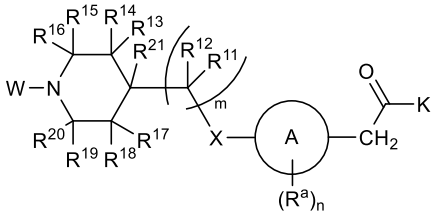
GPR119 AGONISTS

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of US Provisional Application No. 62/911,833 filed on October 7, 2019, which is incorporated herein by reference in its entirety.

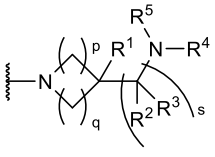
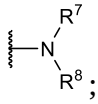
BRIEF SUMMARY

[0001a] In an aspect of the present disclosure, there is provided a compound of Formula (I):



Formula (I)

or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, wherein:

K is  or ;

R^1 is hydrogen, -OH, C_{1-8} alkyl, C_{3-8} cycloalkyl, or 3- to 8-membered heterocycloalkyl, wherein the alkyl, cycloalkyl, and heterocycloalkyl are unsubstituted or substituted by 1-3 substituents independently selected from halogen, -OH, and -O(C_{1-6} alkyl);

each R^2 and R^3 is independently hydrogen, C_{1-6} alkyl, or C_{1-6} fluoroalkyl;

or R^2 and R^3 on the same carbon atom are taken together to form =O;

R^4 is hydrogen, C_{1-8} alkyl, C_{1-8} fluoroalkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl, C_{5-8} cycloalkenyl, 4- to 8-membered heterocycloalkyl, $–[(CH_2)_r–Z]_t–R^6$, $–[(CHR^d)_r–Z]_t–R^6$, or $–[(C(R^d)_2)_r–Z]_t–R^6$; wherein each alkyl, fluoroalkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, and 4- to 8-membered heterocycloalkyl is unsubstituted or substituted by 1-6 R^c groups;

R^5 is C_{1-8} alkyl, C_{1-8} fluoroalkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl, C_{5-8} cycloalkenyl, 4- to 8-membered heterocycloalkyl, $–[(CH_2)_r–Z]_t–R^6$, $–[(CHR^d)_r–Z]_t–R^6$, or $–[(C(R^d)_2)_r–Z]_t–R^6$; wherein each alkyl, fluoroalkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, and 4- to 8-membered heterocycloalkyl is substituted by 1-6 R^c groups;

each Z is independently $–CH_2O–$, $–CH_2NR^d–$, $–CH_2N^+(R^d)_2–$, –NH-C(=O)-NH–, –C(=O)NH–, $–CH_2S(=O)_2–$, or $–CH_2S(=O)–$;

each r is independently 1-6;

each t is independently 1-6;

R^6 is hydrogen, C_{1-8} alkyl, C_{1-8} fluoroalkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl, C_{5-8} cycloalkenyl, or 4- to 8-membered heterocycloalkyl, wherein the alkyl, fluoroalkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, or 4- to 8-membered heterocycloalkyl is unsubstituted or substituted by 1-6 R^c groups;

or R^4 and R^5 are taken together with the nitrogen to which they are attached to form a 4- to 8-membered heterocycloalkyl, which is unsubstituted or substituted by 1-6 R^c groups;

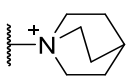
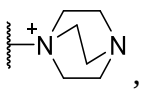
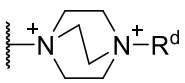
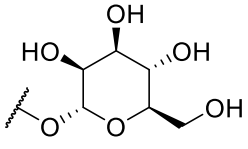
R^7 is hydrogen, C_{1-4} alkyl, or C_{1-4} fluoroalkyl;

R^8 is C_{1-8} alkyl, C_{1-8} fluoroalkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl, C_{5-8} cycloalkenyl, 4- to 8-membered heterocycloalkyl, $–[(CH_2)_r–Z]_t–R^6$, $–[(CHR^d)_r–Z]_t–R^6$, or $–[(CR^d_2)_r–Z]_t–R^6$; wherein each alkyl, fluoroalkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, and 4- to 8-membered heterocycloalkyl is substituted by 1-6 R^e groups;

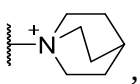
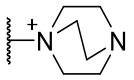
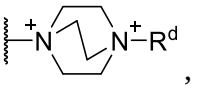
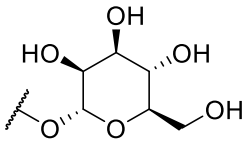
or R^8 is -(C_{1-8} alkyl)-NH-R^9, -(C_{1-8} alkyl)-C(=O)NH-R^9, -(C_{1-8} alkyl)-C(=O)-N(R^9)$_2$, or -(C_{1-8} alkyl)-NHC(=O)NH-R^9; wherein the alkyl is unsubstituted or substituted by 1-6 R^c groups;

each R^9 is independently C_{1-8} alkyl, or C_{1-8} fluoroalkyl which is substituted by 1-6 R^c groups;

or two R^9 are taken together with the nitrogen to which they are attached to form a 4- to 6-membered heterocycloalkyl, which is substituted by 1-6 R^c groups;

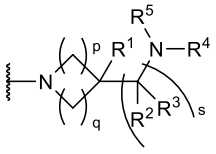
each R^c is independently -OH, -CH_2OH, -CH_2CH_2OH, -NH_2, -CH_2NH_2, -NH(R^d), -CH_2NH(R^d), -N(R^d)$_2$, -CH_2N(R^d)$_2$, -N(R^d)$_3^+$, -C(=O)OH, -CH_2C(=O)OH, -CH_2CH_2C(=O)OH, -S(=O)$_2$OH, -S(=O)OH, -S(=O)$_2NH_2$, -P(=O)(OH)$_2$, -P(=O)(OH)(R^d), -P(=O)(OH)(H), P(=O)(OH)(OR^d), -B(OH)$_2$, -B(OR^d)(OH), -NHCONHS(=O)$_2$(R^d), -N(R^d)CONHS(=O)$_2$(R^d), -NHCON(R^d)S(=O)$_2$(R^d), -C(=O)NHS(=O)$_2$(R^d), -S(=O)$_2$NHC(=O)R^d, -NHC(=NH)NH_2, -NHC(=NH)NHR^d, -NHC(=NH)N(R^d)$_2$, -N(R^d)C(=NH)NH_2, -N(R^d)C(=NH)NH(R^d), -N(R^d)C(=NH)N(R^d)$_2$, -NHC(=N(R^d))NH_2, -NHC(=N(R^d))NHR^d, -NHC(=N(R^d))N(R^d)$_2$, -N(R^d)C(=N(R^d))NH_2, -N(R^d)C(=N(R^d))NHR^d, -N(R^d)C(=N(R^d))N(R^d)$_2$, -NHC(=NH)NHC(=NH)NH_2, -N(R^d)C(=NH)NHC(=NH)NH_2, , , , , or a 4- to 6-membered heterocycle which is unsubstituted or substituted with 1, 2, 3, or 4 substituents selected from C_{1-6} alkyl, –O–(C_{1-6} alkyl), –OH, =O and =S;

each R^d is independently C_{1-6} alkyl, C_{1-6} fluoroalkyl, or C_{3-6} cycloalkyl;

each R^e is independently -OH, -CH_2OH, -CH_2CH_2OH, -$N(R^d)_3^+$, -C(=O)OH, -$CH_2C(=O)OH$, -$CH_2CH_2C(=O)OH$, -$S(=O)_2OH$, -S(=O)OH, -$S(=O)_2NH_2$, -$P(=O)(OH)_2$, -$P(=O)(OH)(R^d)$, -P(=O)(OH)(H), -$P(=O)(OH)(OR^d)$, -$B(OH)_2$, -$B(OR^d)(OH)$, -$NHCONHS(=O)_2(R^d)$, -$N(R^d)CONHS(=O)_2(R^d)$, -$NHCON(R^d)S(=O)_2(R^d)$, -$C(=O)NHS(=O)_2(R^d)$, -$S(O)_2NHC(O)R^d$, -$NHC(=NH)NH_2$, -$NHC(=NH)NHR^d$, -$NHC(=NH)N(R^d)_2$, -$N(R^d)C(=NH)NH_2$, $N(R^d)C(=NH)NH(R^d)$, -$N(R^d)C(=NH)N(R^d)_2$, -$NHC(=N(R^d))NH_2$, -$NHC(=N(R^d))NHR^d$, -$NHC(=N(R^d))N(R^d)_2$, -$N(R^d)C(=N(R^d))NH_2$, -$N(R^d)C(=N(R^d))NHR^d$, -$N(R^d)C(=N(R^d))N(R^d)_2$, -$NHC(=NH)NHC(=NH)NH_2$, $N(R^d)C(=NH)NHC(=NH)NH_2$,  ,  ,  ,  , or a 4- to 6-membered heterocycle which is unsubstituted or substituted with 1, 2, 3, or 4 substituents selected from C_{1-6} alkyl, –O–(C_{1-6} alkyl), –OH, =O and =S;

Ring A is phenyl or 5-6 membered monocyclic heteroaryl;

each R^a is independently halogen, -CN, C_{1-6} alkyl, C_{1-6} fluoroalkyl, or C_{3-6} cycloalkyl;

X, when K is  , is -O-, -NR^N-, *-CH_2O-, *-CH_2NR^N-, *-C(=O)O-, *-$C(=O)NR^N$-, *-$CH_2C(=O)O$-, *-$CH_2C(=O)NR^N$-, *-OC(=O)-, *-$NR^NC(=O)$-, *-$CH_2OC(=O)$-, or *-$CH_2NR^NC(=O)$-, where * represents the attachment point to Ring A;

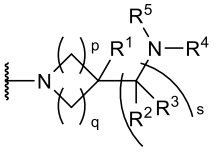
R^N is hydrogen or C_{1-4} alkyl;

or X, when K is  , is -O-, -NR^N-, *-CH_2O-, *-CH_2NR^N-, *-C(=O)O-, *-$C(=O)NR^N$-, *-$CH_2C(=O)O$-, *-$CH_2C(=O)NR^N$-, *-OC(=O)-, *-$CH_2OC(=O)$-, or *-$CH_2NR^NC(=O)$-, where * represents the attachment point to Ring A;

R^N is hydrogen or C_{1-4} alkyl;

each R^{11} is independently hydrogen, fluorine, -OH, C_{1-6} alkyl, or C_{1-6} alkoxy;

each R^{12} is independently hydrogen, fluorine, or C_{1-6} alkyl;

or, when K is  , two R^{11} are taken together with the intervening atoms to which they are attached to form a C_{3-6} cycloalkyl;

or, when K is , two R^{11} are taken together with the intervening atoms to which they are attached to form a C_{4-6} cycloalkyl;

R^{13}, R^{14}, R^{15}, R^{16}, R^{17}, R^{18}, R^{19}, and R^{20} are each independently hydrogen, C_{1-6} alkyl, C_{1-6} alkoxy, or C_{1-6} fluoroalkyl;

or R^{13} and R^{17} or R^{13} and R^{19} or R^{15} and R^{19} are taken together with the intervening atoms to which they are attached to form a ring;

R^{21} is hydrogen, C_{1-6} alkyl, or C_{1-6} fluoroalkyl;

or R^{21} and one R^{11} are taken together with the intervening atoms to which they are attached to form a C_{3-6} cycloalkyl;

W is phenyl or 5-6 membered monocyclic heteroaryl, wherein the phenyl or heteroaryl is unsubstituted or substituted with 1, 2, or 3 substituents selected from R^b;

each R^b is independently halogen, -OH, -CN, -C(O)OH, -C(O)O(C_{1-6} alkyl), C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-6} cycloalkyl, phenyl, or 5- to 6-membered heteroaryl; wherein each alkyl, alkoxy, and cycloalkyl is unsubstituted or substituted with 1, 2, or 3 substituents selected from halogen, -OH, C_{1-6} alkyl, and C_{1-6} alkoxy;

or W is -C(=O)O-R^{22};

R^{22} is C_{1-6} alkyl, C_{3-6} cycloalkyl, or 3- to 6-membered heterocycloalkyl, wherein the alkyl, cycloalkyl, and heterocycloalkyl are unsubstituted or substituted by 1-3 substituents independently selected from fluorine, -OH, C_{1-6} alkyl, C_{1-6} haloalkyl or C_{3-6} cycloalkyl;

m is 1-4;

n is 0-4;

p is 1 or 2;

q is 1 or 2; and

s is 1 or 2.

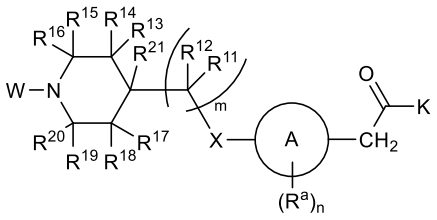
[0001b] In another aspect of the present disclosure, there is provided a pharmaceutical composition comprising a compound disclosed herein, or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, and at least one pharmaceutically acceptable excipient.

[0001c] In a further aspect of the present disclosure, there is provided a use of the compound disclosed herein, or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, in the manufacture of a medicament for the treatment of a condition or disorder involving the gut-brain axis in a subject in need thereof; wherein the condition or disorder is associated with GPR119 activity.

[0001d] In another aspect of the present disclosure, there is provided a compound disclosed herein, or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, for use in therapy.

[0002] Disclosed herein, in certain examples, are G protein-coupled receptor 119 (GPR119) agonists useful for the treatment of conditions or disorders involving the gut-brain axis. In some examples, the GPR119 agonists are gut-restricted or selectively modulate GPR119 located in the gut. In some examples, the condition is selected from the group consisting of: central nervous system (CNS) disorders including mood disorders, anxiety, depression, affective disorders, schizophrenia, malaise, cognition disorders, addiction, autism, epilepsy, neurodegenerative disorders, Alzheimer's disease, and Parkinson's disease, Lewy Body dementia, episodic cluster headache, migraine, pain; metabolic conditions including diabetes and its complications such as chronic kidney disease/diabetic nephropathy, diabetic retinopathy, diabetic neuropathy, and cardiovascular disease, metabolic syndrome, obesity, dyslipidemia, and nonalcoholic steatohepatitis (NASH); eating and nutritional disorders including hyperphagia, cachexia, anorexia nervosa, short bowel syndrome, intestinal failure, intestinal insufficiency and other eating disorders; inflammatory disorders and autoimmune diseases such as inflammatory bowel disease, ulcerative colitis, Crohn's disease, psoriasis, celiac disease, and enteritis, including chemotherapy-induced enteritis or radiation-induced enteritis; necrotizing enterocolitis; diseases/disorders of gastrointestinal barrier dysfunction including environmental enteric dysfunction, spontaneous bacterial peritonitis; functional gastrointestinal disorders such as irritable bowel syndrome, functional dyspepsia, functional abdominal bloating/distension, functional diarrhea, functional constipation, and opioid-induced constipation; gastroparesis; nausea and vomiting; disorders related to microbiome dysbiosis, and other conditions involving the gut-brain axis.

[0003] Disclosed herein, in certain examples, is a compound of Formula (I):



Formula (I)

or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, wherein:

R^{22} is C_{1-6} alkyl, C_{3-6} cycloalkyl, or 3- to 6-membered heterocycloalkyl, wherein the alkyl, cycloalkyl, and heterocycloalkyl are unsubstituted or substituted by 1-3 substituents independently selected from fluorine, -OH, C_{1-6} alkyl, C_{1-6} haloalkyl or C_{3-6} cycloalkyl;

m is 1-4;

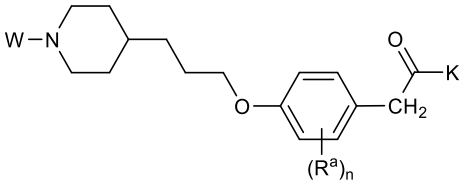
n is 0-4;

p is 1 or 2;

q is 1 or 2; and

s is 1 or 2

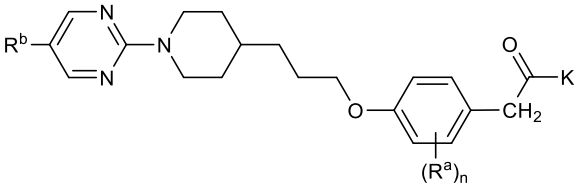
[0004] In some examples, the compound of Formula (I) is a compound of Formula (Ia):



Formula (Ia).

or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof.

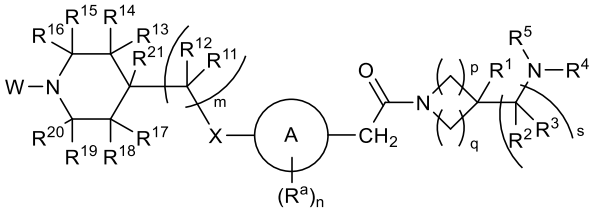
[0005] In some examples, the compound of Formula (I) is a compound of Formula (Ib):



Formula (Ib).

or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof.

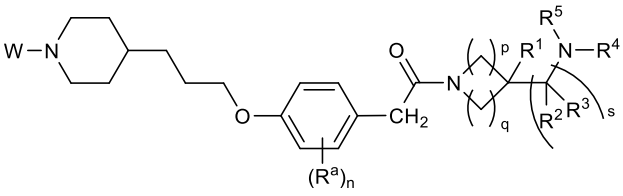
[0006] In some examples, the compound of Formula (I) is a compound of Formula (II):



Formula (II).

or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof.

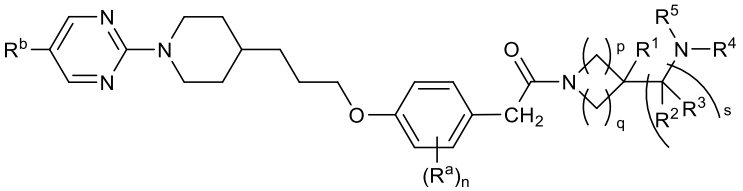
[0007] In some examples, the compound of Formula (II) is a compound of Formula (IIa):



Formula (IIa).

or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof.

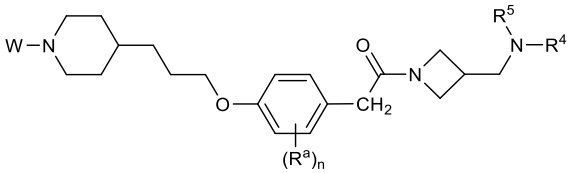
[0008] In some examples, the compound of Formula (II) is a compound of Formula (IIb):



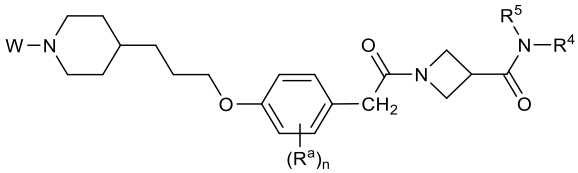
Formula (IIb).

or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof.

[0009] In some examples, the compound of Formula (II) is a compound of Formula (IIc) or Formula (IId):



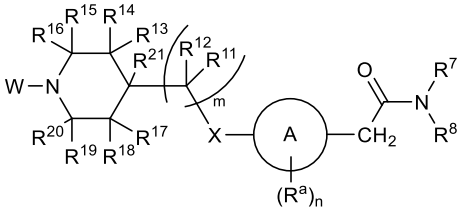
Formula (IIc)



Formula (IId).

or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof.

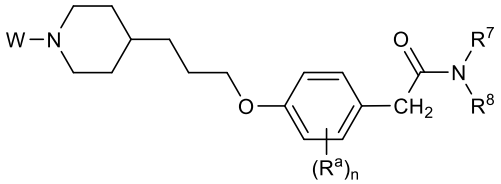
[0010] In some examples, the compound of Formula (I) is a compound of Formula (III):



Formula (III).

or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof.

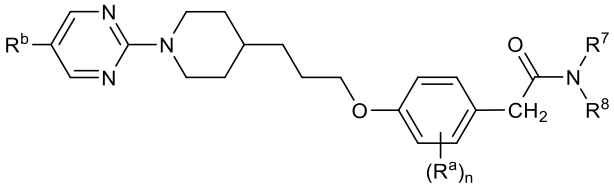
[0011] In some examples, the compound of Formula (III) is a compound of Formula (IIIa):



Formula (IIIa).

or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof.

[0012] In some examples, the compound of Formula (III) is a compound of Formula (IIIb):



Formula (IIIb).

or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof.

[0013] Disclosed herein, in certain examples, are pharmaceutical compositions comprising a compound disclosed herein, or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, and at least one pharmaceutically acceptable excipient.

[0014] Disclosed herein, in certain examples, are methods of treating a condition or disorder involving the gut-brain axis in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of a compound disclosed herein, or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof. In some examples, the condition or disorder is associated with GPR119 activity. In some examples, the condition or disorder is a metabolic disorder. In some examples, the condition or disorder is type 2 diabetes, hyperglycemia, metabolic syndrome, obesity, hypercholesterolemia, nonalcoholic steatohepatitis, or hypertension. In some examples, the condition or disorder is a nutritional disorder. In some examples, the condition or disorder is short bowel syndrome, intestinal failure, or intestinal insufficiency. In some examples, the condition or disorder is chemotherapy-induced enteritis or radiation-induced enteritis. In some examples, the compound disclosed herein is gut-restricted. In some examples, the compound disclosed herein has low systemic exposure.

[0015] In some examples, the methods disclosed herein further comprise administering one or more additional therapeutic agents to the subject. In some examples, the one or more additional therapeutic agents are selected from a TGR5 agonist, a GPR40 agonist, an SSTR5 antagonist, an SSTR5 inverse agonist, a CCK1 agonist, a PDE4 inhibitor, a DPP-4 inhibitor, a GLP-1 receptor agonist, metformin, or a combination thereof. In some examples, the TGR5 agonist, GPR40 agonist, SSTR5 antagonist, SSTR5 inverse agonist, or CCK1 agonist is gut-restricted.

[0016] Also disclosed herein, in certain examples, is the use of a compound disclosed herein, or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, for the preparation of a medicament for the treatment of a condition or disorder involving the gut-brain axis in a subject in need thereof.

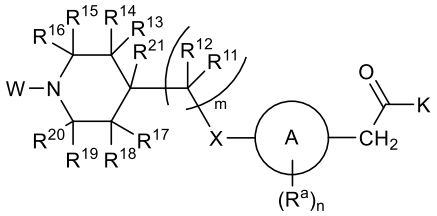
[0017] Also disclosed herein, in certain examples, are methods of treating a condition or disorder involving the gut-brain axis in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of a gut-restricted GPR119 modulator.

[0018] Also disclosed herein, in certain examples, is the use of a gut-restricted GPR119 modulator for the preparation of a medicament for the treatment of a condition or disorder involving the gut-brain axis in a subject in need thereof.

CLAIMS

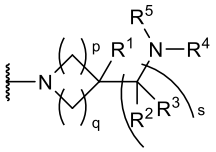
We Claim:

1. A compound of Formula (I):



Formula (I)

or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, wherein:

K is  or ;

R^1 is hydrogen, -OH, C_{1-8} alkyl, C_{3-8} cycloalkyl, or 3- to 8-membered heterocycloalkyl, wherein the alkyl, cycloalkyl, and heterocycloalkyl are unsubstituted or substituted by 1-3 substituents independently selected from halogen, -OH, and -O(C_{1-6} alkyl);

each R^2 and R^3 is independently hydrogen, C_{1-6} alkyl, or C_{1-6} fluoroalkyl;

or R^2 and R^3 on the same carbon atom are taken together to form =O;

R^4 is hydrogen, C_{1-8} alkyl, C_{1-8} fluoroalkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl, C_{5-8} cycloalkenyl, 4- to 8-membered heterocycloalkyl, $–[(CH_2)_r–Z]_t–R^6$, $–[(CHR^d)_r–Z]_t–R^6$, or $–[(C(R^d)_2)_r–Z]_t–R^6$; wherein each alkyl, fluoroalkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, and 4- to 8-membered heterocycloalkyl is unsubstituted or substituted by 1-6 R^c groups;

R^5 is C_{1-8} alkyl, C_{1-8} fluoroalkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl, C_{5-8} cycloalkenyl, 4- to 8-membered heterocycloalkyl, $–[(CH_2)_r–Z]_t–R^6$, $–[(CHR^d)_r–Z]_t–R^6$, or $–[(C(R^d)_2)_r–Z]_t–R^6$; wherein each alkyl, fluoroalkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, and 4- to 8-membered heterocycloalkyl is substituted by 1-6 R^c groups;

each Z is independently $–CH_2O–$, $–CH_2NR^d–$, $–CH_2N^+(R^d)_2–$, –NH-C(=O)-NH–, –C(=O)NH–, $–CH_2S(=O)_2–$, or $–CH_2S(=O)–$;

each r is independently 1-6;

each t is independently 1-6;

R^6 is hydrogen, C_{1-8} alkyl, C_{1-8} fluoroalkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl, C_{5-8} cycloalkenyl, or 4- to 8-membered heterocycloalkyl, wherein the alkyl, fluoroalkyl,

alkenyl, alkynyl, cycloalkyl, cycloalkenyl, or 4- to 8-membered heterocycloalkyl is unsubstituted or substituted by 1-6 R^c groups;

or R^4 and R^5 are taken together with the nitrogen to which they are attached to form a 4- to 8-membered heterocycloalkyl, which is unsubstituted or substituted by 1-6 R^c groups;

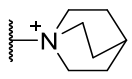
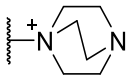
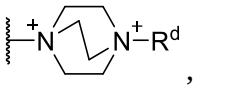
R^7 is hydrogen, C_{1-4} alkyl, or C_{1-4} fluoroalkyl;

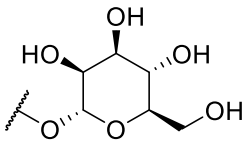
R^8 is C_{1-8} alkyl, C_{1-8} fluoroalkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl, C_{5-8} cycloalkenyl, 4- to 8-membered heterocycloalkyl, $–[(CH_2)_r–Z]_t–R^6$, $–[(CHR^d)_r–Z]_t–R^6$, or $–[(CR^d_2)_r–Z]_t–R^6$; wherein each alkyl, fluoroalkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, and 4- to 8-membered heterocycloalkyl is substituted by 1-6 R^e groups;

or R^8 is -(C_{1-8} alkyl)-NH-R^9, -(C_{1-8} alkyl)-C(=O)NH-R^9, -(C_{1-8} alkyl)-C(=O)-N(R^9)$_2$, or -(C_{1-8} alkyl)-NHC(=O)NH-R^9; wherein the alkyl is unsubstituted or substituted by 1-6 R^c groups;

each R^9 is independently C_{1-8} alkyl, or C_{1-8} fluoroalkyl which is substituted by 1-6 R^c groups;

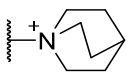
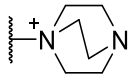
or two R^9 are taken together with the nitrogen to which they are attached to form a 4- to 6-membered heterocycloalkyl, which is substituted by 1-6 R^c groups;

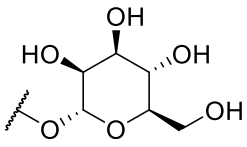
each R^c is independently -OH, -CH_2OH, -CH_2CH_2OH, -NH_2, -CH_2NH_2, -NH(R^d), -CH_2NH(R^d), -N(R^d)$_2$, -CH_2N(R^d)$_2$, -N(R^d)$_3^+$, -C(=O)OH, -CH_2C(=O)OH, -CH_2CH_2C(=O)OH, -S(=O)$_2$OH, -S(=O)OH, -S(=O)$_2$$NH_2$, -P(=O)(OH)$_2$, -P(=O)(OH)($R^d$), -P(=O)(OH)(H), P(=O)(OH)(OR^d), -B(OH)$_2$, -B(OR^d)(OH), -NHCONHS(=O)$_2$(R^d), -N(R^d)CONHS(=O)$_2$(R^d), -NHCON(R^d)S(=O)$_2$(R^d), -C(=O)NHS(=O)$_2$(R^d), -S(=O)$_2$NHC(=O)R^d, -NHC(=NH)NH_2, -NHC(=NH)NHR^d, -NHC(=NH)N(R^d)$_2$, -N(R^d)C(=NH)NH_2, -N(R^d)C(=NH)NH(R^d), -N(R^d)C(=NH)N(R^d)$_2$, -NHC(=N(R^d))NH_2, -NHC(=N(R^d))NHR^d, -NHC(=N(R^d))N(R^d)$_2$, -N(R^d)C(=N(R^d))NH_2, -N(R^d)C(=N(R^d))NHR^d, -N(R^d)C(=N(R^d))N(R^d)$_2$, -NHC(=NH)NHC(=NH)NH_2, -N(R^d)C(=NH)NHC(=NH)NH_2, , , ,

, or a 4- to 6-membered heterocycle which is unsubstituted or substituted with 1, 2, 3, or 4 substituents selected from C_{1-6} alkyl, –O–(C_{1-6} alkyl), –OH, =O and =S;

each R^d is independently C_{1-6} alkyl, C_{1-6} fluoroalkyl, or C_{3-6} cycloalkyl;

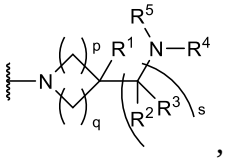
each R^e is independently -OH, -CH_2OH, -CH_2CH_2OH, -N(R^d)$_3^+$, -C(=O)OH, -CH_2C(=O)OH, -CH_2CH_2C(=O)OH, -S(=O)$_2$OH, -S(=O)OH, -S(=O)$_2$$NH_2$, -P(=O)(OH)$_2$,

-P(=O)(OH)(R^d), -P(=O)(OH)(H), -P(=O)(OH)(OR^d), -$B(OH)_2$, -B(OR^d)(OH), -NHCONHS(=O)$_2$(R^d), -N(R^d)CONHS(=O)$_2$(R^d), -NHCON(R^d)S(=O)$_2$(R^d), -C(=O)NHS(=O)$_2$(R^d), -S(O)$_2$NHC(O)R^d, -NHC(=NH)NH_2, -NHC(=NH)NHR^d, -NHC(=NH)N(R^d)$_2$, -N(R^d)C(=NH)NH_2, N(R^d)C(=NH)NH(R^d), -N(R^d)C(=NH)N(R^d)$_2$, -NHC(=N(R^d))NH_2, -NHC(=N(R^d))NHR^d, -NHC(=N(R^d))N(R^d)$_2$, -N(R^d)C(=N(R^d))NH_2, -N(R^d)C(=N(R^d))NHR^d, -N(R^d)C(=N(R^d))N(R^d)$_2$, -NHC(=NH)NHC(=NH)NH_2, N(R^d)C(=NH)NHC(=NH)NH_2,  ,  ,  ,

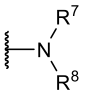
 , or a 4- to 6-membered heterocycle which is unsubstituted or substituted with 1, 2, 3, or 4 substituents selected from C_{1-6} alkyl, –O–(C_{1-6} alkyl), –OH, =O and =S;

Ring A is phenyl or 5-6 membered monocyclic heteroaryl;

each R^a is independently halogen, -CN, C_{1-6} alkyl, C_{1-6} fluoroalkyl, or C_{3-6} cycloalkyl;

X, when K is  , is -O-, -NR^N-, *-CH_2O-, *-CH_2NR^N-, *-C(=O)O-, *-C(=O)NR^N-, *-CH_2C(=O)O-, *-CH_2C(=O)NR^N-, *-OC(=O)-, *-NR^NC(=O)-, *-CH_2OC(=O)-, or *-CH_2NR^NC(=O)-, where * represents the attachment point to Ring A;

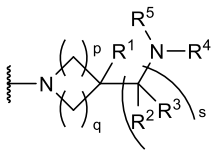
R^N is hydrogen or C_{1-4} alkyl;

or X, when K is  , is -O-, -NR^N-, *-CH_2O-, *-CH_2NR^N-, *-C(=O)O-, *-C(=O)NR^N-, *-CH_2C(=O)O-, *-CH_2C(=O)NR^N-, *-OC(=O)-, *-CH_2OC(=O)-, or *-CH_2NR^NC(=O)-, where * represents the attachment point to Ring A;

R^N is hydrogen or C_{1-4} alkyl;

each R^{11} is independently hydrogen, fluorine, -OH, C_{1-6} alkyl, or C_{1-6} alkoxy;

each R^{12} is independently hydrogen, fluorine, or C_{1-6} alkyl;

or, when K is  , two R^{11} are taken together with the intervening atoms to which they are attached to form a C_{3-6} cycloalkyl;

or, when K is , two R^{11} are taken together with the intervening atoms to which they are attached to form a C_{4-6} cycloalkyl;

R^{13}, R^{14}, R^{15}, R^{16}, R^{17}, R^{18}, R^{19}, and R^{20} are each independently hydrogen, C_{1-6} alkyl, C_{1-6} alkoxy, or C_{1-6} fluoroalkyl;

or R^{13} and R^{17} or R^{13} and R^{19} or R^{15} and R^{19} are taken together with the intervening atoms to which they are attached to form a ring;

R^{21} is hydrogen, C_{1-6} alkyl, or C_{1-6} fluoroalkyl;

or R^{21} and one R^{11} are taken together with the intervening atoms to which they are attached to form a C_{3-6} cycloalkyl;

W is phenyl or 5-6 membered monocyclic heteroaryl, wherein the phenyl or heteroaryl is unsubstituted or substituted with 1, 2, or 3 substituents selected from R^b;

each R^b is independently halogen, -OH, -CN, -C(O)OH, -C(O)O(C_{1-6} alkyl), C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-6} cycloalkyl, phenyl, or 5- to 6-membered heteroaryl; wherein each alkyl, alkoxy, and cycloalkyl is unsubstituted or substituted with 1, 2, or 3 substituents selected from halogen, -OH, C_{1-6} alkyl, and C_{1-6} alkoxy;

or W is -C(=O)O-R^{22};

R^{22} is C_{1-6} alkyl, C_{3-6} cycloalkyl, or 3- to 6-membered heterocycloalkyl, wherein the alkyl, cycloalkyl, and heterocycloalkyl are unsubstituted or substituted by 1-3 substituents independently selected from fluorine, -OH, C_{1-6} alkyl, C_{1-6} haloalkyl or C_{3-6} cycloalkyl;

m is 1-4;

n is 0-4;

p is 1 or 2;

q is 1 or 2; and

s is 1 or 2.

2. The compound of claim 1, or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, wherein:

X is -O-;

each R^{11} is hydrogen;

each R^{12} is hydrogen;

R^{21} is hydrogen;

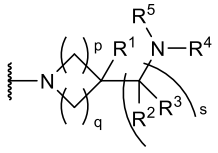
R^{13}, R^{14}, R^{15}, R^{16}, R^{17}, R^{18}, R^{19}, and R^{20} are each hydrogen;

Ring A is phenyl;

each R^a is independently halogen or C_{1-6} alkyl; and

n is 1-3.

3. The compound of claim 1 or claim 2, or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, wherein:

K is , wherein:

R^1 is hydrogen, -OH, or C_{1-8} alkyl, wherein the alkyl is unsubstituted or substituted by -OH or -O(C_{1-6} alkyl);

each R^2 and R^3 is hydrogen;

or R^2 and R^3 on the same carbon atom are taken together to form =O;

p is 1;

q is 1;

R^4 is hydrogen or C_{1-4} alkyl;

R^5 is C_{1-8} alkyl, $–[(CH_2)_r–Z]_t–R^6$, $–[(CHR^d)_r–Z]_t–R^6$, or $–[(C(R^d)_2)_r–Z]_t–R^6$; wherein the alkyl is substituted by 1-6 R^c groups;

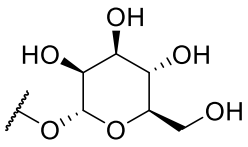
each Z is independently $–CH_2O–$, $–CH_2NR^d–$, or –NH-C(=O)-NH–;

r is 1-3;

t is 1-3;

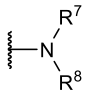
R^6 is hydrogen or C_{1-8} alkyl, wherein the alkyl is substituted by 1-6 R^c groups; and

each R^c is independently -OH, $-CH_2OH$, $-NH_2$, $-N(R^d)_3^+$, -C(=O)OH, or

,

or R^4 is hydrogen; and R^5 is C_{1-8} alkyl which is substituted by 1-6 -OH groups.

4. The compound of claim 1 or claim 2, or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, wherein:

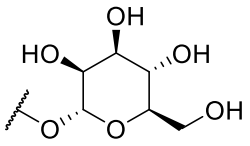
K is , wherein:

R^7 is hydrogen or C_{1-4} alkyl;

R^8 is C_{1-8} alkyl; wherein the alkyl is substituted by 1-6 R^e groups;

or R^8 is -(C_{1-8} alkyl)-NH-R^9, -(C_{1-8} alkyl)-C(=O)NH-R^9, -(C_{1-8} alkyl)-C(=O)-N(R^9)$_2$, or -(C_{1-8} alkyl)-NHC(=O)NH-R^9; wherein the alkyl is unsubstituted; and

each R^e is independently -OH, -CH_2OH, -$N(R^d)_3^+$, -$S(=O)_2OH$, -$S(=O)_2NH_2$, or



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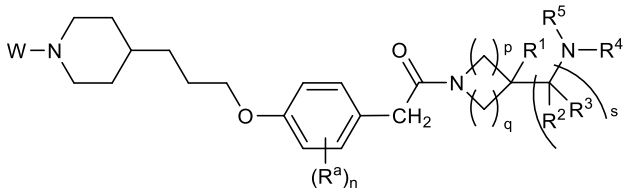
5. The compound of claim 1, or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, wherein the compound has the structure of Formula (IIa), or a pharmaceutically acceptable salt, or solvate thereof:



Formula (IIa),

wherein:

R^1 is hydrogen, -OH, or C_{1-8} alkyl, wherein the alkyl is unsubstituted or substituted by -OH or -O(C_{1-6} alkyl);

each R^2 and R^3 is hydrogen;

or R^2 and R^3 on the same carbon atom are taken together to form =O;

R^4 is hydrogen or C_{1-6} alkyl;

R^5 is C_{1-8} alkyl, C_{3-8} cycloalkyl, 4- to 8-membered heterocycloalkyl, –$[(CH_2)_r–Z]_t–R^6$, –$[(CHR^d)_r–Z]_t–R^6$, or –$[(C(R^d)_2)_r–Z]_t–R^6$; wherein each alkyl, cycloalkyl, and 4- to 8-membered heterocycloalkyl is substituted by 1-6 R^c groups

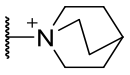
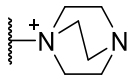
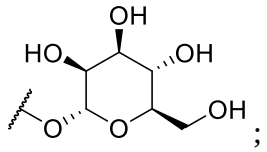
each Z is independently –CH_2O–, –CH_2NR^d–, –$CH_2N^+(R^d)_2$–, or –NH-C(=O)-NH–;

each r is independently 1-6;

each t is independently 1-6;

R^6 is hydrogen, C_{1-8} alkyl, C_{3-8} cycloalkyl, or 4- to 8-membered heterocycloalkyl, wherein the alkyl, cycloalkyl, or 4- to 8-membered heterocycloalkyl is unsubstituted or substituted by 1-6 R^c groups;

or R^4 and R^5 are taken together with the nitrogen to which they are attached to form a 4- to 8-membered heterocycloalkyl, which is unsubstituted or substituted by 1-6 R^c groups;

each R^c is independently -OH, -CH_2OH, -NH_2, -$N(R^d)_3^+$, -C(=O)OH, -$S(=O)_2OH$, -$S(=O)_2NH_2$, -$P(=O)(OH)_2$, -$P(=O)(OH)(R^d)$, -$P(=O)(OH)(OR^d)$, , , , or ;

each R^d is independently C_{1-6} alkyl;

each R^a is independently halogen, -CN, C_{1-6} alkyl, C_{1-6} fluoroalkyl, or C_{3-6} cycloalkyl;

W is phenyl or 5-6 membered monocyclic heteroaryl, wherein the phenyl or heteroaryl is unsubstituted or substituted with 1, 2, or 3 substituents selected from R^b;

each R^b is independently halogen, -OH, -CN, -C(O)OH, -C(O)O(C_{1-6} alkyl), C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-6} cycloalkyl, phenyl, or 5- to 6-membered heteroaryl; wherein each alkyl, alkoxy, and cycloalkyl is unsubstituted or substituted with 1, 2, or 3 substituents selected from halogen, -OH, C_{1-6} alkyl, and C_{1-6} alkoxy;

or W is -C(=O)O-R^{22};

R^{22} is C_{1-6} alkyl, C_{3-6} cycloalkyl, or 3- to 6-membered heterocycloalkyl, wherein the alkyl, cycloalkyl, and heterocycloalkyl are unsubstituted or substituted by 1-3 substituents independently selected from fluorine, -OH, C_{1-6} alkyl, C_{1-6} haloalkyl or C_{3-6} cycloalkyl;

n is 0-4;

p is 1 or 2;

q is 1 or 2; and

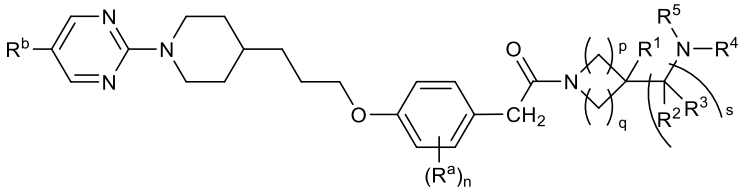
s is 1 or 2.

6. The compound of claim 5, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

W is phenyl or 6-membered monocyclic heteroaryl, wherein the heteroaryl is unsubstituted or substituted with 1 or 2 substituents selected from R^b; and

each R^b is independently halogen, -C(O)OH, -C(O)O(C_{1-6} alkyl), C_{1-6} alkyl, C_{1-6} alkoxy, or C_{3-6} cycloalkyl; wherein each alkyl, alkoxy, and cycloalkyl is unsubstituted or substituted with 1, 2, or 3 substituents selected from halogen, -OH, C_{1-6} alkyl, and C_{1-6} alkoxy.

7. The compound of claim 1, or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, wherein the compound has the structure of Formula (IIb), or a pharmaceutically acceptable salt, or solvate thereof:



Formula (IIb).

8. The compound of any one of claims 5-7, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

p is 1; and

q is 1.

9. The compound of any one of claims 5-8, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

R^4 is hydrogen or C_{1-4} alkyl;

R^5 is C_{1-8} alkyl, $–[(CH_2)_r–Z]_t–R^6$, $–[(CHR^d)_r–Z]_t–R^6$, or $–[(C(R^d)_2)_r–Z]_t–R^6$; wherein the alkyl is substituted by 1-6 R^c groups;

each Z is independently $–CH_2O–$, $–CH_2NR^d–$, or –NH-C(=O)-NH–;

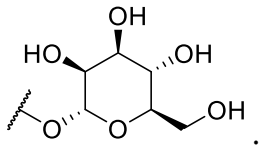
r is 1-3;

t is 1-3; and

R^6 is hydrogen or C_{1-8} alkyl, wherein the alkyl is substituted by 1-6 R^c groups.

10. The compound of any one of claims 5-9, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

each R^c is independently -OH, $-CH_2OH$, $-NH_2$, $-N(R^d)_3^+$, -C(=O)OH, or



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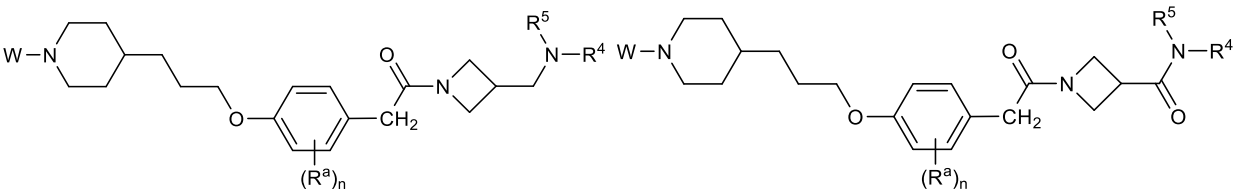
11. The compound of any one of claims 5-8, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

R^4 and R^5 are taken together with the nitrogen to which they are attached to form a 5- or 6-membered heterocycloalkyl, which is unsubstituted or substituted by 1-3 -OH groups.

12. The compound of claim 1, or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, wherein the compound has the structure of Formula (IIc) or Formula (IId), or a pharmaceutically acceptable salt, or solvate thereof:



Formula (IIc) Formula (IId).

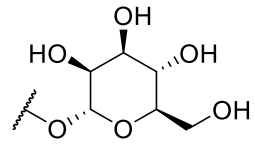
13. The compound of claim 12, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

W is 6-membered monocyclic heteroaryl, wherein the heteroaryl is unsubstituted or substituted with 1 or 2 substituents selected from R^b;

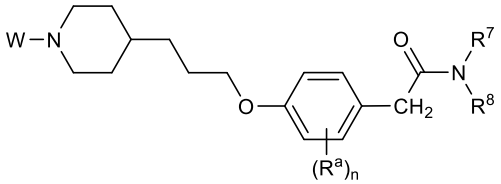
each R^b is independently -F, -Cl, $-CH_3$, $-CH_2CH_3$, $-CH_2CH_2CH_3$, $-CH_2OH$, $-CH_2OCH_3$, $-OCH_3$, $-OCH_2CH_3$, -C(O)OH, or $-C(O)OCH_3$;

R^4 is hydrogen or C_{1-4} alkyl;

R^5 is C_{1-8} alkyl which is substituted by 1-6 R^c groups; and

each R^c is independently -OH, $-CH_2OH$, $-N(R^d)_3^+$, -C(=O)OH, or .

14. The compound of claim 1, or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, wherein the compound has the structure of Formula (IIIa), or a pharmaceutically acceptable salt, or solvate thereof:



Formula (IIIa),

wherein:

R^7 is hydrogen or C_{1-4} alkyl;

R^8 is C_{1-8} alkyl, C_{3-8} cycloalkyl, $–[(CH_2)_r–Z]_t–R^6$, $–[(CHR^d)_r–Z]_t–R^6$, or $–[(CR^d_2)_r–Z]_t–R^6$; wherein the alkyl or cycloalkyl is substituted by 1-6 R^e groups

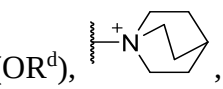
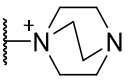
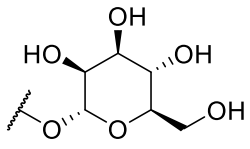
each Z is independently $–CH_2O–$, $–CH_2NR^d–$, $–CH_2N^+(R^d)_2–$, or –NH-C(=O)-NH–;

R^6 is hydrogen, C_{1-8} alkyl, C_{3-8} cycloalkyl, or 4- to 8-membered heterocycloalkyl, wherein the alkyl, cycloalkyl, or 4- to 8-membered heterocycloalkyl is unsubstituted or substituted by 1-6 R^c groups;

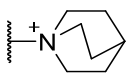
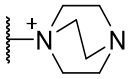
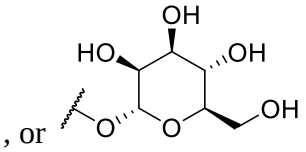
or R^8 is $-(C_{1-8}$ alkyl)-NH-R^9, $-(C_{1-8}$ alkyl)-C(=O)NH-R^9, $-(C_{1-8}$ alkyl)-C(=O)-$N(R^9)_2$, or $-(C_{1-8}$ alkyl)-NHC(=O)NH-R^9; wherein the alkyl is unsubstituted or substituted by 1-6 R^c groups;

each R^9 is independently C_{1-8} alkyl which is substituted by 1-6 R^c groups;

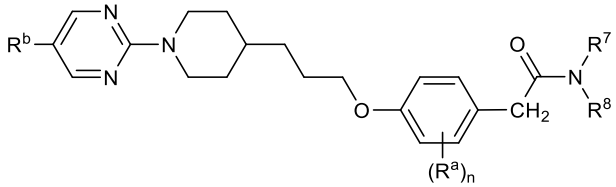
or two R^9 are taken together with the nitrogen to which they are attached to form a 4- to 6-membered heterocycloalkyl, which is substituted by 1-6 R^c groups;

each R^c is independently -OH, -CH_2OH, -NH_2, -$N(R^d)_3^+$, -C(=O)OH, -$S(=O)_2OH$, -$S(=O)_2NH_2$, -$P(=O)(OH)_2$, -P(=O)(OH)(R^d), -P(=O)(OH)(OR^d), , , , or ;

each R^d is independently C_{1-6} alkyl; and

each R^e is independently -OH, -CH_2OH, -$N(R^d)_3^+$, -C(=O)OH, -$S(=O)_2OH$, -$S(=O)_2NH_2$, -$P(=O)(OH)_2$, -P(=O)(OH)(R^d), -P(=O)(OH)(OR^d), , , , , or .

15. The compound of claim 1, or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, wherein the compound has the structure of Formula (IIIb), or a pharmaceutically acceptable salt, or solvate thereof:



Formula (IIIb).

16. The compound of claim 1, or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, selected from:

2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]-N-[5-[[2-hydroxy-1-(hydroxymethyl)ethyl]amino]pentyl]acetamide;

5-[[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]amino]pentyl-triethyl-ammonium;

2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]-N-[5-[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]pentyl]acetamide;

5-[[2-[2,6-difluoro-4-[3-[1-(5-propylpyrimidin-2-yl)-4-piperidyl]propoxy]phenyl]acetyl]amino]pentyl-triethyl-ammonium;

2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]-N-[2-hydroxy-1,1-bis(hydroxymethyl)ethyl]acetamide;

2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2,6-difluoro-phenyl]-N-[2-hydroxy-1,1-bis(hydroxymethyl)ethyl]acetamide;

2-[4-[3-[1-(5-ethylpyrimidin-2-yl)-4-piperidyl]propoxy]-2,6-difluoro-phenyl]-N-[2-hydroxy-1,1-bis(hydroxymethyl)ethyl]acetamide;
2-[2,6-difluoro-4-[3-[1-(5-propylpyrimidin-2-yl)-4-piperidyl]propoxy]phenyl]-N-[2-hydroxy-1,1-bis(hydroxymethyl)ethyl]acetamide;
1-[3,3-bis(hydroxymethyl)azetidin-1-yl]-2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]ethanone;
2-[[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]amino]ethanesulfonic acid;
3-[[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]amino]propane-1-sulfonic acid;
4-[[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]amino]butane-1-sulfonic acid;
2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]-N-(3-sulfamoylpropyl)acetamide;
2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]-N-(4-sulfamoylbutyl)acetamide;
3-[[2-[4-[3-[1-(5-ethylpyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]amino]propyl-trimethyl-ammonium;
2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]-N-[2-[rac-(2S,3S,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydropyran-2-yl]oxyethyl]acetamide;
6-[[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]amino]-N-[2-hydroxy-1-(hydroxymethyl)ethyl]hexanamide;
6-[[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]amino]-N-[2-hydroxy-1,1-bis(hydroxymethyl)ethyl]hexanamide;
3-[[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]amino]-N-[2-hydroxy-1-(hydroxymethyl)ethyl]propenamide;
3-[[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]amino]-N-[2-hydroxy-1,1-bis(hydroxymethyl)ethyl]propenamide;
4-[[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]amino]-N-[2-hydroxy-1-(hydroxymethyl)ethyl]butanamide;
4-[[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]amino]-N-[2-hydroxy-1,1-bis(hydroxymethyl)ethyl]butanamide;
5-[[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]amino]-N-[2-hydroxy-1-(hydroxymethyl)ethyl]pentanamide;

5-[[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]amino]-N-[2-hydroxy-1,1-bis(hydroxymethyl)ethyl]pentanamide;
2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]-N-[6-[(3S,4S)-3,4-dihydroxypyrrolidin-1-yl]-6-oxo-hexyl]acetamide;
1-[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2,6-difluoro-phenyl]acetyl]-N-[2-hydroxy-1,1-bis(hydroxymethyl)ethyl]azetidine-3-carboxamide;
1-[2-[2-fluoro-4-[3-[1-[5-(methoxymethyl)pyrimidin-2-yl]-4-piperidyl]propoxy]phenyl]acetyl]-N-[2-[[2-hydroxy-1,1-bis(hydroxymethyl)ethyl]carbamoylamino]ethyl]azetidine-3-carboxamide;
1-[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]-N-[2-hydroxy-1-(hydroxymethyl)ethyl]azetidine-3-carboxamide;
1-[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]-N-[2-hydroxy-1,1-bis(hydroxymethyl)ethyl]azetidine-3-carboxamide;
1-[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]-N-[2,3-dihydroxy-2-(hydroxymethyl)propyl]azetidine-3-carboxamide;
1-[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]-N-[2-[rac-(2S,3S,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydropyran-2-yl]oxyethyl]azetidine-3-carboxamide;
2-[1-[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]azetidin-3-yl]-N-[2-hydroxy-1,1-bis(hydroxymethyl)ethyl]acetamide;
2-[1-[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]azetidin-3-yl]-N-[2,3-dihydroxy-2-(hydroxymethyl)propyl]acetamide;
2-[1-[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2,6-difluoro-phenyl]acetyl]azetidin-3-yl]-N-[2,3-dihydroxy-2-(hydroxymethyl)propyl]acetamide;
3-[1-[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]azetidin-3-yl]-N-[2,3-dihydroxy-2-(hydroxymethyl)propyl]propenamide;
3-[1-[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2,6-difluoro-phenyl]acetyl]azetidin-3-yl]-N-[2,3-dihydroxy-2-(hydroxymethyl)propyl]propenamide;
1-[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]-N-[rac-(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]azetidine-3-carboxamide;
2-[1-[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]azetidin-3-yl]-N-[rac-(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]acetamide;

1-[2-[2-fluoro-4-[3-[1-[5-(methoxymethyl)pyrimidin-2-yl]-4-piperidyl]propoxy]phenyl]acetyl]-N-[rac-(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]azetidine-3-carboxamide;
3-[[1-[2-[2,6-difluoro-4-[3-[1-(5-propylpyrimidin-2-yl)-4-piperidyl]propoxy]phenyl]acetyl]azetidine-3-carbonyl]amino]propyl-trimethyl-ammonium formate;
1-[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]-N-[2,3-dihydroxy-2-(hydroxymethyl)propyl]piperidine-4-carboxamide;
2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]-1-[3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethanone;
2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]-1-[3-[[[2,3-dihydroxy-2-(hydroxymethyl)propyl]amino]methyl]azetidin-1-yl]ethanone;
2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]-1-[3-[[[2-hydroxy-1,1-bis(hydroxymethyl)ethyl]amino]methyl]azetidin-1-yl]ethanone;
2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]-1-[3-[[[3-hydroxy-2-(hydroxymethyl)propyl]amino]methyl]azetidin-1-yl]ethanone;
2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]-1-[3-[[rac-(3S,4S)-3,4-dihydroxypyrrolidin-1-yl]methyl]azetidin-1-yl]ethanone;
2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]-1-[3-[[rac-(3R,4R)-3,4-dihydroxypyrrolidin-1-yl]methyl]azetidin-1-yl]ethanone;
2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]-1-[3-[[rac-(3S,4R)-3,4-dihydroxypyrrolidin-1-yl]methyl]azetidin-1-yl]ethanone;
2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]-1-[3-[[[rac-(1R,2S,3R,4S)-2,3,4-trihydroxycyclopentyl]amino]methyl]azetidin-1-yl]ethanone;
2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]-1-[3-[[rac-(3R,5S)-3,4,5-trihydroxy-1-piperidyl]methyl]azetidin-1-yl]ethanone;
2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]-1-[3-[[2-[2-(2-hydroxyethoxy)ethoxy]ethylamino]methyl]azetidin-1-yl]ethanone;
1-[3-[[2-[2-(2-aminoethoxy)ethoxy]ethylamino]methyl]azetidin-1-yl]-2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]ethanone;
2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2,6-difluoro-phenyl]-1-[3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethanone;
2-[4-[4-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]butoxy]-2-fluoro-phenyl]-1-[3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethanone;

2-(4-(4-(1-(5-chloropyrimidin-2-yl)piperidin-4-yl)butoxy)-2,6-difluorophenyl)-1-(3-((((2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl)amino)methyl)azetidin-1-yl)ethan-1-one;
2-(4-(3-(1-(5-chloropyrimidin-2-yl)piperidin-4-yl)propoxy)-2-fluorophenyl)-1-(3-(2-((1,3-dihydroxypropan-2-yl)amino)ethyl)azetidin-1-yl)ethan-1-one;
2-(4-(3-(1-(5-chloropyrimidin-2-yl)piperidin-4-yl)propoxy)-2-fluorophenyl)-1-(3-(2-((3-hydroxy-2-(hydroxymethyl)propyl)amino)ethyl)azetidin-1-yl)ethan-1-one;
2-(4-(3-(1-(5-chloropyrimidin-2-yl)piperidin-4-yl)propoxy)-2-fluorophenyl)-1-(3-(2-((2,3-dihydroxy-2-(hydroxymethyl)propyl)amino)ethyl)azetidin-1-yl)ethan-1-one;
2-(4-(3-(1-(5-chloropyrimidin-2-yl)piperidin-4-yl)propoxy)-2-fluorophenyl)-1-(3-(2-((1,3-dihydroxy-2-(hydroxymethyl)propan-2-yl)amino)ethyl)azetidin-1-yl)ethan-1-one;
1-(2-((2-(1-(2-(4-(3-(1-(5-chloropyrimidin-2-yl)piperidin-4-yl)propoxy)-2-fluorophenyl)acetyl)azetidin-3-yl)ethyl)amino)ethyl)-3-(1,3-dihydroxy-2-(hydroxymethyl)propan-2-yl)urea;
2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]-1-[3-[2-[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]ethyl]azetidin-1-yl]ethanone;
2-(4-(3-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yl)propoxy)-2-fluorophenyl)-1-(3-(((3-hydroxy-2-(hydroxymethyl)propyl)amino)methyl)azetidin-1-yl)ethan-1-one;
1-(3-(((2,3-dihydroxy-2-(hydroxymethyl)propyl)amino)methyl)azetidin-1-yl)-2-(4-(3-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yl)propoxy)-2-fluorophenyl)ethan-1-one;
1-(3-(((1,3-dihydroxy-2-(hydroxymethyl)propan-2-yl)amino)methyl)azetidin-1-yl)-2-(4-(3-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yl)propoxy)-2-fluorophenyl)ethan-1-one;
1-(1,3-dihydroxy-2-(hydroxymethyl)propan-2-yl)-3-(2-(((1-(2-(4-(3-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yl)propoxy)-2-fluorophenyl)acetyl)azetidin-3-yl)methyl)amino)ethyl)urea;
(2S,3R,4S,5S)-6-[[1-[2-[4-[3-[1-(5-ethylpyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]azetidin-3-yl]methylamino]-2,3,4,5-tetrahydroxy-hexanoic acid;
1-(3-(((2,3-dihydroxy-2-(hydroxymethyl)propyl)amino)methyl)azetidin-1-yl)-2-(4-(3-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yl)propoxy)-2,6-difluorophenyl)ethan-1-one;
1-(1,3-dihydroxy-2-(hydroxymethyl)propan-2-yl)-3-(2-(((1-(2-(4-(3-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yl)propoxy)-2,6-difluorophenyl)acetyl)azetidin-3-yl)methyl)amino)ethyl)urea;
2-(4-(3-(1-(5-ethylpyrimidin-2-yl)piperidin-4-yl)propoxy)-2,6-difluorophenyl)-1-(3-((((2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl)amino)methyl)azetidin-1-yl)ethan-1-one;
2-(2-fluoro-4-(3-(1-(5-propylpyrimidin-2-yl)piperidin-4-yl)propoxy)phenyl)-1-(3-(((3-hydroxy-2-(hydroxymethyl)propyl)amino)methyl)azetidin-1-yl)ethan-1-one;

1-(3-(((2,3-dihydroxy-2-(hydroxymethyl)propyl)amino)methyl)azetidin-1-yl)-2-(2-fluoro-4-(3-(1-(5-propylpyrimidin-2-yl)piperidin-4-yl)propoxy)phenyl)ethan-1-one;
1-(3-(((1,3-dihydroxy-2-(hydroxymethyl)propan-2-yl)amino)methyl)azetidin-1-yl)-2-(2-fluoro-4-(3-(1-(5-propylpyrimidin-2-yl)piperidin-4-yl)propoxy)phenyl)ethan-1-one;
1-(1,3-dihydroxy-2-(hydroxymethyl)propan-2-yl)-3-(2-(((1-(2-(2-fluoro-4-(3-(1-(5-propylpyrimidin-2-yl)piperidin-4-yl)propoxy)phenyl)acetyl)azetidin-3-yl)methyl)amino)ethyl)urea;
2-(2-fluoro-4-(3-(1-(5-propylpyrimidin-2-yl)piperidin-4-yl)propoxy)phenyl)-1-(3-((((2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl)amino)methyl)azetidin-1-yl)ethan-1-one;
2-(2,6-difluoro-4-(3-(1-(5-propylpyrimidin-2-yl)piperidin-4-yl)propoxy)phenyl)-1-(3-(((2,3-dihydroxy-2-(hydroxymethyl)propyl)amino)methyl)azetidin-1-yl)ethan-1-one;
2-(2,6-difluoro-4-(3-(1-(5-propylpyrimidin-2-yl)piperidin-4-yl)propoxy)phenyl)-1-(3-(((1,3-dihydroxy-2-(hydroxymethyl)propan-2-yl)amino)methyl)azetidin-1-yl)ethan-1-one;
1-(2-(((1-(2-(2,6-difluoro-4-(3-(1-(5-propylpyrimidin-2-yl)piperidin-4-yl)propoxy)phenyl)acetyl)azetidin-3-yl)methyl)amino)ethyl)-3-(1,3-dihydroxy-2-(hydroxymethyl)propan-2-yl)urea;
2-(2,6-difluoro-4-(3-(1-(5-propylpyrimidin-2-yl)piperidin-4-yl)propoxy)phenyl)-1-(3-((((2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl)amino)methyl)azetidin-1-yl)ethan-1-one;
2-[2-fluoro-4-[3-[1-(5-methoxypyrimidin-2-yl)-4-piperidyl]propoxy]phenyl]-1-[3-[[[rac-(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethanone;
2-[4-[3-[1-(5-ethoxypyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]-1-[3-[[[rac-(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethanone;
1-[2-[[1-[2-[2-fluoro-4-[3-[1-[5-(methoxymethyl)pyrimidin-2-yl]-4-piperidyl]propoxy]phenyl]acetyl]azetidin-3-yl]methylamino]ethyl]-3-[2-hydroxy-1,1-bis(hydroxymethyl)ethyl]urea;
(3R,5R)-7-[[1-[2-[2-fluoro-4-[3-[1-[5-(methoxymethyl)pyrimidin-2-yl]-4-piperidyl]propoxy]phenyl]acetyl]azetidin-3-yl]methylamino]-3,5-dihydroxy-heptanoic acid;
2-[2-fluoro-4-[3-[1-[5-(methoxymethyl)pyrimidin-2-yl]-4-piperidyl]propoxy]phenyl]-1-[3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethanone;
2-[2-fluoro-4-[4-[1-[5-(methoxymethyl)pyrimidin-2-yl]-4-piperidyl]butoxy]phenyl]-1-[3-[[[rac-(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethanone;

2-[2,6-difluoro-4-[4-[1-[5-(methoxymethyl)pyrimidin-2-yl]-4-piperidyl]butoxy]phenyl]-1-[3-[[[rac-(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethanone;
2-[4-[2-[(1S,2R)-2-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]cyclopropyl]ethoxy]-2-fluoro-phenyl]-1-[3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethanone;
methyl 2-[4-[3-[3-fluoro-4-[2-oxo-2-[3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethyl]phenoxy]propyl]-1-piperidyl]pyrimidine-5-carboxylate;
2-[4-[2-[1-(5-ethylpyrimidin-2-yl)-4-piperidyl]ethoxymethyl]-2-fluoro-phenyl]-1-[3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]cyclobutyl]ethanone;
2-[4-[2-[1-(5-ethylpyrimidin-2-yl)-4-piperidyl]ethoxymethyl]-3-fluoro-phenyl]-1-[3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]cyclobutyl]ethanone;
2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxymethyl]-2-fluoro-phenyl]-1-[3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethanone;
2-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]ethyl 3-fluoro-4-[2-oxo-2-[3-[[[rac-(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethyl]benzoate;
2-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]ethyl 2-[3-fluoro-4-[2-oxo-2-[3-[[[rac-(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethyl]phenyl]acetate;
2-[2-fluoro-4-[3-[1-[5-(hydroxymethyl)pyrimidin-2-yl]-4-piperidyl]propoxy]phenyl]-1-[3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethanone;
2-[2,6-difluoro-4-[3-[1-[5-(methoxymethyl)pyrimidin-2-yl]-4-piperidyl]propoxy]phenyl]-1-[3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethanone;
[rac-(1R,2R)-2-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]cyclopropyl]methyl 3-fluoro-4-[2-oxo-2-[3-[[[rac-(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethyl]benzoate;
2-[2-fluoro-4-[[(1R,2R)-2-[1-[5-(methoxymethyl)pyrimidin-2-yl]-4-piperidyl]cyclopropyl]methoxymethyl]phenyl]-1-[3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethanone;
2-[2-fluoro-4-[2-[rac-(1S,2R)-2-[1-[5-(methoxymethyl)pyrimidin-2-yl]-4-piperidyl]cyclopropyl]ethoxy]phenyl]-1-[3-[[[rac-(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethanone;

2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]-1-[(3S)-3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]pyrrolidin-1-yl]ethanone;
2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]-1-[(3S)-3-[[[2,3-dihydroxy-2-(hydroxymethyl)propyl]amino]methyl]pyrrolidin-1-yl]ethanone;
2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]-1-[(3R)-3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]pyrrolidin-1-yl]ethanone;
2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]-1-[(3R)-3-[[[2,3-dihydroxy-2-(hydroxymethyl)propyl]amino]methyl]pyrrolidin-1-yl]ethanone;
(3R)-1-[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]-N-[2-hydroxy-1,1-bis(hydroxymethyl)ethyl]pyrrolidine-3-carboxamide;
(3S)-1-[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]-N-[2-hydroxy-1,1-bis(hydroxymethyl)ethyl]pyrrolidine-3-carboxamide;
2-[4-[2-[7-(5-chloropyrimidin-2-yl)-7-azaspiro[3.5]nonan-2-yl]ethoxy]-2-fluoro-phenyl]-1-[3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethanone;
2-[4-[3-[7-(5-chloropyrimidin-2-yl)-7-azaspiro[3.5]nonan-2-yl]propoxy]-2-fluoro-phenyl]-1-[3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethanone;
2-[4-[4-[7-(5-chloropyrimidin-2-yl)-7-azaspiro[3.5]nonan-2-yl]butoxy]-2-fluoro-phenyl]-1-[3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethanone;
2-[4-[[7-(5-chloropyrimidin-2-yl)-7-azaspiro[3.5]nonan-2-yl]methoxymethyl]-2-fluoro-phenyl]-1-[3-[[[2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethanone;
N-[2,3-dihydroxy-2-(hydroxymethyl)propyl]-2-[1-[2-[4-[3-[1-(5-ethoxypyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]azetidin-3-yl]acetamide;
2-[4-[4-[1-(5-chloropyrimidin-2-yl)-4-methyl-4-piperidyl]butoxy]-2-fluoro-phenyl]-1-[3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethanone;
2-[4-[2-[6-(5-chloropyrimidin-2-yl)-6-azaspiro[2.5]octan-2-yl]ethoxy]-2-fluoro-phenyl]-1-[3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethanone;
2-[4-[[6-(5-chloropyrimidin-2-yl)-6-azaspiro[2.5]octan-2-yl]methoxymethyl]-2-fluoro-phenyl]-1-[3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethanone;

isopropyl 4-[3-[3-fluoro-4-[2-oxo-2-[3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethyl]phenoxy]propyl]piperidine-1-carboxylate;

2-[4-[3-[(1R,5S)-3-(5-chloropyrimidin-2-yl)-3-azabicyclo[3.1.0]hexan-6-yl]propoxy]-2-fluoro-phenyl]-1-[3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethanone;

2-[4-[3-[1-(5-ethoxypyrimidin-2-yl)-4-piperidyl]propoxy]-2,6-difluoro-phenyl]-1-[3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethanone;

2-[4-[2-[7-(5-chloropyrimidin-2-yl)-7-azaspiro[3.5]nonan-2-yl]ethoxy]-2,6-difluoro-phenyl]-1-[3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethanone;

2-[4-[3-[7-(5-chloropyrimidin-2-yl)-7-azaspiro[3.5]nonan-2-yl]propoxy]-2,6-difluoro-phenyl]-1-[3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethanone;

isopropyl 2-[3-[3-fluoro-4-[2-oxo-2-[3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethyl]phenoxy]propyl]-7-azaspiro[3.5]nonane-7-carboxylate;

isopropyl 2-[2-[3-fluoro-4-[2-oxo-2-[3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethyl]phenoxy]ethyl]-7-azaspiro[3.5]nonane-7-carboxylate;

(1-methylcyclopropyl) 4-[3-[3-fluoro-4-[2-oxo-2-[3-[[[rac-(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethyl]phenoxy]propyl]piperidine-1-carboxylate;

2-[4-[[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]cyclobutyl]methoxy]-2-fluoro-phenyl]-1-[3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethanone;

2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]-1-[3-(methoxymethyl)-3-[[[r(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]pyrrolidin-1-yl]ethanone;

2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]-1-[3-[[[3-hydroxy-2,2-bis(hydroxymethyl)propyl]amino]methyl]-3-(methoxymethyl)pyrrolidin-1-yl]ethanone;

2-[4-[2-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]cyclobutyl]ethoxy]-2-fluoro-phenyl]-1-[3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethanone;

2-[4-[2-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]cyclobutyl]ethoxy]-2,6-difluoro-phenyl]-1-[3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethanone;

[3-(trifluoromethyl)oxetan-3-yl] 4-[3-[3-fluoro-4-[2-oxo-2-[3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethyl]phenoxy]propyl]piperidine-1-carboxylate;

[3-(trifluoromethyl)oxetan-3-yl] 4-[3-[3,5-difluoro-4-[2-oxo-2-[3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethyl]phenoxy]propyl]piperidine-1-carboxylate;

(3S)-1-[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]-N-[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]pyrrolidine-3-carboxamide;

(3S)-1-[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2,6-difluoro-phenyl]acetyl]-N-[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]pyrrolidine-3-carboxamide;

(3S)-1-[2-[4-[3-[1-(5-ethoxypyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]-N-[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]pyrrolidine-3-carboxamide;

(3S)-1-[2-[4-[3-[1-(5-ethoxypyrimidin-2-yl)-4-piperidyl]propoxy]-2,6-difluoro-phenyl]acetyl]-N-[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]pyrrolidine-3-carboxamide;

(3S)-1-[2-[2,6-difluoro-4-[3-[1-[5-(methoxymethyl)pyrimidin-2-yl]-4-piperidyl]propoxy]phenyl]acetyl]-N-[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]pyrrolidine-3-carboxamide;

2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2,6-difluoro-phenyl]-1-[(3S)-3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]pyrrolidin-1-yl]ethanone;

2-[4-[3-[1-(5-ethoxypyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]-1-[(3S)-3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]pyrrolidin-1-yl]ethanone;

2-[4-[3-[1-(5-ethoxypyrimidin-2-yl)-4-piperidyl]propoxy]-2,6-difluoro-phenyl]-1-[(3S)-3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]pyrrolidin-1-yl]ethanone;

2-[2,6-difluoro-4-[3-[1-[5-(methoxymethyl)pyrimidin-2-yl]-4-piperidyl]propoxy]phenyl]-1-[(3S)-3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]pyrrolidin-1-yl]ethanone;

1-[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]-3-(methoxymethyl)-N-[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]pyrrolidine-3-carboxamide;
1-[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]-N-[3-hydroxy-2,2-bis(hydroxymethyl)propyl]-3-(methoxymethyl)pyrrolidine-3-carboxamide;
2-[4-[2-[7-(5-chloropyrimidin-2-yl)-7-azaspiro[3.5]nonan-3-yl]ethoxy]-2-fluoro-phenyl]-1-[3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethanone;
2-[4-[2-[7-(5-chloropyrimidin-2-yl)-7-azaspiro[3.5]nonan-3-yl]ethoxy]-2,6-difluoro-phenyl]-1-[3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethanone;
isopropyl 3-[2-[3-fluoro-4-[2-oxo-2-[3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethyl]phenoxy]ethyl]-7-azaspiro[3.5]nonane-7-carboxylate;
isopropyl 3-[2-[3,5-difluoro-4-[2-oxo-2-[3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethyl]phenoxy]ethyl]-7-azaspiro[3.5]nonane-7-carboxylate;
2-[4-[3-[6-(5-chloropyrimidin-2-yl)-6-azaspiro[2.5]octan-2-yl]propoxy]-2-fluoro-phenyl]-1-[3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethanone;
2-[4-[3-[6-(5-chloropyrimidin-2-yl)-6-azaspiro[2.5]octan-2-yl]propoxy]-2,6-difluoro-phenyl]-1-[3-[[[2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethanone;
2-[4-[3-[7-(5-chloropyrimidin-2-yl)-7-azaspiro[3.5]nonan-3-yl]propoxy]-2-fluoro-phenyl]-1-[3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethanone;
isopropyl 2-[3-[3-fluoro-4-[2-oxo-2-[3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethyl]phenoxy]propyl]-6-azaspiro[2.5]octane-6-carboxylate;
isopropyl 2-[3-[3,5-difluoro-4-[2-oxo-2-[3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethyl]phenoxy]propyl]-6-azaspiro[2.5]octane-6-carboxylate;
2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]-1-[(3S)-3-[[[3-hydroxy-2,2-bis(hydroxymethyl)propyl]amino]methyl]pyrrolidin-1-yl]ethanone;

2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]-1-[(3S)-3-[[[2-hydroxy-1,1-bis(hydroxymethyl)ethyl]amino]methyl]pyrrolidin-1-yl]ethanone;
2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2,6-difluoro-phenyl]-1-[(3S)-3-[[[2-hydroxy-1,1-bis(hydroxymethyl)ethyl]amino]methyl]pyrrolidin-1-yl]ethanone;
2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2,6-difluoro-phenyl]-1-[(3S)-3-[[[2,3-dihydroxy-2-(hydroxymethyl)propyl]amino]methyl]pyrrolidin-1-yl]ethanone;
2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2,6-difluoro-phenyl]-1-[(3S)-3-[[[3-hydroxy-2,2-bis(hydroxymethyl)propyl]amino]methyl]pyrrolidin-1-yl]ethanone;
2-[4-[3-[1-(5-ethoxypyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]-1-[(3S)-3-[[[2-hydroxy-1,1-bis(hydroxymethyl)ethyl]amino]methyl]pyrrolidin-1-yl]ethanone;
2-[4-[3-[1-(5-ethoxypyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]-1-[(3S)-3-[[[2,3-dihydroxy-2-(hydroxymethyl)propyl]amino]methyl]pyrrolidin-1-yl]ethanone;
2-[4-[3-[1-(5-ethoxypyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]-1-[(3S)-3-[[[3-hydroxy-2,2-bis(hydroxymethyl)propyl]amino]methyl]pyrrolidin-1-yl]ethanone;
2-[4-[3-[1-(5-ethoxypyrimidin-2-yl)-4-piperidyl]propoxy]-2,6-difluoro-phenyl]-1-[(3S)-3-[[[2-hydroxy-1,1-bis(hydroxymethyl)ethyl]amino]methyl]pyrrolidin-1-yl]ethanone;
2-[4-[3-[1-(5-ethoxypyrimidin-2-yl)-4-piperidyl]propoxy]-2,6-difluoro-phenyl]-1-[(3S)-3-[[[2,3-dihydroxy-2-(hydroxymethyl)propyl]amino]methyl]pyrrolidin-1-yl]ethanone;
2-[4-[3-[1-(5-ethoxypyrimidin-2-yl)-4-piperidyl]propoxy]-2,6-difluoro-phenyl]-1-[(3S)-3-[[[3-hydroxy-2,2-bis(hydroxymethyl)propyl]amino]methyl]pyrrolidin-1-yl]ethanone;
2-[2,6-difluoro-4-[3-[1-[5-(methoxymethyl)pyrimidin-2-yl]-4-piperidyl]propoxy]phenyl]-1-[(3S)-3-[[[2-hydroxy-1,1-bis(hydroxymethyl)ethyl]amino]methyl]pyrrolidin-1-yl]ethanone;
2-[2,6-difluoro-4-[3-[1-[5-(methoxymethyl)pyrimidin-2-yl]-4-piperidyl]propoxy]phenyl]-1-[(3S)-3-[[[2,3-dihydroxy-2-(hydroxymethyl)propyl]amino]methyl]pyrrolidin-1-yl]ethanone;
2-[2,6-difluoro-4-[3-[1-[5-(methoxymethyl)pyrimidin-2-yl]-4-piperidyl]propoxy]phenyl]-1-[(3S)-3-[[[3-hydroxy-2,2-bis(hydroxymethyl)propyl]amino]methyl]pyrrolidin-1-yl]ethanone;
2-[2-fluoro-4-[2-[(1S,2R)-2-[1-[5-(methoxymethyl)pyrimidin-2-yl]-4-piperidyl]cyclopropyl]ethoxy]phenyl]-1-[(3S)-3-[[[2-hydroxy-1,1-bis(hydroxymethyl)ethyl]amino]methyl]pyrrolidin-1-yl]ethanone;
2-[2-fluoro-4-[2-[(1S,2R)-2-[1-[5-(methoxymethyl)pyrimidin-2-yl]-4-piperidyl]cyclopropyl]ethoxy]phenyl]-1-[(3S)-3-[[[2,3-dihydroxy-2-(hydroxymethyl)propyl]amino]methyl]pyrrolidin-1-yl]ethanone;

2-[2-fluoro-4-[2-[(1S,2R)-2-[1-[5-(methoxymethyl)pyrimidin-2-yl]-4-piperidyl]cyclopropyl]ethoxy]phenyl]-1-[(3S)-3-[[[3-hydroxy-2,2-bis(hydroxymethyl)propyl]amino]methyl]pyrrolidin-1-yl]ethanone;
2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]-1-[3-[2-[[(2S,3S,4R)-2,3,4,5-tetrahydroxypentyl]amino]ethyl]azetidin-1-yl]ethanone;
2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]-1-[3-[[[(2S,3S,4R)-2,3,4,5-tetrahydroxypentyl]amino]methyl]azetidin-1-yl]ethanone;
2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]-1-[3-[[[(2S,3R,4R)-2,3,4,5-tetrahydroxypentyl]amino]methyl]azetidin-1-yl]ethanone;
2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]-1-[3-[[[(2R,3S,4R)-2,3,4,5-tetrahydroxypentyl]amino]methyl]azetidin-1-yl]ethanone;
2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]-1-[(3R)-3-[[[(2S,3S,4R)-2,3,4,5-tetrahydroxypentyl]amino]methyl]pyrrolidin-1-yl]ethanone;
2-[5-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-pyridyl]-1-[3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethanone;
2-[5-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-3-fluoro-2-pyridyl]-1-[3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethanone;
2-[[1-[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]azetidine-3-carbonyl]amino]ethanesulfonic acid;
3-[[1-[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]azetidine-3-carbonyl]amino]propane-1-sulfonic acid;
4-[[1-[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]azetidine-3-carbonyl]amino]butane-1-sulfonic acid;
5-[[1-[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]azetidine-3-carbonyl]amino]pentane-1-sulfonic acid;
6-[[1-[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]azetidine-3-carbonyl]amino]hexane-1-sulfonic acid;
2-[[2-[1-[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]azetidin-3-yl]acetyl]amino]ethanesulfonic acid;
3-[[2-[1-[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]azetidin-3-yl]acetyl]amino]propane-1-sulfonic acid;
4-[[2-[1-[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]azetidin-3-yl]acetyl]amino]butane-1-sulfonic acid;
2-[6-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-3-pyridyl]-1-[3-[[[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]amino]methyl]azetidin-1-yl]ethanone;

2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]-1-[3-hydroxy-3-[[[3-hydroxy-2,2-bis(hydroxymethyl)propyl]amino]methyl]pyrrolidin-1-yl]ethanone;

1-[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]-3-hydroxy-N-[(2S,3R,4R,5R)-2,3,4,5,6-pentahydroxyhexyl]pyrrolidine-3-carboxamide;

1-[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]-3-hydroxy-N-[3-hydroxy-2,2-bis(hydroxymethyl)propyl]pyrrolidine-3-carboxamide;

2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]-1-[4-hydroxy-4-[[[3-hydroxy-2,2-bis(hydroxymethyl)propyl]amino]methyl]-1-piperidyl]ethanone;

2-[1-[2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]acetyl]-3-hydroxy-azetidin-3-yl]-N-[3-hydroxy-2,2-bis(hydroxymethyl)propyl]acetamide;

2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]-1-[3-hydroxy-3-[[[(2S,3S,4R)-2,3,4,5-tetrahydroxypentyl]amino]methyl]azetidin-1-yl]ethanone;

2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]-1-[3-hydroxy-3-[[[(2S,3S,4R)-2,3,4,5-tetrahydroxypentyl]amino]methyl]pyrrolidin-1-yl]ethanone;

2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2-fluoro-phenyl]-1-[4-hydroxy-4-[[[(2S,3S,4R)-2,3,4,5-tetrahydroxypentyl]amino]methyl]-1-piperidyl]ethanone;

2-[4-[3-[1-(5-chloropyrimidin-2-yl)-4-piperidyl]propoxy]-2,6-difluoro-phenyl]-1-[3-hydroxy-3-[[[3-hydroxy-2,2-bis(hydroxymethyl)propyl]amino]methyl]pyrrolidin-1-yl]ethanone;

2-[4-[3-[1-(5-ethoxypyrimidin-2-yl)-4-piperidyl]propoxy]-2,6-difluoro-phenyl]-1-[3-hydroxy-3-[[[3-hydroxy-2,2-bis(hydroxymethyl)propyl]amino]methyl]pyrrolidin-1-yl]ethanone; and

2-[2,6-difluoro-4-[3-[1-[5-(methoxymethyl)pyrimidin-2-yl]-4-piperidyl]propoxy]phenyl]-1-[3-hydroxy-3-[[[3-hydroxy-2,2-bis(hydroxymethyl)propyl]amino]methyl]pyrrolidin-1-yl]ethanone;

or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof.

17. A pharmaceutical composition comprising a compound of any one of claims 1-16, or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, and at least one pharmaceutically acceptable excipient.

18. Use of the compound of any one of claims 1-16, or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, in the manufacture of a medicament for the treatment of a condition or disorder involving the gut-brain axis in a subject in need thereof; wherein the condition or disorder is associated with GPR119 activity.

19. The use of claim 18, wherein the condition or disorder is a metabolic disorder or a nutritional disorder.

20. The use of claim 19, wherein the condition or disorder is type 2 diabetes, hyperglycemia, metabolic syndrome, obesity, hypercholesterolemia, nonalcoholic steatohepatitis, hypertension, short bowel syndrome, intestinal failure, intestinal insufficiency, chemotherapy-induced enteritis or radiation-induced enteritis.

21. The use of any one of claims 18-20, wherein treatment further comprises the use of one or more additional therapeutic agents;
wherein the one or more additional therapeutic agents are selected from a TGR5 agonist, a GPR40 agonist, an SSTR5 antagonist, an SSTR5 inverse agonist, a CCK1 agonist, a PDE4 inhibitor, a DPP-4 inhibitor, a GLP-1 receptor agonist, metformin, or a combination thereof.

22. A compound of any one of claims 1-16, or a pharmaceutically acceptable salt, solvate, stereoisomer, or prodrug thereof, for use in therapy.