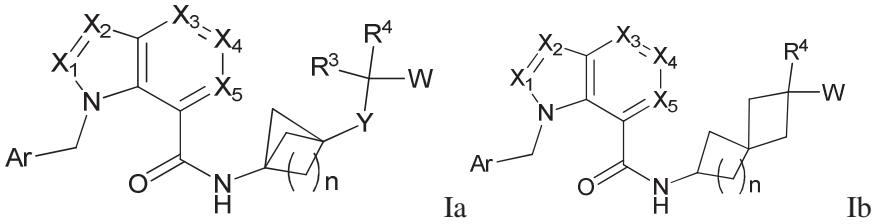
[0053] In some examples, n is 1.

[0053a] In one aspect, provided herein is a compound of Formula Ia or Ib:



Ia Ib

or a pharmaceutically acceptable salt, solvate, solvate of the salt, hydrate, a single stereoisomer, a mixture of stereoisomers, or a racemic mixture of stereoisomers thereof, wherein:

Ar is phenyl and is optionally substituted with 1 to 3 substituents independently selected from:

(a) C_1-C_6 alkyl,

(b) C_3-C_7 cycloalkyl,

(c) heterocycle,

(d) aryl,

(e) heteroaryl,

(f) halogen,

(g) CN,

(h) OR^b,

(i) $N(R^b)C(=O)R^c$,

(j) $C(=O)N(R^b)(R^c)$,

(k) $S(=O)_mR^b$,

(l) $S(=O)_2N(R^b)(R^c)$,

(m) $N(R^b)S(=O)_2R^c$,

(n) SF_5; and

(o) C_1-C_6 haloalkyl;

W is $C(=O)OR^5$, $NHC(=O)NHSO_2R^b$, $C(=O)NHS(=O)_2R^b$, or 1*H*-tetrazole;

X^1, X^2, X^3, X^4, and X^5 are each independently N or CR^a, wherein not more than 2 of X^1, X^2, X^3, X^4, and X^5 are N;

Y is a bond or $-CH_2-$;

R^3 and R^4 are independently selected from H, C_1-C_3 alkyl, and C_1-C_3 haloalkyl;

R^5 is H or C_1-C_6 alkyl;

R^a is selected from:

(a) H,

(b) C_1-C_6 alkyl,

(c) halogen,

(d) aryl,

(e) OR^b,

(f) cyano,

(g) heteroaryl,

(h) C_3-C_6 cycloalkyl, and

(i) C_1-C_6 haloalkyl;

R^b and R^c are independently selected from:

(a) H,

(b) C_1-C_6 alkyl,

(c) aryl,

(d) heteroaryl,

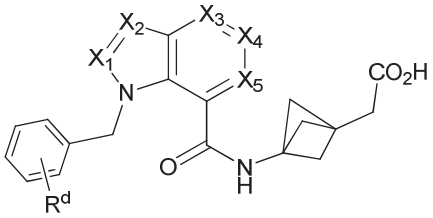
(e) C_3-C_6 cycloalkyl, and

(f) C_1-C_6 haloalkyl; or

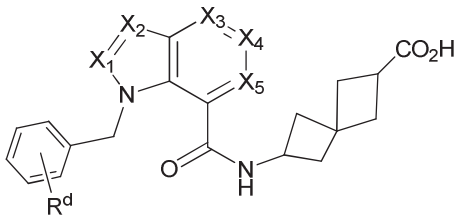
R^b and R^c taken together with the N to which they are both attached form a 3- to 6-membered heterocycle optionally having an additional heteroatom selected from N, O and S;

n is 1, 2 or 3.

[0054] Some examples provided herein describe a compound of Formula I having the Formula Ic or Id:



Ic



Id

or a pharmaceutically acceptable salt, solvate, solvate of the salt, hydrate, a single stereoisomer, a mixture of stereoisomers, a racemic mixture of stereoisomers, or prodrug thereof.

[0055] In some examples, each X^1, X^2, X^3, X^4 and X^5 is independently C-R^a.

[0056] In some examples, one of X^1, X^2, X^3, X^4 and X^5 is N, and the others are each independently C-R^a.

[0057] In some examples, R^a is selected from the group consisting of H and halogen.

[0058] In some examples, R^d is selected from:

(a) CN,

(b) C_1-C_3 alkyl,

(c) SF_5,

(d) C_1-C_3 haloalkyl,

(e) OR^b wherein R^b is C_1-C_6 alkyl, aryl, heteroaryl, C_3-C_6 cycloalkyl or C_1-C_6 haloalkyl,

(f) heterocycle,

(g) aryl, and

(h) heteroaryl.

[0059] In some examples, R^d is selected from the group consisting of: (a) CN, (b) C_1-C_3 alkyl, (c) SF_5, and (d) C_1-C_3 haloalkyl.

[0060] In some examples, each X^1, X^2, X^3, X^4 and X^5 is CH; or one of X^1, X^2, X^3, X^4 and X^5 is C-R^a and the others are CH, and R^a is halogen.

[0061] In some examples, the compound is selected from:

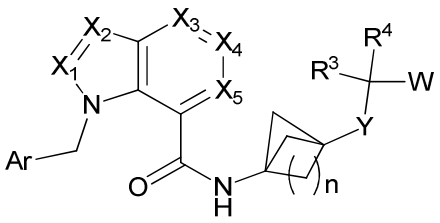
2-(3-(1-(4-cyanobenzyl)-1*H*-indole-7-carboxamido)bicyclo[1.1.1]pentan-1-yl)acetic acid;

2-(3-(1-(4-(trifluoromethyl)benzyl)-1*H*-indole-7-carboxamido)bicyclo[1.1.1]pentan-1-yl)acetic acid;

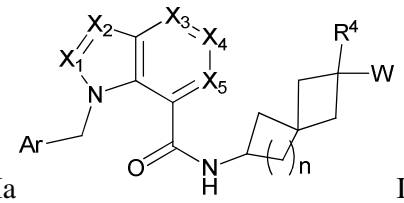
CLAIMS

WHAT IS CLAIMED IS:

1. A compound of Formula Ia or Ib:



Ia



Ib

or a pharmaceutically acceptable salt, solvate, solvate of the salt, hydrate, a single stereoisomer, a mixture of stereoisomers, or a racemic mixture of stereoisomers thereof, wherein:

Ar is phenyl and is optionally substituted with 1 to 3 substituents independently selected from:

(a) C_1-C_6 alkyl,

(b) C_3-C_7 cycloalkyl,

(c) heterocycle,

(d) aryl,

(e) heteroaryl,

(f) halogen,

(g) CN,

(h) OR^b,

(i) $N(R^b)C(=O)R^c$,

(j) $C(=O)N(R^b)(R^c)$,

(k) $S(=O)_mR^b$,

(l) $S(=O)_2N(R^b)(R^c)$,

(m) $N(R^b)S(=O)_2R^c$,

(n) SF_5; and

(o) C_1-C_6 haloalkyl;

W is $C(=O)OR^5$, $NHC(=O)NHSO_2R^b$, $C(=O)NHS(=O)_2R^b$, or 1*H*-tetrazole;

X^1, X^2, X^3, X^4, and X^5 are each independently N or CR^a, wherein not more than 2 of X^1, X^2, X^3, X^4, and X^5 are N;

Y is a bond or $-CH_2-$;

R^3 and R^4 are independently selected from H, C_1-C_3 alkyl, and C_1-C_3 haloalkyl;

R^5 is H or C_1-C_6 alkyl;

R^a is selected from:

(a) H,

(b) C_1-C_6 alkyl,

(c) halogen,

(d) aryl,

(e) OR^b,

(f) cyano,

(g) heteroaryl,

(h) C_3-C_6 cycloalkyl, and

(i) C_1-C_6 haloalkyl;

R^b and R^c are independently selected from:

(a) H,

(b) C_1-C_6 alkyl,

(c) aryl,

(d) heteroaryl,

(e) C_3-C_6 cycloalkyl, and

(f) C_1-C_6 haloalkyl; or

R^b and R^c taken together with the N to which they are both attached form a 3- to 6-membered heterocycle optionally having an additional heteroatom selected from N, O and S;

n is 1, 2 or 3.

2. A compound of Claim 1, or a pharmaceutically acceptable salt, solvate, solvate of the salt, hydrate, a single stereoisomer, a mixture of stereoisomers, or a racemic mixture of stereoisomers thereof, wherein Ar is phenyl optionally substituted with 1 to 3 substituents independently selected from:

(a) halogen,

(b) cyano,

(c) C_1-C_6 alkyl,

(d) SF_5,

(e) C_1-C_6 haloalkyl,

(f) OR^b wherein R^b is C_1-C_6 alkyl, aryl, heteroaryl, C_3-C_6 cycloalkyl or C_1-C_6 haloalkyl;

(g) heterocycle,

(h) aryl, and

(i) heteroaryl.

3. A compound of claim 1 or 2, or a pharmaceutically acceptable salt, solvate, solvate of the salt, hydrate, a single stereoisomer, a mixture of stereoisomers, or a racemic mixture

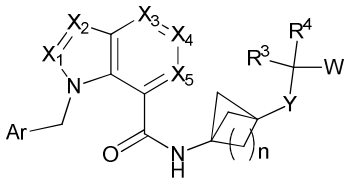
of stereoisomers thereof, wherein each of X^1, X^2, X^3, X^4 and X^5 is independently C-R^a, or one of X^1, X^2, X^3, X^4 and X^5 is N, and the others are each independently C-R^a.

4. A compound of Claim 3, or a pharmaceutically acceptable salt, solvate, solvate of the salt, hydrate, a single stereoisomer, a mixture of stereoisomers, or a racemic mixture of stereoisomers thereof, wherein each of X^1, X^2, X^3, X^4 and X^5 is independently C-R^a.

5. A compound of any of Claims 1 to 4, or a pharmaceutically acceptable salt, solvate, solvate of the salt, hydrate, a single stereoisomer, a mixture of stereoisomers, or a racemic mixture of stereoisomers thereof, wherein R^a is H or a halogen atom.

6. A compound of any of Claims 1 to 5, or a pharmaceutically acceptable salt, solvate, solvate of the salt, hydrate, a single stereoisomer, a mixture of stereoisomers, or a racemic mixture of stereoisomers thereof, wherein W is CO_2H or 1*H*-tetrazole.

7. A compound of Claim 1 having the Formula Ia:



Ia

or a pharmaceutically acceptable salt, solvate, solvate of the salt, hydrate, a single stereoisomer, a mixture of stereoisomers, or a racemic mixture of stereoisomers thereof, wherein

Ar is phenyl optionally substituted with 1 to 3 substituents independently selected from:

(a) halogen,

(b) cyano,

(c) C_1-C_6 alkyl,

(d) SF_5,

(e) C_1-C_6 haloalkyl,

(f) OR^b wherein R^b is C_1-C_6 alkyl, aryl, heteroaryl, C_3-C_6 cycloalkyl or C_1-C_6 haloalkyl,

(g) heterocycle,

(h) aryl, and

(i) heteroaryl;

each X^1, X^2, X^3, X^4 and X^5 is independently C-R^a, or one of X^1, X^2, X^3, X^4 and X^5 is N, and the others are each independently C-R^a;

W is CO_2H or 1*H*-tetrazole;

Y is a bond or -CH_2-;

n is 1 or 2;

R^3 and R^4 are independently selected from:

(a) H,

(b) C_1-C_3 alkyl, and

(c) C_1-C_3 haloalkyl;

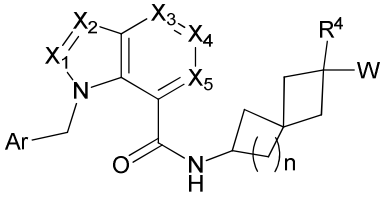
R^a is selected from:

(a) H, and

(b) halogen.

8. A compound of any of Claims 1 to 7, or a pharmaceutically acceptable salt, solvate, solvate of the salt, hydrate, a single stereoisomer, a mixture of stereoisomers, or a racemic mixture of stereoisomers thereof, wherein Y is a bond, and n is 1.

9. A compound of Claim 1 having the Formula Ib:



Ib

or a pharmaceutically acceptable salt, solvate, solvate of the salt, hydrate, a single stereoisomer, a mixture of stereoisomers, or a racemic mixture of stereoisomers thereof, wherein

Ar is phenyl optionally substituted with 1 to 3 substituents independently selected from:

(a) halogen,

(b) cyano,

(c) C_1-C_6 alkyl,

(d) SF_5,

(e) C_1-C_6 haloalkyl,

(f) OR^b wherein R^b is C_1-C_6 alkyl, aryl, heteroaryl, C_3-C_6 cycloalkyl or C_1-C_6 haloalkyl,

(g) heterocycle,

(h) aryl, and

(i) heteroaryl;

each X^1, X^2, X^3, X^4 and X^5 is independently C-R^a, or one of X^1, X^2, X^3, X^4 and X^5 is N, and the others are each independently C-R^a;

W is CO_2H or 1*H*-tetrazole;

n is 1 or 2;

R^4 is selected from:

(a) H,

(b) C_1-C_3 alkyl, and

(c) C_1-C_3 haloalkyl;

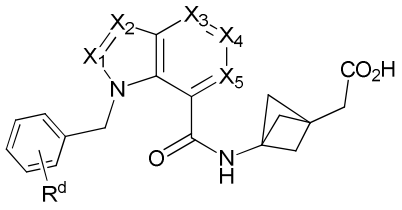
R^a is selected from:

(a) H, and

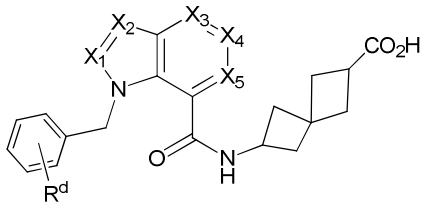
(b) halogen.

10. A compound of Claim 9, or a pharmaceutically acceptable salt, solvate, solvate of the salt, hydrate, a single stereoisomer, a mixture of stereoisomers, or a racemic mixture of stereoisomers thereof, wherein n is 1.

11. A compound of Claim 1 having the Formula Ic or Id:



Ic



Id

or a pharmaceutically acceptable salt, solvate, solvate of the salt, hydrate, a single stereoisomer, a mixture of stereoisomers, or a racemic mixture of stereoisomers thereof, wherein each X^1, X^2, X^3, X^4 and X^5 is independently C-R^a, or one of X^1, X^2, X^3, X^4 and X^5 is N, and the others are each independently C-R^a;

R^a is selected from :

(a) H, and

(b) halogen;

R^d is selected from :

(a) CN,

(b) C_1-C_3 alkyl,

(c) SF_5,

(d) C_1-C_3 haloalkyl,

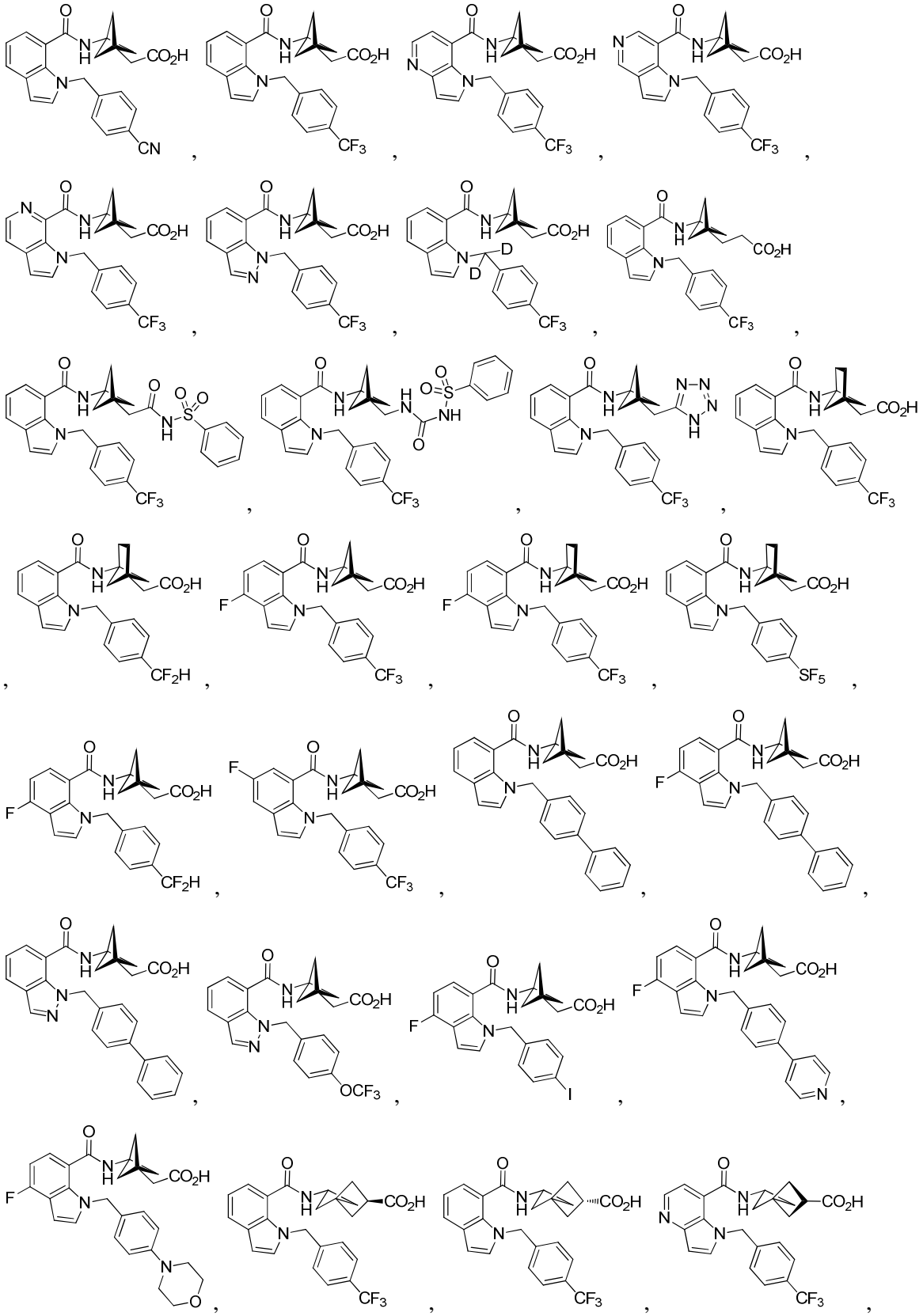
(e) OR^b wherein R^b is C_1-C_6 alkyl, aryl, heteroaryl, C_3-C_6 cycloalkyl or C_1-C_6 haloalkyl,

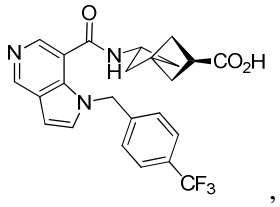
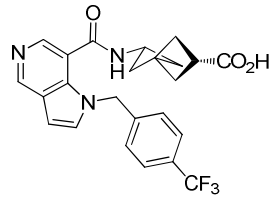
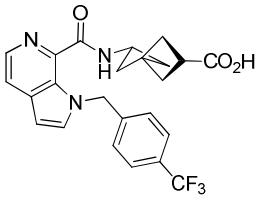
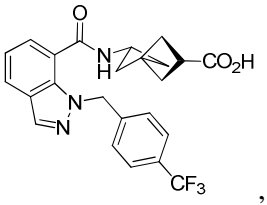
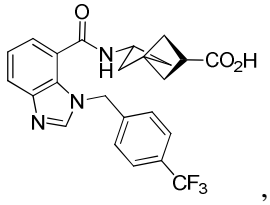
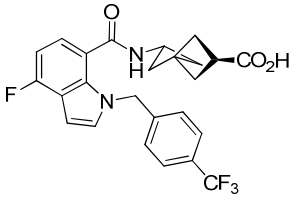
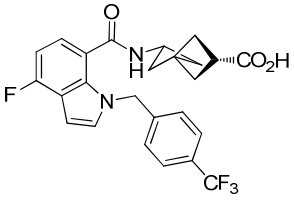
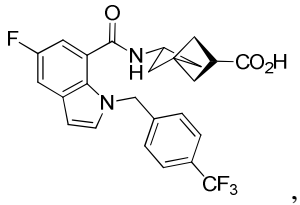
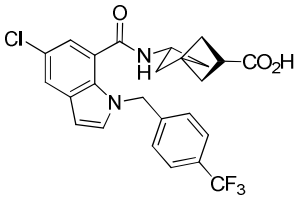
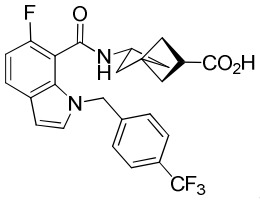
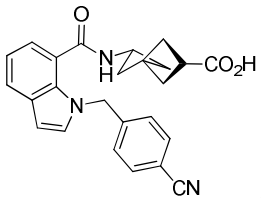
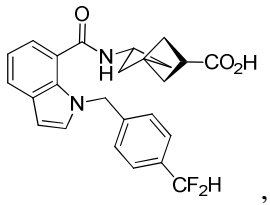
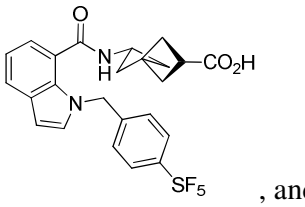
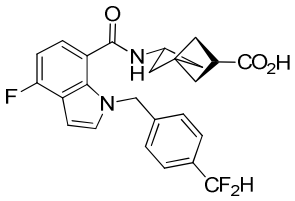
(f) heterocycle,

(g) aryl, and

(h) heteroaryl.

12. A compound of Claim 1 selected from the group consisting of:




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,

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, and

; or a pharmaceutically acceptable salt, solvate, or solvate of the salt thereof.

13. A pharmaceutical composition comprising a compound of any of Claims 1 to 12, or a pharmaceutically acceptable salt, solvate, solvate of the salt, hydrate, a single stereoisomer, a mixture of stereoisomers, or a racemic mixture of stereoisomers thereof, and a pharmaceutically acceptable carrier.

14. Use of a compound of any of Claims 1 to 12, or the pharmaceutical composition of Claim 13 in the manufacture of a medicament for the treatment of cancer, wherein the medicament is to be administered to a patient in need thereof.

15. The use of Claim 14, wherein said cancer is selected from glioblastoma, bone cancer, head and neck cancer, melanoma, basal cell carcinoma, squamous cell carcinoma, adenocarcinoma, oral cancer, esophageal cancer, gastric cancer, intestinal cancer, colon cancer, bladder cancer, hepatocellular carcinoma, renal cell carcinoma, pancreatic cancer, ovarian cancer, cervical cancer, lung cancer, breast cancer, and prostate cancer.

16. The use of Claim 14 or Claim 15, wherein said cancer is selected from colon cancer, bladder cancer, hepatocellular carcinoma, pancreatic cancer, ovarian cancer, cervical cancer, lung cancer, breast cancer, and prostate cancer.

17. The use of any of Claims 14 to 16, wherein the medicament is to be further administered with an additional agent selected from an anti-PD-1 antibody and an anti-PD-L1 antibody.

18. A compound of any of Claims 1 to 12 or the pharmaceutical composition of Claim 13 for use in therapy.