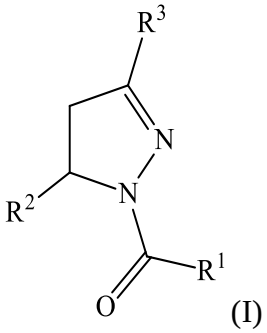
CLAIMS

1. A compound according to Formula (I):



(I)

wherein:

R^1 is (C_1-C_4)alkoxy-CH_2-, phenyl(C_1-C_4)alkoxy-CH_2-, or a substituted or unsubstituted (C_2-C_4)alkynyl, (C_3-C_6)cycloalkyl, (C_3-C_6)cyclo-alkyl-(C_1-C_4)alkyl-group, (C_1-C_4)alkyl or a substituted or unsubstituted 5-6 membered heterocycloalkyl group further optionally substituted by halogen,

wherein said substituted (C_3-C_6)cycloalkyl, (C_3-C_6)cycloalkyl-alkyl-, or 5-6 membered heterocycloalkyl group is substituted by 1, 2 or 3 substituents independently selected from hydroxyl, (benzyloxy)carbonyl)amino, cyano, halogen, (C_1-C_4)alkyl, halo(C_1-C_4)alkyl, (C_1-C_4)alkoxy, (C_1-C_4)alkyl-CO-, cyano(C_1-C_4)-alkyl-CO-, (C_1-C_4)alkoxy-(C_1-C_4)alkyl-CO-, (C_1-C_4)alkoxy-CO-, (C_1-C_4)alkyl-NHCO-, ((C_1-C_4)alkyl)((C_1-C_4)alkyl)NCO-, halo(C_1-C_4)alkyl-CO-, optionally substituted (C_3-C_6)cycloalkyl-CO-, optionally substituted (C_3-C_6)cycloalkyl-(C_1-C_4)-alkyl-CO-, optionally substituted phenyl-CO-, optionally substituted phenyl-SO_2-, optionally substituted phenyl(C_1-C_4)alkyl-CO-, optionally substituted 5-6 membered heteroaryl-CO-, and optionally substituted 9-10 membered heteroaryl-CO-,

wherein said optionally substituted (C_3-C_6)cycloalkyl-CO-, optionally substituted (C_3-C_6)cycloalkyl-(C_1-C_4)alkyl-CO-, optionally substituted phenyl-CO-, optionally substituted phenyl-SO_2-,optionally substituted phenyl(C_1-C_4)alkyl-CO-, optionally substituted 5-6 membered hetero-aryl-CO-, or optionally substituted 9-10 membered heteroaryl-CO- is optionally substituted by 1 or 2 substituents independently selected from halogen, cyano, (C_1-C_4)alkyl, (C_1-C_4)alkoxy, (C_1-C_4)alkyl-CO-, halo(C_1-C_4)alkyl, halo(C_1-C_4)alkyl-CO-, (C_3-C_6)cycloalkyl and 5-6 membered heterocycloalkyl; or

said substituted (C_2-C_4)alkynyl, (C_3-C_6)cycloalkyl or 5-6 membered heterocycloalkyl

group is substituted by an optionally substituted phenyl, 5-6 membered heteroaryl or 9-membered heteroaryl group,

wherein said phenyl, 5-6 membered heteroaryl or 9-membered heteroaryl group is optionally substituted by 1 or 2 substituents independently selected from halogen, (C_1-C_4)alkyl, (C_1-C_4)alkyl-CO-, halo(C_1-C_4)alkyl, and halo(C_1-C_4)alkyl-CO-;

R^2 is a substituted or unsubstituted phenyl, (C_3-C_6)cycloalkyl, 5-6 membered oxygen-containing heterocycloalkyl, 5-6 membered heteroaryl, 9-membered heteroaryl, 9-10 membered carbocyclic-aryl, or 9-10 membered heterocyclic-aryl group,

wherein said substituted phenyl, (C_3-C_6)cycloalkyl, 5-6 membered heterocycloalkyl, 5-6 membered heteroaryl, 9-membered heteroaryl, 9-10 membered carbocyclic-aryl, or 9-10 membered heterocyclic-aryl group is substituted by 1, 2 or 3 substituents independently selected from halogen, (C_1-C_4)alkyl, halo(C_1-C_4)alkyl, (C_1-C_4)alkoxy, halo(C_1-C_4)alkoxy, and cyano;

R^3 is H or halogen; or a salt thereof,

provided the compound is not cyclohexyl(5-phenyl-4,5-dihydro-1H-pyrazol-1-yl)methanone, and provided that the compound also includes:

1-(5-(5-fluoropyridin-3-yl)-4,5-dihydro-1H-pyrazol-1-yl)-2,3-dimethylbutan-1-one;

2,3-dimethyl-1-(5-phenyl-4,5-dihydro-1H-pyrazol-1-yl)butan-1-one;

2,2-dimethyl-3-oxo-3-(5-phenyl-4,5-dihydro-1H-pyrazol-1-yl)propanenitrile;

2-methoxy-2-methyl-1-(5-phenyl-4,5-dihydro-1H-pyrazol-1-yl)propan-1-one;

benzyl ((2*R*)-1-oxo-1-(5-phenyl-4,5-dihydro-1H-pyrazol-1-yl)propan-2-yl)carbamate; and

3-hydroxy-2,2-dimethyl-1-(5-phenyl-4,5-dihydro-1H-pyrazol-1-yl)propan-1-one 2,2,2-trifluoroacetate.

2. The compound, or salt thereof, according to claim 1, wherein:

R^1 is a substituted or unsubstituted (C_4-C_6)cycloalkyl, (C_4-C_6)cycloalkyl-alkyl-, or 5-6 membered heterocycloalkyl group,

wherein said substituted (C_4-C_6)cycloalkyl, (C_4-C_6)cycloalkyl-alkyl-, or 5-6 membered heterocycloalkyl group is substituted by 1, 2 or 3 substituents independently selected from hydroxyl, (benzyloxy)carbonyl)amino, halogen, (C_1-C_4)alkyl, halo(C_1-C_4)alkyl, (C_1-C_4)alkyl-CO-, halo(C_1-C_4)alkyl-CO-, and an optionally substituted 5-6 membered heteroaryl-CO-, wherein said optionally substituted 5-6 membered heteroaryl-CO- is optionally substituted by 1 or 2 substituents independently selected from (C_1-C_4)alkyl, (C_1-C_4)alkyl-CO-, halo(C_1-C_4)alkyl, and halo(C_1-C_4)alkyl-CO-, or

said substituted (C_4-C_6)cycloalkyl or 5-6 membered heterocycloalkyl group is substituted by an optionally substituted phenyl, 5-6 membered heteroaryl or 9-membered heteroaryl optional substituted by 1 or 2 substituents independently selected from halogen, (C_1-C_4)alkyl, (C_1-C_4)alkyl-CO-, halo(C_1-C_4)alkyl, and halo(C_1-C_4)alkyl-CO-;

R^2 is a substituted or unsubstituted phenyl, (C_3-C_6)cycloalkyl, 5-membered oxygen-containing heterocycloalkyl, 5-6 membered heteroaryl or 9-membered heteroaryl group,

wherein said substituted phenyl, (C_3-C_6)cycloalkyl, 5-membered heterocycloalkyl, 5-6 membered heteroaryl or 9-membered heteroaryl group is substituted by 1, 2 or 3 substituents independently selected from halo, (C_1-C_4)alkyl, halo(C_1-C_4)alkyl, (C_1-C_4)alkoxy, and cyano; and

R^3 is H.

3. The compound, or salt thereof, according to claim 1, wherein:

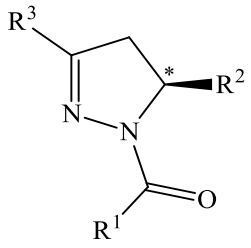
R^1 is a substituted or unsubstituted (C_4-C_6)cycloalkyl, (C_4-C_6)cycloalkyl-alkyl-, or 5-6 membered heterocycloalkyl group,

wherein said substituted (C_4-C_6)cycloalkyl, (C_4-C_6)cycloalkyl-alkyl-, or 5-6 membered heterocycloalkyl group is substituted by 1, 2 or 3 substituents independently selected from hydroxyl, (benzyloxy)carbonyl)amino, halogen, (C_1-C_4)alkyl, halo(C_1-C_4)alkyl, (C_1-C_4)alkyl-CO-, halo(C_1-C_4)alkyl-CO-, and an optionally substituted 5-6 membered heteroaryl-CO-, wherein said optionally substituted 5-6 membered heteroaryl-CO- is optionally substituted by 1 or 2 substituents independently selected from (C_1-C_4)alkyl, (C_1-C_4)alkyl-CO-, halo(C_1-C_4)alkyl, and halo(C_1-C_4)alkyl-CO-, or

said substituted (C_4-C_6)cycloalkyl or 5-6 membered heterocycloalkyl group is substituted by an optionally substituted phenyl, 5-6 membered heteroaryl or 9-membered heteroaryl optional substituted by 1 or 2 substituents independently selected from halogen, (C_1-C_4)alkyl, (C_1-C_4)alkyl-CO-, halo(C_1-C_4)alkyl, and halo(C_1-C_4)alkyl-CO-;

R^2 is a substituted or unsubstituted phenyl, 5-6 membered oxygen-containing heterocycloalkyl, wherein said substituted 5-6 membered heterocycloalkyl is substituted by 1, 2 or 3 substituents independently selected from halo, (C_1-C_4)alkyl, halo(C_1-C_4)alkyl, (C_1-C_4)alkoxy, and cyano; and R^3 is H.

4. The compound, or salt thereof, according to any one of claims 1-3, having Formula (II):



(II).

5. The compound, or salt thereof, according to any one of claims 1-4, wherein R^1 is a substituted or unsubstituted 5-6 membered heterocycloalkyl group.

6. The compound, or salt thereof, according to any one of claims 1-4, wherein R^1 is a substituted or unsubstituted 5-6 membered heterocycloalkyl group further optionally substituted by halogen or $(C_1$-$C_4)$alkyl.

7. The compound, or salt thereof, according to any one of claims 1-4, wherein R^1 is a substituted piperidinyl group, wherein the substituted piperidinyl group is substituted by a substituent selected from $(C_1$-$C_4)$alkyl-CO-, halo$(C_1$-$C_4)$alkyl-CO-, cyano$(C_1$-$C_4)$alkyl-CO-, $(C_1$-$C_4)$alkoxy-$(C_1$-$C_4)$alkyl-CO-, $(C_1$-$C_4)$alkylNHCO-, optionally substituted $(C_3$-$C_6)$cycloalkyl-CO-, optionally substituted $(C_3$-$C_6)$cycloalkyl-$(C_1$-$C_4)$alkyl-CO-, optionally substituted phenyl-CO-, optionally substituted phenyl-SO_2-,optionally substituted phenyl$(C_1$-$C_4)$-alkyl-CO-, optionally substituted 5-6 membered heteroaryl-CO-, and optionally substituted 9-10 membered heteroaryl-CO-, wherein said optionally substituted $(C_3$-$C_6)$cycloalkyl-CO-, optionally substituted $(C_3$-$C_6)$cycloalkyl-$(C_1$-$C_4)$alkyl-CO-, optionally substituted phenyl-CO-, optionally substituted phenyl-SO_2-,optionally substituted phenyl$(C_1$-$C_4)$alkyl-CO-, optionally substituted 5-6 membered heteroaryl-CO-, or optionally substituted 9-10 membered heteroaryl-CO-, is optionally substituted by 1 or 2 substituents independently selected from halogen, cyano, $(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkoxy, $(C_1$-$C_4)$alkyl-CO-, halo$(C_1$-$C_4)$-alkyl, halo$(C_1$-$C_4)$alkyl-CO-, $(C_3$-$C_6)$cycloalkyl and 5-6 membered heterocycloalkyl.

8. The compound, or salt thereof, according to any one of claims 1-4, wherein R^1 is a substituted piperidinyl group, further optionally substituted by halogen or $(C_1$-$C_4)$alkyl, wherein the substituted piperidinyl group is substituted by a substituent selected from $(C_1$-$C_4)$alkyl-CO-, halo$(C_1$-$C_4)$alkyl-CO-, cyano$(C_1$-$C_4)$alkyl-CO-, $(C_1$-$C_4)$alkoxy-$(C_1$-$C_4)$-alkyl-CO-, $(C_1$-$C_4)$alkylNHCO-, optionally substituted $(C_3$-$C_6)$cycloalkyl-CO-, optionally substituted $(C_3$-$C_6)$cycloalkyl-$(C_1$-$C_4)$alkyl-CO-, optionally substituted phenyl-CO-,

optionally substituted phenyl-SO_2-,optionally substituted phenyl(C_1-C_4)alkyl-CO-, optionally substituted 5-6 membered heteroaryl-CO-, and optionally substituted 9-10 membered heteroaryl-CO-, wherein said optionally substituted (C_3-C_6)cycloalkyl-CO-, optionally substituted (C_3-C_6)cycloalkyl-(C_1-C_4)alkyl-CO-, optionally substituted phenyl-CO-, optionally substituted phenyl-SO_2-,optionally substituted phenyl(C_1-C_4)alkyl-CO-, optionally substituted 5-6 membered heteroaryl-CO-, or optionally substituted 9-10 membered heteroaryl-CO- is optionally substituted by 1 or 2 substituents independently selected from halogen, cyano, (C_1-C_4)alkyl, (C_1-C_4)alkoxy, (C_1-C_4)alkyl-CO-, halo(C_1-C_4)alkyl, halo(C_1-C_4)alkyl-CO-, (C_3-C_6)cycloalkyl and 5-6 membered heterocycloalkyl.

9. The compound, or salt thereof, according to any one of claims 1-4, wherein R^1 is a substituted piperidin-4-yl group substituted by CH_3CO-, CF_3CO-, or 1-methyl-1H-pyrrol-2-yl-CO-.

10. The compound, or salt thereof, according to any one of claims 1-4, wherein R^1 is a substituted piperidinyl group, wherein the substituted piperidinyl group is optionally substituted by a halogen or (C_1-C_4)alkyl substituent and is further substituted by an optionally substituted phenyl, 5-6 membered heteroaryl or 9-membered heteroaryl, wherein the optionally substituted phenyl, 6-membered heteroaryl or 9-membered heteroaryl group is optionally substituted by 1 or 2 substituents independently selected from halogen, (C_1-C_4)-alkyl, (C_1-C_4)alkyl-CO-, halo(C_1-C_3)alkyl, and halo(C_1-C_3)alkyl-CO-.

11. The compound, or salt thereof, according to any one of claims 1-10, wherein R^2 is a substituted or unsubstituted phenyl, (C_3-C_6)cycloalkyl, 5-6 membered oxygen-containing heterocycloalkyl, 5-6 membered heteroaryl, 9-membered heteroaryl, 9-10 membered carbocyclic-aryl, or 9-10 membered heterocyclic-aryl group,

wherein said substituted phenyl, (C_3-C_6)cycloalkyl, 5-6 membered heterocycloalkyl, 5-6 membered heteroaryl, 9-membered heteroaryl, 9-10 membered carbocyclic-aryl, or 9-10 membered heterocyclic-aryl group is substituted by 1, 2 or 3 substituents independently selected from halogen, (C_1-C_4)alkyl, halo(C_1-C_4)alkyl, (C_1-C_4)alkoxy, halo(C_1-C_4)alkoxy, and cyano.

12. The compound, or salt thereof, according to any one of claims 1-10, wherein R^2 is unsubstituted phenyl.

13. The compound, or salt thereof, according to any one of claims 1-10, wherein R^2 is phenyl substituted by 1 or 2 substituents independently selected from halo, $(C_1$-$C_4)$alkyl, halo$(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkoxy, halo$(C_1$-$C_4)$alkoxy, and cyano.

14. The compound, or salt thereof, according to any one of claims 1-10, wherein R^2 is an optionally substituted 6-membered heteroaryl containing 1 or 2 nitrogen heteroatoms, wherein the heteroaryl is optionally substituted by 1 or 2 substituents independently selected from halo, $(C_1$-$C_4)$alkyl, halo$(C_1$-$C_4)$alkyl, and $(C_1$-$C_4)$alkoxy.

15. The compound, or salt thereof, according to any one of claims 1-14, wherein R^3 is H.

16. The compound, or salt thereof, according to any one of claims 1-15, wherein the salt is a pharmaceutically acceptable salt.

17. A compound which is (*S*)-1-(4-(5-(3,5-difluorophenyl)-4,5-dihydro-1H-pyrazole-1-carbonyl)piperidin-1-yl)ethanone, or a pharmaceutically acceptable salt thereof.

18. A compound which is (*S*)-1-(4-(5-(3,5-difluorophenyl)-4,5-dihydro-1H-pyrazole-1-carbonyl)piperidin-1-yl)ethanone.

19. The compound according to claim 18, providing a PXRD pattern substantially in accordance with Figure 5.

20. A pharmaceutical composition comprising the compound, or pharmaceutically acceptable salt thereof, according to any one of claims 1-19, and one or more pharmaceutically acceptable excipients.

21. A pharmaceutical composition according to claim 20, which further comprises at least one other therapeutically active agent.

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

23. The compound, or pharmaceutically acceptable salt thereof, according to any one of claims 1-19 for use in the treatment of a RIP1 kinase-mediated disease or disorder, wherein the disease or disorder is amyotrophic lateral sclerosis.

24. Use of the compound, or pharmaceutically acceptable salt thereof, according to any one of claims 1-19 in the manufacture of a medicament for the treatment of a RIP1 kinase-mediated disease or disorder, wherein the disease or disorder is amyotrophic lateral sclerosis.