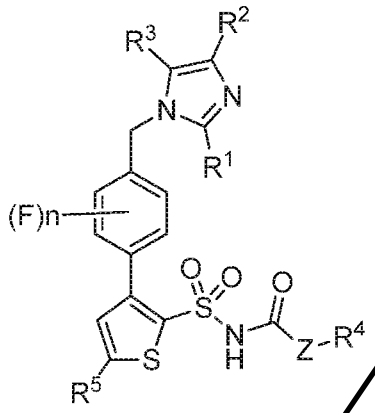
## Claims

1. A compound of formula I,



I

wherein:

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.

2. A compound as claimed in Claim 1, wherein n represents 1.

3. A compound as claimed in Claim 1, wherein, 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 as claimed in any one of the preceding claims, wherein Z represents -O-.

5. A compound as claimed in any one of the preceding claims, wherein $R^1$ represents methyl, ethyl or isopropyl.

6. A compound as claimed in any one of the preceding claims, wherein $R^2$ and $R^3$ independently represent H or methyl.

7. A compound as claimed in any one of the preceding claims, wherein $R^4$ 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 as claimed in any one of the preceding claims, wherein $R^5$ represents methyl, ethyl, n-propyl, n-butyl or isobutyl.

9. A compound as claimed in any one of the preceding claims, wherein $R^6$ 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 as claimed in any one of the preceding claims, wherein $R^7$ represents methyl, ethyl or n-propyl.

11. A compound as claimed in any one of the preceding claims, 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.

12. A compound as defined in any one of Claims 1 to 11, for use as a pharmaceutical.

13. A pharmaceutical formulation comprising a compound as defined in any one of Claims 1 to 11 in admixture with a pharmaceutically-acceptable, adjuvant, diluent or carrier.

14. A compound as defined in any one of Claims 1 to 11, 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. The use of a compound as defined in any one of Claims 1 to 11, 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 method of treatment of an autoimmune disease, a fibrotic disease, a chronic kidney disease, pulmonary hypertension, heart failure and/or myocardial infarction, which comprises administering a compound as defined in any one of Claims 1 to 11 to a patient in need of such treatment.

17. A compound for use as claimed in Claim 14, a use as claimed in Claim 15, or a method of treatment as claimed in Claim 16, wherein the disease is an interstitial lung disease.

18. A compound for use, a use, or a method of treatment as claimed in Claim 17, wherein the interstitial lung disease is idiopathic pulmonary fibrosis or sarcoidosis.

19. A compound for use as claimed in Claim 14, a use as claimed in Claim 15, or a method of treatment as claimed in Claim 16, wherein the autoimmune disease is rheumatoid arthritis or systemic sclerosis.

20. A compound for use as claimed in Claim 14, a use as claimed in Claim 15, or a method of treatment as claimed in Claim 16, wherein the chronic kidney disease is diabetic nephropathy.

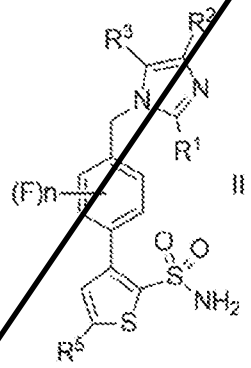
21. A compound for use as claimed in Claim 14, a use as claimed in Claim 15, or a method of treatment as claimed in Claim 16, wherein the pulmonary hypertension is pulmonary arterial hypertension.

22. A compound for use as claimed in Claim 14, a use as claimed in Claim 15, or a method of treatment as claimed in Claim 16, wherein the heart failure is with preserved ejection fraction.

23. A compound for use as claimed in Claim 14, a use as claimed in Claim 15, or a method of treatment as claimed in Claim 16, wherein the viral respiratory tract infection results in virally-induced pneumonia.

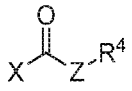
24. A process for the preparation of a compound of formula I as defined in any one of the preceding claims, which process comprises:

(i) reaction of a compound of formula II,



II

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



III

wherein 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

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

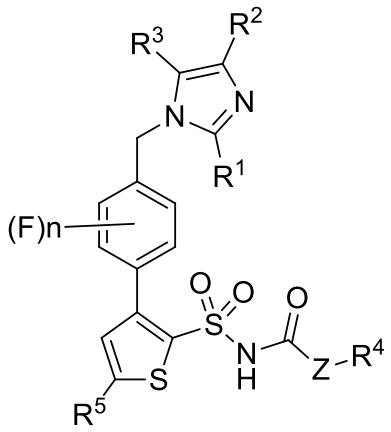
(iii) for compounds of formula I in which Z represents -O-, reaction of a corresponding compound of formula I in which $R^4$ is a lower alkyl group or an optionally substituted aryl group with a compound of formula IV,

$R^{4'}OH$ IV

wherein $R^{4'}$ represents an $R^4$ group other than the one being replaced.

**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-iso-butylthiophen-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-iso-butylthiophen-2-yl)sulfonylcarbamate,

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

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

4-fluorobenzyl (3-(4-((2-ethyl-1H-imidazol-1-yl)methyl)-3-fluorophenyl)-5-iso-butylthiophen-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-iso-butylthiophen-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.

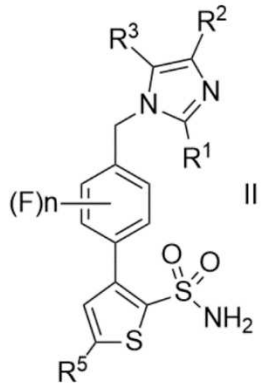
20. A compound for use according to Claim 14 or a use according to Claim 15, in which the pulmonary hypertension is pulmonary arterial hypertension.

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.

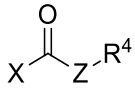
23. A process for the preparation of a pharmaceutical formulation as defined in Claim 13, which comprises preparing a compound of formula I as defined in any one of Claims 1 to 12, or a pharmaceutically acceptable salt thereof, which process comprises:

(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.