CANTOS Trial Group. N Engl J Med, 2017 Sep 21;377(12):1119-1131; and Toldo S and Abbate A Nat Rev Cardiol, 2018 Apr;l5(4):203-214). NLRP3 associated skin diseases include wound healing and scar formation; inflammatory skin diseases such as acne, atopic dermatitis, hidradenitis suppurativa and psoriasis (Kelly et al., Br J Dermatol, 2015 Dec;l 73(6)). NLRP3 inflammasome activity has also been linked to respiratory conditions such as asthma, sarcoidosis, acute respiratory distress syndrome, Severe Acute Respiratory Syndrome (SARS) (Nieto-Torres et al., Virology, 2015 Nov;485:330-9)); and ocular diseases including age-related macular degeneration (AMD) and diabetic retinopathy (Doyle et al., Nat Med, 2012 May;18(5):791-8). Cancers linked to NLRP3 include myeloproliferative neoplasms, leukemias, myelodysplastic syndromes, myelofibrosis, lung cancer and colon cancer (Ridker et al., Lancet, 2017 Oct 21;390(10105): 1833-1842; Derangere et al., Cell Death Differ. 2014 Dec;21(12): 1914-24; Basiorka et al., Lancet Haematol, 2018 Sep;5(9): e393-e402, Zhang et al., Hum Immunol, 2018 Jan;79(1):57-62).

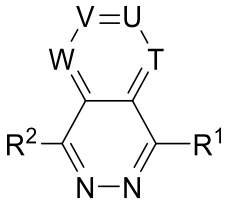
Immune diseases and inflammatory disorders are typically difficult to diagnose or treat efficiently and effectively. Most treatments include treatment of the symptoms, slowing down disease progression, lifestyle changes and surgery.

There remains a need for inhibitors of NLRP3 to provide new treatments for diseases and disorders associated with NLRP3 inflammasome activation and dysregulation. The compounds of the present invention are useful for the treatment and prevention of diseases, disorders and conditions mediated by formation and propogation of the NLRP3 inflammasome.

NLRP3 inhibitors are disclosed in the following publications: *Nat*. 2022, 1; *Cell*. 2021, *184*, 1; *J. Mol. Biol.* 2021, *433*, 167308; *J. Med. Chem*. 2021, *64*, 101; *Nat. Chem. Biol*. 2019, *15*, 556; *Nat*. 2019, *570*, 338; *Nat. Chem. Biol*. 2019, *15*, 560; *PLOS Biol*. 2019, 1; *Nat. Med.* 2015, *21*, 248; *Cell*. 2014, *156*, 1193; *Nat. Immunol*. 2014, *15*, 738; *PNAS*. 2007, *104*, 8041; *Nat*. 2006, *440*, 9; *Immunity*. 2006, *24*, 317. Several patent applications describe NLRP3 inhibitors, including WO 2021/239885, WO 2021/209552, WO 2021/209539, WO 2021/193897, WO 2020/018975, WO 2020/037116, WO 2020/021447, WO 2020/010143, WO 2019/079119, WO 2019/0166621, WO 2019/121691, US 11,319,319, and US 2020/0361898.

SUMMARY

The present disclosure relates to novel compounds of structural formula I:



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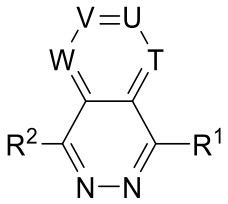
and pharmaceutically acceptable salts thereof.

In one aspect, there is provided a compound of structural Formula I:



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or a pharmaceutically acceptable salt thereof, wherein

T is independently selected from the group: CR^3 and N, provided that one or two of T, U, V and W are N;

U is independently selected from the group:

1) CR^4, and

2) N;

V is independently selected from the group:

1) CR^5, and

2) N;

W is independently selected from the group:

1) CR^6, and

2) N;

R^1 is selected from the group:

1) morpholine,

2) thiomorpholine,

3) piperidine,

4) pyrrolidine,

5) tetrahydropyran,

6) octahydro-1H-pyrrolo[2,3-c]pyridine,

7) 3-azabicyclo[3.1.0]hexane,

8) 5-azaspiro[2.4]heptane,

9) 1-oxa-7-azaspiro[4.4]nonane,

10) 1-oxa-8-azaspiro[4.5]decane,

11) 3-oxa-1,8-diazaspiro[4.5]decane,

12) 2,8-diazaspiro[4.5]decane,

13) 1-oxa-3,8-diazaspiro[4.5]decane,

14) 2-oxa-8-azaspiro[4.5]decane,

15) 1,8-diazaspiro[4.5]decane, and

16) 1-oxa-4,9-diazaspiro[5.5]undecane,

wherein R^1 is unsubstituted or substituted with one to six substituents selected from R^a;

R^2 is selected from the group:

1) aryl, and

2) heteroaryl,

wherein R^2 is unsubstituted or substituted with one to five substituents selected from R^b;

R^3 is selected from the group:

1) hydrogen,

2) OH,

3) CN,

4) CF_3,

5) CF_2H,

6) -C_{1-6}alkyl,

7) -O-C_{1-6}alkyl,

8) halogen, and

9) -C_{1-6}alkyl-O-C_{1-6}alkyl,

wherein R^3 is unsubstituted or substituted with one to five substituents selected from R^d;

R^4 is selected from the group:

1) hydrogen,

2) OH,

3) CN,

4) CF_3,

5) CF_2H,

6) -C_{1-6}alkyl,

7) -O-C_{1-6}alkyl,

8) halogen,

9) -C_{3-6}cycloalkyl,

10) -C_{2-6}cycloheteroalkyl, and

11) -C_{1-6}alkyl-O-C_{1-6}alkyl,

wherein R^4 is unsubstituted or substituted with one to five substituents selected from R^e;

R^5 is selected from the group:

1) hydrogen,

2) OH,

3) CN,

4) CF_3,

5) CF_2H,

6) -C_{1-6}alkyl,

7) -O-C_{1-6}alkyl,

8) halogen,

9) -C_{3-6}cycloalkyl,

10) -C_{2-6}cycloheteroalkyl, and

11) -C_{1-6}alkyl-O-C_{1-6}alkyl,

wherein R^5 is unsubstituted or substituted with one to five substituents selected from R^f;

R^6 is selected from the group:

1) hydrogen,

2) OH,

3) CN,

4) CF_3,

5) CF_2H,

6) -C_{1-6}alkyl,

7) -O-C_{1-6}alkyl,

8) halogen,

9) -C_{3-6}cycloalkyl,

10) -C_{2-6}cycloheteroalkyl, and

11) -C_{1-6}alkyl-O-C_{1-6}alkyl,

wherein R^6 is unsubstituted or substituted with one to five substituents selected from Rg;

each R^a is independently selected from the group:

1) CN,
2) oxo,
3) -OH,
4) halogen,
5) -C_{1-6}alkyl,
6) -O-C_{1-6}alkyl,
7) -C_{2-6}alkenyl,
8) -C_{2-6}alkynyl,
9) -C_{3-6}cycloalkyl,
10) -C_{2-6}cycloheteroalkyl,
11) aryl,
12) heteroaryl, and
13) -C(O)C_{1-6}alkyl,

wherein each R^a is unsubstituted or substituted with one to six substituents selected from halogen, CF_3, OH, C_{1-6}alkyl, and -OC_{1-6}alkyl;

each R^b is independently selected from the group:

1) CN,
2) -OH,
3) -CH_3,
4) -CF_3,
5) -CF_2H,
6) -OCF_2H, and
7) cyclopropane,

wherein each R^b is unsubstituted or substituted with one to six substituents selected from halogen, CF_3, CF_2H, OCF_3, CN, CH_2CF_3, CF_2CH_3, -C_{1-6}alkyl, and -OC_{1-6}alkyl;

each R^d is independently selected from the group:

1) CF_3,
2) halogen, and
3) -C_{1-6}alkyl,

wherein alkyl is unsubstituted or substituted with one to three substituents selected from: CF_3, halogen, OH and -OC_{1-6}alkyl;

each R^e is independently selected from the group:

1) CF_3,
2) halogen, and
3) -C_{1-6}alkyl,

wherein alkyl is unsubstituted or substituted with one to three substituents selected from: CF_3, halogen, OH and -OC_{1-6}alkyl;

each R^f is independently selected from the group:

1) CF_3,
2) halogen, and
3) -C_{1-6}alkyl,

wherein alkyl is unsubstituted or substituted with one to three substituents selected from: CF_3, halogen, OH and -OC_{1-6}alkyl; and

each R^g is independently selected from the group:

1) CF_3,
2) halogen, and
3) -C_{1-6}alkyl,

wherein alkyl is unsubstituted or substituted with one to three substituents selected from: CF_3, halogen, OH and -OC_{1-6}alkyl.

In another aspect, there is provided a compound selected from:

1) (*S*)-1-(4-(2-hydroxy-4-(trifluoromethyl)phenyl)pyrido[3,4-*d*]pyridazin-1-yl)-3-methylpyrrolidin-3-ol;
2) (*S*)-1-(1-(2-hydroxy-4-(trifluoromethyl)phenyl)pyrido[3,4-*d*]-pyridazin-4-yl)-3-methylpyrrolidin-3-ol;
3) (*cis*)-4-(5-(2-(difluoromethoxy)-4-(trifluoromethyl)phenyl)pyrido[2,3-*d*]pyridazin-8-yl)-2,6-dimethylmorpholine;
4) 2-(4-((*cis*)-2,6-dimethylmorpholino)pyrido[3,4-*d*]pyridazin-1-yl)-5-(trifluoromethyl)phenol;
5) 2-(1-((*cis*)-2,6-dimethylmorpholino)pyrido[3,4-*d*]pyridazin-4-yl)-5-(trifluoromethyl)phenol;
6) 2-(5-((*cis*)-2,6-dimethylmorpholino)pyrido[2,3-*d*]pyridazin-8-yl)-5-(trifluoromethyl)phenol;
7) (*cis*)-4-(1-(2-(difluoromethoxy)-4-(trifluoromethyl)phenyl)pyrido[3,4-*d*]pyridazin-4-yl)-2,6-dimethylmorpholine;

8) 2-(8-((*cis*)-2,6-dimethylmorpholino)pyridazino[4,5-*c*]pyridazin-5-yl)-5-(trifluoromethyl)-phenol;

9) 2-(4-((*cis*)-2,6-dimethylmorpholino)pyridazino[4,5-*d*]pyridazin-1-yl)-5-(trifluoromethyl)-phenol;

10) (*S*)-1-(5-(2-hydroxy-4-(trifluoromethyl)phenyl)-2-methylpyrido[2,3-*d*]pyridazin-8-yl)-3-methylpyrrolidin-3-ol;

11) (*cis*)-4-(1-(benzofuran-5-yl)pyrido[3,4-*d*]pyridazin-4-yl)-2,6-dimethylmorpholine;

12) (*S*)-1-(5-(2-hydroxy-4-(trifluoromethyl)phenyl)-2-(trifluoromethyl)pyrido[2,3-*d*]pyridazin-8-yl)-3-methylpyrrolidin-3-ol;

13) (3*S*,4*s*,5*R*)-1-(4-(2-hydroxy-4-(trifluoromethyl)phenyl)pyridazino[4,5-*d*]pyridazin-1-yl)-3,4,5-trimethylpiperidin-4-ol;

14) 2-(4-((*cis*)-2,6-dimethylmorpholino)-5-methylphthalazin-1-yl)-5-(trifluoromethyl)phenol;

15) 2-(4-((*cis*)-2,6-dimethylmorpholino)-8-methylphthalazin-1-yl)-5-(trifluoromethyl)phenol;

16) (3*S*,4*s*,5*R*)-1-(1-(2-hydroxy-4-(trifluoromethyl)phenyl)pyrido[3,4-*d*]pyridazin-4-yl)-3,4,5-trimethylpiperidin-4-ol;

17) (3*S*,4*s*,5*R*)-1-(4-(2-hydroxy-4-(trifluoromethyl)phenyl)pyrido[3,4-*d*]pyridazin-1-yl)-3,4,5-trimethylpiperidin-4-ol;

18) (3*S*,4*r*,5*R*)-1-(1-(2-hydroxy-4-(trifluoromethyl)phenyl)pyrido[3,4-*d*]pyridazin-4-yl)-3,5-dimethylpiperidin-4-ol;

19) (3*S*,4*r*,5*R*)-1-(4-(2-hydroxy-4-(trifluoromethyl)phenyl)pyrido[3,4-*d*]pyridazin-1-yl)-3,5-dimethylpiperidin-4-ol;

20) 2-(4-((*cis*)-2,6-dimethylmorpholino)-6-methylphthalazin-1-yl)-5-(trifluoromethyl)phenol;

21) 2-(4-((*cis*)-2,6-dimethylmorpholino)-7-methylphthalazin-1-yl)-5-(trifluoromethyl)phenol;

22) (*S*)-1-(5-(2-hydroxy-4-(trifluoromethyl)phenyl)pyrido[2,3-*d*]-pyridazin-8-yl)-3-methylpyrrolidin-3-ol;

23) 2-(8-((3a*S*,7a*R*)-6-methyloctahydro-1H-pyrrolo[2,3-*c*]pyridin-1-yl)pyrido[2,3-*d*]pyridazin-5-yl)-5-(trifluoromethyl)phenol;

24) (3*S*,4*s*,5*R*)-1-(5-(2-hydroxy-4-(trifluoromethyl)phenyl)pyrido[2,3-*d*]pyridazin-8-yl)-3,4,5-trimethylpiperidin-4-ol;

25) 8-(5-(2-hydroxy-4-(trifluoromethyl)phenyl)pyrido[2,3-*d*]pyridazin-8-yl)-3-oxa-1,8-diazaspiro[4.5]decan-2-one;

26) (*cis*)-4-(5-(2-hydroxy-4-(trifluoromethyl)phenyl)pyrido[2,3-*d*]pyridazin-8-yl)-2,6-dimethylthiomorpholine 1,1-dioxide;

27) (*R*)-1-(5-(2-hydroxy-4-(trifluoromethyl)phenyl)pyrido[2,3-*d*]pyridazin-8-yl)-3-(trifluoromethyl)pyrrolidin-3-ol;

28) (*S*)-1-(5-(2-hydroxy-4-(trifluoromethyl)phenyl)pyrido[2,3-*d*]pyridazin-8-yl)-3-(trifluoromethyl)pyrrolidin-3-ol;

29) (*R*)-3-(difluoromethyl)-1-(5-(2-hydroxy-4-(trifluoromethyl)phenyl)pyrido[2,3-*d*]pyridazin-8-yl)pyrrolidin-3-ol;

30) (*S*)-3-(difluoromethyl)-1-(5-(2-hydroxy-4-(trifluoromethyl)phenyl)pyrido[2,3-*d*]pyridazin-8-yl)pyrrolidin-3-ol;

31) (*R*)-2-(8-(1-oxa-7-azaspiro[4.4]nonan-7-yl)pyrido[2,3-*d*]pyridazin-5-yl)-5-(trifluoromethyl)phenol;

32) (*S*)-2-(8-(1-oxa-7-azaspiro[4.4]nonan-7-yl)pyrido[2,3-*d*]pyridazin-5-yl)-5-(trifluoromethyl)phenol;

33) 2-(8-(1-oxa-8-azaspiro[4.5]decan-8-yl)pyrido[2,3-*d*]pyridazin-5-yl)-5-(trifluoromethyl)phenol;

34) 2-(8-(2-oxa-8-azaspiro[4.5]decan-8-yl)pyrido[2,3-*d*]pyridazin-5-yl)-5-(trifluoromethyl)phenol;

35) 9-(5-(2-hydroxy-4-(trifluoromethyl)phenyl)pyrido[2,3-*d*]pyridazin-8-yl)-1-oxa-4,9-diazaspiro[5.5]undecan-3-one;

36) 2-(8-((*cis*)-4,4-difluoro-3,5-dimethylpiperidin-1-yl)pyrido[2,3-*d*]pyridazin-5-yl)-5-(trifluoromethyl)phenol;

37) 1-(8-(5-(2-hydroxy-4-(trifluoromethyl)phenyl)pyrido[2,3-*d*]pyridazin-8-yl)-1,8-diazaspiro[4.5]decan-1-yl)ethan-1-one;

38) 1-(8-(5-(2-hydroxy-4-(trifluoromethyl)phenyl)pyrido[2,3-*d*]pyridazin-8-yl)-2,8-diazaspiro[4.5]decan-2-yl)ethan-1-one;

39) 8-(5-(2-hydroxy-4-(trifluoro-methyl)phenyl)pyrido[2,3-*d*]-pyridazin-8-yl)-3-methyl-1-oxa-3,8-diazaspiro[4.5]decan-2-one;

40) 2-(8-(4,4-dimethyl-1-oxa-8-azaspiro[4.5]decan-8-yl)pyrido[2,3-*d*]pyridazin-5-yl)-5-(trifluoromethyl)phenol;

41) (*R*)-1-(5-(2-hydroxy-4-(trifluoromethyl)phenyl)pyrido[2,3-*d*]pyridazin-8-yl)-3-phenylpyrrolidin-3-ol;

42) (*S*)-1-(5-(2-hydroxy-4-(trifluoromethyl)phenyl)pyrido[2,3-*d*]pyridazin-8-yl)-3-phenylpyrrolidin-3-ol;

43) 8-(5-(2-hydroxy-4-(trifluoromethyl)phenyl)pyrido[2,3-*d*]pyridazin-8-yl)-1-methyl-1,8-diazaspiro[4.5]decan-2-one;

44) 8-(5-(2-hydroxy-4-(trifluoromethyl)phenyl)pyrido[2,3-*d*]pyridazin-8-yl)-1-oxa-3,8-diazaspiro[4.5]decan-2-one;

45) 2-(8-(6,6-difluoro-3-azabicyclo[3.1.0]hexan-3-yl)pyrido[2,3-*d*]pyridazin-5-yl)-5-(trifluoromethyl)phenol;

46) 8-(5-(2-hydroxy-4-(trifluoromethyl)phenyl)pyrido[2,3-*d*]pyridazin-8-yl)-1-oxa-8-azaspiro[4.5]decan-2-one;

47) (*R*)-4,4-difluoro-1-(5-(2-hydroxy-4-(trifluoromethyl)phenyl)pyrido[2,3-*d*]pyridazin-8-yl)pyrrolidin-3-ol;

48) (*S*)-4,4-difluoro-1-(5-(2-hydroxy-4-(trifluoromethyl)phenyl)pyrido[2,3-*d*]pyridazin-8-yl)pyrrolidin-3-ol;

49) (*R*)-5-(5-(2-hydroxy-4-(trifluoromethyl)phenyl)pyrido[2,3-*d*]pyridazin-8-yl)-5-azaspiro[2.4]heptan-7-ol;

50) (*S*)-5-(5-(2-hydroxy-4-(trifluoromethyl)phenyl)pyrido[2,3-*d*]pyridazin-8-yl)-5-azaspiro[2.4]heptan-7-ol;

51) (*R*)-3-cyclopropyl-1-(5-(2-hydroxy-4-(trifluoromethyl)phenyl)pyrido[2,3-*d*]pyridazin-8-yl)pyrrolidin-3-ol;

52) (*S*)-3-cyclopropyl-1-(5-(2-hydroxy-4-(trifluoromethyl)phenyl)pyrido[2,3-*d*]pyridazin-8-yl)pyrrolidin-3-ol;

53) (*R*)-3-((dimethylamino)methyl)-1-(5-(2-hydroxy-4-(trifluoromethyl)phenyl)pyrido-[2,3-*d*]pyridazin-8-yl)pyrrolidin-3-ol;

54) (*S*)-3-((dimethylamino)methyl)-1-(5-(2-hydroxy-4-(trifluoromethyl)phenyl)pyrido-[2,3-*d*]pyridazin-8-yl)pyrrolidin-3-ol;

55) (*R*)-3-ethyl-1-(5-(2-hydroxy-4-(trifluoromethyl)phenyl)pyrido[2,3-*d*]pyridazin-8-yl)-pyrrolidin-3-ol;

56) (*S*)-3-ethyl-1-(5-(2-hydroxy-4-(trifluoromethyl)phenyl)pyrido[2,3-*d*]pyridazin-8-yl)-pyrrolidin-3-ol;

57) (*R*)-2-(8-(3-(hydroxymethyl)-3-methylpyrrolidin-1-yl)pyrido[2,3-*d*]pyridazin-5-yl)-5-(trifluoromethyl)phenol;

58) (*S*)-2-(8-(3-(hydroxymethyl)-3-methylpyrrolidin-1-yl)pyrido[2,3-*d*]pyridazin-5-yl)-5-(trifluoromethyl)phenol;

59) (*R*)-2-(8-(3-(2-hydroxypropan-2-yl)pyrrolidin-1-yl)pyrido[2,3-*d*]pyridazin-5-yl)-5-(trifluoromethyl)phenol;

60) (*S*)-2-(8-(3-(2-hydroxypropan-2-yl)pyrrolidin-1-yl)pyrido[2,3-*d*]pyridazin-5-yl)-5-(trifluoromethyl)phenol;

61) 2-(8-((2*R*,6*R*)-2-(hydroxymethyl)-6-methylmorpholino)pyrido[2,3-*d*]pyridazin-5-yl)-5-(trifluoromethyl)phenol;

62) 2-(8-((2*S*,6*S*)-2-(hydroxymethyl)-6-methylmorpholino)pyrido[2,3-*d*]pyridazin-5-yl)-5-(trifluoromethyl)phenol;

63) 2-(8-((2*S*,6*S*)-2-(hydroxymethyl)-6-methylmorpholino)pyrido[2,3-*d*]pyridazin-5-yl)-5-(trifluoromethyl)phenol;

64) 2-(8-((2*R*,6*R*)-2-(hydroxymethyl)-6-methylmorpholino)pyrido[2,3-*d*]pyridazin-5-yl)-5-(trifluoromethyl)phenol;

65) 1-((2*R*,4*r*,6*S*)-2,6-dimethyltetrahydro-2H-pyran-4-yl)-4-(2-methyl-4(trifluoromethyl)-phenyl)phthalazine;

66) (2*R*,4*s*,6*S*)-4-(5-(2-hydroxy-4-(trifluoromethyl)phenyl)pyrido[2,3-*d*]-pyridazin-8-yl)-2,6-dimethyltetrahydro-2*H*-pyran-4-ol;

67) (2*R*,4*r*,6*S*)-4-(5-(2-hydroxy-4-(trifluoromethyl)phenyl)pyrido[2,3-*d*]-pyridazin-8-yl)-2,6-dimethyltetrahydro-2*H*-pyran-4-ol;

68) (*S*)-1-(2-(difluoromethyl)-5-(2-hydroxy-4-(trifluoromethyl)phenyl)pyrido[2,3-*d*]pyridazin-8-yl)-3-methylpyrrolidin-3-ol; and

69) (*S*)-1-(3-(difluoromethyl)-5-(2-hydroxy-4-(trifluoromethyl)phenyl)pyrido[2,3-*d*]pyridazin-8-yl)-3-methylpyrrolidin-3-ol;

or a pharmaceutically acceptable salt thereof.

In another aspect, there is provided a compound selected from:

1) (*S*)-1-(4-(2-hydroxy-4-(trifluoromethyl)phenyl)pyrido[3,4-*d*]pyridazin-1-yl)-3-methylpyrrolidin-3-ol;

2) (*S*)-1-(1-(2-hydroxy-4-(trifluoromethyl)phenyl)pyrido[3,4-*d*]-pyridazin-4-yl)-3-methylpyrrolidin-3-ol;

3) 2-(4-((*cis*)-2,6-dimethylmorpholino)pyridazino[4,5-*d*]pyridazin-1-yl)-5-(trifluoromethyl)phenol;

4) (*S*)-1-(5-(2-hydroxy-4-(trifluoromethyl)phenyl)pyrido[2,3-*d*]-pyridazin-8-yl)-3-methylpyrrolidin-3-ol;

5) 2-(8-((3a*S*,7a*R*)-6-methyloctahydro-1H-pyrrolo[2,3-*c*]pyridin-1-yl)pyrido[2,3-*d*]pyridazin-5-yl)-5-(trifluoromethyl)phenol;

6) (2*R*,4*s*,6*S*)-4-(5-(2-hydroxy-4-(trifluoromethyl)phenyl)pyrido[2,3-*d*]-pyridazin-8-yl)-2,6-dimethyltetrahydro-2*H*-pyran-4-ol; and

7) (2*R*,4*r*,6*S*)-4-(5-(2-hydroxy-4-(trifluoromethyl)phenyl)pyrido[2,3-*d*]-pyridazin-8-yl)-2,6-dimethyltetrahydro-2*H*-pyran-4-ol;

or pharmaceutically acceptable salts thereof.

The compounds of structural formula I, and examples thereof, are inhibitors of NOD-like receptor protein 3 (NLRP3) and may be useful in the treatment and prevention of diseases, disorders and conditions mediated by NLRP3 such as, but not limited to, gout, pseudogout (chondrocalcinosis), cryopyrin-associated periodic syndromes (CAPS), NASH, fibrosis, heart failure, idiophathic pericarditis, atopic dermatitis, inflammatory bowel disease, Alzheimer's Disease, Parkinson's Disease and traumatic brain injury.

The present disclosure also relates to pharmaceutical compositions comprising the compounds of the present disclosure and a pharmaceutically acceptable carrier. In another aspect, there is provided a pharmaceutical composition comprising a compound of the present disclosure, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

The present disclosure also relates to methods for the treatment, management, prevention, alleviation, amelioration, suppression or control of disorders, diseases, and conditions that may be responsive to inhibition of the NLRP3 receptor in a subject in need thereof by administering the compounds and pharmaceutical compositions of the present disclosure.

In another aspect, there is provided a compound of the present disclosure, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of the present disclosure, for use in the treatment of a disorder, condition, or disease that is responsive to the inhibition of NLRP3 in a mammal in need thereof.

In another aspect, there is provided a compound of the present disclosure, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of the present disclosure, for use in therapy.

The present disclosure also relates to the use of compounds of the present disclosure for manufacture of a medicament useful in treating diseases, disorders and conditions that may be responsive to the inhibition of the NLRP3 receptor.

In another aspect, there is provided use of a compound of the present disclosure, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of the present disclosure, in the manufacture of a medicament for the treatment, prevention or control of an

inflammatory disorder, a fibrotic disorder, a cardiovascular disorder, a metabolic disorder and a neurodegenerative disorder.

The present disclosure is also concerned with treatment or prevention of these diseases, disorders and conditions by administering the compounds of the present disclosure in combination with a therapeutically effective amount of another agent that may be useful to treat the disease, disorder and condition. The disclosure is further concerned with processes for preparing the compounds of this disclosure.

DETAILED DESCRIPTION OF THE INVENTION

The present invention is concerned with novel compounds of structural Formula I: