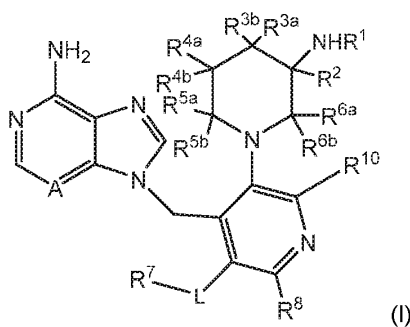


CLAIMS

1. A compound of Formula (I)



- 5 or an enantiomer, an enantiomeric mixture, or a pharmaceutically acceptable salt thereof;
wherein:
- A is N or CR⁹ wherein R⁹ is hydrogen or halo;
- L is a bond or C₁₋₄ alkylene;
- R¹ is H; or
- 10 R¹ and R² together with NH forms a 5-8 membered heterocyclyl containing 1-2 heteroatoms selected from N, O and S as ring members; wherein said 5-8 membered heterocyclyl is unsubstituted or substituted by an oxo substituent;
- R² is selected from the group consisting of:
- (i) hydrogen, -C₁₋₆ alkyl, -haloC₁₋₆ alkyl, -hydroxyC₁₋₆ alkylene, -hydroxyhaloC₁₋₆ alkylene, -C₁₋₆alkoxyC₁₋₆alkylene, -haloC₁₋₆alkoxyC₁₋₆alkylene or -C₃₋₈ cycloalkoxy(C₁₋₆ alkyl);
- 15 (ii) cyano; -cyanoC₁₋₆ alkylene; -C₁₋₆ alkylthioC₁₋₆alkyl; -C₂₋₆ alkenyl; -haloC₂₋₆ alkenyl; -C₂₋₆ alkynyl; -C₁₋₄ alkylSOC₁₋₄alkyl; -C₁₋₄ alkylSO₂C₁₋₄alkyl; -SO₂R⁸ or -C(C₁₋₄ alkyl)=N-O(C₁₋₄ alkyl);
- (iii) -C₁₋₄alkylcarbonyl; -(CR^aR^b)_p-C(=O)-OR¹⁰; or -C(=O)-(CR^aR^b)_qR¹¹-; wherein R¹¹ is C₃₋₇ cycloalkyl, 5-6 membered heterocyclyl or 5-6 membered heteroaryl, each of which is
- 20 independently unsubstituted or substituted with C₁₋₆ alkyl or C₁₋₆ alkoxy;
- (iv) -(CR^aR^b)_r-C(=O)-NR¹²R¹³ wherein R¹² is hydrogen or C₁₋₆ alkyl; R¹³ is hydrogen, -C₁₋₆ alkyl or a 5-6 membered heterocyclic ring; or R¹² and R¹³ together form a 5-6 membered heterocyclic ring; wherein said 5-6 membered heterocyclic ring is unsubstituted or substituted with C₁₋₄ alkyl;
- 25 (v) 5-6 membered heterocyclylC₀₋₆alkyl or 5-6 membered heterocyclyl(haloC₁₋₄ alkyl) wherein each said heterocyclyl radical is unsubstituted or substituted by oxo; and
- (vi) 5-9 membered heteroarylC₀₋₆alkyl or 5-9 membered heteroaryl(haloC₁₋₄alkyl), wherein each said heteroaryl radical is unsubstituted or substituted by -C₁₋₄ alkyl, -haloC₁₋₄ alkyl,

-hydroxyC₁₋₄ alkylene, -C₁₋₄ alkoxy, -haloC₁₋₄ alkoxy, halo, hydroxy, cyano, oxido, -aminocarbonylC₀₋₆alkyl, -C₁₋₄alkylaminocarbonylC₀₋₆alkyl, -diC₁₋₄alkylaminocarbonylC₀₋₆alkyl or -C₃₋₇ cycloalkyl;

5 R^{3a}, R^{3b}, R^{4a}, R^{4b}, R^{5a}, R^{5b}, R^{6a} and R^{6b} are independently hydrogen, halo, cyano, hydroxyl, -C₁₋₆ alkyl, -haloC₁₋₆ alkyl, -hydroxyC₁₋₆ alkylene, -C₁₋₆ alkoxy, -C₁₋₆alkoxyC₁₋₆alkylene, -haloC₁₋₆ alkoxyC₁₋₆ alkylene, -hydroxyhaloC₁₋₆ alkylene, aryl, -C(=O)-OR¹⁴ or -(CR^aR^b)_s-C(=O)-NR¹⁵R¹⁶;

or

R^{3a} and R^{3b}, R^{4a} and R^{4b}, R^{5a} and R^{5b} or R^{6a} and R^{6b} forms an oxo substituent;

R⁷ is H, -C₁₋₄ alkoxy, halo or C₁₋₄ alkyl; or 3-8 membered heterocyclyl, which is unsubstituted

10 or substituted by halo;

R⁸ is C₃₋₈ cycloalkyl(C₀₋₆ alkyl); 4-6 membered heterocyclylC₀₋₆alkyl comprising 1-3 heteroatoms selected from N, O and S; aryl or 5-9 membered heteroarylC₀₋₆alkyl comprising 1-3 heteroatoms selected from N, O and S; wherein R⁸ is unsubstituted or substituted by 1-3 R¹⁷;

15 R¹⁷ is halo, hydroxy, cyano, -C₁₋₆ alkyl, -haloC₁₋₆ alkyl, -C₁₋₆ alkoxy, -haloC₁₋₆ alkoxy, -NR^aC(=O)CR^c=C(R^c)₂ or -(CR^aR^b)_t-NR^a-C(=O)-R¹⁸;

R^a, R^b, R^c, R¹⁰, R¹⁴, R¹⁵ and R¹⁶ are independently hydrogen or -C₁₋₄ alkyl;

R¹⁸ is -C₁₋₄ alkyl or -C₁₋₄ haloalkyl; and

p, q, r, s and t are independently 0-4.

2. The compound of Formula (I) in claim 1 or an enantiomer, an enantiomeric mixture, or a
20 pharmaceutically acceptable salt thereof; wherein A is N.

3. The compound of Formula (I) in claim 1 or 2, or an enantiomer, an enantiomeric mixture, or a pharmaceutically acceptable salt; wherein

R^{3a} is hydrogen or halo; and R^{3b} is hydrogen, halo, -hydroxyl, -C₁₋₆ alkoxy or cyano; or

25 R^{4a} is hydrogen or halo; and R^{4b} is hydrogen, halo, -C₁₋₆alkoxyC₁₋₆alkylene, -C₁₋₆ alkyl or -haloC₁₋₆ alkyl; or

R^{5a} is hydrogen and R^{5b} is hydrogen or -C₁₋₆ alkyl; or

R^{5a} and R^{5b} together form an oxo substituent.

4. The compound of Formula (I) in any one of claims 1-3 or an enantiomer, an enantiomeric mixture, or a pharmaceutically acceptable salt; wherein:

30 R^{6a} is hydrogen or halo;

R^{6b} is hydrogen, -haloC₁₋₆ alkoxyC₁₋₆ alkylene, -hydroxyC₁₋₆ alkylene, -hydroxyhaloC₁₋₆ alkylene, carboxyl, phenyl or -(CR^aR^b)_t-C(O)-NR¹⁵R¹⁶;

R^a, R^b, R¹⁵ and R¹⁶ are independently hydrogen or -C₁₋₄ alkyl; and

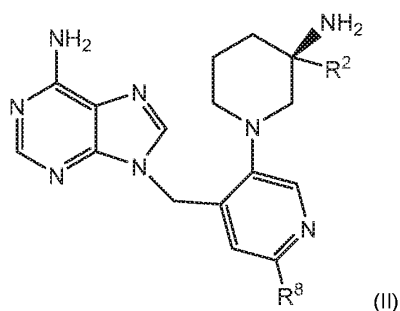
t is 0-1; or

35 R^{6a} and R^{6b} together form an oxo substituent.

5. The compound of Formula (I) in any one of claims 1-4 or an enantiomer, an enantiomeric mixture, or a pharmaceutically acceptable salt thereof; wherein R^7 is H, $-C_{1-4}$ alkoxy or halo.

6. The compound of Formula (I) in any one of claims 1-5 or a pharmaceutically acceptable salt thereof; wherein R^1 , R^{3a} , R^{3b} , R^{4a} , R^{4b} , R^{5a} , R^{5b} , R^{6a} , R^{6b} and R^7 are hydrogen.

7. The compound of Formula (I) in claim 1, wherein said compound is a compound of Formula (II):

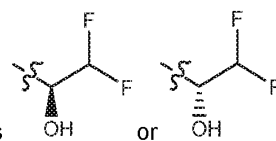


or an enantiomer, an enantiomeric mixture, or a pharmaceutically acceptable salt thereof.

8. The compound according to any one of claims 1-7 or an enantiomer, an enantiomeric mixture, or a pharmaceutically acceptable salt thereof; wherein R^2 is hydrogen, $-C_{1-6}$ alkyl, $-haloC_{1-6}$ alkyl, $-hydroxyC_{1-6}$ alkylene, $-hydroxyhaloC_{1-6}$ alkylene, $-C_{1-6}alkoxyC_{1-6}alkylene$, $-haloC_{1-6}alkoxyC_{1-6}alkylene$ or $-C_{3-8}$ cycloalkoxy(C_{1-6} alkyl).

9. The compound according to any one of claims 1-7 or an enantiomer, an enantiomeric mixture, or a pharmaceutically acceptable salt thereof; wherein R^2 is hydrogen; 2,2-difluoroethyl; 2-methyl-propan-1-yl; ethan-1-yl; 2,2-difluoroethan-1-yl; 2-fluoroethan-1-yl; 2,2,2-trifluoroethan-1-yl; difluoromethoxyl; or 2,2,2-trifluoroethoxyl.

10. The compound according to any one of claims 1-7 or an enantiomer, an enantiomeric



mixture, or a pharmaceutically acceptable salt thereof; wherein R^2 is

11. The compound according to any one of claims 1-7 or an enantiomer, an enantiomeric mixture, or a pharmaceutically acceptable salt thereof; wherein R^2 is $-C_{1-4}alkylcarbonyl$; $-(CR^aR^b)_p-C(O)-OR^{10}$ wherein R^{10} is hydrogen or $-C_{1-4}$ alkyl; $-C(O)-(CR^aR^b)_q-R^{11}$ wherein R^{11} is C_{3-6} cycloalkyl, 5-6 membered heterocyclyl or 5-6 membered heteroaryl, each of which is independently unsubstituted or substituted with

-C₁₋₆ alkyl or -C₁₋₆ alkoxy; or

-(CR^aR^b)_r-C(O)-NR¹²R¹³; wherein

R¹² is hydrogen or -C₁₋₆ alkyl;

R¹³ is hydrogen, -C₁₋₆ alkyl or a 5-6 membered heterocyclic ring; or

5 R¹² and R¹³ together form a 5-6 membered heterocyclic ring; wherein said 5-6 membered heterocyclic ring is unsubstituted or substituted with -C₁₋₄ alkyl; and

R^a, R^b and R¹¹ are independently hydrogen or -C₁₋₄ alkyl; and

p, q and r are independently 0-2.

12. The compound according to any one of claims 1-7 or an enantiomer, an enantiomeric
 10 mixture, or a pharmaceutically acceptable salt thereof; wherein R² is selected from the group:
 pyridin-2-yl, (pyridin-2-yl)methyl or (pyridin-2-yl)ethyl, wherein said pyridin-2-yl is
 independently unsubstituted or substituted with 1-2 -C₁₋₄ alkyl, -C₁₋₄ haloalkyl, hydroxyl,
 -hydroxyC₁₋₄ alkylene, cyano, -C₁₋₄ alkoxy, -C₁₋₆alkoxyC₁₋₆alkylene, -haloC₁₋₄ alkoxy, halo or -C₃₋₇
 cycloalkyl;
 15 thiazol-4-yl, thiazol-2-ylmethyl, oxazol-2-yl, oxazol-2-ylmethyl, pyridazin-3-yl, pyridazin-3-
 ylmethyl, pyrazin-2-yl, pyrazin-2-ylmethyl, pyrimidin-4-yl, pyrimidin-4-ylmethyl, each of which is
 independently unsubstituted or substituted with -C₁₋₄ alkyl or halo;
 1H-pyrazol-3-yl, (1H-pyrazol-3-yl)methyl, 1-methyl-1H-pyrazol-4-yl, (1,2,3-triazol-4-yl),
 isoxazol-3-yl, each of which is independently unsubstituted or substituted with -C₁₋₄ alkyl, halo or
 20 -C₃₋₇ cycloalkyl;
 1,4-dioxan-2-yl;
 pyridin-2(1H)-onyl; and
 pyridin-1-oxide-2-yl.

13. The compound according to any one of claims 1-12 or an enantiomer, an enantiomeric
 25 mixture, or a pharmaceutically acceptable salt thereof; wherein R⁸ is cyclopropyl; cyclobutyl;
 cyclohexyl or azetidyl.

14. The compound according to any one of claims 1-12 or an enantiomer, an enantiomeric
 mixture, or a pharmaceutically acceptable salt thereof; wherein R⁸ is 2,3-dihydrobenzofuran-5-
 yl; 1,3-dihydroisobenzofuran-5-yl; benzo[d][1,3]dioxol-5-yl; imidazo[1,2-a]pyridin-6-yl or
 30 pyrazolo[1,5-a]pyridine-6-yl.

15. The compound according to any one of claims 1-12 or an enantiomer, an enantiomeric
 mixture, or a pharmaceutically acceptable salt thereof; wherein R⁸ is pyridyl, unsubstituted or
 substituted with 1-2 halo, -C₁₋₆ alkyl or -C₁₋₆ alkoxy; 1H-indazol-5-yl unsubstituted or substituted
 with 1-2 halo or -C₁₋₆ alkyl; or 1H-benzo[d]-imidazol-6-yl unsubstituted or substituted with -C₁₋₆
 35 alkyl.

16. The compound according to any one of claims 1-12 or an enantiomer, an enantiomeric mixture, or a pharmaceutically acceptable salt thereof; wherein R⁸ is phenyl substituted with 1-3 R¹⁷;

- 5 R¹⁷ is halo, hydroxy, cyano, -C₁₋₆ alkyl, -haloC₁₋₆ alkyl, -C₁₋₆ alkoxy, -haloC₁₋₆ alkoxy, -NR^dC(O)CR^d=C(R^d)₂ or -(CR^aR^b)_t-NR^d-C(O)-R¹⁸;
 R^a, R^b and R^d are independently hydrogen or -C₁₋₄ alkyl;
 R¹⁸ is C₁₋₄ haloalkyl; and
 t is 0-1.

17. The compound according to any one of claims 1-12 or an enantiomer, an enantiomeric mixture, or a pharmaceutically acceptable salt thereof; wherein R⁸ is phenyl substituted with 1-3 R¹⁷; and R¹⁷ is halo, hydroxy, -C₁₋₆ alkyl, -haloC₁₋₆ alkyl, -C₁₋₆ alkoxy or -haloC₁₋₆ alkoxy.

18. The compound according to claim 1 or an enantiomer, an enantiomeric mixture, or a pharmaceutically acceptable salt thereof; wherein said compound is selected from a compound in Table 2, or a pharmaceutically acceptable salt thereof.

15 19. A pharmaceutical composition comprising a compound according to any one of claims 1-18 or a pharmaceutically acceptable salt thereof, and one or more pharmaceutically acceptable carrier.

20. A combination comprising a compound according to any one of claims 1-18 or a pharmaceutically acceptable salt thereof, and one or more therapeutically active agent.

20 21. The combination according to claim 20, wherein said one or more therapeutically active agent is an anti-cancer agent, an analgesic or an anti-inflammatory agent.

22. A method for treating a disease or condition mediated by nuclear SET domain-containing protein 2 (NSD2), comprising administering to a subject in need of such treatment a therapeutically effective amount of a compound according to any of claims 1-18 or a
 25 pharmaceutically acceptable salt thereof.

23. The method of claim 22, wherein said disease or condition mediated by NSD2 is selected from solid tumors, leukemia, myeloma, lymphoma and hypertension.

24. The method of claim 23, wherein said disease or condition mediated by NSD2 is breast cancer, cervical cancer, skin cancer, ovarian cancer, gastric cancer, prostate cancer, pancreatic
 30 cancer, lung cancer, hepatocellular carcinoma, head and neck cancer, peripheral nerve sheath tumor, osteosarcoma, multiple myeloma, neuroblastoma, leukemia, non-Hodgkin's lymphoma or pulmonary arterial hypertension.

25. The method of claim 22, wherein said disease or condition mediated by NSD2 is acute lymphoblastic leukaemia, skin squamous cell carcinoma or mantle cell lymphoma.

26. Use of a compound according to any one of claims 1-18 and optionally in combination with a second therapeutic agent, in the manufacture of a medicament for a disease or condition mediated by nuclear SET domain-containing protein 2 (NSD2).