

CLAIMS

1. An IL-18 antagonist for use in the treatment and/or prevention of atopic dermatitis or a related condition in a subject in need thereof.
- 5 2. The IL-18 antagonist for use according to claim 1, wherein the IL-18 antagonist specifically binds IL-18, and wherein the IL-18 antagonist does not bind the IL-18/IL-18 binding protein (IL-18 BP) complex.
3. The IL-18 antagonist for use according to any one of the preceding claims, wherein the
10 IL-18 antagonist is an isolated antibody or antibody fragment.
4. The IL-18 antagonist for use according to any one of the preceding claims, wherein the IL-18 antagonist is a human, humanized or chimeric antibody or antibody
15 fragment.
5. The IL-18 antagonist use according to any one of the preceding claims, wherein the IL-18 antagonist binds human IL-18 with a dissociation constant (KD) of 100 pM or less, e.g., 50 pM or less, 25 pM or less, 10 pM or less, 5 pM or less, preferably with a
20 KD of 0.5 pM to 20 pM, in particular as measured by SET.
6. The IL-18 antagonist for use according to any one of the preceding claims, wherein the IL-18 antagonist inhibits IL-18-induced interferon gamma (IFN- γ) production from KG-1 cells with IC₅₀ of less than 5 nM, e.g., 0.1 to 1 nM.
- 25 7. The IL-18 antagonist for use according to any one of the preceding claims, wherein the antibody or the antibody fragment inhibits IL-18-induced interferon gamma (IFN- γ) production in whole blood with IC₅₀ of less than 150 nM, e.g., 5 to 10 nM.
8. The IL-18 antagonist for use according to any one of the preceding claims, wherein
30 the IL-18 antagonist comprises: a heavy chain variable region H-CDR1 comprising

SEQ ID NO: 3, a heavy chain variable region H-CDR2 comprising SEQ ID NO: 9, a heavy chain variable region H-CDR3 comprising SEQ ID NO: 5, a light chain variable region L-CDR1 comprising SEQ ID NO: 6, a light chain variable region L-CDR2 comprising SEQ ID NO: 7, and a light chain variable region L-CDR3 comprising SEQ ID NO: 8.

9. The IL-18 antagonist for use according to claim 8, wherein IL-18 antagonist comprises a heavy chain variable domain comprising SEQ ID NO: 14 or a sequence at least 90% identical thereto; and a light chain variable domain comprising SEQ ID NO: 16 or a sequence at least 90% identical thereto.

10. The IL-18 antagonist for use according to claim 9, wherein the IL-18 antagonist comprises a mutation in the heavy chain framework, wherein the amino acid asparagine at position 30 is replaced with lysine (N30K; numbering according to Kabat).

11. The IL-18 antagonist for use according to any one of claims 8 to 10, wherein the IL-18 antagonist comprises a heavy chain comprising SEQ ID NO: 43 or a sequence at least 90% identical thereto; and a light chain comprising SEQ ID NO: 45 or a sequence at least 90% identical thereto.

12. The IL-18 antagonist for use according to any one of the preceding claims, wherein the treatment results in an improvement in an atopic dermatitis-associated parameter and wherein the improvement in the atopic dermatitis-associated parameter is selected from the group consisting of:

- (a) a decrease from baseline in Investigator's Global Assessment (IGA) score;
- (b) a decrease from baseline in Dermatology Life Quality Index (DLQI);
- (c) a decrease from baseline in a patient global impression of severity (PGIS);
- (d) a decrease from baseline in a patient global impression of change (PGIC);
- (e) a decrease from baseline in Eczema Area and Severity Index (EASI) score; and
- (f) a decrease from baseline in Pruritus Numeric Rating Scale (NRS) score.

13. The IL-18 antagonist for use according to claim 12, wherein the treatment results in an improvement in an atopic dermatitis-associated parameter and wherein the improvement in the atopic dermatitis-associated parameter is selected from the group consisting of:
- (a) a decrease from baseline in Investigator's Global Assessment (IGA) score by at least 2 points, in particular a decrease from baseline in IGA score by at least 2 points and clear or almost clear status;
 - (b) a decrease from baseline in Dermatology Life Quality Index (DLQI) of at least 30%, preferably at least 40%;
 - (c) an improvement from baseline in a patient global impression of severity (PGIS) by at least 1 point;
 - (d) an improvement from baseline in a patient global impression of change (PGIC) by at least 1 point;
 - (e) a decrease from baseline in Eczema Area and Severity Index (EASI) score of at least 50%;
 - (f) percent responders with $\geq 50\%$ improvement in EASI (EASI50);
 - (g) percent responders with $\geq 75\%$ improvement in EASI (EASI75);
 - (h) percent responders with $\geq 90\%$ improvement in EASI (EASI90);
 - (i) percent responders with $\geq 100\%$ improvement in EASI (EASI100);
 - (j) a decrease from baseline in Pruritus Numeric Rating Scale (NRS) score by at least 3 points, preferably by at least 4 points.
14. The IL-18 antagonist for use according to any one of the preceding claims, wherein the atopic dermatitis is moderate-to-severe atopic dermatitis.
15. The IL-18 antagonist for use according to claim 14, wherein the moderate to severe atopic dermatitis is characterized by (i) an Investigator's Global Assessment (IGA) score of 3 or 4, and /or (ii) an Eczema Area and Severity Index (EASI) score of at least 10, particularly at least 12.

16. The IL-18 antagonist for use according to any one of the preceding claims, wherein the atopic dermatitis is accompanied by an infection or wherein the related condition is an infection, in particular a skin infection, more particularly a skin superinfection.
- 5 17. The IL-18 antagonist for use according to claim 16, wherein the infection is (i) a bacterial infection, e.g., staphylococcal bacteria, such as *Staphylococcus* (S.) *aureus*, or streptococcal bacteria, such as *Streptococcus* (S.) *epidermitis*, and / or (ii) a viral infection, e.g., herpes viral infection.
- 10 18. The IL-18 antagonist for use according to any one of the preceding claims, wherein the subject did not adequately respond to a treatment with a topical atopic dermatitis therapy.
- 15 19. The IL-18 antagonist for use according to any one of the preceding claims, wherein the subject was refractory to topical atopic dermatitis therapy or the subject did not adequately respond to a treatment with a topical atopic dermatitis therapy.
- 20 20. The IL-18 antagonist for use according to claim 18 or 19, wherein the topical atopic dermatitis therapy is selected from the group consisting of topical steroid, e.g., corticosteroid, tacrolimus, cyclophosphamide, azathioprine, methotrexate, mycophenolate mofetil, apremilast, calcineurin inhibitor, e.g., topical calcineurin inhibitor, phosphodiesterase 4 (PDE4) inhibitor, e.g., topical PDE4 inhibitor, e.g. Crisaborole, adrenocorticotrophic hormone analogs.
- 25 21. The IL-18 antagonist for use according to claim 20, wherein the topical steroid is selected from the group consisting of a group I topical corticosteroid (TCS), group II topical corticosteroid (TCS) and group III topical corticosteroid (TCS).
- 30 22. The IL-18 antagonist for use according to claim 20, wherein the topical corticosteroid (TCS) is selected from the group consisting of methylprednisolone aceponate, mometasone furoate, fluticasone propionate, betamethasone valerate and

hydrocortisone butyrate.

23. The IL-18 antagonist for use according to any one of the preceding claims, wherein the IL-18 antagonist is to be administered subcutaneously or intravenously to a subject in need thereof.

24. The IL-18 antagonist for use according to any one of the preceding claims, wherein the IL-18 antagonist is to be administered at a dose sufficient to achieve a therapeutically effective serum level.

25. The IL-18 antagonist for use according to claim 24, wherein the serum level is maintained during the treatment course.

26. The IL-18 antagonist for use according to any one of the preceding claims, wherein the IL-18 antagonist is to be administered once a week, once every two weeks, once every three weeks, once every four weeks, once every eight weeks, once every 12 weeks, in particular once every 4 weeks.

27. The IL-18 antagonist for use according to any one of the preceding claims, wherein a second therapeutic agent is to be administered to the subject before, after, or concurrent with the IL-18 antagonist of any one of claims 1 to 11.

28. The IL-18 antagonist for use according to claim 27, wherein the second therapeutic agent is selected from the group consisting of steroid, cyclosporine, tacrolimus, cyclophosphamide, azathioprine, methotrexate, mycophenolate mofetil, apremilast, calcineurin inhibitor, e.g., topical calcineurin inhibitor, phosphodiesterase 4 (PDE4) inhibitor, e.g., topical PDE4 inhibitor, e.g. Crisaborole, adrenocorticotrophic hormone analogs, dupilumab, etanercept, adalimumab, infliximab, omalizumab, secukinumab.

29. The IL-18 antagonist for use according to claim 27, wherein the second therapeutic agent is a low to medium potency steroid, e.g., topical or oral steroid, e.g.,

corticosteroid.

30. The IL-18 antagonist for use according to claim 29, wherein the second therapeutic agent is selected from the group consisting of a group I topical corticosteroid (TCS), group II topical corticosteroid (TCS) and group III topical corticosteroid (TCS).

31. The IL-18 antagonist for use according to claim 29, wherein the topical corticosteroid (TCS) is selected from the group consisting of methylprednisolone aceponate, mometasone furoate, fluticasone propionate, betamethasone valerate and hydrocortisone butyrate.

~~32. A method of treatment and/or prevention of atopic dermatitis or a related condition in a subject in need thereof, comprising administering an IL-18 antagonist.~~

~~33. The method according to claim 32, wherein the IL-18 antagonist specifically binds IL-18, and wherein the IL-18 antagonist does not bind the IL-18/IL-18 binding protein (IL-18 BP) complex.~~

~~34. The method according to claim 32 or 33, wherein the IL-18 antagonist is an isolated antibody or antibody fragment.~~

~~35. The method according to any one of claims 32 to 34, wherein the IL-18 antagonist is a human, humanized or chimeric antibody or antibody fragment.~~

~~36. The method according to any one of claims 32 to 35, wherein the IL-18 antagonist binds human IL-18 with a dissociation constant (KD) of 100 pM or less, e.g., 50 pM or less, 25 pM or less, 10 pM or less, 5 pM or less, preferably with a KD of 0.5 pM to 20 pM, in particular as measured by SET.~~

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37. The method according to any one of claims 32 to 36, wherein the IL-18 antagonist inhibits IL-18 induced interferon gamma (IFN- γ) production from KG-1 cells with IC50 of less than 5 nM, e.g., 0.1 to 1 nM.

38. The method according to any one of claims 32 to 37, wherein IL-18 antagonist inhibits IL-18 induced interferon gamma (IFN- γ) production in whole blood with IC50 of less than 150 nM, e.g., 5 to 10 nM.

39. The method according to any one of claims 32 to 38, wherein the IL-18 antagonist comprises: a heavy chain variable region H-CDR1 comprising SEQ ID NO: 3, a heavy chain variable region H-CDR2 comprising SEQ ID NO: 9, a heavy chain variable region H-CDR3 comprising SEQ ID NO: 5, a light chain variable region L-CDR1 comprising SEQ ID NO: 6, a light chain variable region L-CDR2 comprising SEQ ID NO: 7, and a light chain variable region L-CDR3 comprising SEQ ID NO: 8.

40. The method according to claim 39, wherein the IL-18 antagonist comprises a heavy chain variable domain comprising SEQ ID NO: 14 or a sequence at least 90% identical thereto; and a light chain variable domain comprising SEQ ID NO: 16 or a sequence at least 90% identical thereto.

41. The method according to claim 40, wherein the IL-18 antagonist comprises a mutation in the heavy chain framework, wherein the amino acid asparagine at position 30 is replaced with lysine (N30K; numbering according to Kabat).

42. The method according to any one of claims 39 to 41, wherein the IL-18 antagonist comprises a heavy chain comprising SEQ ID NO: 43 or a sequence at least 90% identical thereto; and a light chain comprising SEQ ID NO: 45 or a sequence at least 90% identical thereto.

43. The method according to any one of claims 32 to 42, wherein the treatment results in an improvement in an atopic dermatitis-associated parameter and wherein the

improvement in the atopic dermatitis-associated parameter is selected from the group consisting of:

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- (a) a decrease from baseline in Investigator's Global Assessment (IGA) score;
- (b) a decrease from baseline in Dermatology Life Quality Index (DLQI);
- (c) a decrease from baseline in a patient global impression of severity (PGIS);
- (d) a decrease from baseline in a patient global impression of change (PGIC);
- (e) a decrease from baseline in Eczema Area and Severity Index (EASI) score; and
- (f) a decrease from baseline in Pruritus Numeric Rating Scale (NRS) score.

44. The method according to any one of claims 32 to 43, wherein the treatment results in an improvement in an atopic dermatitis-associated parameter and wherein the improvement in the atopic dermatitis-associated parameter is selected from the group consisting of:

- (a) a decrease from baseline in Investigator's Global Assessment (IGA) score by at least by 2 points, in particular a decrease from baseline in IGA score by at least by 2 points and clear or almost clear status;
- (b) a decrease from baseline in Dermatology Life Quality Index (DLQI) of at least 30%, preferably at least 40%;
- (c) an improvement from baseline in a patient global impression of severity (PGIS) by at least 1 point;
- (d) an improvement from baseline in a patient global impression of change (PGIC) by at least 1 point;
- (e) a decrease from baseline in Eczema Area and Severity Index (EASI) score of at least 50%;
- (f) percent responders with $\geq 50\%$ improvement in EASI (EASI50);
- (g) percent responders with $\geq 75\%$ improvement in EASI (EASI75);
- (h) percent responders with $\geq 90\%$ improvement in EASI (EASI90);
- (i) percent responders with $\geq 100\%$ improvement in EASI (EASI100);
- (j) a decrease from baseline in Pruritus Numeric Rating Scale (NRS) score by at least 3 points, preferably by at least 4 points.

45. The method according to any one of claims 32 to 44, wherein the atopic dermatitis is moderate to severe atopic dermatitis.

46. The method according to claim 45, wherein the moderate to severe atopic dermatitis is characterized by (i) an Investigator's Global Assessment (IGA) score of 3 or 4, and/or (ii) an Eczema Area and Severity Index (EASI) score of at least 10, in particular at least 12.

47. The method according to any one of claims 32 to 46, wherein the atopic dermatitis is accompanied by an infection or wherein the related condition is an infection, in particular a skin infection, more particularly a skin superinfection.

48. The method according to claim 47, wherein the infection is (i) a bacterial infection, e.g., staphylococcal bacteria, such as *Staphylococcus* (S.) *aureus*, or streptococcal bacteria, such as *Streptococcus* (S.) *epidermitis*, and / or (ii) a viral infection, e.g., herpes viral infection.

49. The method according to any one of claims 32 to 48, wherein the subject did not adequately respond to a treatment with a topical atopic dermatitis therapy.

50. The method according to any one of claims 32 to 49, wherein the subject was refractory to topical atopic dermatitis therapy or the subject did not adequately respond to a treatment with a topical atopic dermatitis therapy.

51. The method according to claim 49 or 50, wherein the topical atopic dermatitis therapy is selected from the group consisting of topical steroid, e.g., corticosteroid, tacrolimus, cyclophosphamide, azathioprine, methotrexate, mycophenolate mofetil, apremilast, calcineurin inhibitor, e.g., topical calcineurin inhibitor, phosphodiesterase 4 (PDE4) inhibitor, e.g., topical PDE4 inhibitor, e.g., Crisaborole, adrenocorticotrophic hormone analogs.

52. The method according to claim 51, wherein the topical steroid is selected from the group consisting of a group I topical corticosteroid (TCS), group II topical corticosteroid (TCS) and group III topical corticosteroid (TCS).

53. The method according to claim 51, wherein the topical corticosteroid (TCS) is selected from the group consisting of methylprednisolone aceponate, mometasone furoate, fluticasone propionate, betamethasone valerate and hydrocortisone butyrate.

54. The method according to any one of claims 32 to 53, wherein the IL-18 antagonist is administered subcutaneously or intravenously to a subject in need thereof.

55. The method according to any one of claims 32 to 54, wherein the IL-18 antagonist is administered at a dose sufficient to achieve a therapeutically effective serum level.

56. The method according to claim 55, wherein the serum level is maintained during the treatment course.

57. The method according to any one of claims 32 to 56, wherein the IL-18 antagonist is administered once a week, once every two weeks, once every three weeks, once every four weeks, once every eight weeks, once every 12 weeks, in particular once every 4 weeks.

58. The method according to any one of claims 32 to 57, wherein a second therapeutic agent is administered to the subject before, after, or concurrent with the isolated antibody or antibody fragment of claims 1 to 11.

59. The method according to claim 58, wherein the second therapeutic agent is selected from the group consisting of steroid, cyclosporine, tacrolimus, cyclophosphamide, azathioprine, methotrexate, mycophenolate mofetil, apremilast, calcineurin inhibitor,

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e.g., topical calcineurin inhibitor, phosphodiesterase 4 (PDE4) inhibitor, e.g., topical PDE4 inhibitor, e.g. Crisaborole, adrenocorticotrophic hormone analogs, dupilumab, etanercept, adalimumab, infliximab, omalizumab, secukinumab.

60. The method according to claim 58, wherein the second therapeutic agent is a low to medium potency steroid, e.g., topical or oral steroid, e.g., corticosteroid.

61. The method according to claim 60, wherein the second therapeutic agent is selected from the group consisting of a group I topical corticosteroid (TCS), group II topical corticosteroid (TCS) and group III topical corticosteroid (TCS).

62. The method according to claim 60, wherein the topical corticosteroid (TCS) is selected from the group consisting of methylprednisolone aceponate, mometasone furoate, fluticasone propionate, betamethasone valerate and hydrocortisone butyrate.

63-32. Use of an IL-18 antagonist for the manufacture of a medicament for treatment and/or prevention of atopic dermatitis or a related condition in a subject in need thereof.

64. Use of an IL-18 antagonist in treatment and/or prevention of atopic dermatitis or a related condition in a subject in need thereof.

65-33. The use according to claim 63-32 or 64, wherein the IL-18 antagonist specifically binds IL-18, and wherein the IL-18 antagonist does not bind the IL-18/IL-18 binding protein (IL-18 BP) complex.

66-34. The use according to any one of claims 63-32 to 65-33, wherein the IL-18 antagonist is an isolated antibody or antibody fragment.

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~~67~~35. The use according to any one of claims ~~63~~32 to ~~66~~34, wherein the IL-18 antagonist is a human, humanized or chimeric antibody or antibody fragment.

5 ~~68~~36. The use according to any one of claims ~~63~~32 to ~~67~~35, wherein the IL-18 antagonist binds human IL-18 with a dissociation constant (KD) of 100 pM or less, e.g., 50 pM or less, 25 pM or less, 10 pM or less, 5 pM or less, preferably with a KD of 0.5 pM to 20 pM, in particular as measured by SET.

10 ~~69~~37. The use according to any one of claims ~~63~~32 to ~~68~~36, wherein the IL-18 antagonist inhibits IL-18-induced interferon gamma (IFN- γ) production from KG-1 cells with IC50 of less than 5 nM, e.g., 0.1 to 1 nM.

15 ~~70~~38. The use according to any one of claims ~~63~~32 to ~~69~~37, wherein the IL-18 antagonist inhibits IL-18-induced interferon gamma (IFN- γ) production in whole blood with IC50 of less than 150 nM, e.g., 5 to 10 nM.

20 ~~71~~39. The use according to any one of claims ~~63~~32 to ~~70~~38, wherein the IL-18 antagonist comprises: a heavy chain variable region H-CDR1 comprising SEQ ID NO: 3, a heavy chain variable region H-CDR2 comprising SEQ ID NO: 9, a heavy chain variable region H-CDR3 comprising SEQ ID NO: 5, a light chain variable region L-CDR1 comprising SEQ ID NO: 6, a light chain variable region L-CDR2 comprising SEQ ID NO: 7, and a light chain variable region L-CDR3 comprising SEQ ID NO: 8.

25 ~~72~~40. The use according to claim ~~71~~39, wherein the IL-18 antagonist comprises a heavy chain variable domain comprising SEQ ID NO: 14 or a sequence at least 90% identical thereto; and a light chain variable domain comprising SEQ ID NO: 16 or a sequence at least 90% identical thereto.

30 ~~73~~41. The use according to claim ~~72~~40, wherein the IL-18 antagonist comprises a mutation in the heavy chain framework, wherein the amino acid asparagine at position

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30 is replaced with lysine (N30K; numbering according to Kabat).

74.42. The use according to any one of claims ~~71-39~~ to ~~7341~~, wherein the IL-18 antagonist comprises a heavy chain comprising SEQ ID NO: 43 or a sequence at least 90% identical thereto; and a light chain comprising SEQ ID NO: 45 or a sequence at least 90% identical thereto.

75.43. The use according to any one of claims ~~63-32~~ to ~~7442~~, wherein the treatment results in an improvement in an atopic dermatitis-associated parameter and wherein the improvement in the atopic dermatitis-associated parameter is selected from the group consisting of:

- (a) a decrease from baseline in Investigator's Global Assessment (IGA) score;
- (b) a decrease from baseline in Dermatology Life Quality Index (DLQI);
- (c) a decrease from baseline in a patient global impression of severity (PGIS);
- (d) a decrease from baseline in a patient global impression of change (PGIC);
- ~~(e)~~ a decrease from baseline in Eczema Area and Severity Index (EASI) score; and
- (f) a decrease from baseline in Pruritus Numeric Rating Scale (NRS) score.

76.44. The use according to claim ~~7543~~, wherein the treatment results in an improvement in an atopic dermatitis-associated parameter and wherein the improvement in the atopic dermatitis-associated parameter is selected from the group consisting of:

- (a) a decrease from baseline in Investigator's Global Assessment (IGA) score by at least 2 points, in particular a decrease from baseline in IGA score by at least 2 points and clear or almost clear status;
- (b) a decrease from baseline in Dermatology Life Quality Index (DLQI) of at least 30%, preferably at least 40%;
- (c) an improvement from baseline in a patient global impression of severity (PGIS) by at least 1 point;
- (d) an improvement from baseline in a patient global impression of change (PGIC) by at least 1 point;

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(e) a decrease from baseline in Eczema Area and Severity Index (EASI) score of at least 50%;

(f) percent responders with $\geq 50\%$ improvement in EASI (EASI50);

(g) percent responders with $\geq 75\%$ improvement in EASI (EASI75);

5 (h) percent responders with $\geq 90\%$ improvement in EASI (EASI90);

(i) percent responders with $\geq 100\%$ improvement in EASI (EASI100);

(j) a decrease from baseline in Pruritus Numeric Rating Scale (NRS) score by at least 3 points, preferably by at least 4 points.

10 ~~77.45.~~ The use according to any one of claims ~~63-32~~ to ~~7644~~, wherein the atopic dermatitis is moderate-to-severe atopic dermatitis.

15 ~~78.46.~~ The use according to claim ~~7745~~, wherein the moderate to severe atopic dermatitis is characterized by (i) an Investigator's Global Assessment (IGA) score of 3 or 4, and /or (ii) an Eczema Area and Severity Index (EASI) score of at least 10, in particular at least 10.

20 ~~79.47.~~ The use according to any one of claims ~~63-32~~ to ~~7846~~, wherein the atopic dermatitis is accompanied by an infection or wherein the related condition is an infection, in particular a skin infection, more particularly a skin superinfection.

25 ~~80.48.~~ The use according to claim ~~7947~~, wherein the infection is (i) a bacterial infection, e.g., staphylococcal bacteria, such as Staphylococcus (S.) aureus, or streptococcal bacteria, such as Streptococcus (S.) epidermitis, and / or (ii) a viral infection, e.g., herpes viral infection.

~~81.49.~~ The use according to any one of claims ~~63-32~~ to ~~8048~~, wherein the subject did not adequately respond to a treatment with a topical atopic dermatitis therapy.

30 ~~82.50.~~ The use according to any one of claims ~~63-32~~ to ~~8149~~, wherein the subject was refractory to a topical atopic dermatitis therapy or the subject did not adequately

respond to a treatment with a topical atopic dermatitis therapy.

83-51. The use according to claim ~~81-49~~ or ~~82-50~~, wherein the topical atopic dermatitis therapy is selected from the group consisting of topical steroid, e.g., corticosteroid, tacrolimus, cyclophosphamide, azathioprine, methotrexate, mycophenolate mofetil, apremilast, calcineurin inhibitor, e.g., topical calcineurin inhibitor, phosphodiesterase 4 (PDE4) inhibitor, e.g., topical PDE4 inhibitor, e.g. Crisaborole, adrenocorticotrophic hormone analogs.

84-52. The use according to claim ~~83-51~~, wherein the topical steroid is selected from the group consisting of a group I topical corticosteroid (TCS), group II topical corticosteroid (TCS) and group III topical corticosteroid (TCS).

85-53. The use according to claim ~~83-52~~, wherein the topical corticosteroid (TCS) is selected from the group consisting of methylprednisolone aceponate, mometasone furoate, fluticasone propionate, betamethasone valerate and hydrocortisone butyrate.

86-54. The use according to any one of claims ~~63-31~~ to ~~85-53~~, wherein the IL-18 antagonist is to be administered subcutaneously or intravenously to a subject in need thereof.

87-55. The use according to any one of claims ~~63-31~~ to ~~86-54~~, wherein the IL-18 antagonist is to be administered at a dose sufficient to achieve a therapeutically effective serum level.

88-56. The use according to claim ~~87-55~~, wherein the serum level is maintained during the treatment course.

89-57. The use according to any one of claims ~~63-32~~ to ~~88-56~~, wherein the IL-18 antagonist is to be administered once a week, once every two weeks, once every three weeks, once every four weeks, once every eight weeks, once every 12 weeks, in

particular once every 4 weeks.

5 | ~~90.58.~~ The use according to any one of claims ~~63-32~~ to ~~8957~~, wherein a second therapeutic agent is to be administered to the subject before, after, or concurrent with the isolated antibody or antibody fragment of claims 1 to 11.

10 | ~~91.59.~~ The use according to claim ~~9058~~, wherein the second therapeutic agent is selected from the group consisting of steroid, cyclosporine, tacrolimus, cyclophosphamide, azathioprine, methotrexate, mycophenolate mofetil, apremilast, calcineurin inhibitor, e.g., topical calcineurin inhibitor, phosphodiesterase 4 (PDE4) inhibitor, e.g., topical PDE4 inhibitor, e.g. Crisaborole, adrenocorticotrophic hormone analogs, dupilumab, etanercept, adalimumab, infliximab, omalizumab, secukinumab.

15 | ~~92.60.~~ The use according to claim ~~9058~~, wherein the second therapeutic agent is a low to medium potency steroid, e.g., topical or oral steroid, e.g., corticosteroid.

20 | ~~93.61.~~ The use according to claim ~~9058~~, wherein the second therapeutic agent is selected from the group consisting of a group I topical corticosteroid (TCS), group II topical corticosteroid (TCS) and group III topical corticosteroid (TCS).

25 | ~~94.62.~~ The use according to claim ~~9058~~, wherein the topical corticosteroid (TCS) is selected from the group consisting of methylprednisolone aceponate, mometasone furoate, fluticasone propionate, betamethasone valerate and hydrocortisone butyrate.