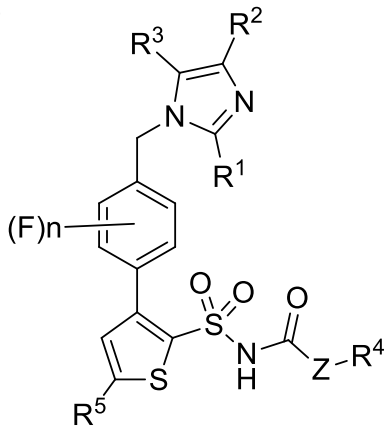
CLAIMS

1. A compound of formula I,



I

in which:

n represents 1 to 4;

Z represents -O- or a direct bond;

R^1 represents C_{1-6} alkyl, optionally substituted by one or more halogen atoms;

R^2 and R^3 each independently represent H or C_{1-6} alkyl, optionally substituted by one or more halogen atoms;

R^4 represents C_{1-8} alkyl, which alkyl group is optionally substituted, and/or terminated, by one or more halogen atoms and/or OR^6 groups; or R^4 represents aryl, C_{1-6} alkylaryl, C_{1-3} alkenylaryl, heteroaryl, C_{1-6} alkylheteroaryl or C_{1-3} alkenylheteroaryl, each of which are optionally substituted by one or more substituents selected from halogen, CF_3, CF_3O, C_{1-6} alkyl, and C_{1-6} alkoxy;

R^5 represents C_{1-6} alkyl, C_{1-6} alkoxy or C_{1-6} alkoxy-C_{1-6} alkyl, each of which is optionally substituted by one or more halogen atoms;

R^6 represents H, $-C(O)R^7$, or C_{1-6} alkyl, aryl, C_{1-6} alkylaryl, C_{1-3} alkenylaryl, heteroaryl, C_{1-6} alkylheteroaryl or C_{1-3} alkenylheteroaryl, each of which latter seven groups are optionally substituted by one or more substituents selected from halogen, CF_3, CF_3O, C_{1-6} alkyl, and C_{1-6} alkoxy; and

R^7 represents C_{1-6} alkyl,

or a pharmaceutically-acceptable salt thereof, for use as a pharmaceutical.

2. A compound for use according to Claim 1, in which n represents 1.

3. A compound for use according to Claim 1, in which, when n is 1, the F atom is ortho, relative to the methylene group that is also attached to the imidazolyl ring.

4. A compound for use according to Claim 1, 2 or 3, in which Z represents -O-.

5. A compound for use according to any preceding claim, in which R^1 represents methyl, ethyl or isopropyl.

6. A compound for use according to any preceding claim, in which R^2 and R^3 independently represent H or methyl.

7. A compound for use according to any preceding claim, in which R^4 represents methyl, ethyl, cyclohexylmethyl, cyclopentylmethyl, n-propyl, n-butyl or isobutyl, each of which is optionally substituted or terminated by up to three F groups and/or one or more OR^6 groups; or C_{1-6} alkylaryl (such as benzyl) optionally substituted by one or more F groups.

8. A compound for use according to any preceding claim, in which R^5 represents methyl, ethyl, n-propyl, n-butyl or isobutyl.

9. A compound for use according to any preceding claim, in which R^6 represents H, methyl, ethyl, n-propyl, n-butyl, optionally substituted or more preferably terminated by up to three fluorine atoms; $-C(O)R^7$; or phenyl.

10. A compound for use according to any preceding claim, in which R^7 represents methyl, ethyl or n-propyl.

11. A compound as defined in any preceding claim, which is:

butyl (3-(3-fluoro-4-((2-methyl-1H-imidazol-1-yl)methyl)phenyl)-5-isobutylthiophen-2-yl)sulfonylcarbamate,

2-phenoxyethyl (3-(3-fluoro-4-((2-methyl-1H-imidazol-1-yl)methyl)phenyl)-5-isobutylthiophen-2-yl)sulfonylcarbamate,

ethyl (3-(3-fluoro-4-((2-methyl-1H-imidazol-1-yl)methyl)phenyl)-5-isobutylthiophen-2-yl)sulfonylcarbamate,

2-methoxyethyl (3-(3-fluoro-4-((2-methyl-1H-imidazol-1-yl)methyl)phenyl)-5-isobutylthiophen-2-yl)sulfonylcarbamate,

2-hydroxyethyl (3-(3-fluoro-4-((2-methyl-1H-imidazol-1-yl)methyl)phenyl)-5-isobutylthiophen-2-yl)sulfonylcarbamate,

3,3,3-trifluoropropyl (3-(3-fluoro-4-((2-ethyl-1H-imidazol-1-yl)methyl)phenyl)-5-isobutylthiophen-2-yl)sulfonylcarbamate,

4-fluorobenzyl (3-(4-((2-ethyl-1H-imidazol-1-yl)methyl)-3-fluorophenyl)-5-isobutylthiophen-2-yl)sulfonylcarbamate,

ethyl (3-(4-((2-ethyl-1H-imidazol-1-yl)methyl)-3-fluorophenyl)-5-isobutylthiophen-2-yl)sulfonylcarbamate,

ethyl (3-(3-fluoro-4-((2-isopropyl-1H-imidazol-1-yl)methyl)phenyl)-5-isobutylthiophen-2-yl)sulfonylcarbamate,

2-hydroxyethyl (3-(3,5-difluoro-4-((2-methyl-1H-imidazol-1-yl)methyl)phenyl)-5-isobutylthiophen-2-yl)sulfonylcarbamate,

methyl (3-(3-fluoro-4-((2-methyl-1H-imidazol-1-yl)methyl)phenyl)-5-isobutylthiophen-2-yl)sulfonylcarbamate,

2-((((3-(3-fluoro-4-((2-methyl-1H-imidazol-1-yl)methyl)phenyl)-5-isobutylthiophen-2-yl)sulfonyl)carbamoyl)oxy)ethyl pivalate,

N-((3-(3-fluoro-4-((2-methyl-1H-imidazol-1-yl)methyl)phenyl)-5-isobutylthiophen-2-yl)sulfonyl)pivalamide,

methyl (3-(4-((2-(tert-butyl)-1H-imidazol-1-yl)methyl)-3-fluorophenyl)-5-isobutylthiophen-2-yl)sulfonylcarbamate,

2-hydroxyethyl (3-(4-((2-(tert-butyl)-1H-imidazol-1-yl)methyl)-3-fluorophenyl)-5-isobutylthiophen-2-yl)sulfonylcarbamate,

2-hydroxy-2-methylpropyl (3-(4-((2-(tert-butyl)-1H-imidazol-1-yl)methyl)-3-fluorophenyl)-5-isobutylthiophen-2-yl)sulfonylcarbamate,

methyl (3-(4-((2-ethyl-1H-imidazol-1-yl)methyl)-3-fluorophenyl)-5-isobutylthiophen-2-yl)sulfonylcarbamate,

2-hydroxyethyl (3-(4-((2-ethyl-1H-imidazol-1-yl)methyl)-3-fluorophenyl)-5-isobutylthiophen-2-yl)sulfonylcarbamate,

N-((3-(4-((2-(tert-butyl)-1H-imidazol-1-yl)methyl)-3-fluorophenyl)-5-isobutylthiophen-2-yl)sulfonyl)benzamide,

N-((3-(4-((2-(tert-butyl)-1H-imidazol-1-yl)methyl)-3-fluorophenyl)-5-isobutylthiophen-2-yl)sulfonyl)picolinamide,

2-hydroxyethyl (3-(3-fluoro-4-((2-isopropylimidazol-1-yl)methyl)phenyl)-5-isobutyl-2-thienyl)sulfonylcarbamate,

methyl (3-(3-fluoro-4-((2-isopropylimidazol-1-yl)methyl)phenyl)-5-isobutyl-2-thienyl)sulfonylcarbamate,

N-[[3-[3-fluoro-4-[(2-isopropylimidazol-1-yl)methyl]phenyl]-5-isobutyl-2-thienyl]sulfonyl]benzamide,

N-[[3-[3-fluoro-4-[(2-isopropylimidazol-1-yl)methyl]phenyl]-5-isobutyl-2-thienyl]sulfonyl]pyridine-2-carboxamide,

N-[[3-[3-fluoro-4-[(2-isopropylimidazol-1-yl)methyl]phenyl]-5-isobutyl-2-thienyl]sulfonyl]-3-(2-pyridyl)propanamide

or a pharmaceutically-acceptable salt of any of these compounds.

12. A compound according to Claim 11, which is:

ethyl (3-(3-fluoro-4-((2-methyl-1H-imidazol-1-yl)methyl)phenyl)-5-isobutylthiophen-2-yl)sulfonylcarbamate,

methyl (3-(3-fluoro-4-((2-methyl-1H-imidazol-1-yl)methyl)phenyl)-5-isobutylthiophen-2-yl)sulfonylcarbamate, or

methyl (3-(4-((2-ethyl-1H-imidazol-1-yl)methyl)-3-fluorophenyl)-5-isobutylthiophen-2-yl)sulfonylcarbamate,

or a pharmaceutically-acceptable salt of any of these compounds.

13. A pharmaceutical formulation comprising a compound as defined in any one of Claims 1 to 12, or a pharmaceutically-acceptable salt thereof, in admixture with a pharmaceutically-acceptable, adjuvant, diluent or carrier.

14. A compound as defined in any one of Claims 1 to 12, for use in the treatment of an autoimmune disease, a fibrotic disease, a chronic kidney disease, pulmonary hypertension, heart failure and/or myocardial infarction.

15. Use of a compound as defined in any one of Claims 1 to 12, or a pharmaceutically-acceptable salt thereof, for the manufacture of a medicament for the treatment of an autoimmune disease, a fibrotic disease, a chronic kidney disease, pulmonary hypertension, heart failure and/or myocardial infarction.

16. A compound for use according to Claim 14 or a use according to Claim 15, in which the disease is an interstitial lung disease.

17. A compound for use or a use according to Claim 16, in which the interstitial lung disease is idiopathic pulmonary fibrosis or sarcoidosis.

18. A compound for use according to Claim 14 or a use according to Claim 15, in which the autoimmune disease is rheumatoid arthritis or systemic sclerosis.

19. A compound for use according to Claim 14 or a use according to Claim 15, in which the chronic kidney disease is diabetic nephropathy.

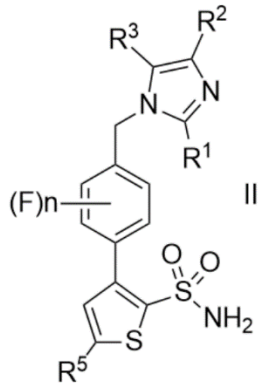
20. A compound for use according to Claim 14 or a use according to Claim 15, in which the pulmonary hypertension is pulmonary arterial hypertension.

21. A compound for use according to Claim 14 or a use according to Claim 15, in which the heart failure is with preserved ejection fraction.

22. A compound for use according to Claim 14 or a use according to Claim 15, in which the viral respiratory tract infection results in virally-induced pneumonia.

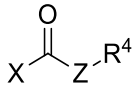
23. A process for the preparation of a pharmaceutical formulation as defined in Claim 13, which comprises preparing a compound of formula I as defined in any one of Claims 1 to 12, or a pharmaceutically acceptable salt thereof, which process comprises:

(i) reaction of a compound of formula II,



II

in which R^1, R^2, R^3 and n are as defined in the relevant preceding claims, with a compound of formula III,



III

in which X represents a suitable leaving group and R^4 and R^5 are as defined in the relevant preceding claims;

(ii) for compounds of formula I in which Z is a bond, reaction of a compound of formula II as defined above with a compound of formula IIIa,

$R^4C(O)OH$ IIIa

in which R^4 is as defined in the relevant preceding claims; or

(iii) for compounds of formula I in which Z represents -O-, reaction of a corresponding compound of formula I in which R^4 is a lower alkyl group or an optionally substituted aryl group with a compound of formula IV,

$R^{4'}OH$ IV

in which $R^{4'}$ represents an R^4 group other than the one being replaced,

followed by admixing the compound or salt with a pharmaceutically-acceptable, adjuvant, diluent or carrier.