

with Examples 11 and 16. In both cases the basic nitrogen atom forms a salt-bridge to Glu275.

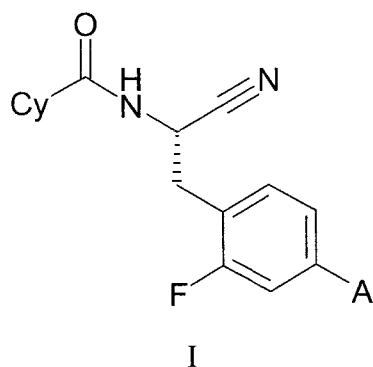
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DETAILED DESCRIPTION

It has surprisingly been found that the problem mentioned above is solved by compounds of formula I of the present disclosure.

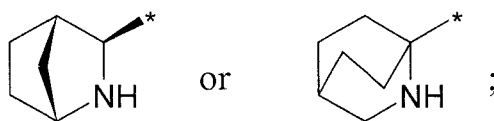
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The present disclosure therefore relates, in one aspect, to a compound of formula I or a pharmaceutically acceptable salt thereof,

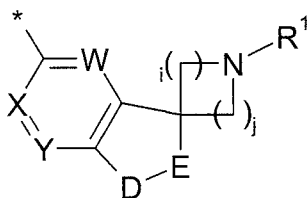


15 wherein

Cy is



A is



20

wherein

W is selected from the group consisting of CH and N;

- X is selected from the group consisting of CH and N;
 Y is selected from the group consisting of CH and N;
 with the proviso that a maximum of one of W, X and Y can be N;
 D-E is selected from the group consisting of $N(R^2)-C(O)$, CH_2CH_2 , $C(O)-O$ and CH_2-O ;
 R^2 is selected from the group consisting of H and C_{1-3} -alkyl;
 R^1 is selected from the group consisting of H, C_{1-3} -alkyl, $CH_3OCH_2CH_2-$, oxetanyl, tetrahydrofuranyl, 4-tetrahydropyranyl and 3-tetrahydropyranyl;
 i is 1, 2 or 3;
 j is 1, 2 or 3;
 with the proviso that the sum of $i+j$ is 2, 3 or 4.

In another aspect, there is provided a compound of formula I as defined herein or a pharmaceutically acceptable salt thereof for use as a medicament.

In another aspect, there is provided a compound of formula I as defined herein or a pharmaceutically acceptable salt thereof for use as a medicament for the treatment of asthma and allergic diseases, gastrointestinal inflammatory diseases, glomerulonephritis, eosinophilic diseases, chronic obstructive pulmonary disease, infection by pathogenic microbes, rheumatoid arthritis, neutrophilic diseases, cystic fibrosis (CF), non-cystic fibrosis, idiopathic pulmonary fibrosis, bronchiectasis, ANCA-associated vasculitis, lung cancer, emphysema, chronic bronchitis, acute lung injury (ALI), acute respiratory distress syndrome (ARDS), pulmonary hypertension, pulmonary arterial hypertension (PAH) and Alpha-1-antitrypsin deficiency (AATD), obesity and related inflammation, insulin resistance, diabetes, fatty liver and liver steatosis.

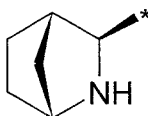
In another aspect, there is provided a pharmaceutical composition, characterised in that it contains one or more compounds of formula I as defined herein or a pharmaceutically active salt thereof.

In another aspect, there is provided use of a compound of formula I as defined herein in the manufacture of a medicament for the treatment or prevention of diseases in which DPPI activity inhibitors have a therapeutic benefit.

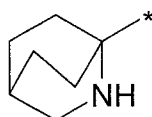
- 5 In another aspect, there is provided a pharmaceutical composition comprising additionally to a compound of formula I as defined herein, a pharmaceutically active compound selected from the group consisting of betamimetics, anticholinergics, corticosteroids, PDE4-inhibitors, LTD4-antagonists, EGFR-inhibitors, CRTH2 inhibitors, 5-LO-inhibitors, Histamine receptor antagonists, CCR9 antagonists and SYK-inhibitors, NE-inhibitors, 10 MMP9 inhibitors, MMP12 inhibitors, but also combinations of two or three active substances.

PREFERRED EMBODIMENTS

- Particularly preferred are the above compounds of formula I, or a pharmaceutically 15 acceptable salt thereof, wherein
Cy is



- Preferred are the above compounds of formula I, or a pharmaceutically acceptable salt 20 thereof, wherein
Cy is



- Preferred are the above compounds of formula I, or a pharmaceutically acceptable salt 25 thereof, wherein
 R^1 is selected from the group consisting of H, CH_3 - and oxetanyl.

Preferred are the above compounds of formula I, or a pharmaceutically acceptable salt thereof, wherein

R^2 is selected from the group consisting of H and CH_3 .

Preferred are the above compounds of formula I, or a pharmaceutically acceptable salt thereof, wherein

R^2 is H.

Preferred are the above compounds of formula I, or a pharmaceutically acceptable salt thereof, wherein

R^2 is CH_3 .

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Preferred are the above compounds of formula I, or a pharmaceutically acceptable salt thereof, wherein

D-E is CH_2-O

15 Preferred are the above compounds of formula I, or a pharmaceutically acceptable salt thereof, wherein

R^1 is selected from the group consisting of H, CH_3 and oxetanyl;

R^2 is CH_3 ;

W is selected from the group consisting of CH and N;

20 X is selected from the group consisting of CH and N;

Y is selected from the group consisting of CH;

with the proviso that a maximum of one of W, X and Y can be N;

D-E is selected from the group consisting of $N(R^2)-C(O)$, CH_2CH_2 , $C(O)-O$ and CH_2-O ;

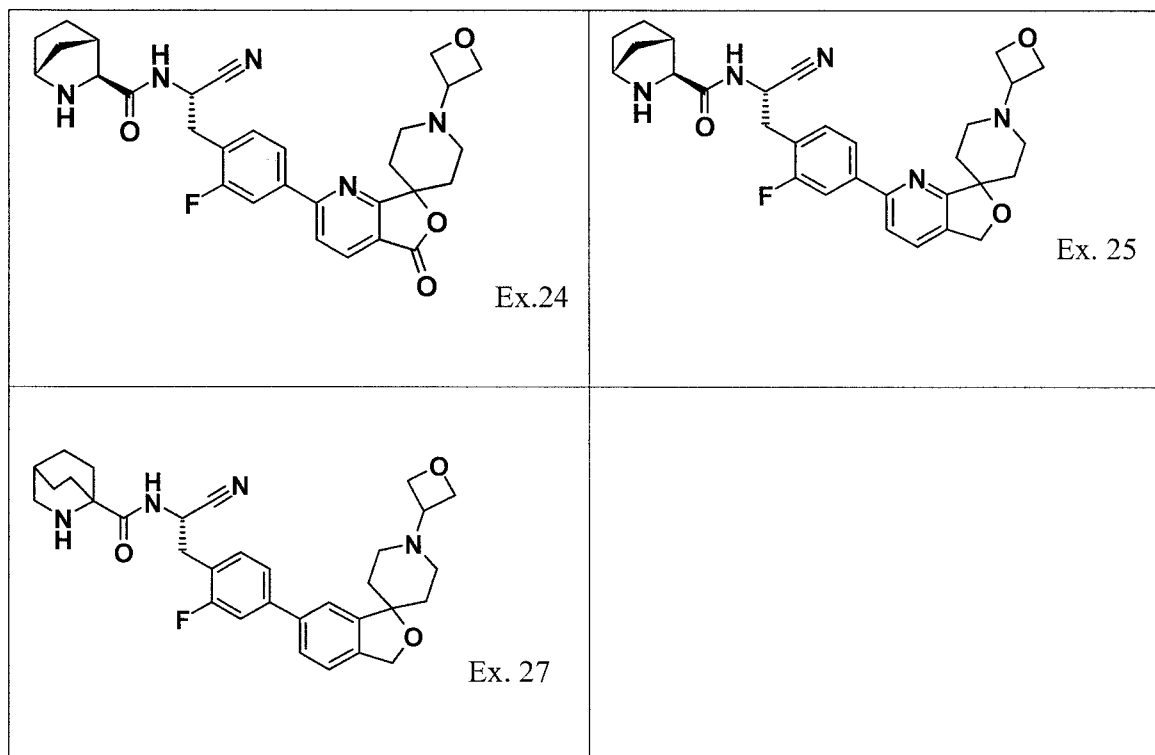
i is 1 or 2;

25 j is 1 or 2;

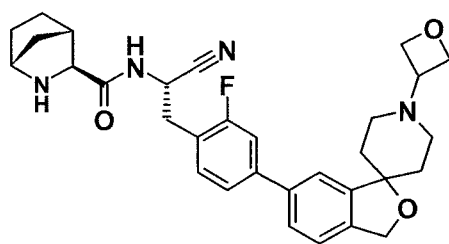
with the proviso that the sum of i+j is 2, 3 or 4.

Preferred are the above compounds of formula I, or a pharmaceutically acceptable salt thereof, wherein

30 A is selected from the group consisting of formulas A1 to A14:



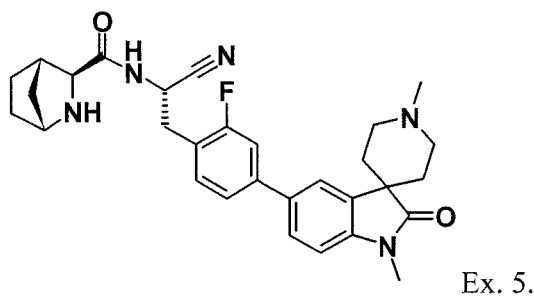
12. A compound of formula I according to claim 1, or a pharmaceutically acceptable salt thereof,



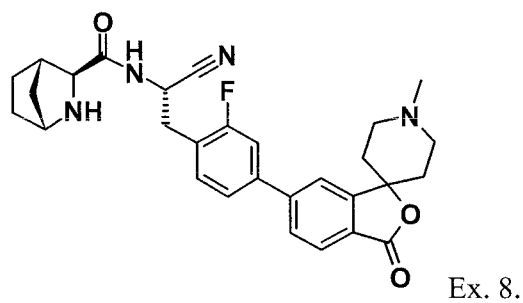
Ex. 1.

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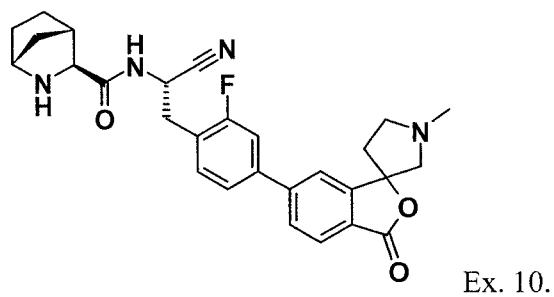
13. A compound of formula I according to claim 1, or a pharmaceutically acceptable salt thereof,



5 14. A compound of formula I according to claim 1, or a pharmaceutically acceptable salt thereof,

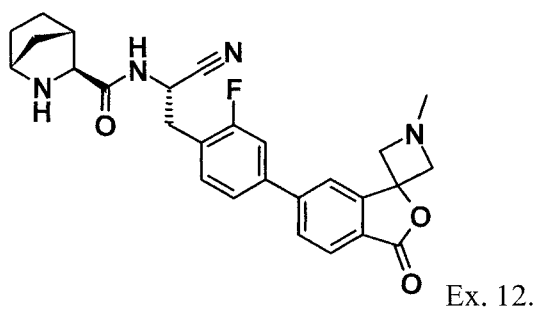


10 15. A compound of formula I according to claim 1, or a pharmaceutically acceptable salt thereof,



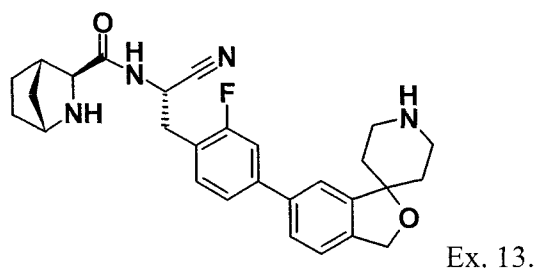
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16. A compound of formula I according to claim 1, or a pharmaceutically acceptable salt thereof,



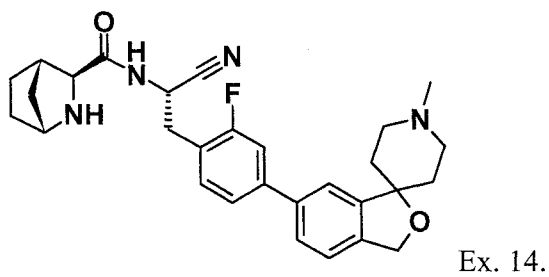
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17. A compound of formula I according to claim 1, or a pharmaceutically acceptable salt thereof,



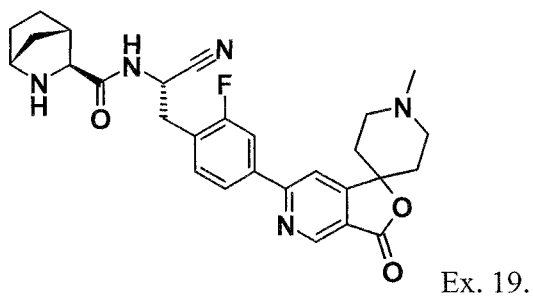
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18. A compound of formula I according to claim 1, or a pharmaceutically acceptable salt thereof,



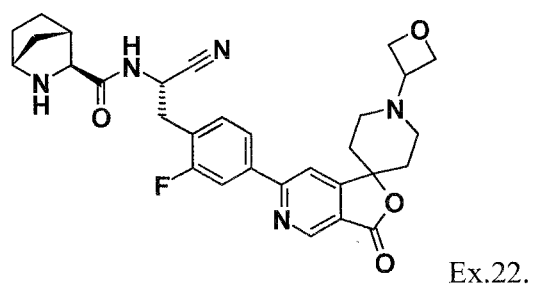
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19. A compound of formula I according to claim 1, or a pharmaceutically acceptable salt thereof,



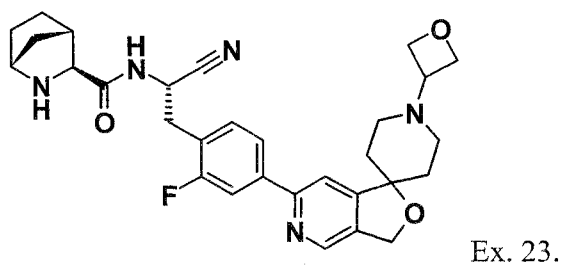
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20. A compound of formula I according to claim 1, or a pharmaceutically acceptable salt thereof,



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21. A compound of formula I according to claim 1, or a pharmaceutically acceptable salt thereof,

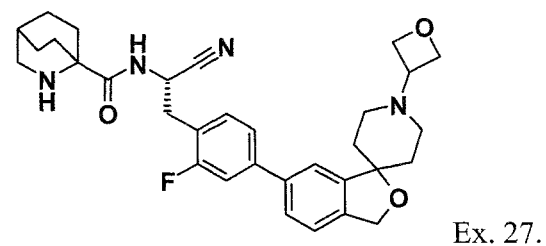


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24. A compound of formula I according to claim 1, or a pharmaceutically acceptable salt thereof,



25. A compound of formula I according to any one of claims 1 to 24 or a pharmaceutically acceptable salt thereof for use as a medicament.

26. A compound of formula I according to any one of claims 1 to 24 or a pharmaceutically acceptable salt thereof for use as a medicament for the treatment of asthma and allergic diseases, gastrointestinal inflammatory diseases, glomerulonephritis, eosinophilic diseases, chronic obstructive pulmonary disease, infection by pathogenic microbes, rheumatoid arthritis, neutrophilic diseases, cystic fibrosis (CF), non-cystic fibrosis, idiopathic pulmonary fibrosis, bronchiectasis, ANCA-associated vasculitis, lung cancer, emphysema, chronic bronchitis, acute lung injury (ALI), acute respiratory distress syndrome (ARDS), pulmonary hypertension, pulmonary arterial hypertension (PAH) and Alpha-1-antitrypsin deficiency (AATD), obesity and related inflammation, insulin resistance, diabetes, fatty liver and liver steatosis.

27. Pharmaceutical composition, characterised in that it contains one or more compounds of formula I according to any one of claims 1 to 24 or a pharmaceutically active salt thereof.

5 28. Use of a compound of formula I according to one of claims 1 to 24 in the manufacture of a medicament for the treatment or prevention of diseases in which DPPI activity inhibitors have a therapeutic benefit.

10 29. A pharmaceutical composition comprising additionally to a compound of formula I, according to any one of claims 1 to 24, a pharmaceutically active compound selected from the group consisting of betamimetics, anticholinergics, corticosteroids, PDE4-inhibitors, LTD4-antagonists, EGFR-inhibitors, CRTH2 inhibitors, 5-LO-inhibitors, Histamine receptor antagonists, CCR9 antagonists and SYK-inhibitors, NE-inhibitors, MMP9 inhibitors, MMP12 inhibitors, but also combinations of two or three active substances.