

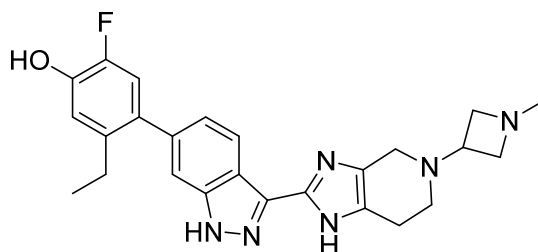
or when  $n$  is 1 and  $R^2$  and  $R^7$  taken together form  $C_2$ alkylene,  $R^4$  and a substituent  $R^x$  on  $C_2$ alkylene taken together form  $C_2$ alkylene;

provided that two substituents  $R^x$  on the same carbon atom are not both fluoro,  
and

- 5 provided that when  $R^x$  is attached to a carbon atom adjacent to a nitrogen atom,  $R^x$  is not -OH, -OC<sub>1-3</sub>alkyl, or halo;  
or a pharmaceutically-acceptable salt thereof.

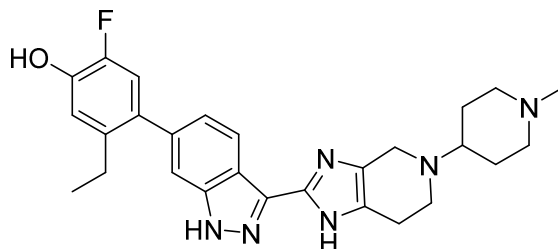
As used hereinafter, the phrase “compound of formula (I)” means a compound of  
formula (I) or a pharmaceutically acceptable salt thereof; i.e., this phrase means a  
10 compound of formula (I) in free base form or in a pharmaceutically acceptable salt form  
unless otherwise indicated.

In another aspect, the disclosure provides a compound of formula



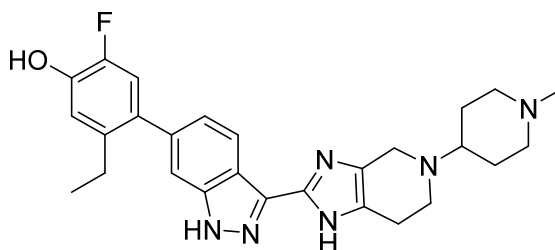
or a pharmaceutically acceptable salt thereof.

- 15 In another aspect, the disclosure provides a compound of formula



or a pharmaceutically acceptable salt thereof.

In another aspect, the disclosure provides a compound of formula

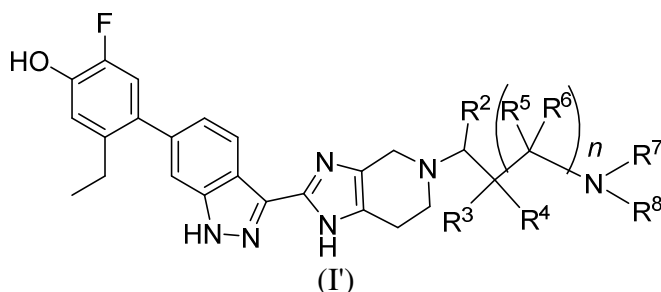


In another aspect, the disclosure provides a crystalline hydrate of 5-ethyl-2-fluoro-4-(3-(5-(1-methylpiperidin-4-yl)-4,5,6,7-tetrahydro-1*H*-imidazo[4,5-*c*]pyridin-2-yl)-1*H*-indazol-6-yl)phenol wherein the crystalline form is characterized by a powder X-ray diffraction pattern comprising diffraction peaks at  $2\theta$  values of  $6.20\pm0.20$ ,  $9.58\pm0.20$ ,  $17.53\pm0.20$ ,  $19.28\pm0.20$ , and  $21.51\pm0.2$ .

In another aspect, the disclosure also provides a pharmaceutical composition comprising a compound or crystalline hydrate as described herein and a pharmaceutically-acceptable carrier.

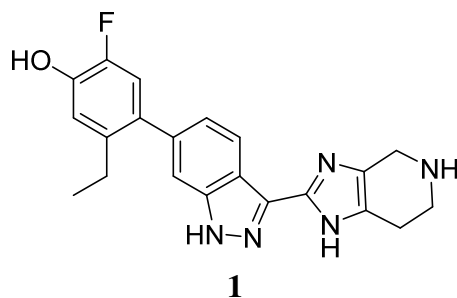
In one embodiment, the disclosure provides a particular compound of formula (I) as a crystalline free base hydrate. The crystalline hydrate of 5-ethyl-2-fluoro-4-(3-(5-(1-methylpiperidin-4-yl)-4,5,6,7-tetrahydro-1*H*-imidazo[4,5-*c*]pyridin-2-yl)-1*H*-indazol-6-yl)phenol has been found to have a melting temperature in the range of about 206 °C to about 216 °C, typically between about 209 °C and about 214 °C, a decomposition onset at about 245 °C, and to exhibit weight changes of less than about 0.12 % when exposed to a range of relative humidity between about 5 % and about 90 % at room temperature.

In another aspect, the disclosure provides a process of preparing a compound of formula (I'):

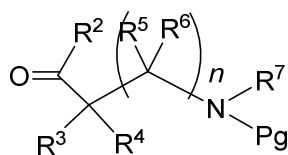


wherein  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ , and  $n$  are defined as described herein, or a pharmaceutically acceptable salt thereof, the process comprising:

(a) reacting a compound of formula **1**:

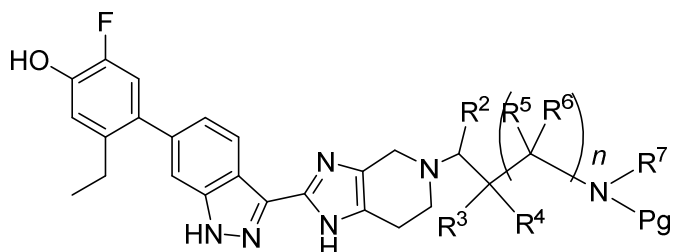


with a compound of formula **2**:



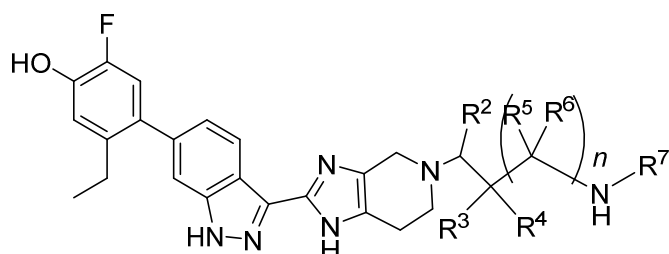
**2**

wherein Pg is an amino-protecting group to provide an intermediate of formula **3**:



**3;**

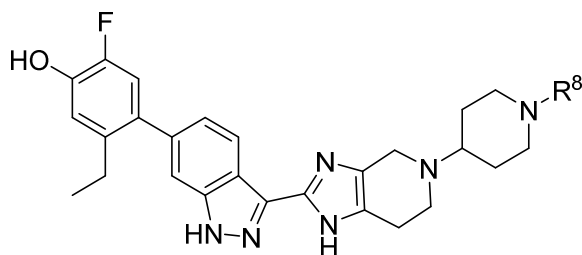
(b) deprotecting intermediate **3** to provide intermediate **4**:



**4;**

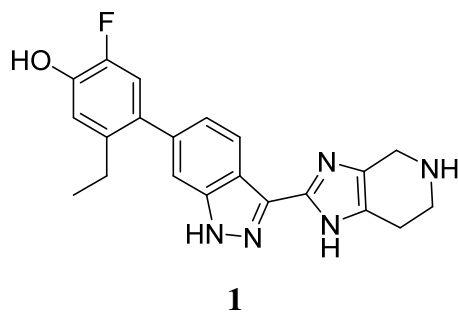
and (c) reacting intermediate **4** with  $R^{8a}-C(=O)-R^{8b}$ , wherein  $R^{8a}$  and  $R^{8b}$  are defined such that  $R^{8a}-C(H)-R^{8b}$  is  $R^8$ , to provide a compound of formula (I') or a pharmaceutically acceptable salt thereof.

In another aspect, the disclosure provides a process of preparing a compound of formula (IV):

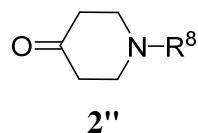


(IV)

or a pharmaceutically acceptable salt thereof, wherein  $R^8$  is selected from hydrogen, methyl,  $C_{2-4}$ alkyl, and  $C_{3-4}$ cycloalkyl, the process comprising reacting a compound of formula **1**:

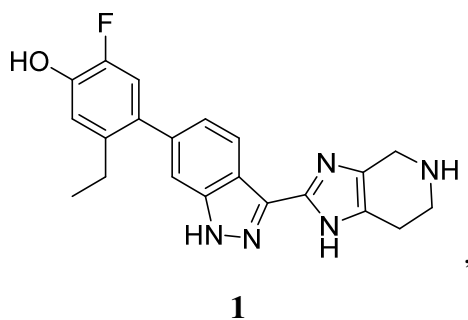


with a compound of formula **2''**:



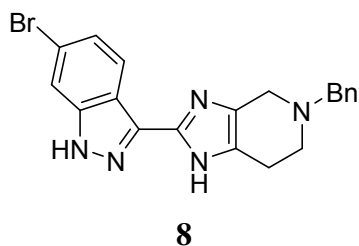
to provide a compound of formula (IV) or a pharmaceutically-acceptable salt thereof.

In another aspect, the disclosure provides a process of preparing a compound of formula **1**:

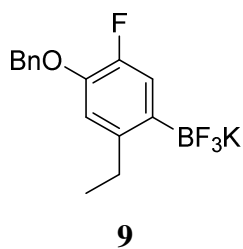


or a salt thereof, the process comprising:

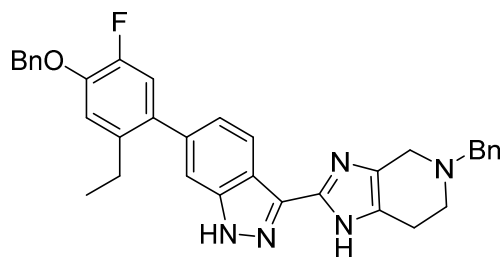
(a) reacting a compound of formula **8**;



wherein Bn represents a benzyl protecting group with a compound of formula **9**:



to form a compound of formula **10**:



**10,**

and (b) deprotecting the compound of formula **10**, to provide a compound of formula **1** or a salt thereof.

5 In another aspect, the disclosure provides a method of preparing the crystalline hydrate of 5-ethyl-2-fluoro-4-(3-(5-(1-methylpiperidin-4-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridin-2-yl)-1H-indazol-6-yl)phenol, the method comprising:

(a) forming a slurry of 5-ethyl-2-fluoro-4-(3-(5-(1-methylpiperidin-4-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridin-2-yl)-1H-indazol-6-yl)phenol in solvate or

10 amorphous form in a diluent including from about 1 to about 30 % v/v water along with an organic solvent selected from methanol, tetrahydrofuran, *tert*-butyl alcohol, acetonitrile, isopropylacetate and acetone;

(b) heating the slurry at a temperature between about 40 °C and about 60 °C for between about 1 hour and about 2 days; and

15 (c) isolating the crystalline hydrate from the slurry.

In another aspect, the disclosure provides a compound or crystalline hydrate as described herein for use in the treatment of an inflammatory or fibrotic respiratory disease in a mammal.

20 In another aspect, the disclosure a use of a compound or crystalline hydrate as described herein for the manufacture of a medicament for the treatment of an inflammatory or fibrotic respiratory disease in a mammal.

In another embodiment, the disclosure also provides a method of treating respiratory disease, in particular, asthma, in a mammal, the method comprising administering to the mammal a therapeutically effective amount of a compound or of a pharmaceutical composition of the invention. In separate and distinct aspects, the  
25 invention also provides synthetic processes and intermediates described herein, which are useful for preparing compounds of the invention.

In another embodiment, the disclosure also provides a compound of the invention as described herein for use in medical therapy, as well as the use of a compound as

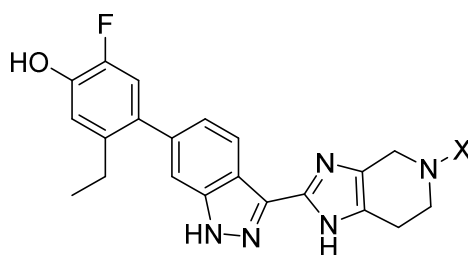
described herein in the manufacture of a formulation or medicament for treating respiratory disease in a mammal.

#### **BRIEF DESCRIPTION OF THE DRAWINGS**

Various aspects of the present invention are illustrated by reference to the  
5 accompanying drawings.

## WHAT IS CLAIMED IS:

1. A compound of formula (I):

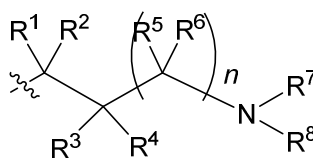


5

(I)

wherein:

X is a group of formula (II):



(II)

10

$n$  is 0 or 1;

R<sup>1</sup> is hydrogen or C<sub>1-3</sub>alkyl;

R<sup>2</sup> is hydrogen or C<sub>1-3</sub>alkyl;

R<sup>3</sup> is hydrogen or C<sub>1-3</sub>alkyl;

or R<sup>2</sup> and R<sup>3</sup> taken together form C<sub>2-4</sub>alkylene;

15

or, when  $n$  is 1, R<sup>3</sup> is selected from hydrogen, -OH, -OC<sub>1-3</sub>alkyl, halo, -C(O)OC<sub>1-3</sub>alkyl, and C<sub>1-3</sub>alkyl, wherein C<sub>1-3</sub>alkyl is optionally substituted with -OH;

R<sup>4</sup> is hydrogen or C<sub>1-3</sub>alkyl;

R<sup>5</sup> is selected from hydrogen, C<sub>1-3</sub>alkyl, -C(O)OC<sub>1-3</sub>alkyl, and phenyl;

20

or when  $n$  is 1, R<sup>2</sup> and R<sup>5</sup> taken together form C<sub>1-3</sub>alkylene;

R<sup>6</sup> is hydrogen or C<sub>1-3</sub>alkyl;

R<sup>7</sup> is hydrogen or C<sub>1-3</sub>alkyl,

or when  $n$  is 0, R<sup>2</sup> and R<sup>7</sup> taken together form C<sub>1-3</sub>alkylene, or

R<sup>4</sup> and R<sup>7</sup> taken together form C<sub>2-4</sub>alkylene or

25

C<sub>1</sub>alkylene-O-C<sub>2</sub>alkylene;

or when  $n$  is 1, R<sup>2</sup> and R<sup>7</sup> taken together form C<sub>2</sub>alkylene, optionally substituted with C<sub>1-3</sub>alkyl or R<sup>x</sup>,

or R<sup>4</sup> and R<sup>7</sup> taken together form C<sub>1-3</sub>alkylene or

-O-C<sub>2</sub>alkylene;

R<sup>8</sup> is selected from

(a) hydrogen,

(b) methyl, optionally substituted with -CN, phenyl or C<sub>3-6</sub>cycloalkyl;

5 (c) C<sub>2-6</sub>alkyl, wherein C<sub>2-6</sub>alkyl is optionally substituted with one or two substituents selected from -OH, -OC<sub>1-3</sub>alkyl, -CN, -SC<sub>1-3</sub>alkyl, phenyl, C<sub>3-6</sub>cycloalkyl, halo, and optionally, in addition with two substituents on a single carbon atom taken together to form C<sub>2-3</sub>alkylene;

10 (d) C<sub>3-6</sub>cycloalkyl, wherein C<sub>3-6</sub>cycloalkyl is optionally substituted with -OH, -CN, -OC<sub>1-3</sub>alkyl, or C<sub>1-3</sub>alkyl, wherein C<sub>1-3</sub>alkyl is optionally substituted with -OC<sub>1-3</sub>alkyl or with one or two halo,

(e) oxetanyl,

(f) tetrahydropyranyl,

(g) tetrahydrothiophenyl 1,1-dioxide, and

15 (h) phenyl,

or R<sup>7</sup> and R<sup>8</sup> taken together form C<sub>3-5</sub>alkylene or C<sub>2</sub>alkylene-O-C<sub>2</sub>alkylene;

wherein C<sub>3-5</sub>alkylene is optionally substituted with one or two R<sup>x</sup>;

R<sup>x</sup> is selected from -OH, -CN, -OC<sub>1-3</sub>alkyl, halo, phenyl, and C<sub>1-3</sub>alkyl which is optionally substituted with -OC<sub>1-3</sub>alkyl or -OH, or

20 two substituents R<sup>x</sup> taken together form C<sub>1-5</sub>alkylene or -CH<sub>2</sub>OCH<sub>2</sub>-,

or when *n* is 1 and R<sup>2</sup> and R<sup>7</sup> taken together form C<sub>2</sub>alkylene, R<sup>4</sup> and a substituent R<sup>x</sup> on C<sub>2</sub>alkylene taken together form C<sub>2</sub>alkylene;

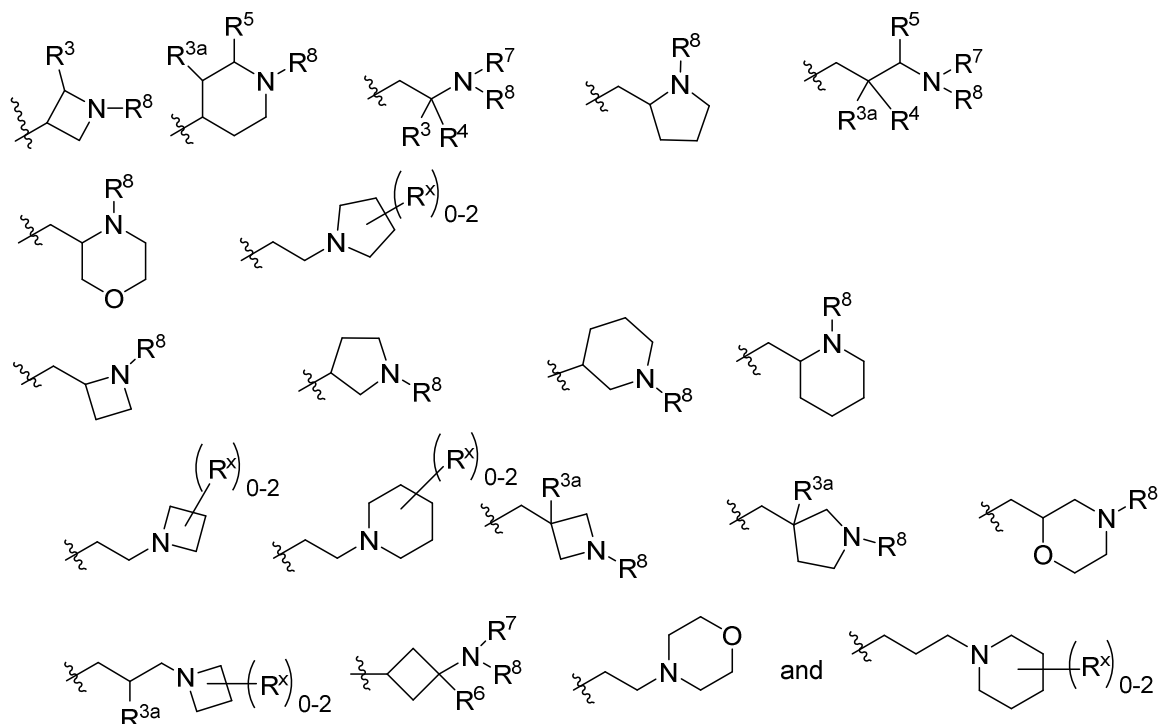
provided that two substituents R<sup>x</sup> on the same carbon atom are not both fluoro,

and

25 provided that when R<sup>x</sup> is attached to a carbon atom adjacent to a nitrogen atom, R<sup>x</sup> is not -OH, -OC<sub>1-3</sub>alkyl, or halo;

or a pharmaceutically-acceptable salt thereof.

2. The compound of Claim 1, or a pharmaceutically acceptable salt thereof, wherein X is selected from:



wherein

5  $R^3$  is hydrogen or  $C_{1-3}$ alkyl;

$R^{3a}$  is selected from hydrogen,  $-OH$ ,  $-OC_{1-3}$ alkyl, halo,  $-C(O)OC_{1-3}$ alkyl, and  $C_{1-3}$ alkyl, wherein  $C_{1-3}$ alkyl is optionally substituted with  $-OH$ ;

$R^4$  is hydrogen or  $C_{1-3}$ alkyl;

$R^5$  is selected from hydrogen,  $C_{1-3}$ alkyl,  $-C(O)OC_{1-3}$ alkyl, and phenyl;

10  $R^6$  is hydrogen or  $C_{1-3}$ alkyl;

$R^7$  is hydrogen or  $C_{1-3}$ alkyl; and

$R^8$  is selected from

(a) hydrogen,

(b) methyl, optionally substituted with  $-CN$ , phenyl or  $C_{3-6}$ cycloalkyl;

15 (c)  $C_{2-6}$ alkyl, wherein  $C_{2-6}$ alkyl is optionally substituted with one or two substituents selected from  $-OH$ ,  $-OC_{1-3}$ alkyl,  $-CN$ ,  $-SC_{1-3}$ alkyl, phenyl,  $C_{3-6}$ cycloalkyl, halo, and optionally, in addition with two substituents on a single carbon atom taken together to form  $C_{2-3}$ alkylene;

(d)  $C_{3-6}$ cycloalkyl, wherein  $C_{3-6}$ cycloalkyl is optionally substituted  
20 with  $-OH$ ,  $-CN$ ,  $-OC_{1-3}$ alkyl, or  $C_{1-3}$ alkyl, wherein  $C_{1-3}$ alkyl is optionally substituted with  $-OC_{1-3}$ alkyl or with one or two halo,

(e) oxetanyl,

- (f) tetrahydropyranyl,
- (g) tetrahydrothiophenyl 1,1-dioxide, and
- (h) phenyl.

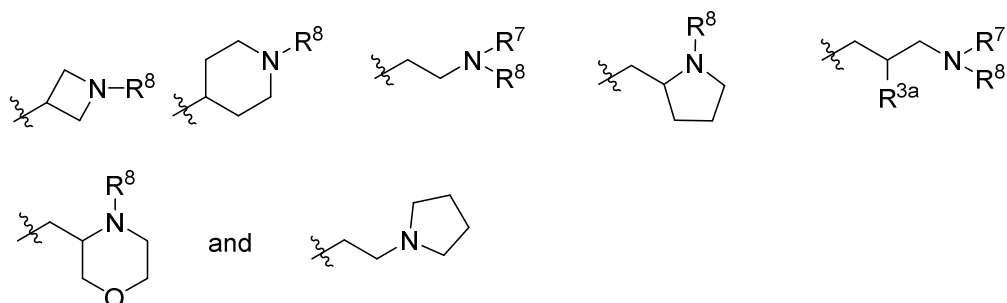
3. The compound of Claim 2, or a pharmaceutically-acceptable salt thereof, wherein:

$R^{3a}$  is selected from hydrogen,  $-OH$ ,  $-OC_{1-3}alkyl$ , halo,  $-C(O)OC_{1-3}alkyl$ , and  $C_{1-3}alkyl$ ; and

$R^8$  is selected from

- (a) hydrogen,
- (b) methyl, optionally substituted with  $C_{3-6}cycloalkyl$ ,
- (c)  $C_{2-4}alkyl$ , wherein  $C_{2-4}alkyl$  is optionally substituted with one substituent selected from  $-OH$ ,  $-OC_{1-3}alkyl$ ,  $-CN$ ,  $-SC_{1-3}alkyl$ ,  $C_{3-4}cycloalkyl$ , and halo and optionally, in addition, with two substituents on a single carbon atom taken together to form  $C_2alkylene$ ;
- (d)  $C_{3-4}cycloalkyl$ , wherein  $C_{3-4}cycloalkyl$  is optionally substituted with  $-OH$ ,  $-CN$ ,  $-OC_{1-3}alkyl$ , or  $C_{1-3}alkyl$ , wherein  $C_{1-3}alkyl$  is optionally substituted with  $-OC_{1-3}alkyl$  or with one or two halo,
- (e) oxetanyl,
- (f) tetrahydropyranyl, and
- (g) tetrahydrothiophenyl 1,1-dioxide.

4. The compound of Claim 2, or a pharmaceutically-acceptable salt thereof, wherein X is selected from:



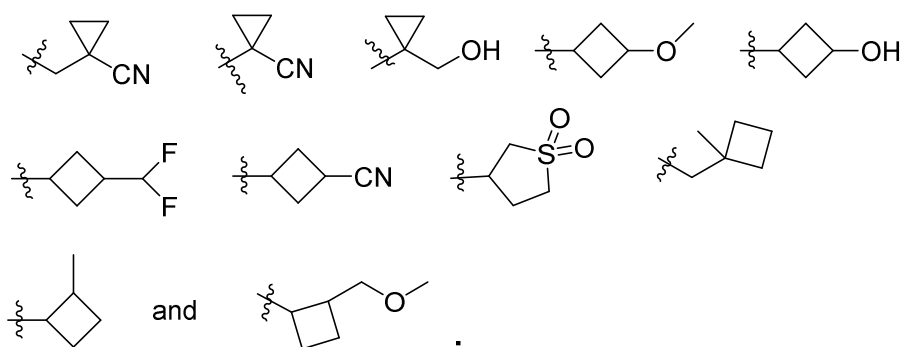
wherein  $R^{3a}$  is halo and

the pyrrolidine ring of is optionally substituted with  $C_{1-3}alkyl$ .

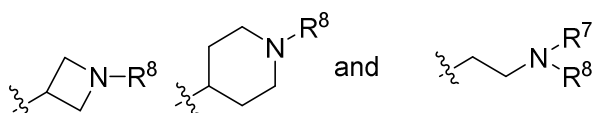
5. The compound of Claim 4, or a pharmaceutically-acceptable salt thereof, wherein  $R^8$  is selected from:

- (a) hydrogen,  
 (b) methyl, optionally substituted with C<sub>3-6</sub>cycloalkyl,  
 (c) C<sub>2-4</sub>alkyl, wherein C<sub>2-4</sub>alkyl is optionally substituted with one  
 substituent selected from -OH, -OC<sub>1-3</sub>alkyl, -CN, -SC<sub>1-3</sub>alkyl, C<sub>3-4</sub>cycloalkyl, and  
 halo and optionally, in addition, with two substituents on a single carbon atom  
 taken together to form C<sub>2</sub>alkylene;  
 (d) C<sub>3-4</sub>cycloalkyl, wherein C<sub>3-4</sub>cycloalkyl is optionally substituted  
 with -OH, -CN, -OC<sub>1-3</sub>alkyl, or C<sub>1-3</sub>alkyl, wherein C<sub>1-3</sub>alkyl is optionally  
 substituted with -OC<sub>1-3</sub>alkyl or with one or two halo,  
 (e) oxetanyl,  
 (f) tetrahydropyranyl, and  
 (g) tetrahydrothiophenyl 1,1-dioxide.

6. The compound of Claim 5, or a pharmaceutically-acceptable salt thereof,  
 wherein R<sup>8</sup> is selected from hydrogen, -CH<sub>3</sub>,  
 -C<sub>2</sub>H<sub>5</sub>, isopropyl, cyclopropyl, cyclobutyl, -CH(CH<sub>3</sub>)C<sub>2</sub>H<sub>5</sub>, -(CH<sub>2</sub>)<sub>2</sub>CN, -CH<sub>2</sub>CH<sub>2</sub>F  
 -CH<sub>2</sub>isopropyl, -CH<sub>2</sub>cyclopropyl, -(CH<sub>2</sub>)<sub>2</sub>OH, (CH<sub>2</sub>)<sub>2-3</sub>OCH<sub>3</sub>, -(CH<sub>2</sub>)<sub>2-3</sub>SCH<sub>3</sub>,  
 -(CH<sub>2</sub>)<sub>2</sub>CH(CH<sub>3</sub>)SCH<sub>3</sub>, tetrahydropyran-4-yl,

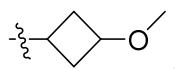


7. The compound of Claim 5, or a pharmaceutically-acceptable salt thereof,  
 wherein X is selected from:

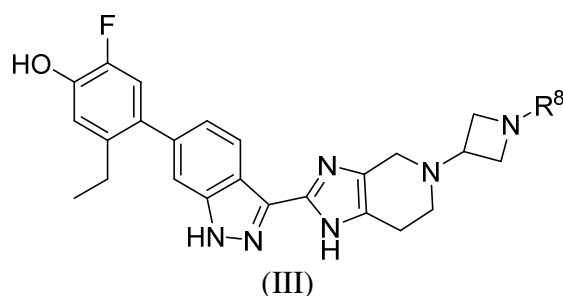


wherein:

R<sup>8</sup> is selected from hydrogen, methyl, C<sub>2-4</sub>alkyl, C<sub>3-4</sub>cycloalkyl, and



8. The compound of Claim 1, or a pharmaceutically-acceptable salt thereof, wherein the compound of formula (I) is a compound of formula (III):



5 wherein  $R^8$  is selected from:

(a) hydrogen,

(b) methyl, optionally substituted with  $C_{3-6}$ cycloalkyl,

(c)  $C_{2-4}$ alkyl, wherein  $C_{2-4}$ alkyl is optionally substituted with one substituent selected from  $-OH$ ,  $-OC_{1-3}$ alkyl,  $-CN$ ,  $-SC_{1-3}$ alkyl,  $C_{3-4}$ cycloalkyl, and halo and optionally, in addition, with two substituents on a single carbon atom taken together to form  $C_2$ alkylene;

(d)  $C_{3-4}$ cycloalkyl, wherein  $C_{3-4}$ cycloalkyl is optionally substituted with  $-OH$ ,  $-CN$ ,  $-OC_{1-3}$ alkyl, or  $C_{1-3}$ alkyl, wherein  $C_{1-3}$ alkyl is optionally substituted with  $-OC_{1-3}$ alkyl or with one or two halo,

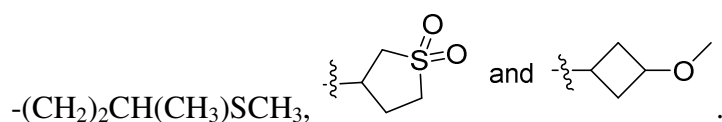
(e) oxetanyl,

(f) tetrahydropyranyl, and

(g) tetrahydrothiophenyl 1,1-dioxide.

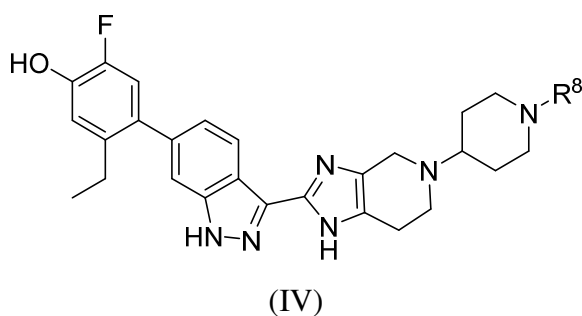
9. The compound of Claim 8, or a pharmaceutically-acceptable salt thereof, wherein  $R^8$  is selected from hydrogen,  $-CH_3$ ,

$-C_2H_5$ , isopropyl, cyclopropyl,  $-CH(CH_3)C_2H_5$ ,  $-(CH_2)_2CN$ ,  $-CH_2CH_2F$ ,  $-CH_2$ isopropyl,  $-CH_2$ cyclopropyl,  $-(CH_2)_2OH$ ,  $(CH_2)_{2-3}OCH_3$ ,  $-(CH_2)_2SCH_3$ ,



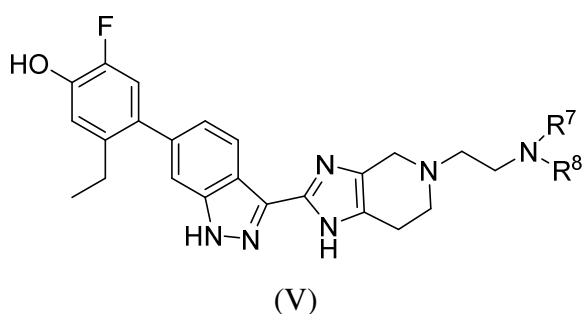
10. The compound of Claim 8, or a pharmaceutically-acceptable salt thereof, wherein  $R^8$  is selected from hydrogen, methyl,  $C_{2-4}$ alkyl, and  $C_3$ cycloalkyl.

11. The compound of Claim 1, or a pharmaceutically-acceptable salt thereof, wherein the compound of formula (I) is a compound of formula (IV):

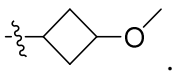


wherein  $R^8$  is selected from hydrogen, methyl,  $C_{2-4}$ alkyl, and  $C_{3-4}$ cycloalkyl.

- 5            12.     The compound of Claim 1, or a pharmaceutically-acceptable salt thereof, wherein the compound of formula (I) is a compound of formula (V):



wherein:

- 10             $R^7$  is hydrogen or  $C_{1-3}$ alkyl and  $R^8$  is methyl,  $C_{2-4}$ alkyl or .

13.     The compound of Claim 1 wherein the compound of formula (I) is selected from:

- 5-ethyl-2-fluoro-4-(3-(5-(1-methylazetidin-3-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridin-2-yl)-1H-indazol-6-yl)phenol,
- 15            4-(3-(5-(azetidin-3-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridin-2-yl)-1H-indazol-6-yl)-5-ethyl-2-fluorophenol,
- 5-ethyl-2-fluoro-4-(3-(5-(1-isopropylazetidin-3-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridin-2-yl)-1H-indazol-6-yl)phenol,
- 20            4-(3-(5-(1-(*sec*-butyl)azetidin-3-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridin-2-yl)-1H-indazol-6-yl)-5-ethyl-2-fluorophenol,

4-(3-(5-(1-cyclopropylazetidin-3-yl)-4,5,6,7-tetrahydro-1*H*-imidazo[4,5-*c*]pyridin-2-yl)-1*H*-indazol-6-yl)-5-ethyl-2-fluorophenol,

5-ethyl-2-fluoro-4-(3-(5-(1-methylpiperidin-4-yl)-4,5,6,7-tetrahydro-1*H*-imidazo[4,5-*c*]pyridin-2-yl)-1*H*-indazol-6-yl)phenol,

5 4-(3-(5-(2-(dimethylamino)ethyl)-4,5,6,7-tetrahydro-1*H*-imidazo[4,5-*c*]pyridin-2-yl)-1*H*-indazol-6-yl)-5-ethyl-2-fluorophenol,

5-ethyl-2-fluoro-4-(3-(5-(2-((3-methoxycyclobutyl)amino)ethyl)-4,5,6,7-tetrahydro-1*H*-imidazo[4,5-*c*]pyridin-2-yl)-1*H*-indazol-6-yl)phenol,

10 5-ethyl-4-(3-(5-(2-(ethyl(methyl)amino)ethyl)-4,5,6,7-tetrahydro-1*H*-imidazo[4,5-*c*]pyridin-2-yl)-1*H*-indazol-6-yl)-2-fluorophenol,

4-(3-(5-(2-(*sec*-butyl(methyl)amino)ethyl)-4,5,6,7-tetrahydro-1*H*-imidazo[4,5-*c*]pyridin-2-yl)-1*H*-indazol-6-yl)-5-ethyl-2-fluorophenol,

(*S*)-5-ethyl-2-fluoro-4-(3-(5-((1-methylpyrrolidin-2-yl)methyl)-4,5,6,7-tetrahydro-1*H*-imidazo[4,5-*c*]pyridin-2-yl)-1*H*-indazol-6-yl)phenol,

15 4-(3-(5-(3-(dimethylamino)-2-fluoropropyl)-4,5,6,7-tetrahydro-1*H*-imidazo[4,5-*c*]pyridin-2-yl)-1*H*-indazol-6-yl)-5-ethyl-2-fluorophenol,

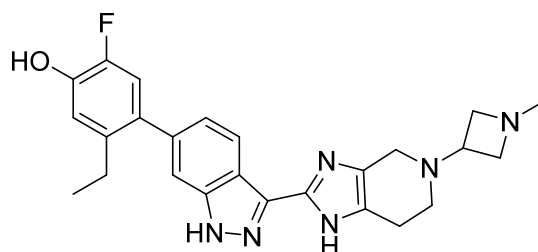
(*S*)-5-ethyl-2-fluoro-4-(3-(5-(morpholin-3-ylmethyl)-4,5,6,7-tetrahydro-1*H*-imidazo[4,5-*c*]pyridin-2-yl)-1*H*-indazol-6-yl)phenol,

20 (*R*)-5-ethyl-2-fluoro-4-(3-(5-(morpholin-3-ylmethyl)-4,5,6,7-tetrahydro-1*H*-imidazo[4,5-*c*]pyridin-2-yl)-1*H*-indazol-6-yl)phenol,

(*S*)-5-ethyl-2-fluoro-4-(3-(5-(2-(2-methylpyrrolidin-1-yl)ethyl)-4,5,6,7-tetrahydro-1*H*-imidazo[4,5-*c*]pyridin-2-yl)-1*H*-indazol-6-yl)phenol,

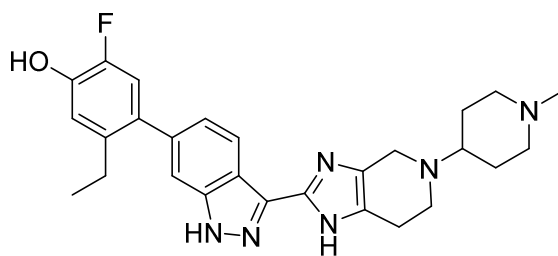
and pharmaceutically acceptable salts thereof.

25 14. A compound of formula



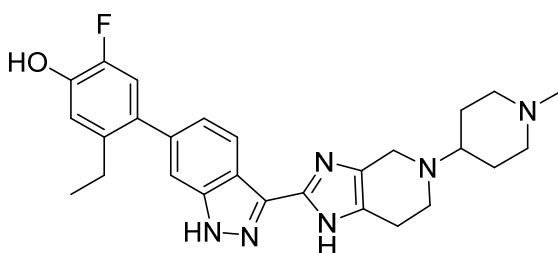
or a pharmaceutically acceptable salt thereof.

15. A compound of formula



or a pharmaceutically acceptable salt thereof.

5 16. A compound of formula



17. A crystalline hydrate of 5-ethyl-2-fluoro-4-(3-(5-(1-methylpiperidin-4-yl)-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridin-2-yl)-1H-indazol-6-yl)phenol wherein the  
10 crystalline form is characterized by a powder X-ray diffraction pattern comprising diffraction peaks at  $2\theta$  values of  $6.20\pm0.20$ ,  $9.58\pm0.20$ ,  $17.53\pm0.20$ ,  $19.28\pm0.20$ , and  $21.51\pm0.2$ .

18. The crystalline hydrate of Claim 17 wherein the powder X-ray diffraction  
15 pattern is further characterized by having two or more additional diffraction peaks at  $2\theta$  values selected from  $10.34\pm0.20$ ,  $11.54\pm0.20$ ,  $12.77\pm0.20$ ,  $13.01\pm0.20$ ,  $16.94\pm0.20$ ,  $20.61\pm0.20$ , and  $22.10\pm0.20$ .

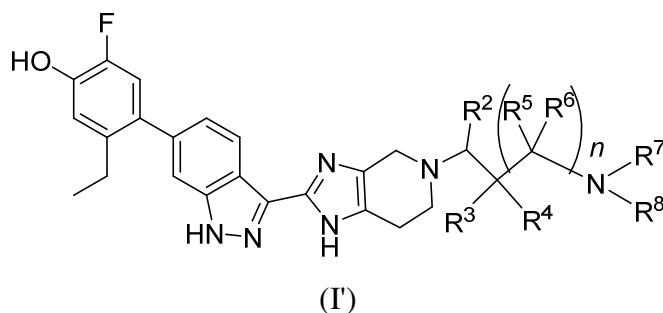
19. The crystalline hydrate of Claim 17, wherein the crystalline form is  
20 characterized by a powder X-ray diffraction pattern in which the peak positions are substantially in accordance with the peak positions of the pattern shown in Figure 1.

20. The crystalline hydrate of Claim 17 wherein the crystalline form is  
characterized by a differential scanning calorimetry trace recorded at a heating rate of  
25  $10\text{ }^{\circ}\text{C}$  per minute which shows a maximum in endothermic heat flow at a temperature between about  $206\text{ }^{\circ}\text{C}$  and about  $216\text{ }^{\circ}\text{C}$ .

21. The crystalline hydrate of Claim 20, wherein the crystalline form is characterized by a differential scanning calorimetry trace substantially in accordance with that shown in Figure 2.

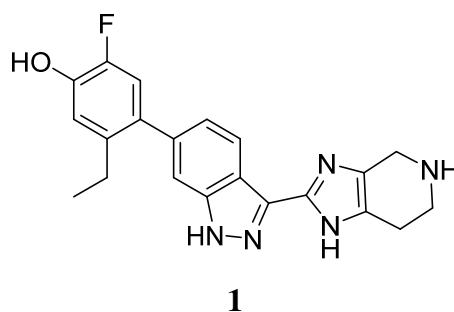
22. A pharmaceutical composition comprising a compound of any one of Claims 1 to 16 or a crystalline hydrate of claim 17 or 18 and a pharmaceutically-acceptable carrier.

23. A process of preparing a compound of formula (I):

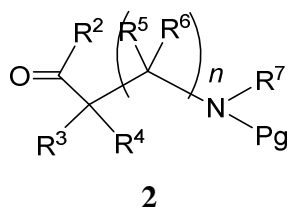


wherein  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ , and  $n$  are defined as in Claim 1, or a pharmaceutically acceptable salt thereof, the process comprising:

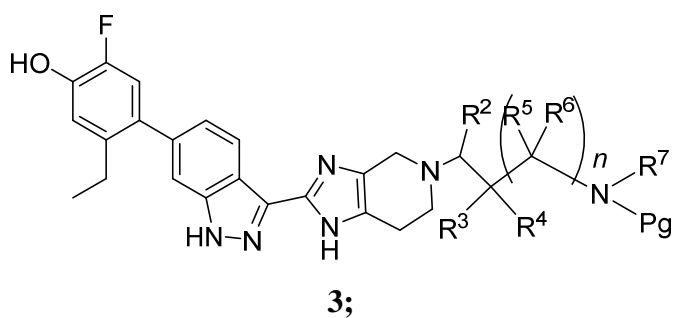
(a) reacting a compound of formula 1:



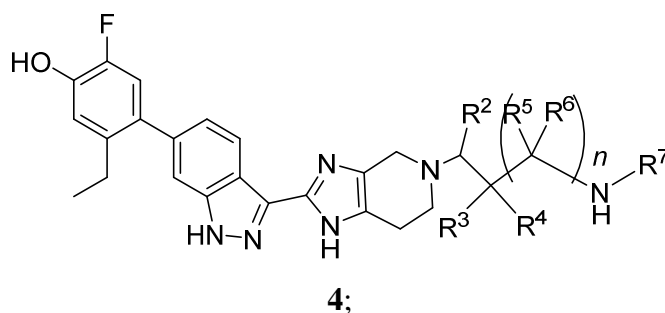
with a compound of formula 2:



wherein Pg is an amino-protecting group to provide an intermediate of formula 3:

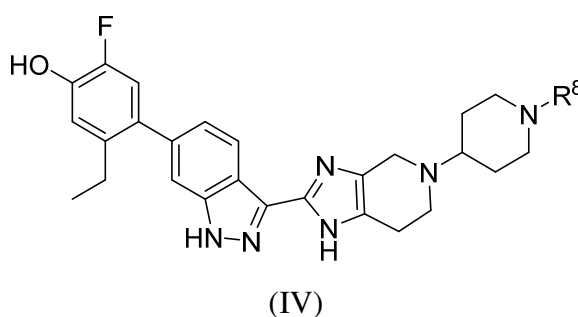


(b) deprotecting intermediate **3** to provide intermediate **4**:

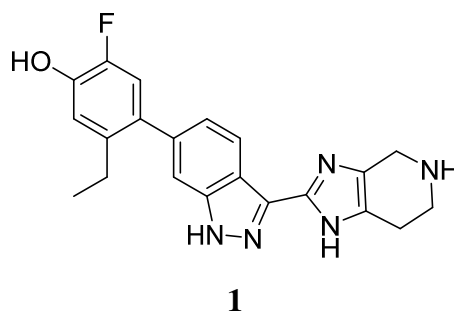


and (c) reacting intermediate **4** with  $R^{8a}-C(=O)-R^{8b}$ , wherein  $R^{8a}$  and  $R^{8b}$  are defined such that  $R^{8a}-C(H)-R^{8b}$  is  $R^8$ , to provide a compound of formula (I') or a pharmaceutically acceptable salt thereof.

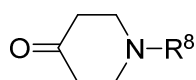
24. A process of preparing a compound of formula (IV):



or a pharmaceutically acceptable salt thereof, wherein  $R^8$  is selected from hydrogen, methyl,  $C_{2-4}$ alkyl, and  $C_{3-4}$ cycloalkyl, the process comprising reacting a compound of formula **1**:



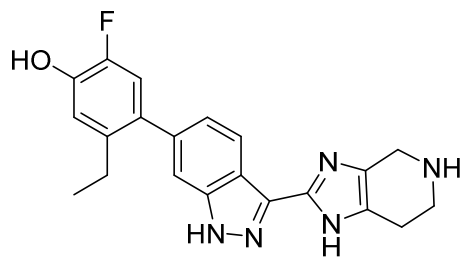
with a compound of formula **2''**:



**2''**

to provide a compound of formula (IV) or a pharmaceutically-acceptable salt thereof.

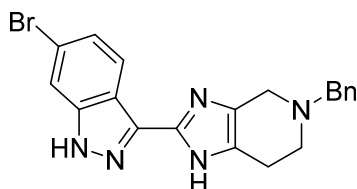
- 5            25.    The process of claim 24, wherein the compound of formula **1**:



**1**

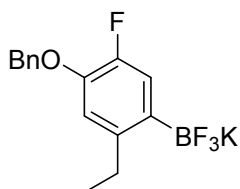
or a salt thereof, is prepared by

- (a) reacting a compound of formula **8**;



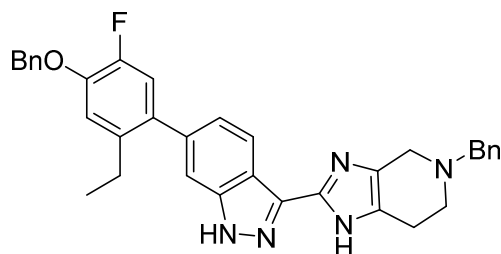
**8**

wherein Bn represents a benzyl protecting group with a compound of formula **9**:



**9**

- 15    to form a compound of formula **10**:



**10,**

and (b) deprotecting the compound of formula **10**, to provide a compound of formula **1** or a salt thereof.

26. A method of preparing the crystalline hydrate of 5-ethyl-2-fluoro-4-(3-(5-(1-methylpiperidin-4-yl)-4,5,6,7-tetrahydro-1*H*-imidazo[4,5-*c*]pyridin-2-yl)-1*H*-indazol-6-yl)phenol, the method comprising:

- 5 (a) forming a slurry of 5-ethyl-2-fluoro-4-(3-(5-(1-methylpiperidin-4-yl)-4,5,6,7-tetrahydro-1*H*-imidazo[4,5-*c*]pyridin-2-yl)-1*H*-indazol-6-yl)phenol in solvate or amorphous form in a diluent including from about 1 to about 30 % v/v water along with an organic solvent selected from methanol, tetrahydrofuran, *tert*-butyl alcohol, acetonitrile, isopropylacetate and acetone;
- 10 (b) heating the slurry at a temperature between about 40 °C and about 60 °C for between about 1 hour and about 2 days; and
- (c) isolating the crystalline hydrate from the slurry.

27. A compound of any one of Claims 1 to 16 or a crystalline hydrate of claim 17 or 18 for use in the treatment of an inflammatory or fibrotic respiratory disease in a mammal.

15

28. The compound or crystalline hydrate for use according to Claim 27 wherein the inflammatory or fibrotic respiratory disease is asthma, chronic obstructive pulmonary disease, cystic fibrosis, pneumonitis, idiopathic pulmonary fibrosis, acute lung injury, acute respiratory distress syndrome, bronchitis, emphysema or bronchiolitis obliterans.

20

29. The compound or crystalline hydrate for use according to Claim 28 wherein the inflammatory or fibrotic respiratory disease is asthma or chronic obstructive pulmonary disease.

25

30. Use of a compound of any one of Claims 1 to 16 or a crystalline hydrate of claim 17 or 18 for the manufacture of a medicament for the treatment of an inflammatory or fibrotic respiratory disease in a mammal.

5           31. The use of Claim 30 wherein the inflammatory or fibrotic respiratory disease is asthma, chronic obstructive pulmonary disease, cystic fibrosis, pneumonitis, idiopathic pulmonary fibrosis, acute lung injury, acute respiratory distress syndrome, bronchitis, emphysema or bronchiolitis obliterans.

10           32. The use of Claim 31 wherein the inflammatory or fibrotic respiratory disease is chronic obstructive pulmonary disease.

33. The compound or crystalline hydrate for use according to Claim 28 wherein the inflammatory or fibrotic respiratory disease is asthma.

15

34. The use of Claim 31 wherein the inflammatory or fibrotic respiratory disease is asthma.

20           35. The compound or crystalline hydrate for use according to Claim 28 wherein the inflammatory or fibrotic respiratory disease is bronchiolitis obliterans.

36. The compound or crystalline hydrate for use according to Claim 28 wherein the inflammatory or fibrotic respiratory disease is acute lung injury.

25           37. The compound or crystalline hydrate for use according to Claim 28 wherein the inflammatory or fibrotic respiratory disease is acute respiratory distress syndrome.

30           38. The use of Claim 31 wherein the inflammatory or fibrotic respiratory disease is bronchiolitis obliterans.

39. The use of Claim 31 wherein the inflammatory or fibrotic respiratory disease is acute lung injury.

40. The use of Claim 31 wherein the inflammatory or fibrotic respiratory disease is acute respiratory distress syndrome