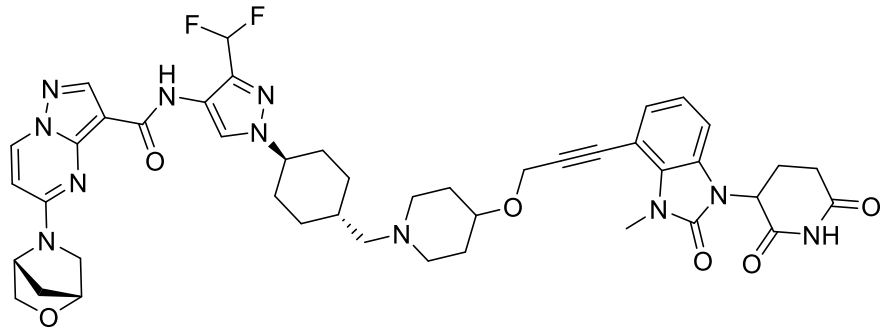
2019/133531 and WO 2020/010227, the contents of which are incorporated herein by reference in their entireties. There remains an unmet need for improved synthesis of such compounds.

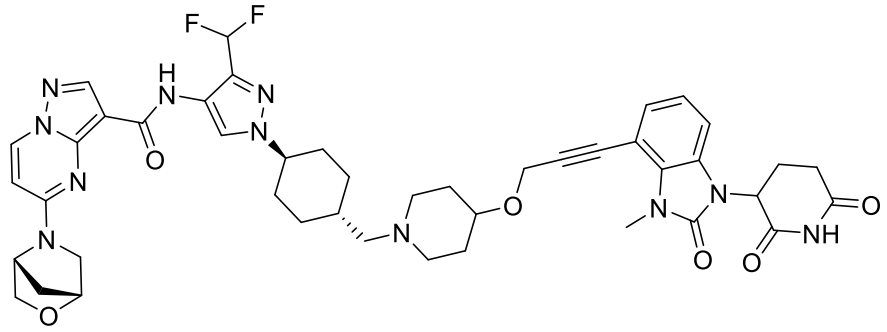
SUMMARY

[0006] It has now been found that a composition of 5-((1R,4R)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)-N-(3-(difluoromethyl)-1-((1r,4R)-4-((4-((3-(1-(2,6-dioxopiperidin-3-yl)-3-methyl-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-4-yl)prop-2-yn-1-yl)oxy)piperidin-1-yl)methyl)cyclohexyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrimidine-3-carboxamide (compound **I-1** herein) or a pharmaceutically acceptable salt thereof may contain a number of impurities.



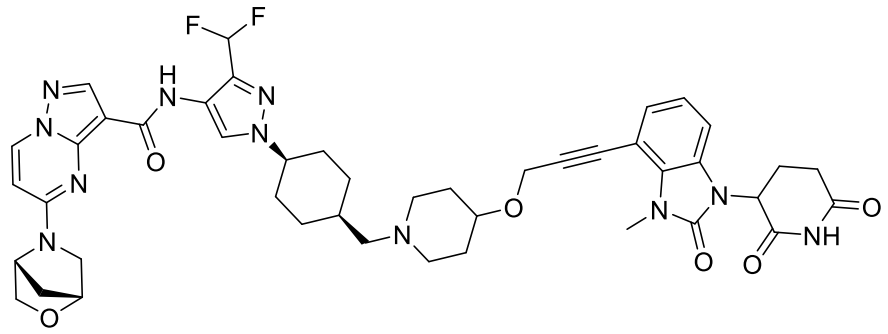
I-1

[0006a] In an aspect of the present disclosure, there is provided a composition comprising compound **I-1**:



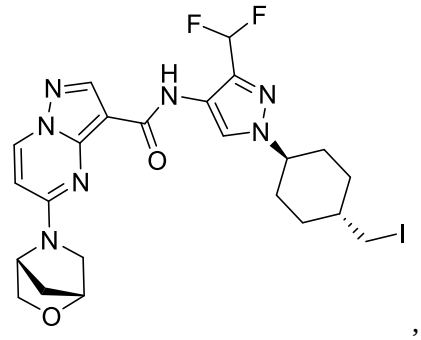
I-1

or a pharmaceutically acceptable salt thereof, and one or more impurity compounds selected from the group consisting of:



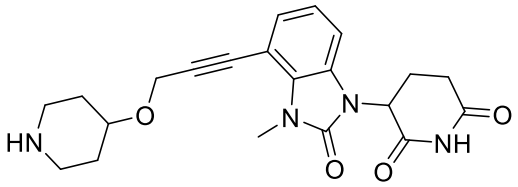
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I-2



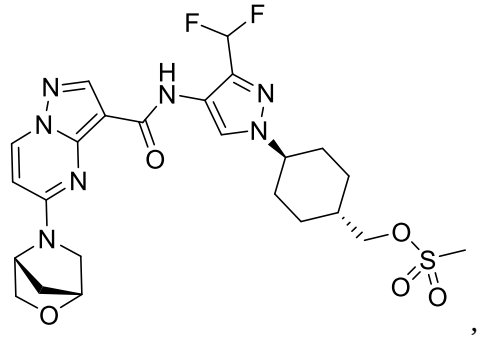
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I-3



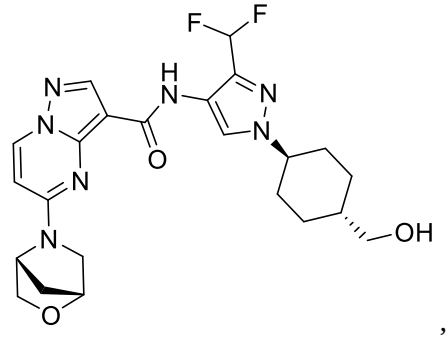
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I-4



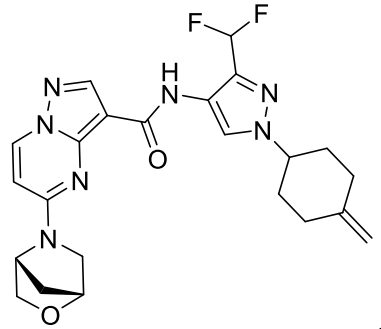
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I-5



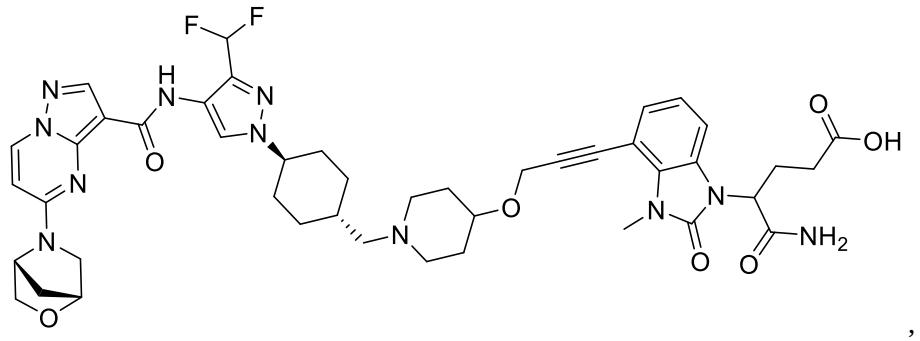
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I-6



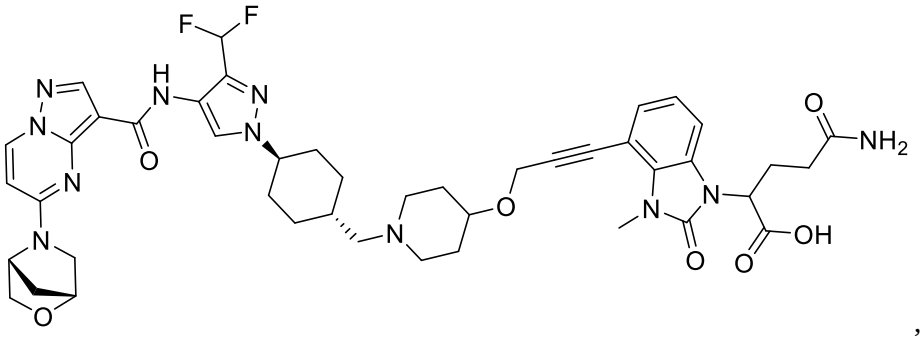
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I-7



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I-8



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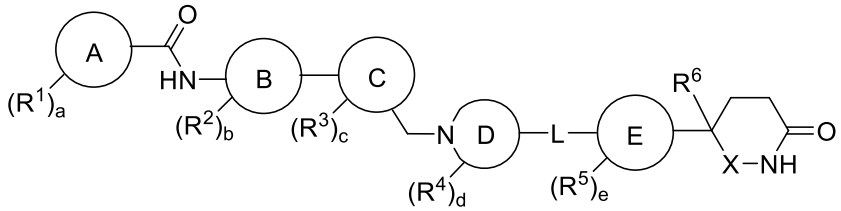
I-9

or a pharmaceutically acceptable salt thereof.

[0006b] In another aspect of the present disclosure, there is provided a pharmaceutical composition comprising a composition disclosed herein, and a pharmaceutically acceptable adjuvant, carrier, or vehicle.

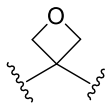
[0006c] In a further aspect of the present disclosure, there is provided a use of a pharmaceutical composition disclosed herein, in the manufacture of a medicament for treating an autoimmune/autoinflammatory disease and/or a hematological malignancy in a patient.

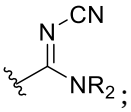
[0006d] In another aspect of the present disclosure, there is provided a process for preparing a compound of formula **I**:



I

or a pharmaceutically acceptable salt thereof, wherein:

X is a bivalent moiety selected from a covalent bond, $–CH_2–$, –C(O)–, –C(S)–, or ;

R^1, R^2, R^3, R^4, and R^5, independently, are selected from hydrogen, deuterium, R^A, halogen, -CN, -NO_2, -OR, -SR, -NR_2, -SO_2R, -SO_2NR_2, -S(O)R, -CFR_2, -CF_2R, -CF_3, -CR_2OR, -$CR_2(NR_2)$, -C(O)R, -C(O)OR, -$C(O)NR_2$, -$C(S)NR_2$, -C(O)NROR, -OC(O)R, -$OC(O)NR_2$, -NRC(O)OR, -NRC(O)R, -$NRC(O)NR_2$, -$NRSO_2R$, -$N^+(O^-)R_2$, -$OP(O)R_2$, -$OP(O)(OR)_2$, -$OP(O)(OR)NR_2$, -$OP(O)(NR_2)_2$, -$P(O)R_2$, -SiR_3, -$Si(OR)R_2$, or ;

each R, independently, is hydrogen, or an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 3-7 membered saturated or partially unsaturated heterocyclic having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or:

two R groups on the same carbon or nitrogen are optionally taken together with their intervening atoms to form a 4-11 membered saturated or partially unsaturated monocyclic, bicyclic, bridged bicyclic, or spirocyclic carbocyclic or heterocyclic ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or a 5-9 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur;

each R^A, independently, is an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur;

a, b, c, d, and e, independently, are selected from 0, 1, 2, 3, or 4;

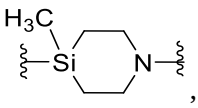
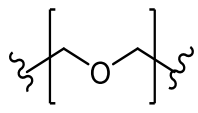
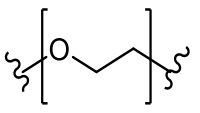
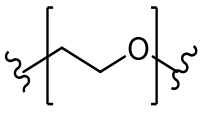
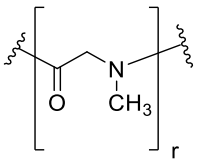
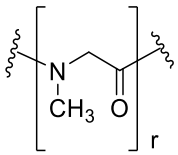
R^6 is hydrogen or C_{1-6} aliphatic;

Ring A, Ring B, and Ring E, independently, are selected from phenyl, naphthyl, a 4-11 membered saturated or partially unsaturated monocyclic, bicyclic, bridged bicyclic, or spirocyclic carbocyclic or heterocyclic ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or a 5-10 membered monocyclic or bicyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur;

Ring C is a 4-6 membered saturated or partially unsaturated carbocyclic or heterocyclic ring having 1-2 heteroatoms selected from nitrogen, oxygen, and sulfur;

Ring D is a 4-6 membered saturated or partially unsaturated heterocyclic ring having, in addition to the nitrogen present, 0-2 heteroatoms selected from nitrogen, oxygen, and sulfur;

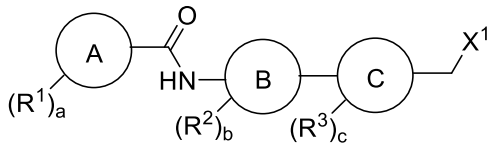
L is a covalent bond or a bivalent, saturated or unsaturated, straight or branched C_{1-10} hydrocarbon chain, wherein 0-6 methylene units of L are independently replaced by -CDH-, -CD_2-, -CRF-, -CF_2-, -Cy-, -O-, -NR-, -SiR_2-, -Si(OH)R-, -$Si(OH)_2$-, -P(O)OR-, -P(O)R-, -$P(O)NR_2$-, -S-, -OC(O)-, -

C(O)O-, -C(O)-, -S(O)-, -SO_2-, -$NRSO_2$-, -SO_2NR-, -NRC(O)-, -C(O)NR-, -OC(O)NR-, -NRC(O)O-, , , , , , or ;

each –Cy–, independently, is an optionally substituted bivalent ring selected from phenylenyl, an 8-10 membered bicyclic arylenyl, a 4-7 membered saturated or partially unsaturated carbocyclylenyl, a 4-12 membered saturated or partially unsaturated spiro carbocyclylenyl, an 8-10 membered bicyclic saturated or partially unsaturated carbocyclylenyl, a 4-7 membered saturated or partially unsaturated heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 4-12 membered saturated or partially unsaturated spiro heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, an 8-10 membered bicyclic saturated or partially unsaturated heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5-6 membered heteroarylenyl having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or an 8-10 membered bicyclic heteroarylenyl having 1-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; and

r is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10,

comprising treating a compound of formula **II**:

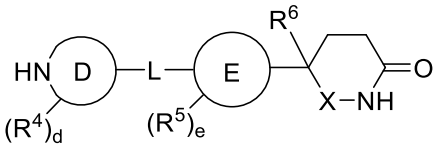


II

or pharmaceutically acceptable salt thereof, wherein:

X^1 is a suitable leaving group,

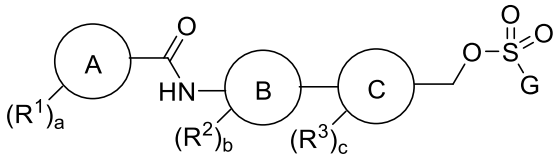
with a compound of formula **III**:



III

under suitable conditions to form the compound of formula **I** or a pharmaceutically acceptable salt thereof.

[0006e] In a further aspect of the present disclosure, there is provided a process for preparing a compound of formula **II** as disclosed herein, the process comprising halogenating a compound of formula **IV**:



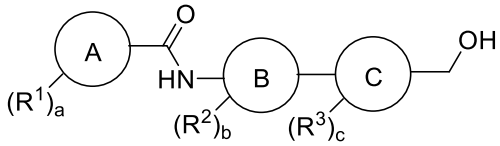
IV

or a pharmaceutically acceptable salt thereof, wherein:

G is an optionally substituted group selected from a C_{1-6} aliphatic, phenyl, naphthyl, a 4-11 membered saturated or partially unsaturated monocyclic, bicyclic, bridged bicyclic, or spirocyclic carbocyclic or heterocyclic ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or a 5-10 membered monocyclic or bicyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur;

under suitable conditions to form the compound of formula **II** or a pharmaceutically acceptable salt thereof.

[0006f] In another aspect of the present disclosure, there is provided a process for preparing a compound of formula **IV** as disclosed herein, the process comprising sulfonating a compound of formula **V**:

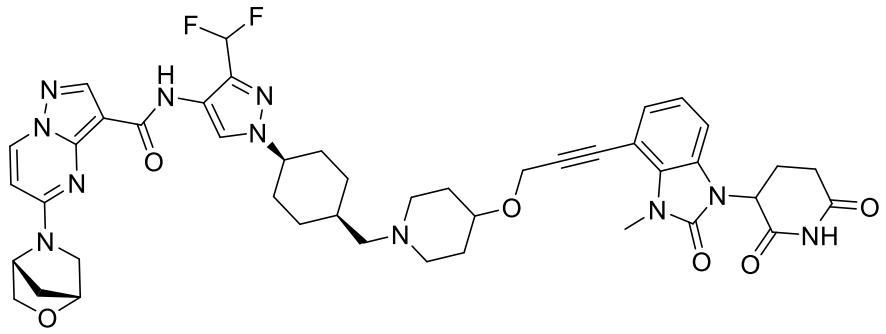


V

or a pharmaceutically acceptable salt thereof, under suitable conditions to form the compound of formula **IV** or a pharmaceutically acceptable salt thereof.

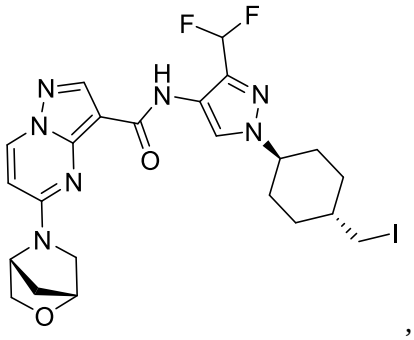
[0006g] In a further aspect of the present disclosure, there is provided a pharmaceutical disclosed herein, for use in therapy.

[0007] In one example, the present disclosure provides a composition comprising compound **I-1** and one or more impurity compounds selected from the group consisting of:

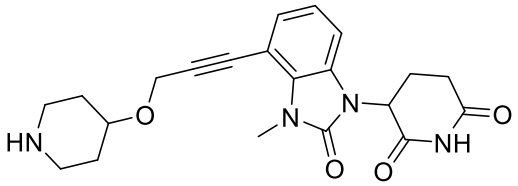


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I-2



,



,

I-4

[0008] Compound **I-1** or a pharmaceutically acceptable salts thereof, and pharmaceutical compositions thereof, as described in the instant application, are useful for treating an autoimmune/autoinflammatory disease. In some examples, the autoimmune/autoinflammatory disease is a cutaneous autoimmune/autoinflammatory disease selected from atopic dermatitis (AD), rheumatoid arthritis (RA), and hidradenitis suppurativa (HS).

[0009] In another example, the present disclosure provides a method for synthesizing compound **I-1**, or a pharmaceutically acceptable salt thereof, and related intermediates.

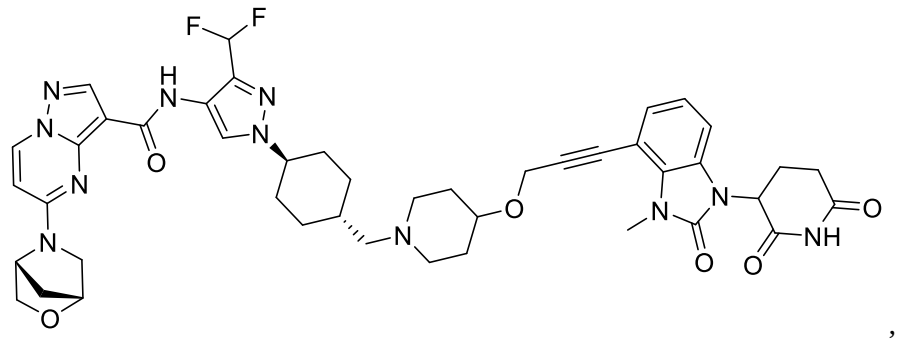
[0010] These and other examples of this disclosure will be apparent upon reference to the following detailed description. To this end, various references are set forth herein which describe in more detail certain background information and procedures and are each hereby incorporated by reference in their entirety.

DETAILED DESCRIPTION OF THE INVENTION

1. General Description of Certain Embodiments of the Invention

[0011] One of ordinary skill in the art will appreciate that impurity profile of an active pharmaceutical agent ("API" or "drug substance") is an important aspect of any pharmaceutical drug product. As such, impurities arising from synthesis or degradation are useful in that they allow for the monitoring of API purity and adherence to regulatory standards.

[0012] In certain embodiments, the present invention provides compositions comprising compound **I-1**:



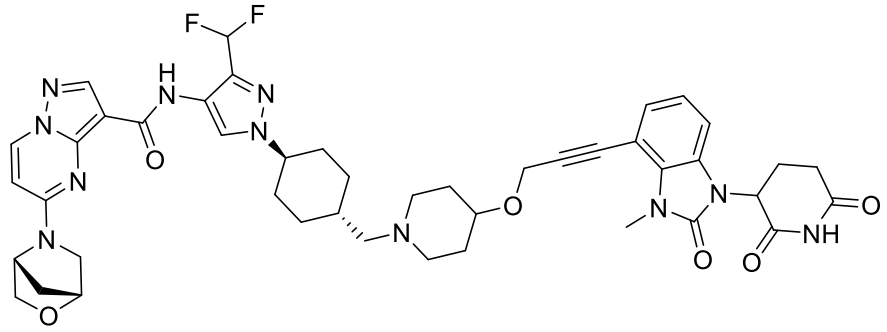
I-1

and one or more impurity compounds (i.e., impurities) therein.

[0013] Compound **I-1** is a potent, highly selective, orally administered heterobifunctional small molecule therapeutic targeting IRAK4 and the E3 ligase CRBN to mediate the selective degradation of IRAK4 via the ubiquitin-proteasome system.

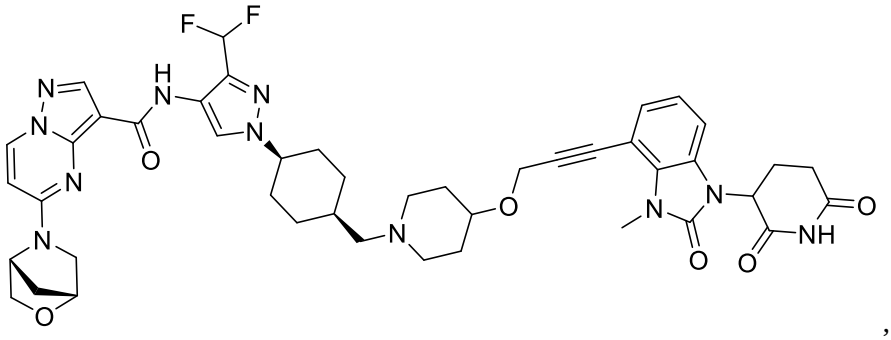
CLAIMS

1. A composition comprising compound **I-1**:



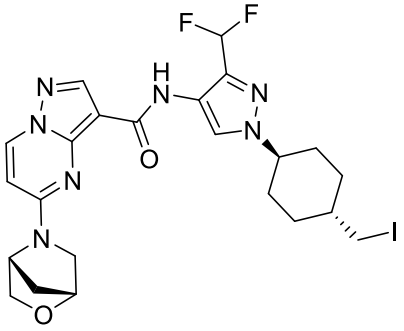
I-1

or a pharmaceutically acceptable salt thereof, and one or more impurity compounds selected from the group consisting of:



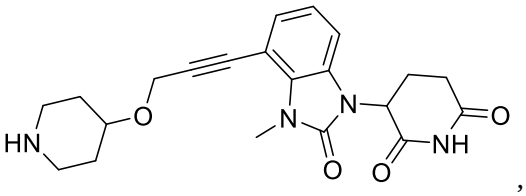
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I-2



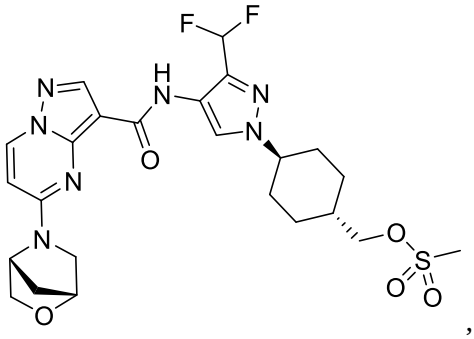
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I-3

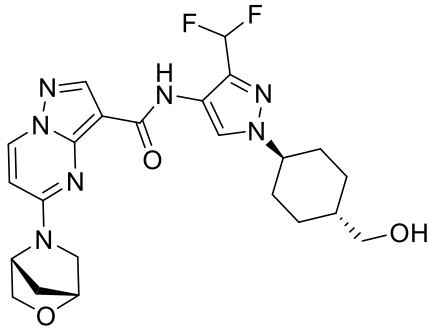


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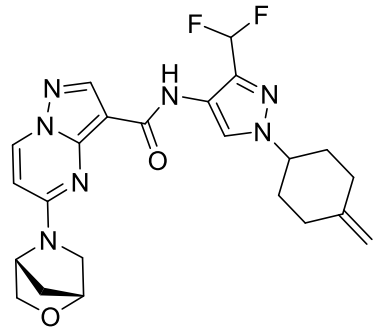
I-4



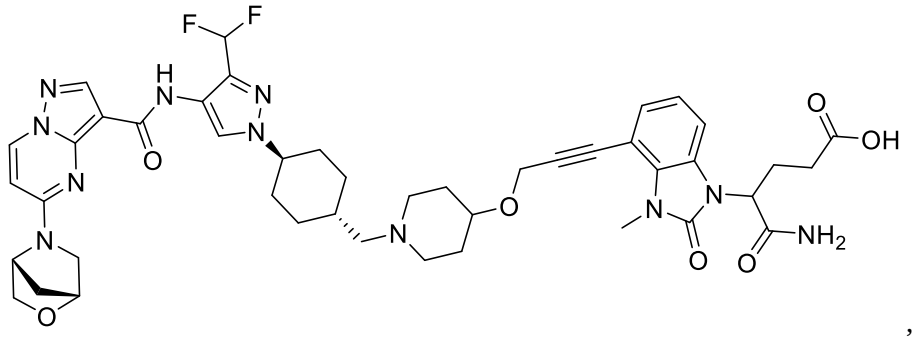
I-5



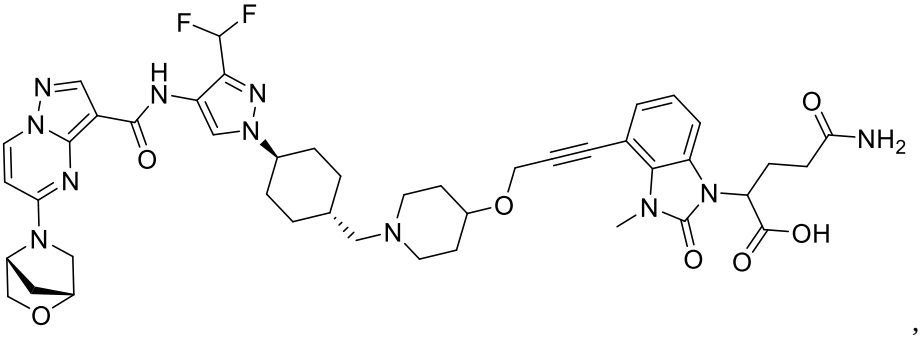
I-6



I-7



I-8



I-9

or a pharmaceutically acceptable salt thereof.

2. The composition of claim 1, wherein the composition comprises one impurity compound selected from the group consisting of **I-2**, **I-3**, **I-4**, **I-5**, **I-6**, **I-7**, **I-8**, and **I-9**, or a pharmaceutically acceptable salt thereof.

3. The composition of claim 1, wherein the composition comprises two impurity compounds selected from the group consisting of **I-2**, **I-3**, **I-4**, **I-5**, **I-6**, **I-7**, **I-8**, and **I-9**, or a pharmaceutically acceptable salt thereof.

4. The composition of claim 1, wherein the composition comprises three impurity compounds selected from the group consisting of **I-2**, **I-3**, **I-4**, **I-5**, **I-6**, **I-7**, **I-8**, and **I-9**, or a pharmaceutically acceptable salt thereof.

5. The composition of claim 1, wherein the composition comprises four impurity compounds selected from the group consisting of **I-2**, **I-3**, **I-4**, **I-5**, **I-6**, **I-7**, **I-8**, and **I-9**, or a pharmaceutically acceptable salt thereof.

6. The composition of claim 1, wherein the composition comprises five impurity compounds selected from the group consisting of **I-2**, **I-3**, **I-4**, **I-5**, **I-6**, **I-7**, **I-8**, and **I-9**, or a pharmaceutically acceptable salt thereof.

7. The composition of claim 1, wherein the composition comprises six impurity compounds selected from the group consisting of **I-2**, **I-3**, **I-4**, **I-5**, **I-6**, **I-7**, **I-8**, and **I-9**, or a pharmaceutically acceptable salt thereof.

8. The composition of claim 1, wherein the composition comprises seven impurity compounds selected from the group consisting of **I-2**, **I-3**, **I-4**, **I-5**, **I-6**, **I-7**, **I-8**, and **I-9**, or a pharmaceutically acceptable salt thereof.

9. The composition of claim 1, wherein the composition comprises each of impurity compounds **I-2**, **I-3**, **I-4**, **I-5**, **I-6**, **I-7**, **I-8**, and **I-9**, or a pharmaceutically acceptable salt thereof.

10. The composition of any one of claims 1-9, wherein the composition comprises one or more impurity compound selected from the group consisting of **I-2**, **I-3**, and **I-5**, or a pharmaceutically acceptable salt thereof.

11. The composition of any one of claims 1-10, wherein the composition comprises one or more impurity compound selected from the group consisting of **I-3** and **I-5**, or a pharmaceutically acceptable salt thereof.

12. The composition of any one of claims 1-11, wherein each of impurity compounds **I-4**, **I-6**, **I-7**, **I-8**, and **I-9**, or a pharmaceutically acceptable salt thereof, is, independently, no more than about 0.7 area percent HPLC of the total weight of the composition.

13. The composition of any one of claims 1-12, wherein impurity compound **I-2** or a pharmaceutically acceptable salt thereof is no more than about 2.0 area percent HPLC of the total weight of the composition.

14. The composition of any one of claims 1-13, wherein each of impurity compounds **I-3** and **I-5**, or a pharmaceutically acceptable salt thereof, is, independently, no more than about 30 ppm.

15. The composition of any one of claims 1-14, wherein the total impurity compounds of **I-2**, **I-3**, **I-4**, **I-5**, **I-6**, **I-7**, **I-8**, and **I-9**, or a pharmaceutically acceptable salt thereof, present in the composition is no more than about 3.0 area percent HPLC.

16. The composition of any one of claims 1-15, wherein the purity of compound **I-1**, or a pharmaceutically acceptable salt thereof, in the composition is at least about 97.0 area percent HPLC.

17. The composition of any one of claims 1-16, further comprising dichloromethane in the composition in an amount of no more than about 600 ppm.

18. The composition of any one of claims 1-17, further comprising N,N-dimethylacetamide in the composition in an amount of no more than about 1090 ppm.

19. The composition of any one of claims 1-18, further comprising tetrahydrofuran in the composition in an amount of no more than about 720 ppm.

20. The composition of any one of claims 1-19, further comprising isopropanol in the composition in an amount of no more than about 5000 ppm.

21. The composition of any one of claims 1-20, further comprising 2-methyltetrahydrofuran in the composition in an amount of no more than about 5000 ppm.

22. The composition of any one of claims 1-21, further comprising isopropyl chloride in the composition in an amount of no more than about 300 ppm.

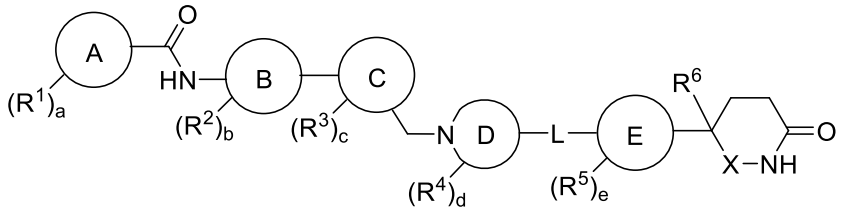
23. A pharmaceutical composition comprising a composition of any one of claims 1-22, and a pharmaceutically acceptable adjuvant, carrier, or vehicle.

24. Use of a pharmaceutical composition of claim 23, in the manufacture of a medicament for treating an autoimmune/autoinflammatory disease and/or a hematological malignancy in a patient.

25. The use of claim 24, wherein the autoimmune/autoinflammatory disease is selected from a cutaneous, rheumatic, and gastrointestinal autoimmune/autoinflammatory disease.

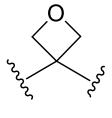
26. The use of claim 24, wherein the autoimmune/autoinflammatory disease is a cutaneous autoimmune/autoinflammatory disease selected from atopic dermatitis (AD) and hidradenitis suppurativa (HS).

27. A process for preparing a compound of formula **I**:



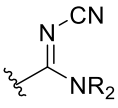
I

or a pharmaceutically acceptable salt thereof, wherein:

X is a bivalent moiety selected from a covalent bond, $–CH_2–$, –C(O)–, –C(S)–, or 

;

R^1, R^2, R^3, R^4, and R^5, independently, are selected from hydrogen, deuterium, R^A, halogen, -CN, $-NO_2$, -OR, -SR, $-NR_2$, $-SO_2R$, $-SO_2NR_2$, -S(O)R, $-CFR_2$, $-CF_2R$, $-CF_3$, $-CR_2OR$, -

$CR_2(NR_2)$, -C(O)R, -C(O)OR, $-C(O)NR_2$, $-C(S)NR_2$, -C(O)NROR, -OC(O)R, $-OC(O)NR_2$, -NRC(O)OR, -NRC(O)R, $-NRC(O)NR_2$, $-NRSO_2R$, $-N^+(O^-)R_2$, $-OP(O)R_2$, $-OP(O)(OR)_2$, -$OP(O)(OR)NR_2$, $-OP(O)(NR_2)_2$, $-P(O)R_2$, $-SiR_3$, $-Si(OR)R_2$, or ;

each R, independently, is hydrogen, or an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 3-7 membered saturated or partially unsaturated heterocyclic having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or:

two R groups on the same carbon or nitrogen are optionally taken together with their intervening atoms to form a 4-11 membered saturated or partially unsaturated monocyclic, bicyclic, bridged bicyclic, or spirocyclic carbocyclic or heterocyclic ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or a 5-9 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur;

each R^A, independently, is an optionally substituted group selected from C_{1-6} aliphatic, phenyl, a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, and a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur;

a, b, c, d, and e, independently, are selected from 0, 1, 2, 3, or 4;

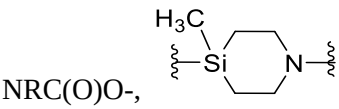
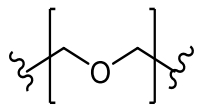
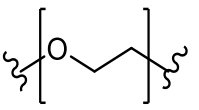
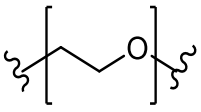
R^6 is hydrogen or C_{1-6} aliphatic;

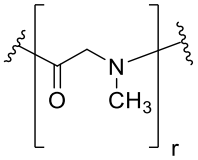
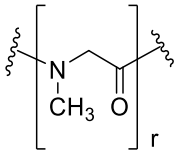
Ring A, Ring B, and Ring E, independently, are selected from phenyl, naphthyl, a 4-11 membered saturated or partially unsaturated monocyclic, bicyclic, bridged bicyclic, or spirocyclic carbocyclic or heterocyclic ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or a 5-10 membered monocyclic or bicyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur;

Ring C is a 4-6 membered saturated or partially unsaturated carbocyclic or heterocyclic ring having 1-2 heteroatoms selected from nitrogen, oxygen, and sulfur;

Ring D is a 4-6 membered saturated or partially unsaturated heterocyclic ring having, in addition to the nitrogen present, 0-2 heteroatoms selected from nitrogen, oxygen, and sulfur;

L is a covalent bond or a bivalent, saturated or unsaturated, straight or branched C_{1-10} hydrocarbon chain, wherein 0-6 methylene units of L are independently replaced by -CDH-, $-CD_2-$, -CRF-, $-CF_2-$, -Cy-, -O-, -NR-, $-SiR_2-$, -Si(OH)R-, $-Si(OH)_2-$, -P(O)OR-, -P(O)R-, $-P(O)NR_2-$, -S-, -OC(O)-, -C(O)O-, -C(O)-, -S(O)-, $-SO_2-$, $-NRSO_2-$, $-SO_2NR-$, -NRC(O)-, -C(O)NR-, -OC(O)NR-, -

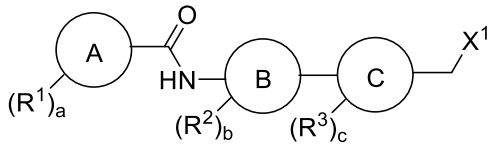
NRC(O)O-, , , , ,

, or ;

each –Cy–, independently, is an optionally substituted bivalent ring selected from phenylenyl, an 8-10 membered bicyclic arylenyl, a 4-7 membered saturated or partially unsaturated carbocyclylenyl, a 4-12 membered saturated or partially unsaturated spiro carbocyclylenyl, an 8-10 membered bicyclic saturated or partially unsaturated carbocyclylenyl, a 4-7 membered saturated or partially unsaturated heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 4-12 membered saturated or partially unsaturated spiro heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, an 8-10 membered bicyclic saturated or partially unsaturated heterocyclylenyl having 1-2 heteroatoms independently selected from nitrogen, oxygen, and sulfur, a 5-6 membered heteroarylenyl having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or an 8-10 membered bicyclic heteroarylenyl having 1-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; and

r is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10,

comprising treating a compound of formula **II**:

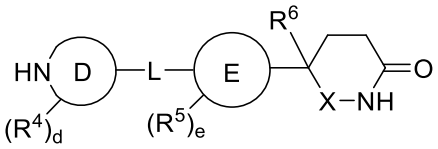


II

or pharmaceutically acceptable salt thereof, wherein:

X^1 is a suitable leaving group,

with a compound of formula **III**:

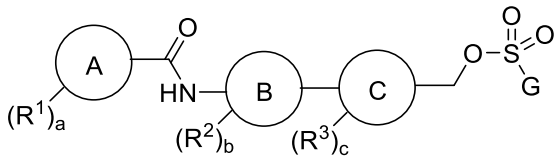


III

under suitable conditions to form the compound of formula **I** or a pharmaceutically acceptable salt thereof.

28. The process of claim 27, wherein X^1 is a halogen.

29. A process for preparing a compound of formula **II** as defined in claim 28, the process comprising halogenating a compound of formula **IV**:



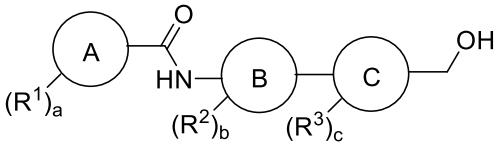
IV

or a pharmaceutically acceptable salt thereof, wherein:

G is an optionally substituted group selected from a C_{1-6} aliphatic, phenyl, naphthyl, a 4-11 membered saturated or partially unsaturated monocyclic, bicyclic, bridged bicyclic, or spirocyclic carbocyclic or heterocyclic ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or a 5-10 membered monocyclic or bicyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur;

under suitable conditions to form the compound of formula **II** or a pharmaceutically acceptable salt thereof.

30. A process for preparing a compound of formula **IV** as defined in claim 29, the process comprising sulfonating a compound of formula **V**:



V

or a pharmaceutically acceptable salt thereof, under suitable conditions to form the compound of formula **IV** or a pharmaceutically acceptable salt thereof.

31. The process of any one of claims 27-30, wherein Ring A is phenyl or a 5-10 membered monocyclic or bicyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur.

32. The process of any one of claims 27-31, wherein Ring B is phenyl or a 5-6 membered heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur.

33. The process of any one of claims 27-32, wherein Ring C is a 6-membered saturated or partially unsaturated carbocyclic or heterocyclic ring having 1-2 heteroatoms selected from nitrogen, oxygen, and sulfur.

34. The process of any one of claims 27-33, wherein Ring D is a 6-membered saturated or partially unsaturated carbocyclic or heterocyclic ring having 1-2 heteroatoms selected from nitrogen, oxygen, and sulfur.

35. The process of any one of claims 27-34, wherein Ring E is a 5-10 membered monocyclic or bicyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur.

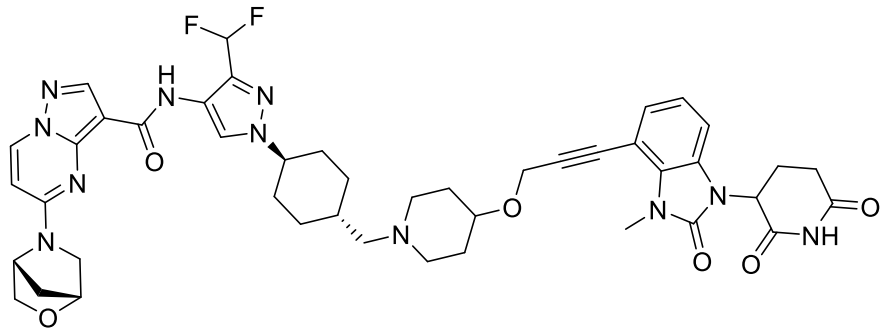
36. The process of any one of claims 27-35, wherein R^1 is halogen, -CN, -NO_2, -OR, -SR, -NR_2, -SO_2R, -SO_2NR_2, -S(O)R, -CFR_2, -CF_2R, -CF_3, -CR_2OR, -$CR_2(NR_2)$, -C(O)R, -C(O)OR, -$C(O)NR_2$, -$C(S)NR_2$, -C(O)NROR, -OC(O)R, -$OC(O)NR_2$, -NRC(O)OR, -NRC(O)R, -$NRC(O)NR_2$, or -$NRSO_2R$.

37. The process of any one of claims 27-36, wherein R^2 is halogen, -CN, -NO_2, -OR, -SR, -NR_2, -SO_2R, -SO_2NR_2, -S(O)R, -CFR_2, -CF_2R, -CF_3, -CR_2OR, -$CR_2(NR_2)$, -C(O)R, -C(O)OR, -$C(O)NR_2$, -$C(S)NR_2$, -C(O)NROR, -OC(O)R, -$OC(O)NR_2$, -NRC(O)OR, -NRC(O)R, -$NRC(O)NR_2$, or -$NRSO_2R$.

38. The process of any one of claims 27-37, wherein c, d, and e are 0.

39. The process of any one of claims 27-38, wherein R^6 is hydrogen.

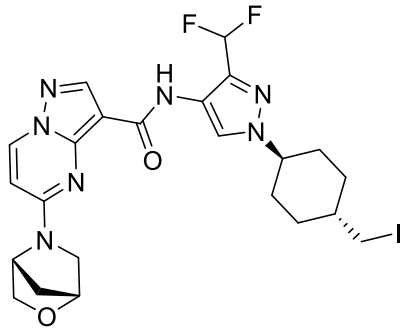
40. The process of any one of claims 27-39, wherein the compound of formula **I** is:



I-1

or a pharmaceutically acceptable salt thereof.

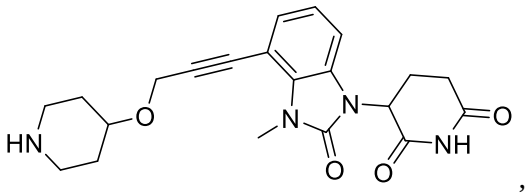
41. The process of any one of claims 27-40, wherein the compound of formula **II** is:



I-3

or a pharmaceutically acceptable salt thereof.

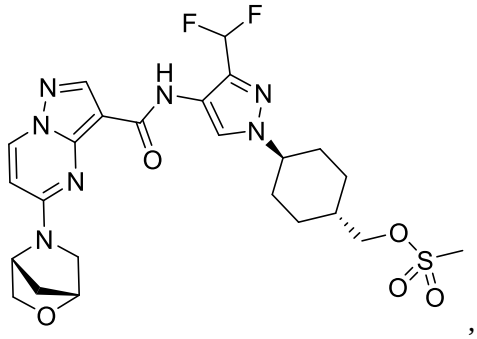
42. The process of any one of claims 27-41, wherein the compound of formula **III** is:



I-4

or a pharmaceutically acceptable salt thereof.

43. The process of any one of claims 29-42, wherein the compound of formula **IV** is:



I-5

or a pharmaceutically acceptable salt thereof.

44. A pharmaceutical composition of claim 23, for use in therapy.