

CLAIMS:

1. An interleukin-13 (IL-13) binding protein for use in ~~a method of treating atopic dermatitis (AD) in a subject, wherein the method comprises the steps of:~~ (a) ~~administering~~ a first dose of the IL-13 binding protein is to be administered to the subject; and (b) ~~administering~~ one or more secondary dose(s) of the IL-13 binding protein are to be administered to the subject, wherein each secondary dose is to be administered to the subject from 15 days to 35 days after the immediately preceding dose, wherein the IL-13 binding protein is an anti-IL-13 antibody, or an IL-13 binding fragment thereof, comprising a heavy chain variable region (HCVR) and a light chain variable region (LCVR), wherein:
 - (i) the heavy chain variable region comprises:
 - a heavy chain complementarity determining region 1 (HCDR1) comprising an amino acid sequence of SEQ ID NO:1; a heavy chain complementarity determining region 2 (HCDR2) comprising an amino acid sequence of SEQ ID NO:2; and a heavy chain complementarity determining region 3 (HCDR3) comprising an amino acid sequence of SEQ ID NO:3; and
 - (ii) the light chain variable region comprises:
 - a light chain complementarity determining region 1 (LCDR1) comprising an amino acid sequence of SEQ ID NO:4; a light chain complementarity determining region 2 (LCDR2) comprising an amino acid sequence of SEQ ID NO:5; and a light chain complementarity determining region 3 (LCDR3) comprising an amino acid sequence of SEQ ID NO:6.

2. ~~A method of treating atopic dermatitis (AD) in a subject in need thereof, wherein the method comprises the steps of: (a) administering a first dose of an IL-13 binding protein to the subject; and (b) administering one or more secondary dose(s) of the IL-13 binding protein to the subject, wherein each secondary dose is administered to the subject from 15 days to 35 days after the immediately preceding dose.~~

3. ~~2.~~ Use of an IL-13 binding protein in the manufacture of a medicament for treating atopic dermatitis (AD) in a subject, wherein ~~the method for treating AD comprises~~

~~the steps of:~~ (a) ~~administering~~ a first dose of the IL-13 binding protein is to be administered to the subject; and (b) ~~administering~~ one or more secondary dose(s) of the IL-13 binding protein are to be administered to the subject, wherein each secondary dose is to be administered to the subject from 15 days to 35 days after the immediately preceding dose, wherein the IL-13 binding protein is an anti-IL-13 antibody, or an IL-13 binding fragment thereof, comprising a heavy chain variable region (HCVR) and a light chain variable region (LCVR), wherein:

(i) the heavy chain variable region comprises:

a heavy chain complementarity determining region 1 (HCDR1) comprising an amino acid sequence of SEQ ID NO:1; a heavy chain complementarity determining region 2 (HCDR2) comprising an amino acid sequence of SEQ ID NO:2; and a heavy chain complementarity determining region 3 (HCDR3) comprising an amino acid sequence of SEQ ID NO:3; and

(ii) the light chain variable region comprises:

a light chain complementarity determining region 1 (LCDR1) comprising an amino acid sequence of SEQ ID NO:4; a light chain complementarity determining region 2 (LCDR2) comprising an amino acid sequence of SEQ ID NO:5; and a light chain complementarity determining region 3 (LCDR3) comprising an amino acid sequence of SEQ ID NO:6.

4.3. The IL-13 binding protein for use, ~~the method~~ or the use according to any one of the preceding claims, wherein the ~~method~~ treatment achieves:

- a. $\geq 50\%$ improvement of Eczema Area and Severity Index (EASI-50) compared to baseline;
- b. at least a 2 point reduction of Investigator's Global Assessment (IGA) score compared to baseline;
- c. at least a 4 point reduction in POEM score compared to baseline;
- d. at least a 1 point reduction, at least a 2 point reduction, at least a 3 point reduction or at least a 4 point reduction in Worst Daily Pruritus Numerical Rating Scale (NRS) compared to baseline;
- e. at least a 0.4 point reduction in eczema-related sleep interference compared to baseline;

- f. at least a 1-point reduction, at least a 2-point reduction, at least a 3-point reduction or at least a 4-point reduction in Hospital Anxiety and Depression Scale (HADS) score compared to baseline;
- g. at least a 4-point increase in SF-36 Physical Component Summary Score and/or at least a 2-point increase in SF-36 Mental Component Summary Score compared to baseline;
- h. at least a 0.2-point increase in EQ-5D-5L index score compared to baseline;
- i. at least a 4-point reduction in DLQI score compared to baseline; and/or
- j. at least a 1-point reduction in PGI-B score compared to baseline.

~~5.4.~~ The IL-13 binding protein for use, ~~the method~~ or the use according to any one of the preceding claims, wherein the AD is moderate-to-severe or severe AD.

~~6.5.~~ The IL-13 binding protein for use, ~~the method~~ or the use according to any one of the preceding claims, wherein the ~~method~~ treatment is for treating a skin infection (e.g. *Staphylococcus aureus* infection), pruritus, eczema-related sleep interference, anxiety and/or depression, or for improving health status and/or quality of life.

~~7.6.~~ The IL-13 binding protein for use, ~~the method~~ or the use according to any one of the preceding claims, wherein each secondary dose is to be administered to the subject from 25 days to 31 days after the immediately preceding dose.

~~8.7.~~ The IL-13 binding protein for use, ~~the method~~ or the use according to any one of the preceding claims, wherein each secondary dose is to be administered to the subject about 4 weeks after the immediately preceding dose.

~~9.8.~~ The IL-13 binding protein for use, ~~the method~~ or the use according to any one of the preceding claims, wherein ~~step (b)~~ is to be continued for at least 8 weeks, at least 12 weeks, at least 3 months, at least 16 weeks, at least 20 weeks, at least 24 weeks, at least 6 months, at least 28 weeks, at least 32 weeks, at least 36 weeks, at least a year, or at least 52 weeks or more.

~~10.9.~~ The IL-13 binding protein for use, ~~the method~~ or the use according to any one of the preceding claims, wherein ~~the method comprises the steps of:~~ (a) ~~administering~~ a first dose of about 300 mg of the IL-13 binding protein is to be administered to the subject; and (b) ~~administering~~ one or more secondary dose(s) of about 300 mg of the IL-13 binding protein are to be administered to the subject, wherein each secondary dose is to be administered to the subject about 4 weeks after the immediately preceding dose.

~~11.10.~~ The IL-13 binding protein for use, ~~the method~~ or the use according to any one of the preceding claims, wherein ~~the method comprises the steps of:~~ (a) ~~subcutaneously administering~~ a first dose of about 300 mg of the IL-13 binding protein is to be subcutaneously administered to the subject; and (b) ~~subcutaneously administering~~ one or more secondary dose(s) of about 300 mg of the IL-13 binding protein are to be subcutaneously administered to the subject, wherein each secondary dose is to be administered to the subject about 4 weeks after the immediately preceding dose.

~~12.11.~~ The IL-13 binding protein for use, ~~the method~~ or the use according to any one of the preceding claims, wherein ~~the method comprises the steps of:~~ (a) ~~subcutaneously administering~~ a first dose of about 300 mg of the IL-13 binding protein is to be subcutaneously administered to the subject; and (b) ~~subcutaneously administering~~ one or more secondary dose(s) of about 300 mg of the IL-13 binding protein are to be subcutaneously administered to the subject, wherein each secondary dose is to be administered to the subject about 4 weeks after the immediately preceding dose, wherein the ~~method~~ treatment is to be carried out for about 12 weeks.

~~13.12.~~ The IL-13 binding protein for use, ~~the method~~ or the use according to any one of the preceding claims, wherein ~~prior to step (a) the method further comprises a step of administering~~ one or more prior dose(s) of the IL-13 binding protein are to be administered to the subject prior to (a).

~~14.13.~~ The IL-13 binding protein for use, ~~the method~~ or the use according to claim ~~13~~12, wherein each prior dose of the IL-13 binding protein is to be administered to the subject from 3 days to 6 weeks after the immediately preceding prior dose.

~~15.14.~~ The IL-13 binding protein for use, ~~the method~~ or the use according to claim ~~13~~12 or claim ~~14~~13, wherein ~~prior to step (a) the method further comprises administering one or more prior dose(s) of the IL-13 binding protein are to be administered to the subject for about 2 weeks, about 4 weeks, about 6 weeks, about 8 weeks, about 12 weeks, about 16 weeks or about 20 weeks or more prior to (a).~~

~~16.15.~~ The IL-13 binding protein for use, ~~the method~~ or the use according to any one of the preceding claims, wherein ~~the method comprises the steps of:~~

- (i) ~~administering~~ one or more prior dose(s) of the IL-13 binding protein are to be administered to the subject for from 2 weeks to 36 weeks, wherein each prior dose is to be administered from 3 days to 2 weeks after the immediately preceding dose;
- (ii) ~~administering~~ a first dose of the IL-13 binding protein is to be administered to the subject; and
- (iii) ~~administering~~ one or more secondary dose(s) of the IL-13 binding protein are to be administered to the subject for at least 8 weeks, wherein each secondary dose of the IL-13 binding protein is to be administered to the subject from 15 days to 35 days after the immediately preceding dose,

wherein each dose is from about 10 to about 600 mg of IL-13 binding protein.

~~17.16.~~ The IL-13 binding protein for use, ~~the method~~ or the use according to any one of the preceding claims, wherein ~~following step (b) the method further comprises a step of:~~ (c) ~~administering~~ one or more tertiary dose(s) of the IL-13 binding protein are to be administered to the subject following (b).

~~18.17.~~ The IL-13 binding protein for use, ~~the method~~ or the use according to claim ~~17~~16, wherein each tertiary dose of the IL-13 binding protein is to be administered from 1 week to 6 weeks after the immediately preceding dose.

~~19.18.~~ The IL-13 binding protein for use, ~~the method~~ or the use according to claim ~~17~~8, wherein each of the one or more tertiary dose(s) of the IL-13 binding protein is to be administered to the subject 2 weeks after the immediately preceding dose.

~~20.19.~~ The IL-13 binding protein for use, ~~the method~~ or the use according to any one of the preceding claims, wherein ~~the method comprises the steps of:~~

- (i) ~~administering~~ one or more prior dose(s) of the IL-13 binding protein are to be administered to the subject for around 8 weeks to 16 weeks, wherein each prior dose is to be administered from 12 days to 16 days after the immediately preceding dose;
- (ii) ~~administering~~ a first dose of the IL-13 binding protein is administered to the subject; and

- (iii) ~~administering~~ one or more secondary dose(s) of the IL-13 binding protein are to be administered to the subject for at least 12 weeks, wherein each secondary dose of the IL-13 binding protein is to be administered to the subject from 26 days to 30 days after the immediately preceding dose,

wherein each dose is from about 250 to about 350 mg of IL-13 binding protein.

~~21.20.~~ The IL-13 binding protein for use, ~~the method~~ or the use according to any one of the preceding claims, wherein ~~the method comprises the steps of:~~

- (i) ~~administering~~ one or more prior dose(s) of the IL-13 binding protein are to be administered to the subject for around 8 weeks to 16 weeks, wherein each prior dose is to be administered from 12 days to 16 days after the immediately preceding dose;
- (ii) ~~administering~~ a first dose of the IL-13 binding protein is to be administered to the subject; and

- (iii) ~~administering~~ one or more secondary dose(s) of the IL-13 binding protein are to be administered to the subject for at least 12 weeks, wherein each secondary dose of the IL-13 binding protein is to administered to the subject from 26 days to 30 days after the immediately preceding dose, wherein the first dose of said one or more prior doses is around 600 mg of IL-13 binding protein and each dose (prior dose(s), first dose, and secondary dose(s)) administered after the first of said one or more prior doses is around 300 mg of IL-13 binding protein.

~~22.21.~~ The IL-13 binding protein for use, ~~the method~~ or the use according to any one of the preceding claims, wherein ~~the method comprises the steps of:~~

- (i) ~~administering~~ one or more prior dose(s) of the IL-13 binding protein is to be administered to the subject for around 12 weeks to 16 weeks, wherein each prior dose is to be administered about 2 weeks after the immediately preceding dose;
- (ii) ~~administering~~ a first dose of the IL-13 binding protein is to be administered to the subject; and
- (iii) ~~administering~~ one or more secondary dose(s) of the IL-13 binding protein is to be administered to the subject for at least 16 weeks, wherein each secondary dose of the IL-13 binding protein is to be administered to the subject around 4 weeks after the immediately preceding dose,

wherein each dose is around 300 mg of IL-13 binding protein.

~~23.22.~~ The IL-13 binding protein for use, ~~the method~~ or the use according to any one of the preceding claims, wherein ~~the method comprises the steps of:~~

- (i) ~~administering~~ one or more prior dose(s) of the IL-13 binding protein is to be administered to the subject for around 12 weeks to 16 weeks, wherein each prior dose is to be administered about 2 weeks after the immediately preceding dose;
- (ii) ~~administering~~ a first dose of the IL-13 binding protein is to be administered to the subject; and
- (iii) ~~administering~~ one or more secondary dose(s) of the IL-13 binding protein is to be administered to the subject for at least 16 weeks, wherein each secondary dose of the IL-13 binding protein is to be administered to the subject around 4 weeks after the immediately preceding dose, wherein the first dose of said one or more prior doses is around 600 mg of IL-13 binding protein and each dose (prior dose(s), first dose, and secondary dose(s)) administered after the first of said one or more prior doses is around 300 mg of IL-13 binding protein.

23. The IL-13 binding protein for use, or the use according to any one of the preceding claims, wherein the administration of one or more prior dose(s) is to be continued until the subject achieves an IGA score of 0 or 1 and/or a 75% improvement of EASI-75 over baseline in the subject.

24. An interleukin-13 (IL-13) binding protein for use in ~~a method of treating a skin infection in a subject with moderate-to-severe or severe AD, wherein the method comprises administering the IL-13 binding protein~~ is to be administered to the subject.

~~25. A method of treating a skin infection in a subject with moderate to severe or severe AD, wherein the method comprises administering an IL-13 binding protein to the subject in a therapeutically effective amount.~~

~~26.~~25. Use of an IL-13 binding protein in the manufacture of a medicament for treating a skin infection in a subject with moderate-to-severe or severe AD, wherein ~~the method of treating a skin infection comprises administering a therapeutically effective amount of the IL-13 binding protein~~ is to be administered to the subject.

~~27.~~26. The IL-13 binding protein for use according to claim 24, ~~the method of claim 25 or the use according to claim 26~~25, wherein the ~~method treatment~~ is as defined in any one of claims 4-23~~1-23~~.

~~28.~~27. An IL-13 binding protein for use in ~~a method of treating pruritus in a subject with moderate-to-severe or severe AD, wherein the method comprises administering an IL-13 binding protein~~ is to be administered to the subject.

~~29. A method of treating pruritus in a subject with moderate to severe or severe AD, wherein the method comprises administering an IL-13 binding protein to the subject.~~

~~30.~~28. Use of an IL-13 binding protein in the manufacture of a medicament for treating pruritus in a subject with moderate-to-severe or severe AD, wherein ~~the method of treating pruritus comprises administering the IL-13 binding protein~~ is to be administered to the subject.

~~31.29.~~ The IL-13 binding protein for use according to claim ~~28~~27, ~~the method of claim~~
~~29~~ or the use according to claim ~~30~~28, wherein the ~~method~~treatment is as defined in
any one of claims ~~4-23~~1-23.

~~32.30.~~ An IL-13 binding protein for use in a ~~method of treating~~ eczema-related sleep
interference in a subject with moderate-to-severe or severe AD, wherein ~~the method~~
~~comprises administering the IL-13 binding protein~~ is to be administered to the
subject.

~~33.~~ A ~~method of treating eczema-related sleep interference in a subject with moderate-~~
~~to severe or severe AD, wherein the method comprises administering the IL-13~~
~~binding protein to the subject.~~

~~34.31.~~ Use of an IL-13 binding protein in the manufacture of a medicament for treating
eczema-related sleep interference in a subject with moderate-to-severe or severe
AD, wherein ~~the method of treating eczema-related sleep interference comprises~~
~~administering the IL-13 binding protein~~ is to be administered to the subject.

~~35.32.~~ The IL-13 binding protein for use according to claim ~~32~~30, ~~the method of claim~~
~~33~~ or the use according to claim ~~34~~31, wherein the ~~method~~treatment is as defined in
any one of claims ~~4-23~~1-23.

~~36.33.~~ An IL-13 binding protein for use in a ~~method of treating~~ anxiety and/or
depression in a subject with moderate-to-severe or severe AD, wherein ~~the method~~
~~comprises administering the IL-13 binding protein~~ is to be administered to the
subject.

~~37.~~ A ~~method of treating anxiety and/or depression in a subject with moderate-to-severe~~
~~or severe AD, wherein the method comprises administering an IL-13 binding protein~~
~~to the subject.~~

~~38.34.~~ Use of an IL-13 binding protein in the manufacture of a medicament for treating anxiety and/or depression in a subject with moderate-to-severe or severe AD, wherein ~~the method of treating anxiety and/or depression comprises administering~~ the IL-13 binding protein is to be administered to the subject.

~~39.35.~~ The IL-13 binding protein for use according to claim ~~3633~~, ~~the method of claim 37~~ or the use according to claim ~~3834~~, wherein the ~~method-treatment~~ is as defined in any one of claims ~~4-231-23~~.

~~40.36.~~ An IL-13 binding protein for use in a ~~method of~~ improving health status and/or quality of life in a subject with moderate-to-severe or severe AD, wherein ~~the method comprises administering~~ the IL-13 binding protein is to be administered to the subject.

~~41.~~ A ~~method of improving health status and/or quality of life in a subject with moderate to severe or severe AD, wherein the method comprises administering an IL-13 binding protein to the subject.~~

~~42.37.~~ Use of an IL-13 binding protein in the manufacture of a medicament for improving health status and/or quality of life in a subject with moderate-to-severe or severe AD, wherein ~~the method of improving health status and/or quality of life comprises administering~~ the IL-13 binding protein is to be administered to the subject.

~~43.38.~~ The IL-13 binding protein for use according to claim ~~4036~~, ~~the method of claim 41~~ or the use according to claim ~~4237~~, wherein the ~~method-administration~~ is as defined in any one of claims ~~4-231-23~~.

~~44.39.~~ The IL-13 binding protein for use, ~~the method~~ or the use according to any one of the preceding claims, wherein each dose of IL-13 binding protein is to be administered in one or two injections.

~~45.40.~~ The IL-13 binding protein for use, ~~the method~~ or the use according to any one of the preceding claims, wherein each dose of the IL-13 binding protein is to be administered subcutaneously.

~~46.41.~~ The IL-13 binding protein for use, ~~the method~~ or the use according to any one of the preceding claims, wherein each dose of the IL-13 binding protein is to be administered as a pharmaceutical composition comprising 50 mM sodium acetate buffer, 85 mM sodium chloride, 0.01% (w/v) polysorbate 80, wherein the pharmaceutical composition has a pH of 5.5.

~~47.42.~~ The IL-13 binding protein for use, ~~the method~~ or the use according to any one of the preceding claims, wherein the IL-13 binding protein is an anti-IL-13 antibody, or an IL-13-binding fragment thereof.

~~48.43.~~ The IL-13 binding protein for use, ~~the method~~ or the use according to any one of the preceding claims, wherein the IL-13 binding protein is a monoclonal anti-IL-13 antibody, or an IL-13-binding fragment thereof.

~~49.44.~~ The IL-13 binding protein for use, ~~the method~~ or the use according to any one of the preceding claims, wherein the IL-13 binding protein is a human anti-IL-13 antibody, or an IL-13-binding fragment thereof.

~~50.45.~~ The IL-13 binding protein for use, ~~the method~~ or the use according to any one of claims ~~47-49~~42-44, wherein the IL-13 antibody is an IgG4 antibody.

~~51.46.~~ The IL-13 binding protein for use, ~~the method~~ or the use according to any one of claims ~~47-50~~42-45, wherein the IL-13-binding fragment is selected from a Fab, Fab', F(ab')₂, Fd, Fv, single-chain Fv (scFv), or disulfide-linked Fvs (sdFv).

~~52.~~ ~~The IL-13 binding protein for use, the method or the use according to any one of claims 47-51, wherein the anti-IL-13 antibody, or the IL-13 binding fragment~~

thereof, comprises a heavy chain variable region (HCVR) and a light chain variable region (LCVR), wherein:

(i) the heavy chain variable region comprises:

a heavy chain complementarity determining region 1 (HCDR1) comprising an amino acid sequence of SEQ ID NO:1;

a heavy chain complementarity determining region 2 (HCDR2) comprising an amino acid sequence of SEQ ID NO:2; and

a heavy chain complementarity determining region 3 (HCDR3) comprising an amino acid sequence of SEQ ID NO:3; and

(ii) the light chain variable region comprises:

a light chain complementarity determining region 1 (LCDR1) comprising an amino acid sequence of SEQ ID NO:4;

a light chain complementarity determining region 2 (LCDR2) comprising an amino acid sequence of SEQ ID NO:5; and

a light chain complementarity determining region 3 (LCDR3) comprising an amino acid sequence of SEQ ID NO:6.

~~53.47.~~ -The IL-13 binding protein for use, the method or the use according to any one of claims ~~47-52~~42-46, wherein the anti-IL-13 antibody, or the IL-13-binding fragment thereof, further comprises:

(i) an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to a heavy chain variable region sequence of SEQ ID NO: 8; and/or

(ii) an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to a light chain variable region sequence of SEQ ID NO: 10.

~~54.48.~~ The IL-13 binding protein for use, the method or the use according to any one of claims ~~47-53~~42-47, wherein the anti-IL-13 antibody, or the IL-13-binding fragment thereof, comprises a heavy chain variable region sequence of SEQ ID NO: 8 and a light chain variable region sequence of SEQ ID NO: 10.

~~55.49.~~ The IL-13 binding protein for use, ~~the method~~ or the use according to any one of claims ~~47-54~~42-48, wherein the anti-IL-13 antibody, or the IL-13-binding fragment thereof, comprises: (i) an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the heavy chain sequence of SEQ ID NO: 11; and/or (ii) an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical to the light chain sequence of SEQ ID NO: 12.

~~56.50.~~ The IL-13 binding protein for use, ~~the method~~ or the use according to any one of claims ~~47-55~~42-49, wherein the anti-IL-13 antibody, or the IL-13-binding fragment thereof, comprises a heavy chain of SEQ ID NO: 11 and a light chain sequence of SEQ ID NO: 12.

~~57.51.~~ The IL-13 binding protein for use, ~~the method~~ or the use according to any one of the preceding claims, wherein the IL-13 binding protein is to be administered as a monotherapy.

~~58.52.~~ The IL-13 binding protein for use, ~~the method~~ or the use according to any one of the preceding claims, wherein the IL-13 binding protein is to be administered in combination with a second therapeutic agent selected from the group consisting of a topical corticosteroid, a topical calcineurin inhibitor, an anti-histamine, an emollient, or an anti-bacterial therapeutic.

53. The IL-13 binding protein for use, or the use according to any one of the preceding claims, wherein the subject has contraindications to cyclosporine A or the atopic dermatitis is not adequately controlled by cyclosporine A.

54. The IL-13 binding protein for use, or the use according to any one of the preceding claims, wherein the subject has experienced conjunctivitis when treated with (i) the IL-13 binding protein in combination with a topical corticosteroid, (ii) an anti-IL4R α antibody, or (iii) an antibody that inhibits IL4/IL13 signalling, e.g. dupilumab.