[0009] EP_2 and EP_4 are highly expressed in endometriosis and there is data that suggests that EP_2/EP_4 inhibition may serve as nonsteroidal therapy for endometriosis (Arosh J.A. *et al., Proc. Natl. Acad. Sci. U.S.A.* **2015**, 112, p. 9716-9721).

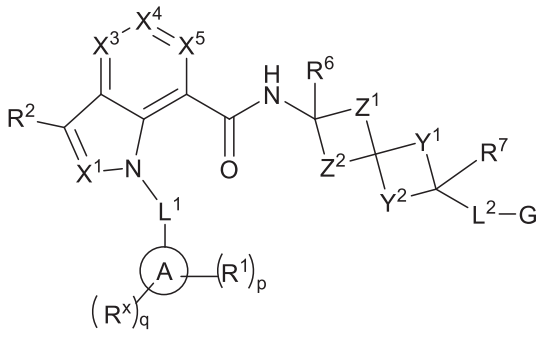
[00010] The EP_4 pathway is also implicated in vascular disease. The EP_4 antagonist ONO-AE3-208 was found to decrease vascular inflammation and to reduce the incidence and severity of abdominal aortic aneurism in the angiotensin II mouse model (Cao R. *et al., Am J Pathol* **2012** 181, p. 313-321). EP_4 overexpression has been associated with enhanced inflammatory reaction in atherosclerotic plaques and EP_4 antagonism has been suggested as a therapy for atherosclerosis and the prevention of acute ischemic syndromes (Cipollone F. *et al., Ateriosclerosis, Thrombosis, and Vascular Biology* **2005**, 25, p. 1925-1931).

[00011] There remains a need to provide novel classes of compounds that are useful in the treatment of EP2 and EP4 receptor-mediated diseases. Such classes of compounds have the potential to be useful in the treatment of inflammatory disease, autoimmune disease, neurodegenerative disease, cardiovascular disease and cancer.

SUMMARY

[00012] Provided herein are compounds of Formula (I) or a pharmaceutically acceptable salt, solvate, solvate of the salt, hydrate, single stereoisomer, mixture of stereoisomers, racemic mixture of stereoisomers, or prodrug thereof. In certain ~~embodiments~~examples, the compounds are modulators of both the EP_2 and EP_4 receptors. In certain examples~~embodiments~~, the compounds are useful as potent and selective antagonists of both the EP_2 and EP_4 receptors, and in this regard, will confer therapeutic benefits associated with the selective blockade of PGE_2-mediated signaling.

[00013] In certain examples~~embodiments~~, provided herein are compound having the Formula (I), 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:



Formula (I)

wherein:

X^1 is N or CH;

X^3 is N or CR^3;

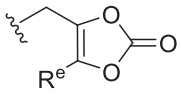
each R^{11} is independently alkyl, deuterated alkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl, wherein cycloalkyl, heterocyclyl, aryl, and heteroaryl are optionally substituted with one, two, or three groups selected from halogen, alkyl, and haloalkyl;

Y^1 and Y^2 are each independently a bond or $-(CR^a_2)_n-$, provided that Y^1 and Y^2 are not both a bond;

Z^1 and Z^2 are each $-CR^a_2-$;

L^2 is $-(CR^c_2)_m-$;

G is $-C(O)OR^{12}$, $-C(O)NHOH$, $-SO_3H$, $-SO_2NH_2$, $-SO_2NHR^d$, $-SO_2NHC(O)R^d$, $-NHC(O)NHSO_2R^d$, -1*H*-tetrazolyl, $-P(O)(OH)_2$, -1,2,4-oxadiazol-5(4*H*)-one, -tetrazol-5(4*H*)-one, or $-C(O)NHSO_2R^d$;

R^{12} is selected from hydrogen, C_1-C_6 alkyl, aryl, aralkyl, $CH(R^{13})OC(=O)R^{14}$, $CH(R^{13})OC(=O)OR^{14}$ and a (5-alkyl-2-oxo-1,3-dioxolen-4-yl)methyl group having the following formula:  wherein R^e is C_1-C_6 alkyl;

R^{13} is hydrogen or C_1-C_6 alkyl;

R^{14} is C_1-C_6 alkyl or C_3-C_6 –cycloalkyl;

each R^a is independently hydrogen, deuterium, optionally deuterated alkyl, halogen, or haloalkyl;

each R^b is independently hydrogen, deuterium, optionally alkyl or haloalkyl, or two R^bs, together with the carbon atom to which they are attached, form optionally cycloalkyl or heterocyclyl;

each R^c is independently hydrogen or halogen;

R^d is alkyl, haloalkyl, cycloalkyl, aryl, or heteroaryl;

m is 0, 1, or 2;

each n is independently 1, 2, or 3;

p is 1 or 2;

q is 0, 1, or 2; and

t is 1, 2 or 3.

[00014] In one example~~embodiment~~, the compound provided herein is a compound of Formula (I). In one example~~embodiment~~, the compound provided herein is a pharmaceutically acceptable salt of the compound of Formula (I). In one example~~embodiment~~, provided herein is a solvate of the compound of Formula (I). In one example~~embodiment~~, provided herein is a solvate of the pharmaceutically acceptable salt of the compound of Formula (I). In one example~~embodiment~~, provided herein is a hydrate of the compound of Formula (I). In one example~~embodiment~~, provided herein is an isotopic variant of the

compound of Formula (I). In one example~~embodiment~~, provided herein is a deuterated compound of Formula (I). In one example~~embodiment~~, provided herein is a prodrug of the compound of Formula (I).

[00015] Also provided are pharmaceutical compositions formulated for administration by an appropriate route and formulations comprising effective concentrations of one or more of the compounds provided herein, or pharmaceutically acceptable salts, solvates, solvates of pharmaceutically acceptable salts, hydrates, and prodrugs thereof and optionally comprising at least one pharmaceutically acceptable carrier.

[00016] In certain examples~~embodiments~~, the compounds are useful for the treatment, prevention or amelioration of cancer, arthritis, pain, endometriosis, neurodegenerative disease, and cardiovascular disease.

[00017] In an example~~aspect~~, the present disclosure provides a method for the treatment of cancer in a patient comprising administering to the patient a compound or pharmaceutical composition as described herein. In some examples~~embodiments~~, the 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. In some examples~~embodiments~~, the cancer is selected from colon cancer, bladder cancer, hepatocellular carcinoma, pancreatic cancer, ovarian cancer, cervical cancer, lung cancer, breast cancer and prostate cancer.

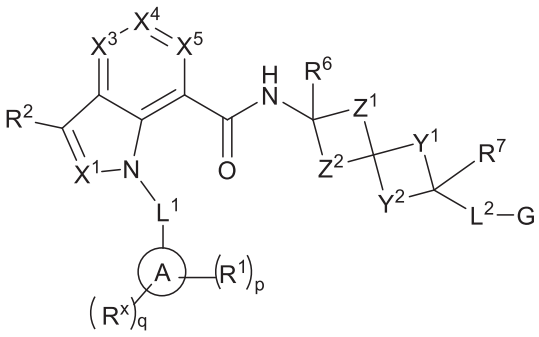
[00018] In another example~~aspect~~, the present disclosure provides a compound or pharmaceutical composition (e.g., as described herein) for use in the treatment of cancer. In some examples~~embodiments~~, the cancer is selected from glioblastoma bone cancer, head and neck cancer, melanoma, basal cell 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. In some examples~~embodiments~~, the cancer is selected from colon cancer, bladder cancer, hepatocellular carcinoma, pancreatic cancer, ovarian cancer, cervical cancer, lung cancer, breast cancer and prostate cancer.

[00019] In another example~~aspect~~, the present disclosure provides a method of treating a neurodegenerative disease in a patient comprising administering to the patient a compound or pharmaceutical composition as described herein. In some examples~~embodiments~~, the neurodegenerative disease is selected from epilepsy, Alzheimer's disease (AD), Parkinson's disease (PD), amyotrophic lateral sclerosis (ALS) and traumatic brain injury (TBI).

[00020] In another example~~aspect~~, the present disclosure provides a method of treating arthritis or inflammatory pain in a patient comprising administering to the patient a compound or pharmaceutical composition as described herein.

[00021] In certain examples~~embodiments~~, the compounds are useful as pharmaceutically acceptable compositions and useful in the treatment of various diseases; in particular cancer, both alone or in combination with radiation, antibodies to cytotoxic t-lymphocyte antigen 4 (i.e. anti-CTLA4 agents such as ipilimumab, or the like), antibodies to programmed death-ligand 1 (i.e. anti-PD-L1 agents such as atezolizumab, avelumab, or the like), antibodies to programmed cell death protein 1 (i.e. anti-PD-1 agents such as nivolumab, pembrolizumab, or the like), activators of stimulator of interferon genes pathway (i.e. STING activators such as ADU-S100, MK-1454, or the like) and cytotoxic agents (i.e. alkylating agents such as cisplatin, dacarbazine, chlorambucil, or the like; anti-metabolites such as methotrexate, fludarabine, gemcitabine, or the like; anti-microtubule agents such as vinblastine, paclitaxel, or the like; topoisomerase inhibitors such as topotecan, doxorubicin, or the like; and others). Also provided herein are processes for the preparation of the compounds of this intervention, as well as for the preparation of intermediates useful for the synthesis of the compounds of Formula (I).

[00021a]In one aspect, the present disclosure refers to a compound of Formula (I), or a pharmaceutically acceptable salt, solvate, solvate of the salt, hydrate, a single stereoisomer, a mixture of stereoisomers, a racemic mixture of stereoisomers, isotopic variant, or prodrug thereof:



Formula (I)

wherein:

X^1 is N;

X^3 is CR^3;

X^4 is CR^4;

X^5 is CR^5;

L^1 is $-CR^b{}_2-$;

Ring A is aryl;

R^1 is aryl optionally substituted with one, two, or three R^y;

each R^y is independently alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, halogen, $-OR^8$, $-NR^8R^9$, -CN, $-C(O)R^{11}$, $-C(O)NR^8R^9$, $-NR^8C(O)R^{11}$, $-NR^8C(O)OR^9$, $-NR^{10}C(O)NR^8R^9$, $-OC(O)NR^8R^9$, $-S(O)_2R^{11}$, $-S(O)R^{11}$, $-SR^8$, $-S(O)_2NR^8R^9$, $-S(O)NR^8R^9$, $-NR^8S(O)R^{11}$, $-NR^8S(O)_2R^{11}$, or $-NR^{10}S(O)_2NR^8R^9$; wherein the alkyl is optionally substituted with $-OR^8$ or $-NR^8R^9$ and wherein the cycloalkyl and heterocyclyl are optionally substituted with one, two, or three groups independently selected from halogen, alkyl, and haloalkyl;

each R^x is independently halogen, methyl, C_1haloalkyl, or -CN;

R^2, R^3, R^4, and R^5 are each independently hydrogen, alkyl, halogen, $-OR^8$, $-NR^8R^9$, $-SR^8$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, -CN, cycloalkyl, or haloalkyl;

R^6 is hydrogen, alkyl, or haloalkyl;

R^7 is hydrogen, halogen, alkyl, alkoxy, haloalkoxy, hydroxyl, or haloalkyl;

each R^8 and each R^9 are independently hydrogen, alkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl, wherein cycloalkyl, heterocyclyl, aryl, and heteroaryl are optionally substituted with one, two, or three groups independently selected from halogen, alkyl, and haloalkyl; or

R^8 and R^9, together with the atom or atoms to which they are attached, form a heterocyclyl optionally substituted with one, two, or three groups independently selected from halogen, alkyl, and haloalkyl;

each R^{10} is independently hydrogen or alkyl;

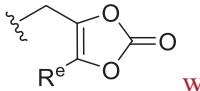
each R^{11} is independently alkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl, wherein cycloalkyl, heterocyclyl, aryl, and heteroaryl are optionally substituted with one, two, or three groups independently selected from halogen, alkyl, and haloalkyl;

Y^1 and Y^2 are each independently a bond or $-(CR^a_2)_n-$, provided that Y^1 and Y^2 are not both a bond;

Z^1 and Z^2 are each $-CR^a_2-$;

L^2 is $-(CR^c_2)_m-$;

G is $-C(O)OR^{12}$, -C(O)NHOH, $-SO_3H$, $-SO_2NH_2$, $-SO_2NHR^d$, $-SO_2NHC(O)R^d$, $-NHC(O)NHSO_2R^d$, -1*H*-tetrazolyl, $-P(O)(OH)_2$, -1,2,4-oxadiazol-5(4*H*)-one, -tetrazol-5(4*H*)-one, or $-C(O)NHSO_2R^d$;

R^{12} is selected from H, C_1-C_6 alkyl, aryl, aralkyl, $CH(R^{13})OC(=O)R^{14}$, $CH(R^{13})OC(=O)OR^{14}$ and a (5-alkyl-2-oxo-1,3-dioxolen-4-yl)methyl group having the following formula:  wherein R^e is C_1-C_6 alkyl;

R^{13} is hydrogen or C_1-C_6 alkyl;

R^{14} is C_1-C_6 alkyl or C_3-C_6 –cycloalkyl;

each R^a is independently hydrogen, alkyl, halogen, or haloalkyl;

each R^b is independently hydrogen, alkyl, or haloalkyl, or

two R^bs, together with the carbon atom to which they are attached, form a cycloalkyl or a heterocyclyl;

each R^c is independently hydrogen or halogen;

R^d is alkyl, haloalkyl, cycloalkyl, aryl, or heteroaryl;

m is 0, 1, or 2;

each n is independently 1, 2, or 3;

p is 1; and

q is 0, 1, or 2.

[00021b] In another aspect, the present disclosure refers to a pharmaceutical composition comprising the compound as described herein, or a pharmaceutically acceptable salt, solvate, solvate of the salt, hydrate, a single stereoisomer, a mixture of stereoisomers, a racemic mixture of stereoisomers, isotopic variant, or prodrug thereof, and a pharmaceutically acceptable carrier.

[00021c] In another aspect, the present disclosure refers to a use of the compound of Formula (I), or a pharmaceutically acceptable salt, solvate, solvate of the salt, hydrate, a single stereoisomer, a mixture of stereoisomers, a racemic mixture of stereoisomers, isotopic variant, or prodrug thereof as described herein, in the manufacture of a medicament for the treatment of an EP4-mediated cancer in a patient, wherein the compound of Formula (I), or a pharmaceutically acceptable salt, solvate, solvate of the salt, hydrate, a single stereoisomer, a mixture of stereoisomers, a racemic mixture of stereoisomers, isotopic variant or prodrug thereof is to be administered to a patient.

[00021d] In yet another aspect, the present disclosure refers to the compound of Formula (I), or a pharmaceutically acceptable salt, solvate, solvate of the salt, hydrate, a single stereoisomer, a mixture of stereoisomers, a racemic mixture of stereoisomers, isotopic variant, or prodrug thereof as described herein, or the pharmaceutical composition as described herein for use in therapy.

[00022] These and other examples~~aspects~~ of the subject matter described herein will become evident upon reference to the following detailed description.

BRIEF DESCRIPTION OF THE DRAWINGS

[00023] FIG. 1 depicts animal tumor growth delay in syngeneic CT26 colon carcinoma mouse model. CT26 tumor bearing mice treated p.o., b.i.d with 50 mg/kg of one of the compounds of Formula (I) (Compound A) for 14 days resulted in a statistically significant (p=0.02) reduction

in tumor size compared to animals treated with vehicle or an internal EP4 selective compound (Compound B).

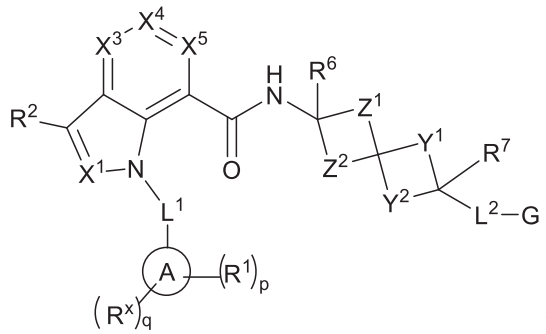
[00024] FIG. 2A-C depict Spider plots of individual CT26 tumor bearing mice treated with one of the compounds of Formula (I) (Compound A) for 14 days (FIG. 2B) which also demonstrate significant tumor growth inhibition compared to animals treated with vehicle (FIG. 2A) or an internal EP4 selective compound Compound B (FIG. 2C).

[00025] FIG 3 depicts animal tumor growth delay in syngeneic CT26 colon carcinoma mouse model. CT26 tumor bearing mice treated p.o., b.i.d with 30 mg/kg of one of the compounds of Formula (I) (Compound A-1) for 14 days resulted in a statistically significant ($p=0.008$) reduction in tumor size compared to animals treated with vehicle or an internal EP4 selective compound (Compound B).

CLAIMS

WHAT IS CLAIMED IS:

1. A compound having the Formula (I), or a pharmaceutically acceptable salt, solvate, solvate of the salt, hydrate, a single stereoisomer, a mixture of stereoisomers, a racemic mixture of stereoisomers, isotopic variant or prodrug thereof:



Formula (I)

wherein:

X^1 is N~~ or CH~~;

X^3 is ~~N or~~ CR^3;

X^4 is ~~N or~~ CR^4;

X^5 is ~~N or~~ CR^5;

~~wherein no more than two of X^3, X^4 and X^5 are N;~~

L^1 is -~~(~~CR^b_2~~)$~~$t$~~-;

Ring A is aryl;

each R^1 is ~~independently C_2-C_9alkyl, C_2-C_9alkenyl, C_2-C_9alkynyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, or $OR^{8'}$, wherein C_2-C_9alkyl, C_2-C_9alkenyl, C_2-C_9alkynyl, cycloalkyl, heterocyclyl,~~ aryl~~, and heteroaryl are~~ optionally substituted with one, two, or three R^y;

~~or two R^1 substituents on adjacent atoms of Ring A are taken together with the atom to which they are attached to form an aromatic or non-aromatic ring containing 0-2 heteroatoms selected from the group consisting of -O-, =N-, NR^{10}-, -S-, and -$S(O)_2$-, wherein the aromatic or non-aromatic ring is optionally deuterated and optionally substituted with one, two, or three R^y;~~

~~each $R^{8'}$ is independently hydrogen, alkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl, wherein cycloalkyl, heterocyclyl, aryl, and heteroaryl are optionally substituted with one, two, or three groups selected from halogen, alkyl, and haloalkyl;~~

each R^y is independently alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, halogen, $-OR^8$, $-NR^8R^9$, -CN, $-C(O)R^{11}$, $-C(O)NR^8R^9$, $-NR^8C(O)R^{11}$, $-NR^8C(O)OR^9$, $-NR^{10}C(O)NR^8R^9$, $-OC(O)NR^8R^9$, $-S(O)_2R^{11}$, $-S(O)R^{11}$, $-SR^8$, $-S(O)_2NR^8R^9$, $-S(O)NR^8R^9$, $-NR^8S(O)R^{11}$, $-NR^8S(O)_2R^{11}$, or $-NR^{10}S(O)_2NR^8R^9$; wherein the alkyl is optionally substituted with $-OR^8$ or $-NR^8R^9$ and wherein the cycloalkyl and heterocyclyl are optionally substituted with one, two, or three groups independently selected from halogen, alkyl, and haloalkyl;

each R^x is independently halogen, methyl, C_1haloalkyl, or -CN;

R^2, R^3, R^4, and R^5 are each independently hydrogen, alkyl, halogen, $-OR^8$, $-NR^8R^9$, $-SR^8$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, -CN, cycloalkyl, or haloalkyl;

R^6 is hydrogen, alkyl, or haloalkyl;

R^7 is hydrogen, halogen, alkyl, alkoxy, haloalkoxy, hydroxyl, or haloalkyl;

each R^8 and each R^9 are independently hydrogen, alkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl, wherein cycloalkyl, heterocyclyl, aryl, and heteroaryl are optionally substituted with one, two, or three groups independently selected from halogen, alkyl, and haloalkyl; or

R^8 and R^9, together with the atom or atoms to which they are attached, form a heterocyclyl optionally substituted with one, two, or three groups independently selected from halogen, alkyl, and haloalkyl;

each R^{10} is independently hydrogen or alkyl;

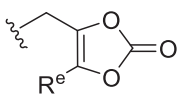
each R^{11} is independently alkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl, wherein cycloalkyl, heterocyclyl, aryl, and heteroaryl are optionally substituted with one, two, or three groups independently selected from halogen, alkyl, and haloalkyl;

Y^1 and Y^2 are each independently a bond or $-(CR^a_2)_n-$, provided that Y^1 and Y^2 are not both a bond;

Z^1 and Z^2 are each $-CR^a_2-$;

L^2 is $-(CR^c_2)_m-$;

G is $-C(O)OR^{12}$, -C(O)NHOH, $-SO_3H$, $-SO_2NH_2$, $-SO_2NHR^d$, $-SO_2NHC(O)R^d$, $-NHC(O)NHSO_2R^d$, -1*H*-tetrazolyl, $-P(O)(OH)_2$, -1,2,4-oxadiazol-5(4*H*)-one, -tetrazol-5(4*H*)-one, or $-C(O)NHSO_2R^d$;

R^{12} is selected from H, C_1-C_6 alkyl, aryl, aralkyl, $CH(R^{13})OC(=O)R^{14}$, $CH(R^{13})OC(=O)OR^{14}$ and a (5-alkyl-2-oxo-1,3-dioxolen-4-yl)methyl group having the following formula:  wherein R^e is C_1-C_6 alkyl;

R^{13} is hydrogen or C_1-C_6 alkyl;

R^{14} is C_1-C_6 alkyl or C_3-C_6 –cycloalkyl;

each R^a is independently hydrogen, alkyl, halogen, or haloalkyl;

each R^b is independently hydrogen, alkyl or haloalkyl, or

two R^bs, together with the carbon atom to which they are attached, form cycloalkyl or heterocyclyl;

each R^c is independently hydrogen or halogen;

R^d is alkyl, haloalkyl, cycloalkyl, aryl, or heteroaryl;

m is 0, 1, or 2;

each n is independently 1, 2, or 3;

p is 1~~ or 2~~;

q is 0, 1, or 2~~; and~~

~~t is 1, 2 or 3~~.

2. The compound of claim 1, or a pharmaceutically acceptable salt, solvate, solvate of the salt, hydrate, a single stereoisomer, a mixture of stereoisomers, a racemic mixture of stereoisomers, isotopic variant, or prodrug thereof, ~~compound of Claim 2~~ wherein:

~~L^1 is $-(CR^b_2)_t-$;~~

~~Ring A is optionally deuterated aryl;~~

~~each R^1 is independently C_2-C_9alkyl, C_2-C_9alkenyl, C_2-C_9alkynyl, cycloalkyl, heterocyclyl, aryl, heteroaryl or $-OR^{8'}$, wherein C_2-C_9alkyl, C_2-C_9alkenyl, C_2-C_9alkynyl, cycloalkyl, heterocyclyl, aryl, and heteroaryl are optionally deuterated and optionally substituted with one, two, or three R^y;~~

~~or two R^1 substituents on adjacent atoms of Ring A are taken together with the atom to which they are attached to form an aromatic or non-aromatic ring containing 0-2 heteroatoms selected from the group consisting of -O-, =N-, -NR^{10}-, -S-, and -$S(O)_2$-, wherein the aromatic or non-aromatic ring is optionally deuterated and optionally substituted with one, two, or three R^y;~~

R^2, R^3, R^4, and R^5 are each independently hydrogen, alkyl, halogen, -OR^8, ~~$-NR^8R^9$, $-SR^8$, $-S(O)R^{11}$, $-S(O)_2R^{11}$,~~ -CN, cycloalkyl, or haloalkyl; each R^b is independently hydrogen, deuterium, optionally deuterated alkyl or haloalkyl, or two R^bs, together with the carbon atom to which they are attached, form optionally deuterated cycloalkyl; and

~~R^7 is hydrogen, deuterium, halogen, optionally deuterated alkyl, alkoxy, haloalkoxy, hydroxyl, or haloalkyl;~~

each R^8 is independently hydrogen, alkyl, deuterated alkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl, wherein cycloalkyl, heterocyclyl, aryl, and heteroaryl are optionally substituted with one, two, or three groups independently selected from halogen, alkyl,

and haloalkyl~~and each R^9 are independently hydrogen, deuterium, alkyl, deuterated alkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl, wherein cycloalkyl, heterocyclyl, aryl, and heteroaryl are optionally substituted with one, two, or three groups selected from halogen, alkyl, and haloalkyl; or~~

~~R^8 and R^9, together with the atom or atoms to which they are attached, form a heterocyclyl optionally substituted with one, two, or three groups selected from halogen, alkyl, and haloalkyl;~~

~~each R^{10} is independently hydrogen, deuterium, alkyl or deuterated alkyl;~~

~~each R^{11} is independently alkyl, deuterated alkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl, wherein cycloalkyl, heterocyclyl, aryl, and heteroaryl are optionally substituted with one, two, or three groups selected from halogen, alkyl, and haloalkyl;~~

~~Y^1 and Y^2 are each independently a bond or $-(CR^a_2)_n-$, provided that Y^1 and Y^2 are not both a bond;~~

~~Z^1 and Z^2 are each $-CR^a_2-$;~~

~~L^2 is $-(CR^e_2)_m-$;~~

~~each R^a is independently hydrogen, deuterium, optionally deuterated alkyl, halogen, or haloalkyl;~~

~~each R^b is independently hydrogen, deuterium, optionally deuterated alkyl or haloalkyl, or~~

~~two R^bs, together with the carbon atom to which they are attached, form optionally deuterated cycloalkyl or heterocyclyl;~~

~~each R^e is independently hydrogen, deuterium or halogen;~~

~~m is 0, 1, or 2;~~

~~each n is independently 1, 2, or 3;~~

~~p is 1 or 2;~~

~~q is 0, 1, or 2; and~~

~~t is 1, 2 or 3~~.

~~3. The compound of claim 1 or 2 wherein:~~

~~R^2, R^3, R^4, and R^5 are each independently hydrogen, alkyl, halogen, $-OR^8$, $-CN$, cycloalkyl, or haloalkyl; each R^b is independently hydrogen, deuterium, optionally deuterated alkyl or haloalkyl, or two R^bs, together with the carbon atom to which they are attached, form optionally deuterated cycloalkyl; and~~

~~R^8 is independently hydrogen, alkyl, deuterated alkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl, wherein cycloalkyl, heterocyclyl, aryl, and~~

~~heteroaryl are optionally substituted with one, two, or three groups selected from halogen, alkyl, and haloalkyl.~~

~~4.~~3. The compound of claim 1~~, 2 or 3,~~ or a pharmaceutically acceptable salt, solvate, solvate of the salt, hydrate, a single stereoisomer, a mixture of stereoisomers, a racemic mixture of stereoisomers, isotopic variant, or prodrug thereof, wherein:

each R^y is independently alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, halogen, $-OR^8$, $-NR^8R^9$, -CN, $-C(O)R^{11}$, $-C(O)NR^8R^9$, $-NR^8C(O)R^{11}$, $-NR^8C(O)OR^9$, $-NR^{10}C(O)NR^8R^9$, $-OC(O)NR^8R^9$, $-S(O)_2R^{11}$, $-S(O)R^{11}$, $-SR^8$, $-S(O)_2NR^8R^9$, $-NR^8S(O)_2R^{11}$, or $-NR^{10}S(O)_2NR^8R^9$ wherein alkyl is optionally substituted with $-OR^8$ or $-NR^8R^9$ and wherein cycloalkyl and heterocyclyl are optionally substituted with one, two, or three groups independently selected from halogen, alkyl, and haloalkyl;

each R^8 and each R^9 are independently hydrogen, alkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl, wherein cycloalkyl, heterocyclyl, aryl, and heteroaryl are optionally substituted with one, two, or three groups independently selected from halogen, alkyl, and haloalkyl; or

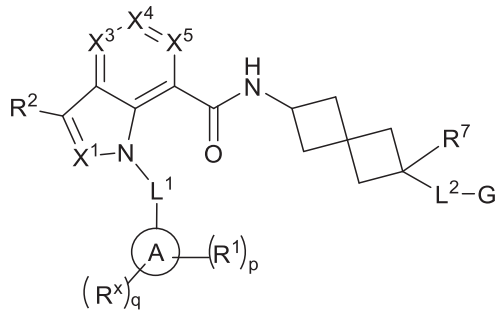
R^8 and R^9, together with the atom or atoms to which they are attached, form a heterocyclyl optionally substituted with one, two, or three groups independently selected from halogen, alkyl, and haloalkyl;

each R^{10} is independently hydrogen or alkyl;

each R^{11} is independently alkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl, wherein cycloalkyl, heterocyclyl, aryl, and heteroaryl are optionally substituted with one, two, or three groups independentlly selected from halogen, alkyl, and haloalkyl; and

each R^b is independently hydrogen or deuterium.

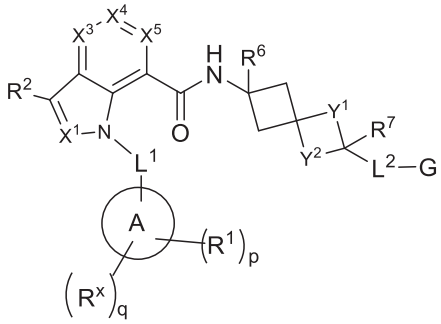
~~5.~~4. The compound of ~~any one of~~ claim~~s~~ 3~~1-4~~ having the Formula (II):



(II)

or a pharmaceutically acceptable salt, solvate, solvate of the salt, hydrate, a single stereoisomer, a mixture of stereoisomers, a racemic mixture of stereoisomers, isotopic variant,or prodrug thereof, wherein L^1 is $-CR^b_2-$ and each R^b is independently hydrogen or deuterium.

~~6.~~5. The compound of ~~any one of~~ claim~~s~~ 3~~1~~ 4 having the Formula (IIc):



(IIc)

or a pharmaceutically acceptable salt, solvate, solvate of the salt, hydrate, a single stereoisomer, a mixture of stereoisomers, a racemic mixture of stereoisomers, isotopic variant, or prodrug thereof, wherein L^1 is $-CR^b_2-$ and each R^b is independently hydrogen or~~,~~ deuterium~~, optionally deuterated alkyl or haloalkyl~~.

~~7.~~6. The compound of claim ~~1,~~ 5 ~~or 6,~~ or a pharmaceutically acceptable salt, solvate, solvate of the salt, hydrate, a single stereoisomer, a mixture of stereoisomers, a racemic mixture of stereoisomers, isotopic variant, or prodrug thereof,wherein:

~~X^3 is CR^3;~~

~~X^4 is N or CR^4;~~

~~X^5 is N or CR^5;~~

R^3, R^4, and R^5 are each independently hydrogen, alkyl, halogen, $-OR^8$, $-NR^8R^9$, $-SR^8$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, -CN, cycloalkyl, or haloalkyl; and

each R^8 and each R^9 are independently hydrogen, deuterium, alkyl, deuterated alkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl, wherein cycloalkyl, heterocyclyl, aryl, and heteroaryl are optionally substituted with one, two, or three groups independently selected from halogen, alkyl, and haloalkyl; or

R^8 and R^9, together with the atom or atoms to which they are attached, form a heterocyclyl optionally substituted with one, two, or three groups independently selected from halogen, alkyl, and haloalkyl; and

each R^{11} is independently alkyl, deuterated alkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl, wherein cycloalkyl, heterocyclyl, aryl, and heteroaryl are optionally substituted with one, two, or three groups independently selected from halogen, alkyl, and haloalkyl.

~~8. The compound of any of claims 1, 5, 6 or 7 wherein:~~

~~X^3 is CR^3;~~

~~X^4 is CR^4;~~

~~X^5 is CR^5;~~

~~R^3, R^4, and R^5 are each independently hydrogen, alkyl, halogen, OR^8, NR^8R^9, SR^8, $S(O)R^{11}$, $S(O)_2R^{11}$, CN, cycloalkyl, or haloalkyl; and~~

~~each R^8 and each R^9 are independently hydrogen, deuterium, alkyl, deuterated alkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl, wherein cycloalkyl, heterocyclyl, aryl, and heteroaryl are optionally substituted with one, two, or three groups selected from halogen, alkyl, and haloalkyl; or~~

~~R^8 and R^9, together with the atom or atoms to which they are attached, form a heterocyclyl optionally substituted with one, two or three groups selected from halogen, alkyl and haloalkyl; and~~

~~each R^{11} is independently alkyl, deuterated alkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl, wherein cycloalkyl, heterocyclyl, aryl, and heteroaryl are optionally substituted with one, two, or three groups selected from halogen, alkyl and haloalkyl.~~

~~9. The compound of claim 1, 5, 6, 7 or 8 wherein X^1 is CH.~~

~~10. The compound of claim 1, 5, 6, 7 or 8 wherein X^1 is N.~~

~~11.~~7. The compound of claim ~~1, 5,~~ 6~~, 7, 8, 9 or 10~~, or a pharmaceutically acceptable salt, solvate, solvate of the salt, hydrate, a single stereoisomer, a mixture of stereoisomers, a racemic mixture of stereoisomers, isotopic variant, or prodrug thereof, wherein:

one of R^3, R^4, and R^5 is alkyl, halogen, $-OR^8$, $-NR^8R^9$, $-SR^8$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, -CN, cycloalkyl, or haloalkyl and the remainder of R^3, R^4, and R^5, when present, are~~is~~ hydrogen~~; and~~

~~R^8 and each R^9 are independently hydrogen, deuterium, alkyl, deuterated alkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl, wherein cycloalkyl,~~

~~heterocyclyl, aryl, and heteroaryl are optionally substituted with one, two, or three groups selected from halogen, alkyl, and haloalkyl; or~~

~~R^8 and R^9, together with the atom or atoms to which they are attached, form a heterocyclyl optionally substituted with one, two or three groups selected from halogen, alkyl and haloalkyl; and~~

~~each R^{11} is independently alkyl, deuterated alkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl, wherein cycloalkyl, heterocyclyl, aryl, and heteroaryl are optionally substituted with one, two, or three groups selected from halogen, alkyl and haloalkyl~~.

~~12. The compound of claim 1, 5, 6, 7, 8, 9 or 10 wherein:~~

~~one of R^3, R^4, and R^5 is halogen and the remainder of R^3, R^4, and R^5, when present, is each independently hydrogen, alkyl, halogen, $-OR^8$, $-NR^8R^9$, $-SR^8$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, -CN, cycloalkyl, or haloalkyl; and~~

~~each R^8 and each R^9 are independently hydrogen, deuterium, alkyl, deuterated alkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl, wherein cycloalkyl, heterocyclyl, aryl, and heteroaryl are optionally substituted with one, two, or three groups selected from halogen, alkyl, and haloalkyl; or~~

~~R^8 and R^9, together with the atom or atoms to which they are attached, form a heterocyclyl optionally substituted with one, two or three groups selected from halogen, alkyl and haloalkyl; and~~

~~each R^{11} is independently alkyl, deuterated alkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, wherein cycloalkyl, heterocyclyl, aryl, and heteroaryl are optionally substituted with one, two or three groups selected from halogen, alkyl and haloalkyl.~~

~~13. The compound of any one of claims 1-12 wherein one of R^3, R^4, or R^5 is halogen and the remainder of R^3, R^4, and R^5, when present, are each hydrogen.~~

~~14.~~8. The compound of ~~any one of claims 1-13~~claim 7, or a pharmaceutically acceptable salt, solvate, solvate of the salt, hydrate, a single stereoisomer, a mixture of stereoisomers, a racemic mixture of stereoisomers, isotopic variant, or prodrug thereof, wherein one of R^3 or R^4 is halogen and the other of R^3 and R^4, when present, is hydrogen and R^5, when present, is hydrogen.

~~15. The compound of any one of claims 1-14, wherein:~~

~~each R^1 is independently cycloalkyl, heterocyclyl, aryl, heteroaryl, or $OR^{8'}$, wherein cycloalkyl, heterocyclyl, aryl, and heteroaryl are each independently optionally deuterated and optionally substituted with one, two, or three R^y;~~

~~each R^y is independently alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, halogen, OR^8, NR^8R^9, CN, $C(O)R^{11}$, $C(O)NR^8R^9$, $NR^8C(O)R^{11}$, $NR^8C(O)OR^9$, $NR^{10}C(O)NR^8R^9$, $OC(O)NR^8R^9$, $S(O)_2R^{11}$, $S(O)R^{11}$, SR^8, $S(O)_2NR^8R^9$, $S(O)NR^8R^9$, $NR^8S(O)R^{11}$, $NR^8S(O)_2R^{11}$, or $NR^{10}S(O)_2NR^8R^9$; wherein alkyl is optionally substituted with OR^8 or NR^8R^9 and wherein cycloalkyl and heterocyclyl are optionally substituted with one, two, or three groups selected from halogen, alkyl, and haloalkyl;~~

~~each R^8 and each R^9 are independently hydrogen, deuterium, alkyl, deuterated alkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl, wherein cycloalkyl, heterocyclyl, aryl, and heteroaryl are optionally substituted with one, two, or three groups selected from halogen, alkyl, and haloalkyl; or~~

~~R^8 and R^9, together with the atom or atoms to which they are attached, form a heterocyclyl optionally substituted with one, two, or three groups selected from halogen, alkyl, and haloalkyl;~~

~~each R^{10} is independently hydrogen, deuterium, alkyl or deuterated alkyl;~~

~~each R^{11} is independently alkyl, deuterated alkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl, wherein cycloalkyl, heterocyclyl, aryl, and heteroaryl are optionally substituted with one, two, or three groups selected from halogen, alkyl, and haloalkyl; and~~

~~each $R^{8'}$ is independently hydrogen, alkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl, wherein cycloalkyl, heterocyclyl, aryl, and heteroaryl are each independently optionally substituted with one, two, or three groups selected from halogen, alkyl, and haloalkyl.~~

~~16.~~9. The compound of ~~any one of claims 1-15~~claim 8, or a pharmaceutically acceptable salt, solvate, solvate of the salt, hydrate, a single stereoisomer, a mixture of stereoisomers, a racemic mixture of stereoisomers, isotopic variant, or prodrug thereof, wherein:

~~each~~ R^1 is ~~independently cycloalkyl, heterocyclyl,~~ aryl~~, or heteroaryl, wherein the heterocyclyl, aryl, and heteroaryl are each independently~~ optionally deuterated and optionally substituted with one or~~,~~ two~~, or three~~ R^y;

each R^y is independently alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, halogen, $-OR^8$, $-NR^8R^9$, -CN, $-C(O)R^{11}$, $-C(O)NR^8R^9$, $-NR^8C(O)R^{11}$, $-NR^8C(O)OR^9$, $-NR^{10}C(O)NR^8R^9$, $-OC(O)NR^8R^9$, $-S(O)_2R^{11}$, $-S(O)R^{11}$, $-SR^8$, $-S(O)_2NR^8R^9$, $-S(O)NR^8R^9$, $-NR^8S(O)R^{11}$, $-NR^8S(O)_2R^{11}$, or $-NR^{10}S(O)_2NR^8R^9$; wherein alkyl is optionally substituted with $-OR^8$ or $-NR^8R^9$ and wherein cycloalkyl and heterocyclyl are optionally substituted with one, two, or three groups independently selected from halogen, alkyl, and haloalkyl;

each R^8 and each R^9 are independently hydrogen, deuterium, alkyl, deuterated alkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl, wherein cycloalkyl, heterocyclyl, aryl, and heteroaryl are optionally substituted with one, two, or three groups independently selected from halogen, alkyl, and haloalkyl; or

R^8 and R^9, together with the atom or atoms to which they are attached, form a heterocyclyl optionally substituted with one, two, or three groups independently selected from halogen, alkyl, and haloalkyl;

each R^{10} is independently hydrogen, deuterium, alkyl or deuterated alkyl; and

each R^{11} is independently alkyl, deuterated alkyl, haloalkyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl, wherein cycloalkyl, heterocyclyl, aryl, and heteroaryl are optionally substituted with one, two, or three groups independently selected from halogen, alkyl, and haloalkyl.

~~17. The compound of any one claims 1-16 wherein p is 1 and R^1 is aryl.~~

~~18.~~10. The compound of ~~any one of claims 1-17~~claim 1, or a pharmaceutically acceptable salt, solvate, solvate of the salt, hydrate, a single stereoisomer, a mixture of stereoisomers, a racemic mixture of stereoisomers, isotopic variant or prodrug thereof, wherein ~~p is 1,~~ Ring A is phenyl and R^1 is phenyl.

~~19.~~11. The compound of claim 10~~any one of claims 1-18~~, or a pharmaceutically acceptable salt, solvate, solvate of the salt, hydrate, a single stereoisomer, a mixture of stereoisomers, a racemic mixture of stereoisomers, isotopic variant, or prodrug thereof, wherein R^7 is hydrogen or deuterium.

20.12. The compound of claim 11any one of claims 1-19, or a pharmaceutically acceptable salt, solvate, solvate of the salt, hydrate, a single stereoisomer, a mixture of stereoisomers, a racemic mixture of stereoisomers, isotopic variant, or prodrug thereof, wherein q is 0 or 1.

21. The compound of any one of claims 1-20, 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, wherein t is 1.

22. The compound of claim 1 wherein the compound is selected from:

6-(4-Fluoro-1-(4-(trifluoromethoxy)benzyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 1);

(*R*$_a$)-6-(4-Fluoro-1-(4-(trifluoromethoxy)benzyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*S*$_a$)-6-(4-Fluoro-1-(4-(trifluoromethoxy)benzyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 8);

6-(1-(4-(tert-butyl)benzyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 2);

(*R*$_a$)-6-(1-(4-(tert-butyl)benzyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*S*$_a$)-6-(1-(4-(tert-butyl)benzyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

6-(1-([1,1'-biphenyl]-4-ylmethyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 3);

(*R*$_a$)-6-(1-([1,1'-biphenyl]-4-ylmethyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*S*$_a$)-6-(1-([1,1'-biphenyl]-4-ylmethyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 9);

6-(4-fluoro-1-(naphthalen-2-ylmethyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 4);

(*R*$_a$)-6-(4-fluoro-1-(naphthalen-2-ylmethyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*S*$_a$)-6-(4-fluoro-1-(naphthalen-2-ylmethyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 26);

6-(4-fluoro-1-((6-fluoronaphthalen-2-yl)methyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 5);

(*R*$_a$) 6 (4 fluoro 1 ((6 fluoronaphthalen 2 yl)methyl) 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;

(*S*$_a$) 6 (4 fluoro 1 ((6 fluoronaphthalen 2 yl)methyl) 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid (Example 37);

6 (4 bromo 1 (4 (*tert* butyl)benzyl) 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid (Example 6);

(*R*$_a$) 6 (4 bromo 1 (4 (*tert* butyl)benzyl) 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;

(*S*$_a$) 6 (4 bromo 1 (4 (*tert* butyl)benzyl) 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;

6 (1 (4 (*tert* Butyl)benzyl) 4 chloro 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid (Example 7);

(*R*$_a$) 6 (1 (4 (*tert* Butyl)benzyl) 4 chloro 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;

(*S*$_a$) 6 (1 (4 (*tert* Butyl)benzyl) 4 chloro 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;

6 (4 Fluoro 1 ((2 fluoro [1,1' biphenyl] 4 yl)methyl) 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid (Example 10);

(*R*$_a$) 6 (4 Fluoro 1 ((2 fluoro [1,1' biphenyl] 4 yl)methyl) 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;

(*S*$_a$) 6 (4 Fluoro 1 ((2 fluoro [1,1' biphenyl] 4 yl)methyl) 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid (Example 65);

6 (4 Fluoro 1 (4 (pyridin 4 yl)benzyl) 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid (Example 11);

(*R*$_a$) 6 (4 Fluoro 1 (4 (pyridin 4 yl)benzyl) 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;

(*S*$_a$) 6 (4 Fluoro 1 (4 (pyridin 4 yl)benzyl) 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid (Example 24);

6 (4 fluoro 1 ((4' methoxy [1,1' biphenyl] 4 yl)methyl) 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid (Example 12);

(*R*$_a$) 6 (4 fluoro 1 ((4' methoxy [1,1' biphenyl] 4 yl)methyl) 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;

(*S*$_a$) 6 (4 fluoro 1 ((4' methoxy [1,1' biphenyl] 4 yl)methyl) 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid (Example 51);

~~6-(1-((4'-cyano-[1,1'-biphenyl]-4-yl)methyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 13);~~

~~(*R*$_a$)-6-(1-((4'-cyano-[1,1'-biphenyl]-4-yl)methyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*S*$_a$)-6-(1-((4'-cyano-[1,1'-biphenyl]-4-yl)methyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~6-(4-fluoro-1-((3'-methoxy-[1,1'-biphenyl]-4-yl)methyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 14);~~

~~(*R*$_a$)-6-(4-fluoro-1-((3'-methoxy-[1,1'-biphenyl]-4-yl)methyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*S*$_a$)-6-(4-fluoro-1-((3'-methoxy-[1,1'-biphenyl]-4-yl)methyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~6-(1-((3'-cyano-[1,1'-biphenyl]-4-yl)methyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 15);~~

~~(*R*$_a$)-6-(1-((3'-cyano-[1,1'-biphenyl]-4-yl)methyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*S*$_a$)-6-(1-((3'-cyano-[1,1'-biphenyl]-4-yl)methyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 55);~~

~~6-(4-fluoro-1-((3'-fluoro-4'-methoxy-[1,1'-biphenyl]-4-yl)methyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 16);~~

~~(*R*$_a$)-6-(4-fluoro-1-((3'-fluoro-4'-methoxy-[1,1'-biphenyl]-4-yl)methyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*S*$_a$)-6-(4-fluoro-1-((3'-fluoro-4'-methoxy-[1,1'-biphenyl]-4-yl)methyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 47);~~

~~6-(1-(4-(5-Chloro-6-methoxypyridin-3-yl)benzyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 17);~~

~~(*R*$_a$)-6-(1-(4-(5-Chloro-6-methoxypyridin-3-yl)benzyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*S*$_a$)-6-(1-(4-(5-Chloro-6-methoxypyridin-3-yl)benzyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~6-(4-fluoro-1-((2'-methoxy-[1,1'-biphenyl]-4-yl)methyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 18);~~

~~(*R*$_a$)-6-(4-fluoro-1-((2'-methoxy-[1,1'-biphenyl]-4-yl)methyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*S*$_a$)-6-(4-fluoro-1-((2'-methoxy-[1,1'-biphenyl]-4-yl)methyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~6-(4-fluoro-1-((4'-fluoro-3'-methoxy-[1,1'-biphenyl]-4-yl)methyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 19);~~

~~(*R*$_a$)-6-(4-fluoro-1-((4'-fluoro-3'-methoxy-[1,1'-biphenyl]-4-yl)methyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*S*$_a$)-6-(4-fluoro-1-((4'-fluoro-3'-methoxy-[1,1'-biphenyl]-4-yl)methyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 46);~~

~~6-(1-((3'-cyano-5'-methoxy-[1,1'-biphenyl]-4-yl)methyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 20);~~

~~(*R*$_a$)-6-(1-((3'-cyano-5'-methoxy-[1,1'-biphenyl]-4-yl)methyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*S*$_a$)-6-(1-((3'-cyano-5'-methoxy-[1,1'-biphenyl]-4-yl)methyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 49);~~

~~6-(1-((3'-Chloro-4'-(oxetan-3-yloxy)-[1,1'-biphenyl]-4-yl)methyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 21);~~

~~(*R*$_a$)-6-(1-((3'-Chloro-4'-(oxetan-3-yloxy)-[1,1'-biphenyl]-4-yl)methyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*S*$_a$)-6-(1-((3'-Chloro-4'-(oxetan-3-yloxy)-[1,1'-biphenyl]-4-yl)methyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~6-(1-(4-(2-(dimethylamino)pyridin-4-yl)benzyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 22);~~

~~(*R*$_a$)-6-(1-(4-(2-(dimethylamino)pyridin-4-yl)benzyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*S*$_a$)-6-(1-(4-(2-(dimethylamino)pyridin-4-yl)benzyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~6-(4-Fluoro-1-((4'-(oxetan-3-yloxy)-[1,1'-biphenyl]-4-yl)methyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 23);~~

~~(*R*$_a$)-6-(4-Fluoro-1-((4'-(oxetan-3-yloxy)-[1,1'-biphenyl]-4-yl)methyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*S*$_a$)-6-(4-Fluoro-1-((4'-(oxetan-3-yloxy)-[1,1'-biphenyl]-4-yl)methyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~6-(1-((3'-Chloro-4'-methoxy-[1,1'-biphenyl]-4-yl)methyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*R*$_a$) 6 (1 ((3' Chloro 4' methoxy [1,1' biphenyl] 4 yl)methyl) 4 fluoro 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(*S*$_a$) 6 (1 ((3' Chloro 4' methoxy [1,1' biphenyl] 4 yl)methyl) 4 fluoro 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid (Example 25);~~

~~6 (1 (4 (*tert* Butyl)benzyl) 4 cyano 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid (Example 27);~~

~~(*R*$_a$) 6 (1 (4 (*tert* Butyl)benzyl) 4 cyano 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(*S*$_a$) 6 (1 (4 (*tert* Butyl)benzyl) 4 cyano 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~6 (1 (4 (cyclopentyloxy)benzyl) 4 fluoro 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid (Example 28);~~

~~(*R*$_a$) 6 (1 (4 (cyclopentyloxy)benzyl) 4 fluoro 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(*S*$_a$) 6 (1 (4 (cyclopentyloxy)benzyl) 4 fluoro 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~6 (1 (4 (cyclohexyloxy)benzyl) 4 fluoro 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid (Example 29);~~

~~(*R*$_a$) 6 (1 (4 (cyclohexyloxy)benzyl) 4 fluoro 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(*S*$_a$) 6 (1 (4 (cyclohexyloxy)benzyl) 4 fluoro 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~6 (4 fluoro 1 (4 ((tetrahydro 2*H* pyran 4 yl)oxy)benzyl) 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid (Example 30);~~

~~(*R*$_a$) 6 (4 fluoro 1 (4 ((tetrahydro 2*H* pyran 4 yl)oxy)benzyl) 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(*S*$_a$) 6 (4 fluoro 1 (4 ((tetrahydro 2*H* pyran 4 yl)oxy)benzyl) 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~6 (4 Fluoro 1 (4 morpholinobenzyl) *1H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid (Example 31);~~

~~(*R*$_a$) 6 (4 Fluoro 1 (4 morpholinobenzyl) *1H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(*S*$_a$) 6 (4 Fluoro 1 (4 morpholinobenzyl) *1H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~6-(1-(4-(Trifluoromethoxy)benzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 32);~~

~~(*R*$_a$)-6-(1-(4-(Trifluoromethoxy)benzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*S*$_a$)-6-(1-(4-(Trifluoromethoxy)benzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~6-(1-([1,1'-biphenyl]-4-ylmethyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 33);~~

~~(*R*$_a$)-6-(1-([1,1'-biphenyl]-4-ylmethyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*S*$_a$)-6-(1-([1,1'-biphenyl]-4-ylmethyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~6-(1-([1,1'-biphenyl]-4-ylmethyl)-4-fluoro-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 34);~~

~~(*R*$_a$)-6-(1-([1,1'-biphenyl]-4-ylmethyl)-4-fluoro-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*S*$_a$)-6-(1-([1,1'-biphenyl]-4-ylmethyl)-4-fluoro-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~6-(4-fluoro-1-((3'-fluoro-[1,1'-biphenyl]-4-yl)methyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 35);~~

~~(*R*$_a$)-6-(4-fluoro-1-((3'-fluoro-[1,1'-biphenyl]-4-yl)methyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*S*$_a$)-6-(4-fluoro-1-((3'-fluoro-[1,1'-biphenyl]-4-yl)methyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 45);~~

~~6-(1-(4-(2-ethoxypyridin-4-yl)benzyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 36);~~

~~(*R*$_a$)-6-(1-(4-(2-ethoxypyridin-4-yl)benzyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*S*$_a$)-6-(1-(4-(2-ethoxypyridin-4-yl)benzyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 48);~~

~~6-(4-fluoro-1-((6-methoxynaphthalen-2-yl)methyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*R*$_a$)-6-(4-fluoro-1-((6-methoxynaphthalen-2-yl)methyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*S*$_a$)-6-(4-fluoro-1-((6-methoxynaphthalen-2-yl)methyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 38);~~

~~6-(4-fluoro-1-((5-methoxynaphthalen-2-yl)methyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*R*$_a$)-6-(4-fluoro-1-((5-methoxynaphthalen-2-yl)methyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*S*$_a$)-6-(4-fluoro-1-((5-methoxynaphthalen-2-yl)methyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 39);~~

~~6-(4-fluoro-1-((7-methoxynaphthalen-2-yl)methyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*R*$_a$)-6-(4-fluoro-1-((7-methoxynaphthalen-2-yl)methyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*S*$_a$)-6-(4-fluoro-1-((7-methoxynaphthalen-2-yl)methyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 40);~~

~~6-(1-((6-cyanonaphthalen-2-yl)methyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*R*$_a$)-6-(1-((6-cyanonaphthalen-2-yl)methyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*S*$_a$)-6-(1-((6-cyanonaphthalen-2-yl)methyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 41);~~

~~6-(1-((6-bromonaphthalen-2-yl)methyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*R*$_a$)-6-(1-((6-bromonaphthalen-2-yl)methyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*S*$_a$)-6-(1-((6-bromonaphthalen-2-yl)methyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 42);~~

~~6-(1-((5-bromonaphthalen-2-yl)methyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*R*$_a$)-6-(1-((5-bromonaphthalen-2-yl)methyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*S*$_a$)-6-(1-((5-bromonaphthalen-2-yl)methyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 43);~~

~~6-(1-((7-bromonaphthalen-2-yl)methyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*R*$_a$) 6 (1 ((7 bromonaphthalen 2 yl)methyl) 4 fluoro 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(*S*$_a$) 6 (1 ((7 bromonaphthalen 2 yl)methyl) 4 fluoro 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid (Example 44);~~

~~6 (1 ((3' (difluoromethoxy) [1,1' biphenyl] 4 yl)methyl) 4 fluoro 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(*R*$_a$) 6 (1 ((3' (difluoromethoxy) [1,1' biphenyl] 4 yl)methyl) 4 fluoro 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(*S*$_a$) 6 (1 ((3' (difluoromethoxy) [1,1' biphenyl] 4 yl)methyl) 4 fluoro 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid (Example 50);~~

~~6 (4 fluoro 1 ((3' methoxy d$_3$ [1,1' biphenyl] 4 yl)methyl) 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(*R*$_a$) 6 (4 fluoro 1 ((3' methoxy d$_3$ [1,1' biphenyl] 4 yl)methyl) 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(*S*$_a$) 6 (4 fluoro 1 ((3' methoxy d$_3$ [1,1' biphenyl] 4 yl)methyl) 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid (Example 52);~~

~~6 (4 fluoro 1 ((3' fluoro 5' methoxy [1,1' biphenyl] 4 yl)methyl) 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(*R*$_a$) 6 (4 fluoro 1 ((3' fluoro 5' methoxy [1,1' biphenyl] 4 yl)methyl) 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(*S*$_a$) 6 (4 fluoro 1 ((3' fluoro 5' methoxy [1,1' biphenyl] 4 yl)methyl) 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid (Example 53);~~

~~6 (1 ((3' ethoxy [1,1' biphenyl] 4 yl)methyl) 4 fluoro 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(*R*$_a$) 6 (1 ((3' ethoxy [1,1' biphenyl] 4 yl)methyl) 4 fluoro 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(*S*$_a$) 6 (1 ((3' ethoxy [1,1' biphenyl] 4 yl)methyl) 4 fluoro 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid (Example 54);~~

~~6 (1 (4 (6 ethoxypyridin 2 yl)benzyl) 4 fluoro 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(*R*$_a$) 6 (1 (4 (6 ethoxypyridin 2 yl)benzyl) 4 fluoro 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(*S*$_a$) 6 (1 (4 (6 ethoxypyridin 2 yl)benzyl) 4 fluoro 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid (Example 56);~~

~~6-(4-fluoro-1-((3'-(oxetane-3-yloxy)-[1,1'-biphenyl]-4-yl)methyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*R*$_a$)-6-(4-fluoro-1-((3'-(oxetane-3-yloxy)-[1,1'-biphenyl]-4-yl)methyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*S*$_a$)-6-(4-fluoro-1-((3'-(oxetane-3-yloxy)-[1,1'-biphenyl]-4-yl)methyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 57);~~

~~6-(1-(4-(2-ethoxypyrimidin-4-yl)benzyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*R*$_a$)-6-(1-(4-(2-ethoxypyrimidin-4-yl)benzyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*S*$_a$)-6-(1-(4-(2-ethoxypyrimidin-4-yl)benzyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 58);~~

~~6-(1-(4-(4-cyano-6-methoxypyridin-2-yl)benzyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*R*$_a$)-6-(1-(4-(4-cyano-6-methoxypyridin-2-yl)benzyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*S*$_a$)-6-(1-(4-(4-cyano-6-methoxypyridin-2-yl)benzyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 59);~~

~~6-(4-fluoro-1-(4-(2-(methylcarbamoyl)pyridin-4-yl)benzyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*R*$_a$)-6-(4-fluoro-1-(4-(2-(methylcarbamoyl)pyridin-4-yl)benzyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*S*$_a$)-6-(4-fluoro-1-(4-(2-(methylcarbamoyl)pyridin-4-yl)benzyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 60);~~

~~6-(1-(4-(2-(ethylcarbamoyl)pyridin-4-yl)benzyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*R*$_a$)-6-(1-(4-(2-(ethylcarbamoyl)pyridin-4-yl)benzyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid:~~

~~(*S*$_a$)-6-(1-(4-(2-(ethylcarbamoyl)pyridin-4-yl)benzyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 61);~~

~~6-(4-fluoro-1-(4-(6-(methylcarbamoyl)pyridin-2-yl)benzyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*R*$_a$)-6-(4-fluoro-1-(4-(6-(methylcarbamoyl)pyridin-2-yl)benzyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(S_a)-6-(4-fluoro-1-(4-(6-(methylcarbamoyl)pyridin-2-yl)benzyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 62);~~

~~6-(4-fluoro-1-(4-(6-(methylcarbamoyl)pyridin-3-yl)benzyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(R_a)-6-(4-fluoro-1-(4-(6-(methylcarbamoyl)pyridin-3-yl)benzyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(S_a)-6-(4-fluoro-1-(4-(6-(methylcarbamoyl)pyridin-3-yl)benzyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 63);~~

~~6-(1-(4-(2-(difluoromethyl)pyridin-4-yl)benzyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(R_a)-6-(1-(4-(2-(difluoromethyl)pyridin-4-yl)benzyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(S_a)-6-(1-(4-(2-(difluoromethyl)pyridin-4-yl)benzyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 64);~~

~~6-(4-fluoro-1-((3-fluoro-[1,1'-biphenyl]-4-yl)methyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(R_a)-6-(4-fluoro-1-((3-fluoro-[1,1'-biphenyl]-4-yl)methyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(S_a)-6-(4-fluoro-1-((3-fluoro-[1,1'-biphenyl]-4-yl)methyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 66);~~

~~6-(4-chloro-1-(4-(pyridin-4-yl)benzyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(R_a)-6-(4-chloro-1-(4-(pyridin-4-yl)benzyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(S_a)-6-4-chloro-1-(4-(pyridin-4-yl)benzyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 67);~~

~~6-(1-([1,1'-biphenyl]-4-ylmethyl)-4-chloro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(R_a)-6-(1-([1,1'-biphenyl]-4-ylmethyl)-4-chloro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(S_a)-6-(1-([1,1'-biphenyl]-4-ylmethyl)-4-chloro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 68);~~

~~6-(4-chloro-1-(4-(2-methoxypyridin-4-yl)benzyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

(*R*$_a$) 6-(4-chloro-1-(4-(2-methoxypyridin-4-yl)benzyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*S*$_a$) 6-(4-chloro-1-(4-(2-methoxypyridin-4-yl)benzyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 69);

6-(4-chloro-1-(4-(2-ethoxypyridin-4-yl)benzyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*R*$_a$) 6-(4-chloro-1-(4-(2-ethoxypyridin-4-yl)benzyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*S*$_a$) 6-(4-chloro-1-(4-(2-ethoxypyridin-4-yl)benzyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 70);

6-(4-chloro-1-(4-morpholinobenzyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*R*$_a$) 6-(4-chloro-1-(4-morpholinobenzyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*S*$_a$) 6-(4-chloro-1-(4-morpholinobenzyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 71);

6-(1-(4-((1*R*, 5*S*)-3-azabicyclo[3.1.0]hexan-3-yl)benzyl)-4-chloro-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*R*$_a$) 6-(1-(4-((1*R*, 5*S*)-3-azabicyclo[3.1.0]hexan-3-yl)benzyl)-4-chloro-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*S*$_a$) 6-(1-(4-((1*R*, 5*S*)-3-azabicyclo[3.1.0]hexan-3-yl)benzyl)-4-chloro-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 72);

6-(1-(4-(1*H*-pyrazol-1-yl)benzyl)-4-chloro-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*R*$_a$) 6-(1-(4-(1*H*-pyrazol-1-yl)benzyl)-4-chloro-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*S*$_a$) 6-(1-(4-(1*H*-pyrazol-1-yl)benzyl)-4-chloro-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 73);

6-(4-chloro-1-(4-(3,3-difluoropyrrolidin-1-yl)benzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*R*$_a$)-6-(4-chloro-1-(4-(3,3-difluoropyrrolidin-1-yl)benzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*S*$_a$) 6-(4-chloro-1-(4-(3,3-difluoropyrrolidin-1-yl)benzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 74);

6-(1-(4-((1*R*,5*S*)-3-azabicyclo[3.1.0]hexan-3-yl)-3-fluorobenzyl)-4-chloro-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*R*$_a$)-6-(1-(4-((1*R*,5*S*)-3-azabicyclo[3.1.0]hexan-3-yl)-3-fluorobenzyl)-4-chloro-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*S*$_a$)-6-(1-(4-((1*R*,5*S*)-3-azabicyclo[3.1.0]hexan-3-yl)-3-fluorobenzyl)-4-chloro-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 75);

6-(4-chloro-1-(4-(1-(difluoromethyl)-3-azabicyclo[3.1.0]hexan-3-yl)-3-fluorobenzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*R*$_a$)-6-(4-chloro-1-(4-((*racemic*)-1-(difluoromethyl)-3-azabicyclo[3.1.0]hexan-3-yl)-3-fluorobenzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*S*$_a$)-6-(4-chloro-1-(4-((*racemic*)-1-(difluoromethyl)-3-azabicyclo[3.1.0]hexan-3-yl)-3-fluorobenzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 76);

6-(1-(1-(4-((1*R*,5*S*)-3-azabicyclo[3.1.0]hexan-3-yl)phenyl)ethyl)-4-chloro-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*R*$_a$)-6-(1-((*racemic*)-1-(4-((1*R*,5*S*)-3-azabicyclo[3.1.0]hexan-3-yl)phenyl)ethyl)-4-chloro-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*S*$_a$)-6-(1-((*racemic*)-1-(4-((1*R*,5*S*)-3-azabicyclo[3.1.0]hexan-3-yl)phenyl)ethyl)-4-chloro-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 77);

(*R*$_a$)-6-(1-((*R*)-1-(4-((1*R*,5*S*)-3-azabicyclo[3.1.0]hexan-3-yl)phenyl)ethyl)-4-chloro-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*R*$_a$)-6-(1-((*S*)-1-(4-((1*R*,5*S*)-3-azabicyclo[3.1.0]hexan-3-yl)phenyl)ethyl)-4-chloro-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*S*$_a$)-6-(1-((*R*)-1-(4-((1*R*,5*S*)-3-azabicyclo[3.1.0]hexan-3-yl)phenyl)ethyl)-4-chloro-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 132);

(*S*$_a$)-6-(1-((*S*)-1-(4-((1*R*,5*S*)-3-azabicyclo[3.1.0]hexan-3-yl)phenyl)ethyl)-4-chloro-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 132);

6-(4-chloro-1-(4-(2-methoxypyridin-4-yl)benzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*R*$_a$)-6-(4-chloro-1-(4-(2-methoxypyridin-4-yl)benzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*S*$_a$) 6-(4-chloro-1-(4-(2-methoxypyridin-4-yl)benzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 78);

6-(4-chloro-1-(4-(2-ethoxypyridin-4-yl)benzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*R*$_a$) 6-(4-chloro-1-(4-(2-ethoxypyridin-4-yl)benzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*S*$_a$) 6-(4-chloro-1-(4-(2-ethoxypyridin-4-yl)benzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 79);

6-(4-chloro-1-(4-(6-ethoxypyridin-2-yl)benzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*R*$_a$) 6-(4-chloro-1-(4-(6-ethoxypyridin-2-yl)benzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

6-(4-chloro-1-((3'-cyano-[1,1'-biphenyl]-4-yl)methyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*R*$_a$) 6-(4-chloro-1-((3'-cyano-[1,1'-biphenyl]-4-yl)methyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*S*$_a$) 6-(4-chloro-1-((3'-cyano-[1,1'-biphenyl]-4-yl)methyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 80);

6-(4-chloro-1-((2-fluoro-2'3'4'5'-tetrahydro-[1,1'-biphenyl]-4-yl)methyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*R*$_a$) 6-(4-chloro-1-((2-fluoro-2'3'4'5'-tetrahydro-[1,1'-biphenyl]-4-yl)methyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*S*$_a$) 6-(4-chloro-1-((2-fluoro-2'3'4'5'-tetrahydro-[1,1'-biphenyl]-4-yl)methyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 81);

6-(4-chloro-1-(4-(cyclopent-1-en-1-yl)-3-fluorobenzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*R*$_a$) 6-(4-chloro-1-(4-(cyclopent-1-en-1-yl)-3-fluorobenzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*S*$_a$) 6-(4-chloro-1-(4-(cyclopent-1-en-1-yl)-3-fluorobenzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 82);

(*S*$_a$)-6-(4-chloro-1-(4-(6-ethoxypyridin-2-yl)benzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 83);

6-(4-chloro-1-(4-(2-ethoxypyrimidin-6-yl)benzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*R*$_a$) 6-(4-chloro-1-(4-(2-ethoxypyrimidin-6-yl)benzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*S*$_a$) 6-(4-chloro-1-(4-(2-ethoxypyrimidin-6-yl)benzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 84);

6-(4-chloro-1-(4-(6-(methylcarbamoyl)pyridin-2-yl)benzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*R*$_a$) 6-(4-chloro-1-(4-(6-(methylcarbamoyl)pyridin-2-yl)benzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*S*$_a$) 6-(4-chloro-1-(4-(6-(methylcarbamoyl)pyridin-2-yl)benzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 85);

6-(4-chloro-1-(4-(6-(trifluoromethoxy)pyridin-2-yl)benzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*R*$_a$) 6-(4-chloro-1-(4-(6-(trifluoromethoxy)pyridin-2-yl)benzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*S*$_a$) 6-(4-chloro-1-(4-(6-(trifluoromethoxy)pyridin-2-yl)benzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 86);

6-(4-chloro-1-(4-(thiazol-2-yl)benzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*R*$_a$) 6-(4-chloro-1-(4-(thiazol-2-yl)benzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*S*$_a$) 6-(4-chloro-1-(4-(thiazol-2-yl)benzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 87);

6-(1-([1,1' biphenyl]-4-ylmethyl)-4-methoxy-1*H*-pyrrolo[3,2-*c*]pyridine-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*R*$_a$) 6-(1-([1,1' biphenyl]-4-ylmethyl)-4-methoxy-1*H*-pyrrolo[3,2-*c*]pyridine-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*S*$_a$) 6-(1-([1,1' biphenyl]-4-ylmethyl)-4-methoxy-1*H*-pyrrolo[3,2-*c*]pyridine-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 88);

6-(1-(4-(2-ethoxypyridin-4-yl)benzyl)-4-methoxy-1*H*-pyrrolo[3,2-*c*]pyridine-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*R*$_a$)-6-(1-(4-(2-ethoxypyridin-4-yl)benzyl)-4-methoxy-1*H*-pyrrolo[3,2-*c*]pyridine-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*S*$_a$) 6-(1-(4-(2-ethoxypyridin-4-yl)benzyl)-4-methoxy-1*H*-pyrrolo[3,2-*c*]pyridine-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 89);

~~6-(1-([1,1'-biphenyl]-4-ylmethyl)-4-ethoxy-1*H*-pyrrolo[3,2-*c*]pyridine-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*R*$_a$)-6-(1-([1,1'-biphenyl]-4-ylmethyl)-4-ethoxy-1*H*-pyrrolo[3,2-*c*]pyridine-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*S*$_a$)-6-(1-([1,1'-biphenyl]-4-ylmethyl)-4-ethoxy-1*H*-pyrrolo[3,2-*c*]pyridine-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 90);~~

~~6-(1-(4-(6-ethoxypyridin-3-yl)benzyl)-4-methoxy-1*H*-pyrrolo[3,2-*c*]pyridine-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*R*$_a$)-6-(1-(4-(6-ethoxypyridin-3-yl)benzyl)-4-methoxy-1*H*-pyrrolo[3,2-*c*]pyridine-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*S*$_a$)-6-(1-(4-(6-ethoxypyridin-3-yl)benzyl)-4-methoxy-1*H*-pyrrolo[3,2-*c*]pyridine-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 91);~~

~~6-(4-methoxy-1-(4-(6-methoxypyridin-2-yl)benzyl)-1*H*-pyrrolo[3,2-*c*]pyridine-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*R*$_a$)-6-(4-methoxy-1-(4-(6-methoxypyridin-2-yl)benzyl)-1*H*-pyrrolo[3,2-*c*]pyridine-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*S*$_a$)-6-(4-methoxy-1-(4-(6-methoxypyridin-2-yl)benzyl)-1*H*-pyrrolo[3,2-*c*]pyridine-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 92);~~

~~6-(1-([1,1'-biphenyl]-4-ylmethyl)-5-chloro-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*R*$_a$)-6-(1-([1,1'-biphenyl]-4-ylmethyl)-5-chloro-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*S*$_a$)-6-(1-([1,1'-biphenyl]-4-ylmethyl)-5-chloro-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 93);~~

~~6-(1-([1,1'-biphenyl]-4-ylmethyl)-4-chloro-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*R*$_a$)-6-(1-([1,1'-biphenyl]-4-ylmethyl)-4-chloro-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*S*$_a$)-6-(1-([1,1'-biphenyl]-4-ylmethyl)-4-chloro-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 94);~~

~~6-(4-chloro-1-(4-(trifluoromethoxy)benzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*R*$_a$)-6-(4-chloro-1-(4-(trifluoromethoxy)benzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(S_a)-6-(4-chloro-1-(4-(trifluoromethoxy)benzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 95);~~

~~6-(4-chloro-1-(naphthalen-2-ylmethyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 96);~~

~~(R_a)-6-(4-chloro-1-(naphthalen-2-ylmethyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(S_a)-6-(4-chloro-1-(naphthalen-2-ylmethyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 96);~~

~~6-(4-chloro-1-(4-isopropylbenzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(R_a)-6-(4-chloro-1-(4-isopropylbenzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(S_a)-6-(4-chloro-1-(4-isopropylbenzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 97);~~

~~6-(4-chloro-1-(4-cyclopropylbenzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(R_a)-6-(4-chloro-1-(4-cyclopropylbenzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(S_a)-6-(4-chloro-1-(4-cyclopropylbenzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 98);~~

~~6-(4-chloro-1-(4-(*tert*-butyl)benzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(R_a)-6-(4-chloro-1-(4-(*tert*-butyl)benzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(S_a)-6-(4-chloro-1-(4-(*tert*-butyl)benzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 99);~~

~~6-(1-([1,1'-biphenyl]-4-ylmethyl)-4-fluoro-1*H*-indole-7-carboxamido)-2-methylspiro[3.3]heptane-2-carboxylic acid (Example 100);~~

~~(R_a)-6-(1-([1,1'-biphenyl]-4-ylmethyl)-4-fluoro-1*H*-indole-7-carboxamido)-2-methylspiro[3.3]heptane-2-carboxylic acid;~~

~~(S_a)-6-(1-([1,1'-biphenyl]-4-ylmethyl)-4-fluoro-1*H*-indole-7-carboxamido)-2-methylspiro[3.3]heptane-2-carboxylic acid;~~

~~6-(1-([1,1'-biphenyl]-4-ylmethyl)-4-fluoro-1*H*-indole-7-carboxamido)-2-deuterospiro[3.3]heptane-2-carboxylic acid (Example 101);~~

~~(*R*$_a$) 6 (1 ([1,1' biphenyl] 4 ylmethyl) 4 fluoro 1*H* indole 7 carboxamido) 2 deuterospiro[3.3]heptane 2 carboxylic acid;~~

~~(*S*$_a$) 6 (1 ([1,1' biphenyl] 4 ylmethyl) 4 fluoro 1*H* indole 7 carboxamido) 2 deuterospiro[3.3]heptane 2 carboxylic acid (Example 105);~~

~~6 (4 chloro 1 (4 (2 (methylcarbamoyl)pyridin 4 yl)benzyl) 1*H* indazole 7 carboxamido) 2 fluorospiro[3.3]heptane 2 carboxylic acid (Example 102);~~

~~(*R*$_a$) 6 (4 chloro 1 (4 (2 (methylcarbamoyl)pyridin 4 yl)benzyl) 1*H* indazole 7 carboxamido) 2 fluorospiro[3.3]heptane 2 carboxylic acid;~~

~~(*S*$_a$) 6 (4 chloro 1 (4 (2 (methylcarbamoyl)pyridin 4 yl)benzyl) 1*H* indazole 7 carboxamido) 2 fluorospiro[3.3]heptane 2 carboxylic acid;~~

~~2 (6 (1 ([1,1' biphenyl] 4 ylmethyl) 4 fluoro 1*H* indole 7 carboxamido)spiro[3.3]heptan 2 yl)acetic acid (Example 106);~~

~~(*R*$_a$) 2 (6 (1 ([1,1' biphenyl] 4 ylmethyl) 4 fluoro 1*H* indole 7 carboxamido)spiro[3.3]heptan 2 yl)acetic acid (Example 104);~~

~~(*S*$_a$) 2 (6 (1 ([1,1' biphenyl] 4 ylmethyl) 4 fluoro 1*H* indole 7 carboxamido)spiro[3.3]heptan 2 yl)acetic acid (Example 103);~~

~~2 (6 (1 ([1,1' biphenyl] 4 ylmethyl) 5 fluoro 1*H* indazole 7 carboxamido)spiro[3.3]heptan 2 yl)acetic acid (Example 107);~~

~~(*R*$_a$) 2 (6 (1 ([1,1' biphenyl] 4 ylmethyl) 5 fluoro 1*H* indazole 7 carboxamido)spiro[3.3]heptan 2 yl)acetic acid;~~

~~(*S*$_a$) 2 (6 (1 ([1,1' biphenyl] 4 ylmethyl) 5 fluoro 1*H* indazole 7 carboxamido)spiro[3.3]heptan 2 yl)acetic acid;~~

~~2 (6 (1 ([1,1' biphenyl] 4 ylmethyl) 4 methoxy 1*H* pyrrolo[3,2 *c*]pyridine 7 carboxamido)spiro[3.3]heptan 2 yl)acetic acid (Example 108);~~

~~(*R*$_a$) 2 (6 (1 ([1,1' biphenyl] 4 ylmethyl) 4 methoxy 1*H* pyrrolo[3,2 *c*]pyridine 7 carboxamido)spiro[3.3]heptan 2 yl)acetic acid;~~

~~(*S*$_a$) 2 (6 (1 ([1,1' biphenyl] 4 ylmethyl) 4 methoxy 1*H* pyrrolo[3,2 *c*]pyridine 7 carboxamido)spiro[3.3]heptan 2 yl)acetic acid;~~

~~2 (6 (1 ([1,1' biphenyl] 4 ylmethyl) 4 chloro 1*H* indazole 7 carboxamido)spiro[3.3]heptan 2 yl)acetic acid (Example 109);~~

~~(*R*$_a$) 2 (6 (1 ([1,1' biphenyl] 4 ylmethyl) 4 chloro 1*H* indazole 7 carboxamido)spiro[3.3]heptan 2 yl)acetic acid;~~

~~(*S*$_a$) 2 (6 (1 ([1,1' biphenyl] 4 ylmethyl) 4 chloro 1*H* indazole 7 carboxamido)spiro[3.3]heptan 2 yl)acetic acid;~~

2-(6-(1-([1,1'-biphenyl]-4-ylmethyl)-5-chloro-1*H*-indazole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid (Example 110);

(*R*$_a$)-2-(6-(1-([1,1'-biphenyl]-4-ylmethyl)-5-chloro-1*H*-indazole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid;

(*S*$_a$)-2-(6-(1-([1,1'-biphenyl]-4-ylmethyl)-5-chloro-1*H*-indazole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid;

4-fluoro-*N*-(6-((methylsulfonyl)carbamoyl)spiro[3.3]heptan-2-yl)-1-(4-(trifluoromethoxy)benzyl)-1*H*-indole-7-carboxamide;

(*R*$_a$)-4-fluoro-*N*-(6-((methylsulfonyl)carbamoyl)spiro[3.3]heptan-2-yl)-1-(4-(trifluoromethoxy)benzyl)-1*H*-indole-7-carboxamide;

(*S*$_a$)-4-fluoro-*N*-(6-((methylsulfonyl)carbamoyl)spiro[3.3]heptan-2-yl)-1-(4-(trifluoromethoxy)benzyl)-1*H*-indole-7-carboxamide (Example 111);

6-(1-(1-([1,1'-biphenyl]-4-yl)-ethyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*R*$_a$)-6-(1-((*racemic*)-1-([1,1'-biphenyl]-4-yl)-ethyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*S*$_a$)-6-(1-((*racemic*)-1-([1,1'-biphenyl]-4-yl)-ethyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 112);

(*R*$_a$)-6-(1-((*R*)-1-([1,1'-biphenyl]-4-yl)-ethyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*R*$_a$)-6-(1-((*S*)-1-([1,1'-biphenyl]-4-yl)-ethyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*S*$_a$)-6-(1-((*R*)-1-([1,1'-biphenyl]-4-yl)-ethyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 125);

(*S*$_a$)-6-(1-((*S*)-1-([1,1'-biphenyl]-4-yl)-ethyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 125);

6-(1-(1-(3'-methoxy-[1,1'-biphenyl]-4-yl)-ethyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*R*$_a$)-6-(1-((*racemic*)-1-(3'-methoxy-[1,1'-biphenyl]-4-yl)-ethyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*S*$_a$)-6-(1-((*racemic*)-1-(3'-methoxy-[1,1'-biphenyl]-4-yl)-ethyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 113);

(*R*$_a$)-6-(1-((*R*)-1-(3'-methoxy-[1,1'-biphenyl]-4-yl)-ethyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

~~(R_a) 6 (1 ((*S*) 1 (3' methoxy [1,1' biphenyl] 4 yl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(S_a) 6 (1 ((*R*) 1 (3' methoxy [1,1' biphenyl] 4 yl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(S_a) 6 (1 ((*S*) 1 (3' methoxy [1,1' biphenyl] 4 yl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~6 (1 (1 (3' cyano 5' methoxy [1,1' biphenyl] 4 yl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(R_a) 6 (1 ((*racemic*) 1 (3' cyano 5' methoxy [1,1' biphenyl] 4 yl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(S_a) 6 (1 ((*racemic*) 1 (3' cyano 5' methoxy [1,1' biphenyl] 4 yl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid (Example 114);~~

~~(R_a) 6 (1 ((*R*) 1 (3' cyano 5' methoxy [1,1' biphenyl] 4 yl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(R_a) 6 (1 ((*S*) 1 (3' cyano 5' methoxy [1,1' biphenyl] 4 yl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(S_a) 6 (1 ((*R*) 1 (3' cyano 5' methoxy [1,1' biphenyl] 4 yl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid (Example 126);~~

~~(S_a) 6 (1 ((*S*) 1 (3' cyano 5' methoxy [1,1' biphenyl] 4 yl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid (Example 126);~~

~~6 (1 (1 (4 (2 ethoxypyridin 4 yl)phenyl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(R_a) 6 (1 ((*racemic*) 1 (4 (2 ethoxypyridin 4 yl)phenyl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(S_a) 6 (1 ((*racemic*) 1 (4 (2 ethoxypyridin 4 yl)phenyl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid (Example 115);~~

~~(R_a) 6 (1 ((*R*) 1 (4 (2 ethoxypyridin 4 yl)phenyl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(R_a) 6 (1 ((*S*) 1 (4 (2 ethoxypyridin 4 yl)phenyl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(S_a) 6 (1 ((*R*) 1 (4 (2 ethoxypyridin 4 yl)phenyl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(S_a) 6 (1 ((*S*) 1 (4 (2 ethoxypyridin 4 yl)phenyl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~6-(1-(1-([1,1'-biphenyl]-4-yl)-ethyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(R_a)-6-(1-((*racemic*)-1-([1,1'-biphenyl]-4-yl)-ethyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(S_a)-6-(1-((*racemic*)-1-([1,1'-biphenyl]-4-yl)-ethyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 116);~~

~~(R_a)-6-(1-((*S*)-1-([1,1'-biphenyl]-4-yl)-ethyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(R_a)-6-(1-((*R*)-1-([1,1'-biphenyl]-4-yl)-ethyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(S_a)-6-(1-((*R*)-1-([1,1'-biphenyl]-4-yl)-ethyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 127);~~

~~(S_a)-6-(1-((*S*)-1-([1,1'-biphenyl]-4-yl)-ethyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 127);~~

~~6-(4-fluoro-1-(1-(3'-methoxy-[1,1'-biphenyl]-4-yl)-ethyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(R_a)-6-(4-fluoro-1-((*racemic*)-1-(3'-methoxy-[1,1'-biphenyl]-4-yl)-ethyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(S_a)-6-(4-fluoro-1-((*racemic*)-1-(3'-methoxy-[1,1'-biphenyl]-4-yl)-ethyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid; (Example 117)~~

~~(R_a)-6-(4-fluoro-1-((*R*)-1-(3'-methoxy-[1,1'-biphenyl]-4-yl)-ethyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(R_a)-6-(4-fluoro-1-((*S*)-1-(3'-methoxy-[1,1'-biphenyl]-4-yl)-ethyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(S_a)-6-(4-fluoro-1-((*R*)-1-(3'-methoxy-[1,1'-biphenyl]-4-yl)-ethyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 128);~~

~~(S_a)-6-(4-fluoro-1-((*S*)-1-(3'-methoxy-[1,1'-biphenyl]-4-yl)-ethyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 128);~~

~~6-(1-(1-(4-(2-ethoxypyridin-4-yl)phenyl)-ethyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(R_a)-6-(1-((*racemic*)-1-(4-(2-ethoxypyridin-4-yl)phenyl)-ethyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(S_a)-6-(1-((*racemic*)-1-(4-(2-ethoxypyridin-4-yl)phenyl)-ethyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 118);~~

~~(R_a)-6-(1-((*R*)-1-(4-(2-ethoxypyridin-4-yl)phenyl)-ethyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(R_a)-6-(1-((*S*)-1-(4-(2-ethoxypyridin-4-yl)phenyl)-ethyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(S_a)-6-(1-((*R*)-1-(4-(2-ethoxypyridin-4-yl)phenyl)-ethyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 129);~~

~~(S_a)-6-(1-((*S*)-1-(4-(2-ethoxypyridin-4-yl)phenyl)-ethyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 129);~~

~~6-(4-fluoro-1-(1-(4-(6-methoxypyridin-3-yl)phenyl)-ethyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(R_a)-6-(4-fluoro-1-((*racemic*)-1-(4-(6-methoxypyridin-3-yl)phenyl)-ethyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(S_a)-6-(4-fluoro-1-((*racemic*)-1-(4-(6-methoxypyridin-3-yl)phenyl)-ethyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 119);~~

~~(R_a)-6-(4-fluoro-1-((*R*)-1-(4-(6-methoxypyridin-3-yl)phenyl)-ethyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(R_a)-6-(4-fluoro-1-((*S*)-1-(4-(6-methoxypyridin-3-yl)phenyl)-ethyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(S_a)-6-(4-fluoro-1-((*R*)-1-(4-(6-methoxypyridin-3-yl)phenyl)-ethyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(S_a)-6-(4-fluoro-1-((*S*)-1-(4-(6-methoxypyridin-3-yl)phenyl)-ethyl)-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~6-(1-(1-(4-(5-chloro-6-methoxypyridin-3-yl)phenyl)-ethyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(R_a)-6-(1-((*racemic*)-1-(4-(5-chloro-6-methoxypyridin-3-yl)phenyl)-ethyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(S_a)-6-(1-((*racemic*)-1-(4-(5-chloro-6-methoxypyridin-3-yl)phenyl)-ethyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 120);~~

~~(R_a)-6-(1-((*R*)-1-(4-(5-chloro-6-methoxypyridin-3-yl)phenyl)-ethyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(R_a)-6-(1-((*S*)-1-(4-(5-chloro-6-methoxypyridin-3-yl)phenyl)-ethyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(S_a)-6-(1-((*R*)-1-(4-(5-chloro-6-methoxypyridin-3-yl)phenyl)-ethyl)-4-fluoro-1*H*-indole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(S_a) 6 (1 ((*S*) 1 (4 (5 chloro 6 methoxypyridin 3 yl)phenyl) ethyl) 4 fluoro 1*H* indole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~6 (1 (1 ([1,1' biphenyl] 4 yl) ethyl) 4 chloro 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(R_a) 6 (1 ((*racemic*) 1 ([1,1' biphenyl] 4 yl) ethyl) 4 chloro 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(S_a) 6 (1 ((*racemic*) 1 ([1,1' biphenyl] 4 yl) ethyl) 4 chloro 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid (Example 121);~~

~~(R_a) 6 (1 ((*R*) 1 ([1,1' biphenyl] 4 yl) ethyl) 4 chloro 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(R_a) 6 (1 ((*S*) 1 ([1,1' biphenyl] 4 yl) ethyl) 4 chloro 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(S_a) 6 (1 ((*R*) 1 ([1,1' biphenyl] 4 yl) ethyl) 4 chloro 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid (Example 130);~~

~~(S_a) 6 (1 ((*S*) 1 ([1,1' biphenyl] 4 yl) ethyl) 4 chloro 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid (Example 130);~~

~~6 (4 chloro 1 (1 (3' methoxy [1,1' biphenyl] 4 yl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(R_a) 6 (4 chloro 1 ((*racemic*) 1 (3' methoxy [1,1' biphenyl] 4 yl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(S_a) 6 (4 chloro 1 ((*racemic*) 1 (3' methoxy [1,1' biphenyl] 4 yl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid (Example 122);~~

~~(R_a) 6 (4 chloro 1 ((*R*) 1 (3' methoxy [1,1' biphenyl] 4 yl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(R_a) 6 (4 chloro 1 ((*S*) 1 (3' methoxy [1,1' biphenyl] 4 yl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(S_a) 6 (4 chloro 1 ((*R*) 1 (3' methoxy [1,1' biphenyl] 4 yl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(S_a) 6 (4 chloro 1 ((*S*) 1 (3' methoxy [1,1' biphenyl] 4 yl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~6 (4 chloro 1 (1 (3' cyano 5' methoxy [1,1' biphenyl] 4 yl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(R_a) 6 (4 chloro 1 ((*racemic*) 1 (3' cyano 5' methoxy [1,1' biphenyl] 4 yl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(*S*$_a$) 6 (4 chloro 1 ((*racemic*) 1 (3' cyano 5' methoxy [1,1' biphenyl] 4 yl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid (Example 123);~~

~~(*R*$_a$) 6 (4 chloro 1 ((*R*) 1 (3' cyano 5' methoxy [1,1' biphenyl] 4 yl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(*R*$_a$) 6 (4 chloro 1 ((*S*) 1 (3' cyano 5' methoxy [1,1' biphenyl] 4 yl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(*S*$_a$) 6 (4 chloro 1 ((*R*) 1 (3' cyano 5' methoxy [1,1' biphenyl] 4 yl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(*S*$_a$) 6 (4 chloro 1 ((*S*) 1 (3' cyano 5' methoxy [1,1' biphenyl] 4 yl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~6 (4 chloro 1 (1 (4 (2 ethoxypyridin 4 yl)phenyl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(*R*$_a$) 6 (4 chloro 1 ((*racemic*) 1 (4 (2 ethoxypyridin 4 yl)phenyl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(*S*$_a$) 6 (4 chloro 1 ((*racemic*) 1 (4 (2 ethoxypyridin 4 yl)phenyl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid (Example 124);~~

~~(*R*$_a$) 6 (4 chloro 1 ((*R*) 1 (4 (2 ethoxypyridin 4 yl)phenyl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(*R*$_a$) 6 (4 chloro 1 ((*S*) 1 (4 (2 ethoxypyridin 4 yl)phenyl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(*S*$_a$) 6 (4 chloro 1 ((*R*) 1 (4 (2 ethoxypyridin 4 yl)phenyl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid (Example 131);~~

~~(*S*$_a$) 6 (4 chloro 1 ((*S*) 1 (4 (2 ethoxypyridin 4 yl)phenyl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid (Example 131);~~

~~6 (1 (1 (4 (6 ethoxypyridin 2 yl)phenyl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(*R*$_a$) 6 (1 ((*racemic*) 1 (4 (6 ethoxypyridin 2 yl)phenyl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(*S*$_a$) 6 (1 ((*racemic*) 1 (4 (6 ethoxypyridin 2 yl)phenyl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid (Example 133);~~

~~(*R*$_a$) 6 (1 ((*R*) 1 (4 (6 ethoxypyridin 2 yl)phenyl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(*R*$_a$) 6 (1 ((*S*) 1 (4 (6 ethoxypyridin 2 yl)phenyl) ethyl) 1*H* indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

(*S*$_a$) 6-(1-((*R*)-1-(4-(6-ethoxypyridin-2-yl)phenyl)-ethyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*S*$_a$) 6-(1-((*S*)-1-(4-(6-ethoxypyridin-2-yl)phenyl)-ethyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

6-(4-chloro-1-(1-(4-(6-ethoxypyridin-2-yl)phenyl)-ethyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*R*$_a$) 6-(4-chloro-1-((*racemic*)-1-(4-(6-ethoxypyridin-2-yl)phenyl)-ethyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*S*$_a$) 6-(4-chloro-1-((*racemic*)-1-(4-(6-ethoxypyridin-2-yl)phenyl)-ethyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 134);

(*R*$_a$) 6-(4-chloro-1-((*R*)-1-(4-(6-ethoxypyridin-2-yl)phenyl)-ethyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*R*$_a$) 6-(4-chloro-1-((*S*)-1-(4-(6-ethoxypyridin-2-yl)phenyl)-ethyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*S*$_a$) 6-(4-chloro-1-((*R*)-1-(4-(6-ethoxypyridin-2-yl)phenyl)-ethyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*S*$_a$) 6-(4-chloro-1-((*S*)-1-(4-(6-ethoxypyridin-2-yl)phenyl)-ethyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

6-(5-chloro-1-(4-(2-methoxypyridin-4-yl)benzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*R*$_a$) 6-(5-chloro-1-(4-(2-methoxypyridin-4-yl)benzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*S*$_a$) 6-(5-chloro-1-(4-(2-methoxypyridin-4-yl)benzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 135);

6-(5-chloro-1-(4-(2-ethoxypyridin-4-yl)benzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*R*$_a$) 6-(5-chloro-1-(4-(2-ethoxypyridin-4-yl)benzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*S*$_a$) 6-(5-chloro-1-(4-(2-ethoxypyridin-4-yl)benzyl)-1*H*-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 136);

2-(6-(4-fluoro-1-(4-(2-methoxyquinolin-6-yl)benzyl)-1H-indole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid;

(*R*$_a$) 2-(6-(4-fluoro-1-(4-(2-methoxyquinolin-6-yl)benzyl)-1H-indole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid;

~~(S_a) 2 (6 (4 fluoro 1 (4 (2 methoxyquinolin 6 yl)benzyl) 1H indole 7 carboxamido)spiro[3.3]heptan 2 yl)acetic acid; (Example 137)~~

~~2 (6 (4 fluoro 1 (4 (6 methoxypyridin 3 yl)benzyl) 1H indole 7 carboxamido)spiro[3.3]heptan 2 yl)acetic acid;~~

~~(R_a) 2 (6 (4 fluoro 1 (4 (6 methoxypyridin 3 yl)benzyl) 1H indole 7 carboxamido)spiro[3.3]heptan 2 yl)acetic acid; (Example 138)~~

~~(S_a) 2 (6 (4 fluoro 1 (4 (6 methoxypyridin 3 yl)benzyl) 1H indole 7 carboxamido)spiro[3.3]heptan 2 yl)acetic acid;~~

~~2 (6 (4 fluoro 1 (4 (2 methoxypyridin 4 yl)benzyl) 1H indole 7 carboxamido)spiro[3.3]heptan 2 yl)acetic acid;~~

~~(R_a) 2 (6 (4 fluoro 1 (4 (2 methoxypyridin 4 yl)benzyl) 1H indole 7 carboxamido)spiro[3.3]heptan 2 yl)acetic acid; (Example 139)~~

~~(S_a) 2 (6 (4 fluoro 1 (4 (2 methoxypyridin 4 yl)benzyl) 1H indole 7 carboxamido)spiro[3.3]heptan 2 yl)acetic acid;~~

~~2 (6 (4 fluoro 1 (4 (2 methoxyquinolin 6 yl)benzyl) 1H indole 7 carboxamido)spiro[3.3]heptan 2 yl)acetic acid;~~

~~(R_a) 2 (6 (4 fluoro 1 (4 (2 methoxyquinolin 6 yl)benzyl) 1H indole 7 carboxamido)spiro[3.3]heptan 2 yl)acetic acid; (Example 140)~~

~~(S_a) 2 (6 (4 fluoro 1 (4 (2 methoxyquinolin 6 yl)benzyl) 1H indole 7 carboxamido)spiro[3.3]heptan 2 yl)acetic acid;~~

~~2 (6 (1 ([1,1' biphenyl] 4 ylmethyl) 4 chloro 1H indazole 7 carboxamido)spiro[3.3]heptan 2 yl)acetic acid;~~

~~(S_a) 2 (6 (1 ([1,1' biphenyl] 4 ylmethyl) 4 chloro 1H indazole 7 carboxamido)spiro[3.3]heptan 2 yl)acetic acid; (Example 141)~~

~~(R_a) 2 (6 (1 ([1,1' biphenyl] 4 ylmethyl) 4 chloro 1H indazole 7 carboxamido)spiro[3.3]heptan 2 yl)acetic acid; (Example 142)~~

~~2 (6 (4 chloro 1 ((2' fluoro [1,1' biphenyl] 4 yl)methyl) 1H indazole 7 carboxamido)spiro[3.3]heptan 2 yl)acetic acid;~~

~~(R_a) 2 (6 (4 chloro 1 ((2' fluoro [1,1' biphenyl] 4 yl)methyl) 1H indazole 7 carboxamido)spiro[3.3]heptan 2 yl)acetic acid; (Example 143)~~

~~(S_a) 2 (6 (4 chloro 1 ((2' fluoro [1,1' biphenyl] 4 yl)methyl) 1H indazole 7 carboxamido)spiro[3.3]heptan 2 yl)acetic acid;~~

~~2 (6 (4 chloro 1 ((3' cyano [1,1' biphenyl] 4 yl)methyl) 1H indazole 7 carboxamido)spiro[3.3]heptan 2 yl)acetic acid;~~

~~(*R*$_a$) 2-(6-(4-chloro-1-((3'-cyano-[1,1'-biphenyl]-4-yl)methyl)-1H-indazole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid; (Example 144)~~

~~(*S*$_a$) 2-(6-(4-chloro-1-((3'-cyano-[1,1'-biphenyl]-4-yl)methyl)-1H-indazole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid;~~

~~2-(6-(4-chloro-1-((4'-cyano-[1,1'-biphenyl]-4-yl)methyl)-1H-indazole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid;~~

~~(*R*$_a$) 2-(6-(4-chloro-1-((4'-cyano-[1,1'-biphenyl]-4-yl)methyl)-1H-indazole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid; (Example 145)~~

~~(*S*$_a$) 2-(6-(4-chloro-1-((4'-cyano-[1,1'-biphenyl]-4-yl)methyl)-1H-indazole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid;~~

~~2-(6-(4-chloro-1-(4-(2-methoxyquinolin-6-yl)benzyl)-1H-indazole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid;~~

~~(*R*$_a$) 2-(6-(4-chloro-1-(4-(2-methoxyquinolin-6-yl)benzyl)-1H-indazole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid; (Example 146)~~

~~(*S*$_a$) 2-(6-(4-chloro-1-(4-(2-methoxyquinolin-6-yl)benzyl)-1H-indazole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid;~~

~~2-(6-(5-chloro-1-(4-(2-methoxyquinolin-6-yl)benzyl)-1H-indazole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid;~~

~~(*R*$_a$) 2-(6-(5-chloro-1-(4-(2-methoxyquinolin-6-yl)benzyl)-1H-indazole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid; (Example 147)~~

~~(*S*$_a$) 2-(6-(5-chloro-1-(4-(2-methoxyquinolin-6-yl)benzyl)-1H-indazole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid;~~

~~2-(6-(1-([1,1'-biphenyl]-4-ylmethyl)-5-chloro-1H-indazole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid;~~

~~(*R*$_a$) 2-(6-(1-([1,1'-biphenyl]-4-ylmethyl)-5-chloro-1H-indazole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid;~~

~~(*S*$_a$) 2-(6-(1-([1,1'-biphenyl]-4-ylmethyl)-5-chloro-1H-indazole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid; (Example 148)~~

~~2-(6-(4-chloro-1-(4-(6-methoxypyridin-2-yl)benzyl)-1H-indazole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid;~~

~~(*R*$_a$)-2-(6-(4-chloro-1-(4-(6-methoxypyridin-2-yl)benzyl)-1H-indazole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid; (Example 149)~~

~~(*S*$_a$) 2-(6-(4-chloro-1-(4-(6-methoxypyridin-2-yl)benzyl)-1H-indazole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid;~~

~~2-(6-(4-fluoro-1-(4-(6-methoxypyridin-2-yl)benzyl)-1H-indole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid;~~

~~(*R*$_a$)-2-(6-(4-fluoro-1-(4-(6-methoxypyridin-2-yl)benzyl)-1H-indole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid; (Example 150)~~

~~(*S*$_a$)-2-(6-(4-fluoro-1-(4-(6-methoxypyridin-2-yl)benzyl)-1H-indole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid;~~

~~2-(6-(5-chloro-1-((2-fluoro-[1,1'-biphenyl]-4-yl)methyl)-1H-indazole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid;~~

~~(*R*$_a$)-2-(6-(5-chloro-1-((2-fluoro-[1,1'-biphenyl]-4-yl)methyl)-1H-indazole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid; (Example 151)~~

~~(*S*$_a$)-2-(6-(5-chloro-1-((2-fluoro-[1,1'-biphenyl]-4-yl)methyl)-1H-indazole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid; (Example 152)~~

~~6-(5-chloro-1-((2-fluoro-[1,1'-biphenyl]-4-yl)methyl)-1H-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*R*$_a$)-6-(5-chloro-1-((2-fluoro-[1,1'-biphenyl]-4-yl)methyl)-1H-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*S*$_a$)-6-(5-chloro-1-((2-fluoro-[1,1'-biphenyl]-4-yl)methyl)-1H-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid; (Example 153)~~

~~6-(5-chloro-1-(3-fluoro-4-(2-methoxypyridin-4-yl)benzyl)-1H-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*R*$_a$)-6-(5-chloro-1-(3-fluoro-4-(2-methoxypyridin-4-yl)benzyl)-1H-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*S*$_a$)-6-(5-chloro-1-(3-fluoro-4-(2-methoxypyridin-4-yl)benzyl)-1H-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid; (Example 154)~~

~~6-(5-chloro-1-((3-fluoro-[1,1'-biphenyl]-4-yl)methyl)-1H-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*R*$_a$)-6-(5-chloro-1-((3-fluoro-[1,1'-biphenyl]-4-yl)methyl)-1H-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*S*$_a$)-6-(5-chloro-1-((3-fluoro-[1,1'-biphenyl]-4-yl)methyl)-1H-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid; (Example 155)~~

~~6-(5-chloro-1-(2-fluoro-4-(2-methoxypyridin-4-yl)benzyl)-1H-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*R*$_a$)-6-(5-chloro-1-(2-fluoro-4-(2-methoxypyridin-4-yl)benzyl)-1H-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(S_a) 6 (5 chloro 1 (2 fluoro 4 (2 methoxypyridin 4 yl)benzyl) 1H indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid; (Example 156)~~

~~6 (1 (([1,1' biphenyl] 4 yl 2,3,5,6 d4)methyl d2) 4 chloro 1H indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(R_a) 6 (1 (([1,1' biphenyl] 4 yl 2,3,5,6 d4)methyl d2) 4 chloro 1H indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(S_a) 6 (1 (([1,1' biphenyl] 4 yl 2,3,5,6 d4)methyl d2) 4 chloro 1H indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid; (Example 157)~~

~~6 (1 ([1,1' biphenyl] 4 ylmethyl) 5 bromo 1H indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(R_a) 6 (1 ([1,1' biphenyl] 4 ylmethyl) 5 bromo 1H indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(S_a) 6 (1 ([1,1' biphenyl] 4 ylmethyl) 5 bromo 1H indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid; (Example 158)~~

~~6 (1 ([1,1' biphenyl] 4 ylmethyl) 5 methoxy 1H indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(R_a) 6 (1 ([1,1' biphenyl] 4 ylmethyl) 5 methoxy 1H indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(S_a) 6 (1 ([1,1' biphenyl] 4 ylmethyl) 5 methoxy 1H indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid; (Example 159)~~

~~6 (1 ([1,1' biphenyl] 4 ylmethyl) 5 methyl 1H indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(R_a) 6 (1 ([1,1' biphenyl] 4 ylmethyl) 5 methyl 1H indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid;~~

~~(S_a) 6 (1 ([1,1' biphenyl] 4 ylmethyl) 5 methyl 1H indazole 7 carboxamido)spiro[3.3]heptane 2 carboxylic acid; (Example 160)~~

~~2 (6 (1 ([1,1' biphenyl] 4 ylmethyl) 4 methoxy 1H indazole 7 carboxamido)spiro[3.3]heptan 2 yl)acetic acid;~~

~~(R_a) 2 (6 (1 ([1,1' biphenyl] 4 ylmethyl) 4 methoxy 1H indazole 7 carboxamido)spiro[3.3]heptan 2 yl)acetic acid;~~

~~(S_a) 2 (6 (1 ([1,1' biphenyl] 4 ylmethyl) 4 methoxy 1H indazole 7 carboxamido)spiro[3.3]heptan 2 yl)acetic acid; (Example 161)~~

~~2 (6 (1 ([1,1' biphenyl] 4 ylmethyl) 4 (difluoromethoxy) 1H indazole 7 carboxamido)spiro[3.3]heptan 2 yl)acetic acid;~~

(*R*$_a$) 2-(6-(1-([1,1'-biphenyl]-4-ylmethyl)-4-(difluoromethoxy)-1H-indazole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid;

(*S*$_a$) 2-(6-(1-([1,1'-biphenyl]-4-ylmethyl)-4-(difluoromethoxy)-1H-indazole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid; (Example 162)

6-(1-([1,1'-biphenyl]-4-ylmethyl)-5-(difluoromethoxy)-1H-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*R*$_a$) 6-(1-([1,1'-biphenyl]-4-ylmethyl)-5-(difluoromethoxy)-1H-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*S*$_a$) 6-(1-([1,1'-biphenyl]-4-ylmethyl)-5-(difluoromethoxy)-1H-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid; (Example 163)

2-(6-(1-([1,1'-biphenyl]-4-ylmethyl)-5-methoxy-1H-indazole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid;

(*R*$_a$) 2-(6-(1-([1,1'-biphenyl]-4-ylmethyl)-5-methoxy-1H-indazole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid; (Example 164)

(*S*$_a$) 2-(6-(1-([1,1'-biphenyl]-4-ylmethyl)-5-methoxy-1H-indazole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid;

2-(6-(1-([1,1'-biphenyl]-4-ylmethyl)-5-(difluoromethoxy)-1H-indazole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid;

(*R*$_a$) 2-(6-(1-([1,1'-biphenyl]-4-ylmethyl)-5-(difluoromethoxy)-1H-indazole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid; (Example 165)

(*S*$_a$) 2-(6-(1-([1,1'-biphenyl]-4-ylmethyl)-5-(difluoromethoxy)-1H-indazole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid;

6-(1-(1-([1,1'-biphenyl]-4-yl)ethyl-1,2,2,2-d4)-4-chloro-1H-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*R*$_a$) 6-(1-((*racemic*)-1-([1,1'-biphenyl]-4-yl)ethyl-1,2,2,2-d4)-4-chloro-1H-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*S*$_a$) 6-(1-((*racemic*)-1-([1,1'-biphenyl]-4-yl)ethyl-1,2,2,2-d4)-4-chloro-1H-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid; (Example 166)

6-(1-((*R*) or (*S*)-1-([1,1'-biphenyl]-4-yl)ethyl-1,2,2,2-d4)-4-chloro-1H-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*R*$_a$)-6-(1-((*R*) or (*S*)-1-([1,1'-biphenyl]-4-yl)ethyl-1,2,2,2-d4)-4-chloro-1H-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(*S*$_a$) 6-(1-((*R*) or (*S*)-1-([1,1'-biphenyl]-4-yl)ethyl-1,2,2,2-d4)-4-chloro-1H-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid; (Example 167)

6-(1-(1-([1,1'-biphenyl]-4-yl)ethyl-1,2,2,2-d4)-1H-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(R_a)-6-(1-((racemic)-1-([1,1'-biphenyl]-4-yl)ethyl-1,2,2,2-d4)-1H-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(S_a)-6-(1-((racemic)-1-([1,1'-biphenyl]-4-yl)ethyl-1,2,2,2-d4)-1H-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid; (Example 168)

(R_a)-6-(1-((*R*) or (*S*)-1-([1,1'-biphenyl]-4-yl)ethyl-1,2,2,2-d4)-1H-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(S_a)-6-(1-((*R*) or (*S*)-1-([1,1'-biphenyl]-4-yl)ethyl-1,2,2,2-d4)-1H-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid; (Example 169)

2-(6-(1-([1,1'-biphenyl]-4-ylmethyl)-5-chloro-4-fluoro-1H-indazole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid;

(R_a)-2-(6-(1-([1,1'-biphenyl]-4-ylmethyl)-5-chloro-4-fluoro-1H-indazole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid; (Example 170)

(S_a)-2-(6-(1-([1,1'-biphenyl]-4-ylmethyl)-5-chloro-4-fluoro-1H-indazole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid;

2-(6-(1-([1,1'-biphenyl]-4-ylmethyl)-5-chloro-4-methoxy-1H-indazole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid;

(R_a)-2-(6-(1-([1,1'-biphenyl]-4-ylmethyl)-5-chloro-4-methoxy-1H-indazole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid; (Example 171)

(S_a)-2-(6-(1-([1,1'-biphenyl]-4-ylmethyl)-5-chloro-4-methoxy-1H-indazole-7-carboxamido)spiro[3.3]heptan-2-yl)acetic acid; (Example 171)

6-(4-chloro-1-(4-cyclobutyl-3-fluorobenzyl)-1H-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(R_a)-6-(4-chloro-1-(4-cyclobutyl-3-fluorobenzyl)-1H-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(S_a)-6-(4-chloro-1-(4-cyclobutyl-3-fluorobenzyl)-1H-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid; (Example 172)

6-(1-(1-([1,1'-biphenyl]-4-yl)ethyl)-5-chloro-1H-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(R_a)-6-(1-((*racemic*)1-([1,1'-biphenyl]-4-yl)ethyl)-5-chloro-1H-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;

(S_a)-6-(1-((*racemic*)1-([1,1'-biphenyl]-4-yl)ethyl)-5-chloro-1H-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid; (Example 173)

~~6-(1-(1-([1,1'-biphenyl]-4-yl)ethyl)-5-chloro-1H-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*R*$_a$)-6-(1-((*R*)-1-([1,1'-biphenyl]-4-yl)ethyl)-5-chloro-1H-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*S*$_a$)-6-(1-((*S*)-1-([1,1'-biphenyl]-4-yl)ethyl)-5-chloro-1H-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~6-(4-chloro-1-((2-methoxyquinolin-7-yl)methyl)-1H-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*R*$_a$)-6-(4-chloro-1-((2-methoxyquinolin-7-yl)methyl)-1H-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

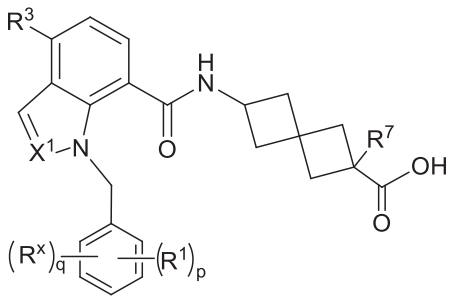
~~(*S*$_a$)-6-(4-chloro-1-((2-methoxyquinolin-7-yl)methyl)-1H-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid; (Example 175)~~

~~6-(1-(3-([1,1'-biphenyl]-4-yl)oxetan-3-yl)-4-chloro-1H-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid;~~

~~(*R*$_a$)-6-(1-(3-([1,1'-biphenyl]-4-yl)oxetan-3-yl)-4-chloro-1H-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid; and~~

~~(*S*$_a$)-6-(1-(3-([1,1'-biphenyl]-4-yl)oxetan-3-yl)-4-chloro-1H-indazole-7-carboxamido)spiro[3.3]heptane-2-carboxylic acid (Example 176).~~

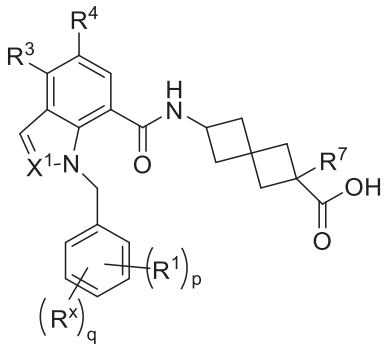
13. The compound of claim 1 having the Formula (V):



(V)

or a pharmaceutically acceptable salt, solvate, solvate of the salt, hydrate, a single stereoisomer, a mixture of stereoisomers, a racemic mixture of stereoisomers, isotopic variant, or prodrug thereof; wherein p is 1 and R^1 is phenyl optionally substituted with one, two, or three R^y.

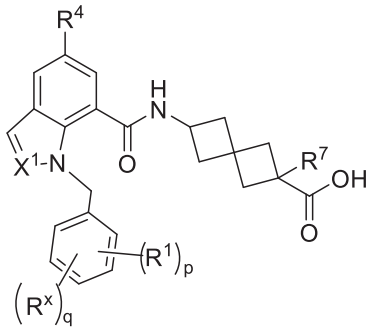
14. The compound of claim 1 having the Formula (Va):



(Va)

or a pharmaceutically acceptable salt, solvate, solvate of the salt, hydrate, a single stereoisomer, a mixture of stereoisomers, a racemic mixture of stereoisomers, isotopic variant, or prodrug thereof; wherein p is 1 and R^1 is phenyl optionally substituted with one, two, or three R^y.

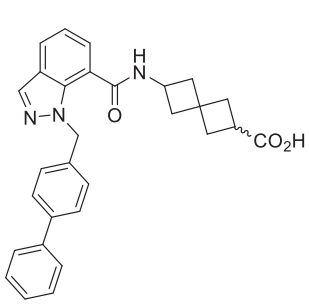
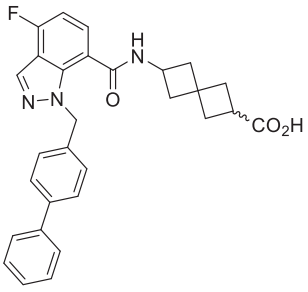
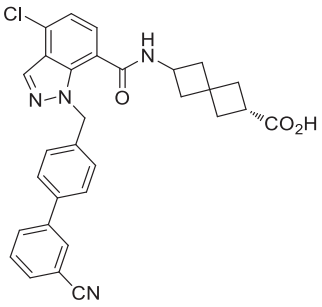
15. The compound of claim 1 having the Formula (Vb):

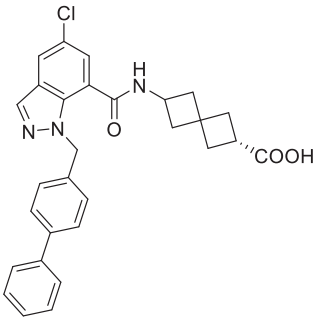
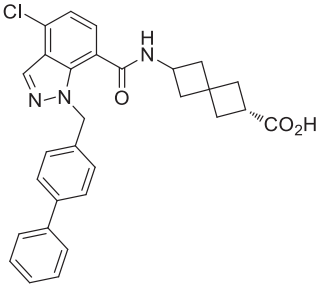
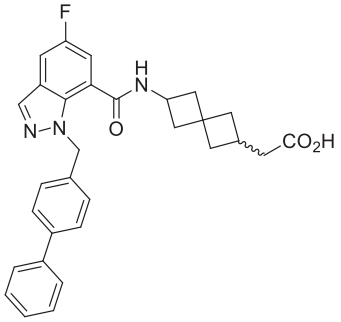


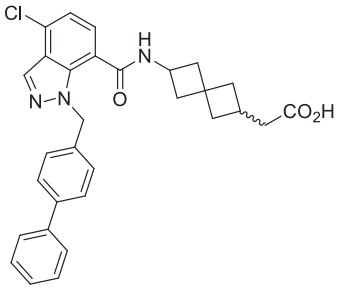
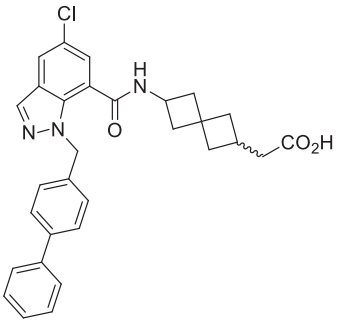
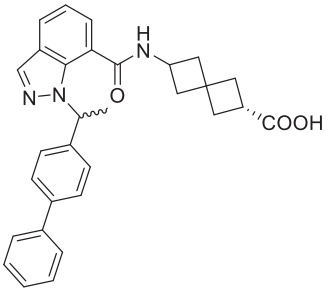
(Vb)

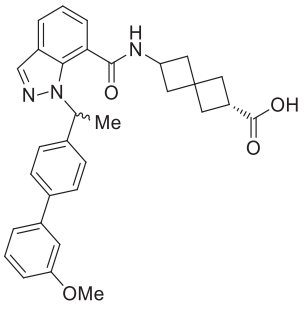
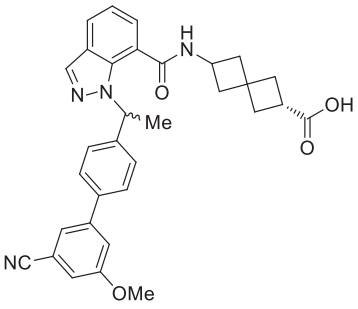
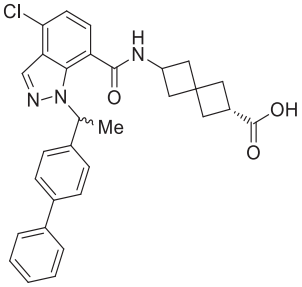
or a pharmaceutically acceptable salt, solvate, solvate of the salt, hydrate, a single stereoisomer, a mixture of stereoisomers, a racemic mixture of stereoisomers, isotopic variant, or prodrug thereof; wherein p is 1 and R^1 is phenyl optionally substituted with one, two, or three R^y.

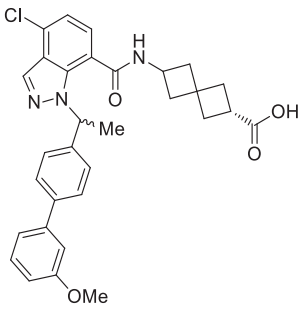
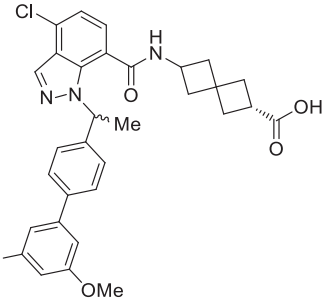
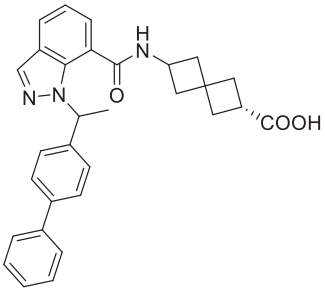
16. The compound of claim 1 wherein the compound is selected from:

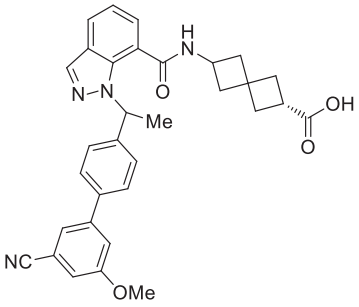
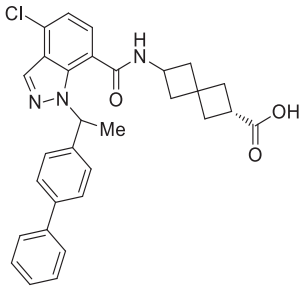
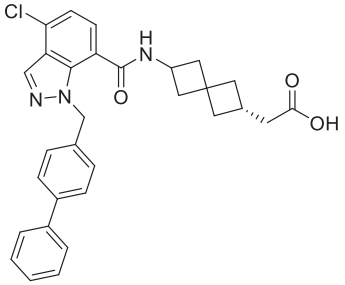
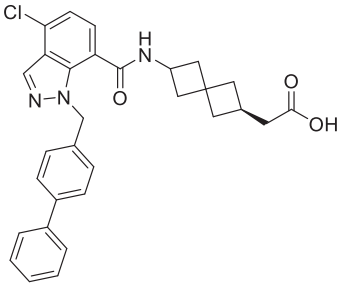
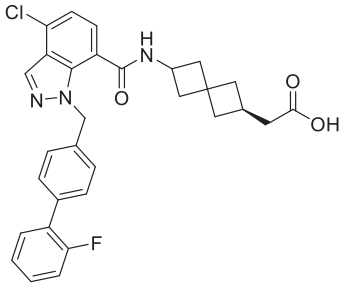
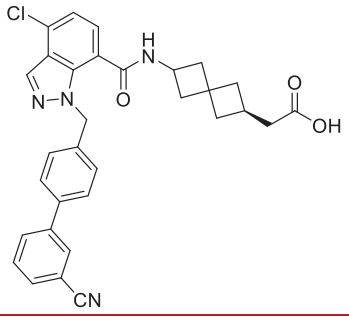
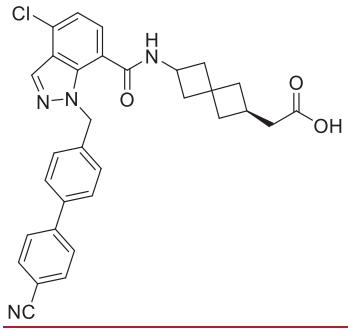
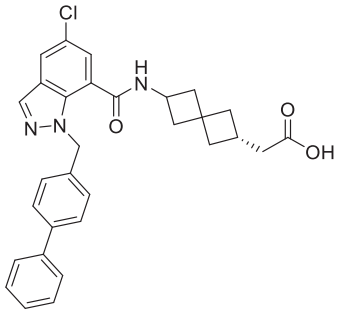
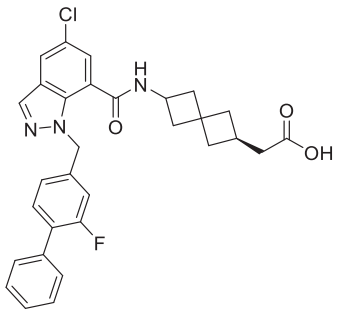
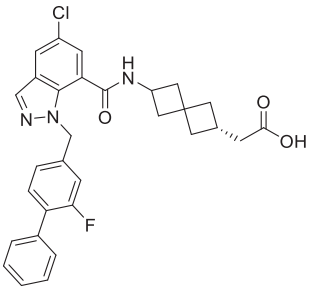
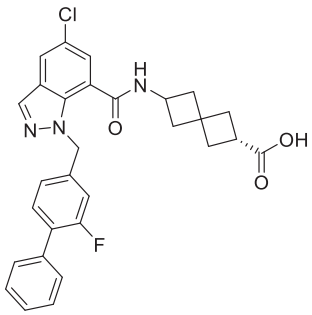
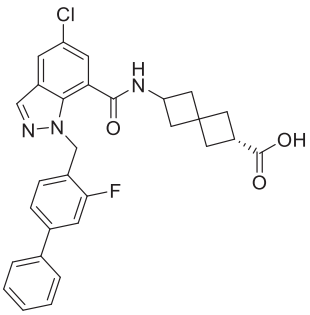
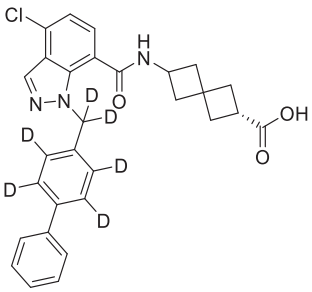
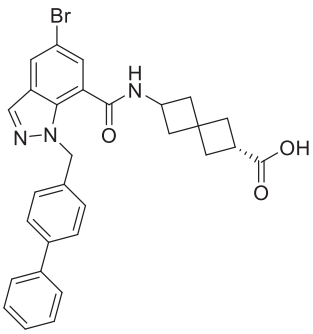
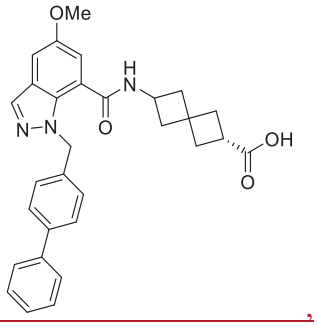




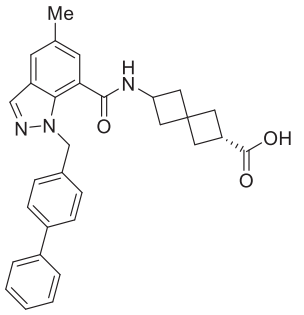
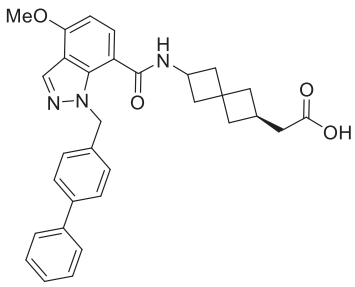
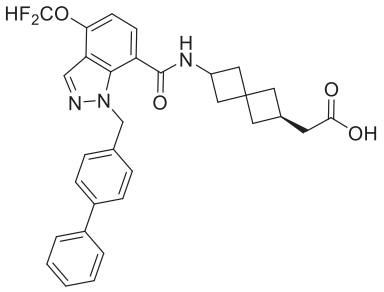




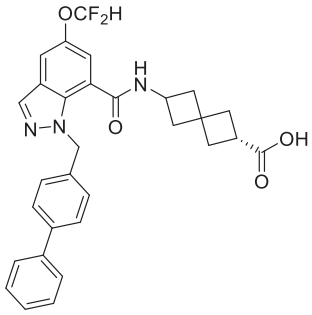
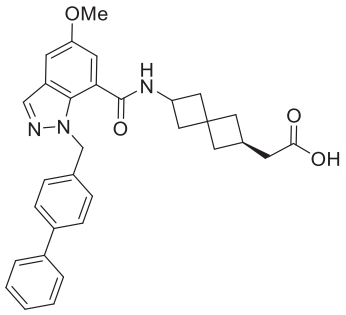
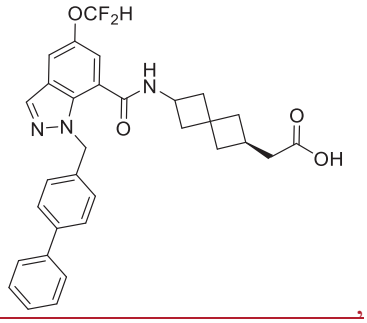




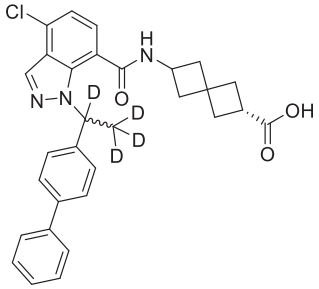
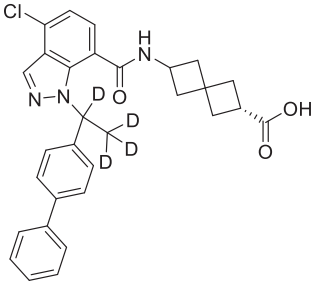
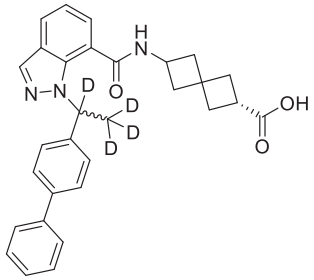




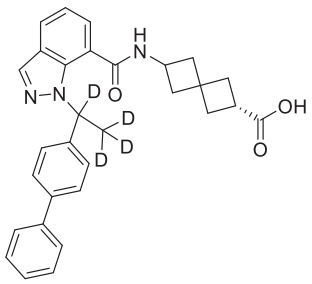
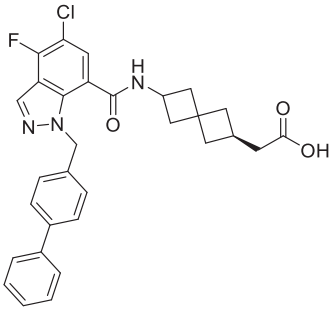
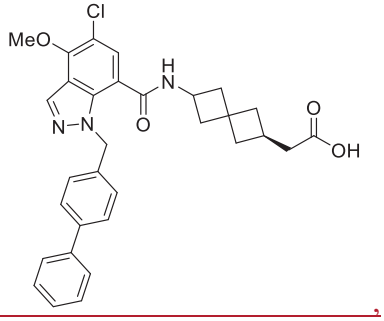




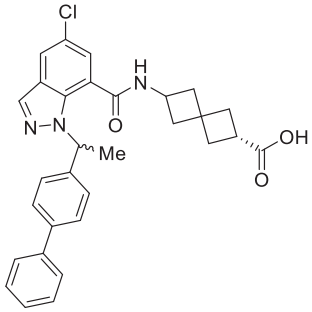
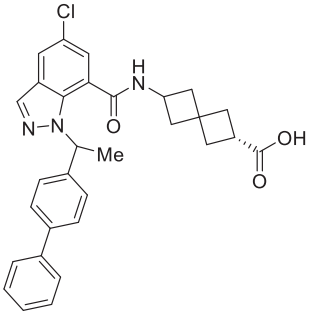
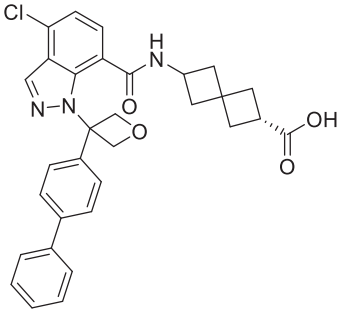

















,

,

,


,

,

,


,

,

,


,

,

,


,

, and

,

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

~~23.~~17. A pharmaceutical composition comprising a compound of ~~any one of claims 1-22~~claim 1, or a pharmaceutically acceptable salt, solvate, solvate of the salt, hydrate, a single stereoisomer, a mixture of stereoisomers, a racemic mixture of stereoisomers, isotopic variant, or prodrug thereof, and a pharmaceutically acceptable carrier.

~~24.~~18. Use of the compound of Formula (I), or a pharmaceutically acceptable salt, solvate, solvate of the salt, hydrate, a single stereoisomer, a mixture of stereoisomers, a racemic mixture of stereoisomers, isotopic variant, or prodrug thereof of any one of claims 1 to 16, in the manufacture of a medicament for the treatment of an EP4-mediated cancer in a patient, wherein the compound of Formula (I), or a pharmaceutically acceptable salt, solvate, solvate of the salt, hydrate, a single stereoisomer, a mixture of stereoisomers, a racemic mixture of stereoisomers, isotopic variant or prodrug thereof is to be administered to a patient~~A method for the treatment of cancer in a patient comprising administering to the patient a compound of any of claims 1-22 or the pharmaceutical composition of claim 23~~.

19. The use of claim 18, wherein the pharmaceutical composition of claim 17 is to be further administered to the patient.

~~25.~~20. The use~~method~~ of claim 18 or 19~~24~~, wherein said EP4-mediated 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.

~~26.~~21. The ~~method~~ use of claim 20~~24 or 25~~, wherein said EP4-mediated cancer is selected from colon cancer, bladder cancer, hepatocellular carcinoma, pancreatic cancer, ovarian cancer, cervical cancer, lung cancer, breast cancer and prostate cancer.

22. The use of claim 18 or 19, wherein said EP4-mediated cancer is selected from colorectal cancer (CRC), lung cancer, squamous cell carcinoma of the head and neck (SCCHN), bladder cancer, endometrial cancer, and gastric cancer.

23. The use of claim 18 or 19, wherein said EP4-mediated cancer is colorectal cancer (CRC).

~~27.~~24. The compound of Formula (I), or a pharmaceutically acceptable salt, solvate, solvate of the salt, hydrate, a single stereoisomer, a mixture of stereoisomers, a racemic mixture of stereoisomers, isotopic variant, or prodrug thereof of any one of claims 1 to 16, or the pharmaceutical composition of claim 17 ~~of any one of claims 1-22~~ for use in therapy~~the treatment of cancer~~.

~~28. The compound for use of claim 27 wherein the 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.~~

~~29. A method of treating neurodegenerative disease in a patient comprising administering to the patient a compound of any of claims 1-22 or the pharmaceutical composition of claim 23.~~

~~30. The method of claim 29 wherein said neurodegenerative disease is selected from epilepsy, Alzheimer's disease (AD), Parkinson's disease (PD), amyotrophic lateral sclerosis (ALS) and traumatic brain injury (TBI).~~

~~31. A method of treating inflammatory disease or symptom in a patient comprising administering to the patient a compound of any of claims 1-22 or the pharmaceutical composition of claim 23.~~

~~32. The method of claim 31 wherein said inflammatory disease or symptom is arthritis, immune dysfunction, autoimmune disease or inflammatory pain.~~