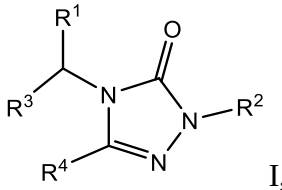
Degterev A, et al., *Chemical inhibitor of nonapoptotic cell death with therapeutic potential for ischemic brain injury*, Nat Chem Biol 2005, 1(2):112-119.

Therefore, there is a need for inhibitors of RIPK1 that offer high selectivity which can penetrate the blood–brain barrier, thus offering the possibility to target neuroinflammation and cell death which drive various neurologic conditions including Alzheimer's disease, ALS, and multiple sclerosis as well as acute neurological diseases such as stroke and traumatic brain injuries.

SUMMARY

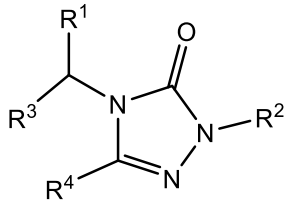
Described herein are compounds of Formula I:



I,

and pharmaceutically acceptable salts thereof, wherein R^1, R^2, R^3 and R^4 are described below.

In a first aspect of the present disclosure, there is provided a compound of Formula I:



(I), or a pharmaceutically acceptable salt thereof, wherein:

R^1 is selected from C_3-C_6cycloalkyl, aryl and heteroaryl, wherein each of the C_3-C_6cycloalkyl, aryl and heteroaryl is optionally substituted with one to four substituents independently selected from:

(1) halogen;

(2) -CN;

(3) -C_1-C_6alkyl, optionally substituted with one to four substituents independently selected from halogen and -CN;

(4) -C_2-C_6alkynyl;

(5) -C_3-C_6cycloalkyl;

(6) -O-C_1-C_6alkyl; and

(7) -OH

R^2 is selected from C_3-C_{10}cycloalkyl, heterocycloalkyl, aryl and heteroaryl, wherein each of the C_3-C_{10}cycloalkyl, heterocycloalkyl, aryl and heteroaryl is optionally substituted with one to four substituents independently selected from:

(1) halogen;

(2) -CN;

(3) -C_1-C_6alkyl, optionally substituted with one to four substituents independently selected from halogen, -CN, -OH, -O-C_1-C_6alkyl, and a heteroaryl;

(4) -O-C_1-C_6alkyl, optionally substituted with one to four substituents independently selected from halogen and -CN;

(5) –C(O)-R^a, wherein is R^a is selected from -OH, -C_1-C_6alkyl, -O-C_1-C_6alkyl, and -NR^bR^c, each of R^b and R^c is independently selected from hydrogen and -C_1-C_6alkyl optionally substituted with an heteroaryl; and

(6) aryl, optionally substituted with one to three halogens; and

R^3 and R^4 together with the atoms to which they are attached, form a 5- or 6-membered ring fused to the triazole ring, wherein the 5- or 6-membered ring optionally comprises heteroatoms selected from N, O, or S and is optionally substituted with one to four substituents independently selected from halogen, -OH, and -C_1-C_6alkyl.

The compounds described herein are RIPK1 inhibitors, which can be useful in the prevention, treatment or amelioration of neurodegenerative, autoimmune, inflammatory diseases and other RIPK1-related diseases.

Also described herein are methods of treating neurodegenerative, autoimmune, and inflammatory diseases comprising administering to a patient in need thereof a compound described herein, or a pharmaceutically acceptable salt thereof.

Also described herein are uses of a compound described herein, or a pharmaceuticall acceptable salt thereof, to treat neurodegenerative, autoimmune, and inflammatory diseases in a patient in need thereof.

In another aspect of the present disclosure, there is provided a use of a compound, or pharmaceutically acceptable salt thereof, as disclosed herein in the manufacture of a medicament for the treatment of RIPK1 dependent inflammation and cell death that occurs in inherited and sporadic diseases including Alzheimer's disease, amyotrophic lateral sclerosis, multiple sclerosis, Parkinson's disease, chronic traumatic encephalopathy, rheumatoid arthritis, ulcerative colitis, inflammatory bowel disease, psoriasis as well as acute tissue injury caused by stroke, traumatic brain injury, encephalitis.

In yet another aspect of the present disclosure, there is provided a use of a compound, or pharmaceutically acceptable salt thereof, as disclosed herein in the manufacture of a medicament for the treatment of amyotrophic lateral sclerosis.

In a further aspect of the present disclosure, there is provided a compound, or pharmaceutically acceptable salt thereof, as disclosed herein for use in therapy.

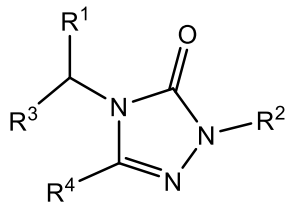
Also described herein are pharmaceutical compositions comprising a compound described herein, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

Also described herein are pharmaceutical compositions comprising a compound described herein and a pharmaceutically acceptable carrier.

Also described herein are methods of treating neurodegenerative, autoimmune, and inflammatory diseases comprising administering to a patient in need thereof a compound described herein, or a pharmaceutically acceptable salt thereof, and at least one additional therapeutic agent.

WHAT IS CLAIMED IS:

1. A compound of Formula I:



(I),

or a pharmaceutically acceptable salt thereof, wherein:

R^1 is selected from C_3-C_6cycloalkyl, aryl and heteroaryl, wherein each of the C_3-C_6cycloalkyl, aryl and heteroaryl is optionally substituted with one to four substituents independently selected from:

(1) halogen;

(2) -CN;

(3) -C_1-C_6alkyl, optionally substituted with one to four substituents independently selected from halogen and -CN;

(4) -C_2-C_6alkynyl;

(5) -C_3-C_6cycloalkyl;

(6) -O-C_1-C_6alkyl; and

(7) -OH

R^2 is selected from C_3-C_{10}cycloalkyl, heterocycloalkyl, aryl and heteroaryl, wherein each of the C_3-C_{10}cycloalkyl, heterocycloalkyl, aryl and heteroaryl is optionally substituted with one to four substituents independently selected from:

(1) halogen;

(2) -CN;

(3) -C_1-C_6alkyl, optionally substituted with one to four substituents independently selected from halogen, -CN, -OH, -O-C_1-C_6alkyl, and a heteroaryl;

(4) -O-C_1-C_6alkyl, optionally substituted with one to four substituents independently selected from halogen and -CN;

(5) –C(O)-R^a, wherein is R^a is selected from -OH, -C_1-C_6alkyl, -O-C_1-C_6alkyl, and -NR^bR^c, each of R^b and R^c is independently selected from hydrogen and -C_1-C_6alkyl optionally substituted with an heteroaryl; and

(6) aryl, optionally substituted with one to three halogens; and

R^3 and R^4 together with the atoms to which they are attached, form a 5- or 6-membered ring fused to the triazole ring, wherein the 5- or 6-membered ring optionally comprises heteroatoms selected from N, O, or S and is optionally substituted with one to four substituents independently selected from halogen, -OH, and -C_1-C_6alkyl.

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

R^1 is selected from -C_4-C_6cycloalkyl, phenyl and heteroaryl, wherein the heteroaryl is selected from pyridyl, oxazolyl, imidazolyl, triazolyl, furyl, triazinyl, thienyl, pyrimidyl, pyrazinyl, pyridazinyl, indolizinyl, cinnolinyl, phthalazinyl, quinazolinyl, naphthyridinyl, quinoxalinyl, purinyl, benzimidazolyl, quinolyl and isoquinolyl;

wherein the -C_4-C_6cycloalkyl, phenyl and heteroaryl is optionally substituted with one to three substituents selected from:

(1) halogen;

(2) -CN;

(3) -CH_3, optionally substituted with one to three substituents independently selected from halogen and -CN;

(4) -CH_2CH_3, optionally substituted with one to three substituents independently selected from halogen and -CN;

(5) ethynyl;

(6) cyclopropyl;

(7) -O-CH_3; and

(8) -O-CH_2CH_3.

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

R^1 is selected from cyclobutyl, cyclopentyl, cyclohexyl, phenyl, pyridyl, and pyrazinyl, wherein the cyclobutyl, cyclopentyl, phenyl, pyridyl, and pyrazinyl is optionally substituted with one to three substituents selected from:

(1) halogen;

(2) -CN;

(3) -CH_3, optionally substituted with one to three substituents independently selected from halogen and -CN;

(4) ethynyl;

(5) cyclopropyl; and

(6) -O-CH_3.

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

R^1 is phenyl, optionally substituted with one to three substituents selected from:

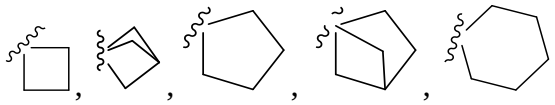
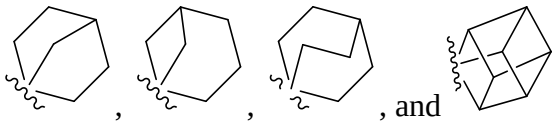
(1) halogen;

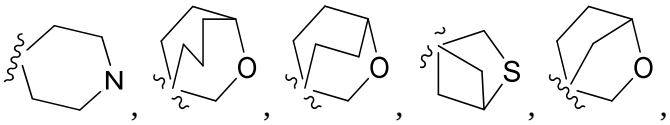
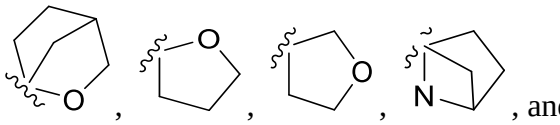
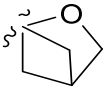
(2) -CN; and

(3) -CH_3, optionally substituted with one to three substituents independently selected from halogen and -CN.

5. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein:

R^2 is selected from C_3-C_{10}cycloalkyl, heterocycloalkyl, phenyl and heteroaryl, wherein:

the C_3-C_{10}cycloalkyl is selected from , , and ;

the heterocycloalkyl is selected from , , and ; and

the heteroaryl is selected from pyridyl, oxazolyl, imidazolyl, triazolyl, furyl, triazinyl, thienyl, pyrimidyl, pyrazinyl, pyridazinyl, indolizinyl, cinnolinyl, phthalazinyl, quinazolinyl, naphthyridinyl, quinoxalinyl, purinyl, benzimidazolyl, quinolyl and isoquinolyl;

wherein each of the C_3-C_{10}cycloalkyl, heterocycloalkyl, phenyl and heteroaryl is optionally substituted with one to three substituents independently selected from:

(1) halogen;

(2) -CN;

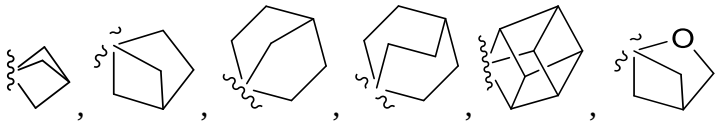
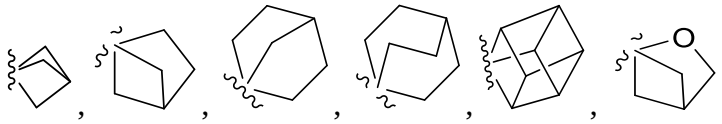
(3) -C_1-C_4alkyl, optionally substituted with one to three substituents independently selected from halogen, -CN, -OH, and -O-C_1-C_4alkyl;

(4) -O-C_1-C_4alkyl, optionally substituted with one to three substituents independently selected from halogen and -CN;

(5) –C(O)-R^a, wherein is R^a is selected from -OH, -C_1-C_6alkyl, -O-C_1-C_6alkyl, and -NHR^c, and R^c is selected from hydrogen and -C_1-C_4alkyl optionally substituted with an heteroaryl selected from pyridyl, oxazolyl, imidazolyl, triazolyl, furyl, triazinyl, thienyl, pyrimidyl, pyrazinyl, pyridazinyl, indolizinyl, cinnolinyl, phthalazinyl, quinazolinyl, naphthyridinyl, quinoxalinyl, purinyl, benzimidazolyl, quinolyl and isoquinolyl; and

(6) phenyl, optionally substituted with one to three halogens.

6. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein:

R^2 is selected from , and phenyl, wherein each of the , and phenyl is optionally substituted with one to three substituents independently selected from:

(1) halogen;

(2) -CN;

(3) -CH_3, optionally substituted with one to three substituents independently selected from halogen, -CN, -OH and -O-CH_3;

(4) -O-CH_3, optionally substituted with one to three substituents independently selected from halogen and -CN;

(5) –C(O)-R^a, wherein is R^a is selected from -OH, -CH_3, -O-CH_3, and -NHR^c; and R^c is selected from hydrogen and -CH_3 optionally substituted with a thienyl; and

(6) phenyl, optionally substituted with one to three halogens.

7. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein:

R^2 is , optionally substituted with one to three substituents independently selected from:

(1) halogen;

(2) -CN;

(3) $-CH_3$, optionally substituted with one to three substituents independently selected from halogen, -CN, -OH and $-O-CH_3$;

(4) -C(O)OMe;

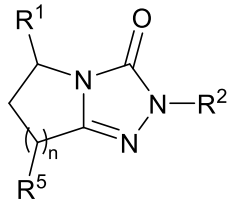
(5) $-C(O)CH_2$-thienyl; and

(6) phenyl.

8. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein:

R^3 and R^4 together with the atoms to which they are attached, form a 5-membered aliphatic ring fused to the triazole ring, wherein the 5-membered aliphatic ring is optionally substituted with one to four substituents independently selected from halogen, -OH, $-CH_3$, $-CH_2CH_3$, and $-CH_2CH_2CH_3$.

9. The compound of claim 1, of Formula Ia:



(Ia),

or a pharmaceutically acceptable salt thereof, wherein:

n is 1 or 2;

R^1 is selected from C_3-C_6cycloalkyl, aryl and heteroaryl, wherein each of the C_3-C_6cycloalkyl, aryl and heteroaryl is optionally substituted with one to three substituents independently selected from:

(1) halogen;

(2) -CN;

(3) $-C_1$-C_6alkyl, optionally substituted with one to four substituents independently selected from halogen and -CN;

(4) $-C_2$-C_6alkynyl;

(5) -C_3-C_6cycloalkyl; and

(6) -O-C_1-C_6alkyl;

R^2 is selected from C_3-C_{10}cycloalkyl, heterocycloalkyl, aryl and heteroaryl, wherein each of the C_3-C_{10}cycloalkyl, heterocycloalkyl, aryl and heteroaryl is optionally substituted with one to four substituents independently selected from:

(1) halogen;

(2) -CN;

(3) -C_1-C_6alkyl, optionally substituted with one to four substituents independently selected from halogen, -CN, -OH, -O-C_1-C_6alkyl, and a heteroaryl;

(4) -O-C_1-C_6alkyl, optionally substituted with one to four substituents independently selected from halogen and -CN;

(5) –C(O)-R^a, wherein is R^a is selected from -OH, -C_1-C_6alkyl, -O-C_1-C_6alkyl, and -NR^bR^c, each of R^b and R^c is independently selected from hydrogen and -C_1-C_6alkyl optionally substituted with an heteroaryl; and

(6) aryl, optionally substituted with one to three halogens; and

each occurrence of R^5 is independently selected from hydrogen, halogen, -C_1-C_6alkyl and -OH.

10. The compound of claim 8, or a pharmaceutically acceptable salt thereof, wherein n is 1.

11. The compound of claim 10, or a pharmaceutically acceptable salt thereof, wherein:

R^1 is selected from -C_4-C_6cycloalkyl, phenyl and heteroaryl, wherein the heteroaryl is selected from pyridyl, oxazolyl, imidazolyl, triazolyl, furyl, triazinyl, thienyl, pyrimidyl, pyrazinyl, pyridazinyl, indolizinyl, cinnolinyl, phthalazinyl, quinazolinyl, naphthyridinyl, quinoxalinyl, purinyl, benzimidazolyl, quinolyl and isoquinolyl;

wherein the -C_4-C_6cycloalkyl, phenyl and heteroaryl is optionally substituted with one to three substituents selected from:

(1) halogen;

(2) -CN;

(3) -CH_3, optionally substituted with one to three substituents independently selected from halogen and -CN;

(4) -CH_2CH_3, optionally substituted with one to three substituents independently selected from halogen and -CN;

(5) ethynyl;

(6) cyclopropyl;

(7) -O-CH_3; and

(8) -O-CH_2CH_3.

12. The compound of claim 10, or a pharmaceutically acceptable salt thereof, wherein:

R^1 is selected from cyclobutyl, cyclopentyl, cyclohexyl, phenyl, pyridyl and pyrazinyl, wherein the cyclobutyl, cyclopentyl, cyclohexyl, phenyl, pyridyl and pyrazinyl is optionally substituted with one to three substituents selected from:

(1) halogen;

(2) -CN;

(3) -CH_3, optionally substituted with one to three substituents independently selected from halogen and -CN;

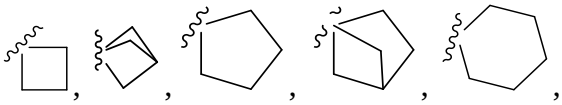
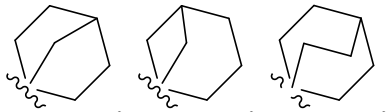
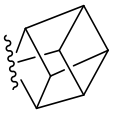
(4) ethynyl;

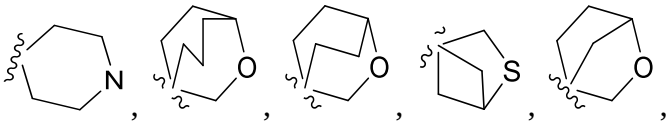
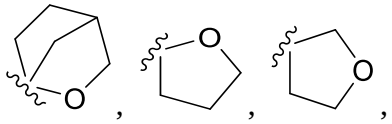
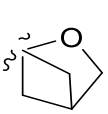
(5) cyclopropyl; and

(6) -O-CH_3.

13. The compound of claim 10, or a pharmaceutically acceptable salt thereof, wherein:

R^2 is selected from C_3-C_{10}cycloalkyl, heterocycloalkyl, phenyl and heteroaryl, wherein:

the C_3-C_{10}cycloalkyl is selected from , , and ;

the heterocycloalkyl is selected from , , and ; and

the heteroaryl is selected from pyridyl, oxazolyl, imidazolyl, triazolyl, furyl, triazinyl, thienyl, pyrimidyl, pyrazinyl, pyridazinyl, indolizinyl, cinnolinyl, phthalazinyl, quinazolinyl, naphthyridinyl, quinoxalinyl, purinyl, benzimidazolyl, quinolyl and isoquinolyl;

wherein each of the C_3-C_{10}cycloalkyl, heterocycloalkyl, phenyl and heteroaryl is optionally substituted with one to three substituents independently selected from:

(1) halogen;

(2) -CN;

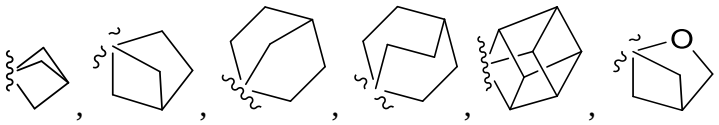
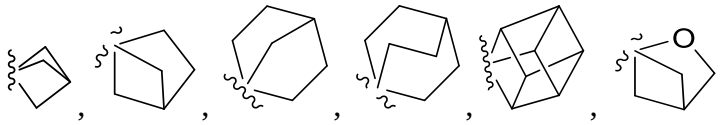
(3) -C_1-C_4alkyl, optionally substituted with one to three substituents independently selected from halogen, -CN, -OH, and -O-C_1-C_4alkyl;

(4) -O-C_1-C_4alkyl, optionally substituted with one to four substituents independently selected from halogen and -CN;

(5) –C(O)-R^a, wherein is R^a is selected from -OH, -C_1-C_6alkyl, -O-C_1-C_6alkyl, and -NHR^c, and R^c is selected from hydrogen and -C_1-C_4alkyl optionally substituted with an heteroaryl selected from pyridyl, oxazolyl, imidazolyl, triazolyl, furyl, triazinyl, thienyl, pyrimidyl, pyrazinyl, pyridazinyl, indolizinyl, cinnolinyl, phthalazinyl, quinazolinyl, naphthyridinyl, quinoxalinyl, purinyl, benzimidazolyl, quinolyl and isoquinolyl; and

(6) phenyl, optionally substituted with one to three halogens.

14. The compound of claim 10, or a pharmaceutically acceptable salt thereof, wherein:

R^2 is selected from , and phenyl, wherein each of the , and phenyl is optionally substituted with one to three substituents independently selected from:

(1) halogen;

(2) -CN;

(3) -CH_3, optionally substituted with one to three substituents independently selected from halogen, -CN, -OH and -O-CH_3;

(4) -O-CH_3, optionally substituted with one to three substituents independently selected from halogen and -CN;

(5) –C(O)-R^a, wherein is R^a is selected from -OH, -CH_3, -O-CH_3, and -NHR^c; and R^c is selected from hydrogen and -CH_3 optionally substituted with a thienyl; and

(6) phenyl, optionally substituted with one to three halogens.

15. The compound of claim 10, or a pharmaceutically acceptable salt thereof, wherein:

R^1 is selected from -C_4-C_6cycloalkyl, phenyl and heteroaryl, wherein the heteroaryl is selected from pyridyl, oxazolyl, imidazolyl, triazolyl, furyl, triazinyl, thienyl, pyrimidyl, pyrazinyl, pyridazinyl, indolizinyl, cinnolinyl, phthalazinyl, quinazolinyl, naphthyridinyl, quinoxalinyl, purinyl, benzimidazolyl, quinolyl and isoquinolyl;

wherein the -C_4-C_6cycloalkyl, phenyl and heteroaryl is optionally substituted with one to three substituents selected from:

(1) halogen;

(2) -CN;

(3) -CH_3, optionally substituted with one to three substituents independently selected from halogen and -CN;

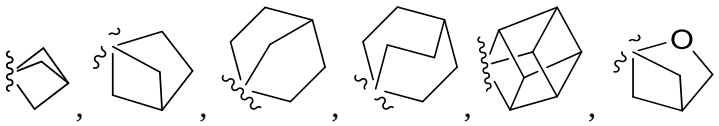
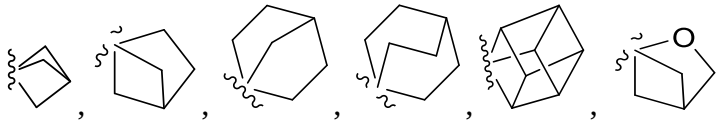
(4) -CH_2CH_3, optionally substituted with one to three substituents independently selected from halogen and -CN;

(5) ethynyl;

(6) cyclopropyl;

(7) -O-CH_3; and

(8) -O-CH_2CH_3;

R^2 is selected from , and phenyl, wherein each of the , and phenyl is optionally substituted with one to three substituents independently selected from:

(1) halogen;

(2) -CN;

(3) -CH_3, optionally substituted with one to three substituents independently selected from halogen, -CN, -OH and -O-CH_3;

(4) -O-CH_3, optionally substituted with one to three substituents independently selected from halogen and -CN;

(5) –C(O)-R^a, wherein is R^a is selected from -OH, -CH_3, -O-CH_3, and -NHR^c; and R^c is selected from hydrogen and -CH_3 optionally substituted with a thienyl; and

(6) phenyl, optionally substituted with one to three halogens; and

R^5 is selected from hydrogen, halogen, -C_1-C_4alkyl and -OH.

16. The compound of claim 10, or a pharmaceutically acceptable salt thereof, wherein:

R^1 is phenyl, optionally substituted with one to three substituents selected from:

(1) halogen;

(2) -CN;

(3) -CH_3, optionally substituted with one to three substituents independently selected from halogen and -CN;

(4) cyclopropyl; and

(5) -O-CH_3;

R^2 is , optionally substituted with one to three substituents independently selected from:

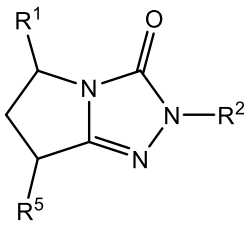
(1) halogen;

(2) -CN; and

(3) -CH_3, optionally substituted with one to three substituents independently selected from halogen, -CN, -OH and -O-CH_3; and

R^5 is selected from hydrogen, halogen, -CH_3, and -OH.

17. The compound of claim 1 of Formula Ib:



(Ib),

or a pharmaceutically acceptable salt thereof, wherein:

R^1 is selected from C_3-C_6cycloalkyl, phenyl and heteroaryl, wherein each of the C_3-C_6cycloalkyl, phenyl and heteroaryl is optionally substituted with one to three substituents independently selected from:

(1) halogen;

(2) -CN;

(3) -C_1-C_6alkyl, optionally substituted with one to three substituents independently selected from halogen and -CN;

(4) -C_2-C_6alkynyl;

(5) -C_3-C_6cycloalkyl; and

(6) -O-C_1-C_6alkyl;

R^2 is selected from C_3-C_{10}cycloalkyl and heterocycloalkyl, wherein each of the C_3-C_{10}cycloalkyl and heterocycloalkyl is optionally substituted with one to three substituents independently selected from:

(1) halogen;

(2) -CN;

(3) -C_1-C_6alkyl, optionally substituted with one to three substituents independently selected from halogen, -CN, -OH, and -O-C_1-C_6alkyl;

(4) -O-C_1-C_6alkyl, optionally substituted with one to three substituents independently selected from halogen and -CN;

(5) –C(O)-R^a, wherein is R^a is selected from -OH, -C_1-C_6alkyl, -O-C_1-C_6alkyl, and -NR^bR^c, each of R^b and R^c is independently selected from hydrogen and -C_1-C_6alkyl optionally substituted with an heteroaryl; and

(6) aryl, optionally substituted with one to three halogens; and

R^5 is selected from hydrogen, halogen, -C_1-C_6alkyl and -OH.

18. The compound of claim 17, or a pharmaceutically acceptable salt thereof, wherein:

R^1 is phenyl, substituted with one to three substituents selected from:

(1) halogen;

(2) -CN;

(3) -CH_3, optionally substituted with one to three substituents independently selected from halogen and -CN;

(4) cyclopropyl; and

(5) -O-CH_3;

R^2 is , substituted with one to three substituents independently selected from:

(1) halogen;

(2) -CN;

(3) -CH_3, optionally substituted with one to three substituents independently selected from halogen, -CN, -OH and -O-CH_3;

(4) -C(O)O-CH_3;

(5) -C(O)CH_2-thienyl; and

(6) phenyl; and

R^5 is hydrogen.

19. The compound of claim 1, or a pharmaceutically acceptable salt thereof, selected from:

(5S)-2-(bicyclo[2.2.1]heptan-1-yl)-5-phenyl-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,

(5S)-5-(3,5-difluorophenyl)-2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,

(5S)-5-(3,5-difluorophenyl)-2-(4-fluorobicyclo[2.2.1]heptan-1-yl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,

(5S)-2-(bicyclo[2.1.1]hexan-1-yl)-5-(3,5-difluorophenyl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,

3-[(5S)-5-(3,5-difluorophenyl)-3-oxo-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl]bicyclo[1.1.1]pentane-1-carbonitrile,

(5S)-2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-5-phenyl-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,

(5S)-2-(bicyclo[1.1.1]pentan-1-yl)-5-(3,5-difluorophenyl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,

(5S)-2-(3-chlorobicyclo[1.1.1]pentan-1-yl)-5-(3,5-difluorophenyl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,

(5S)-2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-5-(2-fluorophenyl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,

(5S)-2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-5-(5-fluoropyridin-3-yl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
3-[(5S)-5-(5-fluoropyridin-3-yl)-3-oxo-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl]bicyclo[1.1.1]pentane-1-carbonitrile,
(5S)-5-(3,5-difluorophenyl)-2-(3-phenylbicyclo[1.1.1]pentan-1-yl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
(5S)-5-(5-fluoropyridin-3-yl)-2-(3-phenylbicyclo[1.1.1]pentan-1-yl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
(5S)-5-(3,5-difluorophenyl)-2-(1-methyl-2-oxabicyclo[2.1.1]hexan-4-yl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
(5S)-2-(3-chlorobicyclo[1.1.1]pentan-1-yl)-5-(5-fluoropyridin-3-yl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
(S)-2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-5-(3-fluorophenyl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
3-[(5S)-3-oxo-5-phenyl-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl]bicyclo[1.1.1]pentane-1-carbonitrile,
methyl 3-[(5S)-5-(3,5-difluorophenyl)-3-oxo-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl]bicyclo[1.1.1]pentane-1-carboxylate,
methyl 3-[(5S)-3-oxo-5-phenyl-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl]bicyclo[1.1.1]pentane-1-carboxylate,
(5S)-5-(3,5-difluorophenyl)-2-(4-fluoropentacyclo[4.2.0.0~2,5~.0~3,8~.0~4,7~]octan-1-yl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
4-[(5S)-5-(3,5-difluorophenyl)-3-oxo-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl]pentacyclo[4.2.0.0~2,5~.0~3,8~.0~4,7~]octane-1-carbonitrile,
(S)-3-(5-(5-chloropyridin-3-yl)-3-oxo-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl)bicyclo[1.1.1]pentane-1-carbonitrile,
3-[(5S)-5-(2-fluorophenyl)-3-oxo-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl]bicyclo[1.1.1]pentane-1-carbonitrile,
(S)-3-(5-(3-fluorophenyl)-3-oxo-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl)bicyclo[1.1.1]pentane-1-carbonitrile,
(5S)-2-(bicyclo[2.2.2]octan-1-yl)-5-(3,5-difluorophenyl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,

(5S)-5-(3,5-difluorophenyl)-2-(4-methoxybicyclo[2.2.1]heptan-1-yl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
(5S)-2-[4-(difluoromethyl)bicyclo[2.2.1]heptan-1-yl]-5-(3,5-difluorophenyl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
(5S)-2-[3-(difluoromethyl)bicyclo[1.1.1]pentan-1-yl]-5-(3,5-difluorophenyl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
4-[(5S)-5-(3,5-difluorophenyl)-3-oxo-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl]bicyclo[2.2.1]heptane-1-carbonitrile,
4-[(5S)-3-oxo-5-phenyl-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl]bicyclo[2.2.1]heptane-1-carbonitrile,
(5S)-2-[3-(difluoromethyl)bicyclo[1.1.1]pentan-1-yl]-5-phenyl-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
(5S)-2-[3-(1,1-difluoroethyl)bicyclo[1.1.1]pentan-1-yl]-5-phenyl-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
(5S)-2-[3-(difluoromethyl)bicyclo[1.1.1]pentan-1-yl]-5-(3-fluorophenyl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
(5S)-2-[3-(1,1-difluoroethyl)bicyclo[1.1.1]pentan-1-yl]-5-(3-fluorophenyl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
4-[(5S)-5-(3,5-difluorophenyl)-3-oxo-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl]bicyclo[2.1.1]hexane-1-carbonitrile,
methyl 3-[(5S)-5-(3,5-difluorophenyl)-3-oxo-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl]-2,2-difluorobicyclo[1.1.1]pentane-1-carboxylate,
(5S)-2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-5-(4-fluorophenyl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
3-[(5S)-5-(4-fluorophenyl)-3-oxo-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl]bicyclo[1.1.1]pentane-1-carbonitrile,
4-[(5S)-3-oxo-5-phenyl-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl]bicyclo[2.1.1]hexane-1-carbonitrile,
(S)-5-(2,6-difluorophenyl)-2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
(5S)-2-(3-chlorobicyclo[1.1.1]pentan-1-yl)-5-phenyl-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,

(S)-2-(3-chlorobicyclo[1.1.1]pentan-1-yl)-5-(3-fluorophenyl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
(S)-3-(5-(2,6-difluorophenyl)-3-oxo-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl)bicyclo[1.1.1]pentane-1-carbonitrile,
(S)-3-(5-(3,4-difluorophenyl)-3-oxo-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl)bicyclo[1.1.1]pentane-1-carbonitrile,
(S)-5-(4-chlorophenyl)-2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
(S)-3-(5-(4-chlorophenyl)-3-oxo-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl)bicyclo[1.1.1]pentane-1-carbonitrile,
(S)-3-(5-(2,4-difluorophenyl)-3-oxo-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl)bicyclo[1.1.1]pentane-1-carbonitrile,
(S)-5-(2,4-difluorophenyl)-2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
(S)-3-(3-oxo-5-(3-(trifluoromethyl)phenyl)-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl)bicyclo[1.1.1]pentane-1-carbonitrile,
(S)-3-(3-oxo-5-(4-(trifluoromethyl)phenyl)-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl)bicyclo[1.1.1]pentane-1-carbonitrile,
(S)-3-(5-(3,5-difluoro-4-methylphenyl)-3-oxo-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl)bicyclo[1.1.1]pentane-1-carbonitrile,
3-[5-(S or R)-(3,5-difluorophenyl)-6-(S or R)-methyl-3-oxo-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl]bicyclo[1.1.1]pentane-1-carbonitrile,
(S)-3-(5-(3,5-difluorophenyl)-3-oxo-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-2(3H)-yl)bicyclo[1.1.1]pentane-1-carbonitrile,
3-(5-(S or R)-cyclopentyl-3-oxo-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl)bicyclo[1.1.1]pentane-1-carbonitrile,
3-(5-(S or R)-cyclohexyl-3-oxo-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl)bicyclo[1.1.1]pentane-1-carbonitrile,
(5S)-5-(3,5-difluorophenyl)-2-[3-(methoxymethyl)bicyclo[1.1.1]pentan-1-yl]-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
3-[(5S)-5-(3,5-difluorophenyl)-3-oxo-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl]-N-[(thiophen-2-yl)methyl]bicyclo[1.1.1]pentane-1-carboxamide,

3-[(5S)-5-(3,5-difluorophenyl)-3-oxo-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl]-N-[(thiophen-3-yl)methyl]bicyclo[1.1.1]pentane-1-carboxamide,

(S)-2-(3-(5-(3,5-difluorophenyl)-3-oxo-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl)bicyclo[1.1.1]pentan-1-yl)acetonitrile,

(5S)-2-(3-acetylbicyclo[1.1.1]pentan-1-yl)-5-(3,5-difluorophenyl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,

3-[(5S)-5-(3,5-difluorophenyl)-3-oxo-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl]-2,2-difluorobicyclo[1.1.1]pentane-1-carbonitrile,

2,2-difluoro-3-[(5S)-3-oxo-5-phenyl-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl]bicyclo[1.1.1]pentane-1-carbonitrile,

(±)-3-(3-oxo-5-(pyrazin-2-yl)-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl)bicyclo[1.1.1]pentane-1-carbonitrile,

(±)-2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-5-(3-fluoro-5-methoxyphenyl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,

(±)-3-[2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-3-oxo-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-5-yl]benzonitrile,

(±)-5-(3-ethynylphenyl)-2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,

(±)-5-(2,3-difluorophenyl)-2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,

(±)-2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-5-(3-fluoro-5-methylphenyl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,

(S)-3-(3-oxo-5-(p-tolyl)-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl)bicyclo[1.1.1]pentane-1-carbonitrile,

(S)-3-(3-oxo-5-(pyrazin-2-yl)-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl)bicyclo[1.1.1]pentane-1-carbonitrile,

(S)-5-(3-fluoro-5-methylphenyl)-2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,

(S)-5-(4-(difluoromethyl)phenyl)-2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,

(S)-5-(4-cyclopropylphenyl)-2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,

(S)-2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-5-(pyrazin-2-yl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
(S)-2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-5-(6-methylpyrazin-2-yl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
(S)-2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-5-(5-methylpyrazin-2-yl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
(5S,7R)-5-(3,5-difluorophenyl)-2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-7-hydroxy-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
(5S,7S)-5-(3,5-difluorophenyl)-2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-7-hydroxy-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
(5S)-5-(3,5-difluorophenyl)-7-(S or R)-fluoro-2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
(5S)-5-(3,5-difluorophenyl)-7-(S or R)-fluoro-2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
(5S)-7-(S or R)-fluoro-2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-5-phenyl-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
(5S)-7-(S or R)-fluoro-2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-5-phenyl-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
3-[(5S)-5-(3,5-difluorophenyl)-7-(S or R)-fluoro-3-oxo-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl]bicyclo[1.1.1]pentane-1-carbonitrile,
3-[(5S)-5-(3,5-difluorophenyl)-7-(S or R)-fluoro-3-oxo-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl]bicyclo[1.1.1]pentane-1-carbonitrile,
3-[(5S)-7-(S or R)-fluoro-3-oxo-5-phenyl-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl]bicyclo[1.1.1]pentane-1-carbonitrile,
3-[(5S)-7-(S or R)-fluoro-3-oxo-5-phenyl-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl]bicyclo[1.1.1]pentane-1-carbonitrile,
3-[(5S)-7-(S or R)-fluoro-5-(2-fluorophenyl)-3-oxo-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl]bicyclo[1.1.1]pentane-1-carbonitrile,
3-[(5S)-7-(S or R)-fluoro-5-(2-fluorophenyl)-3-oxo-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl]bicyclo[1.1.1]pentane-1-carbonitrile,
(S)-5-(3,5-difluoro-4-methylphenyl)-2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,

(S)-2-(3-(difluoromethyl)bicyclo[1.1.1]pentan-1-yl)-5-(5-fluoropyridin-3-yl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
(S)-5-(3,5-difluorophenyl)-2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-3(2H)-one,
(S)-2-(3-chlorobicyclo[1.1.1]pentan-1-yl)-5-(pyrazin-2-yl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
(S)-4-(3-oxo-5-(pyrazin-2-yl)-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl)bicyclo[2.1.1]hexane-1-carbonitrile,
(S)-2-(bicyclo[2.1.1]hexan-1-yl)-5-(pyrazin-2-yl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
(S)-3-(5-(3-chlorophenyl)-3-oxo-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl)bicyclo[1.1.1]pentane-1-carbonitrile,
(S)-5-(3-chlorophenyl)-2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
(S)-3-(5-(3,5-difluorophenyl)-3-oxo-5,6-dihydrothiazolo[2,3-c][1,2,4]triazol-2(3H)-yl)bicyclo[1.1.1]pentane-1-carbonitrile,
(R)-3-(5-(3,5-difluorophenyl)-3-oxo-5,6-dihydrothiazolo[2,3-c][1,2,4]triazol-2(3H)-yl)bicyclo[1.1.1]pentane-1-carbonitrile,
(S)-2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-5-(4-methoxyphenyl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
(S)-4-(2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-3-oxo-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-5-yl)benzonitrile,
(S)-2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-5-(6-methylpyrazin-2-yl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
3-((5S,7R)-5-(3,5-difluorophenyl)-7-methyl-3-oxo-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl)bicyclo[1.1.1]pentane-1-carbonitrile,
3-((5S,7S)-5-(3,5-difluorophenyl)-7-methyl-3-oxo-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl)bicyclo[1.1.1]pentane-1-carbonitrile,
(S)-2-(3-chlorobicyclo[1.1.1]pentan-1-yl)-5-(5-fluoropyridin-2-yl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
(S)-5-(3-chloro-5-fluoro-4-methylphenyl)-2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,

(S)-5-(3,5-difluoro-4-hydroxyphenyl)-2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
(S)-5-(2,6-difluoro-4-methylphenyl)-2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
(S)-5-(4-chloro-3-fluorophenyl)-2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
(S)-2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-5-(3,4,5-trifluorophenyl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
(S)-5-(4-chloro-3,5-difluorophenyl)-2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
(R)-2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-5-phenyl-2,5,6,8-tetrahydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-3-one,
(R)-3-(5-(3,5-difluorophenyl)-3-oxo-5,6-dihydro-3H-[1,2,4]triazolo[3,4-c][1,4]oxazin-2(8H)-yl)bicyclo[1.1.1]pentane-1-carbonitrile,
(S)-2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-5-phenyl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridin-3(2H)-one,
3-[(5S)-5-(3,5-difluorophenyl)-3-oxo-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl]-2,2-difluorobicyclo[1.1.1]pentane-1-carbonitrile,
methyl (S)-2,2-difluoro-3-(3-oxo-5-phenyl-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl)bicyclo[1.1.1]pentane-1-carboxylate,
2,2-difluoro-3-[(5S)-3-oxo-5-phenyl-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl]bicyclo[1.1.1]pentane-1-carbonitrile,
(S)-2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-5-(o-tolyl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
(S)-2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-5-(5-(trifluoromethyl)pyrazin-2-yl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one,
(5S,7S)-7-fluoro-2-(3-fluorobicyclo[1.1.1]pentan-1-yl)-5-(pyrazin-2-yl)-2,5,6,7-tetrahydro-3H-pyrrolo[2,1-c][1,2,4]triazol-3-one, and
(*S*)-3-(5-(4-(difluoromethyl)phenyl)-3-oxo-6,7-dihydro-3H-pyrrolo[2,1-c][1,2,4]triazol-2(5H)-yl)bicyclo[1.1.1]pentane-1-carbonitrile.

20. Use of a compound, or pharmaceutically acceptable salt thereof, of any one of claims 1-19 in the manufacture of a medicament for the treatment of RIPK1 dependent

inflammation and cell death that occurs in inherited and sporadic diseases including Alzheimer's disease, amyotrophic lateral sclerosis, multiple sclerosis, Parkinson's disease, chronic traumatic encephalopathy, rheumatoid arthritis, ulcerative colitis, inflammatory bowel disease, psoriasis as well as acute tissue injury caused by stroke, traumatic brain injury, encephalitis.

21. Use of a compound, or pharmaceutically acceptable salt thereof, of any one of claims 1-19 in the manufacture of a medicament for the treatment of amyotrophic lateral sclerosis.

22. A compound, or pharmaceutically acceptable salt thereof, of any one of claims 1-19 for use in therapy.

23. A pharmaceutical composition comprising a compound of any one of claims 1-19, or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

24. A pharmaceutical composition comprising a compound of any one of claims 1-19 and a pharmaceutically acceptable carrier.