 antibody.

9. The use of claim 8, wherein the PD-L1 inhibitor is selected from atezolizumab, avelumab, and durvalumab.

10. The use of claim 1 or 7, wherein the PD-L1 inhibitor is a small molecule inhibitor.

11. The use of claim 7 or 10, wherein the PD-L1 inhibitor is a compound of the following formula

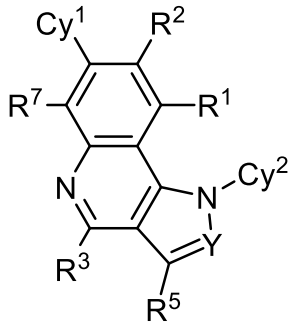


or a pharmaceutically acceptable salt thereof.

12. The use of any one of claims 1 to 11, wherein the KRAS G12D inhibitor has an IC_{50} of about 100 nM or lower.

13. The use of any one of claims 1 to 12, wherein the KRAS G12D inhibitor is selective for inhibiting G12D versus wild-type KRAS.

14. The use of any one of claims 1 to 13, wherein the KRAS G12D inhibitor is a compound of Formula I:



I

or a pharmaceutically acceptable salt thereof, wherein:

Y is N or CR^6;

R^1 is selected from H, C_{1-3} alkyl, C_{1-3} haloalkyl, cyclopropyl, halo, D, CN, and OR^{a1}; wherein said C_{1-3} alkyl and cyclopropyl are each optionally substituted with 1 or 2 substituents independently selected from R^g;

R^2 is selected from H, C_{1-3} alkyl, C_{1-3} haloalkyl, 4-6 membered heterocycloalkyl, phenyl, 5-6 membered heteroaryl, 4-6 membered heterocycloalkyl-C_{1-3} alkylene, phenyl-C_{1-3} alkylene, 5-6 membered heteroaryl-C_{1-3} alkylene, halo, D, CN, and OR^{a2}; wherein said C_{1-3} alkyl, 4-6 membered heterocycloalkyl, phenyl, 5-6 membered heteroaryl, 4-6 membered heterocycloalkyl-C_{1-3} alkylene, phenyl-C_{1-3} alkylene, 5-6 membered heteroaryl-C_{1-3} alkylene are each optionally substituted with 1 or 2 substituents independently selected from R^g;

Cy^1 is selected from C_{3-10} cycloalkyl, 4-10 membered heterocycloalkyl, C_{6-10} aryl and 6-10 membered heteroaryl; wherein the 4-10 membered heterocycloalkyl and 6-10 membered heteroaryl each has at least one ring-forming carbon atom and 1, 2, 3, or 4 ring-forming heteroatoms independently selected from N, O, and S; wherein a ring-forming carbon atom of 6-10 membered heteroaryl and 4-10 membered heterocycloalkyl is optionally substituted by oxo to form a carbonyl group; and wherein the C_{3-10} cycloalkyl, 4-10 membered heterocycloalkyl, C_{6-10} aryl and 6-10 membered heteroaryl are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from R^{10};

R^3 is selected from H, C_{1-3} alkyl, C_{1-3} haloalkyl, C_{3-6} cycloalkyl, 4-6 membered heterocycloalkyl, phenyl, 5-6 membered heteroaryl, C_{3-6} cycloalkyl-C_{1-3} alkylene, 4-6 membered heterocycloalkyl-C_{1-3} alkylene, phenyl-C_{1-3} alkylene, 5-6 membered heteroaryl-C_{1-3} alkylene, halo, D, CN, OR^{f3}, $C(O)NR^{c3}R^{d3}$, $NR^{c3}R^{j3}$, and $NR^{c3}C(O)R^{b3}$; wherein said C_{1-3} alkyl, C_{3-6} cycloalkyl, 4-6 membered heterocycloalkyl, phenyl, 5-6 membered heteroaryl, C_{3-6}

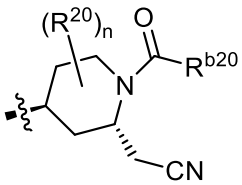
cycloalkyl-C_{1-3} alkylene, 4-6 membered heterocycloalkyl-C_{1-3} alkylene, phenyl-C_{1-3} alkylene, and 5-6 membered heteroaryl-C_{1-3} alkylene are each optionally substituted with 1, 2, or 3 substituents independently selected from R^{30};

R^5 is selected from H, C_{1-3} alkyl, C_{1-3} haloalkyl, cyclopropyl, halo, D, CN, and OR^{a5}; wherein said C_{1-3} alkyl and cyclopropyl are each optionally substituted with 1 or 2 substituents independently selected from R^g;

R^6 is selected from H, C_{1-3} alkyl, C_{1-3} haloalkyl, C_{3-6} cycloalkyl, 4-9 membered heterocycloalkyl, phenyl, 5-6 membered heteroaryl, C_{3-6} cycloalkyl-C_{1-3} alkylene, 4-6 membered heterocycloalkyl-C_{1-3} alkylene, phenyl-C_{1-3} alkylene, 5-6 membered heteroaryl-C_{1-3} alkylene, halo, D, CN, OR^{a6}, and $C(O)NR^{c6}R^{d6}$; wherein said C_{1-3} alkyl, C_{3-6} cycloalkyl, 4-9 membered heterocycloalkyl, phenyl, 5-6 membered heteroaryl, C_{3-6} cycloalkyl-C_{1-3} alkylene, 4-6 membered heterocycloalkyl-C_{1-3} alkylene, phenyl-C_{1-3} alkylene, and 5-6 membered heteroaryl-C_{1-3} alkylene are each optionally substituted with 1 or 2 substituents independently selected from R^{60};

R^7 is selected from H, C_{1-3} alkyl, C_{1-3} haloalkyl, cyclopropyl, halo, D, CN, and OR^{a7}; wherein said C_{1-3} alkyl and cyclopropyl are each optionally substituted with 1 or 2 substituents independently selected from R^g;

Cy^2 is selected from



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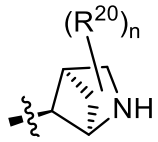
and



;

Cy^2-a Cy^2-b

wherein n is 0, 1, or 2;

each R^{10} is independently selected from C_{1-3} alkyl, C_{1-3} haloalkyl, halo, D, CN, OR^{a10}, $C(O)R^{b10}$, $C(O)NR^{c10}R^{d10}$, $C(O)OR^{a10}$, $NR^{c10}R^{d10}$, and $S(O)_2R^{b10}$;

each R^{20} is independently selected from C_{1-3} alkyl, C_{1-3} haloalkyl, halo, D, CN, and OR^{a20};

each R^{30} is independently selected from C_{1-3} alkyl, C_{1-3} haloalkyl, C_{3-6} cycloalkyl, 4-6 membered heterocycloalkyl, phenyl, 5-6 membered heteroaryl, halo, D, CN, OR^{a30}, $C(O)R^{b30}$, $C(O)NR^{c30}R^{d30}$, $C(O)OR^{a30}$, $NR^{c30}R^{d30}$, and $S(O)_2R^{b30}$; wherein said C_{1-3} alkyl, C_{3-6} cycloalkyl, 4-6 membered heterocycloalkyl, phenyl, and 5-6 membered heteroaryl are each optionally substituted with 1 or 2 substituents independently selected from R^{31};

each R^{31} is independently selected from C_{1-3} alkyl, C_{1-3} haloalkyl, halo, D, CN, OR^{a31}, $C(O)R^{b31}$, $C(O)NR^{c31}R^{d31}$, $C(O)OR^{a31}$, $NR^{c31}R^{d31}$, and $S(O)_2R^{b31}$;

each R^{33} is independently selected from C_{1-3} alkyl, C_{1-3} haloalkyl, C_{3-6} cycloalkyl, 4-membered heterocycloalkyl, 6-membered heterocycloalkyl, phenyl, 5-6 membered heteroaryl, halo, D, CN, OR^{a30}, $C(O)NR^{c30}R^{d30}$, and $NR^{c30}R^{d30}$; wherein said C_{1-3} alkyl, C_{3-6} cycloalkyl, 4-membered heterocycloalkyl, 6-membered heterocycloalkyl, phenyl, and 5-6 membered heteroaryl are each optionally substituted with 1 or 2 substituents independently selected from R^{31};

each R^{60} is independently selected from C_{1-3} alkyl, C_{1-3} haloalkyl, 4-6 membered heterocycloalkyl, 5-6 membered heteroaryl, halo, D, CN, OR^{a60}, $C(O)R^{b60}$, $C(O)NR^{c60}R^{d60}$, $NR^{c60}C(O)R^{b60}$, $C(O)OR^{a60}$, $NR^{c60}C(O)OR^{a60}$, $NR^{c60}R^{d60}$, $NR^{c60}S(O)_2R^{b60}$, and $S(O)_2R^{b60}$; wherein said C_{1-3} alkyl, 4-6 membered heterocycloalkyl, and 5-6 membered heteroaryl are each optionally substituted with 1 or 2 substituents independently selected from R^{61};

each R^{61} is independently selected from C_{1-3} alkyl, C_{1-3} haloalkyl, halo, D, CN, OR^{a61}, and $NR^{c61}R^{d61}$;

R^{a1} is selected from H, C_{1-3} alkyl, and C_{1-3} haloalkyl;

each R^{a2} is independently selected from H, C_{1-3} alkyl, and C_{1-3} haloalkyl;

each R^{b3}, R^{c3} and R^{d3} is independently selected from H, C_{1-3} alkyl, C_{1-3} haloalkyl, C_{3-6} cycloalkyl, 4-6 membered heterocycloalkyl, phenyl and 5-6 membered heteroaryl; wherein said C_{1-3} alkyl, C_{3-6} cycloalkyl, 4-6 membered heterocycloalkyl, phenyl, and 5-6 membered heteroaryl are each optionally substituted with 1, 2, or 3 substituents independently selected from R^{30};

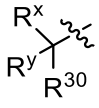
or R^{c3} and R^{d3} attached to the same N atom, together with the N atom to which they are attached, form a 4-, 5-, or 6-membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents independently selected from R^{30};

R^{j3} is selected from C_{1-3} alkyl, C_{1-3} haloalkyl, C_{3-6} cycloalkyl, 4-6 membered heterocycloalkyl, phenyl, and 5-6 membered heteroaryl; wherein said C_{1-3} alkyl, C_{3-6} cycloalkyl, 4-6 membered heterocycloalkyl, phenyl, and 5-6 membered heteroaryl are each optionally substituted with 1, 2, or 3 substituents independently selected from R^{30};

or R^{c3} and R^{j3} attached to the same N atom, together with the N atom to which they are attached, form a 4-, 5-, or 6-membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents independently selected from R^{30};

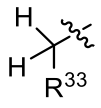
R^{f3} is selected from C_{1-3} haloalkyl, C_{3-6} cycloalkyl, 4-6 membered heterocycloalkyl, phenyl and 5-6 membered heteroaryl; wherein said C_{1-3} haloalkyl, C_{3-6} cycloalkyl, 4-6 membered heterocycloalkyl, phenyl, and 5-6 membered heteroaryl are each optionally substituted with 1, 2, or 3 substituents independently selected from R^{30}; or

R^{f3} is selected from



R^{f3}-a

and



R^{f3}-b

wherein R^x is H or C_{1-2} alkyl and R^y is C_{1-2} alkyl;

or R^x and R^y, together with the C atom to which they are attached, form a 3-, or 4-membered cycloalkyl group;

R^{a5} is selected from H, C_{1-3} alkyl, and C_{1-3} haloalkyl;

each R^{a6}, R^{c6} and R^{d6} is independently selected from H, C_{1-3} alkyl, C_{1-3} haloalkyl, C_{3-6} cycloalkyl, 4-6 membered heterocycloalkyl, phenyl and 5-6 membered heteroaryl; wherein said C_{1-3} alkyl, C_{3-6} cycloalkyl, 4-6 membered heterocycloalkyl, phenyl and 5-6 membered heteroaryl are each optionally substituted with 1 or 2 substituents independently selected from R^{60};

R^{a7} is selected from H, C_{1-3} alkyl, and C_{1-3} haloalkyl;

each R^{a10}, R^{b10}, R^{c10} and R^{d10} is independently selected from H, C_{1-3} alkyl, and C_{1-3} haloalkyl;

each R^{a20} is independently selected from H, C_{1-3} alkyl, and C_{1-3} haloalkyl;

R^{b20} is selected from NH_2, C_{1-3} alkyl, and C_{1-3} haloalkyl;

each R^{a30}, R^{b30}, R^{c30} and R^{d30} is independently selected from H, C_{1-3} alkyl, and C_{1-3} haloalkyl;

each R^{a31}, R^{b31}, R^{c31} and R^{d31} is independently selected from H, C_{1-3} alkyl, and C_{1-3} haloalkyl;

each R^{a60}, R^{b60}, R^{c60} and R^{d60} is independently selected from H, C_{1-3} alkyl, C_{1-3} haloalkyl, C_{3-6} cycloalkyl, 4-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; wherein said C_{1-3} alkyl, C_{3-6} cycloalkyl, 4-6 membered heterocycloalkyl, and 5-6 membered heteroaryl are each optionally substituted with 1 or 2 substituents independently selected from R^{61};

or any R^{c60} and R^{d60} attached to the same N atom, together with the N atom to which they are attached, form a 4-, 5-, or 6-membered heterocycloalkyl group optionally substituted with 1 or 2 substituents independently selected from R^{61};

each R^{a61}, R^{c61}, and R^{d61}, is independently selected from H, C_{1-3} alkyl, and C_{1-3} haloalkyl; and

each R^g is independently selected from D, OH, CN, halo, C_{1-3} alkyl, C_{1-3} haloalkyl, C_{1-3} alkoxy, C_{1-3} haloalkoxy, amino, C_{1-3} alkylamino, and di(C_{1-3} alkyl)amino.

15. The use of claim 14, wherein

Y is CR^6;

R^1 is selected from H, C_{1-3} alkyl, and C_{1-3} haloalkyl;

R^2 is selected from H, C_{1-3} alkyl, C_{1-3} haloalkyl, halo, D, CN, and OR^{a2}; wherein said C_{1-3} alkyl is optionally substituted with 1 or 2 substituents independently selected from R^g;

Cy^1 is selected from C_{3-10} cycloalkyl, 4-10 membered heterocycloalkyl, C_{6-10} aryl and 6-10 membered heteroaryl; wherein the 4-10 membered heterocycloalkyl and 6-10 membered heteroaryl each has at least one ring-forming carbon atom and 1, 2, 3, or 4 ring-forming heteroatoms independently selected from N, O, and S; wherein a ring-forming carbon atom of 6-10 membered heteroaryl and 4-10 membered heterocycloalkyl is optionally substituted by oxo to form a carbonyl group; and wherein the C_{3-10} cycloalkyl, 4-10 membered heterocycloalkyl, C_{6-10} aryl and 6-10 membered heteroaryl are each optionally substituted with 1, 2, 3, or 4 substituents independently selected from R^{10};

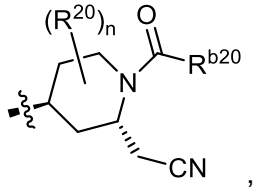
R^3 is selected from H, C_{1-3} alkyl, C_{1-3} haloalkyl, C_{3-6} cycloalkyl, 4-6 membered heterocycloalkyl, phenyl, 5-6 membered heteroaryl, halo, D, CN, $C(O)NR^{c3}R^{d3}$, and $NR^{c3}C(O)R^{b3}$; wherein said C_{1-3} alkyl, C_{3-6} cycloalkyl, 4-6 membered heterocycloalkyl, phenyl, and 5-6 membered heteroaryl are each optionally substituted with 1, 2, or 3 substituents independently selected from R^{30};

R^5 is selected from H, C_{1-3} alkyl, C_{1-3} haloalkyl, and halo;

R^6 is selected from H, C_{1-3} haloalkyl, C_{3-6} cycloalkyl, 4-8 membered heterocycloalkyl, phenyl, 5-6 membered heteroaryl, halo, D, CN, OR^{a6}, and $C(O)NR^{c6}R^{d6}$; wherein said C_{3-6} cycloalkyl, 4-8 membered heterocycloalkyl, phenyl, and 5-6 membered heteroaryl are each optionally substituted with 1 or 2 substituents independently selected from R^{60};

R^7 is selected from H, C_{1-3} alkyl, C_{1-3} haloalkyl, halo, and CN;

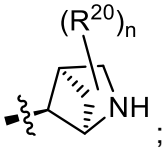
Cy^2 is selected from



,

Cy^2-a

and



;

Cy^2-b

wherein n is 0, 1, or 2;

each R^{10} is independently selected from C_{1-3} alkyl, C_{1-3} haloalkyl, halo, D, CN, OR^{a10}, $C(O)R^{b10}$, $C(O)NR^{c10}R^{d10}$, $C(O)OR^{a10}$, $NR^{c10}R^{d10}$, and $S(O)_2R^{b10}$;

each R^{20} is independently selected from C_{1-3} alkyl, C_{1-3} haloalkyl, halo, D, CN, and OR^{a20};

each R^{30} is independently selected from C_{1-3} alkyl, C_{1-3} haloalkyl, C_{3-6} cycloalkyl, 4-6 membered heterocycloalkyl, phenyl, 5-6 membered heteroaryl, halo, D, CN, OR^{a30}, $C(O)R^{b30}$, $C(O)NR^{c30}R^{d30}$, $C(O)OR^{a30}$, $NR^{c30}R^{d30}$, and $S(O)_2R^{b30}$; wherein said C_{1-3} alkyl, C_{3-6} cycloalkyl,

4-6 membered heterocycloalkyl, phenyl, and 5-6 membered heteroaryl are each optionally substituted with 1 or 2 substituents independently selected from R^{31};

each R^{31} is independently selected from C_{1-3} alkyl, C_{1-3} haloalkyl, halo, D, CN, OR^{a31}, $C(O)R^{b31}$, $C(O)NR^{c31}R^{d31}$, $C(O)OR^{a31}$, $NR^{c31}R^{d31}$, and $S(O)_2R^{b31}$;

each R^{60} is independently selected from C_{1-3} alkyl, C_{1-3} haloalkyl, C_{1-3} haloalkoxy, 4-6 membered heterocycloalkyl, 5-6 membered heteroaryl, halo, D, CN, OR^{a60}, $C(O)R^{b60}$, $C(O)NR^{c60}R^{d60}$, $NR^{c60}C(O)R^{b60}$, $C(O)OR^{a60}$, $NR^{c60}C(O)OR^{a60}$, $NR^{c60}R^{d60}$, $NR^{c60}S(O)_2R^{b60}$, and $S(O)_2R^{b60}$; wherein said C_{1-3} alkyl, 4-6 membered heterocycloalkyl, and 5-6 membered heteroaryl are each optionally substituted with 1 or 2 substituents independently selected from R^{61};

each R^{61} is independently selected from C_{1-3} alkyl, C_{1-3} haloalkyl, halo, D, CN, OR^{a61}, and $NR^{c61}R^{d61}$;

each R^{a2} is independently selected from H, C_{1-3} alkyl, and C_{1-3} haloalkyl;

each R^{b3}, R^{c3} and R^{d3} is independently selected from H, C_{1-3} alkyl, C_{1-3} haloalkyl, C_{3-6} cycloalkyl, 4-6 membered heterocycloalkyl, phenyl and 5-6 membered heteroaryl; wherein said , C_{1-3} alkyl, C_{3-6} cycloalkyl, 4-6 membered heterocycloalkyl, phenyl and 5-6 membered heteroaryl are each optionally substituted with 1, 2, or 3 substituents independently selected from R^{30};

or R^{c3} and R^{d3} attached to the same N atom, together with the N atom to which they are attached, form a 4-, 5-, or 6-membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents independently selected from R^{30};

each R^{a6}, R^{c6} and R^{d6} is independently selected from H, C_{1-3} alkyl, C_{1-3} haloalkyl, C_{3-6} cycloalkyl, 4-6 membered heterocycloalkyl, phenyl and 5-6 membered heteroaryl; wherein said C_{1-3} alkyl, C_{3-6} cycloalkyl, 4-6 membered heterocycloalkyl, phenyl and 5-6 membered heteroaryl are each optionally substituted with 1 or 2 substituents independently selected from R^{60};

each R^{a10}, R^{b10}, R^{c10} and R^{d10} is independently selected from H, C_{1-3} alkyl, and C_{1-3} haloalkyl;

each R^{a20} is independently selected from H, C_{1-3} alkyl, and C_{1-3} haloalkyl;

R^{b20} is selected from NH_2, C_{1-3} alkyl, and C_{1-3} haloalkyl;

each R^{a30}, R^{b30}, R^{c30} and R^{d30} is independently selected from H, C_{1-3} alkyl, and C_{1-3} haloalkyl;

each R^{a31}, R^{b31}, R^{c31} and R^{d31} is independently selected from H, C_{1-3} alkyl, and C_{1-3} haloalkyl;

each R^{a60}, R^{b60}, R^{c60} and R^{d60} is independently selected from H, C_{1-3} alkyl, C_{1-3} haloalkyl, C_{3-6} cycloalkyl, 4-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; wherein said C_{1-3} alkyl, C_{3-6} cycloalkyl, 4-6 membered heterocycloalkyl, and 5-6 membered

heteroaryl are each optionally substituted with 1 or 2 substituents independently selected from R^{61};

or any R^{c60} and R^{d60} attached to the same N atom, together with the N atom to which they are attached, form a 4-, 5-, or 6-membered heterocycloalkyl group optionally substituted with 1 or 2 substituents independently selected from R^{61}; and

each R^{a61}, R^{c61}, and R^{d61}, is independently selected from H, C_{1-3} alkyl, and C_{1-3} haloalkyl; and

each R^{g} is independently selected from D, CN, halo, C_{1-3} alkyl, and C_{1-3} haloalkyl.

16. The use of claim 14 or 15, wherein

Y is CR^6;

R^1 is H;

R^2 is selected from C_{1-3} alkyl, C_{1-3} haloalkyl, halo, CN, and $-CH_2CH_2CN$;

Cy^1 is selected from C_{3-10} cycloalkyl, C_{6-10} aryl and 6-10 membered heteroaryl; wherein the 6-10 membered heteroaryl has at least one ring-forming carbon atom and 1, ring-forming heteroatoms independently selected from N and S; and wherein the C_{3-10} cycloalkyl, C_{6-10} aryl and 6-10 membered heteroaryl are each optionally substituted with 1 or 2 substituents independently selected from R^{10};

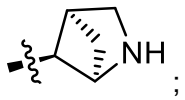
R^3 is selected from H, C_{1-3} alkyl, C_{1-3} haloalkyl, 4-6 membered heterocycloalkyl, phenyl, and 5-6 membered heteroaryl; wherein said C_{1-3} alkyl, 4-6 membered heterocycloalkyl, phenyl, and 5-6 membered heteroaryl are each optionally substituted with 1, 2, or 3 substituents independently selected from R^{30};

R^5 is selected from H and halo;

R^6 is selected from H, C_{1-3} haloalkyl, 4-8 membered heterocycloalkyl, and 5-6 membered heteroaryl; wherein said 4-8 membered heterocycloalkyl and 5-6 membered heteroaryl are each optionally substituted with 1 or 2 substituents independently selected from R^{60}; or

R^7 is halo;

Cy^2 is



;

Cy^2-b

each R^{10} is independently selected from C_{1-3} alkyl, C_{1-3} haloalkyl, halo, D, CN, and OR^{a10};

each R^{30} is independently selected from C_{1-3} alkyl, C_{1-3} haloalkyl, 4-6 membered heterocycloalkyl, halo, D, CN, OR^{a30}, $C(O)NR^{c30}R^{d30}$, and $NR^{c30}R^{d30}$; wherein said C_{1-3} alkyl

and 4-6 membered heterocycloalkyl are each optionally substituted with 1 or 2 substituents independently selected from R^{31};

each R^{31} is independently selected from C_{1-3} alkyl, C_{1-3} haloalkyl, halo, CN, OR^{a31}, and $NR^{c31}R^{d31}$;

each R^{60} is independently selected from C_{1-3} alkyl, C_{1-3} haloalkyl, C_{1-3} haloalkoxy, 4-6 membered heterocycloalkyl, 5-6 membered heteroaryl, halo, D, CN, OR^{a60}, $C(O)R^{b60}$, $C(O)NR^{c60}R^{d60}$, $NR^{c60}C(O)R^{b60}$, $C(O)OR^{a60}$, $NR^{c60}C(O)OR^{a60}$, $NR^{c60}R^{d60}$, $NR^{c60}S(O)_2R^{b60}$, and $S(O)_2R^{b60}$; wherein said C_{1-3} alkyl, 4-6 membered heterocycloalkyl, and 5-6 membered heteroaryl are each optionally substituted with 1 or 2 substituents independently selected from R^{61};

each R^{61} is independently selected from C_{1-3} alkyl, C_{1-3} haloalkyl, halo, and CN;

each R^{a10} is independently selected from H and C_{1-3} alkyl;

each R^{a30}, R^{c30} and R^{d30} is independently selected from H and C_{1-3} alkyl;

each R^{a31}, R^{c31} and R^{d31} is independently selected from H and C_{1-3} alkyl;

each R^{a60}, R^{b60}, R^{c60} and R^{d60} is independently selected from H, C_{1-3} alkyl, C_{1-3} haloalkyl, C_{3-6} cycloalkyl, 4-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; wherein said C_{1-3} alkyl, C_{3-6} cycloalkyl, 4-6 membered heterocycloalkyl, and 5-6 membered heteroaryl are each optionally substituted with 1 or 2 substituents independently selected from R^{61};

or any R^{c60} and R^{d60} attached to the same N atom, together with the N atom to which they are attached, form a 4-, 5-, or 6-membered heterocycloalkyl group optionally substituted with 1 or 2 substituents independently selected from R^{61}.

17. The use of any one of claims 14 to 16, wherein

Y is CR^6;

R^1 is H;

R^2 is $-CH_2CH_2CN$;

Cy^1 is phenyl; wherein the phenyl is optionally substituted with 1 or 2 substituents independently selected from R^{10};

R^3 is selected from H, C_{1-3} alkyl, phenyl, and 5-6 membered heteroaryl; wherein said C_{1-3} alkyl, phenyl, and 5-6 membered heteroaryl are each optionally substituted with 1, 2 or 3 substituents independently selected from R^{30};

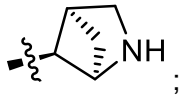
R^5 is selected from H and halo;

R^6 is selected from 4-8 membered heterocycloalkyl; wherein said 4-8 membered heterocycloalkyl is optionally substituted with 1 or 2 substituents independently selected from R^{60}; or

R^6 is selected from C_{1-3} alkyl; wherein said C_{1-3} alkyl is substituted with 1 or 2 substituents independently selected from R^{60};

R^7 is halo;

Cy^2 is



;

Cy^2-b

each R^{10} is independently selected from C_{1-3} alkyl and halo;

each R^{30} is independently selected from C_{1-3} alkyl, halo, D, OH, and $C(O)NR^{c30}R^{d30}$; wherein said C_{1-3} alkyl is optionally substituted with 1 substituent independently selected from R^{31};

each R^{31} is OR^{a31};

each R^{60} is independently selected from C_{1-3} alkyl, C_{1-3} haloalkoxy, 4-6 membered heterocycloalkyl, 5-6 membered heteroaryl, halo, $C(O)R^{b60}$, $C(O)NR^{c60}R^{d60}$, $NR^{c60}C(O)R^{b60}$, $C(O)OR^{a60}$, $NR^{c60}C(O)OR^{a60}$, and $NR^{c60}S(O)_2R^{b60}$; wherein said C_{1-3} alkyl, 4-6 membered heterocycloalkyl, and 5-6 membered heteroaryl are each optionally substituted with 1 or 2 substituents independently selected from R^{61};

each R^{61} is independently selected from C_{1-3} alkyl, and halo;

each R^{c30} and R^{d30} is independently selected from H and C_{1-3} alkyl;

each R^{a31} is independently selected from H and C_{1-3} alkyl; and

each R^{a60}, R^{b60}, R^{c60} and R^{d60} is independently selected from H, C_{1-3} alkyl, C_{1-3} haloalkyl, C_{3-6} cycloalkyl, 4-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; wherein said C_{1-3} alkyl, C_{3-6} cycloalkyl, 4-6 membered heterocycloalkyl, and 5-6 membered heteroaryl are each optionally substituted with 1 or 2 substituents independently selected from R^{61};

or any R^{c60} and R^{d60} attached to the same N atom, together with the N atom to which they are attached, form a 4-, 5-, or 6-membered heterocycloalkyl group optionally substituted with 1 or 2 substituents independently selected from R^{61}.

18. The use of any one of claims 14 to 17, wherein

Y is CR^6;

R^1 is H;

R^2 is $-CH_2CH_2CN$;

Cy^1 is phenyl; wherein the phenyl is optionally substituted with 1 or 2 substituents independently selected from R^{10};

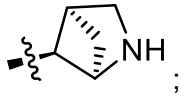
R^3 is selected from H, methyl, ethyl, phenyl, 1,2,4-triazolyl, pyrazyl, and pyridyl; wherein said methyl, phenyl, 1,2,4-triazolyl, pyrazyl, and pyridyl are each optionally substituted with 1, 2 or 3 substituents independently selected from R^{30};

R^5 is selected from H and chloro;

R^6 is selected from pyrrolidinyl, 2-azabicyclo[3.1.0]hexanyl, 2-azabicyclo[2.2.1]heptanyl, and 5-oxo-1,2,3,5-tetrahydroindolizin-3-yl; wherein said pyrrolidinyl, 2-azabicyclo[3.1.0]hexanyl, 2-azabicyclo[2.2.1]heptanyl ,and 5-oxo-1,2,3,5-tetrahydroindolizin-3-yl are optionally substituted with 1 or 2 substituents independently selected from R^{60};

R^7 is fluoro;

Cy^2 is



;

Cy^2-b

each R^{10} is independently selected from methyl, fluoro, and chloro;

each R^{30} is independently selected from methyl, fluoro, OH, D, and $C(O)NR^{c30}R^{d30}$; wherein said methyl is optionally substituted with 1 substituent that is R^{31};

each R^{31} is OR^{a31};

each R^{60} is independently selected from methyl, fluoro, C_{1-2} haloalkoxy, 3-oxomorpholinyl, 2-oxopyrazin-1(2*H*)-yl), $C(O)R^{b60}$, $C(O)NR^{c60}R^{d60}$, $NR^{c60}C(O)R^{b60}$, $C(O)OR^{a60}$, $NR^{c60}C(O)OR^{a60}$, and $NR^{c60}S(O)_2R^{b60}$; wherein said 3-oxomorpholinyl, and 2-oxopyrazin-1(2*H*)-yl) are each optionally substituted with 1 or 2 substituents independently selected from R^{61};

each R^{61} is independently selected from methyl and fluoro;

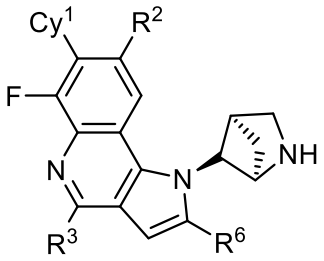
each R^{c30} and R^{d30} is independently selected from H and methyl;

each R^{a31} is independently selected from H and methyl; and

each R^{a60}, R^{b60}, R^{c60} and R^{d60} is independently selected from H, C_{1-2} alkyl, C_1 haloalkyl, cyclopropyl, tetrahydrofuranyl, and thiazolyl; wherein said C_{1-2} alkyl, cyclopropyl, tetrahydrofuranyl, and thiazolyl are each optionally substituted with 1 or 2 substituents independently selected from R^{61};

or any R^{c60} and R^{d60} attached to the same N atom, together with the N atom to which they are attached, form an azetidinyl group optionally substituted with 1 or 2 substituents independently selected from R^{61}.

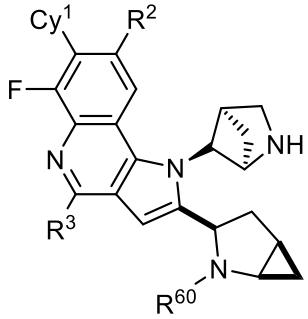
19. The use of any one of claims 14 to 18, wherein the compound of Formula I is a compound of Formula II:



II

or a pharmaceutically acceptable salt thereof.

20. The use of any one of claims 14 to 19, wherein the compound of Formula I is a compound of Formula III:



III

or a pharmaceutically acceptable salt thereof.

21. The use of any one of claims 1 to 20, wherein the KRAS G12D inhibitor is selected from

3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(7-chloro-3-hydroxynaphthalen-1-yl)-6-fluoro-2-methyl-4-(1H-1,2,4-triazol-1-yl)-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(5,7-difluoro-1H-indol-3-yl)-6-fluoro-2-methyl-4-((*S*)-1-((*S*)-1-methylpyrrolidin-2-yl)ethoxy)-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-6-fluoro-7-(6-fluoro-5-methyl-1*H*-indol-3-yl)-2-methyl-4-((*S*)-1-((*S*)-1-methylpyrrolidin-2-yl)ethoxy)-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile;

3-(2-(3-(azetidin-1-yl)-3-oxopropyl)-1-((*1R,4R,5S*)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-((*S*)-1-((*S*)-1-methylpyrrolidin-2-yl)ethoxy)-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile;

3-((1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-6-fluoro-7-(3-hydroxynaphthalen-1-yl)-8-methyl-4-((*S*)-1-((*S*)-1-methylpyrrolidin-2-yl)ethoxy)-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)methyl)oxazolidin-2-one;

8-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-6-fluoro-2,8-dimethyl-4-((*S*)-1-((*S*)-1-methylpyrrolidin-2-yl)ethoxy)-1*H*-pyrrolo[3,2-*c*]quinolin-7-yl)-1-naphthonitrile;

1-((2*S*,4*S*)-1-acetyl-2-(cyanomethyl)piperidin-4-yl)-7-(8-cyanonaphthalen-1-yl)-6-fluoro-4-((*S*)-1-((*S*)-1-methylpyrrolidin-2-yl)ethoxy)-1*H*-pyrazolo[4,3-*c*]quinoline-8-carbonitrile;

8-(1-((*1R*,*4R*,*5S*)-2-azabicyclo[2.1.1]hexan-5-yl)-6-fluoro-8-methyl-4-((*S*)-1-((*S*)-1-methylpyrrolidin-2-yl)ethoxy)-2-((3-oxomorpholino)methyl)-1*H*-pyrrolo[3,2-*c*]quinolin-7-yl)-1-naphthonitrile;

3-(7-(benzo[*b*]thiophen-3-yl)-1-((*1R*,*4R*,*5S*)-2-azabicyclo[2.1.1]hexan-5-yl)-6-fluoro-4-((*S*)-1-((*S*)-1-methylpyrrolidin-2-yl)ethoxy)-2-((2-oxopyrrolidin-1-yl)methyl)-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile;

3-(1-((*1R*,*4R*,*5S*)-2-azabicyclo[2.1.1]hexan-5-yl)-4-(((*S*)-1-(dimethylamino)propan-2-yl)oxy)-6-fluoro-7-(7-fluoronaphthalen-1-yl)-2-((2-oxopyrrolidin-1-yl)methyl)-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile;

8-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-6-fluoro-2-methyl-4-((*S*)-1-((*S*)-1-methylpyrrolidin-2-yl)ethoxy)-1*H*-pyrrolo[3,2-*c*]quinolin-7-yl)-1-naphthonitrile;

3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(2,3-dichloro-5-hydroxyphenyl)-6-fluoro-2-methyl-4-((*S*)-1-((*S*)-1-methylpyrrolidin-2-yl)ethoxy)-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile;

3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-6-fluoro-4-((3-fluoro-1-methylazetidin-3-yl)methoxy)-7-(3-hydroxynaphthalen-1-yl)-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)-*N*,*N*-dimethylpropanamide;

3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-6-fluoro-7-(3-hydroxynaphthalen-1-yl)-2-methyl-4-(5-methylpyrazin-2-yl)-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile;

3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-6-fluoro-7-(7-fluoronaphthalen-1-yl)-4-methyl-2-((4-methyl-2-oxopiperazin-1-yl)methyl)-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile;

3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(2,3-dichloro-5-hydroxyphenyl)-4-ethoxy-6-fluoro-2-((4-isopropyl-2-oxopiperazin-1-yl)methyl)-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile;

3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-4-(3-(dimethylamino)-3-methylazetidin-1-yl)-6-fluoro-7-(7-fluoronaphthalen-1-yl)-2-((3-oxomorpholino)methyl)-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile;

3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-4-ethoxy-6-fluoro-7-(3-hydroxynaphthalen-1-yl)-2-(1-(3-oxomorpholino)ethyl)-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile;

3-(1-((endo)-2-azabicyclo[2.1.1]hexan-5-yl)-6-fluoro-7-(3-hydroxynaphthalen-1-yl)-4-((*S*)-1-((*S*)-1-methylpyrrolidin-2-yl)ethoxy)-2-(pyridin-3-yl)-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile;

3-(2-(3-(azetidin-1-yl)-3-oxopropyl)-1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(7,8-difluoronaphthalen-1-yl)-6-fluoro-4-((S)-1-((S)-1-methylpyrrolidin-2-yl)ethoxy)-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(2-(3-(azetidin-1-yl)-3-oxopropyl)-1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(6,7-difluoronaphthalen-1-yl)-6-fluoro-4-((S)-1-((S)-1-methylpyrrolidin-2-yl)ethoxy)-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-6-fluoro-7-(7-fluoro-3-hydroxynaphthalen-1-yl)-2-methyl-4-((S)-1-((S)-1-methylpyrrolidin-2-yl)ethoxy)-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

1-(1-((2*S*,4*S*)-1-acetyl-2-(cyanomethyl)piperidin-4-yl)-8-chloro-6-fluoro-4-((*S*)-1-((*S*)-1-methylpyrrolidin-2-yl)ethoxy)-1*H*-pyrazolo[4,3-*c*]quinolin-7-yl)isoquinoline-8-carbonitrile;

8-(1-((2*S*,4*S*)-1-acetyl-2-(cyanomethyl)piperidin-4-yl)-8-chloro-6-fluoro-4-((*S*)-1-((*S*)-1-methylpyrrolidin-2-yl)ethoxy)-1*H*-pyrrolo[3,2-*c*]quinolin-7-yl)-1-naphthonitrile;

8-(1-((2*S*,4*S*)-1-acetyl-2-(cyanomethyl)piperidin-4-yl)-8-chloro-6-fluoro-4-((*S*)-1-((*S*)-1-methylpyrrolidin-2-yl)ethoxy)-1*H*-pyrazolo[4,3-*c*]quinolin-7-yl)-1-naphthonitrile;

3-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-6-fluoro-7-(7-fluoro-3-hydroxynaphthalen-1-yl)-2-methyl-4-(1*H*-1,2,4-triazol-1-yl)-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile;

3-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-6-fluoro-7-(7-fluoronaphthalen-1-yl)-2-methyl-4-((S)-1-((S)-1-methylpyrrolidin-2-yl)ethoxy)-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

(2*R*)-2-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-(1*H*-1,2,4-triazol-1-yl)-1*H*-pyrrolo[3,2-c]quinolin-2-yl)-*N*,*N*-dimethylpyrrolidine-1-carboxamide;

methyl (2*R*)-2-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(2-chloro-3-methylphenyl)-8-(2-cyanoethyl)-6-fluoro-4-(1*H*-1,2,4-triazol-1-yl)-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)pyrrolidine-1-carboxylate;

methyl (1S,3R,5S)-3-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-4-(6-(dimethylcarbamoyl)pyridin-3-yl)-6-fluoro-1H-pyrrolo[3,2-c]quinolin-2-yl)-2-azabicyclo[3.1.0]hexane-2-carboxylate;

3-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-2-(5-oxo-1,2,3,5-tetrahydroindolizin-3-yl)-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

methyl (2R)-2-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-4-(6-(dimethylcarbamoyl)pyridin-3-yl)-6-fluoro-1H-pyrrolo[3,2-c]quinolin-2-yl)pyrrolidine-1-carboxylate;

methyl (2R)-2-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-(6-(methylcarbamoyl)pyridin-3-yl)-1H-pyrrolo[3,2-c] quinolin-2-yl)pyrrolidine-1-carboxylate;

3-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(2-chloro-3-fluorophenyl)-2-((R)-1-(cyclopropanecarbonyl)pyrrolidin-2-yl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

8-(2-((R)-1-acetylpyrrolidin-2-yl)-1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-6-fluoro-8-methyl-4-(2-methylpyridin-4-yl)-1H-pyrrolo[3,2-c]quinolin-7-yl)-1,2,3,4-tetrahydronaphthalene-1-carbonitrile;

5-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(3-chloro-2-methylphenyl)-8-(2-cyanoethyl)-6-fluoro-2-((R)-1-(2-oxopyrazin-1(2H)-yl)ethyl)-1H-pyrrolo[3,2-c]quinolin-4-yl)-N-methylpicolinamide;

3-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-6-fluoro-7-(7-fluoronaphthalen-1-yl)-4-(6-(2-hydroxypropan-2-yl)pyridin-3-yl)-2-((R)-1-(2-oxopyrazin-1(2H)-yl)ethyl)-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(3-chloro-2-methylphenyl)-6-fluoro-4-(5-methylpyrazin-2-yl)-2-((R)-1-(2-oxopyrazin-1(2H)-yl)ethyl)-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

methyl (2R)-2-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-(5-fluoro-6-(methylcarbamoyl)pyridin-3-yl)-1H-pyrrolo[3,2-c]quinolin-2-yl)pyrrolidine-1-carboxylate;

methyl (2R)-2-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-(6-(2-hydroxypropan-2-yl)pyridin-3-yl)-1H-pyrrolo[3,2-c]quinolin-2-yl)pyrrolidine-1-carboxylate;

ethyl (2R)-2-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-(6-(2-hydroxypropan-2-yl)pyridin-3-yl)-1H-pyrrolo[3,2-c]quinolin-2-yl)pyrrolidine-1-carboxylate;

3-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(2,3-dichlorophenyl)-2-((R)-1-(3,3-difluoroazetidine-1-carbonyl)pyrrolidin-2-yl)-6-fluoro-4-(methyl-d3)-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(2,3-dichlorophenyl)-2-((R)-1-(3,3-difluoroazetidine-1-carbonyl)pyrrolidin-2-yl)-6-fluoro-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(3-chloro-2-methylphenyl)-6-fluoro-4-(5-methylpyrazin-2-yl)-2-((R)-1-(3-oxomorpholino)ethyl)-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

5-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-6-fluoro-7-(7-fluoronaphthalen-1-yl)-2-((R)-1-(3-oxomorpholino)ethyl)-1H-pyrrolo[3,2-c]quinolin-4-yl)-N-methylpicolinamide;

3-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-6-fluoro-7-(7-fluoronaphthalen-1-yl)-4-(6-(2-hydroxypropan-2-yl)pyridin-3-yl)-2-((R)-1-(3-oxomorpholino)ethyl)-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-6-fluoro-7-(7-fluoronaphthalen-1-yl)-4-(5-methylpyrazin-2-yl)-2-((R)-1-(3-oxomorpholino)ethyl)-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

methyl (1R,3R,5R)-3-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-4-(6-(dimethylcarbamoyl)pyridin-3-yl)-6-fluoro-1H-pyrrolo[3,2-c]quinolin-2-yl)-2-azabicyclo[3.1.0]hexane-2-carboxylate;

3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile;

3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-(6-(2-hydroxypropan-2-yl)pyridin-3-yl)-2-((*R*)-1-(2-oxopyrazin-1(2*H*)-yl)ethyl)-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile;

methyl (2*R*,4*S*)-2-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-(6-(2-hydroxypropan-2-yl)pyridin-3-yl)-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)-4-fluoropyrrolidine-1-carboxylate;

methyl (2*R*,5*R*)-2-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-(6-(2-hydroxypropan-2-yl)pyridin-3-yl)-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)-5-methylpyrrolidine-1-carboxylate;

methyl (2*R*)-2-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-3-chloro-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-(6-(2-hydroxypropan-2-yl)pyridin-3-yl)-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)pyrrolidine-1-carboxylate;

4-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-2-((*R*)-1-(2-oxopyrazin-1(2*H*)-yl)ethyl)-1*H*-pyrrolo[3,2-c]quinolin-4-yl)-2-fluoro-*N*-methylbenzamide;

methyl ((1*R*)-1-(1-((*1R*,*4R*,*5S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)ethyl)carbamate;

N-((1*R*)-1-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)ethyl)-2,2-difluoroacetamide;

N-((1*R*)-1-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)ethyl)-2,2-difluoroacetamide;

(2*S*)-*N*-((1*R*)-1-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)ethyl)tetrahydrofuran-2-carboxamide;

N-((1*R*)-1-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)ethyl)cyclopropanesulfonamide;

N-((1*R*)-1-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)ethyl)thiazole-4-carboxamide;

N-((1*R*)-1-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)ethyl)-*N*-methylcyclopropanecarboxamide;

N-((1*R*)-1-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-(1-hydroxyethyl)-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)ethyl)-1-methylcyclopropane-1-carboxamide;

3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-(1-hydroxyethyl)-2-((1*R*,3*R*,5*R*)-2-(1-methylcyclopropane-1-carbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile;

3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(2,3-dichlorophenyl)-6-fluoro-2-((1*R*,3*R*,5*R*)-2-(1-fluorocyclopropane-1-carbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-4-(1-hydroxyethyl)-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile;

3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(2,3-dichlorophenyl)-6-fluoro-2-((1*R*,3*R*,5*R*)-2-(1-fluorocyclopropane-1-carbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile;

N-((1*R*)-1-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-(1-hydroxyethyl)-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)ethyl)-1-fluorocyclopropane-1-carboxamide;

N-((1*R*)-1-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-(1-hydroxyethyl)-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)ethyl)-1-fluorocyclobutane-1-carboxamide;

3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(3-chloro-2-methylphenyl)-2-(1-(2,6-dimethyl-3-oxo-2,3-dihydropyridazin-4-yl)ethyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile;

N-((1*R*)-1-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)ethyl)pyrimidine-4-carboxamide;

N-((1*R*)-1-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)ethyl)pyridazine-3-carboxamide;

N-((1*R*)-1-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)ethyl)-3,3-difluoroazetidine-1-carboxamide;

3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-2-((*R*)-1-((1-methyl-1*H*-pyrazol-4-yl)amino)ethyl)-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile;

5-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-2-((*R*)-1-(1-fluorocyclopropane-1-carbonyl)pyrrolidin-2-yl)-1*H*-pyrrolo[3,2-*c*]quinolin-4-yl)-N,N-dimethylpicolinamide; and

methyl (2*R*)-2-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-4-(4-((dimethylamino)methyl)-2,3-difluorophenyl)-6-fluoro-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)pyrrolidine-1-carboxylate;

and pharmaceutically acceptable salts thereof.

22. The use of any one of claims 1 to 21, wherein the KRAS G12D inhibitor is 3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile, or a pharmaceutically acceptable salt thereof.

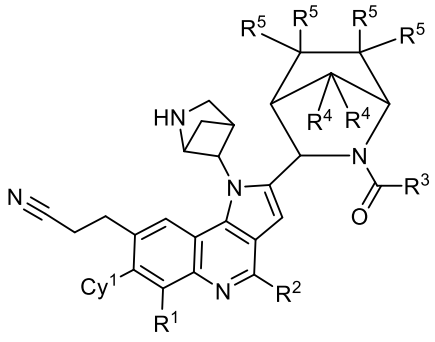
23. The use of any one of claims 1 to 22, wherein the KRAS G12D inhibitor is 3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile hydrochloride dihydrate.

24. The use of any one of claims 1 to 22, wherein the KRAS G12D inhibitor is 3-((R_a)-1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile hydrochloride dihydrate.

25. The use of any one of claims 1 to 22, wherein the KRAS G12D inhibitor is 3-((S_a)-1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-

azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile hydrochloride dihydrate.

26. The use of any one of claims 1 to 13, wherein the KRAS G12D inhibitor is a compound of Formula IV:



(**IV**)

or a pharmaceutically acceptable salt thereof, wherein:

Cy^1 is phenyl optionally substituted with 1, 2, 3, or 4 substituents each selected from D, C_{1-3} alkyl, C_{1-3} haloalkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, halo, OH, C_{1-3} alkoxy, and C_{1-3} haloalkoxy;

R^1 is halogen;

R^2 is selected from H, D, C_{1-3} alkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, C_{1-3} haloalkyl, C_{3-5} cycloalkyl, 4-6 membered heterocycloalkyl, phenyl, 5-6 membered heteroaryl, C_{3-6} cycloalkyl-C_{1-3} alkylene, 4-6 membered heterocycloalkyl-C_{1-3} alkylene, phenyl-C_{1-3} alkylene, 5-6 membered heteroaryl-C_{1-3} alkylene, halo, CN, OR^{a2}, $C(O)R^{b2}$, $C(O)NR^{c2}R^{d2}$, $NR^{c2}R^{e2}$, and $NR^{c2}C(O)R^{b2}$; wherein the C_{3-5} cycloalkyl, 4-6 membered heterocycloalkyl, phenyl, 5-6 membered heteroaryl, C_{3-6} cycloalkyl-C_{1-3} alkylene, 4-6 membered heterocycloalkyl-C_{1-3} alkylene, phenyl-C_{1-3} alkylene, and 5-6 membered heteroaryl-C_{1-3} alkylene forming R^2 are each optionally substituted with 1, 2, or 3 substituents independently selected from R^{2A}; wherein the ring-forming atoms of the 4-6 membered heterocycloalkyl, 5-6 membered heteroaryl, C_{3-6} cycloalkyl-C_{1-3} alkylene, and 4-6 membered heterocycloalkyl-C_{1-3} alkylene forming R^2 consist of at least one carbon atom and 1, 2, 3, or 4 heteroatoms selected from O, N, and S; wherein a ring-forming carbon atom of the 4-6 membered heterocycloalkyl, 5-6 membered heteroaryl, C_{3-6} cycloalkyl-C_{1-3} alkylene, and 4-6 membered heterocycloalkyl-C_{1-3} alkylene forming R^2 is optionally substituted by oxo to form a carbonyl group; and wherein the C_{1-3} alkyl, C_{2-3} alkenyl, and C_{2-3} alkynyl forming R^2 are each optionally substituted with 1, 2, or 3 substituents independently selected from R^{2B};

each R^{a2} is independently selected from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-3} haloalkyl, C_{3-6} cycloalkyl, 4-6 membered heterocycloalkyl, phenyl, and 5-6 membered heteroaryl; wherein the C_{3-6} cycloalkyl, 4-6 membered heterocycloalkyl, phenyl, and 5-6

membered heteroaryl forming R^{a2} are each optionally substituted with 1, 2, or 3 substituents independently selected from R^{2A}; wherein the ring-forming atoms of the 4-6 membered heterocycloalkyl and 5-6 membered heteroaryl forming R^{a2} consist of at least one carbon atom and 1, 2, 3, or 4 heteroatoms selected from O, N, and S; wherein a ring-forming carbon atom of the 4-6 membered heterocycloalkyl and 5-6 membered heteroaryl forming R^{a2} is optionally substituted by oxo to form a carbonyl group; and wherein the C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl forming R^{a2} are each optionally substituted with 1, 2, or 3 substituents independently selected from R^{2B};

each R^{b2}, R^{c2}, and R^{d2} is independently selected from H, C_{1-3} alkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, C_{1-3} haloalkyl, C_{3-6} cycloalkyl, 4-6 membered heterocycloalkyl, phenyl, and 5-6 membered heteroaryl; wherein the C_{3-6} cycloalkyl, 4-6 membered heterocycloalkyl, phenyl, and 5-6 membered heteroaryl forming R^{b2}, R^{c2}, and R^{d2} are each optionally substituted with 1, 2, or 3 substituents independently selected from R^{2A}; the ring-forming atoms of the 4-6 membered heterocycloalkyl and 5-6 membered heteroaryl forming R^{b2}, R^{c2}, and R^{d2} consist of at least one carbon atom and 1, 2, 3, or 4 heteroatoms selected from O, N, and S; wherein a ring-forming carbon atom of the 4-6 membered heterocycloalkyl and 5-6 membered heteroaryl forming R^{b2}, R^{c2}, and R^{d2} is optionally substituted by oxo to form a carbonyl group; and wherein the C_{1-3} alkyl, C_{2-3} alkenyl, and C_{2-3} alkynyl forming R^{b2}, R^{c2}, and R^{d2} are each optionally substituted with 1, 2, or 3 substituents independently selected from R^{2B}; or

any R^{c2} and R^{d2} attached to the same N atom, together with the N atom to which they are attached, form a 4-, 5-, or 6-membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents independently selected from R^{2B};

each R^{e2} is independently selected from C_{1-3} alkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, C_{1-3} haloalkyl, C_{3-6} cycloalkyl, 4-6 membered heterocycloalkyl, phenyl and 5-6 membered heteroaryl; wherein the C_{3-6} cycloalkyl, 4-6 membered heterocycloalkyl, phenyl and 5-6 membered heteroaryl forming R^{e2} are each optionally substituted with 1, 2, or 3 substituents independently selected from R^{2A}; wherein the ring-forming atoms of the 4-6 membered heterocycloalkyl and 5-6 membered heteroaryl forming R^{e2} consist of at least one carbon atom and 1, 2, 3, or 4 heteroatoms selected from O, N, and S; wherein a ring-forming carbon atom of the 4-6 membered heterocycloalkyl and 5-6 membered heteroaryl forming R^{e2} is optionally substituted by oxo to form a carbonyl group; and wherein the C_{1-3} alkyl, C_{2-3} alkenyl, and C_{2-3} alkynyl, forming R^{e2} are each optionally substituted with 1, 2, or 3 substituents independently selected from R^{2B}; or

R^{c2} and R^{e2} attached to the same N atom, together with the N atom to which they are attached, form a 4-, 5-, or 6-membered heterocycloalkyl group optionally substituted with 1, 2, or 3 substituents independently selected from R^{2B};

each R^{2A} is independently selected from C_{1-3} alkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, C_{1-3} haloalkyl, and R^{2B}, wherein the C_{1-3} alkyl, C_{2-3} alkenyl, and C_{2-3} alkynyl, forming R^{2A} are each optionally substituted with 1, 2 or 3 substituents independently selected from R^{2B};

each R^{2B} is independently selected from C_{3-6} cycloalkyl, 4-10 membered heterocycloalkyl, phenyl, 5-6 membered heteroaryl, halo, D, CN, OR^{a2B}, $C(O)R^{b2B}$, $C(O)NR^{c2B}R^{d2B}$, $C(O)OR^{a2B}$, $NR^{c2B}R^{d2B}$, and $S(O)_2R^{b2B}$; wherein the C_{1-3} alkyl, C_{3-6} cycloalkyl, 4-6 membered heterocycloalkyl, phenyl, and 5-6 membered heteroaryl are each optionally substituted with 1, 2, or 3 substituents independently selected from R^{2C};

each R^{2C} is independently selected from C_{1-3} alkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, C_{1-3} haloalkyl, C_{3-6} cycloalkyl, 4-6 membered heterocycloalkyl, phenyl, 5-6 membered heteroaryl, halo, D, CN, OR^{a2C}, $C(O)R^{b2C}$, $C(O)NR^{c2C}R^{d2C}$, $C(O)OR^{a2C}$, $NR^{c2C}R^{d2C}$, and $S(O)_2R^{b2C}$;

each R^{a2B}, R^{b2B}, R^{c2B} and R^{d2B} is independently selected from H, C_{1-3} alkyl, and C_{1-3} haloalkyl;

each R^{a2C}, R^{b2C}, R^{c2C} and R^{d2C} is independently selected from H, C_{1-3} alkyl, and C_{1-3} haloalkyl;

R^3 is selected from C_{1-3} alkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, C_{3-10} cycloalkyl, 4-10 membered heterocycloalkyl, C_{6-10} aryl, 5-10 membered heteroaryl, OR^{3A}, and $NR^{3B}R^{3C}$; wherein the C_{3-10} cycloalkyl, 4-10 membered heterocycloalkyl, C_{6-10} aryl, and 5-10 membered heteroaryl C_{1-3} alkyl forming R^3 are each optionally substituted with 1, 2, or 3 substituents independently selected from R^{3D}; wherein the ring-forming atoms of the 4-10 membered heterocycloalkyl and 5-10 membered heteroaryl forming R^3 consist of at least one carbon atom and 1, 2, 3, or 4 heteroatoms selected from O, N, and S; wherein a ring-forming carbon atom of the 4-10 membered heterocycloalkyl or 5-10 membered heteroaryl forming R^3 is optionally substituted by oxo to form a carbonyl group; and wherein the C_{1-3} alkyl, C_{2-3} alkenyl, and C_{2-3} alkynyl forming R^3 are each optionally substituted with 1, 2, or 3 substituents independently selected from R^{3E};

R^{3A} is selected from C_{1-3} alkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, C_{3-10} cycloalkyl, 4-10 membered heterocycloalkyl, C_{6-10} aryl, and 5-10 membered heteroaryl; wherein the C_{3-10} cycloalkyl, 4-10 membered heterocycloalkyl, C_{6-10} aryl, and 5-10 membered heteroaryl C_{1-3} alkyl forming R^{3A} are each optionally substituted with 1, 2, or 3 substituents independently selected from R^{3D}; wherein the ring-forming atoms of the 4-10 membered heterocycloalkyl and 5-10 membered heteroaryl forming R^{3A} consist of at least one carbon atom and 1, 2, 3, or 4 heteroatoms selected from O, N, and S; wherein a ring-forming carbon atom of the 4-10 membered heterocycloalkyl or 5-10 membered heteroaryl forming R^{3A} is optionally substituted by oxo to form a carbonyl group; and wherein the C_{1-3} alkyl, C_{2-3} alkenyl, and C_{2-3} alkynyl forming R^{3A} are each optionally substituted with 1, 2, or 3 substituents independently selected from R^{3E};

R^{3B} is selected from H, C_{1-3} alkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, C_{3-10} cycloalkyl, 4-10 membered heterocycloalkyl, C_{6-10} aryl, and 5-10 membered heteroaryl; wherein the C_{3-10} cycloalkyl, 4-10 membered heterocycloalkyl, C_{6-10} aryl, and 5-10 membered heteroaryl forming R^{3B} are each optionally substituted with 1, 2, or 3 substituents independently selected from R^{3D}; wherein the ring-forming atoms of the 4-10 membered heterocycloalkyl and 5-10 membered heteroaryl forming R^{3B} consist of at least one carbon atom and 1, 2, 3, or 4 heteroatoms selected from O, N, and S; wherein a ring-forming carbon atom of the 4-10 membered heterocycloalkyl and 5-10 membered heteroaryl forming R^{3B} is optionally substituted by oxo to form a carbonyl group; and wherein the C_{1-3} alkyl, C_{2-3} alkenyl, and C_{2-3} alkynyl forming R^{3B} are each optionally substituted with 1, 2, or 3 substituents independently selected from R^{3E};

R^{3B} and R^{3C}, together with the N atom to which they are both attached, optionally form a 4-, 5-, 6-, or 7-membered heterocycloalkyl group that is optionally substituted with 1, 2, or 3 substituents independently selected from independently selected from R^{3D};

R^{3C} is selected from H, C_{1-3} alkyl, C_{2-3} alkenyl, and C_{2-3} alkynyl; wherein the C_{1-3} alkyl, C_{2-3} alkenyl, and C_{2-3} alkynyl forming R^{3C} are each optionally substituted with 1, 2, or 3 substituents independently selected from R^{3E};

each R^{3D} is independently selected from C_{1-3} alkyl, C_{1-3} haloalkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, and R^{3E}; wherein each of the C_{1-3} alkyl, C_{2-3} alkenyl, and C_{2-3} alkynyl forming R^{3D} is optionally substituted with 1, 2, or 3 substituents independently selected from R^{3E};

each R^{3E} is independently selected from D, halo, CN, OR^{a3}, SR^{a3}, $C(O)R^{b3}$, $C(O)NR^{c3}R^{d3}$, $C(O)OR^{a3}$, $OC(O)R^{b3}$, $OC(O)NR^{c3}R^{d3}$, $NR^{c3}R^{d3}$, $NR^{c3}C(O)R^{b3}$, $NR^{c3}C(O)NR^{c3}R^{d3}$, $NR^{c3}C(O)OR^{a3}$, $C(=NR^{e3})NR^{c3}R^{d3}$, $NR^{c3}C(=NR^{e3})NR^{c3}R^{d3}$, $S(O)R^{b3}$, $S(O)NR^{c3}R^{d3}$, $S(O)_2R^{b3}$, $NR^{c3}S(O)_2R^{b3}$, and $S(O)_2NR^{c3}R^{d3}$;

R^{a3}, R^{b3}, R^{c3}, and R^{d3} are each independently selected from H, C_{1-3} alkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, C_{6-10} aryl, C_{3-7} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C_{6-10} aryl-C_{1-3} alkyl, 5-10 membered heteroaryl-C_{1-3} alkyl, C_{3-7} cycloalkyl-C_{1-3} alkyl, and 4-10 membered heterocycloalkyl-C_{1-3} alkyl; wherein the C_{6-10} aryl-C_{1-3} alkyl, 5-10 membered heteroaryl-C_{1-3} alkyl, C_{3-7} cycloalkyl-C_{1-3} alkyl, and 4-10 membered heterocycloalkyl-C_{1-3} alkyl forming R^{a3}, R^{b3}, R^{c3}, and R^{d3} are each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from C_{1-3} alkyl, C_{1-3} haloalkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, halo, CN, OR^{a3A}, SR^{a3A}, $C(O)R^{b3A}$, $C(O)NR^{c3A}R^{d3A}$, $C(O)OR^{a3A}$, $OC(O)R^{b3A}$, $OC(O)NR^{c3A}R^{d3A}$, $NR^{c3A}R^{d3A}$, $NR^{c3A}C(O)R^{b3A}$, $NR^{c3A}C(O)NR^{c3A}R^{d3A}$, $NR^{c3A}C(O)OR^{a3A}$, $C(=NR^{e3A})NR^{c3A}R^{d3A}$, $NR^{c3A}C(=NR^{e3A})NR^{c3A}R^{d3A}$, $S(O)R^{b3A}$, $S(O)NR^{c3A}R^{d3A}$, $S(O)_2R^{b3A}$, $NR^{c3A}S(O)_2R^{b3A}$, and $S(O)_2NR^{c3A}R^{d3A}$; wherein the ring-forming atoms of the 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, 5-10 membered heteroaryl-C_{1-3} alkyl, and 4-10 membered heterocycloalkyl-C_{1-3} alkyl forming R^{a3}, R^{b3}, R^{c3}, and R^{d3} consist of at least one

carbon atom and 1, 2, 3, or 4 heteroatoms selected from O, N, and S; wherein a ring-forming carbon atom of the 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, 5-10 membered heteroaryl-C_{1-3} alkyl, and 4-10 membered heterocycloalkyl-C_{1-3} alkyl forming R^{a3}, R^{b3}, R^{c3}, and R^{d3} is optionally substituted by oxo to form a carbonyl group; or

R^{c3} and R^{d3} attached to the same N atom, together with the N atom to which they are both attached, form a 4-, 5-, 6-, or 7-membered heterocycloalkyl group or 5-membered heteroaryl group, each optionally substituted with 1, 2, or 3 substituents independently selected from C_{1-3} alkyl, C_{1-3} haloalkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, halo, CN, OR^{a3A}, SR^{a3A}, $C(O)R^{b3A}$, $C(O)NR^{c3A}R^{d3A}$, $C(O)OR^{a3A}$, $OC(O)R^{b3A}$, $OC(O)NR^{c3A}R^{d3A}$, $NR^{c3A}R^{d3A}$, $NR^{c3A}C(O)R^{b3A}$, $NR^{c3A}C(O)NR^{c3A}R^{d3A}$, $NR^{c3A}C(O)OR^{a3A}$, $C(=NR^{e3A})NR^{c3A}R^{d3A}$, $NR^{c3A}C(=NR^{e3A})NR^{c3A}R^{d3A}$, $S(O)R^{b3A}$, $S(O)NR^{c3A}R^{d3A}$, $S(O)_2R^{b3A}$, $NR^{c3A}S(O)_2R^{b3A}$, and $S(O)_2NR^{c3A}R^{d3A}$;

R^{a3A}, R^{b3A}, R^{c3A}, and R^{d3A} are each independently selected from H, C_{1-3} alkyl, C_{1-3} haloalkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, aryl, C_{6-10} aryl-C_{1-3} alkyl, 5-10 membered heteroaryl-C_{1-3} alkyl, C_{3-7} cycloalkyl-C_{1-3} alkyl, and 4-10 membered heterocycloalkyl-C_{1-3} alkyl; wherein the C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl C_{6-10} aryl-C_{1-3} alkyl, 5-10 membered heteroaryl-C_{1-3} alkyl, C_{3-7} cycloalkyl-C_{1-3} alkyl, and 4-10 membered heterocycloalkyl-C_{1-3} alkyl forming R^{a3A}, R^{b3A}, R^{c3A}, and R^{d3A} are each optionally substituted with 1, 2, or 3 substituents independently selected from OH, CN, amino, NH(C_{1-6} alkyl), N(C_{1-6} alkyl)$_2$, halo, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, and C_{1-6} haloalkoxy; wherein the ring-forming atoms of the 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, 5-10 membered heteroaryl-C_{1-3} alkyl, and 4-10 membered heterocycloalkyl-C_{1-3} alkyl forming R^{a3A}, R^{b3A}, R^{c3A}, and R^{d3A} consist of at least one carbon atom, and 1, 2, 3, or 4 heteroatoms selected from O, N, and S; and wherein a ring-forming carbon atom of the 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl, 5-10 membered heteroaryl-C_{1-3} alkyl, and 4-10 membered heterocycloalkyl-C_{1-3} alkyl forming R^{a3A}, R^{b3A}, R^{c3A}, and R^{d3A} is optionally substituted by oxo to form a carbonyl group; or

R^{c3A} and R^{d3A} attached to the same N atom, together with the N atom to which they are both attached, form a 4-, 5-, 6-, or 7-membered heterocycloalkyl group or 5-membered heteroaryl group, each optionally substituted with 1, 2, or 3 substituents independently selected from OH, CN, amino, NH(C_{1-6} alkyl), N(C_{1-6} alkyl)$_2$, halo, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, and C_{1-6} haloalkoxy;R^{e3}, and R^{e3A} are each, independently, H, CN or NO_2;

each R^4 is independently selected from H, D, C_{1-3} alkyl, C_{1-3} haloalkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, halo, and OR^{a4};

each R^{a4} is independently selected from H, C_{1-3} alkyl, and C_{1-3} haloalkyl;

one R^5 is R^{5A}; and each other R^5 is independently selected from H, D, halo, C_{1-3} alkyl, OR^{a5}, C_{1-3} haloalkyl, C_{2-3} alkenyl, and C_{2-3} alkynyl; or, optionally, two other R^5 attached to the

same carbon atom, together with the carbon atom to which they are both attached, form a spiro C_{3-6} cycloalkyl ring that is optionally substituted with 1, 2, 3, or 4 substituents each selected from D, C_{1-3} alkyl, and halo; or, optionally, two other R^5 attached to adjacent carbon atoms, together with the carbon atoms to which they are each attached, form a fused C_{3-6} cycloalkyl ring that is optionally substituted with 1, 2, 3, or 4 substituents each selected from D, C_{1-3} alkyl, and halo;

R^{5A} is H, D, C_{1-3} alkyl, C_{1-3} haloalkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, halo, OR^{a5A}, CN, or Cy^2; wherein the C_{1-3} alkyl forming R^{5A} is optionally substituted with 1, 2, 3 or 4 substituents each selected from R^{5B} and also optionally substituted with Cy^2, or, optionally, R^{5A} and R^5 attached to the same carbon atom, together with the carbon atom to which they are both attached, form a spiro C_{3-6} cycloalkyl ring that is optionally substituted with 1, 2, 3, or 4 substituents each selected from D, C_{1-3} alkyl, and halo; or, optionally, R^{5A} and R^5 attached to adjacent carbon atoms, together with the carbon atoms to which they are each attached, form a fused C_{3-6} cycloalkyl ring that is optionally substituted with 1, 2, 3, or 4 substituents each selected from D, C_{1-3} alkyl, and halo;

each R^{5B} is independently selected from D and halo;

each R^{a5} is independently selected from H, C_{1-3} alkyl, and C_{1-3} haloalkyl;

R^{a5A} is selected from H, C_{1-3} alkyl, C_{1-3} haloalkyl, and Cy^2, wherein the C_{1-3} alkyl forming R^{a5A} is optionally substituted with 1, 2, 3 or 4 substituents each selected from R^{5B} and also optionally substituted with Cy^2;

Cy^2 is selected from C_{3-7} cycloalkyl, 4-10 membered heterocycloalkyl, C_{6-10} aryl, and 5-10 membered heteroaryl; wherein the C_{3-7} cycloalkyl, 4-10 membered heterocycloalkyl, C_{6-10} aryl, 5-10 membered heteroaryl, C_{6-10} aryl, and 5-10 membered heteroaryl forming Cy^2 is optionally substituted with 1, 2, 3, or 4 substituents independently selected from R^{Cy2}; wherein the ring-forming atoms of the 4-10 membered heterocycloalkyl and 5-10 membered heteroaryl forming Cy^2 consist of at least one carbon atom and 1, 2, 3, or 4 heteroatoms independently selected from N, O, and S; and wherein a ring-forming carbon atom of the 4-10 membered heterocycloalkyl and 5-10 membered heteroaryl forming Cy^2 is optionally substituted by oxo to form a carbonyl group;

each R^{Cy2} is independently selected from D, C_{1-3} alkyl, C_{1-3} haloalkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, C_{3-6} cycloalkyl, 4-10 membered heterocycloalkyl, C_{6-10} aryl, 5-10 membered heteroaryl, halo, CN, OR^{aCy21}, SR^{aCy21}, $C(O)R^{bCy21}$, $C(O)NR^{cCy21}R^{dCy21}$, $C(O)OR^{aCy21}$, $OC(O)R^{bCy21}$, $OC(O)NR^{cCy21}R^{dCy21}$, $NR^{cCy21}R^{dCy21}$, $NR^{cCy21}C(O)R^{bCy21}$, $NR^{cCy21}C(O)NR^{cCy21}R^{dCy21}$, $NR^{cCy21}C(O)OR^{aCy21}$, $C(=NR^{eCy21})NR^{cCy21}R^{dCy21}$, $NR^{cCy21}C(=NR^{eCy21})NR^{cCy21}R^{dCy21}$, $S(O)R^{bCy21}$, $S(O)NR^{cCy21}R^{dCy21}$, $S(O)_2R^{bCy21}$, $NR^{cCy21}S(O)_2R^{bCy21}$, and $S(O)_2NR^{cCy21}R^{dCy21}$; wherein the C_{3-6} cycloalkyl, 4-10 membered heterocycloalkyl, C_{6-10} aryl, and 5-10 membered heteroaryl forming R^{Cy2} are each optionally

substituted by 1, 2, 3, or 4 substituents independently selected from R^{Cy2A}; wherein the ring-forming atoms of the 4-10 membered heterocycloalkyl and 5-10 membered heteroaryl forming R^{Cy2} consist of at least one carbon atom and 1, 2, 3, or 4 heteroatoms independently selected from N, O, and S; wherein a ring-forming carbon atom of the 4-10 membered heterocycloalkyl and 5-10 membered heteroaryl forming R^{Cy2} is optionally substituted by oxo to form a carbonyl group; and wherein the C_{1-3} alkyl, C_{2-3} alkenyl, and C_{2-3} alkynyl forming R^{Cy2} are each optionally substituted by 1, 2, or 3 substituents independently selected from R^{Cy2B};

each R^{Cy2A} is independently selected from C_{1-3} alkyl, C_{1-3} haloalkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, and R^{Cy2B}; wherein the C_{1-3} alkyl, C_{2-3} alkenyl, and C_{2-3} alkynyl forming R^{Cy2A} are each optionally substituted by 1, 2, or 3 substituents independently selected from R^{Cy2B},

each R^{Cy2B} is independently selected from D, halo, CN, OR^{aCy21}, SR^{aCy21}, $C(O)R^{bCy21}$, $C(O)NR^{cCy21}R^{dCy21}$, $C(O)OR^{aCy21}$, $OC(O)R^{bCy21}$, $OC(O)NR^{cCy21}R^{dCy21}$, $NR^{cCy21}R^{dCy21}$, $NR^{cCy21}C(O)R^{bCy21}$, $NR^{cCy21}C(O)NR^{cCy21}R^{dCy21}$, $NR^{cCy21}C(O)OR^{aCy21}$, $C(=NR^{eCy21})NR^{cCy21}R^{dCy21}$, $NR^{cCy21}C(=NR^{eCy21})NR^{cCy21}R^{dCy21}$, $S(O)R^{bCy21}$, $S(O)NR^{cCy21}R^{dCy21}$, $S(O)_2R^{bCy21}$, $NR^{cCy21}S(O)_2R^{bCy21}$, and $S(O)_2NR^{cCy21}R^{dCy21}$,

R^{aCy21}, R^{bCy21}, R^{cCy21}, and R^{dCy21} are each independently selected from H, C_{1-3} alkyl, C_{1-3} haloalkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, C_{6-10} aryl, C_{3-7} cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, C_{6-10} aryl-C_{1-3} alkyl, 5-10 membered heteroaryl-C_{1-3} alkyl, C_{3-7} cycloalkyl-C_{1-3} alkyl, and 4-10 membered heterocycloalkyl-C_{1-3} alkyl; wherein the C_{6-10} aryl-C_{1-3} alkyl, 5-10 membered heteroaryl-C_{1-3} alkyl, C_{3-7} cycloalkyl-C_{1-3} alkyl, and 4-10 membered heterocycloalkyl-C_{1-3} alkyl forming R^{aCy21}, R^{bCy21}, R^{cCy21}, and R^{dCy21} are each optionally substituted with 1, 2, or 3 substituents independently selected from C_{1-3} alkyl, C_{1-3} haloalkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, halo, CN, OR^{aCy22}, SR^{aCy22}, $C(O)R^{bCy22}$, $C(O)NR^{cCy22}R^{dCy22}$, $C(O)OR^{aCy22}$, $OC(O)R^{bCy22}$, $OC(O)NR^{cCy22}R^{dCy22}$, $NR^{cCy22}R^{dCy22}$, $NR^{cCy22}C(O)R^{bCy22}$, $NR^{cCy22}C(O)NR^{cCy22}R^{dCy22}$, $NR^{cCy22}C(O)OR^{aCy22}$, $C(=NR^{eCy22})NR^{cCy22}R^{dCy22}$, $NR^{cCy22}C(=NR^{eCy22})NR^{cCy22}R^{dCy22}$, $S(O)R^{bCy22}$, $S(O)NR^{cCy22}R^{dCy22}$, $S(O)_2R^{bCy22}$, $NR^{cCy22}S(O)_2R^{bCy22}$, and $S(O)_2NR^{cCy22}R^{dCy22}$; wherein the ring-forming atoms each of the 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl-C_{1-3} alkyl, and 4-10 membered heterocycloalkyl-C_{1-3} alkyl forming R^{aCy21}, R^{bCy21}, R^{cCy21}, and R^{dCy21} consist of at least one carbon atom and 1, 2, 3, or 4 heteroatoms independently selected from N, O, and S; and wherein a ring-forming carbon atom of the 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl-C_{1-3} alkyl, and 4-10 membered heterocycloalkyl-C_{1-3} alkyl forming R^{aCy21}, R^{bCy21}, R^{cCy21}, and R^{dCy21} is optionally substituted by oxo to form a carbonyl group;

or R^{cCy21} and R^{dCy21} attached to the same N atom, together with the N atom to which they are both attached, form a 4-, 5-, 6-, or 7-membered heterocycloalkyl group or 5-

membered heteroaryl group, each optionally substituted with 1, 2, or 3 substituents independently selected from C_{1-3} alkyl, C_{1-3} haloalkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, halo, CN, OR^{aCy22}, SR^{aCy22}, $C(O)R^{bCy22}$, $C(O)NR^{cCy22}R^{dCy22}$, $C(O)OR^{aCy22}$, $OC(O)R^{bCy22}$, $OC(O)NR^{cCy22}R^{dCy22}$, $NR^{cCy22}R^{dCy22}$, $NR^{cCy22}C(O)R^{bCy22}$, $NR^{cCy22}C(O)NR^{cCy22}R^{dCy22}$, $NR^{cCy22}C(O)OR^{aCy22}$, $C(=NR^{eCy22})NR^{cCy22}R^{dCy22}$, $NR^{cCy22}C(=NR^{eCy22})NR^{cCy22}R^{dCy22}$, $S(O)R^{bCy22}$, $S(O)NR^{cCy22}R^{dCy22}$, $S(O)_2R^{bCy22}$, $NR^{cCy22}S(O)_2R^{bCy22}$, and $S(O)_2NR^{cCy22}R^{dCy22}$;

R^{aCy22}, R^{bCy22}, R^{cCy22}, and R^{dCy22} are each independently selected from H, C_{1-3} alkyl, C_{1-3} haloalkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, aryl, C_{6-10} aryl-C_{1-3} alkyl, 5-10 membered heteroaryl-C_{1-3} alkyl, C_{3-7} cycloalkyl-C_{1-3} alkyl, and 4-10 membered heterocycloalkyl-C_{1-3} alkyl; wherein the C_{1-3} alkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, C_{6-10} aryl-C_{1-3} alkyl, 5-10 membered heteroaryl-C_{1-3} alkyl, C_{3-7} cycloalkyl-C_{1-3} alkyl, and 4-10 membered heterocycloalkyl-C_{1-3} alkyl forming R^{aCy22}, R^{bCy22}, R^{cCy22}, and R^{dCy22} are each optionally substituted with 1, 2, or 3 substituents independently selected from OH, CN, amino, NH(C_{1-3} alkyl), N(C_{1-3} alkyl)$_2$, halo, C_{1-3} alkyl, C_{1-3} alkoxy, C_{1-3} haloalkyl, and C_{1-3} haloalkoxy; wherein the ring-forming atoms each of the 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl-C_{1-3} alkyl, and 4-10 membered heterocycloalkyl-C_{1-3} alkyl forming R^{aCy22}, R^{bCy22}, R^{cCy22}, and R^{dCy22} consist of at least one carbon atom and 1, 2, 3, or 4 heteroatoms independently selected from N, O, and S; and wherein a ring-forming carbon atom of the 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, 5-10 membered heteroaryl-C_{1-3} alkyl, and 4-10 membered heterocycloalkyl-C_{1-3} alkyl forming R^{aCy22}, R^{bCy22}, R^{cCy22}, and R^{dCy22} is optionally substituted by oxo to form a carbonyl group; or

R^{cCy22} and R^{dCy22} attached to the same N atom, together with the N atom to which they are both attached, form a 4-, 5-, 6-, or 7-membered heterocycloalkyl group or 5-membered heteroaryl group, each optionally substituted with 1, 2, or 3 substituents independently selected from OH, CN, amino, NH(C_{1-6} alkyl), N(C_{1-6} alkyl)$_2$, halo, C_{1-3} alkyl, C_{1-3} alkoxy, C_{1-3} haloalkyl, and C_{1-3} haloalkoxy; and

R^{eCy21} and R^{eCy22} are each, independently, H, CN or NO_2.

27. The use of claim 26, wherein

Cy^1 is phenyl optionally substituted with 1 or 2 substituents each selected from D, C_{1-3} alkyl, C_{1-3} haloalkyl, halo, OH, and C_{1-3} alkoxy;

R^1 is halo;

R^2 is C_{1-3} alkyl optionally substituted with OH;

R^3 is C_{3-10} cycloalkyl optionally substituted with halo;

each R^4 is H;

one R^5 is R^{5A}; and each other R^5 is independently selected from H, D, halo, C_{1-3} alkyl, OC_{1-3} alkyl, C_{1-3} haloalkyl; or, optionally, two other R^5 attached to adjacent carbon atoms,

together with the carbon atoms to which they are each attached, form a fused C_{3-6} cycloalkyl ring that is optionally substituted with 1 or 2 substituents each selected from D, C_{1-3} alkyl, and halo; and

R^{5A} is H, halo, or OR^{a5A};

R^{a5A} is selected from C_{1-3} alkyl, C_{1-3} haloalkyl, and Cy^2, wherein the C_{1-3} alkyl forming R^{a5A} is optionally substituted with 1, 2, or 3 D, and also optionally substituted with Cy^2; and

Cy^2 is selected from C_{6-10} aryl and 5-10 membered heteroaryl.

28. The use of claim 26 or 27, wherein

Cy^1 is phenyl optionally substituted with 1 or 2 substituents each selected from D, C_{1-3} alkyl, C_{1-3} haloalkyl, halo, OH, and C_{1-3} alkoxy;

R^1 is halo;

R^2 is C_{1-3} alkyl optionally substituted with OH;

R^3 is OR^{3A} or C_{3-10} cycloalkyl optionally substituted with halo;

R^{3A} is C_{1-3} alkyl;

each R^4 is H;

one R^5 is R^{5A}; and each other R^5 is independently selected from H, D, halo, C_{1-3} alkyl, OC_{1-3} alkyl, C_{1-3} haloalkyl; or, optionally, two other R^5 attached to adjacent carbon atoms, together with the carbon atoms to which they are each attached, form a fused C_{3-6} cycloalkyl ring that is optionally substituted with 1 or 2 substituents each selected from D, C_{1-3} alkyl, and halo;

R^{5A} is H, halo, or OR^{a5A};

R^{a5A} is selected from C_{1-3} alkyl, C_{1-3} haloalkyl, and Cy^2, wherein the C_{1-3} alkyl forming R^{a5A} is optionally substituted with 1, 2, or 3 D, and also optionally substituted with Cy^2; and

Cy^2 is selected from C_{6-10} aryl and 5-10 membered heteroaryl.

29. The use of any one of claims 26 to 28, wherein

Cy^1 is phenyl optionally substituted with 1 or 2 substituents each selected from C_{1-3} alkyl, C_{1-3} haloalkyl, halo, OH, and C_{1-3} alkoxy;

R^1 is halo;

R^2 is C_{1-3} alkyl optionally substituted with OH;

R^3 is OR^{3A} or C_{3-10} cycloalkyl optionally substituted with halo;

R^{3A} is C_{1-3} alkyl;

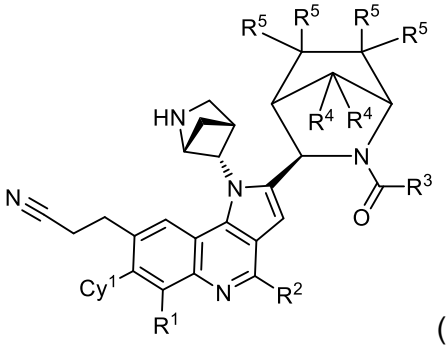
each R^4 is H;

one R^5 is R^{5A}; and each other R^5 is independently selected from H, halo, C_{1-3} alkyl, OC_{1-3} alkyl, C_{1-3} haloalkyl;

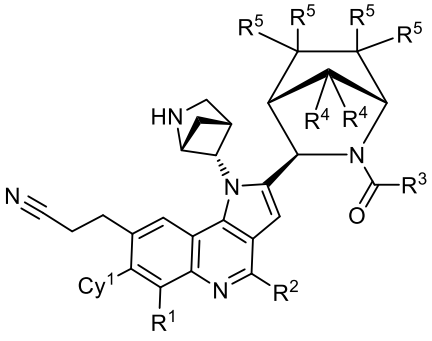
R^{5A} is H, halo, or OR^{a5A}; and

R^{a5A} is selected from C_{1-3} alkyl and C_{1-3} haloalkyl, wherein the C_{1-3} alkyl forming R^{a5A} is optionally substituted with 1, 2, or 3 D.

30. The use of any one of claims 26 to 29, wherein the compound of Formula IV is a compound of Formula IV-A or Formula IV-B:



(**IV-A**)



(**IV-B**)

or a pharmaceutically acceptable salt thereof.

31. The use of any one of claims 26 to 30, wherein the compound of Formula IV is selected from:

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-2-(2-(cyclopropanecarbonyl)-5-methoxy-2-azabicyclo[2.2.1]heptan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-2-(2-(cyclopropanecarbonyl)-5-fluoro-2-azabicyclo[2.2.1]heptan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-2-(6-(cyclopropanecarbonyl)-6-azatricyclo[3.2.1.02,4]octan-7-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-2-(2-(cyclopropanecarbonyl)-5-(methoxy-d3)-2-azabicyclo[2.2.1]heptan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-2-(2-(cyclopropanecarbonyl)-5-(pyridin-3-yloxy)-2-azabicyclo[2.2.1]heptan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(2-(5-(benzyloxy)-2-(cyclopropanecarbonyl)-2-azabicyclo[2.2.1]heptan-3-yl)-1-(2-azabicyclo[2.1.1]hexan-5-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-2-(2-(cyclopropanecarbonyl)-5-(difluoromethoxy)-2-azabicyclo[2.2.1]heptan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-7-(2,3-dichlorophenyl)-6-fluoro-2-(5-fluoro-2-(1-fluorocyclopropane-1-carbonyl)-2-azabicyclo[2.2.1]heptan-3-yl)-4-((R)-1-hydroxyethyl)-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-2-(2-(cyclopropanecarbonyl)-5-(difluoromethyl)-2-azabicyclo[2.2.1]heptan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-2-(2-(cyclopropanecarbonyl)-2-azabicyclo[2.2.1]heptan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

5-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-2-(2-(cyclopropanecarbonyl)-2-azabicyclo[2.2.1]heptan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-1H-pyrrolo[3,2-c]quinolin-4-yl)-N,N-dimethylpicolinamide;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-2-(2-(cyclopropanecarbonyl)-2-azabicyclo[2.2.1]heptan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-(6-(2-hydroxypropan-2-yl)pyridin-3-yl)-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

4-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-2-(2-(cyclopropanecarbonyl)-2-azabicyclo[2.2.1]heptan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-1H-pyrrolo[3,2-c]quinolin-4-yl)-2-fluoro-N-methylbenzamide;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-2-(2-(cyclopropanecarbonyl)-5-methyl-2-azabicyclo[2.2.1]heptan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-2-(2-(cyclopropanecarbonyl)-5-hydroxy-2-azabicyclo[2.2.1]heptan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-2-(2-(cyclopropanecarbonyl)-5-(pyridin-2-yloxy)-2-azabicyclo[2.2.1]heptan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-2-(2-(cyclopropanecarbonyl)-5-(pyridin-4-yloxy)-2-azabicyclo[2.2.1]heptan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-7-(2,3-dichlorophenyl)-2-(5-(difluoromethoxy)-2-(1-fluorocyclopropane-1-carbonyl)-2-azabicyclo[2.2.1]heptan-3-yl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-7-(2,3-dichlorophenyl)-6-fluoro-2-(5-fluoro-2-(1-fluorocyclopropane-1-carbonyl)-2-azabicyclo[2.2.1]heptan-3-yl)-4-(1-hydroxyethyl)-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-2-(5-chloro-2-(1-fluorocyclopropane-1-carbonyl)-2-azabicyclo[2.2.1]heptan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-(1-hydroxyethyl)-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-2-(2-(cyclopropanecarbonyl)-5-(trifluoromethoxy)-2-azabicyclo[2.2.1]heptan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-7-(2,3-dichlorophenyl)-2-(5-(difluoromethoxy)-2-(1-fluorocyclopropane-1-carbonyl)-2-azabicyclo[2.2.1]heptan-3-yl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-2-(2-(cyclopropanecarbonyl)-5-cyclopropoxy-2-azabicyclo[2.2.1]heptan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-7-(2,3-dichlorophenyl)-2-(5-(difluoromethoxy)-2-(1-fluorocyclopropane-1-carbonyl)-2-azabicyclo[2.2.1]heptan-3-yl)-6-fluoro-4-(1-hydroxyethyl)-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-2-(5-cyclopropoxy-2-(1-fluorocyclopropane-1-carbonyl)-2-azabicyclo[2.2.1]heptan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-(1-hydroxyethyl)-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

methyl 3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-2-yl)-5-(trifluoromethoxy)-2-azabicyclo[2.2.1]heptane-2-carboxylate;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-7-(2,3-dichlorophenyl)-6-fluoro-2-(2-(1-fluorocyclopropane-1-carbonyl)-5-(trifluoromethoxy)-2-azabicyclo[2.2.1]heptan-3-yl)-4-methyl-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

methyl 3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-2-yl)-5-(difluoromethyl)-2-azabicyclo[2.2.1]heptane-2-carboxylate; and

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-7-(2,3-dichlorophenyl)-2-(5-(difluoromethyl)-2-(1-fluorocyclopropane-1-carbonyl)-2-azabicyclo[2.2.1]heptan-3-yl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

and pharmaceutically acceptable salts thereof.

32. The use of any one of claims 26 to 31, wherein the KRAS G12D inhibitor is methyl (1*R*,3*R*,4*R*,5*S*)-3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-

dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)-5-(difluoromethoxy)-2-azabicyclo[2.2.1]heptane-2-carboxylate, or a pharmaceutically acceptable salt thereof.

33. The use of any one of claims 1 to 32, wherein the KRAS G12D inhibitor is to be administered in a pharmaceutical composition comprising the KRAS G12D inhibitor, or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier or excipient.

34. The use of any one of claims 1 to 33, wherein the PD-1 inhibitor or PD-L1 inhibitor is to be administered in a pharmaceutical composition comprising the PD-1 inhibitor or PD-L1, or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier or excipient.

35. Use of:

a pharmaceutical composition comprising a KRAS G12D inhibitor, or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier or excipient; and

a pharmaceutical composition comprising a PD-1 inhibitor or a PD-L1 inhibitor, or pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier or excipient,

in the manufacture of a medicament for treating cancer.

36. Use of a KRAS G12D inhibitor that is 3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile, or a pharmaceutically acceptable salt thereof, and a PD-1 inhibitor that is retifanlimab, in the manufacture of a medicament for treating cancer.

37. The use of claim 36, wherein the KRAS G12D inhibitor is 3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile hydrochloride dihydrate.

38. The use of claim 36 or 37, wherein the KRAS G12D inhibitor is 3-((R_a)-1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile hydrochloride dihydrate.

39. The use of claim 36 or 37, wherein the KRAS G12D inhibitor is 3-((S_a)-1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile hydrochloride dihydrate.

40. The use of any one of claims 1 to 39, wherein the KRAS G12D inhibitor is to be administered twice daily (BID).

41. The use of any one of claims 1 to 39, wherein the KRAS G12D inhibitor is to be administered once daily (QD).

42. The use of any one of claims 1 to 41, wherein the KRAS G12D inhibitor is to be administered orally (PO).

43. The use of any one of claims 1 to 42, wherein the PD-1 inhibitor is to be administered twice a week (BIW).

44. The use of any one of claims 1 to 43, wherein the PD-1 inhibitor is to be administered as an intraperitoneal injection (IP).

45. The use of any one of claims 1 to 44, wherein the cancer is selected from carcinomas, hematological cancers, sarcomas, and glioblastoma.

46. The use of any one of claims 1 to 45, wherein the cancer is a cancer comprising abnormally proliferating cells having a KRAS G12D mutation.

47. The use of any one of claims 1 to 45, wherein the use further comprises identifying the presence of abnormally proliferating cells having a KRAS G12D mutation.

48. The use of any one of claims 45 to 47, wherein the cancer is a hematological cancer selected from myeloproliferative neoplasms, myelodysplastic syndrome, chronic and juvenile myelomonocytic leukemia, acute myeloid leukemia, acute lymphocytic leukemia, and multiple myeloma.

49. The use of any one of claims 45 to 47, wherein the cancer is a carcinoma selected from pancreatic, colorectal, lung, bladder, gastric, esophageal, breast, head and neck, cervical, skin, and thyroid carcinomas.

50. The use of claim 49, wherein the carcinoma is colorectal carcinoma.

51. The use of claim 49, wherein the carcinoma is lung carcinoma.

52. The use of claim 49, wherein the carcinoma is pancreatic carcinoma.

53. The use of any one of claims 1 to 47, wherein the cancer is colorectal cancer.

54. The use of any one of claims 1 to 47, wherein the cancer is non-small cell lung cancer (NSCLC).

55. The use of any one of claims 1 to 47, wherein the cancer is pancreatic ductal adenocarcinoma.

56. The use of any one of claims 1 to 55, wherein the cancer is metastatic.

57. A pharmaceutical composition comprising

a) a KRAS G12D inhibitor, or a pharmaceutically acceptable salt thereof;

b) a PD-1 inhibitor or a PD-L1 inhibitor, or a pharmaceutically acceptable salt thereof; and

c) at least one pharmaceutically acceptable carrier or excipient.

58. The pharmaceutical composition of claim 57, wherein the KRAS G12D inhibitor is selected from

3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(7-chloro-3-hydroxynaphthalen-1-yl)-6-fluoro-2-methyl-4-(1H-1,2,4-triazol-1-yl)-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(5,7-difluoro-1H-indol-3-yl)-6-fluoro-2-methyl-4-((*S*)-1-((*S*)-1-methylpyrrolidin-2-yl)ethoxy)-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-6-fluoro-7-(6-fluoro-5-methyl-1*H*-indol-3-yl)-2-methyl-4-((*S*)-1-((*S*)-1-methylpyrrolidin-2-yl)ethoxy)-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile;

3-(2-(3-(azetidin-1-yl)-3-oxopropyl)-1-((*1R,4R,5S*)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-((*S*)-1-((*S*)-1-methylpyrrolidin-2-yl)ethoxy)-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile;

3-((1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-6-fluoro-7-(3-hydroxynaphthalen-1-yl)-8-methyl-4-((*S*)-1-((*S*)-1-methylpyrrolidin-2-yl)ethoxy)-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)methyl)oxazolidin-2-one;

8-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-6-fluoro-2,8-dimethyl-4-((*S*)-1-((*S*)-1-methylpyrrolidin-2-yl)ethoxy)-1*H*-pyrrolo[3,2-*c*]quinolin-7-yl)-1-naphthonitrile;

1-((2*S*,4*S*)-1-acetyl-2-(cyanomethyl)piperidin-4-yl)-7-(8-cyanonaphthalen-1-yl)-6-fluoro-4-((*S*)-1-((*S*)-1-methylpyrrolidin-2-yl)ethoxy)-1*H*-pyrazolo[4,3-*c*]quinoline-8-carbonitrile;

8-(1-((*1R*,*4R*,*5S*)-2-azabicyclo[2.1.1]hexan-5-yl)-6-fluoro-8-methyl-4-((*S*)-1-((*S*)-1-methylpyrrolidin-2-yl)ethoxy)-2-((3-oxomorpholino)methyl)-1*H*-pyrrolo[3,2-*c*]quinolin-7-yl)-1-naphthonitrile;

3-(7-(benzo[*b*]thiophen-3-yl)-1-((*1R*,*4R*,*5S*)-2-azabicyclo[2.1.1]hexan-5-yl)-6-fluoro-4-((*S*)-1-((*S*)-1-methylpyrrolidin-2-yl)ethoxy)-2-((2-oxopyrrolidin-1-yl)methyl)-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile;

3-(1-((*1R*,*4R*,*5S*)-2-azabicyclo[2.1.1]hexan-5-yl)-4-(((*S*)-1-(dimethylamino)propan-2-yl)oxy)-6-fluoro-7-(7-fluoronaphthalen-1-yl)-2-((2-oxopyrrolidin-1-yl)methyl)-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile;

8-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-6-fluoro-2-methyl-4-((*S*)-1-((*S*)-1-methylpyrrolidin-2-yl)ethoxy)-1*H*-pyrrolo[3,2-*c*]quinolin-7-yl)-1-naphthonitrile;

3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(2,3-dichloro-5-hydroxyphenyl)-6-fluoro-2-methyl-4-((*S*)-1-((*S*)-1-methylpyrrolidin-2-yl)ethoxy)-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile;

3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-6-fluoro-4-((3-fluoro-1-methylazetidin-3-yl)methoxy)-7-(3-hydroxynaphthalen-1-yl)-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)-*N*,*N*-dimethylpropanamide;

3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-6-fluoro-7-(3-hydroxynaphthalen-1-yl)-2-methyl-4-(5-methylpyrazin-2-yl)-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile;

3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-6-fluoro-7-(7-fluoronaphthalen-1-yl)-4-methyl-2-((4-methyl-2-oxopiperazin-1-yl)methyl)-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile;

3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(2,3-dichloro-5-hydroxyphenyl)-4-ethoxy-6-fluoro-2-((4-isopropyl-2-oxopiperazin-1-yl)methyl)-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile;

3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-4-(3-(dimethylamino)-3-methylazetidin-1-yl)-6-fluoro-7-(7-fluoronaphthalen-1-yl)-2-((3-oxomorpholino)methyl)-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile;

3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-4-ethoxy-6-fluoro-7-(3-hydroxynaphthalen-1-yl)-2-(1-(3-oxomorpholino)ethyl)-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile;

3-(1-((endo)-2-azabicyclo[2.1.1]hexan-5-yl)-6-fluoro-7-(3-hydroxynaphthalen-1-yl)-4-((*S*)-1-((*S*)-1-methylpyrrolidin-2-yl)ethoxy)-2-(pyridin-3-yl)-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile;

3-(2-(3-(azetidin-1-yl)-3-oxopropyl)-1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(7,8-difluoronaphthalen-1-yl)-6-fluoro-4-((S)-1-((S)-1-methylpyrrolidin-2-yl)ethoxy)-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(2-(3-(azetidin-1-yl)-3-oxopropyl)-1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(6,7-difluoronaphthalen-1-yl)-6-fluoro-4-((S)-1-((S)-1-methylpyrrolidin-2-yl)ethoxy)-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-6-fluoro-7-(7-fluoro-3-hydroxynaphthalen-1-yl)-2-methyl-4-((S)-1-((S)-1-methylpyrrolidin-2-yl)ethoxy)-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

1-(1-((2*S*,4*S*)-1-acetyl-2-(cyanomethyl)piperidin-4-yl)-8-chloro-6-fluoro-4-((*S*)-1-((*S*)-1-methylpyrrolidin-2-yl)ethoxy)-1*H*-pyrazolo[4,3-*c*]quinolin-7-yl)isoquinoline-8-carbonitrile;

8-(1-((2*S*,4*S*)-1-acetyl-2-(cyanomethyl)piperidin-4-yl)-8-chloro-6-fluoro-4-((*S*)-1-((*S*)-1-methylpyrrolidin-2-yl)ethoxy)-1*H*-pyrrolo[3,2-*c*]quinolin-7-yl)-1-naphthonitrile;

8-(1-((2*S*,4*S*)-1-acetyl-2-(cyanomethyl)piperidin-4-yl)-8-chloro-6-fluoro-4-((*S*)-1-((*S*)-1-methylpyrrolidin-2-yl)ethoxy)-1*H*-pyrazolo[4,3-*c*]quinolin-7-yl)-1-naphthonitrile;

3-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-6-fluoro-7-(7-fluoro-3-hydroxynaphthalen-1-yl)-2-methyl-4-(1*H*-1,2,4-triazol-1-yl)-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile;

3-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-6-fluoro-7-(7-fluoronaphthalen-1-yl)-2-methyl-4-((S)-1-((S)-1-methylpyrrolidin-2-yl)ethoxy)-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

(2*R*)-2-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-(1*H*-1,2,4-triazol-1-yl)-1*H*-pyrrolo[3,2-c]quinolin-2-yl)-*N*,*N*-dimethylpyrrolidine-1-carboxamide;

methyl (2*R*)-2-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(2-chloro-3-methylphenyl)-8-(2-cyanoethyl)-6-fluoro-4-(1*H*-1,2,4-triazol-1-yl)-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)pyrrolidine-1-carboxylate;

methyl (1S,3R,5S)-3-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-4-(6-(dimethylcarbamoyl)pyridin-3-yl)-6-fluoro-1H-pyrrolo[3,2-c]quinolin-2-yl)-2-azabicyclo[3.1.0]hexane-2-carboxylate;

3-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-2-(5-oxo-1,2,3,5-tetrahydroindolizin-3-yl)-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

methyl (2R)-2-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-4-(6-(dimethylcarbamoyl)pyridin-3-yl)-6-fluoro-1H-pyrrolo[3,2-c]quinolin-2-yl)pyrrolidine-1-carboxylate;

methyl (2R)-2-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-(6-(methylcarbamoyl)pyridin-3-yl)-1H-pyrrolo[3,2-c] quinolin-2-yl)pyrrolidine-1-carboxylate;

3-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(2-chloro-3-fluorophenyl)-2-((R)-1-(cyclopropanecarbonyl)pyrrolidin-2-yl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

8-(2-((R)-1-acetylpyrrolidin-2-yl)-1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-6-fluoro-8-methyl-4-(2-methylpyridin-4-yl)-1H-pyrrolo[3,2-c]quinolin-7-yl)-1,2,3,4-tetrahydronaphthalene-1-carbonitrile;

5-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(3-chloro-2-methylphenyl)-8-(2-cyanoethyl)-6-fluoro-2-((R)-1-(2-oxopyrazin-1(2H)-yl)ethyl)-1H-pyrrolo[3,2-c]quinolin-4-yl)-N-methylpicolinamide;

3-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-6-fluoro-7-(7-fluoronaphthalen-1-yl)-4-(6-(2-hydroxypropan-2-yl)pyridin-3-yl)-2-((R)-1-(2-oxopyrazin-1(2H)-yl)ethyl)-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(3-chloro-2-methylphenyl)-6-fluoro-4-(5-methylpyrazin-2-yl)-2-((R)-1-(2-oxopyrazin-1(2H)-yl)ethyl)-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

methyl (2R)-2-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-(5-fluoro-6-(methylcarbamoyl)pyridin-3-yl)-1H-pyrrolo[3,2-c]quinolin-2-yl)pyrrolidine-1-carboxylate;

methyl (2R)-2-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-(6-(2-hydroxypropan-2-yl)pyridin-3-yl)-1H-pyrrolo[3,2-c]quinolin-2-yl)pyrrolidine-1-carboxylate;

ethyl (2R)-2-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-(6-(2-hydroxypropan-2-yl)pyridin-3-yl)-1H-pyrrolo[3,2-c]quinolin-2-yl)pyrrolidine-1-carboxylate;

3-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(2,3-dichlorophenyl)-2-((R)-1-(3,3-difluoroazetidine-1-carbonyl)pyrrolidin-2-yl)-6-fluoro-4-(methyl-d3)-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(2,3-dichlorophenyl)-2-((R)-1-(3,3-difluoroazetidine-1-carbonyl)pyrrolidin-2-yl)-6-fluoro-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(3-chloro-2-methylphenyl)-6-fluoro-4-(5-methylpyrazin-2-yl)-2-((R)-1-(3-oxomorpholino)ethyl)-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

5-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-6-fluoro-7-(7-fluoronaphthalen-1-yl)-2-((R)-1-(3-oxomorpholino)ethyl)-1H-pyrrolo[3,2-c]quinolin-4-yl)-N-methylpicolinamide;

3-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-6-fluoro-7-(7-fluoronaphthalen-1-yl)-4-(6-(2-hydroxypropan-2-yl)pyridin-3-yl)-2-((R)-1-(3-oxomorpholino)ethyl)-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-6-fluoro-7-(7-fluoronaphthalen-1-yl)-4-(5-methylpyrazin-2-yl)-2-((R)-1-(3-oxomorpholino)ethyl)-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

methyl (1R,3R,5R)-3-(1-((1R,4R,5S)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-4-(6-(dimethylcarbamoyl)pyridin-3-yl)-6-fluoro-1H-pyrrolo[3,2-c]quinolin-2-yl)-2-azabicyclo[3.1.0]hexane-2-carboxylate;

3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile;

3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-(6-(2-hydroxypropan-2-yl)pyridin-3-yl)-2-((*R*)-1-(2-oxopyrazin-1(2*H*)-yl)ethyl)-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile;

methyl (2*R*,4*S*)-2-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-(6-(2-hydroxypropan-2-yl)pyridin-3-yl)-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)-4-fluoropyrrolidine-1-carboxylate;

methyl (2*R*,5*R*)-2-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-(6-(2-hydroxypropan-2-yl)pyridin-3-yl)-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)-5-methylpyrrolidine-1-carboxylate;

methyl (2*R*)-2-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-3-chloro-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-(6-(2-hydroxypropan-2-yl)pyridin-3-yl)-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)pyrrolidine-1-carboxylate;

4-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-2-((*R*)-1-(2-oxopyrazin-1(2*H*)-yl)ethyl)-1*H*-pyrrolo[3,2-c]quinolin-4-yl)-2-fluoro-*N*-methylbenzamide;

methyl ((1*R*)-1-(1-((*1R*,*4R*,*5S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)ethyl)carbamate;

N-((1*R*)-1-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)ethyl)-2,2-difluoroacetamide;

N-((1*R*)-1-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)ethyl)-2,2-difluoroacetamide;

(2*S*)-*N*-((1*R*)-1-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)ethyl)tetrahydrofuran-2-carboxamide;

N-((1*R*)-1-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)ethyl)cyclopropanesulfonamide;

N-((1*R*)-1-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)ethyl)thiazole-4-carboxamide;

N-((1*R*)-1-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)ethyl)-*N*-methylcyclopropanecarboxamide;

N-((1*R*)-1-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-(1-hydroxyethyl)-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)ethyl)-1-methylcyclopropane-1-carboxamide;

3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-(1-hydroxyethyl)-2-((1*R*,3*R*,5*R*)-2-(1-methylcyclopropane-1-carbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile;

3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(2,3-dichlorophenyl)-6-fluoro-2-((1*R*,3*R*,5*R*)-2-(1-fluorocyclopropane-1-carbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-4-(1-hydroxyethyl)-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile;

3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(2,3-dichlorophenyl)-6-fluoro-2-((1*R*,3*R*,5*R*)-2-(1-fluorocyclopropane-1-carbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile;

N-((1*R*)-1-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-(1-hydroxyethyl)-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)ethyl)-1-fluorocyclopropane-1-carboxamide;

N-((1*R*)-1-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-(1-hydroxyethyl)-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)ethyl)-1-fluorocyclobutane-1-carboxamide;

3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(3-chloro-2-methylphenyl)-2-(1-(2,6-dimethyl-3-oxo-2,3-dihydropyridazin-4-yl)ethyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile;

N-((1*R*)-1-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)ethyl)pyrimidine-4-carboxamide;

N-((1*R*)-1-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)ethyl)pyridazine-3-carboxamide;

N-((1*R*)-1-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)ethyl)-3,3-difluoroazetidine-1-carboxamide;

3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-2-((*R*)-1-((1-methyl-1*H*-pyrazol-4-yl)amino)ethyl)-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile;

5-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-2-((*R*)-1-(1-fluorocyclopropane-1-carbonyl)pyrrolidin-2-yl)-1*H*-pyrrolo[3,2-*c*]quinolin-4-yl)-N,N-dimethylpicolinamide; and

methyl (2*R*)-2-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-4-(4-((dimethylamino)methyl)-2,3-difluorophenyl)-6-fluoro-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)pyrrolidine-1-carboxylate;

and pharmaceutically acceptable salts thereof.

59. The pharmaceutical composition of claim 57 or 58, wherein the KRAS G12D inhibitor is 3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile, or a pharmaceutically acceptable salt thereof.

60. The pharmaceutical composition of any one of claims 57 to 59, wherein the KRAS G12D inhibitor is 3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile hydrochloride dihydrate.

61. The pharmaceutical composition of any one of claims 57 to 60, wherein the KRAS G12D inhibitor is 3-((R_a)-1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile hydrochloride dihydrate.

62. The pharmaceutical composition of any one of claims 57 to 60, wherein the KRAS G12D inhibitor is 3-((S_a)-1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile hydrochloride dihydrate.

63. The pharmaceutical composition of claim 57, wherein the KRAS G12D inhibitor is selected from:

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-2-(2-(cyclopropanecarbonyl)-5-methoxy-2-azabicyclo[2.2.1]heptan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-2-(2-(cyclopropanecarbonyl)-5-fluoro-2-azabicyclo[2.2.1]heptan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-2-(6-(cyclopropanecarbonyl)-6-azatricyclo[3.2.1.02,4]octan-7-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-2-(2-(cyclopropanecarbonyl)-5-(methoxy-d3)-2-azabicyclo[2.2.1]heptan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-2-(2-(cyclopropanecarbonyl)-5-(pyridin-3-yloxy)-2-azabicyclo[2.2.1]heptan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(2-(5-(benzyloxy)-2-(cyclopropanecarbonyl)-2-azabicyclo[2.2.1]heptan-3-yl)-1-(2-azabicyclo[2.1.1]hexan-5-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-2-(2-(cyclopropanecarbonyl)-5-(difluoromethoxy)-2-azabicyclo[2.2.1]heptan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-7-(2,3-dichlorophenyl)-6-fluoro-2-(5-fluoro-2-(1-fluorocyclopropane-1-carbonyl)-2-azabicyclo[2.2.1]heptan-3-yl)-4-((R)-1-hydroxyethyl)-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-2-(2-(cyclopropanecarbonyl)-5-(difluoromethyl)-2-azabicyclo[2.2.1]heptan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-2-(2-(cyclopropanecarbonyl)-2-azabicyclo[2.2.1]heptan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

5-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-2-(2-(cyclopropanecarbonyl)-2-azabicyclo[2.2.1]heptan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-1H-pyrrolo[3,2-c]quinolin-4-yl)-N,N-dimethylpicolinamide;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-2-(2-(cyclopropanecarbonyl)-2-azabicyclo[2.2.1]heptan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-(6-(2-hydroxypropan-2-yl)pyridin-3-yl)-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

4-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-2-(2-(cyclopropanecarbonyl)-2-azabicyclo[2.2.1]heptan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-1H-pyrrolo[3,2-c]quinolin-4-yl)-2-fluoro-N-methylbenzamide;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-2-(2-(cyclopropanecarbonyl)-5-methyl-2-azabicyclo[2.2.1]heptan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-2-(2-(cyclopropanecarbonyl)-5-hydroxy-2-azabicyclo[2.2.1]heptan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-2-(2-(cyclopropanecarbonyl)-5-(pyridin-2-yloxy)-2-azabicyclo[2.2.1]heptan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-2-(2-(cyclopropanecarbonyl)-5-(pyridin-4-yloxy)-2-azabicyclo[2.2.1]heptan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-7-(2,3-dichlorophenyl)-2-(5-(difluoromethoxy)-2-(1-fluorocyclopropane-1-carbonyl)-2-azabicyclo[2.2.1]heptan-3-yl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-7-(2,3-dichlorophenyl)-6-fluoro-2-(5-fluoro-2-(1-fluorocyclopropane-1-carbonyl)-2-azabicyclo[2.2.1]heptan-3-yl)-4-(1-hydroxyethyl)-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-2-(5-chloro-2-(1-fluorocyclopropane-1-carbonyl)-2-azabicyclo[2.2.1]heptan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-(1-hydroxyethyl)-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-2-(2-(cyclopropanecarbonyl)-5-(trifluoromethoxy)-2-azabicyclo[2.2.1]heptan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-7-(2,3-dichlorophenyl)-2-(5-(difluoromethoxy)-2-(1-fluorocyclopropane-1-carbonyl)-2-azabicyclo[2.2.1]heptan-3-yl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-2-(2-(cyclopropanecarbonyl)-5-cyclopropoxy-2-azabicyclo[2.2.1]heptan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-7-(2,3-dichlorophenyl)-2-(5-(difluoromethoxy)-2-(1-fluorocyclopropane-1-carbonyl)-2-azabicyclo[2.2.1]heptan-3-yl)-6-fluoro-4-(1-hydroxyethyl)-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-2-(5-cyclopropoxy-2-(1-fluorocyclopropane-1-carbonyl)-2-azabicyclo[2.2.1]heptan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-(1-hydroxyethyl)-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

methyl 3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-2-yl)-5-(trifluoromethoxy)-2-azabicyclo[2.2.1]heptane-2-carboxylate;

3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-7-(2,3-dichlorophenyl)-6-fluoro-2-(2-(1-fluorocyclopropane-1-carbonyl)-5-(trifluoromethoxy)-2-azabicyclo[2.2.1]heptan-3-yl)-4-methyl-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

methyl 3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-2-yl)-5-(difluoromethyl)-2-azabicyclo[2.2.1]heptane-2-carboxylate; and

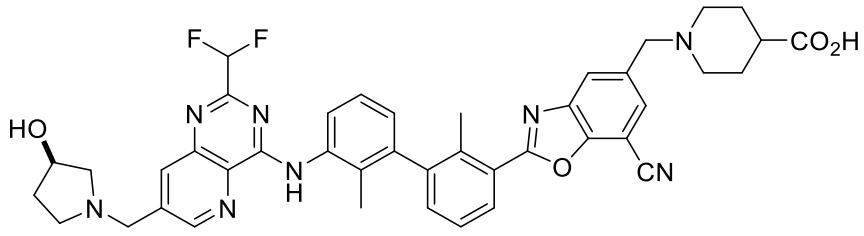
3-(1-(2-azabicyclo[2.1.1]hexan-5-yl)-7-(2,3-dichlorophenyl)-2-(5-(difluoromethyl)-2-(1-fluorocyclopropane-1-carbonyl)-2-azabicyclo[2.2.1]heptan-3-yl)-6-fluoro-4-methyl-1H-pyrrolo[3,2-c]quinolin-8-yl)propanenitrile;

and pharmaceutically acceptable salts thereof.

64. The pharmaceutical composition of claim 57 or 63, wherein the KRAS G12D inhibitor is methyl (1*R*,3*R*,4*R*,5*S*)-3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)-5-(difluoromethoxy)-2-azabicyclo[2.2.1]heptane-2-carboxylate, or a pharmaceutically acceptable salt thereof.

65. The pharmaceutical composition of any one of claims 57 to 64, wherein the PD-1 inhibitor is retifanlimab.

66. The pharmaceutical composition of any one of claims 57 to 64, wherein the PD-L1 inhibitor is



or a pharmaceutically acceptable salt thereof.

67. A pharmaceutical combination comprising a KRAS G12D inhibitor, or a pharmaceutically acceptable salt thereof, and a PD-1 inhibitor or a PD-L1 inhibitor, or pharmaceutically acceptable salt thereof.

68. The pharmaceutical combination of claim 67, wherein the KRAS G12D inhibitor is 3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile, or a pharmaceutically acceptable salt thereof.

69. The pharmaceutical combination of claim 67 or 68, wherein the KRAS G12D inhibitor is 3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile hydrochloride dihydrate.

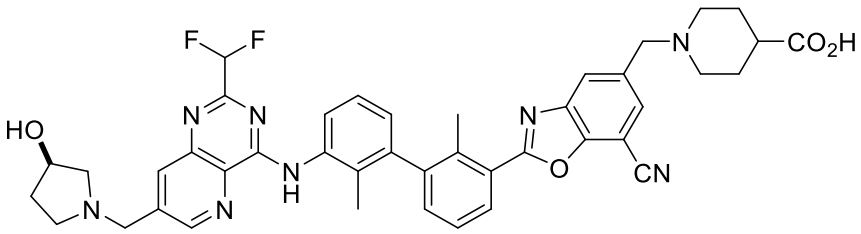
70. The pharmaceutical combination of any one of claims 67 to 69, wherein the KRAS G12D inhibitor is 3-((R_a)-1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile hydrochloride dihydrate.

71. The pharmaceutical combination of any one of claims 67 to 69, wherein the KRAS G12D inhibitor is 3-((S_a)-1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile hydrochloride dihydrate.

72. The pharmaceutical combination of claim 67, wherein the KRAS G12D inhibitor is the KRAS G12D inhibitor is methyl (1*R*,3*R*,4*R*,5*S*)-3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-8-(2-cyanoethyl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-2-yl)-5-(difluoromethoxy)-2-azabicyclo[2.2.1]heptane-2-carboxylate, or a pharmaceutically acceptable salt thereof.

73. The pharmaceutical combination of any one of claims 67 to 72, wherein the PD-1 inhibitor is retifanlimab.

74. The pharmaceutical combination of any one of claims 67 to 72, wherein the PD-L1 inhibitor is



or a pharmaceutically acceptable salt thereof.