694 (1994), Molecular Vision 18: 194 (2012)). Reducing or eliminating aldehydes should thus ameliorate the symptoms and slow the progression of these pathological conditions.

MDA, HNE and other toxic aldehydes are generated by a myriad of metabolic mechanisms involving: fatty alcohols, sphingolipids, glycolipids, phytol, fatty acids, arachidonic acid metabolism (Rizzo (2007)), polyamine metabolism (Wood *et al.* (2006)), lipid peroxidation, oxidative metabolism (Buddi *et al.* (2002), Zhou *et al.* (2005)), and glucose metabolism (Pozzi *et al.* (2009)). Aldehydes can cross link with primary amino groups and other chemical moieties on proteins, phospholipids, carbohydrates, and DNA, leading in many cases to toxic consequences, such as mutagenesis and carcinogenesis (Marnett (2002)). MDA is associated with diseased corneas, keratoconus, bullous and other keratopathy, and Fuch's endothelial dystrophy corneas (Buddi *et al.* (2002)). Also, skin disorders, *e.g.*, Sjögren-Larsson Syndrome, are likely connected with the accumulation of fatty aldehydes such as octadecanal and hexadecanal (Rizzo *et al.* (2010)). Further, increased lipid peroxidation and resultant aldehyde generation are associated with the toxic effects of blister agents (Sciuto *et al.* (2004) and Pal *et al.* (2009)).

There has been no suggestion in the art for treating the various conditions associated with toxic aldehydes by the administration of small molecule therapeutics acting as a scavenger for aldehydes, such as MDA and/or HNE. Thus, there is a need for treating, preventing, and/or reducing a risk of a disease or disorder in which aldehyde toxicity is implicated in the pathogenesis. The present invention addresses such a need.

SUMMARY ~~OF THE INVENTION~~

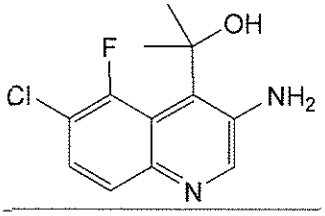
The ~~invention~~ present disclosure relates to a method of treating, preventing, and/or reducing a risk of a disease, disorder, or condition in which aldehyde toxicity is implicated in the pathogenesis, by administering a compound (*e.g.*, a primary amine compound) described herein. The present disclosure ~~invention~~ also relates to the use of a compound (*e.g.*, a primary amine compound) described herein in the manufacture of a medicament for the treatment, prevention, and/or reduction of a risk of a disease, disorder, or condition in which aldehyde toxicity is implicated in the pathogenesis, or the use of a compound (*e.g.*, a primary amine compound) described herein in treating, preventing, and/or reducing a risk of a disease, disorder, or condition in which aldehyde toxicity is implicated in the pathogenesis.

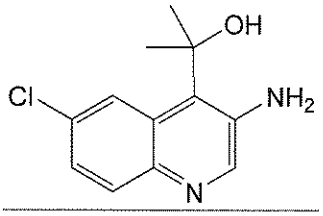
In one aspect of the present disclosure, there is provided a use of a compound comprising a primary amine in the manufacture of a medicament for treating, preventing, or

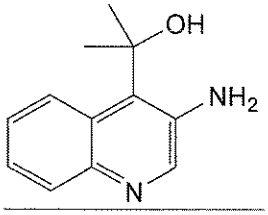
reducing a risk of a disease, disorder, condition, or cosmetic indication in which aldehyde toxicity is implicated in a subject in need thereof, provided that the disease, disorder, or condition is not macular degeneration or Stargardt disease.

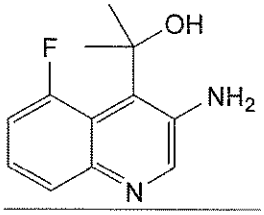
In another aspect of the present disclosure, there is provided a use of a compound comprising a primary amine in the manufacture of a medicament for treating, preventing, or reducing a risk of a disease, disorder, condition, or cosmetic indication associated with aldehyde toxicity, provided that the disease, disorder, or condition is not macular degeneration or Stargardt disease.

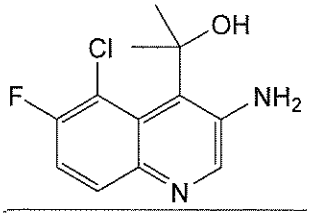
In a further aspect of the present disclosure, there is provided a use of an amine compound in the manufacture of a medicament for treating, preventing, or reducing a risk of a disease, disorder, or condition in which aldehyde toxicity is implicated in a subject in need thereof, wherein the amine compound is selected from the group consisting of:

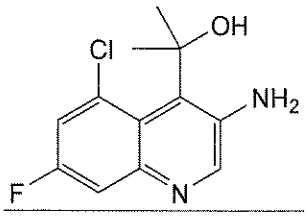


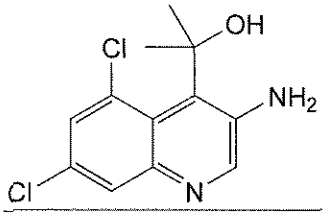


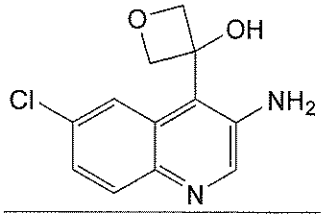


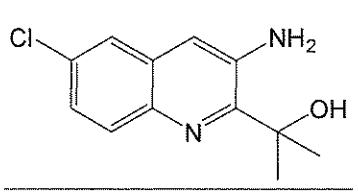
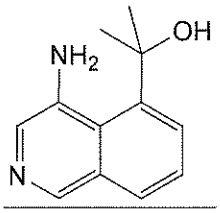
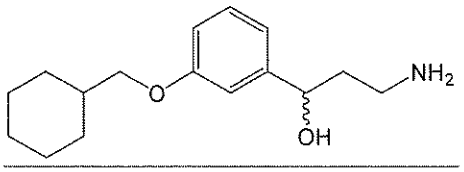
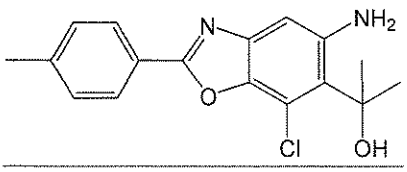
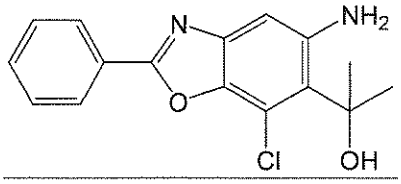
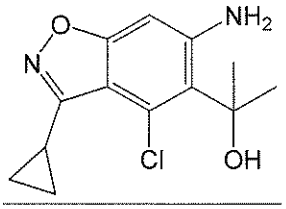
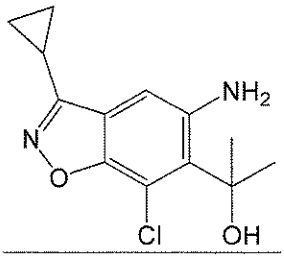
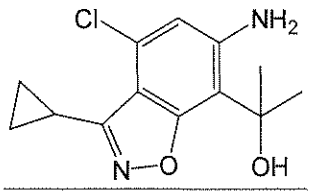
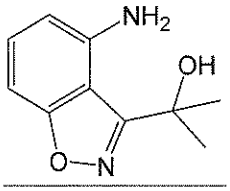
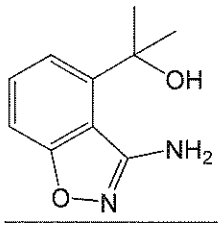
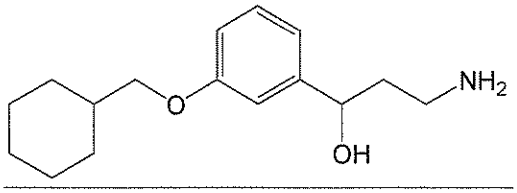
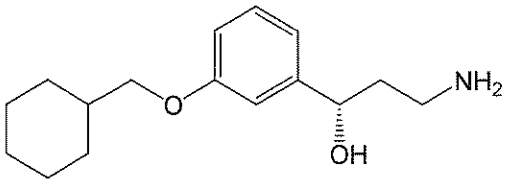
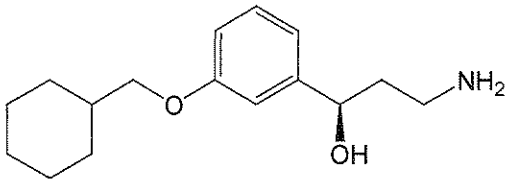
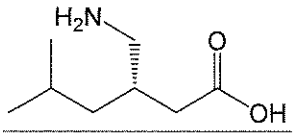
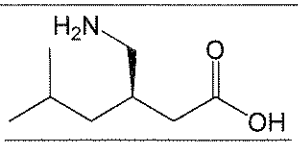










, and

or a pharmaceutically acceptable salt thereof, and wherein the disease, disorder, or condition is selected from the group consisting of:

an ocular disorder selected from the group consisting of dry eye syndrome, cataracts, keratoconus, bullous and other keratopathy, Fuch's endothelial dystrophy, allergic conjunctivitis, ocular cicatricial pemphigoid, conditions associated with PRK healing and

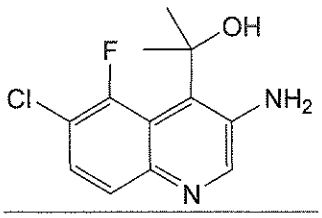
other corneal healing, conditions associated with tear lipid degradation or lacrimal gland dysfunction, uveitis, sclcritis, ocular Stevens Johnson Syndrome, and ocular rosacea,

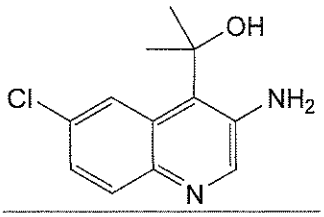
a skin disease, disorder, or condition selected from the group consisting of psoriasis, topical (discoid) lupus, contact dermatitis, atopic dermatitis, allergic dermatitis, radiation dermatitis, acne vulgaris, Sjogren-Larsson Syndrome and other ichthyosis, and a cosmetic indication selected from the group consisting of solar elastosis/wrinkles, skin tone firmness,puffiness, eczema, smoke or irritant induced skin changes, dermal incision, and a skin condition associated with burn or wound,

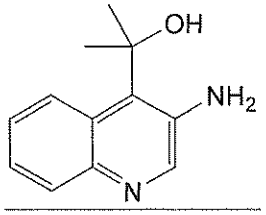
a condition associated with the toxic effects of blister agents or burns from alkali agents, and

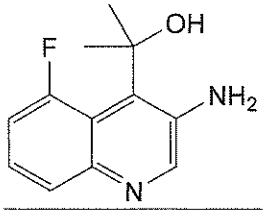
an autoimmune, immune-mediated, inflammatory, cardiovascular, or neurological disease, diabetes, metabolic syndrome, and a fibrotic disease.

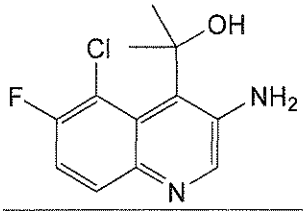
In another aspect of the present disclosure, there is provided a use of an amine compound in the manufacture of a medicament for treating, preventing, or reducing a risk of a disease, disorder, or condition associated with aldehyde toxicity, wherein the amine compound is selected from the group consisting of:

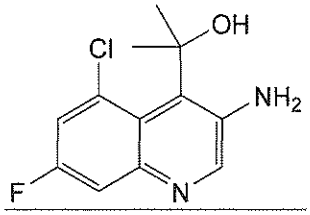


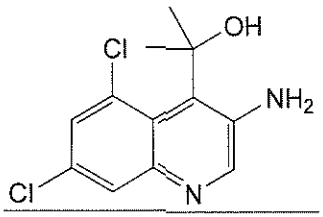


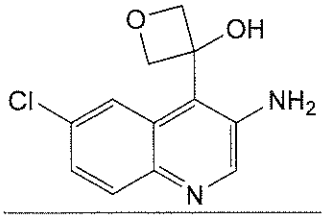


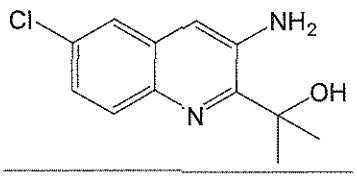


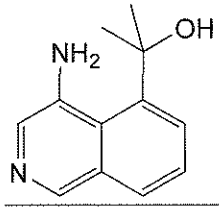


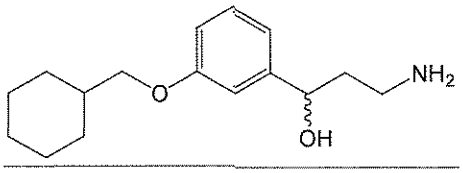


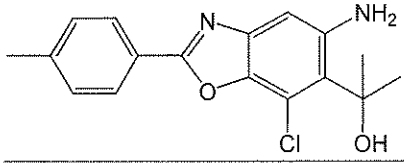


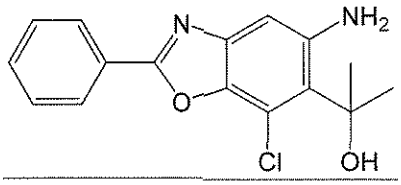


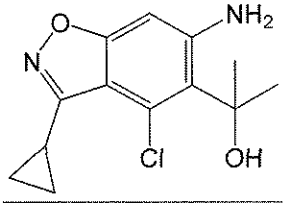


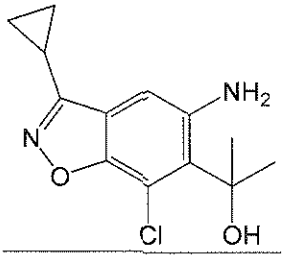


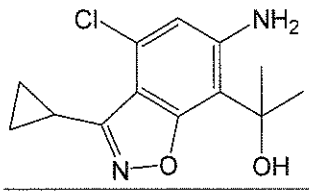


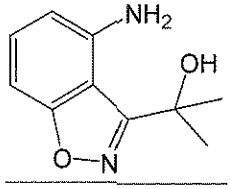


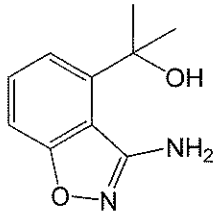


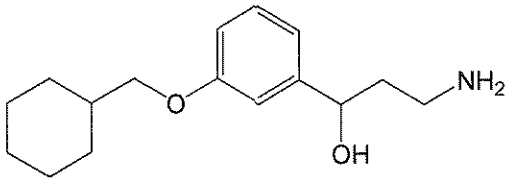


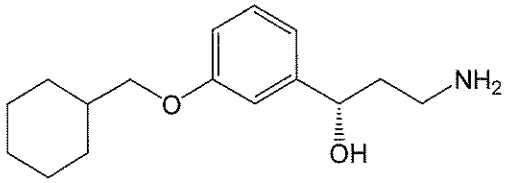


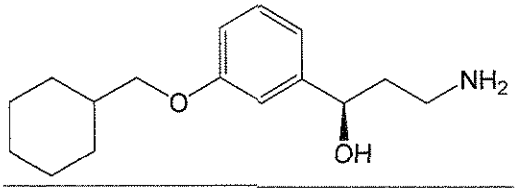


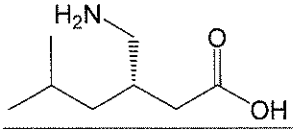




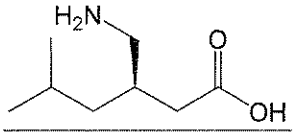








, and



or a pharmaceutically acceptable salt thereof, and wherein the disease, disorder, or condition is selected from the group consisting of:

an ocular disorder selected from the group consisting of dry eye syndrome, cataracts, keratoconus, bullous and other keratopathy, Fuch's endothelial dystrophy, allergic conjunctivitis, ocular cicatricial pemphigoid, conditions associated with PRK healing and other corneal healing, conditions associated with tear lipid degradation or lacrimal gland dysfunction, uveitis, scleritis, ocular Stevens Johnson Syndrome, and ocular rosacea,

a skin disease, disorder, or condition selected from the group consisting of psoriasis, topical (discoid) lupus, contact dermatitis, atopic dermatitis, allergic dermatitis, radiation dermatitis, acne vulgaris, Sjogren-Larsson Syndrome and other ichthyosis, and a cosmetic indication selected from the group consisting of solar elastosis/wrinkles, skin tone firmness, puffiness, eczema, smoke or irritant induced skin changes, dermal incision, and a skin condition associated with burn or wound,

a condition associated with the toxic effects of blister agents or burns from alkali agents, and

an autoimmune, immune-mediated, inflammatory, cardiovascular, or neurological disease, diabetes, metabolic syndrome, and a fibrotic disease.

In one embodiment, a disease, disorder, or condition in which aldehyde toxicity is implicated in the pathogenesis is an ocular disease, disorder, or condition, including, but not

limited to, a corneal disease (*e.g.*, dry eye syndrome, cataracts, keratoconus, bullous and other keratopathy, and Fuch's endothelial dystrophy), other ocular disorders or conditions (*e.g.*, allergic conjunctivitis, ocular cicatricial pemphigoid, conditions associated with PRK healing and other corneal healing, and conditions associated with tear lipid degradation or lacrimal gland dysfunction), and other ocular conditions associated with high aldehyde levels as a result of inflammation (*e.g.*, uveitis, scleritis, ocular Stevens Johnson Syndrome, and ocular rosacea (with or without meibomian gland dysfunction)).

In a second embodiment, a disease, disorder, or condition in which aldehyde toxicity is implicated in the pathogenesis is a skin disorder or condition or a cosmetic indication. For example, the disease, disorder, or condition includes, but is not limited to, psoriasis, scleroderma, topical (discoid) lupus, contact dermatitis, atopic dermatitis, allergic dermatitis, radiation dermatitis, acne vulgaris, Sjögren-Larsson Syndrome and other ichthyosis, and the cosmetic indication is solar elastosis/wrinkles, skin tone firmness, puffiness, eczema, smoke or irritant induced skin changes, dermal incision, and a skin condition associated with burn and/or wound.

In a third embodiment, a disease, disorder, or condition in which aldehyde toxicity is implicated in the pathogenesis is a condition associated with the toxic effects of blister agents or burns from alkali agents.

In a fourth embodiment, a disease, disorder, or condition in which aldehyde toxicity is implicated in the pathogenesis is an autoimmune, immune-mediated, inflammatory, cardiovascular, or neurological disease. For example, the disease, disorder, or condition includes, but is not limited to, lupus, scleroderma, asthma, chronic obstructive pulmonary disease (COPD), rheumatoid arthritis, inflammatory bowel disease, sepsis, atherosclerosis, ischemic-reperfusion injury, Parkinson's disease, Alzheimer's disease, multiple sclerosis, amyotrophic lateral sclerosis, diabetes, metabolic syndrome, and fibrotic diseases.

A compound (*e.g.*, a primary amine compound) described herein can be administered topically or systemically, as described in detail below.

Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this ~~invention~~ present disclosure belongs. In the case of conflict, the present specification, including definitions, will control. In the specification, the singular forms also include the plural unless the context clearly dictates otherwise. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present ~~invention~~disclosure, suitable methods and

materials are described below. All publications, patent applications, patents, and other references mentioned herein are incorporated by reference. The references cited herein are not admitted to be prior art to the ~~claimed invention~~present disclosure. In addition, the materials, methods, and examples are illustrative only and are not intended to be limiting.

Other features and advantages of the ~~invention~~ present disclosure will be apparent from the following detailed description and claims.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1. A plot showing that Compound 9 rapidly reacts with and traps the two most common pathogenic aldehydes: malondialdehye (MDA) and 4-hydroxynonenal (HNE)

Figure 2. Bar graphs showing that Compound 9 prevents aldehyde-mediated cell death in neurons

Figure 3. A bar graph showing broad downregulation of inflammatory cytokines by a single dose of Compound 9

Figure 4. Bar graphs showing the anti-inflammatory profile of a single-dose of Compound 9 in response to LPS treatment

Figure 5. Bar graphs showing the efficacy of a single dose of Compound 9 in (A) contact dermatitis and (B) allergic dermatitis

Figure 6. (A) a plot and a table showing the mucositis score over time in hamsters subject to 40 Gy irradiation and treated with or without Compound 9, (B) photographs of cheeks of hamsters subject to 40 Gy irradiation and treated with or without Compound 9

Figure 7. A bar plot showing that Compound 9 treatment diminishes radiation induced fibrosis in hamsters subject to 40 Gy irradiation

DETAILED DESCRIPTION OF THE INVENTION

The invention relates to compounds (*e.g.*, a primary amine compound) for the treatment, prevention, and/or reduction of a risk of diseases, disorders, or conditions in which aldehyde toxicity is implicated in the pathogenesis.

Examples of the diseases, disorders, or conditions in which aldehyde toxicity is implicated include an ocular disease, disorder, or condition, including, but not limited to, a corneal disease (*e.g.*, dry eye syndrome, cataracts, keratoconus, bullous and other keratopathy, and Fuch's endothelial dystrophy), other ocular disorders or conditions (*e.g.*, allergic conjunctivitis, ocular cicatricial pemphigoid, conditions associated with PRK healing

CLAIMS

1. Use of a compound comprising a primary amine in the manufacture of a medicament for ~~A method of~~ treating, preventing, or reducing a risk of a disease, disorder, condition, or cosmetic indication in which aldehyde toxicity is implicated in a subject in need thereof~~, comprising administering topically or systemically to the subject a compound comprising a primary amine~~, provided that the disease, disorder, or condition is not macular degeneration or Stargardt disease.

2. Use of a compound comprising a primary amine in the manufacture of a medicament for treating, preventing, or reducing a risk of a disease, disorder, condition, or cosmetic indication associated with aldehyde toxicity, provided that the disease, disorder, or condition is not macular degeneration or Stargardt disease.

~~2~~3. The ~~method of~~ use according to any one of claims 1 or 2, wherein the disease, disorder, or condition is an ocular disorder, provided that the ocular disorder is not macular degeneration or Stargardt disease.

~~3~~4. The ~~method of~~ use according to claim ~~2~~3, wherein the ocular disorder is selected from the group consisting of dry eye syndrome, cataracts, keratoconus, bullous and other keratopathy, Fuch's endothelial dystrophy, allergic conjunctivitis, ocular cicatricial pemphigoid, conditions associated with PRK healing and other corneal healing, conditions associated with tear lipid degradation or lacrimal gland dysfunction, uveitis, scleritis, ocular Stevens Johnson Syndrome, and ocular rosacea.

~~4~~5. The ~~method of~~ use according to claim ~~3~~4, wherein the ocular disorder is dry eye syndrome.

~~5~~6. The ~~method of~~ use according to claim ~~3~~4, wherein the ocular disorder is a condition associated with PRK healing and other corneal healing.

~~6~~7. The ~~method of~~ use according to claim ~~3~~4, wherein the ocular disorder is selected from the group consisting of uveitis, scleritis, ocular Stevens Johnson Syndrome, and ocular rosacea.

~~7~~8. The ~~method of~~ use according to claim ~~6~~7, wherein the ocular disorder is ocular rosacea or uveitis.

~~8~~9. The ~~method of~~ use according to claim ~~3~~4, wherein the ocular disorder is selected from the group consisting of keratoconus, cataracts, bullous and other keratopathy, Fuchs' endothelial dystrophy, ocular cicatricial pemphigoid, and allergic conjunctivitis.

~~9~~10. The ~~method of~~ use according to any one of claims 1 or 2, wherein the disease, disorder, or condition is a skin disease, disorder, or condition selected from the group consisting of psoriasis, topical (discoid) lupus,

contact dermatitis, atopic dermatitis, allergic dermatitis, radiation dermatitis, acne vulgaris, Sjögren-Larsson Syndrome and other ichthyosis, and the cosmetic indication is selected from the group consisting of solar elastosis/wrinkles, skin tone firmness, puffiness, eczema, smoke or irritant induced skin changes, dermal incision, and a skin condition associated with burn or wound.

~~10~~11. The ~~method of~~ use according to claim ~~9~~10, wherein the skin disease, disorder, or condition is selected from the group consisting of psoriasis, scleroderma, topical (discoid) lupus, contact dermatitis, atopic dermatitis, allergic dermatitis, radiation dermatitis, acne vulgaris, and Sjögren-Larsson Syndrome and other ichthyosis.

~~11~~12. The ~~method of~~ use according to claim ~~10~~11, wherein the skin disease, disorder, or condition is contact dermatitis, atopic dermatitis, allergic dermatitis, or radiation dermatitis.

~~12~~13. The ~~method of~~ use according to claim ~~10~~11, wherein the skin disease, disorder, or condition is Sjögren-Larsson Syndrome.

~~13~~14. The ~~method of~~ use according to claim ~~9~~10, wherein the cosmetic indication is selected from the group consisting of solar elastosis/wrinkles, skin tone firmness, puffiness, eczema, smoke or irritant induced skin changes, dermal incision, and a skin condition associated with burn or wound.

~~14~~15. The ~~method of~~ use according to any one of claims 1 or 2, wherein the disease, disorder, or condition is a condition associated with the toxic effects of blister agents or burns from alkali agents.

~~15~~16. The ~~method of~~ use according to claim ~~14~~15, wherein the blister agent is sulfur mustard, nitrogen mustard, or phosgene oxime.

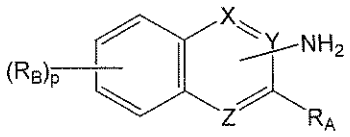
~~16~~17. The ~~method of~~ use according to claim ~~14~~15, wherein the alkali agent is lime, lye, ammonia, or a drain cleaner.

~~17~~18. The ~~method of~~ use according to any one of claims 1 or 2, wherein the disease, disorder, or condition is an autoimmune, immune-mediated, inflammatory, cardiovascular, or neurological disease, or diabetes, metabolic syndrome, or a fibrotic disease.

~~18~~19. The ~~method of~~ use according to claim ~~17~~18, wherein the disease, disorder, or condition is selected from the group consisting of lupus, scleroderma, asthma, chronic obstructive pulmonary disease (COPD), rheumatoid arthritis, inflammatory bowel disease, sepsis, atherosclerosis, ischemic-reperfusion injury, Parkinson's disease, Alzheimer's disease, multiple sclerosis, and amyotrophic lateral sclerosis.

~~19~~20. The ~~method of~~ use according to claim ~~17~~18, wherein the fibrotic disease is a renal, hepatic, pulmonary, or cardiac fibrosis.

~~20~~21. The ~~method of~~ use according to any one of claims 1 to ~~19~~20, wherein the primary amine compound is a compound of formula (I):



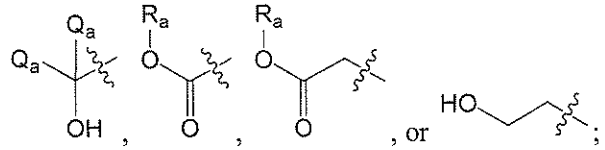
(I),

or a pharmaceutically acceptable salt thereof, wherein:

X, Y, and Z are each independently N, CH, or C with the $-NH_2$ attached, provided that at least one of X, Z and Y is N;

p is 0, 1, 2, or 3;

each R_B is independently halogen, hydroxyl, carbamoyl, amino, or unsubstituted or substituted aryl;

R_A is 

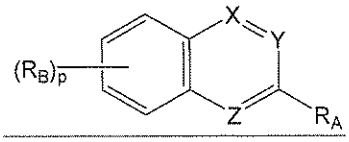
, or ;

Q_a is C_1-C_6 straight chain alkyl; and

R_a is unsubstituted or substituted C_1-C_8 straight chain or C_3-C_8 branched alkyl.

22. The use according to claim 21, wherein X is CH; Z is N and Y is $C(NH_2)$.

23. The use according to any one of claims 1 to 20, wherein the primary amine compound is a compound of formula (I):



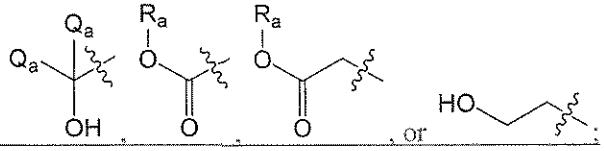
(I),

or a pharmaceutically acceptable salt thereof, wherein:

X is CH; Z is N and Y is $C(NH_2)$, provided that at least one of X, Z and Y is N;

p is 0, 1, 2, or 3;

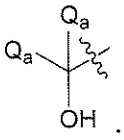
each R_B is independently halogen, hydroxyl, carbamoyl, amino, or unsubstituted or substituted aryl;

R_A is ;

Q_a is C_1-C_6 straight chain alkyl; and

R_a is unsubstituted or substituted C_1-C_8 straight chain or C_3-C_8 branched alkyl.

24 ~~21~~. The ~~method of~~ use according to any one of claims ~~20~~ 21 to 23, wherein p is 1.

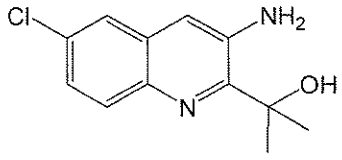
25 ~~22~~. The ~~method of~~ use according to any one of claims ~~20~~ 21 to 23, wherein R_A is .

26 ~~23~~. The ~~method of~~ use according to any one of claims ~~20~~21 to 23, wherein R_B is halogen, hydroxyl, carbamoyl, amino, or aryl.

27 ~~24~~. The ~~method of~~ use according to claim ~~23~~26, wherein R_B is halogen.

28 ~~25~~. The ~~method of~~ use according to claim ~~24~~27, wherein R_B is chlorine.

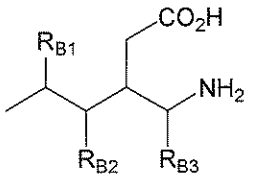
29 ~~26~~. The ~~method of~~ use according to any one of claims ~~20~~ 21 to 23, wherein the compound is



(9),

or a pharmaceutically acceptable salt thereof.

30 ~~27~~. The ~~method of~~ use according to any one of claims 1 to ~~19~~20, wherein the primary amine compound is a compound of formula (II):



(II),

or a pharmaceutically acceptable salt thereof, wherein:

R_{B1} is unsubstituted or substituted C_1-C_8 straight chain or C_3-C_8 branched alkyl, C_2-C_8 straight chain or C_3-C_8 branched alkenyl, C_1-C_6 alkoxy, C_3-C_7 cycloalkyl, C_1-C_6 alkyl-C_3-C_7 cycloalkyl, hydroxyl, C_1-C_6 alkylphenoxy, phenyl, or substituted phenyl;

R_{B2} is H, unsubstituted or substituted C_1-C_6 straight chain or C_3-C_6 branched alkyl, phenyl, or substituted phenyl; and

R_{B3} is H, unsubstituted or substituted C_1-C_6 straight chain or branched C_3-C_6 alkyl, or carboxyl.

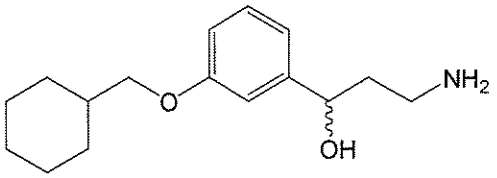
31 ~~28~~. The ~~method of~~ use according to claim ~~27~~30, wherein the compound is selected from the group consisting of:

3-aminomethyl-5-methylhexanoic acid, 3-aminomethyl-5-methylheptanoic acid, 3-aminomethyl-5-methyl-octanoic acid, 3-aminomethyl-5-methyl-nonanoic acid, 3-aminomethyl-5-methyl-decanoic acid, 3-aminomethyl-5-methyl-undecanoic acid, 3-aminomethyl-5-methyl-dodecanoic acid, 3-aminomethyl-5-methyl-tridecanoic acid, 3-aminomethyl-5-cyclopropyl-hexanoic acid, 3-aminomethyl-5-cyclobutyl-hexanoic acid, 3-aminomethyl-5-cyclopentyl-hexanoic acid, 3-aminomethyl-5-cyclohexyl-hexanoic acid, 3-

(3S,5R)-3-aminomethyl-7-cyclopentyl-5-methyl-heptanoic acid, (3S,5R)-3-aminomethyl-7-cyclohexyl-5-methyl-heptanoic acid, (3S,5R)-3-aminomethyl-8-cyclopropyl-5-methyl-octanoic acid, (3S,5R)-3-aminomethyl-8-cyclobutyl-5-methyl-octanoic acid, (3S,5R)-3-aminomethyl-8-cyclopentyl-5-methyl-octanoic acid, (3S,5R)-3-aminomethyl-8-cyclohexyl-5-methyl-octanoic acid, (3S,5S)-3-aminomethyl-6-fluoro-5-methyl-hexanoic acid, (3S,5S)-3-aminomethyl-7-fluoro-5-methyl-heptanoic acid, (3S,5R)-3-aminomethyl-8-fluoro-5-methyl-octanoic acid, (3S,5R)-3-aminomethyl-9-fluoro-5-methyl-nonanoic acid, (3S,5S)-3-aminomethyl-7,7,7-trifluoro-5-methyl-heptanoic acid, (3S,5R)-3-aminomethyl-8,8,8-trifluoro-5-methyl-octanoic acid, (3S,5R)-3-aminomethyl-5-methyl-8-phenyl-octanoic acid, (3S,5S)-3-aminomethyl-5-methyl-6-phenyl-hexanoic acid, and (3S,5R)-3-aminomethyl-5-methyl-7-phenyl-heptanoic acid,
or a pharmaceutically acceptable salt thereof.

32 ~~29~~. The ~~method of~~ use according to claim ~~28~~ 31, wherein the compound is (S)-3-(aminomethyl)-5-methylhexanoic acid or (R)-3-(aminomethyl)-5-methylhexanoic acid, or a pharmaceutically acceptable salt or racemic mixture thereof.

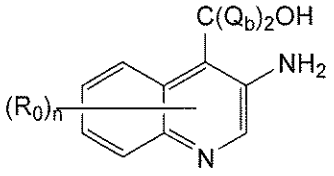
33 ~~30~~. The ~~method of~~ use according to any one of claims 1 to ~~19~~20, wherein the primary amine compound is



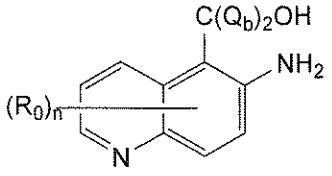
(11),

or a pharmaceutically acceptable salt thereof.

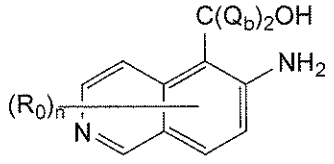
34 ~~31~~. The ~~method of~~ use according to any one of claims 1 to ~~19~~20, wherein the primary amine compound is a compound of one of formula (IIIa)-(IIIf):



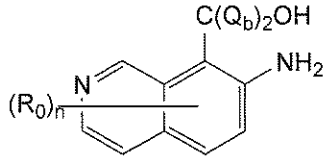
(IIIa),



(IIIb),



(IIIc),



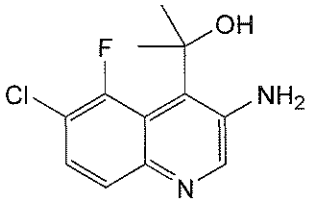
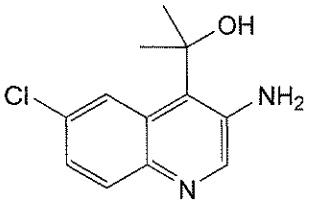
(IIId),

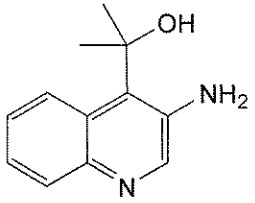
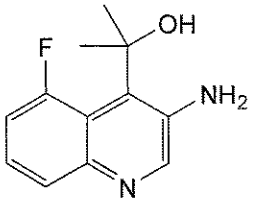
each Q_b is independently H, C_1-C_6 straight chain or C_3-C_6 branched alkyl, or C_1-C_6 straight chain or C_3-C_6 branched alkyl substituted with 1-6 F, or

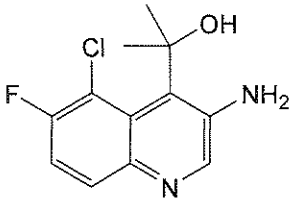
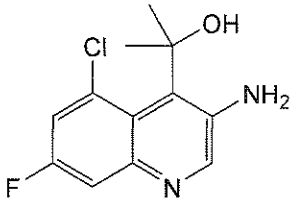
both Q_b, together with the carbon atom to which they are attached, form a C_3-C_6 carbocycle or a saturated heterocycle selected from , ,  and , wherein "*" denotes the position of the carbon atom to which both Q_b are attached, wherein the carbocycle or the heterocycle is optionally substituted with one or more R_{b3}; and

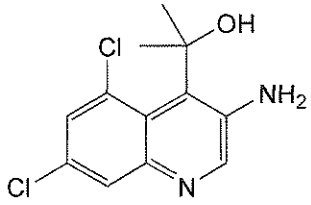
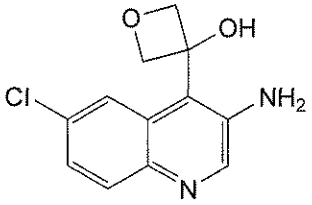
n is 0,1, 2, or 3.

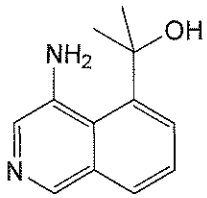
35 ~~32~~. The use according to claim ~~31~~ 34, wherein the compound is selected from the group consisting of:

, ,

, ,

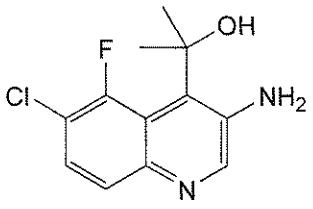
, ,

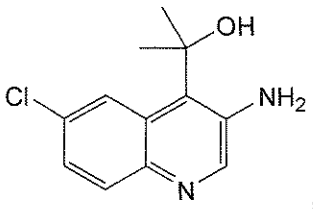
, , and

,

or a pharmaceutically acceptable salt thereof.

36 ~~33~~. The ~~method of~~ use according to claim ~~32~~ 35, wherein the compound is

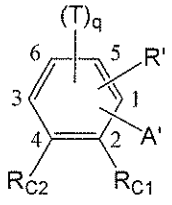


or


,

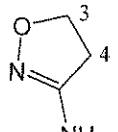
or a pharmaceutically acceptable salt thereof.

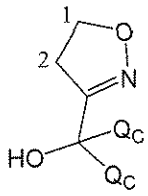
37 ~~34~~. The ~~method of~~ use according to any one of claims 1 to ~~19~~20, wherein the primary amine compound is a compound of formula (IV):



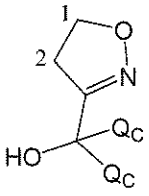
(IV),

or a pharmaceutically acceptable salt thereof, wherein:

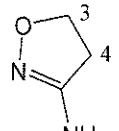
A' and R', together with the two adjacent carbon atoms to which they are attached, form a five-membered heteroaryl ring containing one nitrogen atom and one oxygen atom, wherein the heteroaryl ring is substituted with R_C', wherein "1", "2", "3", "4", "5", and "6" denote the points of attachment of the heteroaryl ring to the phenyl ring, provided that when the heteroaryl ring is 

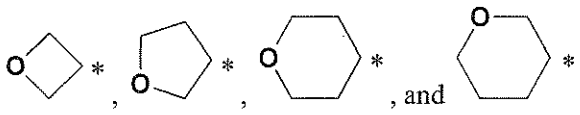
, then R_{C1} is $C(Q_C)_2OH$, R_{C2} is absent, and R_C' is absent, and that when the heteroaryl ring is 

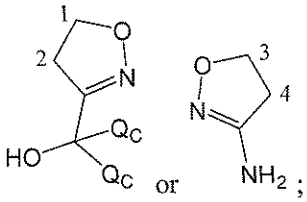
, then R_{C1} is absent, R_{C2} is NH_2, and R_C' is absent;

R_{C1} is $C(Q_C)_2OH$, or R_{C1} is absent when A' and R', together with the two adjacent carbon atoms to which they are attached, form 

;

R_{C2} is NH_2, or R_{C2} is absent when A' and R', together with the two adjacent carbon atoms to which they are attached, form ;

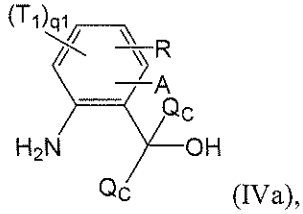
each Q_C is independently C_1-C_6 alkyl or C_3-C_6 cycloalkyl, or two Q_C, together with the carbon atom to which they are attached, form a C_3-C_6 carbocyclic ring or a saturated heterocycle selected from , wherein "*" denotes the position of the carbon atom to which the two Q_C are attached;

R_C' is C_1-C_{10} alkyl, C_1-C_{10} alkyl substituted with C_3-C_6 cycloalkyl, C_3-C_6 cycloalkyl, aryl, aryl substituted with C_1-C_6 alkyl, or C_1-C_6 alkoxy, or R_C' is absent when A' and R', together with the two adjacent carbon atoms to which they are attached, form ;

q is 0, 1, or 2, provided that when R_C' is phenyl, q is not 0; and

each T is independently halogen, C_1-C_{10} alkyl, C_1-C_{10} alkyl substituted with C_3-C_6 cycloalkyl, C_3-C_6 cycloalkyl, or cyano.

38 ~~35~~. The ~~method of~~ use according to claim ~~34~~ 37, wherein the compound is a compound of formula (IVa):


(IVa),

or a pharmaceutically acceptable salt thereof, wherein:

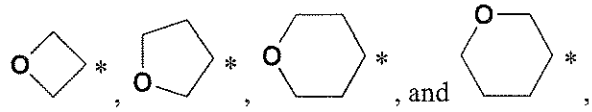
A and R, together with the two adjacent carbon atoms to which they are attached, form a five-membered heteroaryl ring containing one nitrogen atom and one oxygen atom, wherein the heteroaryl ring is substituted with R_C;

R_C is C_1-C_{10} alkyl, C_1-C_{10} alkyl substituted with C_3-C_6 cycloalkyl, C_3-C_6 cycloalkyl, aryl, aryl substituted with C_1-C_6 alkyl, or C_1-C_6 alkoxy;

q_1 is 1 or 2;

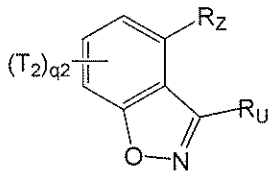
each T_1 is independently halogen, C_1-C_{10} alkyl, C_1-C_{10} alkyl substituted with C_3-C_6 cycloalkyl, C_3-C_6 cycloalkyl, or cyano; and

each Q_C is independently C_1-C_6 alkyl or C_3-C_6 cycloalkyl, or two Q_C, together with the carbon atom to which they are attached, form a C_3-C_6 carbocyclic ring or a saturated heterocycle selected from



, wherein "*" denotes the position of the carbon atom to which the two Q_C are attached.

39 ~~36~~. The ~~method of~~ use according to claim ~~34~~ 37, wherein the compound is a compound of formula (IVb):

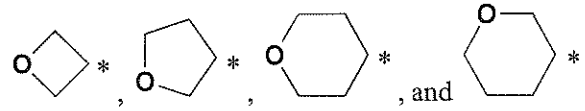


(IVb),

or a pharmaceutically acceptable salt thereof, wherein:

one of R_U and R_Z is $C(Q_C)_2OH$, and the other is NH_2;

each Q_C is independently C_1-C_6 alkyl or C_3-C_6 cycloalkyl, or two Q_C, together with the carbon atom to which they are attached, form a C_3-C_6 carbocyclic ring or a saturated heterocycle selected from

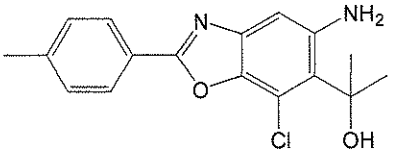


, wherein "*" denotes the position of the carbon atom to which the two Q_C are attached;

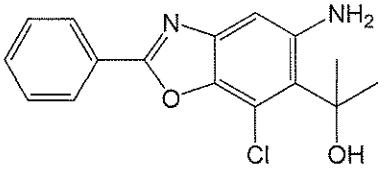
q_2 is 0, 1, or 2; and

each T_2 is independently halogen, C_1-C_{10} alkyl, C_1-C_{10} alkyl substituted with C_3-C_6 cycloalkyl, C_3-C_6 cycloalkyl, or cyano.

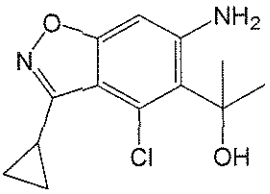
40 ~~37~~. The ~~method of~~ use according to claim ~~34~~ 37, wherein the compound is a compound selected from the group consisting of:

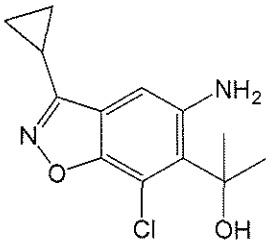


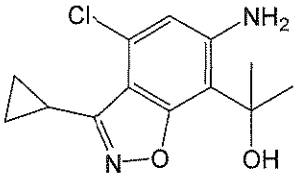
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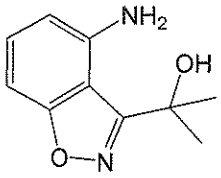


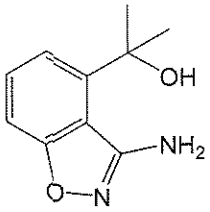
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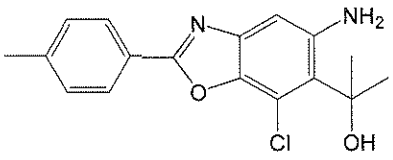
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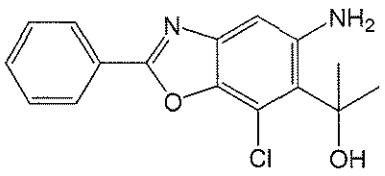
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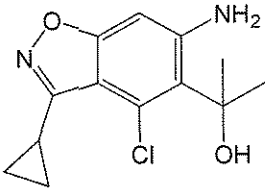
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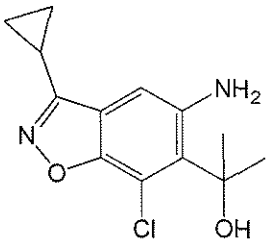
,
or a pharmaceutically acceptable salt thereof.

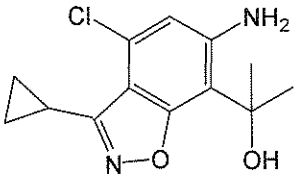
41 ~~38~~. The ~~method of~~ use according to claim ~~37~~ 40, wherein the compound is



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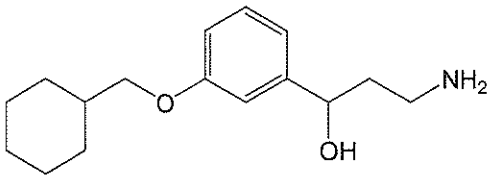
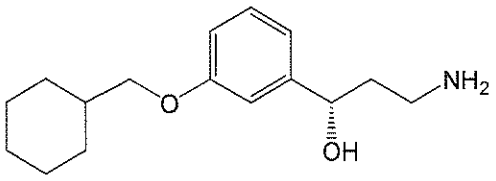
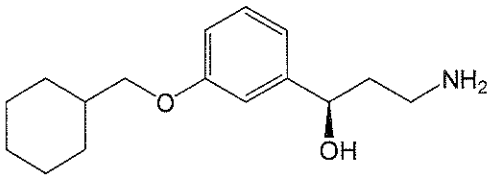
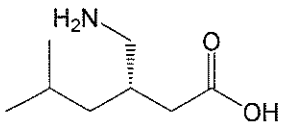
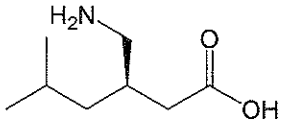
,


,


, and


,
or a pharmaceutically acceptable salt thereof.

42 ~~39~~. ~~A method of~~ Use of an amine compound in the manufacture of a medicament for treating, preventing, or reducing a risk of a disease, disorder, or condition in which aldehyde toxicity is implicated in a subject in need thereof~~, comprising administered topically or systemically to the subject a compound,~~ wherein the amine compound is selected from the group consisting of:

, and

or a pharmaceutically acceptable salt thereof, and wherein the disease, disorder, or condition is selected from the group consisting of:

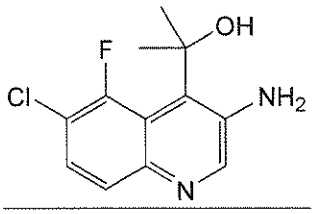
an ocular disorder selected from the group consisting of dry eye syndrome, cataracts, keratoconus, bullous and other keratopathy, Fuch's endothelial dystrophy, allergic conjunctivitis, ocular cicatricial pemphigoid, conditions associated with PRK healing and other corneal healing, conditions associated with tear lipid degradation or lacrimal gland dysfunction, uveitis, scleritis, ocular Stevens Johnson Syndrome, and ocular rosacea,

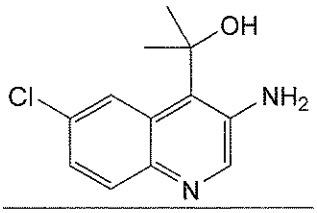
a skin disease, disorder, or condition selected from the group consisting of psoriasis, topical (discoid) lupus, contact dermatitis, atopic dermatitis, allergic dermatitis, radiation dermatitis, acne vulgaris, Sjogren-Larsson Syndrome and other ichthyosis, and a cosmetic indication selected from the group consisting of solar elastosis/wrinkles, skin tone firmness, puffiness, eczema, smoke or irritant induced skin changes, dermal incision, and a skin condition associated with burn or wound,

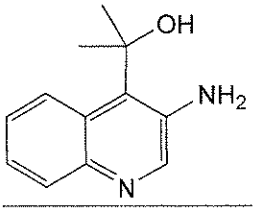
a condition associated with the toxic effects of blister agents or burns from alkali agents, and

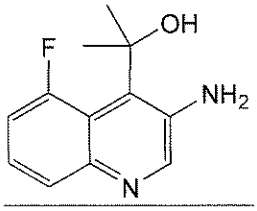
an autoimmune, immune-mediated, inflammatory, cardiovascular, or neurological disease, diabetes, metabolic syndrome, and a fibrotic disease.

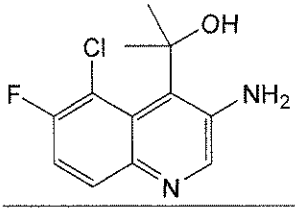
43. Use of an amine compound in the manufacture of a medicament for treating, preventing, or reducing a risk of a disease, disorder, or condition associated with aldehyde toxicity, wherein the amine compound is selected from the group consisting of:

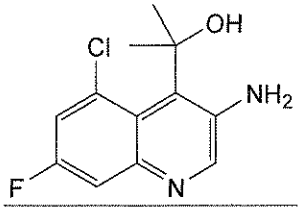

OH
F
Cl
NH2
N

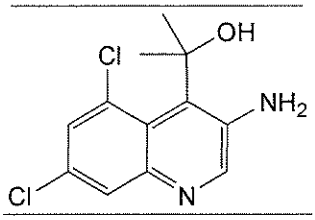

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Cl
NH2
N

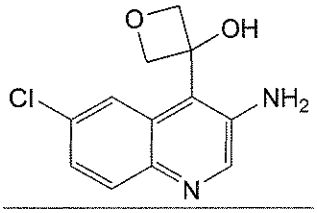

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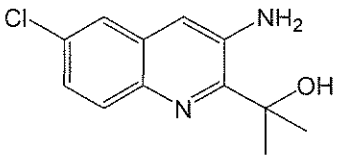

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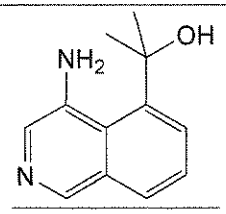

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NH2
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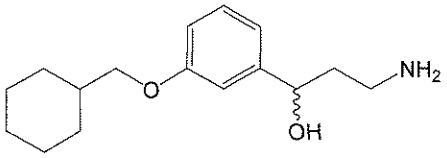

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NH2
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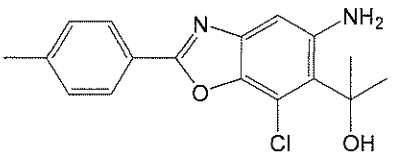

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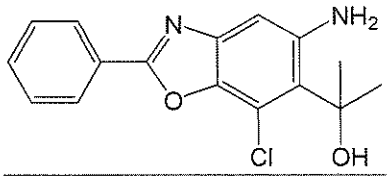

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NH2
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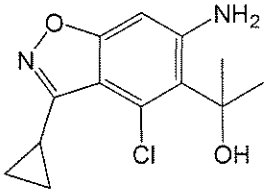

Cl
NH2
N
OH

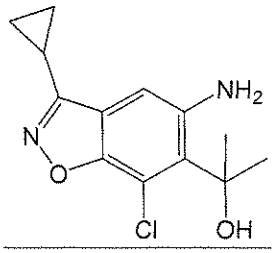

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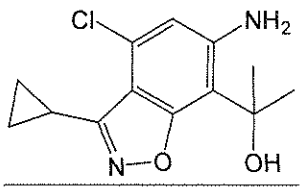

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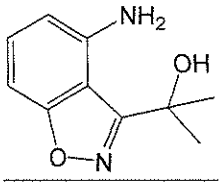

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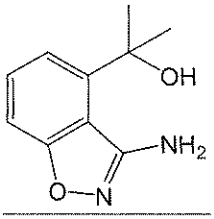

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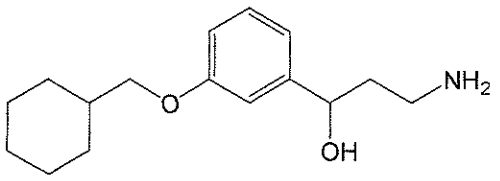

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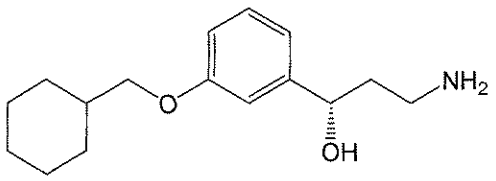


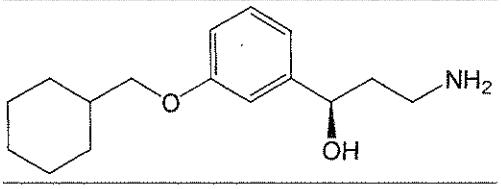


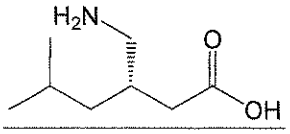




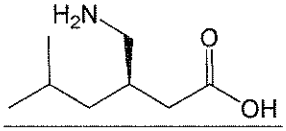








, and



or a pharmaceutically acceptable salt thereof, and wherein the disease, disorder, or condition is selected from the group consisting of:

an ocular disorder selected from the group consisting of dry eye syndrome, cataracts, keratoconus, bullous and other keratopathy, Fuch's endothelial dystrophy, allergic conjunctivitis, ocular cicatricial pemphigoid, conditions associated with PRK healing and other corneal healing, conditions associated with tear lipid degradation or lacrimal gland dysfunction, uveitis, scleritis, ocular Stevens Johnson Syndrome, and ocular rosacea,

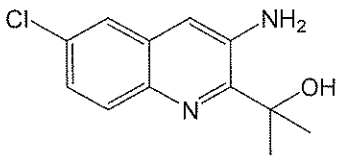
a skin disease, disorder, or condition selected from the group consisting of psoriasis, topical (discoid) lupus, contact dermatitis, atopic dermatitis, allergic dermatitis, radiation dermatitis, acne vulgaris, Sjogren-Larsson Syndrome and other ichthyosis, and a cosmetic indication selected from the group consisting of solar elastosis/wrinkles, skin tone firmness, puffiness, eczema, smoke or irritant induced skin changes, dermal incision, and a skin condition associated with burn or wound,

a condition associated with the toxic effects of blister agents or burns from alkali agents, and

an autoimmune, immune-mediated, inflammatory, cardiovascular, or neurological disease,

diabetes, metabolic syndrome, and a fibrotic disease.

4440. The ~~method of~~ use according to any one of claims ~~39~~ 42 or 43, wherein the compound is



, or a pharmaceutically acceptable salt thereof.

41. Use of a compound comprising a primary amine in the manufacture of a medicament for the treatment, prevention, or reduction of a risk of a disease, disorder, condition, or a cosmetic indication in which aldehyde toxicity is implicated in a subject, provided that the disease, disorder or condition is not macular degeneration or Stargradt disease.

42. Use of a compound comprising a primary amine in treating, preventing, or reducing a risk of a disease, disorder, condition, or a cosmetic indication in which aldehyde toxicity is implicated in a subject, provided that the disease, disorder or condition is not macular degeneration or Stargradt disease.