USES OF PLASMINOGEN ACTIVATOR INHIBITOR 1 (PAI-1) INHIBITORS

Cross-Reference To Related Applications

[0001] This application claims priority to United States Provisional Application No. 62/731,076, filed September 13, 2018, the entirety of which is incorporated herein by reference.

Background

[0002] Hair loss or alopecia often promote significant anxiety; many people go to great lengths to re-grow their hair, particularly if hair loss occurs prematurely. Previously available therapies have largely proven unsatisfactory, hence new treatment options are needed.

Summary

[0002a] In an aspect of the present disclosure, there is provided a non-therapeutic method of ~~use of a plasminogen activator inhibitor-1 (PAI-1) inhibitor in the manufacture of a medicament for~~ treating ~~one or more treatable conditions of~~hair loss in a subject,

wherein the ~~treating~~ method comprises:

providing a composition that comprises or delivers ~~the~~ a plasminogen activator inhibitor-1 (PAI-1) inhibitor;

administering the composition to a site of the subject, wherein the site contains or did contain a plurality of hair follicles, each hair follicle optionally comprising a hair disposed therein, so that the PAI-1 inhibitor is delivered to the subject,

wherein the PAI-1 inhibitor is selected from a group consisting of: 5-Chloro-2-{[(2-{[3-(furan-3-yl)phenyl]amino}-2-oxoethoxy)acetyl]amino benzoic acid, 5-Chloro-2-{[{[3-(furan-3-yl)phenyl]amino}(oxo)acetyl]amino} benzoic acid.

~~wherein the subject is suffering from one or more treatable conditions, and~~

~~wherein the one or more treatable conditions is/are selected from the group consisting of androgenetic alopecia, alopecia areata, frontal fibrosing alopecia, and senescent alopecia.~~

[0002b] In another aspect of the present disclosure, there is provided a non-therapeutic method of ~~use of a plasminogen activator inhibitor-1 (PAI-1) inhibitor in the manufacture of a medicament for~~ treating ~~one or more treatable conditions of~~hair loss in a subject,

wherein the ~~treating~~ method comprises:

providing a composition that comprises or delivers a plasminogen activator inhibitor-1 (PAI-1) inhibitor;

administering the composition to a subject, wherein a site of the subject contains or did contain a plurality of hair follicles, each hair follicle optionally comprising a hair disposed therein, so that the PAI-1 inhibitor is delivered to the subject,

wherein the PAI-1 inhibitor is selected from a group consisting of: 5-Chloro-2-{[(2-{[3-(furan-3-yl)phenyl]amino}-2-oxoethoxy)acetyl]amino benzoic acid, 5-Chloro-2-{[{[3-(furan-3-yl)phenyl]amino}(oxo)acetyl]amino} benzoic acid.

~~wherein the subject is suffering from one or more treatable conditions, and~~

~~wherein the one or more treatable conditions is/are selected from the group consisting of androgenetic alopecia, alopecia areata, frontal fibrosing alopecia, and senescent alopecia.~~

[0002c] In a further aspect of the present disclosure, there is provided a ~~use of a plasminogen activator inhibitor-1 (PAI-1) inhibitor in the manufacture of a medicament for~~non-therapeutic method of preventing the occurrence ~~or progression of one or more conditions~~of hair loss in a subject, ~~the preventing comprising~~wherein the method comprises:

(a) providing a composition that comprises or delivers ~~the~~ a plasminogen activator inhibitor (PAI-1) inhibitor,

wherein the PAI-1 inhibitor is selected from a group consisting of: 5-Chloro-2-{[(2-{[3-(furan-3-yl)phenyl]amino}-2-oxoethoxy)acetyl]amino benzoic acid, 5-Chloro-2-{[{[3-(furan-3-yl)phenyl]amino}(oxo)acetyl]amino} benzoic acid;

~~-~~(b) administering the composition topically to a site of the subject, wherein the site is a skin surface that contains or contained a plurality of hair follicles, each optionally comprising a hair disposed therein; and~~,~~

~~wherein the one or more conditions is/are selected from the group consisting of androgenetic alopecia, alopecia areata, frontal fibrosing alopecia senescent alopecia, and combinations thereof; and~~

~~-~~(c) leaving the composition on the site for a period of time, so that the PAI-1 inhibitor is delivered to the subject.

[0002d] In another aspect of the present disclosure, there is provided a composition comprising a therapeutically effective amount of a PAI-1 inhibitor ~~and a pharmaceutically acceptable carrier~~ effective for treating hair loss, and a pharmaceutically acceptable carrier, formulated for topical administration to a site of a subject, wherein the site contains or did

contain a plurality of hair follicles, each with a hair disposed therein, wherein the PAI-1 inhibitor is selected from a group consisting of: 5-Chloro-2-{[(2-{[3-(furan-3-yl)phenyl]amino}-2-oxoethoxy)acetyl]amino benzoic acid, 5-Chloro-2-{[{[3-(furan-3-yl)phenyl]amino}(oxo)acetyl]amino} benzoic acid.

[0002e] In a further aspect of the present disclosure, there is provided a kit comprising a composition comprising a PAI-1 inhibitor as disclosed herein and a patch for use in covering the composition comprising the PAI-1 inhibitor after administration to thea site.

[0002f] In another aspect of the present disclosure, there is provided a kit comprising a composition comprising a PAI-1 inhibitor as disclosed herein, a device for facilitating penetration of a composition comprising the PAI-1 inhibitor into thea site on a subject, and instructions for administering the composition to the site.

[0003] The present disclosure provides, *inter alia*, new technologies (e.g., methods, kits, compositions, etc) for treatment and/or prevention of certain types of alopecia (hair loss). Among other things, the present disclosure provides an insight that plasminogen activator inhibitor -1 (PAI-1) inhibitors may be useful in the treatment and/or prevention only of certain types of alopecia, but not for other types of hair loss. Specifically, the present disclosure provides new technologies (e.g., methods, kits, compositions, etc.) which in some examples, may be particularly useful in the treatment and/or prevention of specific types of hair loss (or alopecia), including androgenetic alopecia (also called androgenic alopecia), alopecia areata, frontal fibrosing alopecia, and senescent alopecia. Furthermore, the present disclosure provides insight that the new technologies that may not be particularly useful in the treatment and/or prevention of other types of alopecia such as radiation-induced alopecia, chemotherapy-induced alopecia, and alopecia due to chronic discoid lupus erythematosus.

Claims

We claim:

1. A non-therapeutic method of~~Use of a plasminogen activator inhibitor-1 (PAI-1) inhibitor in the manufacture of a medicament for~~ treating ~~one or more treatable conditions of~~hair loss in a subject,

wherein the ~~treating~~ method comprises:

providing a composition that comprises or delivers a plasminogen activator inhibitor-1~~the~~ (PAI-1) inhibitor;

administering the composition to a site of the subject, wherein the site contains or did contain a plurality of hair follicles, each hair follicle optionally comprising a hair disposed therein, so that the PAI-1 inhibitor is delivered to the subject,

wherein the PAI-1 inhibitor is selected from a group consisting of: 5-Chloro-2-{[(2-{[3-(furan-3-yl)phenyl]amino}-2-oxoethoxy)acetyl]amino benzoic acid, 5-Chloro-2-{[{[3-(furan-3-yl)phenyl]amino}(oxo)acetyl]amino} benzoic acid.

~~wherein the subject is suffering from one or more treatable conditions, and~~

~~wherein the one or more treatable conditions is/are selected from the group consisting of androgenetic alopecia, alopecia areata, frontal fibrosing alopecia, and senescent alopecia.~~

2. The ~~use~~method of claim 1, wherein the administering is by topically applying to a site on a skin surface.

3. The ~~use~~method of claim 2, wherein the administering comprises maintaining the composition on the skin surface for a period of time.

~~4. The use of claim 1, wherein the administering is by injection.~~

4~~5~~. ~~Use of a plasminogen activator inhibitor-1 (PAI-1) inhibitor in the manufacture of a medicament for~~ A non-therapeutic method of treating ~~one or more treatable conditions of~~hair loss in a subject,

wherein the ~~treating~~ method comprises:

providing a composition that comprises or delivers a plasminogen activator inhibitor-1 (PAI-1) inhibitor;

administering the composition to a subject, wherein a site of the subject contains or did contain a plurality of hair follicles, each hair follicle optionally comprising a hair disposed therein, so that the PAI-1 inhibitor is delivered to the subject,

wherein the PAI-1 inhibitor is selected from a group consisting of: 5-Chloro-2-{[(2-{[3-(furan-3-yl)phenyl]amino}-2-oxoethoxy)acetyl]amino benzoic acid, 5-Chloro-2-{[{[3-(furan-3-yl)phenyl]amino}(oxo)acetyl]amino} benzoic acid.

~~wherein the subject is suffering from one or more treatable conditions, and~~

~~wherein the one or more treatable conditions is/are selected from the group consisting of androgenetic alopecia, alopecia areata, frontal fibrosing alopecia, and senescent alopecia.~~

~~6. The use of claim 5, wherein the administering is by oral administration.~~

5~~7~~. The ~~use~~method of claim 3, wherein the ~~treating~~ method further comprises, after the period of time, removing remaining composition from the site.

6~~8~~. The ~~use~~method of any one of claims 3~~, 4, or 7~~ to 5, wherein the step of administering the composition comprises massaging the composition into the site.

7~~9~~. The ~~use~~method of claim 3, wherein the period of time is at least 1 minute.

8~~10~~. The ~~use~~method of claim 3, wherein the period of time is at least 1 hour.

9~~11~~. The method of claim 3~~7~~, wherein the period of time is within a range of 1 to 10 minutes.

~~12. The use of any of the preceding claims, wherein the PAI-1 inhibitor is selected from the group consisting of: polypeptides, nucleic acids, lipids, carbohydrates, small molecules, metals, polymers, therapeutic antibodies, and combinations thereof.~~

~~13. The use of claim 12, wherein the nucleic acid is or comprises siRNA.~~

~~14. The use of claim 12, wherein the PAI-1 inhibitor is selected from a group consisting of : 5-Chloro-2-{[(2-{[3-(furan-3-yl)phenyl]amino}-2-oxoethoxy)acetyl]amino benzoic acid, 5-Chloro-2-{[{[3-(furan-3-yl)phenyl]amino}(oxo-)acetyl]amino}-benzoic acid, a benzopyran compound, a butadiene, spironolactone, imidapril, an angiotensin converting enzyme inhibitor (ACEI, captopril, or enalapril), an angiotensin II receptor antagonist (AIIRA), a defibrotide (a polydeoxyribonucleotide) and any combination thereof.~~

10~~15~~. The ~~use~~method of claim~~s~~ 1 or 4, wherein the PAI-1 inhibitor is 5-Chloro-2-{[(2-{[3-(furan-3-yl)phenyl]amino}-2-oxoethoxy)acetyl]amino benzoic acid.

11~~16~~. The ~~use~~method of any one of the preceding claims, further comprising administering one or more other active agents, wherein the one or more other active agents is selected from the group comprising of minoxidil, finasteride, dutasteride, platelet-rich plasma, and combinations thereof.

12~~17~~. The ~~use~~method of any one of the preceding claims, wherein the composition comprising the PAI-1 inhibitor is or comprises a suspension.

13~~18~~. The ~~use~~method of any one of the preceding claims, wherein the composition comprising the PAI-1 inhibitor is or comprises a foam.

14~~19~~. The ~~use~~method of any one of the preceding claims, wherein the composition comprising the PAI-1 inhibitor comprises an emulsion.

15~~20~~. The ~~use~~method of claim 14~~19~~, wherein the emulsion is a nanoemulsion.

~~21. The use of any one of the claims 1-3 or 7-20, wherein the treating further comprises a step of administering a penetrating treatment.~~

~~22. The use of claim 21, wherein the penetrating treatment is or comprises a non-irritating chemical agent.~~

~~23. The use of claim 21, wherein the penetrating treatment is or comprises administration of an electric or magnetic field.~~

~~24. The use of claim 21, wherein the penetrating treatment is or comprises microneedling.~~

~~25. The use of claim 21, wherein the penetrating treatment is or comprises laser treatment.~~

~~26. The use of any one of the claims 1-3 or 7-25, wherein the PAI-1 inhibitor penetrates the site within about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 minutes of administration.~~

~~27. The use of any one of the claims 1-3 or 7-26, wherein the PAI-1 inhibitor penetrates the site within about 5 to about 60 minutes, about 5 to about 12 minutes, about 5 to about 15 minutes, or about 15 to about 30 minutes of administration.~~

~~28. The use of any one of the claims 1-3 or 7-27, wherein the PAI-1 inhibitor penetrates the site within about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 or 24 hours of administration.~~

~~29. The use of any one of the claims 1-3 or 7-28, wherein the PAI-1 inhibitor penetrates the site within about 1 to about 12 hours, about 8 to about 12 hours or 12 hours to about 24 hours of administration.~~

16~~30~~. The ~~use~~method of any one of the preceding claims, comprising more than one administration of the composition over time.

17~~31~~. The ~~use~~method of claim 16~~30~~, wherein each administration comprising the PAI-1 inhibitor is separated by a specified period of time.

~~32. The use of claim 31, wherein the specified period of time is longer as compared to the specified period of time for administering a reference treatment regimen.~~

18~~33~~. The ~~use~~method any one of the preceding claims, wherein the hair is not gray.

19~~34~~. The ~~use~~method of any one of claims 1 to 17~~32~~, wherein the hair is gray.

20~~35~~. The ~~use~~method of any one of the claims 1-3 or ~~7-34~~5-19, wherein the composition is formulated as a suspension, a foam, a lotion, a cream, a gel, an oil, a powder, a liniment, or drops.

21~~36~~. ~~Use of a plasminogen activator inhibitor-1 (PAI-1) inhibitor in the manufacture of a medicament for~~A non-therapeutic method of preventing the occurrence ~~or progression of one or more conditions~~ of hair loss in a subject, ~~the preventing comprising~~wherein the method comprises:

(a) providing a composition that comprises or delivers ~~the~~ a plasminogen activator inhibitor-1 (PAI-1) inhibitor,

wherein the PAI-1 inhibitor is selected from a group consisting of: 5-Chloro-2-{[(2-{[3-(furan-3-yl)phenyl]amino}-2-oxoethoxy)acetyl]amino benzoic acid, 5-Chloro-2-{[{[3-(furan-3-yl)phenyl]amino}(oxo)acetyl]amino} benzoic acid;

(b) administering the composition topically to a site of the subject, wherein the site is a skin surface that contains or contained a plurality of hair follicles, each optionally comprising a hair disposed therein; and~~,~~

~~wherein the one or more conditions is/are selected from the group consisting of androgenetic alopecia, alopecia areata, frontal fibrosing alopecia senescent alopecia, and combinations thereof; and~~

~~-~~(c) leaving the composition on the site for a period of time, so that the PAI-1 inhibitor is delivered to the subject.

22~~37~~. The ~~use~~method of claim ~~36~~21, wherein the ~~preventing~~ method further comprises, after the period of time, removing remaining composition from the site.

2338. The ~~use~~method of claim 2136 or claim 2237, wherein the step of administering the composition comprises massaging the composition into the site.

2439. The ~~use~~method of any of claims 2136 to 2338, wherein the period of time is within a range of ~~about~~ 1 to ~~about~~ 10 minutes, ~~about~~ 5 to ~~about~~ 60 minutes, ~~about~~ 5 to ~~about~~ 12 minutes, ~~about~~ 5 to ~~about~~ 15 minutes, or ~~about~~ 15 to ~~about~~ 30 minutes, ~~about~~ 1 to ~~about~~ 12 hours, ~~about~~ 8 to ~~about~~ 12 hours or 12 hours to ~~about~~ 24 hours.

~~40. The use of any of claims 36 to 39, wherein the PAI-1 inhibitor is selected from the group consisting of: polypeptides, nucleic acids, lipids, carbohydrates, small molecules, metals, polymers, therapeutic antibodies, and combinations thereof.~~

~~41. The use of claim 40, wherein the nucleic acid is or comprises siRNA.~~

~~42. The use of claim 40, wherein the PAI-1 inhibitor is selected from a group consisting of : 5-Chloro-2-{[(2-{[3-(furan-3-yl)phenyl]amino}-2-oxoethoxy)acetyl]amino benzoic acid, 5-Chloro-2-{{{[3-(furan-3-yl)phenyl]amino}(oxo)acetyl]amino}-benzoic acid, a benzopyran compound, a butadiene, spironolactone, imidapril, an angiotensin converting enzyme inhibitor (ACEI, captopril, or enalapril), an angiotensin II receptor antagonist (AIIRA), a defibrotide (a polydeoxyribonucleotide) and any combination thereof.~~

2543. The ~~use~~method of claims ~~42~~21 to 24, wherein the PAI-1 inhibitor is 5-Chloro-2-{[(2-{[3-(furan-3-yl)phenyl]amino}-2-oxoethoxy)acetyl]amino benzoic acid.

2644. The ~~use~~method of any one of claims 2136 to 2543, wherein the ~~prevention~~ method further comprises administering one or more other active agents~~-~~, wherein the one or more other active agents is selected from the group comprising of minoxidil, finasteride, dutasteride, platelet-rich plasma, and combinations thereof.

2745. The ~~use~~method of any one of claims 2136 to 2644, wherein the composition comprising the PAI-1 inhibitor is or comprises a suspension.

2846. The ~~use~~method of any one of claims 2136 to 2644, wherein the composition comprising the PAI-1 inhibitor is or comprises a foam.

2947. The ~~use~~method of any one of claims 2136 to 2644, wherein the composition comprising the PAI-1 inhibitor comprises an emulsion.

3048. The ~~use~~method of claim ~~47~~29, wherein the emulsion is a nanoemulsion.

~~49. The use of any one of claims 36 to 48, wherein the preventing further comprises a step of administering a penetrating treatment.~~

~~50. The use of claim 49, wherein the penetrating treatment is or comprises a non-irritating chemical agent.~~

~~51. The use of claim 49, wherein the penetrating treatment is or comprises administration of an electric or magnetic field.~~

~~52. The use of claim 49, wherein the penetrating treatment is or comprises microneedling.~~

~~53. The use of claim 49, wherein the penetrating treatment is or comprises laser treatment.~~

~~54. The use of any one of claims 36 to 53, wherein the PAI-1 inhibitor penetrates the site within about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 minutes of administration.~~

~~55. The use of any one of claims 36 to 54, wherein the PAI-1 inhibitor penetrates the site within about 5 to about 60 minutes, about 5 to about 12 minutes, about 5 to about 15 minutes, or about 15 to about 30 minutes of administration.~~

~~56. The use of any one of claims 36 to 55, wherein the PAI-1 inhibitor penetrates the site within about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 or 24 hours of administration.~~

~~57. The use of any one of the claims 36 to 56, wherein the PAI-1 inhibitor penetrates the site within about 1 to about 12 hours, about 8 to about 12 hours or 12 hours to about 24 hours of administration.~~

3158. The ~~use~~method of any one of claims 2136 to 3057, comprising more than one administration of the composition comprising the PAI-1 inhibitor over time.

3259. The ~~use~~method of claim 3158, wherein each administration comprising the PAI-1 inhibitor is separated by a specified period of time.

~~60. The use of claim 59, wherein the specified period of time is longer as compared to the specified period of time for administering a reference treatment regimen.~~

3361. The ~~use~~method any one of claims 2136 to 3260, wherein the hair is gray.

3462. The ~~use~~method of any one of claims 2136 to 3260, wherein the hair is not gray.

3563. The ~~use~~method of any one of claims 2136 to 3462, wherein the composition is formulated as a suspension, a foam, a lotion, a cream, ~~-~~a gel, an oil, a powder, a liniment, or drops.

3664. A composition comprising a therapeutically effective amount of a PAI-1 inhibitor effective for treating hair loss, and a pharmaceutically acceptable carrier, formulated for topical administration to a site of a subject, wherein the site contains or did contain a plurality of hair follicles, each with a hair disposed therein, wherein the PAI-1 inhibitor is selected from a group consisting of: 5-Chloro-2-{[(2-{[3-(furan-3-yl)phenyl]amino}-2-oxoethoxy)acetyl]amino benzoic acid, 5-Chloro-2-{[{[3-(furan-3-yl)phenyl]amino}(oxo)acetyl]amino} benzoic acid~~and a pharmaceutically acceptable carrier~~.

~~65. The composition of claim 64, wherein the composition is formulated for topical administration.~~

3766. The composition of claim 3665, wherein the therapeutically effective amount is less than ~~about~~ 0.1% w/w to ~~about~~ 5 % w/w, ~~about~~ 0.1 % to ~~about~~ 10% w/w, ~~about~~ 0.1% to ~~about~~ 15% w/w, ~~about~~ 0.1% w/w to ~~about~~ 20% w/w, or ~~about~~ 1% w/w to ~~about~~ 5% w/w.

~~67. The composition of claim 64, wherein the composition is formulated for oral administration.~~

~~68. The composition of claim 67, wherein the therapeutically effective amount is about 10 mg/day to about 100 mg/day, about 10 mg/day to about 200 mg/day, about 10 mg/day to about 300 mg/day, about 10 mg/day to about 400 mg/day, about 10 mg/day to about 500 mg/day, about 10 mg/day to about 600 mg/day, about 10 mg/day to about 700 mg/day, about 10 mg/day to about 800 mg/day, about 10 mg/day to about 900 mg/day, or about 10 mg/day to about 1000 mg/day.~~

~~69. The composition of claim any one of claims 64 to 68, wherein the PAI-1 inhibitor is selected from the group consisting of : polypeptides, nucleic acids, lipids, carbohydrates, small molecules, metals, polymers, therapeutic antibodies, and combinations thereof.~~

~~70. The composition of claim 69, wherein the nucleic acid is or comprises siRNA.~~

~~71. The composition of claim 69, wherein the PAI-1 inhibitor is selected from a group consisting of : 5-Chloro-2-{[(2-{[3-(furan-3-yl)phenyl]amino}-2-oxoethoxy)acetyl]amino benzoic acid, 5-Chloro-2-{[{[3-(furan-3-yl)phenyl]amino}(oxo)acetyl]amino} benzoic acid, a benzopyran compound, a butadiene, spironolactone, imidapril, an angiotensin converting enzyme inhibitor (ACEI, captopril, or enalapril), an angiotensin II receptor antagonist (AIIRA), a defibrotide (a polydeoxyribonucleotide) and any combination thereof.~~

3872. The composition of claim 3671, wherein the PAI-1 inhibitor is 5-Chloro-2-{[(2-{[3-(furan-3-yl)phenyl]amino}-2-oxoethoxy)acetyl]amino benzoic acid.

3973. The composition of any one of claims 3664 to 3872, wherein the composition comprising the PAI-1 inhibitor is or comprises a suspension.

4074. The composition of any one of claims 3664 to 3872, wherein the composition comprising the PAI-1 inhibitor is or comprises a foam.

4175. The composition of any one of claims 3664 to 3872, wherein the composition comprising the PAI-1 inhibitor comprises an emulsion.

4276. The composition of claim 4175, wherein the emulsion is a nanoemulsion.

4377. The composition of any one of claims 3664 to 4276, wherein the composition comprising the PAI-1 inhibitor is formulated as a suspension, a foam, a lotion, a cream, a gel, an oil, a powder, a liniment, or drops.

4478. A kit comprising a composition comprising a PAI-1 inhibitor as claimed in claim 36, and a patch for use in covering the composition comprising the PAI-1 inhibitor after administration to thea site.

4579. The kit of claim 4478, wherein the composition comprising the PAI-1 inhibitor is incorporated into the patch.

4680. The kit of claim 4478 or claim 4579, wherein the patch comprises microneedles.

4781. The kit of any one of claims 4478 to 4680, wherein the composition comprising the PAI-1 inhibitor is or comprises a suspension.

4882. The kit of any one of claims 4478 to 4680, wherein the composition comprising the PAI-1 inhibitor is or comprises a foam.

4983. The kit of any one of claims 4478 to 4680, wherein the composition comprising the PAI-1 inhibitor comprises an emulsion.

5084. The kit of claim 4983, wherein the emulsion is a nanoemulsion.

5185. A kit comprising a composition comprising a PAI-1 inhibitor as claimed in claim 36, a device for facilitating penetration of a composition comprising the PAI-1 inhibitor into thea site on a subject, and instructions for administering the composition to the site.

5286. The kit of any one of claim 5185, wherein the composition comprising the PAI-1 inhibitor is or comprises a suspension.

5387. The kit of any one of claim 5185, wherein the composition comprising the PAI-1 inhibitor is or comprises a foam.

5488. The kit of claim 5185, wherein the composition comprising the PAI-1 inhibitor comprises an emulsion.

5589. The kit of claim 5488, wherein the emulsion is a nanoemulsion.

5690. The kit of any one of claims 5185 to 5589, wherein the device is a brush or a comb.

5791. The kit of any one of claims 5185 to 5690, wherein the device is a patch, a roller, or a pen.

5892. The kit of any one of claims 4478 to 5791, wherein the composition comprising the PAI-1 inhibitor is formulated as a suspension, a foam, a lotion, a cream, a powder, an ointment, a liniment, a gel, or drops.