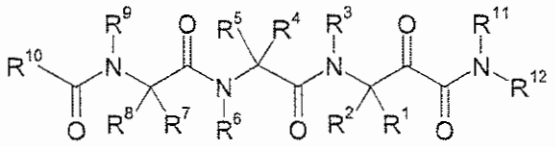
SUMMARY ~~OF THE INVENTION~~

One ~~aspect~~embodiment of the ~~invention~~present disclosure pertains to certain pyruvamide compounds (for convenience, collectively referred to herein as "PVA compounds"), as described herein. In an aspect, there is provided a compound selected from compounds of the following formula, and pharmaceutically acceptable salts, hydrates, and solvates thereof:



wherein:

$-R^1$ is independently -H or $-R^{1A}$;

$-R^{1A}$ is saturated aliphatic C_{1-6}alkyl, and is optionally substituted with one or more substituents $-R^{X1}$;

$-R^2$ is -H;

$-R^3$ is independently -H or $-R^{3A}$;

$-R^{3A}$ is saturated aliphatic C_{1-3}alkyl;

$-R^4$ is $-R^{4A}$;

$-R^{4A}$ is -Me;

$-R^5$ is -H;

$-R^6$ is -H or $-R^{6A}$;

$-R^{6A}$ is saturated aliphatic C_{1-3}alkyl;

$-R^7$ is -H, $-R^{7A}$, or $-R^{7B}$;

$-R^{7A}$ is saturated aliphatic C_{1-6}alkyl;

$-R^{7B}$ is independently $-L^{7B1}-R^{7BB}$ or $-R^{7BB}$;

$-L^{7B1}-$ is saturated aliphatic C_{1-3}alkylene;

$-R^{7BB}$ is independently $-R^{7BB1}$, $-R^{7BB2}$, $-R^{7BB3}$, or $-R^{7BB4}$;

$-R^{7BB1}$ is independently phenyl or naphthyl, and is optionally substituted with one or more substituents $-R^{X3}$;

$-R^{7BB2}$ is C_{5-10}heteroaryl, and is optionally substituted with one or more substituents $-R^{X3}$;

$-R^{7BB3}$ is C_{3-7}cycloalkyl, and is optionally substituted with one or more substituents $-R^{X2}$, or is optionally fused to a benzene ring which is optionally subtituted with one or more substituents $-R^{X3}$;

$-R^{7BB4}$ is saturated bridged C_{5-10}cycloalkyl, and is optionally substituted with one or more substituents $-R^{X2}$;

$-R^8$ is -H;

$-R^9$ is independently -H or $-R^{9A}$;

$-R^{9A}$ is saturated aliphatic C_{1-4}alkyl;

$-R^{10}$ is independently $-R^{10A}$, $-R^{10B}$, $-R^{10C}$, or $-R^{10D}$;

$-R^{10A}$ is independently phenyl or naphthyl, and is optionally substituted with one or more substituents $-R^{X3}$;

$-R^{10B}$ is C_{5-10}heteroaryl, and is optionally substituted with one or more substituents $-R^{X3}$;

$-R^{10C}$ is saturated C_{3-7}cycloalkyl, and is optionally substituted with one or more substituents $-R^{X2}$;

$-R^{10D}$ is non-aromatic C_{3-10}heterocyclyl, and is optionally substituted with one or more substituents $-R^{X2}$;

or $-R^{9}$ and $-R^{10}$, taken together with the nitrogen atom and carbon atom to which they are respectively attached, form a non-aromatic C_{5-7}heterocyclic lactam ring, which is optionally substituted with one or more substituents $-R^{X2}$, or which is optionally fused to a benzene ring which is optionally substituted with one or more substituents $-R^{X3}$;

$-R^{11}$ is independently -H, $-R^{11A}$, or $-R^{11B}$;

$-R^{11A}$ is independently $-R^{Z1}$, $-R^{Z2}$, $-R^{Z3}$, $-R^{Z4}$, $-R^{Z5}$, $-L^{Z}-R^{Z2}$, $-L^{Z}-R^{Z3}$, $-L^{Z}-R^{Z4}$, or $-L^{Z}-R^{Z5}$;

$-R^{Z1}$ is saturated aliphatic C_{1-6}alkyl, and is optionally substituted with one or more substituents $-R^{X1}$;

each $-R^{Z2}$ is saturated C_{3-7}cycloalkyl, and is optionally substituted with one or more substituents $-R^{X2}$;

each $-R^{Z3}$ is independently $-R^{Z3A}$ or $-R^{Z3B}$;

each $-R^{Z3A}$ is non-aromatic C_{3-7}heterocyclyl, and is optionally substituted with one or more substituents $-R^{X2}$;

each $-R^{Z3B}$ is saturated bridged C_{5-10}heterocyclyl, and is optionally substituted with one or more substituents $-R^{X2}$;

each $-R^{Z4}$ is independently phenyl or naphthyl, and is optionally substituted with one or more substituents $-R^{X3}$;

each $-R^{Z5}$ is C_{5-10}heteroaryl, and is optionally substituted with one or more substituents $-R^{X3}$;

each $-L^{Z}-$ is saturated aliphatic C_{1-4}alkylene;

$-R^{11B}$ is $-CR^{J1}R^{J2}-C(=O)-NR^{J3}R^{J4}$;

$-R^{J1}$ is independently -H or saturated aliphatic C_{1-4}alkyl;

$-R^{J2}$ is independently -H or saturated aliphatic C_{1-4}alkyl;

$-R^{J3}$ is independently -H, saturated aliphatic C_{1-4}alkyl, phenyl, or benzyl;

$-R^{J4}$ is independently -H, saturated aliphatic C_{1-4}alkyl, phenyl, or benzyl;

or $-NR^{J3}R^{J4}$ is a C_{3-10}heterocyclyl group, and is optionally substituted with one or more substituents $-R^{X2}$;

$-R^{12}$ is independently-H or $-R^{12A}$;

$-R^{12A}$ is saturated aliphatic C_{1-4}alkyl;

wherein each $-R^{X1}$ is independently selected from:

-F, -Cl, -Br, -I, phenyl, $-CF_3$, -OH, $-OR^S$, $-OCF_3$, $-NH_2$, $-NHR^S$, $-NR^S{}_2$, pyrrolidino, piperidino, morpholino, piperizino, N-(C_{1-4}alkyl)-piperizino, $-NHC(=O)R^S$, $-NR^SC(=O)R^S$, $-C(=O)R^S$, -C(=O)OH, $-C(=O)OR^S$, $-C(=O)NH_2$, $-C(=O)NHR^S$, $-C(=O)NR^S{}_2$, -C(=O)-pyrrolidino, -C(=O)-piperidino, -C(=O)-morpholino, -C(=O)-piperizino, -C(=O)-{N-(C_{1-4}alkyl)-piperizino}-, $-SR^S$, $-S(=O)R^S$, and $-S(=O)_2R^S$;

wherein each $-R^S$ is independently saturated aliphatic C_{1-6}alkyl, phenyl, or $-CH_2$-phenyl;

wherein each phenyl is optionally substituted with one or more groups selected from: -F, -Cl, -Br, -I, $-R^{SS}$, $-CF_3$, -OH, $-OR^{SS}$, or $-OCF_3$, wherein each $-R^{SS}$ is saturated aliphatic C_{1-4}alkyl;

and wherein each $-R^{X2}$ is independently selected from:

-F, -Cl, -Br, -I, $-R^T$, phenyl, -OH, $-OR^T$, $-C(=O)R^T$, $-NH_2$, $-NHR^T$, $-NR^T{}_2$, pyrrolidino, piperidino, morpholino, piperizino, N-(C_{1-4}alkyl)-piperizino, $-NHC(=O)R^T$, and $-NR^TC(=O)R^T$;

wherein each $-R^T$ is independently saturated aliphatic C_{1-6}alkyl, phenyl, or $-CH_2$-phenyl;

wherein each phenyl is optionally substituted with one or more groups selected from: -F, -Cl, -Br, -I, $-R^{TT}$, $-CF_3$, -OH, $-OR^{TT}$, or $-OCF_3$, wherein each $-R^{TT}$ is saturated aliphatic C_{1-4}alkyl;

and wherein each $-R^{X3}$ is independently selected from:

-F, -Cl, -Br, -I,

$-R^V$,

$-CH=CH_2$, -C≡CH, cyclopropyl,

$-CF_3$, $-CHF_2$, $-OCF_3$, $-OCHF_2$,

-CN,

$-NO_2$,

-OH, $-OR^V$,

$-L^V$-OH, $-L^V-OR^V$,

$-O-L^V$-OH, $-O-L^V-OR^V$,

$-NH_2$, $-NHR^V$, $-NR^V{}_2$,

pyrrolidino, piperidino, morpholino,

piperizino, N-(C_{1-4}alkyl)-piperizino,

-L^V-NH_2, -L^V-NHR^V, -L^V-NR^V_2,

-L^V-pyrrolidino, -L^V-piperidino, -L^V-morpholino,

-L^V-piperizino, -L^V-{N-(C_{1-4}alkyl)-piperizino},

-L^V-imidazol-2-yl, -L^V-{N-(C_{1-4}alkyl)-imidazol-2-yl},

-O-L^V-NH_2, -O-L^V-NHR^V, -O-L^V-NR^V_2,

-O-L^V-pyrrolidino, -O-L^V-piperidino, -O-L^V-morpholino,

-O-L^V-piperizino, -O-L^V-{N-(C_{1-4}alkyl)-piperizino},

-O-L^V-imidazol-2-yl, -O-L^V-{N-(C_{1-4}alkyl)-imidazol-2-yl},

-$NHC(=O)R^V$, -$NR^VC(=O)R^V$,

-$C(=O)R^V$,

-C(=O)OH, -$C(=O)OR^V$,

-$C(=O)NH_2$, -$C(=O)NHR^V$, -$C(=O)NR^V_2$,

-C(=O)-pyrrolidino, -C(=O)-piperidino, -C(=O)-morpholino,

-C(=O)-piperizino, -C(=O)-{N-(C_{1-4}alkyl)-piperizino}-,

-$NHC(=O)NH_2$, -$NHC(=O)NHR^V$, -$NHC(=O)NR^V_2$,

-NHC(=O)-pyrrolidino, -NHC(=O)-piperidino, -NHC(=O)-morpholino,

-NHC(=O)-piperizino, -NHC(=O)-{N-(C_{1-4}alkyl)-piperizino}-,

-$S(=O)_2R^V$,

-$S(=O)_2NH_2$, -$S(=O)_2NHR^V$, -$S(=O)_2NR^V_2$, and

=O;

wherein each -L^V- is saturated aliphatic C_{1-4}alkylene;

wherein each -R^V is independently saturated aliphatic C_{1-6}alkyl, phenyl, -CH_2-phenyl, C_{5-6}heteroaryl, or -CH_2-C_{5-6}heteroaryl;

wherein each phenyl is optionally substituted with one or more groups selected from: -F, -Cl, -Br, -I, -R^{VV}, -CF_3, -OH, -OR^{VV}, or -OCF_3;

wherein each C_{5-6}heteroaryl is optionally substituted with one or more groups selected from: -F, -Cl, -Br, -I, -R^{VV}, -CF_3, -OH, -OR^{VV}, or -OCF_3;

wherein each -R^{VV} is saturated aliphatic C_{1-4}alkyl;

and additionally, two adjacent groups -R^{X3} may together form -OCH_2O-, -OCH_2CH_2O-, -CH_2OCH_2- or -OCH_2CH_2-;

and additionally, two adjacent groups -R^{X3} may, together with the ring atoms to which they are attached, form a C_{5-7}carbocyclic ring or a C_{5-7}heterocyclic ring.

Another ~~aspect~~embodiment of the ~~invention~~present disclosure pertains to a composition (e.g., a pharmaceutical composition) comprising a PVA compound, as described herein, and a pharmaceutically acceptable carrier or diluent. In another aspect, there is provided a composition comprising a compound as defined herein, and a pharmaceutically acceptable carrier, diluent, or excipient.

Another ~~aspect~~embodiment of the ~~invention~~present disclosure pertains to a composition (e.g., a pharmaceutical composition) comprising the step of admixing a PVA compound, as described herein, and a pharmaceutically acceptable carrier or diluent. In another aspect, there is provided a method of preparing a composition comprising admixing a compound as defined herein and a pharmaceutically acceptable carrier, diluent, or excipient.

Another ~~aspect~~embodiment of the present ~~invention~~disclosure pertains to a method of inhibiting a dust mite Group 1 peptidase allergen (e.g., Der p 1, Der f 1, Eur m 1), *in vitro* or *in vivo*, comprising contacting a dust mite Group 1 peptidase allergen with an effective amount of a PVA compound, as described herein. In another aspect, there is provided a method of inhibiting a dust mite Group 1 peptidase allergen, *in vitro*, comprising contacting said dust mite Group 1 peptidase allergen with an effective amount of a compound as described herein.

Another ~~aspect~~embodiment of the present ~~invention~~disclosure pertains to a method of inhibiting a dust mite Group 1 peptidase allergen in a cell, *in vitro* or *in vivo*, comprising contacting the cell with an effective amount of a PVA compound, as described herein. In another aspect, there is provided a method of inhibiting a dust mite Group 1 peptidase allergen in a cell, *in vitro*, comprising contacting the cell with an effective amount of a compound as defined herein.

Another ~~aspect~~embodiment of the present ~~invention~~disclosure pertains to a method of treatment comprising administering to a subject in need of treatment a therapeutically-effective amount of a PVA compound, as described herein, preferably in the form of a pharmaceutical composition.

Another aspect of the present ~~invention~~disclosure pertains to a PVA compound as described herein for use in a method of treatment of the human or animal body by therapy.

Another ~~aspect~~embodiment of the present ~~invention~~disclosure pertains to use of a PVA compound, as described herein, in the manufacture of a medicament for use in treatment.

In one embodiment, the treatment is treatment of a disease or condition that is mediated by a dust mite Group 1 peptidase allergen.

In one embodiment, the treatment is treatment of a disease or condition that is ameliorated by the inhibition of a dust mite Group 1 peptidase allergen.

In one embodiment, the treatment is treatment of: asthma, for example, atopic asthma; allergic asthma; atopic bronchial IgE-mediated asthma; bronchial asthma; extrinsic

asthma; allergen-induced asthma; allergic asthma exacerbated by respiratory virus infection; infective asthma; infective asthma caused by bacterial infection; infective asthma caused by fungal infection; infective asthma caused by protozoal infection; or infective asthma caused by viral infection.

In one embodiment, the treatment is treatment of: bronchial hyperreactivity associated with asthma; or bronchial hyperresponsiveness associated with asthma.

In one embodiment, the treatment is treatment of: airway remodelling associated with an allergic lung disease, for example, airway remodelling associated with asthma.

In one embodiment, the treatment is treatment of: asthma co-presented with a chronic obstructive lung disease, for example, asthma co-presented with emphysema; or asthma co-presented with chronic bronchitis.

In one embodiment, the treatment is treatment of: rhinitis, for example, allergic rhinitis; perennial rhinitis; persistent rhinitis; or IgE-mediated rhinitis.

In one embodiment, the treatment is treatment of: allergic conjunctivitis, including, for example, IgE-mediated conjunctivitis.

In one embodiment, the treatment is treatment of: atopic dermatitis.

In one embodiment, the treatment is treatment of: an allergic condition which is triggered by dust mites.

In one embodiment, the treatment is treatment of: an allergic condition which is triggered by a dust mite Group 1 peptidase allergen (e.g., Der p 1, Der f 1, Eur m 1).

In one embodiment, the treatment is treatment of: canine atopy.

In one embodiment, the treatment further comprises treatment with one or more additional therapeutic agents, for example, one or more additional therapeutic agents selected from agents used, or likely to be used, in the treatment of a respiratory disease.

In another aspect, there is provided a compound as defined herein for use in a method of treatment of:

asthma, for example, atopic asthma; allergic asthma; atopic bronchial IgE-mediated asthma; bronchial asthma; extrinsic asthma; allergen-induced asthma; allergic asthma exacerbated by respiratory virus infection; infective asthma; infective asthma caused by bacterial infection; infective asthma caused by fungal infection; infective asthma caused by protozoal infection; or infective asthma caused by viral infection;

bronchial hyperreactivity associated with asthma; or bronchial hyperresponsiveness associated with asthma;

airway remodelling associated with an allergic lung disease, for example, airway remodelling associated with asthma;

asthma co-presented with a chronic obstructive lung disease, for example, asthma co-presented with emphysema; or asthma co-presented with chronic bronchitis;

rhinitis, for example, allergic rhinitis; perennial rhinitis; persistent rhinitis; or IgE-mediated rhinitis;

allergic conjunctivitis, for example, IgE-mediated conjunctivitis;

atopic dermatitis;

an allergic condition which is triggered by dust mites;

an allergic condition which is triggered by dust mite Group 1 peptidase allergen; or

canine atopy.

In another aspect, there is provided the use of a compound as defined herein in the manufacture of a medicament for the treatment of:

asthma, for example, atopic asthma; allergic asthma; atopic bronchial IgE-mediated asthma; bronchial asthma; extrinsic asthma; allergen-induced asthma; allergic asthma exacerbated by respiratory virus infection; infective asthma; infective asthma caused by bacterial infection; infective asthma caused by fungal infection; infective asthma caused by protozoal infection; or infective asthma caused by viral infection;

bronchial hyperreactivity associated with asthma; or bronchial hyperresponsiveness associated with asthma;

airway remodelling associated with an allergic lung disease, for example, airway remodelling associated with asthma;

asthma co-presented with a chronic obstructive lung disease, for example, asthma co-presented with emphysema; or asthma co-presented with chronic bronchitis;

rhinitis, for example, allergic rhinitis; perennial rhinitis; persistent rhinitis; or IgE-mediated rhinitis;

allergic conjunctivitis, for example, IgE-mediated conjunctivitis;

atopic dermatitis;

an allergic condition which is triggered by dust mites;

an allergic condition which is triggered by dust mite Group 1 peptidase allergen; or

canine atopy.

Another aspect of the present ~~invention~~disclosure pertains to a PVA compound, as described herein, for use as an acaricide.

Another aspect of the present ~~invention~~disclosure pertains to a composition comprising a PVA compound, as described herein, for use as an acaricide.

Another aspect of the present ~~invention~~disclosure pertains to an acaricide composition comprising a PVA compound, as described herein.

Another aspect of the present ~~invention~~disclosure pertains to the use of a PVA compound, as described herein, as an acaricide.

Another aspect of the present ~~invention~~disclosure pertains to a method of killing mites (e.g., dust mites), comprising exposing said mites to an effective amount of a PVA compound, as described herein.

Another aspect of the present ~~invention~~disclosure pertains to a method of controlling (e.g., limiting) a mite (e.g., dust mite) population comprising exposing mites to an effective amount of a PVA compound, as described herein.

Another ~~aspect~~embodiment of the present ~~invention~~disclosure pertains to a kit comprising (a) a PVA compound, as described herein, preferably provided as a pharmaceutical composition and in a suitable container and/or with suitable packaging; and (b) instructions for use, for example, written instructions on how to administer the compound.

Another ~~aspect~~embodiment of the present ~~invention~~disclosure pertains to a PVA compound *obtainable* by a method of synthesis as described herein, or a method comprising a method of synthesis as described herein.

Another ~~aspect~~embodiment of the present ~~invention~~disclosure pertains to a PVA compound *obtainable* by a method of synthesis as described herein, or a method comprising a method of synthesis as described herein.

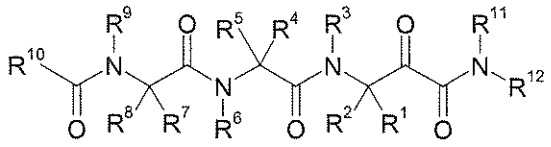
Another ~~aspect~~embodiment of the present ~~invention~~disclosure pertains to novel intermediates, as described herein, which are suitable for use in the methods of synthesis described herein.

Another ~~aspect~~embodiment of the present ~~invention~~disclosure pertains to the use of such novel intermediates, as described herein, in the methods of synthesis described herein.

As will be appreciated by one of skill in the art, features and preferred embodiments of one aspect of the ~~invention~~present disclosure will also pertain to other aspect of the ~~invention~~present disclosure.

CLAIMS

1. A compound selected from compounds of the following formula, and pharmaceutically acceptable salts, hydrates, and solvates thereof:



wherein:

$-R^1$ is independently -H or $-R^{1A}$;

$-R^{1A}$ is saturated aliphatic C_{1-6}alkyl, and is optionally substituted with one or more substituents $-R^{X1}$;

$-R^2$ is -H;

$-R^3$ is independently -H or $-R^{3A}$;

$-R^{3A}$ is saturated aliphatic C_{1-3}alkyl;

$-R^4$ is $-R^{4A}$;

$-R^{4A}$ is -Me;

$-R^5$ is -H;

$-R^6$ is -H or $-R^{6A}$;

$-R^{6A}$ is saturated aliphatic C_{1-3}alkyl;

$-R^7$ is -H, $-R^{7A}$, or $-R^{7B}$;

$-R^{7A}$ is saturated aliphatic C_{1-6}alkyl;

$-R^{7B}$ is independently $-L^{7B1}-R^{7BB}$ or $-R^{7BB}$;

$-L^{7B1}-$ is saturated aliphatic C_{1-3}alkylene;

$-R^{7BB}$ is independently $-R^{7BB1}$, $-R^{7BB2}$, $-R^{7BB3}$, or $-R^{7BB4}$;

$-R^{7BB1}$ is independently phenyl or naphthyl, and is optionally substituted with one or more substituents $-R^{X3}$;

$-R^{7BB2}$ is C_{5-10}heteroaryl, and is optionally substituted with one or more substituents $-R^{X3}$;

$-R^{7BB3}$ is C_{3-7}cycloalkyl, and is optionally substituted with one or more substituents $-R^{X2}$, or is optionally fused to a benzene ring which is optionally subtituted with one or more substituents $-R^{X3}$;

$-R^{7BB4}$ is saturated bridged C_{5-10}cycloalkyl, and is optionally substituted with one or more substituents $-R^{X2}$;

$-R^8$ is -H;

$-R^9$ is independently -H or $-R^{9A}$;

$-R^{9A}$ is saturated aliphatic C_{1-4}alkyl;

$-R^{10}$ is independently $-R^{10A}$, $-R^{10B}$, $-R^{10C}$, or $-R^{10D}$;

$-R^{10A}$ is independently phenyl or naphthyl, and is optionally substituted with one or more substituents $-R^{X3}$;

$-R^{10B}$ is C_{5-10}heteroaryl, and is optionally substituted with one or more substituents $-R^{X3}$;

$-R^{10C}$ is saturated C_{3-7}cycloalkyl, and is optionally substituted with one or more substituents $-R^{X2}$;

$-R^{10D}$ is non-aromatic C_{3-10}heterocyclyl, and is optionally substituted with one or more substituents $-R^{X2}$;

or $-R^{9}$ and $-R^{10}$, taken together with the nitrogen atom and carbon atom to which they are respectively attached, form a non-aromatic C_{5-7}heterocyclic lactam ring, which is optionally substituted with one or more substituents $-R^{X2}$, or which is optionally fused to a benzene ring which is optionally substituted with one or more substituents $-R^{X3}$;

$-R^{11}$ is independently -H, $-R^{11A}$, or $-R^{11B}$;

$-R^{11A}$ is independently $-R^{Z1}$, $-R^{Z2}$, $-R^{Z3}$, $-R^{Z4}$, $-R^{Z5}$, $-L^{Z}-R^{Z2}$, $-L^{Z}-R^{Z3}$, $-L^{Z}-R^{Z4}$, or $-L^{Z}-R^{Z5}$;

$-R^{Z1}$ is saturated aliphatic C_{1-6}alkyl, and is optionally substituted with one or more substituents $-R^{X1}$;

each $-R^{Z2}$ is saturated C_{3-7}cycloalkyl, and is optionally substituted with one or more substituents $-R^{X2}$;

each $-R^{Z3}$ is independently $-R^{Z3A}$ or $-R^{Z3B}$;

each $-R^{Z3A}$ is non-aromatic C_{3-7}heterocyclyl, and is optionally substituted with one or more substituents $-R^{X2}$;

each $-R^{Z3B}$ is saturated bridged C_{5-10}heterocyclyl, and is optionally substituted with one or more substituents $-R^{X2}$;

each $-R^{Z4}$ is independently phenyl or naphthyl, and is optionally substituted with one or more substituents $-R^{X3}$;

each $-R^{Z5}$ is C_{5-10}heteroaryl, and is optionally substituted with one or more substituents $-R^{X3}$;

each $-L^{Z}-$ is saturated aliphatic C_{1-4}alkylene;

$-R^{11B}$ is $-CR^{J1}R^{J2}-C(=O)-NR^{J3}R^{J4}$;

$-R^{J1}$ is independently -H or saturated aliphatic C_{1-4}alkyl;

$-R^{J2}$ is independently -H or saturated aliphatic C_{1-4}alkyl;

$-R^{J3}$ is independently -H, saturated aliphatic C_{1-4}alkyl, phenyl, or benzyl;

$-R^{J4}$ is independently -H, saturated aliphatic C_{1-4}alkyl, phenyl, or benzyl;

or $-NR^{J3}R^{J4}$ is a C_{3-10}heterocyclyl group, and is optionally substituted with one or more substituents $-R^{X2}$;

$-R^{12}$ is independently-H or $-R^{12A}$;

$-R^{12A}$ is saturated aliphatic C_{1-4}alkyl;

wherein each $-R^{X1}$ is independently selected from:

-F, -Cl, -Br, -I, phenyl, $-CF_3$, -OH, $-OR^S$, $-OCF_3$, $-NH_2$, $-NHR^S$, $-NR^S{}_2$, pyrrolidino, piperidino, morpholino, piperizino, N-(C_{1-4}alkyl)-piperizino, $-NHC(=O)R^S$, $-NR^SC(=O)R^S$, $-C(=O)R^S$, -C(=O)OH, $-C(=O)OR^S$, $-C(=O)NH_2$, $-C(=O)NHR^S$, $-C(=O)NR^S{}_2$, -C(=O)-pyrrolidino, -C(=O)-piperidino, -C(=O)-morpholino, -C(=O)-piperizino, -C(=O)-{N-(C_{1-4}alkyl)-piperizino}-, $-SR^S$, $-S(=O)R^S$, and $-S(=O)_2R^S$;

wherein each $-R^S$ is independently saturated aliphatic C_{1-6}alkyl, phenyl, or $-CH_2$-phenyl;

wherein each phenyl is optionally substituted with one or more groups selected from: -F, -Cl, -Br, -I, $-R^{SS}$, $-CF_3$, -OH, $-OR^{SS}$, or $-OCF_3$, wherein each $-R^{SS}$ is saturated aliphatic C_{1-4}alkyl;

and wherein each $-R^{X2}$ is independently selected from:

-F, -Cl, -Br, -I, $-R^T$, phenyl, -OH, $-OR^T$, $-C(=O)R^T$, $-NH_2$, $-NHR^T$, $-NR^T{}_2$, pyrrolidino, piperidino, morpholino, piperizino, N-(C_{1-4}alkyl)-piperizino, $-NHC(=O)R^T$, and $-NR^TC(=O)R^T$;

wherein each $-R^T$ is independently saturated aliphatic C_{1-6}alkyl, phenyl, or $-CH_2$-phenyl;

wherein each phenyl is optionally substituted with one or more groups selected from: -F, -Cl, -Br, -I, $-R^{TT}$, $-CF_3$, -OH, $-OR^{TT}$, or $-OCF_3$, wherein each $-R^{TT}$ is saturated aliphatic C_{1-4}alkyl;

and wherein each $-R^{X3}$ is independently selected from:

-F, -Cl, -Br, -I,

$-R^V$,

$-CH=CH_2$, $-C\equiv CH$, cyclopropyl,

$-CF_3$, $-CHF_2$, $-OCF_3$, $-OCHF_2$,

-CN,

$-NO_2$,

-OH, $-OR^V$,

$-L^V$-OH, $-L^V-OR^V$,

$-O-L^V$-OH, $-O-L^V-OR^V$,

$-NH_2$, $-NHR^V$, $-NR^V{}_2$,

pyrrolidino, piperidino, morpholino,
piperizino, N-(C_{1-4}alkyl)-piperizino,
-L^V-NH_2, -L^V-NHR^V, -L^V-NR^V_2,
-L^V-pyrrolidino, -L^V-piperidino, -L^V-morpholino,
-L^V-piperizino, -L^V-{N-(C_{1-4}alkyl)-piperizino},
-L^V-imidazol-2-yl, -L^V-{N-(C_{1-4}alkyl)-imidazol-2-yl},
-O-L^V-NH_2, -O-L^V-NHR^V, -O-L^V-NR^V_2,
-O-L^V-pyrrolidino, -O-L^V-piperidino, -O-L^V-morpholino,
-O-L^V-piperizino, -O-L^V-{N-(C_{1-4}alkyl)-piperizino},
-O-L^V-imidazol-2-yl, -O-L^V-{N-(C_{1-4}alkyl)-imidazol-2-yl},
-NHC(=O)R^V, -NR^VC(=O)R^V,
-C(=O)R^V,
-C(=O)OH, -C(=O)OR^V,
-C(=O)NH_2, -C(=O)NHR^V, -C(=O)NR^V_2,
-C(=O)-pyrrolidino, -C(=O)-piperidino, -C(=O)-morpholino,
-C(=O)-piperizino, -C(=O)-{N-(C_{1-4}alkyl)-piperizino}-,
-NHC(=O)NH_2, -NHC(=O)NHR^V, -NHC(=O)NR^V_2,
-NHC(=O)-pyrrolidino, -NHC(=O)-piperidino, -NHC(=O)-morpholino,
-NHC(=O)-piperizino, -NHC(=O)-{N-(C_{1-4}alkyl)-piperizino}-,
-$S(=O)_2R^V$,
-$S(=O)_2NH_2$, -$S(=O)_2NHR^V$, -$S(=O)_2NR^V_2$, and
=O;

wherein each -L^V- is saturated aliphatic C_{1-4}alkylene;

wherein each -R^V is independently saturated aliphatic C_{1-6}alkyl, phenyl, -CH_2-phenyl, C_{5-6}heteroaryl, or -CH_2-C_{5-6}heteroaryl;

wherein each phenyl is optionally substituted with one or more groups selected from: -F, -Cl, -Br, -I, -R^{VV}, -CF_3, -OH, -OR^{VV}, or -OCF_3;

wherein each C_{5-6}heteroaryl is optionally substituted with one or more groups selected from: -F, -Cl, -Br, -I, -R^{VV}, -CF_3, -OH, -OR^{VV}, or -OCF_3;

wherein each -R^{VV} is saturated aliphatic C_{1-4}alkyl;

and additionally, two adjacent groups -R^{X3} may together form -OCH_2O-, -OCH_2CH_2O-, -CH_2OCH_2- or -OCH_2CH_2-;

and additionally, two adjacent groups -R^{X3} may, together with the ring atoms to which they are attached, form a C_{5-7}carbocyclic ring or a C_{5-7}heterocyclic ring.

2. A compound according to claim 1, wherein $-R^1$ is $-R^{1A}$, wherein $-R^{1A}$ is -iPr.

3. A compound according to claim 1 or 2, wherein $-R^3$ is -H and $-R^6$ is -H.

4. A compound according to any one of claims 1 to 3, wherein $-R^7$ is $-R^{7A}$, and $-R^{7A}$ is -tBu.

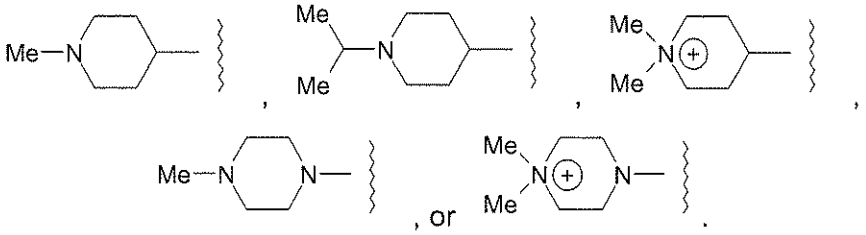
5. A compound according to any one of claims 1 to 3, wherein $-R^7$ is $-R^{7B}$; $-R^{7B}$ is $-L^{7B1}-R^{7BB}$; $-L^{7B1}-$ is $-CH_2-$; $-R^{7BB}$ is $-R^{7BB1}$; and $-R^{7BB1}$ is phenyl.

6. A compound according to any one of claims 1 to 5, wherein $-R^9$ is -H; $-R^{10}$ is $-R^{10A}$; and $-R^{10A}$ is phenyl, and is optionally substituted with one or more substituents $-R^{X3}$.

7. A compound according to any one of claims 1 to 5, wherein $-R^9$ is -H; $-R^{10}$ is $-R^{10B}$; and $-R^{10B}$ is pyridyl, and is optionally substituted with one or more substituents $-R^{X3}$.

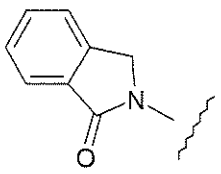
8. A compound according to any one of claims 1 to 5, wherein $-R^9$ is -H; $-R^{10}$ is $-R^{10B}$; and $-R^{10B}$ is independently indazolyl, benzimidazolyl, benzothiazolyl, quinolinyl, or isoquinolinyl, and is optionally substituted with one or more substituents $-R^{X3}$.

9. A compound according to any one of claims 1 to 5, wherein $-R^9$ is -H; $-R^{10}$ is $-R^{10D}$; and $-R^{10D}$ is independently:



, or .

10. A compound according to any one of claims 1 to 5, wherein the group $-N(R^9)-C(=O)-R^{10}$ is the following group:



.

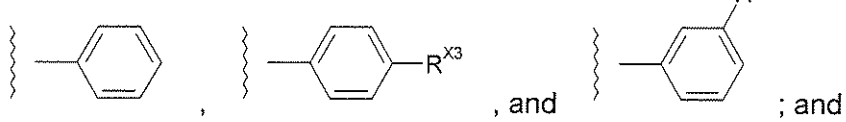
11. A compound according to any one of claims 1 to 10, wherein:

$-R^{11}$ is $-R^{11A}$;

$-R^{11A}$ is $-L^{Z}-R^{Z4}$;

$-L^{Z}-$ is $-CH_2-$ or -CH(Me)-; and

$-R^{Z4}$ is independently selected from:



; and

$-R^{12}$ is -H.

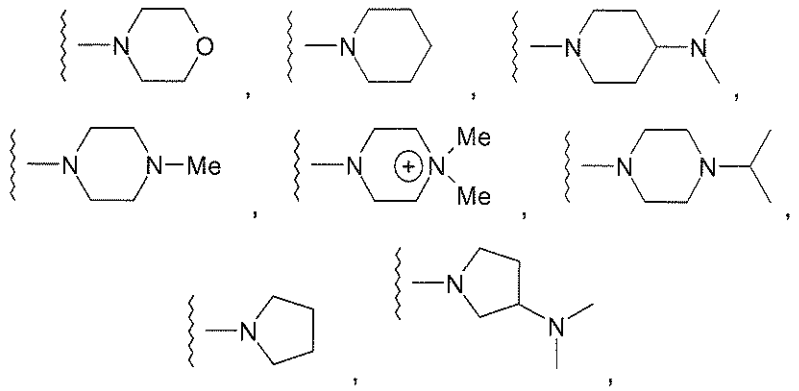
12. A compound according to any one of claims 1 to 10, wherein:

$-R^{11}$ is $-R^{11B}$;

$-R^{J1}$ is independently -H, -Me, -Et, -nPr, or -iPr;

$-R^{J2}$ is -H;

$-NR^{J3}R^{J4}$ is independently selected from:



1,2,3,4-tetrahydro-isoquinolin-2-yl, and

2,3-dihydro-1H-indol-1-yl; and

$-R^{12}$ is -H.

13. A compound according to any one of claims 1 to 12, wherein

each $-R^{X1}$, if present, is independently selected from: -F, -Cl, -Br, -I, -OH, $-OR^{S}$, $-NH_2$, $-NHR^{S}$, $-NR^{S}{}_2$, pyrrolidino, piperidino, morpholino, piperizino, N-(C_{1-4}alkyl)-piperizino, $-NHC(=O)R^{S}$, $-NR^{S}C(=O)R^{S}$, $-C(=O)NH_2$, $-C(=O)NHR^{S}$, $-C(=O)NR^{S}{}_2$, -C(=O)-pyrrolidino, -C(=O)-piperidino, -C(=O)-morpholino, -C(=O)-piperizino, and -C(=O)-{N-(C_{1-4}alkyl)-piperizino}-; and

each $-R^{X2}$, if present, is independently selected from: $-R^{T}$, -OH, $-OR^{T}$, $-C(=O)R^{T}$, $-NH_2$, $-NHR^{T}$, $-NR^{T}{}_2$, pyrrolidino, piperidino, morpholino, piperizino, N-(C_{1-4}alkyl)-piperizino, $-NHC(=O)R^{T}$, and $-NR^{T}C(=O)R^{T}$.

14. A compound according to any one of claims 1 to 13, wherein each $-R^{X3}$, if present, is independently selected from: -F, -Cl, -Br, -I, $-R^V$, -CN, -OH, $-OR^V$, $-NH_2$, $-NHR^V$, $-NR^V_2$, pyrrolidino, piperidino, morpholino, piperizino, N-(C_{1-4}alkyl)-piperizino, $-L^V-NH_2$, $-L^V-NHR^V$, $-L^V-NR^V_2$, $-L^V$-pyrrolidino, $-L^V$-piperidino, $-L^V$-morpholino, $-L^V$-piperizino, $-L^V$-{N-(C_{1-4}alkyl)-piperizino}, -C(=O)OH, $-C(=O)OR^V$, $-C(=O)NH_2$, $-C(=O)NHR^V$, $-C(=O)NR^V_2$, $-NHC(=O)NH_2$, $-S(=O)_2NH_2$, $-S(=O)_2NHR^V$, $-S(=O)_2NR^V_2$, and =O.

15. A compound according to any one of claims 1 to 13, wherein each $-R^{X3}$, if present, is independently selected from: -F, -Cl, -Br, -I, $-R^V$, -OH, $-OR^V$, $-NH_2$, $-NHR^V$, $-NR^V_2$, pyrrolidino, piperidino, morpholino, piperizino, and N-(C_{1-4}alkyl)-piperizino.

16. A compound according to claim 1, selected from the following compounds and pharmaceutically acceptable salts, hydrates, and solvates thereof:
PVA-001 to PVA-005,
PVA-008 to PVA-013,
PVA-015 to PVA-017,
PVA-019 to PVA-086,
PVA-089,
PVA-092 to PVA-099,
PVA-102 to PVA-122,
PVA-124 to PVA-138,
PVA-141-PVA-144, and
PVA-146-PVA-216.

17. A composition comprising a compound according to any one of claims 1 to 16, and a pharmaceutically acceptable carrier, diluent, or excipient.

18. A method of preparing a composition comprising admixing a compound according to any one of claims 1 to 16 and a pharmaceutically acceptable carrier, diluent, or excipient.

19. A compound according to any one of claims 1 to 16 for use in a method of treatment of the human or animal body by therapy.

20. A compound according to any one of claims 1 to 16 for use in a method of treatment of:

asthma, for example, atopic asthma; allergic asthma; atopic bronchial IgE-mediated asthma; bronchial asthma; extrinsic asthma; allergen-induced asthma; allergic asthma exacerbated by respiratory virus infection; infective asthma; infective asthma caused by bacterial infection; infective asthma caused by fungal infection; infective asthma caused by protozoal infection; or infective asthma caused by viral infection;

bronchial hyperreactivity associated with asthma; or bronchial hyperresponsiveness associated with asthma;

airway remodelling associated with an allergic lung disease, for example, airway remodelling associated with asthma;

asthma co-presented with a chronic obstructive lung disease, for example, asthma co-presented with emphysema; or asthma co-presented with chronic bronchitis;

rhinitis, for example, allergic rhinitis; perennial rhinitis; persistent rhinitis; or IgE-mediated rhinitis;

allergic conjunctivitis, for example, IgE-mediated conjunctivitis;

atopic dermatitis;

an allergic condition which is triggered by dust mites;

an allergic condition which is triggered by dust mite Group 1 peptidase allergen; or

canine atopy.

21. A compound according to claim 20, wherein the treatment further comprises treatment with one or more additional therapeutic agents selected from agents used, or likely to be used, in the treatment of a respiratory disease.

22. Use of a compound according to any one of claims 1 to 16 in the manufacture of a medicament for the treatment of:

asthma, for example, atopic asthma; allergic asthma; atopic bronchial IgE-mediated asthma; bronchial asthma; extrinsic asthma; allergen-induced asthma; allergic asthma exacerbated by respiratory virus infection; infective asthma; infective asthma caused by bacterial infection; infective asthma caused by fungal infection; infective asthma caused by protozoal infection; or infective asthma caused by viral infection;

bronchial hyperreactivity associated with asthma; or bronchial hyperresponsiveness associated with asthma;

airway remodelling associated with an allergic lung disease, for example, airway remodelling associated with asthma;

asthma co-presented with a chronic obstructive lung disease, for example, asthma co-presented with emphysema; or asthma co-presented with chronic bronchitis;

rhinitis, for example, allergic rhinitis; perennial rhinitis; persistent rhinitis; or IgE-mediated rhinitis;

allergic conjunctivitis, for example, IgE-mediated conjunctivitis;

atopic dermatitis;

an allergic condition which is triggered by dust mites;

an allergic condition which is triggered by dust mite Group 1 peptidase allergen; or

canine atopy.

23. Use according to claim 22, wherein the treatment further comprises treatment with one or more additional therapeutic agents selected from agents used, or likely to be used, in the treatment of a respiratory disease.

24. A method of inhibiting a dust mite Group 1 peptidase allergen, *in vitro,* comprising contacting said dust mite Group 1 peptidase allergen with an effective amount of a compound according to any one of claims 1 to 16.

25. A method of inhibiting a dust mite Group 1 peptidase allergen in a cell, *in vitro,* comprising contacting the cell with an effective amount of a compound according to any one of claims 1 to 16.

26. A compound according to any one of claims 1 to 16, for use as an acaricide.

27. A composition comprising a compound according to any one of claims 1 to 16, for use as an acaricide.

28. An acaricide composition comprising a compound according to any one of claims 1 to 16.

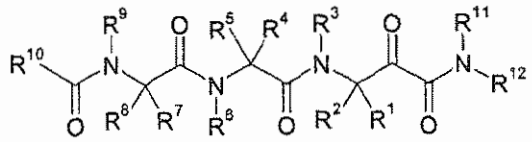
29. Use of a compound according to any one of claims 1 to 16 as an acaricide.

30. A method of killing mites, comprising exposing said mites to an effective amount of a compound according to any one of claims 1 to 16.

31. A method of controlling a mite population comprising exposing mites to an effective amount of a compound according to any one of claims 1 to 16.

CLAIMS

1. A compound selected from compounds of the following formula, and pharmaceutically acceptable salts, hydrates, and solvates thereof:



wherein:

$-R^1$ is independently -H or $-R^{1A}$;

$-R^{1A}$ is independently saturated aliphatic C_{1-6}alkyl, and is optionally substituted with one or more substituents $-R^{X1}$;

$-R^2$ is independently -H;

$-R^3$ is independently -H or $-R^{3A}$;

$-R^{3A}$ is independently saturated aliphatic C_{1-3}alkyl;

$-R^4$ is independently $-R^{4A}$;

$-R^{4A}$ is independently -Me;

$-R^5$ is independently -H;

$-R^6$ is independently -H or $-R^{6A}$;

$-R^{6A}$ is independently saturated aliphatic C_{1-3}alkyl;

$-R^7$ is independently -H, $-R^{7A}$, or $-R^{7B}$;

$-R^{7A}$ is independently saturated aliphatic C_{1-6}alkyl;

$-R^{7B}$ is independently $-L^{7B1}-R^{7BB}$ or $-R^{7BB}$;

$-L^{7B1}-$ is independently saturated aliphatic C_{1-3}alkylene;

$-R^{7BB}$ is independently $-R^{7BB1}$, $-R^{7BB2}$, $-R^{7BB3}$, or $-R^{7BB4}$;

$-R^{7BB1}$ is independently phenyl or naphthyl, and is optionally substituted with one or more substituents $-R^{X3}$;

$-R^{7BB2}$ is independently C_{5-10}heteroaryl, and is optionally substituted with one or more substituents $-R^{X3}$;

$-R^{7BB3}$ is independently C_{3-7}cycloalkyl, and is optionally substituted with one or more substituents $-R^{X2}$, or is optionally fused to a benzene ring which is optionally substituted with one or more substituents $-R^{X3}$;

-R^{7BB4} is independently saturated bridged C_{5-10}cycloalkyl, and is optionally substituted with one or more substituents -R^{X2};

-R^{8} is independently -H;

-R^{9} is independently -H or -R^{9A};

-R^{9A} is independently saturated aliphatic C_{1-4}alkyl;

-R^{10} is independently -R^{10A}, -R^{10B}, -R^{10C}, or -R^{10D};

-R^{10A} is independently phenyl or naphthyl, and is optionally substituted with one or more substituents -R^{X3};

-R^{10B} is independently C_{5-10}heteroaryl, and is optionally substituted with one or more substituents -R^{X3};

-R^{10C} is independently saturated C_{3-7}cycloalkyl, and is optionally substituted with one or more substituents -R^{X2};

-R^{10D} is independently non-aromatic C_{3-10}heterocyclyl, and is optionally substituted with one or more substituents -R^{X2};

or -R^{9} and -R^{10}, taken together with the nitrogen atom and carbon atom to which they are respectively attached, form a non-aromatic C_{5-7}heterocyclic lactam ring, which is optionally substituted with one or more substituents -R^{X2}, or which is optionally fused to a benzene ring which is optionally substituted with one or more substituents -R^{X3};

-R^{11} is independently -H, -R^{11A}, or -R^{11B};

-R^{11A} is independently -R^{Z1}, -R^{Z2}, -R^{Z3}, -R^{Z4}, -R^{Z5}, -L^{Z}-R^{Z2}, -L^{Z}-R^{Z3}, -L^{Z}-R^{Z4}, or -L^{Z}-R^{Z5};

-R^{Z1} is independently saturated aliphatic C_{1-6}alkyl, and is optionally substituted with one or more substituents -R^{X1};

each -R^{Z2} is independently saturated C_{3-7}cycloalkyl, and is optionally substituted with one or more substituents -R^{X2};

each -R^{Z3} is independently -R^{Z3A} or -R^{Z3B};

each -R^{Z3A} is independently non-aromatic C_{3-7}heterocyclyl, and is optionally substituted with one or more substituents -R^{X2};

each -R^{Z3B} is independently saturated bridged C_{5-10}heterocyclyl, and is optionally substituted with one or more substituents -R^{X2};

each -R^{Z4} is independently phenyl or naphthyl, and is optionally substituted with one or more substituents -R^{X3};

each -R^{Z5} is independently C_{5-10}heteroaryl, and is optionally substituted with one or more substituents -R^{X3};

each -L^Z- is independently saturated aliphatic C_{1-4}alkylene;

-R^{11B} is independently -$CR^{J1}R^{J2}$-C(=O)-$NR^{J3}R^{J4}$;
-R^{J1} is independently -H or saturated aliphatic C_{1-4}alkyl;
-R^{J2} is independently -H or saturated aliphatic C_{1-4}alkyl;
-R^{J3} is independently -H, saturated aliphatic C_{1-4}alkyl, phenyl, or benzyl;
-R^{J4} is independently -H, saturated aliphatic C_{1-4}alkyl, phenyl, or benzyl;
or -$NR^{J3}R^{J4}$ is independently a C_{3-10}heterocyclyl group, and is optionally substituted with one or more substituents -R^{X2};

-R^{12} is independently-H or -R^{12A};
-R^{12A} is independently saturated aliphatic C_{1-4}alkyl;

wherein each -R^{X1} is independently selected from:
-F, -Cl, -Br, -I, phenyl, -CF_3, -OH, -OR^S, -OCF_3, -NH_2, -NHR^S, -NR^S_2, pyrrolidino, piperidino, morpholino, piperizino, N-(C_{1-4}alkyl)-piperizino, -NHC(=O)R^S, -NR^SC(=O)R^S, -C(=O)R^S, -C(=O)OH, -C(=O)OR^S, -C(=O)NH_2, -C(=O)NHR^S, -C(=O)NR^S_2, -C(=O)-pyrrolidino, -C(=O)-piperidino, -C(=O)-morpholino, -C(=O)-piperizino, -C(=O)-{N-(C_{1-4}alkyl)-piperizino}-, -SR^S, -S(=O)R^S, and -$S(=O)_2R^S$;
wherein each -R^S is independently saturated aliphatic C_{1-6}alkyl, phenyl, or -CH_2-phenyl;
wherein each phenyl is optionally substituted with one or more groups selected from: -F, -Cl, -Br, -I, -R^{SS}, -CF_3, -OH, -OR^{SS}, or -OCF_3, wherein each -R^{SS} is independently saturated aliphatic C_{1-4}alkyl;

and wherein each -R^{X2} is independently selected from:
-F, -Cl, -Br, -I, -R^T, phenyl, -OH, -OR^T, -C(=O)R^T, -NH_2, -NHR^T, -NR^T_2, pyrrolidino, piperidino, morpholino, piperizino, N-(C_{1-4}alkyl)-piperizino, -NHC(=O)R^T, and -NR^TC(=O)R^T;
wherein each -R^T is independently saturated aliphatic C_{1-6}alkyl, phenyl, or -CH_2-phenyl;
wherein each phenyl is optionally substituted with one or more groups selected from: -F, -Cl, -Br, -I, -R^{TT}, -CF_3, -OH, -OR^{TT}, or -OCF_3, wherein each -R^{TT} is independently saturated aliphatic C_{1-4}alkyl.

and wherein each -R^{X3} is independently selected from:
-F, -Cl, -Br, -I,
-R^V,
-$CH=CH_2$, -C≡CH, cyclopropyl,
-CF_3, -CHF_2, -OCF_3, -$OCHF_2$,

-CN,
-NO_2,
-OH, -OR^V,
-L^V-OH, -L^V-OR^V,
-O-L^V-OH, -O-L^V-OR^V,
-NH_2, -NHR^V, -NR^V_2,
pyrrolidino, piperidino, morpholino,
piperizino, N-(C_{1-4}alkyl)-piperizino,
-L^V-NH_2, -L^V-NHR^V, -L^V-NR^V_2,
-L^V-pyrrolidino, -L^V-piperidino, -L^V-morpholino,
-L^V-piperizino, -L^V-{N-(C_{1-4}alkyl)-piperizino},
-L^V-imidazol-2-yl, -L^V-{N-(C_{1-4}alkyl)-imidazol-2-yl},
-O-L^V-NH_2, -O-L^V-NHR^V, -O-L^V-NR^V_2,
-O-L^V-pyrrolidino, -O-L^V-piperidino, -O-L^V-morpholino,
-O-L^V-piperizino, -O-L^V-{N-(C_{1-4}alkyl)-piperizino},
-O-L^V-imidazol-2-yl, -O-L^V-{N-(C_{1-4}alkyl)-imidazol-2-yl},
-NHC(=O)R^V, -NR^VC(=O)R^V,
-C(=O)R^V,
-C(=O)OH, -C(=O)OR^V,
-C(=O)NH_2, -C(=O)NHR^V, -C(=O)NR^V_2,
-C(=O)-pyrrolidino, -C(=O)-piperidino, -C(=O)-morpholino,
-C(=O)-piperizino, -C(=O)-{N-(C_{1-4}alkyl)-piperizino}-,
-NHC(=O)NH_2, -NHC(=O)NHR^V, -NHC(=O)NR^V_2,
-NHC(=O)-pyrrolidino, -NHC(=O)-piperidino, -NHC(=O)-morpholino,
-NHC(=O)-piperizino, -NHC(=O)-{N-(C_{1-4}alkyl)-piperizino}-,
-$S(=O)_2R^V$,
-$S(=O)_2NH_2$, -$S(=O)_2NHR^V$, -$S(=O)_2NR^V_2$, and
=O;

wherein each -L^V- is independently saturated aliphatic C_{1-4}alkylene;

wherein each -R^V is independently saturated aliphatic C_{1-6}alkyl, phenyl, -CH_2-phenyl, C_{5-6}heteroaryl, or -CH_2-C_{5-6}heteroaryl;

wherein each phenyl is optionally substituted with one or more groups selected from: -F, -Cl, -Br, -I, -R^{VV}, -CF_3, -OH, -OR^{VV}, or -OCF_3;

wherein each C_{5-6}heteroaryl is optionally substituted with one or more groups selected from: -F, -Cl, -Br, -I, -R^{VV}, -CF_3, -OH, -OR^{VV}, or -OCF_3;

wherein each -R^{VV} is independently saturated aliphatic C_{1-4}alkyl;

and additionally, two adjacent groups -R^{X3} may together form -OCH_2O-, -OCH_2CH_2O-, -CH_2OCH_2- or -OCH_2CH_2-;

and additionally, two adjacent groups -R^{X3} may, together with the ring atoms to which they are attached, form a C_{5-7}carbocyclic ring or a C_{5-7}heterocyclic ring.

2. A compound according to claim 1, wherein $-R^1$ is independently $-R^{1A}$.

3. A compound according to claim 1 or 2, wherein $-R^{1A}$, if present, is independently saturated aliphatic C_{1-6}alkyl.

4. A compound according to claim 1 or 2, wherein $-R^{1A}$, if present, is independently saturated aliphatic C_{3-4}alkyl.

5. A compound according to claim 1 or 2, wherein $-R^{1A}$, if present, is independently -iPr or -nBu.

6. A compound according to claim 1 or 2, wherein $-R^{1A}$, if present, is independently -iPr.

7. A compound according to any one of claims 1 to 6, wherein $-R^3$ is independently -H.

8. A compound according to any one of claims 1 to 7, wherein $-R^6$ is independently -H.

9. A compound according to any one of claims 1 to 8, wherein $-R^7$ is independently $-R^{7A}$ or $-R^{7B}$.

10. A compound according to any one of claims 1 to 8, wherein $-R^7$ is independently $-R^{7A}$.

11. A compound according to any one of claims 1 to 8, wherein $-R^7$ is independently $-R^{7B}$.

12. A compound according to any one of claims 1 to 11, wherein $-R^{7A}$, if present, is independently saturated aliphatic C_{3-4}alkyl.

13. A compound according to any one of claims 1 to 11, wherein $-R^{7A}$, if present, is independently -tBu.

14. A compound according to any one of claims 1 to 13, wherein $-R^{7B}$, if present, is independently $-L^{7B1}-R^{7BB}$ or $-R^{7BB}$.

15. A compound according to any one of claims 1 to 13, wherein $-R^{7B}$, if present, is independently $-L^{7B1}-R^{7BB}$.

16. A compound according to any one of claims 1 to 13, wherein $-R^{7B}$, if present, is independently $-R^{7BB}$.

17. A compound according to any one of claims 1 to 16, wherein $-L^{7B1}-$, if present, is independently $-CH_2-$, $-CH(Me)-$, $-C(Me)_2-$, $-CH_2CH_2-$, or $-CH_2CH_2CH_2-$.

18. A compound according to any one of claims 1 to 17, wherein $-R^{7BB}$, if present, is independently $-R^{7BB1}$.

19. A compound according to any one of claims 1 to 17, wherein $-R^{7BB}$, if present, is independently $-R^{7BB4}$.

20. A compound according to any one of claims 1 to 19, wherein $-R^{7BB1}$, if present, is independently phenyl or naphthyl, and is optionally substituted with one or more substituents $-R^{X3}$.

21. A compound according to any one of claims 1 to 19, wherein $-R^{7BB1}$, if present, is independently phenyl, and is optionally substituted with one or more substituents $-R^{X3}$.

22. A compound according to any one of claims 1 to 19, wherein $-R^{7BB1}$, if present, is independently phenyl, and is optionally substituted with one or more substituents independently selected from -F, -Cl, -Br, -I, -Me, $-CF_3$, -Ph, $-NH_2$, -NHMe, $-NMe_2$, pyrrolidino, piperidino, morpholino, piperizino, and N-(methyl)-piperizino.

23. A compound according to any one of claims 1 to 19, wherein $-R^{7BB1}$, if present, is independently phenyl.

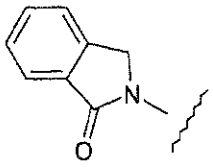
24. A compound according to any one of claims 1 to 19, wherein $-R^{7BB1}$, if present, is independently naphthyl.

25. A compound according to any one of claims 1 to 24, wherein $-R^{7BB4}$, if present, is independently adamantyl.

26. A compound according to any one of claims 1 to 25, wherein $-R^{9}$ is independently -H.

27. A compound according to any one of claims 1 to 26, wherein $-R^{9A}$, if present, is independently -Me.

28. A compound according to any one of claims 1 to 25, wherein the group $-N(R^9)-C(=O)-R^{10}$ is the following group:



29. A compound according to any one of claims 1 to 27, wherein $-R^{10}$ is independently $-R^{10A}$.

30. A compound according to any one of claims 1 to 27, wherein $-R^{10}$ is independently $-R^{10B}$.

31. A compound according to any one of claims 1 to 27, wherein $-R^{10}$ is independently $-R^{10D}$.

32. A compound according to any one of claims 1 to 27 and 29 to 31, wherein $-R^{10A}$, if present, is independently phenyl or naphthyl, and is optionally substituted with one or more substituents $-R^{X3}$.

33. A compound according to any one of claims 1 to 27 and 29 to 31, wherein $-R^{10A}$, if present, is independently phenyl, and is optionally substituted with one or more substituents $-R^{X3}$.

34. A compound according to any one of claims 1 to 27 and 29 to 31, wherein $-R^{10A}$, if present, is independently phenyl, and is optionally substituted with one or more substituents independently selected from:
-F, -Cl, -Br, -I, $-CF_3$,
$-C(=O)OH$, $-C(=O)O(C_{1-4}alkyl)$,
$-S(=O)_2(C_{1-4}alkyl)$,
phenyl, -O-phenyl,
$-NH_2$, $-NH(C_{1-4}alkyl)$, $-N(C_{1-4}alkyl)_2$,
pyrrolidino, piperidino, morpholino, piperizino, $N-(C_{1-4}alkyl)$-piperizino,
$-O-CH_2CH_2-NH_2$, $-O-CH_2CH_2-NH(C_{1-4}alkyl)$, $-O-CH_2CH_2-N(C_{1-4}alkyl)_2$,
$-O-CH_2CH_2$-pyrrolidino, $-O-CH_2CH_2$-piperidino, $-O-CH_2CH_2$-morpholino,
$-O-CH_2CH_2$-piperizino, $-O-CH_2CH_2-\{N-(C_{1-4}alkyl)$-piperizino$\}$,
$-O-CH_2$-imidazol-2-yl, and $-O-CH_2-\{N-(C_{1-4}alkyl)$-imidazol-2-yl$\}$.

35. A compound according to any one of claims 1 to 27 and 29 to 31, wherein $-R^{10A}$, if present, is independently naphthyl.

36. A compound according to any one of claims 1 to 27 and 29 to 35, wherein $-R^{10B}$, if present, is independently C_{5-10}heteroaryl, and is optionally substituted with one or more substituents $-R^{X3}$.

37. A compound according to any one of claims 1 to 27 and 29 to 35, wherein $-R^{10B}$, if present, is independently C_{5-6}heteroaryl, and is optionally substituted with one or more substituents independently selected from:
saturated aliphatic C_{1-4}alkyl,
$-NH_2$, $-NH(C_{1-4}alkyl)$, $-N(C_{1-4}alkyl)_2$,
pyrrolidino, piperidino, morpholino, piperizino, N-(C_{1-4}alkyl)-piperizino,
$-NHC(=O)(C_{1-4}alkyl)$, and
-OH.

38. A compound according to any one of claims 1 to 27 and 29 to 35, wherein $-R^{10B}$, if present, is independently pyridyl, and is optionally substituted with one or more substituents $-R^{X3}$.

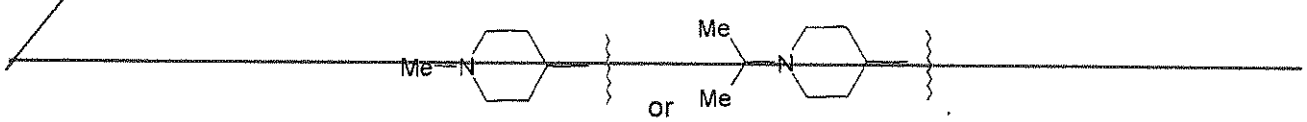
39. A compound according to any one of claims 1 to 27 and 29 to 35, wherein $-R^{10B}$, if present, is independently indazolyl, benzimidazolyl, benzothiazolyl, quinolinyl, or isoquinolinyl, and is optionally substituted with one or more substituents $-R^{X3}$.

40. A compound according to any one of claims 1 to 27 and 29 to 35, wherein $-R^{10B}$, if present, is independently indazolyl, and is optionally substituted with one or more substituents $-R^{X3}$.

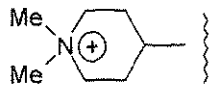
41. A compound according to any one of claims 1 to 27 and 29 to 35, wherein $-R^{10B}$, if present, is independently benzimidazolyl, and is optionally substituted with one or more substituents $-R^{X3}$.

42. A compound according to any one of claims 1 to 27 and 29 to 35, wherein $-R^{10B}$, if present, is independently quinolinyl or isoquinolinyl, and is optionally substituted with one or more substituents $-R^{X3}$.

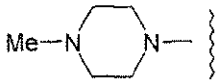
43. A compound according to any one of claims 1 to 27 and 29 to 42, wherein $-R^{10D}$ is independently:



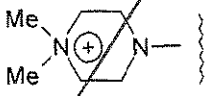
44. A compound according to any one of claims 1 to 27 and 29 to 42, wherein $-R^{10D}$ is independently:



45. A compound according to any one of claims 1 to 27 and 29 to 42, wherein $-R^{10D}$ is independently:



46. A compound according to any one of claims 1 to 27 and 29 to 42, wherein $-R^{10D}$ is independently:



47. A compound according to any one of claims 1 to 46, wherein $-R^{11}$ is independently $-R^{11A}$.

48. A compound according to any one of claims 1 to 46, wherein $-R^{11}$ is independently $-R^{11B}$.

49. A compound according to any one of claims 1 to 46, wherein $-R^{11}$ is independently -H.

50. A compound according to any one of claims 1 to 49, wherein $-R^{11A}$, if present, is independently $-R^{Z1}$, $-R^{Z2}$, $-L^{Z}-R^{Z4}$, or $-L^{Z}-R^{Z5}$.

51. A compound according to any one of claims 1 to 49, wherein $-R^{11A}$, if present, is independently $-R^{Z2}$ or $-L^{Z}-R^{Z4}$.

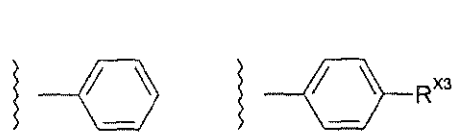
52. A compound according to any one of claims 1 to 51, wherein $-R^{Z1}$, if present, is independently -Me.

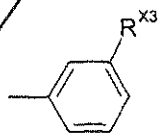
53. A compound according to any one of claims 1 to 52, wherein each $-R^{Z2}$, if present, is independently cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl.

54. A compound according to any one of claims 1 to 53, wherein each -R^{Z4}, if present, is independently phenyl or naphthyl, and is optionally substitutedwith one or more substituents -R^{X3}.

55. A compound according to any one of claims 1 to 53, wherein each -R^{Z4}, if present, is independently phenyl, and is optionally substituted with one or more substituents -R^{X3}.

56. A compound according to any one of claims 1 to 53, wherein each -R^{Z4}, if present, is independently selected from:



, and 

.

57. A compound according to any one of claims 1 to 53, wherein each -R^{Z4}, if present, is independently phenyl, and is optionally substitutedwith one or more substituents independently selected from -F, -Cl, -Br, -I, -Me, -Et, -nPr, -iPr, -tBu, -C(=O)OH, -C(=O)OMe, -C(=O)OEt, -C(=O)O(nPr), -C(=O)O(iPr), -C(=O)O(tBu), -OH, -OMe, -OEt, -CF_3, -OCF_3, -CN, -$S(=O)_2NH_2$, -$S(=O)_2NHMe$, -$C(=O)NH_2$, -C(=O)NHMe, piperizino, N-(methyl)-piperizino, -CH_2-NMe_2, -CH_2-piperidino, -$NHC(=O)NH_2$, and -OCH_2O-.

58. A compound according to any one of claims 1 to 53, wherein each -R^{Z4}, if present, is independently phenyl, and is optionally substituted at the meta- or para-position with a substituent independently selected from -C(=O)OH, -C(=O)OMe, -C(=O)OEt, -C(=O)O(nPr), -C(=O)O(iPr), -C(=O)O(tBu), -$S(=O)_2NH_2$, -$S(=O)_2NHMe$, -$C(=O)NH_2$, -C(=O)NHMe, piperizino, N-(methyl)-piperizino, -CH_2-NMe_2, -CH_2-piperidino, or -$NHC(=O)NH_2$.

59. A compound according to any one of claims 1 to 53, wherein each -R^{Z4}, if present, is independently phenyl.

60. A compound according to any one of claims 1 to 59, wherein each -R^{Z5}, if present, is independently pyridyl, and is optionally substitutedwith one or more substituents independently selected from:
-NH_2, -$NH(C_{1-4}alkyl)$, -$N(C_{1-4}alkyl)_2$,
pyrrolidino, piperidino, morpholino, piperizino, N-(C_{1-4}alkyl)-piperizino,
-$NHC(=O)(C_{1-4}alkyl)$, and
-OH.

61. A compound according to any one of claims 1 to 59, wherein each $-R^{Z5}$, if present, is independently pyridyl or pyridonyl.

62. A compound according to any one of claims 1 to 59, wherein each $-R^{Z5}$, if present, is independently imidazolyl, pyrazolyl, oxazolyl, isoxazolyl, and is optionally substituted with one or more substituents selected from C_{1-4}alkyl.

63. A compound according to any one of claims 1 to 59, wherein each $-R^{Z5}$, if present, is independently pyrazolyl, and is optionally substitutedwith one or more substituents selected from C_{1-4}alkyl.

64. A compound according to any one of claims 1 to 63, wherein each $-L^{Z}-$, if present, is independently $-CH_2-$ or -CH(Me)-.

65. A compound according to any one of claims 1 to 64, wherein $-R^{J1}$, if present, is independently -H, -Me, or -Et.

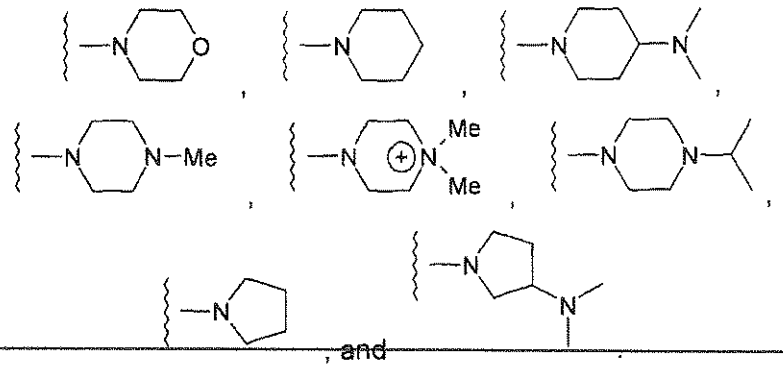
66. A compound according to any one of claims 1 to 64, wherein $-R^{J1}$, if present, is independently -H.

67. A compound according to any one of claims 1 to 66, wherein $-R^{J2}$, if present, is independently -H.

68. A compound according to any one of claims 1 to 67, wherein $-NR^{J3}R^{J4}$, if present, is independently a C_{3-10}heterocyclyl group, and is optionally substituted with one or more substituents $-R^{X2}$.

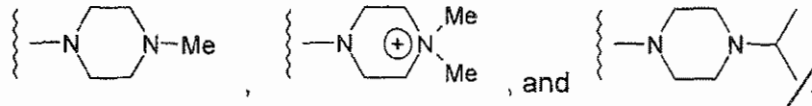
69. A compound according to any one of claims 1 to 67, wherein $-NR^{J3}R^{J4}$, if present, is independently 1,2,3,4-tetrahydro-isoquinolin-2-yl or 2,3-dihydro-1H-indol-1-yl.

70. A compound according to any one of claims 1 to 67, wherein $-NR^{J3}R^{J4}$, if present, is independently selected from:

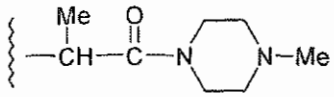


, and .

71. A compound according to any one of claims 1 to 67, wherein $-NR^{J3}R^{J4}$, if present, is independently selected from:



72. A compound according to any one of claims 1 to 64, wherein $-R^{1B}$, if present, is independently:



73. A compound according to any one of claims 1 to 72, wherein $-R^{12}$ is independently -H.

74. A compound according to any one of claims 1 to 73, wherein each $-R^{X1}$, if present, is independently selected from:
-F, -Cl, -Br, -I, -OH, $-OR^S$, $-NH_2$, $-NHR^S$, $-NR^S{}_2$, pyrrolidino, piperidino, morpholino, piperizino, N-(C_{1-4}alkyl)-piperizino, $-NHC(=O)R^S$, $-NR^SC(=O)R^S$, $-C(=O)NH_2$, $-C(=O)NHR^S$, $-C(=O)NR^S{}_2$, -C(=O)-pyrrolidino, -C(=O)-piperidino, -C(=O)-morpholino, -C(=O)-piperizino, and -C(=O)-{N-(C_{1-4}alkyl)-piperizino}-.

75. A compound according to any one of claims 1 to 73, wherein each $-R^{X1}$, if present, is independently selected from:
-OH, $-OR^S$, $-NH_2$, $-NHR^S$, $-NR^S{}_2$, pyrrolidino, piperidino, morpholino, piperizino, N-(C_{1-4}alkyl)-piperizino, $-NHC(=O)R^S$, $-NR^SC(=O)R^S$, $-C(=O)NH_2$, $-C(=O)NHR^S$, $-C(=O)NR^S{}_2$, -C(=O)-pyrrolidino, -C(=O)-piperidino, -C(=O)-morpholino, -C(=O)-piperizino, and -C(=O)-{N-(C_{1-4}alkyl)-piperizino}-.

76. A compound according to any one of claims 1 to 75, wherein each $-R^S$, if present, is independently saturated aliphatic C_{1-4}alkyl.

77. A compound according to any one of claims 1 to 76, wherein each $-R^{X2}$, if present, is independently selected from:
$-R^T$, -OH, $-OR^T$, $-C(=O)R^T$, $-NH_2$, $-NHR^T$, $-NR^T{}_2$, pyrrolidino, piperidino, morpholino, piperizino, N-(C_{1-4}alkyl)-piperizino, $-NHC(=O)R^T$, and $-NR^TC(=O)R^T$.

78. A compound according to any one of claims 1 to 77, wherein each $-R^T$, if present, is independently saturated aliphatic C_{1-4}alkyl.

79. A compound according to any one of claims 1 to 78, wherein each $-R^{X3}$, if present, is independently selected from:
-F, -Cl, -Br, -I,
$-R^{V}$,
-OH, $-OR^{V}$,
$-NH_2$, $-NHR^{V}$, $-NR^{V}_2$,
pyrrolidino, piperidino, morpholino,
piperizino, and N-(C_{1-4}alkyl)-piperizino.

80. A compound according to any one of claims 1 to 79, wherein each $-L^{V}-$, if present, is independently $-CH_2CH_2-$, $-CH_2CH_2CH_2-$, or $-CH_2CH_2CH_2CH_2-$.

81. A compound according to any one of claims 1 to 80, wherein each $-R^{V}$, if present, is independently saturated aliphatic C_{1-4}alkyl.

82. A composition comprising a compound according to any one of claims 1 to 81, and a pharmaceutically acceptable carrier, diluent, or excipient.

83. A method of preparing a composition comprising admixing a compound according to any one of claims 1 to 81 and a pharmaceutically acceptable carrier, diluent, or excipient.

84. A compound according to any one of claims 1 to 81 for use in a method of treatment of the human or animal body by therapy.

85. A compound according to any one of claims 1 to 81 for use in a method of treatment of:

asthma, for example, atopic asthma; allergic asthma; atopic bronchial IgE-mediated asthma; bronchial asthma; extrinsic asthma; allergen-induced asthma; allergic asthma exacerbated by respiratory virus infection; infective asthma; infective asthma caused by bacterial infection; infective asthma caused by fungal infection; infective asthma caused by protozoal infection; or infective asthma caused by viral infection;

bronchial hyperreactivity associated with asthma; or bronchial hyperresponsiveness associated with asthma;

airway remodelling associated with an allergic lung disease, for example, airway remodelling associated with asthma;

asthma co-presented with a chronic obstructive lung disease, for example, asthma co-presented with emphysema; or asthma co-presented with chronic bronchitis;

rhinitis, for example, allergic rhinitis; perennial rhinitis; persistent rhinitis; or IgE-mediated rhinitis;

allergic conjunctivitis, for example, IgE-mediated conjunctivitis;

atopic dermatitis;

an allergic condition which is triggered by dust mites;

an allergic condition which is triggered by dust mite Group 1 peptidase allergen (e.g., Der p 1, Der f 1, Eur m 1); or

canine atopy.

86. Use of a compound according to any one of claims 1 to 81 in the manufacture of a medicament for the treatment of:

asthma, for example, atopic asthma; allergic asthma; atopic bronchial IgE-mediated asthma; bronchial asthma; extrinsic asthma; allergen-induced asthma; allergic asthma exacerbated by respiratory virus infection; infective asthma; infective asthma caused by bacterial infection; infective asthma caused by fungal infection; infective asthma caused by protozoal infection; or infective asthma caused by viral infection;

bronchial hyperreactivity associated with asthma; or bronchial hyperresponsiveness associated with asthma;

airway remodelling associated with an allergic lung disease, for example, airway remodelling associated with asthma;

asthma co-presented with a chronic obstructive lung disease, for example, asthma co-presented with emphysema; or asthma co-presented with chronic bronchitis;

rhinitis, for example, allergic rhinitis; perennial rhinitis; persistent rhinitis; or IgE-mediated rhinitis;

allergic conjunctivitis, for example, IgE-mediated conjunctivitis;

atopic dermatitis;

an allergic condition which is triggered by dust mites;

an allergic condition which is triggered by dust mite Group 1 peptidase allergen (e.g., Der p 1, Der f 1, Eur m 1); or

canine atopy.

87. A method of treatment, comprising administering to a subject in need of treatment a therapeutically-effective amount of a compound according to any one of claims 1 to 81, wherin the treatment is treatment of:

asthma, for example, atopic asthma; allergic asthma; atopic bronchial IgE-mediated asthma; bronchial asthma; extrinsic asthma; allergen-induced asthma; allergic asthma exacerbated by respiratory virus infection; infective asthma; infective asthma caused by bacterial infection; infective asthma caused

by fungal infection; infective asthma caused by protozoal infection; or infective asthma caused by viral infection;

bronchial hyperreactivity associated with asthma; or bronchial hyperresponsiveness associated with asthma;

airway remodelling associated with an allergic lung disease, for example, airway remodelling associated with asthma;

asthma co-presented with a chronic obstructive lung disease, for example, asthma co-presented with emphysema; or asthma co-presented with chronic bronchitis;

rhinitis, for example, allergic rhinitis; perennial rhinitis; persistent rhinitis; or IgE-mediated rhinitis;

allergic conjunctivitis, for example, IgE-mediated conjunctivitis;

atopic dermatitis;

an allergic condition which is triggered by dust mites;

an allergic condition which is triggered by dust mite Group 1 peptidase allergen (e.g., Der p 1, Der f 1, Eur m 1); or

canine atopy.

88. A compound according to claim 85, use according to claim 86, or a method according to claim 87, wherein the treatment further comprises treatment with one or more additional therapeutic agents selected from agents used, or likely to be used, in the treatment of a respiratory disease.

89. A method of inhibiting a dust mite Group 1 peptidase allergen (e.g., Der p 1, Der f 1, Eur m 1), *in vitro* or *in vivo,* comprising contacting a dust mite Group 1 peptidase allergen (e.g., Der p 1, Der f 1, Eur m 1) with an effective amount of a compound according to any one of claims 1 to 81.

90. A method of inhibiting a dust mite Group 1 peptidase allergen (e.g., Der p 1, Der f 1, Eur m 1) in a cell, *in vitro* or *in vivo,* comprising contacting the cell with an effective amount of a compound according to any one of claims 1 to 81.

91. A compound according to any one of claims 1 to 81, for use as an acaricide.

92. A composition comprising a compound according to any one of claims 1 to 81, for use as an acaricide.

93. An acaricide composition comprising a compound according to any one of claims 1 to 81.

94. Use of a compound according to any one of claims 1 to 81 as an acaricide.

95. A method of killing mites (e.g., dust mites), comprising exposing said mites to an effective amount of a compound according to any one of claims 1 to 81.

96. A method of controlling (e.g., limiting) a mite (e.g., dust mite) population comprising exposing mites to an effective amount of a compound according to any one of claims 1 to 81.