

protease inhibitor Kazal-type 5 (SPINK5). See Descargues et al., Nat Genet. 2005 Jan;37(1):56-65 (2004). SPINK5 has been shown to inhibit several members of the KLK serine protease family (e.g. KLK5 and KLK7). See Wang et al., Exp Dermatol. Jul;23(7):524-6 (2014). The absence of SPINK5 in Netherton Syndrome results in unopposed KLKs activities. KLK5 hyperactivity is thought to be a key element in the pathophysiology of Netherton Syndrome as KLK5 is a regulator of proteolysis in the epidermis. Ablation of KLK5 and KLK7 rescues lethality of Netherton Syndrome-like phenotype. See Briot et al., J Exp Med. May 11;206(5):1135-47 (2009); Furio et al., J Exp Med. Mar 10;211(3):499-513 (2014); and Kasparek et al., PLoS Genet. 2017 Jan 17;13(1):e1006566 (2017). Netherton Syndrome is a complex systemic disease with multiple effects for which currently no satisfactory treatment is available.

[005] Asthma is a clinically heterogeneous disorder associated with both genetic and environmental risk factors. Estimates of heritability from asthma twin studies vary from 35% to 80%, indicating an important role for genetic risk. See e.g., Ulleymar et al., Allergy 71, 230-238 (2016). Several large scale GWAS have been performed for asthma and asthma related phenotypes, and many of the loci identified such as those near ORMDL3, IL13, IL1RL1 and TSLP genes have been confirmed in multiple study populations. See e.g., Bonnelykke et al., Nat Genet 46, 51-55 (2014). Recent studies identified a SNP at the KLK4/5 locus which is protective for the risk regarding periostin low, or type 2 low inflammation asthma. In the same study, KLK5 levels were found to be elevated in bronchoalveolar lavage of severe asthma patients supporting the hypothesis that KLK5 plays a role in bronchial obstruction and asthma pathogenesis.

[006] Despite the advances in the field of diseases such as Netherton Syndrome and asthma, there remains a need to identify targets and develop means that can supplement or enhance the efficacy of existing therapies.

SUMMARY

[007] The ~~invention-disclosure~~ provides anti-KLK7 antibodies, anti-KLK5 antibodies, anti-KLK5/KLK7 multispecific antibodies, and methods of using the same.

Embodiment 1. An isolated antibody that binds to human kallikrein related peptidase 7 (KLK7), wherein the antibody:

Embodiment 259. A method of ameliorating skin rash and/or scaling in an individual with Netherton Syndrome comprising administering to the individual an anti-KLK5 antibody and an anti-KLK7 antibody, wherein the anti-KLK5 antibody inhibits KLK5 protease activity, and wherein the anti-KLK7 antibody inhibits KLK7 protease activity.

Embodiment 260. The use of any one of embodiments 192, 193, 240, or 247 or the method of any one of embodiments 205, 206, 209, 243, or 254-257, or the antibody, bispecific antibody, or pharmaceutical composition for use of embodiment 237, wherein the skin inflammatory cytokines are one or more of IL-8, TNF α , IL-6, IL-4, and/or G-CSF.

Embodiment 261. A bispecific antibody comprising a first binding domain and a second binding domain, wherein the first binding domain binds human KLK7 and the second binding domain binds human KLK5, wherein the first binding domain comprises a heavy chain amino acid sequence of SEQ ID NO: 194, and a light chain amino acid sequence of SEQ ID NO: 113, and the second binding domain comprises a heavy chain amino acid sequence of SEQ ID NO: 195, and a light chain amino acid sequence of SEQ ID NO: 115.

Embodiment 262. A bispecific antibody comprising a first binding domain and a second binding domain, wherein the first binding domain binds human KLK7 and the second binding domain binds human KLK5, wherein the first binding domain comprises a heavy chain amino acid sequence of SEQ ID NO: 112, and a light chain amino acid sequence of SEQ ID NO: 113, and the second binding domain comprises a heavy chain amino acid sequence of SEQ ID NO: 195, and a light chain amino acid sequence of SEQ ID NO: 115.

Embodiment 263. A bispecific antibody comprising a first binding domain and a second binding domain, wherein the first binding domain binds human KLK7 and the second binding domain binds human KLK5, wherein the first binding domain comprises a heavy chain amino acid sequence of SEQ ID NO: 194, and a light chain amino acid sequence of SEQ ID NO: 113, and the second binding domain comprises a heavy chain amino acid sequence of SEQ ID NO: 114, and a light chain amino acid sequence of SEQ ID NO: 115.

[007a] In one aspect, the present disclosure refers to an antibody that binds to human KLK5, wherein the antibody comprises:

- a) a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 39, (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO: 41, and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO: 42, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 43, (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 45, and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO: 47; or

b) a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 107, (b) CDR-H2 comprising an amino acid sequence selected from SEQ ID NOs: 40 and 41, and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO: 42, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising an amino acid sequence selected from SEQ ID NOs: 43 and 44, (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 45, and (f) CDR-L3 comprising an amino acid sequence selected from SEQ ID NOs: 46-49; or

c) a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising an amino acid sequence selected from SEQ ID NOs: 39 and 107, (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO: 41, and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO: 42, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising an amino acid sequence selected from SEQ ID NOs: 43 and 44, (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 45, and (f) CDR-L3 comprising an amino acid sequence selected from SEQ ID NOs: 46-49; or

d) a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising an amino acid sequence selected from SEQ ID NOs: 39 and 107, (b) CDR-H2 comprising an amino acid sequence selected from SEQ ID NOs: 40 and 41, and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO: 42, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NOs: 44, (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 45, and (f) CDR-L3 comprising an amino acid sequence selected from SEQ ID NOs: 46-49; or

e) a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising an amino acid sequence selected from SEQ ID NOs: 39 and 107, (b) CDR-H2 comprising an amino acid sequence selected from SEQ ID NOs: 40 and 41, and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO: 42, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising an amino acid sequence selected from SEQ ID NOs: 43 and 44, (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 45, and (f) CDR-L3 comprising an amino acid sequence selected from SEQ ID NOs: 47-49; or

f) a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 68, (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO: 70, and (c) CDR-H3 comprising an amino acid sequence selected from SEQ ID NOs: 71 and 72, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 73, (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 74, and (f) CDR-L3 comprising an amino acid sequence selected from SEQ ID NOs: 75-78; or

g) a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 68, (b) CDR-H2 comprising an amino acid sequence selected from SEQ ID NOs: 69 and 70, and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO: 72, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 73, (e)

CDR-L2 comprising the amino acid sequence of SEQ ID NO: 74, and (f) CDR-L3 comprising an amino acid sequence selected from SEQ ID NOs: 75-78; or
h) a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 68, (b) CDR-H2 comprising an amino acid sequence selected from SEQ ID NOs: 69 and 70, and (c) CDR-H3 comprising an amino acid sequence selected from SEQ ID NOs: 71 and 72, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 73, (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 74, and (f) CDR-L3 comprising an amino acid sequence selected from SEQ ID NOs: 76-78.

[007b] In one aspect, the present disclosure refers to an isolated antibody that binds to human kallikrein related peptidase 7 (KLK7), wherein the antibody:

- a) inhibits human KLK7-mediated cleavage of a substrate comprising the amino acid sequence RPKPVE-Nval-WRK (SEQ ID NO: 121), wherein Nval is norvaline; and/or
- b) binds human KLK7 with an K_D of less than 10 pM, or less than 9 pM, or less than 8 pM, or less than 7 pM, or less than 6 pM, or less than 5 pM as measured by surface plasmon resonance;
- c) binds an epitope within amino acids R71-N82, K152-S158, and/or Q211-K222 of KLK7 (SEQ ID NO: 4); and/or
- d) binds an epitope comprising one or more of amino acids H72, P73, G74, S76, Q78, N82, N157, K211, and/or T213 of KLK7 (SEQ ID NO: 4).

[007c] In one aspect, the present disclosure refers to an antibody that binds to human KLK7, wherein the antibody comprises a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 7, (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO: 8, and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO: 9, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 10, (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 11, and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO: 12.

[007d] In one aspect, the present disclosure refers to an antibody that specifically binds human KLK7, which competes for binding to human KLK7 with the antibody of any one of paragraphs [007c] or [007d], optionally wherein the antibody:

- a) inhibits human KLK7-mediated cleavage of a substrate comprising the amino acid sequence RPKPVE-Nval-WRK (SEQ ID NO: 121), wherein Nval is norvaline, with an IC_{50} of less than 5 nM, or less than 3 nM, or less than 2 nM, or less than 1 nM; and/or
- b) binds human KLK7 with a K_D of less than 10 pM, or less than 9 pM, or less than 8 pM, or less than 7 pM, or less than 6 pM, or less than 5 pM as measured by surface plasmon resonance.

[007e] In one aspect, the present disclosure refers to an isolated nucleic acid encoding the antibody disclosed herein.

[007f] In one aspect, the present disclosure refers to an isolated host cell comprising the nucleic acid disclosed herein.

[007g] In one aspect, the present disclosure refers to an isolated host cell that expresses the antibody disclosed herein.

[007h] In one aspect, the present disclosure refers to a method of producing an antibody comprising culturing the host cell disclosed herein under conditions suitable for the expression of the antibody, and optionally recovering the antibody from the host cell.

[007i] In one aspect, the present disclosure refers to a bispecific antibody comprising a first binding domain and a second binding domain, wherein the first binding domain binds human KLK7 and the second binding domain binds human KLK5, wherein the second binding domain comprises

a) a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 39, (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO: 41, and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO: 42, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 43, (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 45, and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO: 47; or

b) a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 107, (b) CDR-H2 comprising an amino acid sequence selected from SEQ ID NOs: 40 and 41, and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO: 42, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NOs: 43 or 44, (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 45, and (f) CDR-L3 comprising an amino acid sequence selected from SEQ ID NOs: 46-49; or

c) a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising an amino acid sequence selected from SEQ ID NOs: 39 and 107, (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO: 41, and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO: 42, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising an amino acid sequence selected from SEQ ID NOs: 43 and 44, (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 45, and (f) CDR-L3 comprising an amino acid sequence selected from SEQ ID NOs: 46-49; or

d) a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 39 or 107, (b) CDR-H2 comprising an amino acid sequence selected from SEQ ID NOs: 40 and 41, and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO: 42, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NOs: 44, (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 45, and (f) CDR-L3 comprising an amino acid sequence selected from SEQ ID NOs: 46-49; or

e) a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising an amino acid sequence selected from SEQ ID NOs: 39 and 107, (b) CDR-H2 comprising an amino acid sequence selected from SEQ ID NOs: 40 and 41, and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO: 42, and a light chain

variable domain (VL) comprising (d) CDR-L1 comprising an amino acid sequence selected from SEQ ID NOs: 43 and 44, (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 45, and (f) CDR-L3 comprising an amino acid sequence selected from SEQ ID NOs: 47-49; or

f) a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 68, (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO: 70, and (c) CDR-H3 comprising an amino acid sequence selected from SEQ ID NOs: 71 and 72, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 73, (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 74, and (f) CDR-L3 comprising an amino acid sequence selected from SEQ ID NOs: 75-78; or

g) a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 68, (b) CDR-H2 comprising an amino acid sequence selected from SEQ ID NOs: 69 and 70, and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO: 72, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 73, (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 74, and (f) CDR-L3 comprising an amino acid sequence selected from SEQ ID NOs: 75-78; or

h) a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 68, (b) CDR-H2 comprising an amino acid sequence selected from SEQ ID NOs: 69 and 70, and (c) CDR-H3 comprising an amino acid sequence selected from SEQ ID NOs: 71 and 72, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 73, (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 74, and (f) CDR-L3 comprising an amino acid sequence selected from SEQ ID NOs: 76-78.

[007j] In one aspect, the present disclosure refers to a bispecific antibody comprising a first binding domain and a second binding domain, wherein the first binding domain binds human KLK7 and the second binding domain binds human KLK5, wherein the first binding domain comprises a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 7, (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO: 8, and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO: 9, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 10, (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 11, and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO: 12.

[007k] In one aspect, the present disclosure refers to a bispecific antibody comprising a first binding domain and a second binding domain, wherein the first binding domain binds human KLK7 and the second binding domain binds human KLK5, wherein (i) the first binding domain comprises a heavy chain amino acid sequence of SEQ ID NO: 108 or 192, and a light chain amino acid sequence of SEQ ID NO: 109, and the second binding domain comprises a heavy chain amino acid sequence of SEQ ID NO: 110 or 193, and a light chain amino acid sequence of SEQ ID NO: 111; or (ii) the first binding domain comprises a heavy chain amino acid sequence of SEQ ID NO: 112 or 194, and a light chain amino acid sequence of SEQ ID

NO: 113, and the second binding domain comprises a heavy chain amino acid sequence of SEQ ID NO: 114 or 195, and a light chain amino acid sequence of SEQ ID NO: 115; or (iii) the first binding domain comprises a heavy chain amino acid sequence of SEQ ID NO: 108 and a light chain amino acid sequence of SEQ ID NO: 109, and the second binding domain comprises a heavy chain amino acid sequence of SEQ ID NO: 110 and a light chain amino acid sequence of SEQ ID NO: 111; or (iv) the first binding domain comprises a heavy chain amino acid sequence of SEQ ID NO: 112 and a light chain amino acid sequence of SEQ ID NO: 113, and the second binding domain comprises a heavy chain amino acid sequence of SEQ ID NO: 114 and a light chain amino acid sequence of SEQ ID NO: 115.

[007l] In one aspect, the present disclosure refers to an isolated nucleic acid encoding the bispecific antibody disclosed herein.

[007m] In one aspect, the present disclosure refers to an isolated nucleic acid encoding the first binding domain and/or the second binding domain of the bispecific antibody disclosed herein.

[007n] In one aspect, the present disclosure refers to an isolated host cell comprising the isolated nucleic acid encoding the bispecific antibody disclosed herein or the isolated nucleic acid encoding the first binding domain and/or the second binding domain of the bispecific antibody disclosed herein.

[007o] In one aspect, the present disclosure refers to an isolated host cell that expresses the bispecific antibody disclosed herein.

[007p] In one aspect, the present disclosure refers to an isolated host cell that expresses the first binding domain and/or the second binding domain of the bispecific antibody disclosed herein.

[007q] In one aspect, the present disclosure refers to a method of producing a bispecific antibody that binds to human KLK5 and human KLK7, comprising culturing the host cell disclosed herein under conditions suitable for the expression of the antibody, and optionally recovering the antibody from the host cell.

[007r] In one aspect, the present disclosure refers to a pharmaceutical composition comprising the antibody disclosed herein and a pharmaceutically acceptable carrier, optionally wherein the pharmaceutical composition further comprises an additional therapeutic agent, optionally wherein the additional therapeutic agent is a KLK5 inhibitor, optionally wherein the KLK5 inhibitor is an anti-KLK5 antibody.

[007s] In one aspect, the present disclosure refers to a pharmaceutical composition comprising the antibody disclosed herein and a pharmaceutically acceptable carrier, optionally wherein the pharmaceutical composition further comprises an additional therapeutic agent, optionally wherein the additional therapeutic agent is a KLK7 inhibitor, optionally wherein the KLK7 inhibitor is an anti-KLK7 antibody, optionally wherein the anti-KLK7 antibody is an antibody disclosed herein.

[007t] In one aspect, the present disclosure refers to an isolated antibody that binds human KLK7, wherein when bound to human KLK7 results in a conformational change of

human KLK7, wherein the conformational change allosterically results in the disruption of the substrate binding site and/or the active site of human KLK7.

[007u] In one aspect, the present disclosure refers to a bispecific antibody comprising a first binding domain and a second binding domain, wherein the first binding domain binds human KLK7 and the second binding domain binds human KLK5, wherein when bound to human KLK7 results in a conformational change of human KLK7, wherein the conformational change allosterically results in the disruption of the substrate binding site and/or the active site of human KLK7; and/or wherein when bound to human KLK5 results in a conformational change of human KLK5, wherein the conformational change allosterically results in the disruption of the substrate binding site and/or the active site of human KLK5.

[007v] In one aspect, the present disclosure refers to a pharmaceutical composition comprising the antibody or bispecific antibody disclosed herein.

[007w] In one aspect, the present disclosure refers to the antibody disclosed herein, the bispecific antibody disclosed herein, or the pharmaceutical composition disclosed herein for use as a medicament.

[007x] In one aspect, the present disclosure refers to the antibody disclosed herein, the bispecific antibody disclosed herein, or the pharmaceutical composition disclosed herein for use in treating disease selected from Netherton Syndrome, asthma, atopic dermatitis, psoriasis, eosinophilic esophagitis, and rosacea.

[007y] In one aspect, the present disclosure refers to use of the antibody disclosed herein, the bispecific antibody disclosed herein, or the pharmaceutical composition disclosed herein in the manufacture of a medicament for treating disease selected from Netherton Syndrome, asthma, atopic dermatitis, psoriasis, eosinophilic esophagitis, and rosacea.

[007z] In one aspect, the present disclosure refers to a combination of an antibody of paragraph [007a] and an antibody of any one of paragraphs [007b] to [007d], for use as a medicament.

[007aa] In one aspect, the present disclosure refers to a combination of an antibody of paragraph [007a] and an antibody of any one of paragraphs [007b] to [007d], for use in treating disease selected from Netherton Syndrome, asthma, atopic dermatitis, psoriasis, eosinophilic esophagitis, and rosacea.

[007bb] In one aspect, the present disclosure refers to use of a combination of an antibody of paragraph [007a] and an antibody of any one of paragraphs [007b] to [007d] in the manufacture of a medicament for treating disease selected from Netherton Syndrome, asthma, atopic dermatitis, psoriasis, eosinophilic esophagitis, and rosacea.

[007cc] In one aspect, the present disclosure refers to use of the antibody disclosed herein, the bispecific antibody disclosed herein, or the pharmaceutical composition disclosed herein in the manufacture of a medicament for reducing epithelium inflammation, reducing epithelium permeability, reducing transepidermal water loss, reducing dermal infiltrates, reducing parakeratosis, restoring the epithelial barrier, and/or reducing skin inflammatory cytokines.

[007dd] In one aspect, the present disclosure refers to use of a combination of an antibody of paragraph [007a] and an antibody of any one of paragraphs [007b] to [007d] in the manufacture of a medicament for reducing epithelium inflammation, reducing epithelium permeability, reducing transepidermal water loss, reducing dermal infiltrates, reducing parakeratosis, restoring the epithelial barrier, and/or reducing skin inflammatory cytokines.

[007ee] In one aspect, the present disclosure refers to the antibody disclosed herein, the bispecific antibody disclosed herein, or the pharmaceutical composition disclosed herein for use in reducing epithelium inflammation, reducing epithelium permeability, reducing transepidermal water loss, reducing dermal infiltrates, reducing parakeratosis, restoring the epithelial barrier, and/or reducing skin inflammatory cytokines in an individual.

[007ff] In one aspect, the present disclosure refers to a combination of a) an effective amount of the antibody of paragraph [007a]; and b) an effective amount of the antibody of any one of paragraphs [007b] to [007d], for use in reducing epithelium inflammation, reducing epithelium permeability, reducing transepidermal water loss, reducing dermal infiltrates, reducing parakeratosis, restoring the epithelial barrier, and/or reducing skin inflammatory cytokines in an individual.

[007gg] In one aspect, the present disclosure refers to use of (a) a bispecific antibody, wherein the bispecific antibody comprises a first binding domain and second binding domain, wherein the first binding domain binds human KLK7 and inhibits KLK7 protease activity and the second binding domain binds human KLK5 and inhibits KLK5 protease activity; or (b) an anti-KLK5 antibody and an anti-KLK7 antibody, wherein the anti-KLK5 antibody inhibits KLK5 protease activity, and wherein the anti-KLK7 antibody inhibits KLK7 protease activity, in the manufacture of a medicament for treating an individual having a disease selected from Netherton Syndrome, asthma, atopic dermatitis, psoriasis, eosinophilic esophagitis, and rosacea.

[007hh] In one aspect, the present disclosure refers to use of (a) a KLK5 antagonist and a KLK7 antagonist, optionally wherein the KLK5 antagonist is an anti-KLK5 antibody and/or the KLK7 antagonist is an anti-KLK7 antibody, optionally wherein the anti-KLK5 antibody inhibits KLK5 protease activity, and wherein the anti-KLK7 antibody inhibits KLK7 protease activity; or (b) a bispecific antibody, wherein the bispecific antibody comprises a first binding domain and second binding domain, wherein the first binding domain binds human KLK7 and inhibits KLK7 protease activity and the second binding domain binds human KLK5 and inhibits KLK5 protease activity, in the manufacture of a medicament for reducing epithelium inflammation, reducing epithelium permeability, reducing transepidermal water loss, reducing dermal infiltrates, reducing parakeratosis, restoring the epithelial barrier and/or reducing skin inflammatory cytokines in an individual.

[007ii] In one aspect, the present disclosure refers to use of (a) a bispecific antibody, wherein the bispecific antibody comprises a first binding domain and second binding domain, wherein the first binding domain binds human KLK7 and inhibits KLK7 protease activity and the second binding domain binds human KLK5 and inhibits KLK5 protease activity; or (b) an anti-KLK5 antibody and an anti-KLK7 antibody, wherein the anti-KLK5 antibody inhibits KLK5 protease activity, and wherein the anti-KLK7 antibody inhibits KLK7 protease activity, in the manufacture of a medicament for ameliorating skin rash and/or scaling in an individual with Netherton Syndrome.

BRIEF DESCRIPTION OF THE FIGURES

[008] Figures 1A-1B show an alignment of anti-KLK7 antibody rb.14H11c-LC light chain variable region with certain humanized versions of the light chain variable regions (1A) and anti-KLK7 antibody rb.14H11c-HC heavy chain variable region with certain humanized versions of the heavy chain variable regions (1B). CDRs according to Chothia, Kabat, and contact residues are indicated. Differences in the humanized versions relative to the rabbit parental variable regions are shown in white with a black background.

WHAT IS CLAIMED IS:

1. An antibody that binds to human KLK5, wherein the antibody comprises:
 - a) a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 39, (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO: 41, and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO: 42, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 43, (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 45, and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO: 47; or
 - b) a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 107, (b) CDR-H2 comprising an amino acid sequence selected from SEQ ID NOs: 40 and 41, and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO: 42, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising an amino acid sequence selected from SEQ ID NOs: 43 and 44, (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 45, and (f) CDR-L3 comprising an amino acid sequence selected from SEQ ID NOs: 46-49; or
 - c) a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising an amino acid sequence selected from SEQ ID NOs: 39 and 107, (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO: 41, and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO: 42, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising an amino acid sequence selected from SEQ ID NOs: 43 and 44, (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 45, and (f) CDR-L3 comprising an amino acid sequence selected from SEQ ID NOs: 46-49; or
 - d) a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising an amino acid sequence selected from SEQ ID NOs: 39 and 107, (b) CDR-H2 comprising an amino acid sequence selected from SEQ ID NOs: 40 and 41, and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO: 42, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NOs: 44, (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 45, and (f) CDR-L3 comprising an amino acid sequence selected from SEQ ID NOs: 46-49; or

e) a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising an amino acid sequence selected from SEQ ID NOs: 39 and 107, (b) CDR-H2 comprising an amino acid sequence selected from SEQ ID NOs: 40 and 41, and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO: 42, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising an amino acid sequence selected from SEQ ID NOs: 43 and 44, (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 45, and (f) CDR-L3 comprising an amino acid sequence selected from SEQ ID NOs: 47-49; or

f) a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 68, (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO: 70, and (c) CDR-H3 comprising an amino acid sequence selected from SEQ ID NOs: 71 and 72, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 73, (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 74, and (f) CDR-L3 comprising an amino acid sequence selected from SEQ ID NOs: 75-78; or

g) a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 68, (b) CDR-H2 comprising an amino acid sequence selected from SEQ ID NOs: 69 and 70, and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO: 72, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 73, (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 74, and (f) CDR-L3 comprising an amino acid sequence selected from SEQ ID NOs: 75-78; or

h) a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 68, (b) CDR-H2 comprising an amino acid sequence selected from SEQ ID NOs: 69 and 70, and (c) CDR-H3 comprising an amino acid sequence selected from SEQ ID NOs: 71 and 72, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 73, (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 74, and (f) CDR-L3 comprising an amino acid sequence selected from SEQ ID NOs: 76-78.

2. The antibody of claim 1, comprising a sequence selected from:

a) a VH sequence comprising an amino acid sequence selected from SEQ ID NOs: 50, 52, 53, 105, and 106;

b) a VL sequence comprising an amino acid sequence selected from SEQ ID NOs: 51 and 54-67; and

c) a VH sequence as defined in (a) and a VL sequence as defined in (b);

d) a VH sequence comprising an amino acid sequence selected from SEQ ID NOs: 79 and 81-87;

e) a VL sequence comprising an amino acid sequence selected from SEQ ID NOs: 80 and 88-94; and

f) a VH sequence as defined in (d) and a VL sequence as defined in (e).

3. The antibody of claim 1 or claim 2, wherein the antibody binds human KLK5 with a K_D of less than 60 pM, less than 30 pM, less than 20 pM, less than 10 pM, or less than 5 pM, as measured by surface plasmon resonance; and/or wherein the antibody inhibits human KLK5 protease activity with an IC_{50} of less than 5 nM, or less than 3 nM, or less than 2 nM, or less than 1 nM; optionally wherein inhibition of human KLK5 protease activity is inhibition of human KLK5-mediated cleavage of the substrate Boc-Val-Pro-Arg-AMC.

4.4. An isolated antibody that binds to human kallikrein related peptidase 7 (KLK7), wherein the antibody:

- a) inhibits human KLK7-mediated cleavage of a substrate comprising the amino acid sequence RPKPVE-Nval-WRK (SEQ ID NO: 121), wherein Nval is norvaline; and/or
- b) binds human KLK7 with an K_D of less than 10 pM, or less than 9 pM, or less than 8 pM, or less than 7 pM, or less than 6 pM, or less than 5 pM as measured by surface plasmon resonance;
- c) binds an epitope within amino acids R71-N82, K152-S158, and/or Q211-K222 of KLK7 (SEQ ID NO: 4); and/or
- d) binds an epitope comprising one or more of amino acids H72, P73, G74, S76, Q78, N82, N157, K211, and/or T213 of KLK7 (SEQ ID NO: 4).

2.5. An antibody that binds to human KLK7, wherein the antibody comprises a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 7, (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO: 8, and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO: 9, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID

NO: 10, (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 11, and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO: 12.

3.6. The antibody of claim ~~14~~, comprising a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 7, (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO: 8, and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO: 9, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 10, (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 11, and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO: 12.

~~4. The antibody of any one of claims 1 to 3, which is a monoclonal antibody.~~

~~5. The antibody of any one of claims 1 to 4, which is a humanized, or chimeric antibody.~~

~~6. The antibody of any one of claims 1 to 5, which is an antibody fragment that binds to human KLK7.~~

~~7. The antibody of any of claims 1 to 6, wherein the antibody binds human KLK7 with a K_D of less than 10 pM, or less than 9 pM, or less than 8 pM, or less than 7 pM, or less than 6 pM, or less than 5 pM as measured by surface plasmon resonance; and/or binds to cynomolgus monkey KLK7 with a K_D of less than 10 pM, or less than 9 pM, or less than 8 pM, or less than 7 pM, or less than 6 pM, or less than 5 pM as measured by surface plasmon resonance.~~

~~8. The antibody of any one of claims 1 to 7, wherein the heavy chain variable region comprises an FR1 comprising an amino acid sequence selected from SEQ ID NO: 123-128, an FR2 comprising an amino acid sequence selected from SEQ ID NO: 130-133, an FR3 comprising an amino acid sequence of SEQ ID NO: 135-143, and/or an FR4 comprising an amino acid sequence selected from SEQ ID NO: 144-145.~~

~~9. The antibody of any one of claims 1 to 8, wherein the light chain variable region comprises an FR1 comprising an amino acid sequence selected from SEQ ID NO: 147-150, an FR2 comprising an amino acid sequence selected from SEQ ID NO: 152-154, an FR3 comprising an amino acid sequence selected from SEQ ID NO: 156-158, and/or an FR4 comprising an amino acid sequence selected from SEQ ID NO: 160.~~

~~10. The antibody of any of claims 1 to 9, comprising a sequence selected from:~~

~~(a) a VH sequence having at least 95% sequence identity to an amino acid sequence selected from SEQ ID NOs: 15-30;~~

~~(b) a VL sequence having at least 95% sequence identity to an amino acid sequence selected from SEQ ID NO:31-38; and~~

~~(c) a VH sequence as defined in (a) and a VL sequence as defined in (b).~~

~~11.7.~~ The antibody of any one of claims 1-4 to 106, comprising a sequence selected from:

(a) a VH sequence comprising an amino acid sequence selected from SEQ ID NOs: 15-30;

(b) a VL sequence comprising an amino acid sequence selected from SEQ ID NO:31-38;
and

(c) a VH sequence as defined in (a) and a VL sequence as defined in (b).

~~12.—The antibody of any of claims 1 to 11, comprising a VH sequence of SEQ ID NO: 29 and a VL sequence of SEQ ID NO: 32.~~

~~13.—The antibody of any of claims 1 to 11, comprising a VH sequence of SEQ ID NO: 30 and a VL sequence of SEQ ID NO: 38.~~

~~14.—An antibody that specifically binds to human KLK7 comprising a VH sequence of SEQ ID NO: 29 and a VL sequence of SEQ ID NO: 32.~~

~~15.—An antibody that specifically binds to human KLK7 comprising a VH sequence of SEQ ID NO: 30 and a VL sequence of SEQ ID NO: 38.~~

~~16.—The antibody of any one of claims 1 to 15, wherein the antibody comprises a heavy chain constant region and a light chain constant region, wherein the heavy chain constant region comprises a S183K substitution (EU numbering) and/or an S183E substitution (EU numbering); and/or the light chain constant region comprises a V133K substitution (EU numbering) and/or a V133E substitution (EU numbering).~~

~~17.—The antibody of any of claims 1 to 16, which is a full length IgG1 antibody.~~

~~18.—The antibody of claim 17, wherein the antibody comprises a N297G substitution (EU numbering).~~

~~19.—The antibody of any one of claims 16 to 18, wherein the antibody comprises a M428L substitution (EU numbering) and/or an N434S substitution (EU numbering).~~

~~20.8.~~ The antibody of any one of claims 1-4 to 197, wherein the antibody binds human KLK7 with a K_D of less than 20 pM, or less than 15 pM, or less than 10 pM, less than 5 pM, or less than 3 pM, or less than 2 pM, or less than 1 pM, as measured by surface plasmon resonance; and wherein the antibody inhibits human KLK7 protease activity with an IC50 of

less than 5 nM, or less than 3 nM, or less than 2 nM, or less than 1 nM, optionally, wherein inhibition of human KLK7 protease activity is inhibition of human KLK7-mediated cleavage of a substrate comprising the amino acid sequence RPKPVE-Nval-WRK (SEQ ID NO: 121), wherein Nval is norvaline.

~~21.—The antibody of any one of claims 1 to 20, wherein the antibody inhibits human KLK7 protease activity with an IC₅₀ of less than 5 nM, or less than 3 nM, or less than 2 nM, or less than 1 nM.~~

~~22.—The antibody of any one of claims 1 to 21, wherein the antibody binds human KLK7 with a K_D of less than 20 pM, or less than 15 pM, or less than 10 pM, less than 5 pM, or less than 3 pM, or less than 2 pM, or less than 1 pM, as measured by surface plasmon resonance; and wherein the antibody inhibits human KLK7 protease activity with an IC₅₀ of less than 5 nM, or less than 3 nM, or less than 2 nM, or less than 1 nM.~~

~~23.—The antibody of claim 21 or claim 22, wherein inhibition of human KLK7 protease activity is inhibition of human KLK7 mediated cleavage of a substrate comprising the amino acid sequence RPKPVE Nval WRK (SEQ ID NO: 121), wherein Nval is norvaline.~~

~~24.—The antibody of any of claims 1 to 23, wherein the antibody is a multispecific antibody.~~

~~25.—The antibody of claim 24, which is a bispecific antibody.~~

26.9. An antibody that specifically binds human KLK7, which competes for binding to human KLK7 with the antibody of any one of claims 1-4 to 258, optionally wherein the antibody:-

- a) inhibits human KLK7-mediated cleavage of a substrate comprising the amino acid sequence RPKPVE-Nval-WRK (SEQ ID NO: 121), wherein Nval is norvaline, with an IC₅₀ of less than 5 nM, or less than 3 nM, or less than 2 nM, or less than 1 nM; and/or
- b) binds human KLK7 with a K_D of less than 10 pM, or less than 9 pM, or less than 8 pM, or less than 7 pM, or less than 6 pM, or less than 5 pM as measured by surface plasmon resonance.

~~27.—The antibody of claim 26, wherein the antibody:-~~

- a) ~~inhibits human KLK7 mediated cleavage of a substrate comprising the amino acid sequence RPKPVE Nval WRK (SEQ ID NO: 121), wherein Nval is norvaline, with an IC₅₀ of less than 5 nM, or less than 3 nM, or less than 2 nM, or less than 1 nM; and/or~~
- b) ~~binds human KLK7 with a K_D of less than 10 pM, or less than 9 pM, or less than 8 pM, or less than 7 pM, or less than 6 pM, or less than 5 pM as measured by surface plasmon resonance.~~
28. ~~An isolated nucleic acid encoding the antibody of any of claims 1 to 27.~~
29. ~~An isolated host cell comprising the nucleic acid of claim 28.~~
30. ~~An isolated host cell that expresses the antibody of any one of claims 1 to 27.~~
31. ~~A method of producing an antibody that binds to human KLK7 comprising culturing the host cell of claim 29 or claim 30 under conditions suitable for the expression of the antibody.~~
32. ~~The method of claim 31, further comprising recovering the antibody from the host cell.~~
33. ~~An antibody produced by the method of claim 32.~~
34. ~~An antibody that binds to human KLK5, wherein the antibody comprises:~~
- ~~a) a heavy chain variable domain (VH) comprising (a) CDR H1 comprising the amino acid sequence of SEQ ID NO: 107, (b) CDR H2 comprising an amino acid sequence selected from SEQ ID NOs: 40 and 41, and (c) CDR H3 comprising the amino acid sequence of SEQ ID NO: 42, and a light chain variable domain (VL) comprising (d) CDR L1 comprising an amino acid sequence selected from SEQ ID NOs: 43 and 44, (e) CDR L2 comprising the amino acid sequence of SEQ ID NO: 45, and (f) CDR L3 comprising an amino acid sequence selected from SEQ ID NOs: 46-49; or~~
- ~~b) a heavy chain variable domain (VH) comprising (a) CDR H1 comprising an amino acid sequence selected from SEQ ID NOs: 39 and 107, (b) CDR H2 comprising the amino acid sequence of SEQ ID NO: 41, and (c) CDR H3 comprising the amino acid sequence of SEQ ID NO: 42, and a light chain variable domain (VL) comprising (d) CDR L1 comprising an amino acid sequence selected from SEQ ID NOs: 43 and 44, (e) CDR L2 comprising the amino acid sequence of SEQ ID NO: 45, and (f) CDR L3 comprising an amino acid sequence selected from SEQ ID NOs: 46-49; or~~

~~e) a heavy chain variable domain (VH) comprising (a) CDR H1 comprising an amino acid sequence selected from SEQ ID NOs: 39 and 107, (b) CDR H2 comprising an amino acid sequence selected from SEQ ID NOs: 40 and 41, and (c) CDR H3 comprising the amino acid sequence of SEQ ID NO: 42, and a light chain variable domain (VL) comprising (d) CDR L1 comprising the amino acid sequence of SEQ ID NOs: 44, (e) CDR L2 comprising the amino acid sequence of SEQ ID NO: 45, and (f) CDR L3 comprising an amino acid sequence selected from SEQ ID NOs: 46-49; or~~

~~d) a heavy chain variable domain (VH) comprising (a) CDR H1 comprising an amino acid sequence selected from SEQ ID NOs: 39 and 107, (b) CDR H2 comprising an amino acid sequence selected from SEQ ID NOs: 40 and 41, and (c) CDR H3 comprising the amino acid sequence of SEQ ID NO: 42, and a light chain variable domain (VL) comprising (d) CDR L1 comprising an amino acid sequence selected from SEQ ID NOs: 43 and 44, (e) CDR L2 comprising the amino acid sequence of SEQ ID NO: 45, and (f) CDR L3 comprising an amino acid sequence selected from SEQ ID NOs: 47-49; or~~

~~e) a heavy chain variable domain (VH) comprising (a) CDR H1 comprising the amino acid sequence of SEQ ID NO: 68, (b) CDR H2 comprising the amino acid sequence of SEQ ID NO: 70, and (c) CDR H3 comprising an amino acid sequence selected from SEQ ID NOs: 71 and 72, and a light chain variable domain (VL) comprising (d) CDR L1 comprising the amino acid sequence of SEQ ID NO: 73, (e) CDR L2 comprising the amino acid sequence of SEQ ID NO: 74, and (f) CDR L3 comprising an amino acid sequence selected from SEQ ID NOs: 75-78; or~~

~~f) a heavy chain variable domain (VH) comprising (a) CDR H1 comprising the amino acid sequence of SEQ ID NO: 68, (b) CDR H2 comprising an amino acid sequence selected from SEQ ID NOs: 69 and 70, and (c) CDR H3 comprising the amino acid sequence of SEQ ID NO: 72, and a light chain variable domain (VL) comprising (d) CDR L1 comprising the amino acid sequence of SEQ ID NO: 73, (e) CDR L2 comprising the amino acid sequence of SEQ ID NO: 74, and (f) CDR L3 comprising an amino acid sequence selected from SEQ ID NOs: 75-78; or~~

~~g) a heavy chain variable domain (VH) comprising (a) CDR H1 comprising the amino acid sequence of SEQ ID NO: 68, (b) CDR H2 comprising an amino acid sequence selected from SEQ ID NOs: 69 and 70, and (c) CDR H3 comprising an~~

~~amino acid sequence selected from SEQ ID NOs: 71 and 72, and a light chain variable domain (VL) comprising (d) CDR L1 comprising the amino acid sequence of SEQ ID NO: 73, (e) CDR L2 comprising the amino acid sequence of SEQ ID NO: 74, and (f) CDR L3 comprising an amino acid sequence selected from SEQ ID NOs: 76-78.~~

~~35.—The antibody of claim 34, wherein the antibody comprises a heavy chain variable domain (VH) comprising (a) CDR H1 comprising the amino acid sequence of SEQ ID NO: 39, (b) CDR H2 comprising the amino acid sequence of SEQ ID NO: 41, and (c) CDR H3 comprising the amino acid sequence of SEQ ID NO: 42, and a light chain variable domain (VL) comprising (d) CDR L1 comprising the amino acid sequence of SEQ ID NOs: 43, (e) CDR L2 comprising the amino acid sequence of SEQ ID NO: 45, and (f) CDR L3 comprising the amino acid sequence of SEQ ID NO: 47.~~

~~36.—The antibody of claim 34, wherein the antibody comprises a heavy chain variable domain (VH) comprising (a) CDR H1 comprising the amino acid sequence of SEQ ID NO: 68, (b) CDR H2 comprising the amino acid sequence of SEQ ID NO: 70, and (c) CDR H3 comprising the amino acid sequence of SEQ ID NO: 72, and a light chain variable domain (VL) comprising (d) CDR L1 comprising the amino acid sequence of SEQ ID NO: 73, (e) CDR L2 comprising the amino acid sequence of SEQ ID NO: 74, and (f) CDR L3 comprising the amino acid sequence of SEQ ID NO: 76.~~

~~37.—The antibody of any one of claims 34 to 36, which is a monoclonal antibody.~~

~~38.—The antibody of any one of claims 34 to 37, which is a humanized, or chimeric antibody.~~

~~39.—The antibody of any one of claims 34 to 38, which is an antibody fragment that binds human KLK5.~~

~~40.—The antibody of any of claims 34 to 39, wherein the antibody binds human KLK5 with a K_D of less than 1 nM, or less than 500 pM, or less than 300 pM, or less than 200 pM, or less than 100 pM, or less than 50 pM as measured by surface plasmon resonance; and/or binds to cynomolgus monkey KLK5 with a K_D of less than 1 nM, or less than 500 pM, or less than 300 pM, or less than 200 pM, or less than 100 pM, or less than 50 pM as measured by surface plasmon resonance.~~

~~41.—The antibody of any one of claims 34 to 40, wherein the heavy chain variable region comprises:~~

a) ~~an FR1 comprising the amino acid sequence selected of SEQ ID NO: 161, an FR2 comprising the amino acid sequence of SEQ ID NO: 162-163, an FR3 comprising the amino acid sequence of SEQ ID NO: 164, and/or an FR4 comprising the amino acid sequence of SEQ ID NO: 165; or~~

b) ~~an FR1 comprising the amino acid sequence of SEQ ID NO: 171, an FR2 comprising an amino acid sequence selected from SEQ ID NO: 172-173, an FR3 comprising the amino acid sequence of SEQ ID NO: 174, and/or an FR4 comprising the amino acid sequence of SEQ ID NO: 175.~~

42. ~~The antibody of any one of claims 34 to 41, wherein the light chain variable region comprises:~~

a) ~~an FR1 comprising the amino acid sequence of SEQ ID NO: 166, an FR2 comprising an amino acid sequence selected from SEQ ID NO: 167-168, an FR3 comprising the amino acid sequence of SEQ ID NO: 169, and/or an FR4 comprising the amino acid sequence of SEQ ID NO: 170; or~~

b) ~~an FR1 comprising the amino acid sequence of SEQ ID NO: 176, an FR2 comprising an amino acid sequence selected from SEQ ID NO: 177-178, an FR3 comprising the amino acid sequence of SEQ ID NO: 179, and/or an FR4 comprising the amino acid sequence of SEQ ID NO: 180.~~

43. ~~The antibody of any of claims 34 to 42, comprising a sequence selected from:~~

a) ~~a VH sequence having at least 95% sequence identity to an amino acid sequence selected from SEQ ID NOs: 50, 52, 53, 105, and 106;~~

b) ~~a VL sequence having at least 95% sequence identity to an amino acid sequence selected from SEQ ID NOs: 51 and 54-67; and~~

c) ~~a VH sequence as defined in (a) and a VL sequence as defined in (b);~~

d) ~~a VH sequence having at least 95% sequence identity to an amino acid sequence selected from SEQ ID NOs: 79 and 81-87;~~

e) ~~a VL sequence having at least 95% sequence identity to an amino acid sequence selected from SEQ ID NOs: 80 and 88-94; and~~

f) ~~a VH sequence as defined in (d) and a VL sequence as defined in (e).~~

44. ~~The antibody of any of claims 34 to 43, comprising a sequence selected from:~~

~~a) a VH sequence comprising an amino acid sequence selected from SEQ ID NOs: 50, 52, 53, 105, and 106;~~

~~b) a VL sequence comprising an amino acid sequence selected from SEQ ID NOs: 51 and 54-67; and~~

~~c) a VH sequence as defined in (a) and a VL sequence as defined in (b);~~

~~d) a VH sequence comprising an amino acid sequence selected from SEQ ID NOs: 79 and 81-87;~~

~~e) a VL sequence comprising an amino acid sequence selected from SEQ ID NOs: 80 and 88-94; and~~

~~f) a VH sequence as defined in (d) and a VL sequence as defined in (e).~~

~~45. The antibody of any of claims 34 to 44, comprising a VH sequence of SEQ ID NO: 52 and a VL sequence of SEQ ID NO: 55.~~

~~46. The antibody of any of claims 34 to 44, comprising a VH sequence of SEQ ID NO: 53 and a VL sequence of SEQ ID NO: 62.~~

~~47. An antibody that specifically binds to human KLK5 comprising a VH sequence of SEQ ID NO: 52 and a VL sequence of SEQ ID NO: 55.~~

~~48. An antibody that specifically binds to human KLK5 comprising a VH sequence of SEQ ID NO: 53 and a VL sequence of SEQ ID NO: 62.~~

~~49. The antibody of any of claims 34 to 44, comprising a VH sequence of SEQ ID NO: 83 and a VL sequence of SEQ ID NO: 88.~~

~~50. The antibody of any of claims 34 to 44, comprising a VH sequence of SEQ ID NO: 87 and a VL sequence of SEQ ID NO: 92.~~

~~51. An antibody that specifically binds to human KLK5 comprising a VH sequence of SEQ ID NO: 83 and a VL sequence of SEQ ID NO: 88.~~

~~52. An antibody that specifically binds to human KLK5 comprising a VH sequence of SEQ ID NO: 87 and a VL sequence of SEQ ID NO: 92.~~

~~53. The antibody of any one of claims 34 to 52, wherein the antibody comprises a heavy chain constant region and a light chain constant region, wherein the heavy chain constant region comprises a S183K substitution (EU numbering) and/or an S183E substitution (EU numbering);~~

and/or the light chain constant region comprises a ~~V133K~~ substitution (EU numbering) and/or a ~~V133E~~ substitution (EU numbering).

~~54.—The antibody of any of claims 34 to 53, which is a full length IgG1 antibody.~~

~~55.—The antibody of claim 54, wherein the antibody comprises a N297G substitution (EU numbering).~~

~~56.—The antibody of any one of claims 53 to 55, wherein the antibody comprises a M428L substitution (EU numbering) and/or an N434S substitution (EU numbering).~~

~~57.—The antibody of any of claims 34 to 56, wherein the antibody binds human KLK5 with a K_D of less than 60 pM, less than 30 pM, less than 20 pM, less than 10 pM, or less than 5 pM, as measured by surface plasmon resonance.~~

~~58.—The antibody of any one of claims 34 to 57, wherein the antibody inhibits human KLK5 protease activity with an IC_{50} of less than 5 nM, or less than 3 nM, or less than 2 nM, or less than 1 nM.~~

~~59.—The antibody of any one of claims 34 to 58, wherein the antibody binds human KLK5 with a K_D of less than 60 pM, less than 30 pM, less than 20 pM, less than 10 pM, or less than 5 pM, as measured by surface plasmon resonance; and wherein the antibody inhibits human KLK5 protease activity with an IC_{50} of less than 5 nM, or less than 3 nM, or less than 2 nM, or less than 1 nM.~~

~~60.—The antibody of claim 58 or claim 59, wherein inhibition of human KLK5 protease activity is inhibition of human KLK5 mediated cleavage of the substrate Boc-Val-Pro-Arg-AMC.~~

61.10. The antibody of any one of claims 34.1 to 60.9, wherein the antibody is a multispecific antibody, optionally wherein the antibody is a bispecific antibody.

~~62.—The antibody of claim 61, wherein the antibody is a bispecific antibody.~~

63.11. An isolated nucleic acid encoding the antibody of any one of claims 34.1 to 62.10.

64.12. An isolated host cell comprising the nucleic acid of claim 63.11.

65.13. An isolated host cell that expresses the antibody of any one of claims 34.1 to 62.9.

66.14. A method of producing an antibody ~~that binds to human KLK5~~ comprising culturing the host cell of claim 64.12 or claim 65.13 under conditions suitable for the expression of the antibody, and optionally recovering the antibody from the host cell.

~~67. The method of claim 66, further comprising recovering the antibody from the host cell.~~

15. A bispecific antibody comprising a first binding domain and a second binding domain, wherein the first binding domain binds human KLK7 and the second binding domain binds human KLK5, wherein the second binding domain comprises

a) a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 39, (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO: 41, and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO: 42, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 43, (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 45, and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO: 47; or

b) a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 107, (b) CDR-H2 comprising an amino acid sequence selected from SEQ ID NOS: 40 and 41, and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO: 42, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NOS: 43 or 44, (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 45, and (f) CDR-L3 comprising an amino acid sequence selected from SEQ ID NOS: 46-49; or

c) a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising an amino acid sequence selected from SEQ ID NOS: 39 and 107, (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO: 41, and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO: 42, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising an amino acid sequence selected from SEQ ID NOS: 43 and 44, (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 45, and (f) CDR-L3 comprising an amino acid sequence selected from SEQ ID NOS: 46-49; or

d) a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 39 or 107, (b) CDR-H2 comprising an amino acid sequence selected from SEQ ID NOS: 40 and 41, and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO: 42, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NOS: 44,

(e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 45, and (f) CDR-L3 comprising an amino acid sequence selected from SEQ ID NOs: 46-49; or

e) a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising an amino acid sequence selected from SEQ ID NOs: 39 and 107, (b) CDR-H2 comprising an amino acid sequence selected from SEQ ID NOs: 40 and 41, and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO: 42, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising an amino acid sequence selected from SEQ ID NOs: 43 and 44, (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 45, and (f) CDR-L3 comprising an amino acid sequence selected from SEQ ID NOs: 47-49; or

f) a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 68, (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO: 70, and (c) CDR-H3 comprising an amino acid sequence selected from SEQ ID NOs: 71 and 72, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 73, (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 74, and (f) CDR-L3 comprising an amino acid sequence selected from SEQ ID NOs: 75-78; or

g) a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 68, (b) CDR-H2 comprising an amino acid sequence selected from SEQ ID NOs: 69 and 70, and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO: 72, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 73, (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 74, and (f) CDR-L3 comprising an amino acid sequence selected from SEQ ID NOs: 75-78; or

h) a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 68, (b) CDR-H2 comprising an amino acid sequence selected from SEQ ID NOs: 69 and 70, and (c) CDR-H3 comprising an amino acid sequence selected from SEQ ID NOs: 71 and 72, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 73, (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 74, and (f) CDR-L3 comprising an amino acid sequence selected from SEQ ID NOs: 76-78.

16. The bispecific antibody of claim 15, wherein the second binding domain comprises a sequence selected from:

a) a VH sequence comprising an amino acid sequence selected from SEQ ID NOs: 50, 52, 53, 105, and 106;

b) a VL sequence comprising an amino acid sequence selected from SEQ ID NOs: 51 and 54-67; and

c) a VH sequence as defined in (a) and a VL sequence as defined in (b);

d) a VH sequence comprising an amino acid sequence selected from SEQ ID NOs: 79 and 81-87;

e) a VL sequence comprising an amino acid sequence selected from SEQ ID NOs: 80 and 88-94; and

f) a VH sequence as defined in (d) and a VL sequence as defined in (e).

~~68.—An antibody produced by the method of claim 67.~~

69.17. A bispecific antibody comprising a first binding domain and a second binding domain, wherein the first binding domain binds human KLK7 and the second binding domain binds human KLK5, wherein the first binding domain comprises a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 7, (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO: 8, and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO: 9, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 10, (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 11, and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO: 12.

~~70.—The bispecific antibody of claim 69, wherein the first binding domain is humanized.~~

~~71.—The bispecific antibody of claim 69 or claim 70, wherein the first binding domain comprises a sequence selected from:~~

~~(a) a VH sequence having at least 95% sequence identity to an amino acid sequence selected from SEQ ID NOs: 15-30;~~

~~(b) a VL sequence having at least 95% sequence identity to an amino acid sequence selected from SEQ ID NO: 31-38; and~~

~~(c) a VH sequence as defined in (a) and a VL sequence as defined in (b).~~

72.18. The bispecific antibody of ~~any one of claims 69 to 71~~claim 17, wherein the first binding domain comprises a sequence selected from:

- (a) a VH sequence comprising an amino acid sequence selected from SEQ ID NOs: 15-30;
- (b) a VL sequence comprising an amino acid sequence selected from SEQ ID NO: 31-38;
- and
- (c) a VH sequence as defined in (a) and a VL sequence as defined in (b).

~~73. The bispecific antibody of any one of claims 69 to 72, wherein the first binding domain comprises a VH sequence of SEQ ID NO: 29 and a VL sequence of SEQ ID NO: 32.~~

~~74. The bispecific antibody of any one of claims 69 to 72, wherein the first binding domain comprises a VH sequence of SEQ ID NO: 30 and a VL sequence of SEQ ID NO: 38.~~

75.19. The bispecific antibody of ~~any one of claims 69 to 74~~claim 17 or claim 18, wherein the second binding domain comprises:

- a) a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising an amino acid sequence selected from SEQ ID NOs: 39 and 107, (b) CDR-H2 comprising an amino acid sequence selected from SEQ ID NOs: 40 and 41, and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO: 42, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising an amino acid sequence selected from SEQ ID NOs: 43 and 44, (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 45, and (f) CDR-L3 comprising an amino acid sequence selected from SEQ ID NOs: 46-49; or
- b) a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 68, (b) CDR-H2 comprising an amino acid sequence selected from SEQ ID NOs: 69 and 70, and (c) CDR-H3 comprising an amino acid sequence selected from SEQ ID NOs: 71 and 72, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 73, (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 74, and (f) CDR-L3 comprising an amino acid sequence selected from SEQ ID NOs: 75-78.

~~76. The bispecific antibody of any one of claims 69 to 75, wherein the second binding domain comprises a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 39, (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO: 41, and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO: 42, and a~~

~~light chain variable domain (VL) comprising (d) CDR L1 comprising the amino acid sequence of SEQ ID NOs: 43, (e) CDR L2 comprising the amino acid sequence of SEQ ID NO: 45, and (f) CDR L3 comprising the amino acid sequence of SEQ ID NO: 47.~~

~~77.—The bispecific antibody of any one of claims 69 to 75, wherein the second binding domain comprises a heavy chain variable domain (VH) comprising (a) CDR H1 comprising the amino acid sequence of SEQ ID NO: 68, (b) CDR H2 comprising the amino acid sequence of SEQ ID NO: 70, and (c) CDR H3 comprising the amino acid sequence of SEQ ID NO: 72, and a light chain variable domain (VL) comprising (d) CDR L1 comprising the amino acid sequence of SEQ ID NO: 73, (e) CDR L2 comprising the amino acid sequence of SEQ ID NO: 74, and (f) CDR L3 comprising the amino acid sequence of SEQ ID NO: 76.~~

~~78.—The bispecific antibody of any one of claims 69 to 77, wherein the second binding domain is humanized.~~

~~79.—The bispecific antibody of any one of claims 75 to 78, wherein the second binding domain comprises a sequence selected from:~~

- ~~a) a VH sequence having at least 95% sequence identity to an amino acid sequence selected from SEQ ID NOs: 50, 52, 53, 105, and 106;~~
- ~~b) a VL sequence having at least 95% sequence identity to an amino acid sequence selected from SEQ ID NOs: 51 and 54-67; and~~
- ~~c) a VH sequence as defined in (a) and a VL sequence as defined in (b);~~
- ~~d) a VH sequence having at least 95% sequence identity to an amino acid sequence selected from SEQ ID NOs: 79 and 81-87;~~
- ~~e) a VL sequence having at least 95% sequence identity to an amino acid sequence selected from SEQ ID NOs: 80 and 88-94; and~~
- ~~f) a VH sequence as defined in (d) and a VL sequence as defined in (e).~~

~~80.—The bispecific antibody of any one of claims 75 to 78, wherein the second binding domain comprises a sequence selected from:~~

- ~~a) a VH sequence having at least 95% sequence identity to an amino acid sequence selected from SEQ ID NOs: 52, 53, 105, and 106;~~
- ~~b) a VL sequence having at least 95% sequence identity to an amino acid sequence selected from SEQ ID NOs: 54-67; and~~
- ~~c) a VH sequence as defined in (a) and a VL sequence as defined in (b);~~

~~d) a VH sequence having at least 95% sequence identity to an amino acid sequence selected from SEQ ID NOs: 81-87;~~

~~e) a VL sequence having at least 95% sequence identity to an amino acid sequence selected from SEQ ID NOs: 88-94; and~~

~~f) a VH sequence as defined in (d) and a VL sequence as defined in (e).~~

81.20. The bispecific antibody of any one of claims ~~69-17~~ to ~~78~~19, wherein the second binding domain comprises a sequence selected from:

a) a VH sequence comprising an amino acid sequence selected from SEQ ID NOs: 50, 52, 53, 105, and 106;

b) a VL sequence comprising an amino acid sequence selected from SEQ ID NOs: 51 and 54-67; and

c) a VH sequence as defined in (a) and a VL sequence as defined in (b);

d) a VH sequence comprising an amino acid sequence selected from SEQ ID NOs: 79 and 81-87;

e) a VL sequence comprising an amino acid sequence selected from SEQ ID NOs: 80 and 88-94; and

f) a VH sequence as defined in (d) and a VL sequence as defined in (e).

~~82. — The bispecific antibody of any one of claims 69 to 78, wherein the second binding domain comprises a sequence selected from:~~

~~a) a VH sequence comprising an amino acid sequence selected from SEQ ID NOs: 52, 53, 105, and 106;~~

~~b) a VL sequence comprising an amino acid sequence selected from SEQ ID NOs: 54-67; and~~

~~c) a VH sequence as defined in (a) and a VL sequence as defined in (b);~~

~~d) a VH sequence comprising an amino acid sequence selected from SEQ ID NOs: 81-87;~~

~~e) a VL sequence comprising an amino acid sequence selected from SEQ ID NOs: 88-94; and~~

~~f) a VH sequence as defined in (d) and a VL sequence as defined in (e).~~

83.21. The bispecific antibody of any one of claims ~~69-17~~ to ~~79~~20, wherein the first binding domain comprises a VH amino acid sequence of SEQ ID NO: 29 or SEQ ID NO: 30 and a VL amino acid sequence of SEQ ID NO: 32 or SEQ ID NO: 38, and the second binding domain comprises a VH sequence of SEQ ID NO: 52 or SEQ ID NO: 53 and a VL amino acid sequence of SEQ ID NO: 55 or SEQ ID NO: 62.

~~84. — The bispecific antibody of claim 83, wherein (i) the first binding domain comprises a VH amino acid sequence of SEQ ID NO: 29 and a VL amino acid sequence of SEQ ID NO: 32, or a VH amino acid sequence of SEQ ID NO: 30 and a VL amino acid sequence of SEQ ID NO: 38; and (ii) the second binding domain comprises a VH sequence of SEQ ID NO: 52 and a VL amino acid sequence of SEQ ID NO: 55; or a VH sequence of SEQ ID NO: 53 and a VL amino acid sequence of SEQ ID NO: 62.~~

~~85. — The bispecific antibody of any one of claims 69 to 79, wherein the first binding domain comprises a VH sequence of SEQ ID NO: 30 and a VL sequence of SEQ ID NO: 38, and the second binding domain comprises a VH sequence of SEQ ID NO: 53 and a VL sequence of SEQ ID NO: 62.~~

~~86. — A bispecific antibody comprising a first binding domain and a second binding domain, wherein the first binding domain binds human KLK7 and the second binding domain binds human KLK5, wherein the first binding domain comprises a heavy chain variable domain (VH) amino acid sequence of SEQ ID NO: 30 and a light chain variable domain (VL) amino acid sequence of SEQ ID NO: 38, and the second binding domain comprises a VH amino acid sequence of SEQ ID NO: 53 and a VL amino acid sequence of SEQ ID NO: 62.~~

87.22. The bispecific antibody of any one of claims ~~69-17~~ to ~~86~~21, wherein the first binding domain comprises a first heavy chain variable domain and a first light chain variable domain, wherein the first heavy chain variable domain is linked to a first heavy chain constant region and the first light chain variable domain is linked to a first light chain constant region; and the second binding domain comprises a second heavy chain variable domain and a second light chain variable domain, wherein the second heavy chain variable domain is linked to a second heavy chain constant region and the second light chain variable domain is linked to a second light chain constant region; and wherein:

a) the first heavy chain constant region further comprises a S183K substitution (EU numbering) and the first light chain constant region comprises a V133E substitution (EU numbering), and the second heavy chain constant region further comprises a S183E

substitution (EU numbering) and the second light chain constant region comprises a V133K substitution (EU numbering); or

b) the first heavy chain constant region further comprises a S183E substitution (EU numbering) and the first light chain constant region comprises a V133K substitution (EU numbering), and the second heavy chain constant region further comprises a S183K substitution (EU numbering) and the second light chain constant region comprises a V133E substitution (EU numbering);

c) the first heavy chain constant region comprises an amino acid sequence selected from SEQ ID NOs: 96, 184, 98, 186, 117, 188, 119, and 190 and the first light chain constant region comprises the amino acid sequence of SEQ ID NO: 103; and the heavy chain constant region comprises an amino acid sequence selected from SEQ ID NOs: 97, 185, 99, 187, 118, 189, 120, and 191 and the second light chain constant region comprising the amino acid sequence of SEQ ID NO: 104; or

d) the second heavy chain constant region comprises an amino acid sequence selected from SEQ ID NOs: 96, 184, 98, 186, 117, 188, 119, and 190 and the second light chain constant region comprises the amino acid sequence of SEQ ID NO: 103; and the first heavy chain constant region comprises an amino acid sequence selected from SEQ ID NOs: 97, 185, 99, 187, 118, 189, 120, and 191 and the first light chain constant region comprises the amino acid sequence of SEQ ID NO: 104.

~~88.—The bispecific antibody of claim 87, wherein the first heavy chain constant region comprises a knob mutation and the second heavy chain constant region comprises a hole mutation; or wherein the first heavy chain constant region comprises a hole mutation and the second heavy chain constant region comprises a knob mutation.~~

~~89.—The bispecific antibody of claim 88, wherein the antibody is an IgG1 antibody and wherein the knob mutation comprises a T366W substitution.~~

~~90.—The bispecific antibody of claim 88 or claim 89, wherein the antibody is an IgG1 antibody and wherein the hole mutation comprises at least one, at least two, or three substitutions selected from T366S, L368A, and Y407V.~~

~~91.—The bispecific antibody of claim 90, wherein the antibody is an IgG1 antibody and wherein the hole mutation comprises T366S, L368A, and Y407V substitutions.~~

~~92.—The bispecific antibody of any one of claims 87 to 91, wherein the first heavy chain constant region and/or the second heavy chain constant region comprises a N297G substitution (EU numbering).~~

~~93.—The bispecific antibody of claim 92, wherein the first heavy chain constant region and the second heavy chain constant region each comprises a N297G substitution (EU numbering).~~

~~94.—The bispecific antibody of any one of claims 87 to 93, wherein:~~

~~a) —the first heavy chain constant region further comprises a S183K substitution (EU numbering) and the first light chain constant region comprises a V133E substitution (EU numbering), and the second heavy chain constant region further comprises a S183E substitution (EU numbering) and the second light chain constant region comprises a V133K substitution (EU numbering); or~~

~~b) —the first heavy chain constant region further comprises a S183E substitution (EU numbering) and the first light chain constant region comprises a V133K substitution (EU numbering), and the second heavy chain constant region further comprises a S183K substitution (EU numbering) and the second light chain constant region comprises a V133E substitution (EU numbering).~~

~~95.—The bispecific antibody of any one of claims 87 to 94, wherein the first heavy chain constant region and/or the second heavy chain constant region further comprises at least one substitution selected from M428L and N434S (EU numbering).~~

~~96.—The bispecific antibody of claim 95, wherein the first heavy chain constant region and the second heavy chain constant region each further comprises at least one substitution selected from M428L and N434S (EU numbering).~~

~~97.—The bispecific antibody of claim 96, wherein the first heavy chain constant region and the second heavy chain constant region each further comprises M428L and N434S substitutions (EU numbering).~~

~~98.—The bispecific antibody of any one of claims 87 to 97, wherein:~~

~~a) —the first heavy chain constant region comprises an amino acid sequence selected from SEQ ID NOs: 96, 184, 98, 186, 117, 188, 119, and 190 and the first light chain constant region comprises the amino acid sequence of SEQ ID NO: 103; and the heavy chain constant region comprises an amino acid sequence selected from SEQ ID~~

~~NOs: 97, 185, 99, 187, 118, 189, 120, and 191 and the second light chain constant region comprising the amino acid sequence of SEQ ID NO: 104; or~~

~~b) — the second heavy chain constant region comprises an amino acid sequence selected from SEQ ID NOs: 96, 184, 98, 186, 117, 188, 119, and 190 and the second light chain constant region comprises the amino acid sequence of SEQ ID NO: 103; and the first heavy chain constant region comprises an amino acid sequence selected from SEQ ID NOs: 97, 185, 99, 187, 118, 189, 120, and 191 and the first light chain constant region comprises the amino acid sequence of SEQ ID NO: 104.~~

~~99. — The bispecific antibody of claim 98, wherein:~~

~~a) the first heavy chain constant region comprises the amino acid sequence of SEQ ID NOs: 96 or 184 and the first light chain constant region comprises the amino acid sequence of SEQ ID NO: 103, and the second heavy chain constant region comprises the amino acid sequence of SEQ ID NO: 97 or 185 and the second light chain constant region comprises the amino acid sequence of SEQ ID NO: 104; or~~

~~b) the first heavy chain constant region comprises the amino acid sequence of SEQ ID NO: 98 or 186 and the first light chain constant region comprises the amino acid sequence of SEQ ID NO: 103, and the second heavy chain constant region comprises the amino acid sequence of SEQ ID NO: 99 or 187 and the second light chain constant region comprises the amino acid sequence of SEQ ID NO: 104; or~~

~~c) the second heavy chain constant region comprises the amino acid sequence of SEQ ID NOs: 96 or 184 and the second light chain constant region comprises the amino acid sequence of SEQ ID NO: 103, and the first heavy chain constant region comprises the amino acid sequence of SEQ ID NO: 97 or 185 and the first light chain constant region comprises the amino acid sequence of SEQ ID NO: 104; or~~

~~d) the second heavy chain constant region comprises the amino acid sequence of SEQ ID NO: 98 or 186 and the second light chain constant region comprises the amino acid sequence of SEQ ID NO: 103, and the first heavy chain constant region comprises the amino acid sequence of SEQ ID NO: 99 or 187 and the first light chain constant region comprises the amino acid sequence of SEQ ID NO: 104; or~~

~~e) the first heavy chain constant region comprises the amino acid sequence of SEQ ID NOs: 118 or 189 and the first light chain constant region comprises the amino acid sequence of SEQ ID NO: 103, and the second heavy chain constant region comprises the~~

~~amino acid sequence of SEQ ID NO: 117 or 188 and the second light chain constant region comprises the amino acid sequence of SEQ ID NO: 104; or~~

~~f) the first heavy chain constant region comprises the amino acid sequence of SEQ ID NO: 120 or 191 and the first light chain constant region comprises the amino acid sequence of SEQ ID NO: 103, and the second heavy chain constant region comprises the amino acid sequence of SEQ ID NO: 119 or 190 and the second light chain constant region comprises the amino acid sequence of SEQ ID NO: 104; or~~

~~g) the second heavy chain constant region comprises the amino acid sequence of SEQ ID NOs: 118 or 189 and the second light chain constant region comprises the amino acid sequence of SEQ ID NO: 103, and the first heavy chain constant region comprises the amino acid sequence of SEQ ID NO: 117 or 188 and the first light chain constant region comprises the amino acid sequence of SEQ ID NO: 104; or~~

~~h) the second heavy chain constant region comprises the amino acid sequence of SEQ ID NO: 120 or 191 and the second light chain constant region comprises the amino acid sequence of SEQ ID NO: 103, and the first heavy chain constant region comprises the amino acid sequence of SEQ ID NO: 119 or 190 and the first light chain constant region comprises the amino acid sequence of SEQ ID NO: 104.~~

100:23. A bispecific antibody comprising a first binding domain and a second binding domain, wherein the first binding domain binds human KLK7 and the second binding domain binds human KLK5, wherein (i) the first binding domain comprises a heavy chain amino acid sequence of SEQ ID NO: 108 or 192, and a light chain amino acid sequence of SEQ ID NO: 109, and the second binding domain comprises a heavy chain amino acid sequence of SEQ ID NO: 110 or 193, and a light chain amino acid sequence of SEQ ID NO: 111; or (ii) the first binding domain comprises a heavy chain amino acid sequence of SEQ ID NO: 112 or 194, and a light chain amino acid sequence of SEQ ID NO: 113, and the second binding domain comprises a heavy chain amino acid sequence of SEQ ID NO: 114 or 195, and a light chain amino acid sequence of SEQ ID NO: 115; or (iii) the first binding domain comprises a heavy chain amino acid sequence of SEQ ID NO: 108 and a light chain amino acid sequence of SEQ ID NO: 109, and the second binding domain comprises a heavy chain amino acid sequence of SEQ ID NO: 110 and a light chain amino acid sequence of SEQ ID NO: 111; or (iv) the first binding domain comprises a heavy chain amino acid sequence of SEQ ID NO: 112 and a light chain amino acid sequence of SEQ ID NO: 113, and the second binding domain comprises a heavy chain amino acid sequence of SEQ ID NO: 114 and a light chain amino acid sequence of SEQ ID NO: 115.

~~101. A bispecific antibody comprising a first binding domain and a second binding domain, wherein the first binding domain binds human KLK7 and the second binding domain binds human KLK5, wherein the first binding domain comprises a heavy chain amino acid sequence of SEQ ID NO: 112 or 194, and a light chain amino acid sequence of SEQ ID NO: 113, and the second binding domain comprises a heavy chain amino acid sequence of SEQ ID NO: 114 or 195, and a light chain amino acid sequence of SEQ ID NO: 115.~~

~~102. A bispecific antibody comprising a first binding domain and a second binding domain, wherein the first binding domain binds human KLK7 and the second binding domain binds human KLK5, wherein the first binding domain comprises a heavy chain amino acid sequence of SEQ ID NO: 108 and a light chain amino acid sequence of SEQ ID NO: 109, and the second binding domain comprises a heavy chain amino acid sequence of SEQ ID NO: 110 and a light chain amino acid sequence of SEQ ID NO: 111.~~

~~103. A bispecific antibody comprising a first binding domain and a second binding domain, wherein the first binding domain binds human KLK7 and the second binding domain binds human KLK5, wherein the first binding domain comprises a heavy chain amino acid sequence of SEQ ID NO: 112 and a light chain amino acid sequence of SEQ ID NO: 113, and the second binding domain comprises a heavy chain amino acid sequence of SEQ ID NO: 114 and a light chain amino acid sequence of SEQ ID NO: 115.~~

~~104. A bispecific antibody comprising a first binding domain and a second binding domain, wherein the first binding domain binds human KLK7 and the second binding domain binds human KLK5, wherein the second binding domain comprises~~

- ~~a) a heavy chain variable domain (VH) comprising (a) CDR H1 comprising the amino acid sequence of SEQ ID NO: 107, (b) CDR H2 comprising an amino acid sequence selected from SEQ ID NOs: 40 and 41, and (c) CDR H3 comprising the amino acid sequence of SEQ ID NO: 42, and a light chain variable domain (VL) comprising (d) CDR L1 comprising the amino acid sequence of SEQ ID NOs: 43 or 44, (e) CDR L2 comprising the amino acid sequence of SEQ ID NO: 45, and (f) CDR L3 comprising an amino acid sequence selected from SEQ ID NOs: 46-49; or~~
- ~~b) a heavy chain variable domain (VH) comprising (a) CDR H1 comprising an amino acid sequence selected from SEQ ID NOs: 39 and 107, (b) CDR H2 comprising the amino acid sequence of SEQ ID NO: 41, and (c) CDR H3 comprising the amino acid sequence of SEQ ID NO: 42, and a light chain variable domain (VL) comprising (d) CDR L1 comprising an amino acid sequence selected~~

~~from SEQ ID NOs: 43 and 44, (e) CDR L2 comprising the amino acid sequence of SEQ ID NO: 45, and (f) CDR L3 comprising an amino acid sequence selected from SEQ ID NOs: 46-49; or~~

~~e) a heavy chain variable domain (VH) comprising (a) CDR H1 comprising the amino acid sequence of SEQ ID NO: 39 or 107, (b) CDR H2 comprising an amino acid sequence selected from SEQ ID NOs: 40 and 41, and (c) CDR H3 comprising the amino acid sequence of SEQ ID NO: 42, and a light chain variable domain (VL) comprising (d) CDR L1 comprising the amino acid sequence of SEQ ID NOs: 44, (e) CDR L2 comprising the amino acid sequence of SEQ ID NO: 45, and (f) CDR L3 comprising an amino acid sequence selected from SEQ ID NOs: 46-49; or~~

~~d) a heavy chain variable domain (VH) comprising (a) CDR H1 comprising an amino acid sequence selected from SEQ ID NOs: 39 and 107, (b) CDR H2 comprising an amino acid sequence selected from SEQ ID NOs: 40 and 41, and (c) CDR H3 comprising the amino acid sequence of SEQ ID NO: 42, and a light chain variable domain (VL) comprising (d) CDR L1 comprising an amino acid sequence selected from SEQ ID NOs: 43 and 44, (e) CDR L2 comprising the amino acid sequence of SEQ ID NO: 45, and (f) CDR L3 comprising an amino acid sequence selected from SEQ ID NOs: 47-49; or~~

~~e) a heavy chain variable domain (VH) comprising (a) CDR H1 comprising the amino acid sequence of SEQ ID NO: 68, (b) CDR H2 comprising the amino acid sequence of SEQ ID NO: 70, and (c) CDR H3 comprising an amino acid sequence selected from SEQ ID NOs: 71 and 72, and a light chain variable domain (VL) comprising (d) CDR L1 comprising the amino acid sequence of SEQ ID NO: 73, (e) CDR L2 comprising the amino acid sequence of SEQ ID NO: 74, and (f) CDR L3 comprising an amino acid sequence selected from SEQ ID NOs: 75-78; or~~

~~f) a heavy chain variable domain (VH) comprising (a) CDR H1 comprising the amino acid sequence of SEQ ID NO: 68, (b) CDR H2 comprising an amino acid sequence selected from SEQ ID NOs: 69 and 70, and (c) CDR H3 comprising the amino acid sequence of SEQ ID NO: 72, and a light chain variable domain (VL) comprising (d) CDR L1 comprising the amino acid sequence of SEQ ID NO: 73, (e) CDR L2 comprising the amino acid sequence of SEQ ID NO: 74, and (f) CDR L3 comprising an amino acid sequence selected from SEQ ID NOs: 75-78; or~~

~~g) a heavy chain variable domain (VH) comprising (a) CDR H1 comprising the amino acid sequence of SEQ ID NO: 68, (b) CDR H2 comprising an amino acid sequence selected from SEQ ID NOs: 69 and 70, and (c) CDR H3 comprising an amino acid sequence selected from SEQ ID NOs: 71 and 72, and a light chain variable domain (VL) comprising (d) CDR L1 comprising the amino acid sequence of SEQ ID NO: 73, (e) CDR L2 comprising the amino acid sequence of SEQ ID NO: 74, and (f) CDR L3 comprising an amino acid sequence selected from SEQ ID NOs: 76-78.~~

~~105. The bispecific antibody of claim 104, wherein the second binding domain comprises a heavy chain variable domain (VH) comprising (a) CDR H1 comprising the amino acid sequence of SEQ ID NO: 39, (b) CDR H2 comprising the amino acid sequence of SEQ ID NO: 41, and (c) CDR H3 comprising the amino acid sequence of SEQ ID NO: 42, and a light chain variable domain (VL) comprising (d) CDR L1 comprising the amino acid sequence of SEQ ID NOs: 43, (e) CDR L2 comprising the amino acid sequence of SEQ ID NO: 45, and (f) CDR L3 comprising the amino acid sequence of SEQ ID NO: 47.~~

~~106. The bispecific antibody of claim 104, wherein the second binding domain comprises a heavy chain variable domain (VH) comprising (a) CDR H1 comprising the amino acid sequence of SEQ ID NO: 68, (b) CDR H2 comprising the amino acid sequence of SEQ ID NO: 70, and (c) CDR H3 comprising the amino acid sequence of SEQ ID NO: 72, and a light chain variable domain (VL) comprising (d) CDR L1 comprising the amino acid sequence of SEQ ID NO: 73, (e) CDR L2 comprising the amino acid sequence of SEQ ID NO: 74, and (f) CDR L3 comprising the amino acid sequence of SEQ ID NO: 76.~~

~~107. The bispecific antibody of any one of claims 104 to 106, wherein the second binding domain is humanized.~~

~~108. The bispecific antibody of any one of claims 104 to 107, wherein the second binding domain comprises a sequence selected from:~~

~~a) a VH sequence having at least 95% sequence identity to an amino acid sequence selected from SEQ ID NOs: 50, 52, 53, 105, and 106;~~

~~b) a VL sequence having at least 95% sequence identity to an amino acid sequence selected from SEQ ID NOs: 51 and 54-67; and~~

~~c) a VH sequence as defined in (a) and a VL sequence as defined in (b);~~

~~d) a VH sequence having at least 95% sequence identity to an amino acid sequence selected from SEQ ID NOs: 79 and 81-87;~~

~~e) a VL sequence having at least 95% sequence identity to an amino acid sequence selected from SEQ ID NOs: 80 and 88-94; and~~

~~f) a VH sequence as defined in (d) and a VL sequence as defined in (e).~~

~~109. The bispecific antibody of any one of claims 104 to 107, wherein the second binding domain comprises a sequence selected from:~~

~~a) a VH sequence having at least 95% sequence identity to an amino acid sequence selected from SEQ ID NOs: 52, 53, 105, and 106;~~

~~b) a VL sequence having at least 95% sequence identity to an amino acid sequence selected from SEQ ID NOs: 54-67; and~~

~~c) a VH sequence as defined in (a) and a VL sequence as defined in (b);~~

~~d) a VH sequence having at least 95% sequence identity to an amino acid sequence selected from SEQ ID NOs: 81-87;~~

~~e) a VL sequence having at least 95% sequence identity to an amino acid sequence selected from SEQ ID NOs: 88-94; and~~

~~f) a VH sequence as defined in (d) and a VL sequence as defined in (e).~~

~~110. The bispecific antibody of any one of claims 104 to 107, wherein the second binding domain comprises a sequence selected from:~~

~~a) a VH sequence comprising an amino acid sequence selected from SEQ ID NOs: 50, 52, 53, 105, and 106;~~

~~b) a VL sequence comprising an amino acid sequence selected from SEQ ID NOs: 51 and 54-67; and~~

~~c) a VH sequence as defined in (a) and a VL sequence as defined in (b);~~

~~d) a VH sequence comprising an amino acid sequence selected from SEQ ID NOs: 79 and 81-87;~~

~~e) a VL sequence comprising an amino acid sequence selected from SEQ ID NOs: 80 and 88-94; and~~

~~f) a VH sequence as defined in (d) and a VL sequence as defined in (e).~~

~~111. The bispecific antibody of any one of claims 104 to 107, wherein the second binding domain comprises a sequence selected from:~~

- ~~a) a VH sequence comprising an amino acid sequence selected from SEQ ID NOs: 52, 53, 105, and 106;~~
- ~~b) a VL sequence comprising an amino acid sequence selected from SEQ ID NOs: 54-67; and~~
- ~~c) a VH sequence as defined in (a) and a VL sequence as defined in (b);~~
- ~~d) a VH sequence comprising an amino acid sequence selected from SEQ ID NOs: 81-87;~~
- ~~e) a VL sequence comprising an amino acid sequence selected from SEQ ID NOs: 88-94; and~~
- ~~f) a VH sequence as defined in (d) and a VL sequence as defined in (e).~~

~~112. The bispecific antibody of any one of claims 104 to 107, wherein the second half amino acid antibody comprises a VH sequence of SEQ ID NO: 52 or SEQ ID NO: 53 and a VL amino acid sequence of SEQ ID NO: 55 or SEQ ID NO: 62.~~

~~113. The bispecific antibody of claim 112, wherein the second half amino acid antibody comprises a VH sequence of SEQ ID NO: 52 and a VL amino acid sequence of SEQ ID NO: 55; or a VH sequence of SEQ ID NO: 53 and a VL amino acid sequence of SEQ ID NO: 62.~~

~~114. The bispecific antibody of any one of claims 104 to 113, wherein the first binding domain is humanized.~~

~~115.~~24. The bispecific antibody of any one of claims ~~104-15~~ to ~~114~~23, wherein the first binding domain comprises a first heavy chain variable domain and a first light chain variable domain, wherein the first heavy chain variable domain is linked to a first heavy chain constant region and the first light chain variable domain is linked to a first light chain constant region; and the second binding domain comprises a second heavy chain variable domain and a second light chain variable domain, wherein the second heavy chain variable domain is linked to a second heavy chain constant region and the second light chain variable domain is linked to a second light chain constant region; optionally wherein the first heavy chain constant region comprises a knob mutation and the second heavy chain constant region comprises a hole mutation; or wherein the first heavy chain constant region comprises a hole mutation and the second heavy chain constant region comprises a knob mutation.

~~116. The bispecific antibody of claim 115, wherein the first heavy chain constant region comprises a knob mutation and the second heavy chain constant region comprises a hole mutation; or wherein the first heavy chain constant region comprises a hole mutation and the second heavy chain constant region comprises a knob mutation.~~

~~117. The bispecific antibody of claim 116, wherein the antibody is an IgG1 antibody and wherein the knob mutation comprises a T366W mutation.~~

~~118. The bispecific antibody of claim 116 or claim 117, wherein the antibody is an IgG1 antibody and wherein the hole mutation comprises at least one, at least two, or three mutations selected from T366S, L368A, and Y407V.~~

~~119. The bispecific antibody of claim 118, wherein the antibody is an IgG1 antibody and wherein the hole mutation comprises T366S, L368A, and Y407V mutations.~~

~~120. The bispecific antibody of any one of claims 115 to 119, wherein the first heavy chain constant region and/or the second heavy chain constant region comprises a N297G substitution (EU numbering).~~

~~121. The bispecific antibody of claim 120, wherein the first heavy chain constant region and the second heavy chain constant region each comprises a N297G substitution (EU numbering).~~

~~122;25.~~ The bispecific antibody of ~~any one of claims 115 to 121~~claim 24, wherein:

a) the first heavy chain constant region further comprises a S183K substitution (EU numbering) and the first light chain constant region comprises a V133E substitution (EU numbering), and the second heavy chain constant region further comprises a S183E substitution (EU numbering) and the second light chain constant region comprises a V133K substitution (EU numbering); or

b) the first heavy chain constant region further comprises a S183E substitution (EU numbering) and the first light chain constant region comprises a V133K substitution (EU numbering), and the second heavy chain constant region further comprises a S183K substitution (EU numbering) and the second light chain constant region comprises a V133E substitution (EU numbering).

~~123;26.~~ The bispecific antibody of ~~any one of claims 115 to 122~~claim 24 or claim 25, wherein the first heavy chain constant region and/or the second heavy chain constant region further comprises at least one substitution selected from M428L and N434S (EU numbering).

~~124. The bispecific antibody of claim 123, wherein the first heavy chain constant region and the second heavy chain constant region each further comprises at least one substitution selected from M428L and N434S (EU numbering);~~

~~125. The bispecific antibody of claim 124, wherein the first heavy chain constant region and the second heavy chain constant region each further comprises M428L and N434S substitutions (EU numbering);~~

~~126.~~27. The bispecific antibody of any one of claims ~~115-24~~ to ~~125~~26, wherein:

a) the first heavy chain constant region comprises an amino acid sequence selected from SEQ ID NOs: 96, 184, 98, 186, 117, 188, 119, and 190 and the first light chain constant region comprises the amino acid sequence of SEQ ID NO: 103; and the heavy chain constant region comprises an amino acid sequence selected from SEQ ID NOs: 97, 185, 99, 187, 118, 189, 120, and 191 and the second light chain constant region comprising the amino acid sequence of SEQ ID NO: 104; or

b) the second heavy chain constant region comprises an amino acid sequence selected from SEQ ID NOs: 96, 184, 98, 186, 117, 188, 119, and 190 and the second light chain constant region comprises the amino acid sequence of SEQ ID NO: 103; and the first heavy chain constant region comprises an amino acid sequence selected from SEQ ID NOs: 97, 185, 99, 187, 118, 189, 120, and 191 and the first light chain constant region comprises the amino acid sequence of SEQ ID NO: 104.

~~127. The bispecific antibody of claim 126, wherein:~~

~~a) the first heavy chain constant region comprises the amino acid sequence of SEQ ID NOs: 96 or 184 and the first light chain constant region comprises the amino acid sequence of SEQ ID NO: 103, and the second heavy chain constant region comprises the amino acid sequence of SEQ ID NO: 97 or 185 and the second light chain constant region comprises the amino acid sequence of SEQ ID NO: 104; or~~

~~b) the first heavy chain constant region comprises the amino acid sequence of SEQ ID NO: 98 or 186 and the first light chain constant region comprises the amino acid sequence of SEQ ID NO: 103, and the second heavy chain constant region comprises the amino acid sequence of SEQ ID NO: 99 or 187 and the second light chain constant region comprises the amino acid sequence of SEQ ID NO: 104; or~~

~~c) the second heavy chain constant region comprises the amino acid sequence of SEQ ID NOs: 96 or 184 and the second light chain constant region comprises the amino~~

~~acid sequence of SEQ ID NO: 103, and the first heavy chain constant region comprises the amino acid sequence of SEQ ID NO: 97 or 185 and the first light chain constant region comprises the amino acid sequence of SEQ ID NO: 104; or~~

~~d) the second heavy chain constant region comprises the amino acid sequence of SEQ ID NO: 98 or 186 and the second light chain constant region comprises the amino acid sequence of SEQ ID NO: 103, and the first heavy chain constant region comprises the amino acid sequence of SEQ ID NO: 99 or 187 and the first light chain constant region comprises the amino acid sequence of SEQ ID NO: 104; or~~

~~e) the first heavy chain constant region comprises the amino acid sequence of SEQ ID NOs: 118 or 189 and the first light chain constant region comprises the amino acid sequence of SEQ ID NO: 103, and the second heavy chain constant region comprises the amino acid sequence of SEQ ID NO: 117 or 188 and the second light chain constant region comprises the amino acid sequence of SEQ ID NO: 104; or~~

~~f) the first heavy chain constant region comprises the amino acid sequence of SEQ ID NO: 120 or 191 and the first light chain constant region comprises the amino acid sequence of SEQ ID NO: 103, and the second heavy chain constant region comprises the amino acid sequence of SEQ ID NO: 119 or 190 and the second light chain constant region comprises the amino acid sequence of SEQ ID NO: 104; or~~

~~g) the second heavy chain constant region comprises the amino acid sequence of SEQ ID NOs: 118 or 189 and the second light chain constant region comprises the amino acid sequence of SEQ ID NO: 103, and the first heavy chain constant region comprises the amino acid sequence of SEQ ID NO: 117 or 188 and the first light chain constant region comprises the amino acid sequence of SEQ ID NO: 104; or~~

~~h) the second heavy chain constant region comprises the amino acid sequence of SEQ ID NO: 120 or 191 and the second light chain constant region comprises the amino acid sequence of SEQ ID NO: 103, and the first heavy chain constant region comprises the amino acid sequence of SEQ ID NO: 119 or 190 and the first light chain constant region comprises the amino acid sequence of SEQ ID NO: 104.~~

128:28. The bispecific antibody of any one of claims ~~69-15~~ to 127, wherein the antibody binds human KLK5 with a K_D of less than 60 pM, less than 30 pM, less than 20 pM, less than 10 pM, or less than 5 pM, as measured by surface plasmon resonance; and/or wherein the antibody inhibits human KLK5 protease activity with an IC_{50} of less than 5 nM, or less than 3 nM, or less

than 2 nM, or less than 1 nM, optionally wherein inhibition of human KLK5 protease activity is inhibition of human KLK5-mediated cleavage of the substrate Boc-Val-Pro-Arg-AMC.

~~129. The bispecific antibody of any one of claims 69 to 128, wherein the antibody inhibits human KLK5 protease activity with an IC₅₀ of less than 5 nM, or less than 3 nM, or less than 2 nM, or less than 1 nM.~~

~~130. The antibody of any one of claims 69 to 129, wherein the antibody binds human KLK5 with a K_D of less than 60 pM, less than 30 pM, less than 20 pM, less than 10 pM, or less than 5 pM, as measured by surface plasmon resonance; and wherein the antibody inhibits human KLK5 protease activity with an IC₅₀ of less than 5 nM, or less than 3 nM, or less than 2 nM, or less than 1 nM.~~

~~131. The bispecific antibody of claim 129 or claim 130, wherein inhibition of human KLK5 protease activity is inhibition of human KLK5-mediated cleavage of the substrate Boc-Val-Pro-Arg-AMC.~~

132.29. The bispecific antibody of any one of claims 69-15 to 13128, wherein the antibody binds human KLK7 with a K_D of less than 20 pM, or less than 15 pM, or less than 10 pM, less than 5 pM, or less than 3 pM, or less than 2 pM, or less than 1 pM, as measured by surface plasmon resonance; and/or wherein the antibody inhibits human KLK7 protease activity with an IC₅₀ of less than 5 nM, or less than 3 nM, or less than 2 nM, or less than 1 nM, optionally wherein inhibition of human KLK7 protease activity is inhibition of human KLK7-mediated cleavage of a substrate comprising the amino acid sequence RPKPVE- Nval-WRK (SEQ ID NO: 121), wherein Nval is norvaline.

~~133. The bispecific antibody of any one of claims 69 to 132, wherein the antibody inhibits human KLK7 protease activity with an IC₅₀ of less than 5 nM, or less than 3 nM, or less than 2 nM, or less than 1 nM.~~

~~134. The bispecific antibody of any one of claims 69 to 133, wherein the antibody binds human KLK7 with a K_D of less than 20 pM, or less than 15 pM, or less than 10 pM, less than 5 pM, or less than 3 pM, or less than 2 pM, or less than 1 pM, as measured by surface plasmon resonance; and wherein the antibody inhibits human KLK7 protease activity with an IC₅₀ of less than less than 5 nM, or less than 3 nM, or less than 2 nM, or less than 1 nM.~~

~~135. The bispecific antibody of claim 133 or claim 134, wherein inhibition of human KLK7 protease activity is inhibition of human KLK7-mediated cleavage of a substrate~~

~~comprising the amino acid sequence RPKPVE Nval WRK (SEQ ID NO: 121), wherein Nval is norvaline.~~

~~136. The bispecific antibody of any one of claims 69 to 135, wherein the K_D of the bispecific antibody for human KLK5 and the K_D of the antibody for human KLK7 are within 3-fold, or within 2.5 fold, or within 2 fold, or within 1.5 fold of one another.~~

~~137.~~30. An isolated nucleic acid encoding the bispecific antibody of any one of claims ~~69~~15 to ~~136~~29.

~~138.~~31. An isolated nucleic acid encoding the first binding domain ~~of the bispecific antibody of any one of claims 69 to 136~~ and/or the second binding domain of the bispecific antibody of any one of claims 15 to 29.

~~139. An isolated nucleic acid encoding the second binding domain of the bispecific antibody of any one of claims 69 to 136.~~

~~140.~~32. An isolated host cell comprising the isolated nucleic acid of claim ~~137~~30 or claim 31.

~~141. An isolated host cell comprising the isolated nucleic acid of claim 138.~~

~~142. An isolated host cell comprising the isolated nucleic acid of claim 139.~~

~~143.~~33. An isolated host cell that expresses the bispecific antibody of any one of claims ~~69~~15 to ~~136~~29.

~~144.~~34. An isolated host cell that expresses the first binding domain ~~of the bispecific antibody of any one of claims 69 to 136~~ and/or the second binding domain of the bispecific antibody of any one of claims 15 to 29.

~~145. An isolated host cell that expresses the second binding domain of the bispecific antibody of any one of claims 69 to 136.~~

~~146.~~35. A method of producing a bispecific antibody that binds to human KLK5 and human KLK7, comprising culturing the host cell of claim ~~140~~33 or claim ~~143~~34 under conditions suitable for the expression of the antibody, and optionally recovering the antibody from the host cell.

~~147. The method of claim 146, further comprising recovering the antibody from the host cell.~~

~~148. A method of producing a bispecific antibody that binds to human KLK5 and human KLK7, comprising (i) culturing the host cell of claim 141 or claim 144 under conditions suitable~~

~~for the expression of the first binding domain; and (ii) culturing the host cell of claim 142 or claim 145 under conditions suitable for expression of the second binding domain.~~

~~149. The method of claim 148, further comprising recovering the first binding domain and the second binding domain and assembling the bispecific antibody.~~

~~150.36.~~ A pharmaceutical composition comprising the antibody of any of claims ~~14~~ to ~~27~~ 9 and a pharmaceutically acceptable carrier, optionally wherein the pharmaceutical composition further comprises an additional therapeutic agent, optionally wherein the additional therapeutic agent is a KLK5 inhibitor, optionally wherein the KLK5 inhibitor is an anti-KLK5 antibody.

~~151. The pharmaceutical composition of claim 150, further comprising an additional therapeutic agent.~~

~~152. The pharmaceutical composition of claim 151, wherein the additional therapeutic agent is a KLK5 inhibitor.~~

~~153. The pharmaceutical composition of claim 152, wherein the KLK5 inhibitor is an anti-KLK5 antibody.~~

~~154.37.~~ -The pharmaceutical composition of claim ~~153~~36, wherein the anti-KLK5 antibody comprises:

a) a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising an amino acid sequence selected from SEQ ID NOs: 39 and 107, (b) CDR-H2 comprising an amino acid sequence selected from SEQ ID NOs: 40 and 41, and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO: 42, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising an amino acid sequence selected from SEQ ID NOs: 43 and 44, (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 45, and (f) CDR-L3 comprising an amino acid sequence selected from SEQ ID NOs: 46-49; or

b) a heavy chain variable domain (VH) comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 68, (b) CDR-H2 comprising an amino acid sequence selected from SEQ ID NOs: 69 and 70, and (c) CDR-H3 comprising an amino acid sequence selected from SEQ ID NOs: 71 and 72, and a light chain variable domain (VL) comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 73, (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 74, and (f) CDR-L3 comprising an amino acid sequence selected from SEQ ID NOs: 75-78.

~~155. The pharmaceutical composition of claim 153 or claim 154, wherein the anti-KLK5 antibody comprises a heavy chain variable domain (VH) comprising (a) CDR H1 comprising the amino acid sequence of SEQ ID NO: 39, (b) CDR H2 comprising the amino acid sequence of SEQ ID NO: 41, and (c) CDR H3 comprising the amino acid sequence of SEQ ID NO: 42, and a light chain variable domain (VL) comprising (d) CDR L1 comprising the amino acid sequence of SEQ ID NOs: 43, (e) CDR L2 comprising the amino acid sequence of SEQ ID NO: 45, and (f) CDR L3 comprising the amino acid sequence of SEQ ID NO: 47.~~

~~156. The pharmaceutical composition of claim 153 or claim 154, wherein the anti-KLK5 antibody comprises a heavy chain variable domain (VH) comprising (a) CDR H1 comprising the amino acid sequence of SEQ ID NO: 68, (b) CDR H2 comprising the amino acid sequence of SEQ ID NO: 70, and (c) CDR H3 comprising the amino acid sequence of SEQ ID NO: 72, and a light chain variable domain (VL) comprising (d) CDR L1 comprising the amino acid sequence of SEQ ID NO: 73, (e) CDR L2 comprising the amino acid sequence of SEQ ID NO: 74, and (f) CDR L3 comprising the amino acid sequence of SEQ ID NO: 76.~~

~~157. The pharmaceutical composition of any one of claims 153 to 156, wherein the anti-KLK5 antibody is a monoclonal antibody.~~

~~158. The pharmaceutical composition of any one of claims 153 to 157, wherein the anti-KLK5 antibody is a humanized, or chimeric antibody.~~

~~159.~~38. The pharmaceutical composition of ~~any one of claims 153 to 158~~claim 36, wherein the anti-KLK5 antibody is an antibody ~~fragment that binds human KLK5~~of any one of claims 1 to 3.

~~160. The pharmaceutical composition of any one of claims 153-159, wherein the anti-KLK5 antibody comprises a sequence selected from:~~

~~a) a VH sequence having at least 95% sequence identity to an amino acid sequence selected from SEQ ID NOs: 50, 52, 53, 105 and 106;~~

~~b) a VL sequence having at least 95% sequence identity to an amino acid sequence selected from SEQ ID NOs: 51 and 54-67; and~~

~~c) a VH sequence as defined in (a) and a VL sequence as defined in (b);~~

~~d) a VH sequence having at least 95% sequence identity to an amino acid sequence selected from SEQ ID NOs: 79 and 81-87;~~

~~e) a VL sequence having at least 95% sequence identity to an amino acid sequence selected from SEQ ID NOs: 80 and 88-94; and~~

~~f) a VH sequence as defined in (d) and a VL sequence as defined in (e).~~

~~161. The pharmaceutical composition of any one of claims 153-159, wherein the anti-KLK5 antibody comprises a sequence selected from:~~

~~a) a VH sequence having at least 95% sequence identity to an amino acid sequence selected from SEQ ID NOs: 52, 53, 105 and 106;~~

~~b) a VL sequence having at least 95% sequence identity to an amino acid sequence selected from SEQ ID NOs: 54-67; and~~

~~c) a VH sequence as defined in (a) and a VL sequence as defined in (b);~~

~~d) a VH sequence having at least 95% sequence identity to an amino acid sequence selected from SEQ ID NOs: 81-87;~~

~~e) a VL sequence having at least 95% sequence identity to an amino acid sequence selected from SEQ ID NOs: 88-94; and~~

~~f) a VH sequence as defined in (d) and a VL sequence as defined in (e).~~

~~162. The pharmaceutical composition of any one of claims 153-159, wherein the anti-KLK5 antibody comprises a sequence selected from:~~

~~a) a VH sequence comprising an amino acid sequence selected from SEQ ID NOs: 50, 52, 53, 105, and 106;~~

~~b) a VL sequence comprising an amino acid sequence selected from SEQ ID NOs: 51 and 54-67; and~~

~~c) a VH sequence as defined in (a) and a VL sequence as defined in (b);~~

~~d) a VH sequence comprising an amino acid sequence selected from SEQ ID NOs: 79 and 81-87;~~

~~e) a VL sequence comprising an amino acid sequence selected from SEQ ID NOs: 80 and 88-94; and~~

~~f) a VH sequence as defined in (d) and a VL sequence as defined in (e).~~

~~163. The pharmaceutical composition of any one of claims 153-159, wherein the anti-KLK5 antibody comprises a sequence selected from:~~

~~a) a VH sequence comprising an amino acid sequence selected from SEQ ID NOs: 52, 53, 105, and 106;~~

~~b) a VL sequence comprising an amino acid sequence selected from SEQ ID NOs: 54-67;
and~~

~~e) a VH sequence as defined in (a) and a VL sequence as defined in (b);~~

~~d) a VH sequence comprising an amino acid sequence selected from SEQ ID NOs: 81-87;~~

~~e) a VL sequence comprising an amino acid sequence selected from SEQ ID NOs: 88-94;
and~~

~~f) a VH sequence as defined in (d) and a VL sequence as defined in (e).~~

~~164. The pharmaceutical composition of claim 153, wherein the anti-KLK5 antibody is
an antibody of any one of claims 34 to 62.~~

~~165. The pharmaceutical composition of claim 153, wherein the anti-KLK5 antibody is
an antibody of any one of claims 47, 48, 51, and 52.~~

~~166.~~39. A pharmaceutical composition comprising the antibody of any of claims ~~34-1~~ to ~~62-3~~ and a pharmaceutically acceptable carrier, optionally wherein the pharmaceutical composition further comprises an additional therapeutic agent, optionally wherein the additional therapeutic agent is a KLK7 inhibitor, optionally wherein the KLK7 inhibitor is an anti-KLK7 antibody, optionally wherein the anti-KLK7 antibody is an antibody of any one of claims 4 to 9.

40. An isolated antibody that binds human KLK7, wherein when bound to human KLK7 results in a conformational change of human KLK7, wherein the conformational change allosterically results in the disruption of the substrate binding site and/or the active site of human KLK7.

41. The isolated antibody of claim 40, which is a bispecific antibody, optionally wherein the bispecific antibody binds human KLK7 and human KLK5, optionally wherein when bound to human KLK5 results in a conformational change of human KLK5, wherein the conformational change allosterically results in the disruption of the substrate binding site and/or the active site of human KLK5.

42. The isolated antibody of claim 41, wherein the antibody binds to an epitope on human KLK5 comprising one or more amino acid residues selected from Pro130, Ser131, Ala132, Gly133, Val162, Leu163, Ser164, Gln165, Lys166, Arg167, Glu169, Asp170, Ala171, Tyr172, Pro173, Arg174, Gln174A, Ile176, Asp177, Asp178, Gly184, Asp185, Lys186, Ala186A, Arg188, Asn223, Arg224, Pro225, and Lys233 according to standard protease numbering; or wherein the antibody binds to an epitope on human KLK5 comprising one or more amino acid residues selected from the group consisting of Pro130, Ser131, Ala132,

Val162, Leu163, Ser164, Gln165, Lys166, Arg167, Glu169, Asp170, Ala171, Tyr172, Pro173, Arg174, Gln174A, Ile176, Asp177, Asp178, Arg224, and Lys233 according to standard protease numbering; or wherein the antibody binds to an epitope on human KLK5 comprising one or more amino acid residues selected from Pro130, Ser131, Ala132, Gly133, Val162, Leu163, Ser164, Gln165, Lys166, Arg167, Glu169, Asp170, Ala171, Tyr172, Pro173, Arg174, Gln174A, Ile176, Asp177, and Lys233 according to standard protease numbering; or wherein the antibody binds to an epitope on human KLK5 comprising one or more amino acid residues selected from Ser131, Ala132, Gly133, Leu163, Ser164, Gln165, Lys166, Arg167, Glu169, Asp170, Ala171, Pro173, Arg174, Gly184, Asp185, Lys186, Ala186A, Arg188, Asn223, Arg224, and Pro225 according to standard protease numbering.

43. The isolated antibody of any one of claims 40 to 42, wherein the antibody binds an epitope within amino acids R71-N82, K152-S158, and/or Q211-K222 of KLK7 (SEQ ID NO: 4); optionally wherein the antibody binds an epitope comprising one or more of amino acids H72, P73, G74, S76, Q78, N82, N157, K211, and/or T213 of KLK7 (SEQ ID NO: 4).

44. A bispecific antibody comprising a first binding domain and a second binding domain, wherein the first binding domain binds human KLK7 and the second binding domain binds human KLK5, wherein when bound to human KLK7 results in a conformational change of human KLK7, wherein the conformational change allosterically results in the disruption of the substrate binding site and/or the active site of human KLK7; and/or wherein when bound to human KLK5 results in a conformational change of human KLK5, wherein the conformational change allosterically results in the disruption of the substrate binding site and/or the active site of human KLK5.

~~167. The pharmaceutical composition of claim 166, further comprising an additional therapeutic agent.~~

~~168. The pharmaceutical composition of claim 167, wherein the additional therapeutic agent is a KLK7 inhibitor.~~

~~169. The pharmaceutical composition of claim 168, wherein the KLK7 inhibitor is an anti-KLK7 antibody.~~

~~170. The pharmaceutical composition of claim 169, wherein the anti-KLK7 antibody is an antibody of any one of claims 1 to 27.~~

~~171.45.~~ A pharmaceutical composition comprising the antibody or bispecific antibody of any one of claims 1-40 to 27-44 ~~and an antibody of any one of claims 34 to 62, and a pharmaceutically acceptable carrier.~~

~~172. The pharmaceutical composition of any one of claims 150 to 171, comprising an additional therapeutic agent selected from an anti-inflammatory agent and an antibiotic.~~

~~173. A pharmaceutical composition comprising the bispecific antibody of any one of claims 69 to 136.~~

~~174. The pharmaceutical composition of claim 173, further comprising an additional therapeutic agent.~~

~~175. The pharmaceutical composition of claim 174, wherein the additional therapeutic agent is an anti-inflammatory agent.~~

~~176. The pharmaceutical composition of any one of claims 150 to 175, wherein the pharmaceutical composition is for topical administration.~~

~~177. The pharmaceutical composition of any one of claims 150 to 175, wherein the pharmaceutical composition is for subcutaneous or intravenous administration.~~

~~178.46.~~ The antibody of any one of claims 1 to 27-9 and 34-40 to 62-43, the bispecific antibody of any one of claims 69-15 to 136-29 and 44, or the pharmaceutical composition of any one of claims 150-36 to 177-39 and 45 for use as a medicament.

~~179.47.~~ The antibody of any one of claims 1 to 27-9 and 34-40 to 62-43, the bispecific antibody of any one of claims 69-15 to 136-29 and 44, or the pharmaceutical composition of any one of claims 150-36 to 177-39 and 45 for use in treating disease selected from Netherton Syndrome, asthma, atopic dermatitis, psoriasis, eosinophilic esophagitis, and rosacea.

48. Use of the antibody of any one of claims 1 to 9 and 40 to 43, the bispecific antibody of any one of claims 15 to 29 and 44, or the pharmaceutical composition of any one of claims 36 to 39 and 45 in the manufacture of a medicament for treating disease selected from Netherton Syndrome, asthma, atopic dermatitis, psoriasis, eosinophilic esophagitis, and rosacea.

~~180.49.~~ The antibody, bispecific antibody, or pharmaceutical composition for use of claim 47, or the use of claim 48 ~~The antibody, bispecific antibody, or pharmaceutical composition for use of claim 179,~~ wherein the asthma is selected from atopic asthma, allergic asthma, non-allergic asthma, exercise-induced asthma, aspirin sensitive/exacerbated asthma, mild asthma, moderate to severe asthma, corticosteroid naïve asthma, chronic asthma, corticosteroid resistant asthma, corticosteroid refractory asthma, newly diagnosed and untreated

asthma, asthma due to smoking, asthma uncontrolled on corticosteroids, T helper lymphocyte type 2 (Th2) or type 2 (Th2) high, or Type 2 (T2)-driven asthma, eosinophilic asthma, periostin-high asthma, eosinophil-high asthma, Th2-low asthma or nonTh2-driven asthma, periostin-low asthma, and eosinophil-low asthma.

~~181.—The antibody, bispecific antibody, or pharmaceutical composition for use of claim 180, wherein the asthma is eosinophil low asthma.~~

~~182-50.~~ A combination of an antibody of any one of claims 1 to ~~27-3~~ and an antibody of any one of claims ~~34-4~~ to ~~629~~, for use as a medicament.

~~183-51.~~ A combination of an antibody of any one of claims 1 to ~~27-3~~ and an antibody of any one of claims ~~34-4~~ to ~~629~~, for use in treating disease selected from Netherton Syndrome, asthma, atopic dermatitis, psoriasis, eosinophilic esophagitis, and rosacea.

~~52. Use of a combination of the antibody of any one of claims 1 to 3 and the antibody of any one of claims 4 to 9 in the manufacture of a medicament for treating disease selected from Netherton Syndrome, asthma, atopic dermatitis, psoriasis, eosinophilic esophagitis, and rosacea.~~

~~184-53.~~ The combination for use of claim ~~183-51~~, or the use of claim ~~52~~, wherein the asthma is selected from atopic asthma, allergic asthma, non-allergic asthma, exercise-induced asthma, aspirin sensitive/exacerbated asthma, mild asthma, moderate to severe asthma, corticosteroid naïve asthma, chronic asthma, corticosteroid resistant asthma, corticosteroid refractory asthma, newly diagnosed and untreated asthma, asthma due to smoking, asthma uncontrolled on corticosteroids, T helper lymphocyte type 2 (Th2) or type 2 (Th2) high, or Type 2 (T2)-driven asthma, eosinophilic asthma, periostin-high asthma, eosinophil-high asthma, Th2-low asthma or nonTh2-driven asthma, periostin-low asthma, and eosinophil-low asthma.

~~185.—The combination of claim 184, wherein the asthma is eosinophil low asthma.~~

~~186.—Use of the antibody of any one of claims 1 to 27 and 34 to 62, the bispecific antibody of any one of claims 69 to 136, or the pharmaceutical composition of any one of claims 150 to 177 in the manufacture of a medicament for treating disease selected from Netherton Syndrome, asthma, atopic dermatitis, psoriasis, eosinophilic esophagitis, and rosacea.~~

~~187.—The use of claim 186, wherein the asthma is selected from atopic asthma, allergic asthma, non-allergic asthma, exercise-induced asthma, aspirin sensitive/exacerbated asthma, mild asthma, moderate to severe asthma, corticosteroid naïve asthma, chronic asthma, corticosteroid resistant asthma, corticosteroid refractory asthma, newly diagnosed and untreated asthma, asthma due to smoking, asthma uncontrolled on corticosteroids, T helper lymphocyte~~

~~type 2 (Th2) or type 2 (Th2) high, or Type 2 (T2) driven asthma, eosinophilic asthma, periostin-high asthma, eosinophil high asthma, Th2 low asthma or nonTh2 driven asthma, periostin low asthma, and eosinophil low asthma.~~

~~188.—The use of claim 187, wherein the asthma is eosinophil low asthma.~~

~~189.—Use of a combination of the antibody of any one of claims 1 to 27 and the antibody of any one of claims 34 to 62 in the manufacture of a medicament for treating disease selected from Netherton Syndrome, asthma, atopic dermatitis, psoriasis, eosinophilic esophagitis, and rosacea.~~

~~190.—The use of claim 189, wherein the asthma is selected from atopic asthma, allergic asthma, non-allergic asthma, exercise induced asthma, aspirin sensitive/exacerbated asthma, mild asthma, moderate to severe asthma, corticosteroid naïve asthma, chronic asthma, corticosteroid resistant asthma, corticosteroid refractory asthma, newly diagnosed and untreated asthma, asthma due to smoking, asthma uncontrolled on corticosteroids, T helper lymphocyte type 2 (Th2) or type 2 (Th2) high, or Type 2 (T2) driven asthma, eosinophilic asthma, periostin-high asthma, eosinophil high asthma, Th2 low asthma or nonTh2 driven asthma, periostin low asthma, and eosinophil low asthma.~~

~~191.—The use of claim 190, wherein the asthma is eosinophil low asthma.~~

192.54. Use of the antibody of any one of claims 1 to 27.9 and 34.40 to 62.43, the bispecific antibody of any one of claims 69.15 to 136.29 and 44, or the pharmaceutical composition of any one of claims 150.36 to 177.39 and 45 in the manufacture of a medicament for reducing epithelium inflammation, reducing epithelium permeability, reducing transepidermal water loss, reducing dermal infiltrates, reducing parakeratosis, restoring the epithelial barrier, and/or reducing skin inflammatory cytokines.

193.55. Use of a combination of the antibody of any one of claims 1 to 27.3 and the antibody of any one of claims 34.4 to 62.9 in the manufacture of a medicament for reducing epithelium inflammation, reducing epithelium permeability, reducing transepidermal water loss, reducing dermal infiltrates, reducing parakeratosis, restoring the epithelial barrier, and/or reducing skin inflammatory cytokines.

~~194.—A method of treating an individual having a disease selected from Netherton Syndrome, asthma, atopic dermatitis, psoriasis, eosinophilic esophagitis, and rosacea, comprising administering to the individual an effective amount of the antibody of any one of~~

~~claims 1 to 27 and 34 to 62, the bispecific antibody of any one of claims 69 to 136, or the pharmaceutical composition of any one of claims 150 to 177.~~

~~195.—A method of treating an individual having a disease selected from Netherton Syndrome, asthma, atopic dermatitis, psoriasis, eosinophilic esophagitis, and rosacea, comprising administering to the individual a) an effective amount of the antibody of any one of claims 1 to 27; and b) an effective amount of the antibody of any one of claims 34 to 62.~~

~~196.—The method of claim 195, wherein the antibody of (a) and the antibody of (b) are administered simultaneously.~~

~~197.—The method of claim 195, wherein the antibody of (a) and the antibody of (b) are administered sequentially.~~

~~198.—A method of treating an individual having a disease selected from Netherton Syndrome, asthma, atopic dermatitis, psoriasis, eosinophilic esophagitis, and rosacea, comprising administering to the individual an effective amount of the bispecific antibody of any one of claims 69 to 136, or an effective amount of the pharmaceutical composition of any one of claims 150 to 177.~~

~~199.—The method of any one of claims 194 to 198, wherein the asthma is selected from atopic asthma, allergic asthma, non-allergic asthma, exercise-induced asthma, aspirin sensitive/exacerbated asthma, mild asthma, moderate to severe asthma, corticosteroid naïve asthma, chronic asthma, corticosteroid resistant asthma, corticosteroid refractory asthma, newly diagnosed and untreated asthma, asthma due to smoking, asthma uncontrolled on corticosteroids, T helper lymphocyte type 2 (Th2) or type 2 (Th2) high, or Type 2 (T2) driven asthma, eosinophilic asthma, periostin high asthma, eosinophil high asthma, Th2 low asthma or nonTh2 driven asthma, periostin low asthma, and eosinophil low asthma.~~

~~200.—The method of claim 199, wherein the asthma is eosinophil low asthma.~~

~~201.—The method of any one of claims 194 to 198, wherein the individual has Netherton Syndrome.~~

~~202.—The method of any one of claims 194 to 198, wherein the individual has rosacea.~~

~~203.—The method of any one of claims 194 to 202, further comprising administering an additional therapeutic agent to the individual.~~

~~204.—The method of claim 203 wherein the additional therapeutic agent is an anti-inflammatory agent.~~

205.56. The antibody of any one of claims 1 to 9 and 40 to 43, the bispecific antibody of any one of claims 15 to 29 and 44, or the pharmaceutical composition of any one of claims 36 to 39 and 45 for use in~~A method of~~ reducing epithelium inflammation, reducing epithelium permeability, reducing transepidermal water loss, reducing dermal infiltrates, reducing parakeratosis, restoring the epithelial barrier, and/or reducing skin inflammatory cytokines in an individual ~~comprising administering to the individual an effective amount of the antibody of any one of claims 1 to 27 and 34 to 62, the bispecific antibody of any one of claims 69 to 136, or the pharmaceutical composition of any one of claims 150 to 177 to reduce epithelium inflammation, reduce epithelium permeability, reduce transepidermal water loss, reduce dermal infiltrates, reduce parakeratosis, and/or restore the epithelial barrier.~~

206.57. A combination of a) an effective amount of the antibody of any one of claims 1 to 3; and b) an effective amount of the antibody of any one of claims 4 to 9, for use in~~A method of~~ reducing epithelium inflammation, reducing epithelium permeability, reducing transepidermal water loss, reducing dermal infiltrates, reducing parakeratosis, restoring the epithelial barrier, and/or reducing skin inflammatory cytokines in an individual ~~comprising administering to the individual a) an effective amount of the antibody of any one of claims 1 to 27; and b) an effective amount of the antibody of any one of claims 34 to 62, to reduce epithelium inflammation, reduce epithelium permeability, reduce transepidermal water loss, reduce dermal infiltrates, reduce parakeratosis, and/or restore the epithelial barrier.~~

~~207. The method of claim 206, wherein the antibody of (a) and the antibody of (b) are administered simultaneously.~~

~~208. The method of claim 206, wherein the antibody of (a) and the antibody of (b) are administered sequentially.~~

58. Use of (a) a bispecific antibody, wherein the bispecific antibody comprises a first binding domain and second binding domain, wherein the first binding domain binds human KLK7 and inhibits KLK7 protease activity and the second binding domain binds human KLK5 and inhibits KLK5 protease activity; or (b) an anti-KLK5 antibody and an anti-KLK7 antibody, wherein the anti-KLK5 antibody inhibits KLK5 protease activity, and wherein the anti-KLK7 antibody inhibits KLK7 protease activity, in the manufacture of a medicament for treating an individual having a disease selected from Netherton Syndrome, asthma, atopic dermatitis, psoriasis, eosinophilic esophagitis, and rosacea.

209.59. A method of reducing epithelium inflammation, reducing epithelium permeability, reducing transepidermal water loss, reducing dermal infiltrates, reducing

~~parakeratosis, restoring the epithelial barrier, and/or reducing skin inflammatory cytokines in an individual comprising administering to the individual~~Use of (a) a KLK5 antagonist and a KLK7 antagonist, optionally wherein the KLK5 antagonist is an anti-KLK5 antibody and/or the KLK7 antagonist is an anti-KLK7 antibody, optionally wherein the anti-KLK5 antibody inhibits KLK5 protease activity, and wherein the anti-KLK7 antibody inhibits KLK7 protease activity; or (b) a bispecific antibody of any one of claims 69 to 136, or an effective amount of the pharmaceutical composition of any one of claims 150 to 177, to reduce epithelium inflammation, reduce epithelium permeability, reduce transepidermal water loss, reduce dermal infiltrates, reduce parakeratosis, and/or restore the epithelial barrier, wherein the bispecific antibody comprises a first binding domain and second binding domain, wherein the first binding domain binds human KLK7 and inhibits KLK7 protease activity and the second binding domain binds human KLK5 and inhibits KLK5 protease activity, in the manufacture of a medicament for reducing epithelium inflammation, reducing epithelium permeability, reducing transepidermal water loss, reducing dermal infiltrates, reducing parakeratosis, restoring the epithelial barrier and/or reducing skin inflammatory cytokines in an individual.

~~210.— The method of any one of claims 194 to 209, wherein the administering is subcutaneous or intravenous administration.~~

~~211.— The method of any one of claims 194 to 209, wherein the administering is topical administration.~~

~~212.— The method of any one of claims 194 to 209, wherein the administering is intravenous administration.~~

~~213.— An isolated antibody that binds human KLK7, wherein when bound to human KLK7 results in a conformational change of human KLK7, wherein the conformational change allosterically results in the disruption of the substrate binding site and/or the active site of human KLK7.~~

~~214.— The isolated antibody of claim 213, which is a bispecific antibody.~~

~~215.— The isolated antibody of claim 214, wherein the bispecific antibody binds human KLK7 and human KLK5.~~

~~216.— The isolated antibody of claim 215, wherein when bound to human KLK5 results in a conformational change of human KLK5, wherein the conformational change allosterically results in the disruption of the substrate binding site and/or the active site of human KLK5.~~

~~217.—The isolated antibody of claim 216, wherein the antibody binds to an epitope on human KLK5 comprising one or more amino acid residues selected from Pro130, Ser131, Ala132, Gly133, Val162, Leu163, Ser164, Gln165, Lys166, Arg167, Glu169, Asp170, Ala171, Tyr172, Pro173, Arg174, Gln174A, Ile176, Asp177, Asp178, Gly184, Asp185, Lys186, Ala186A, Arg188, Asn223, Arg224, Pro225, and Lys233 according to standard protease numbering.~~

~~218.—The isolated antibody of claim 217, wherein the antibody binds to an epitope on human KLK5 comprising one or more amino acid residues selected from the group consisting of Pro130, Ser131, Ala132, Val162, Leu163, Ser164, Gln165, Lys166, Arg167, Glu169, Asp170, Ala171, Tyr172, Pro173, Arg174, Gln174A, Ile176, Asp177, Asp178, Arg224, and Lys233 according to standard protease numbering.~~

~~219.—The isolated antibody of claim 217, wherein the antibody binds to an epitope on human KLK5 comprising one or more amino acid residues selected from Pro130, Ser131, Ala132, Gly133, Val162, Leu163, Ser164, Gln165, Lys166, Arg167, Glu169, Asp170, Ala171, Tyr172, Pro173, Arg174, Gln174A, Ile176, Asp177, and Lys233 according to standard protease numbering.~~

~~220.—The isolated antibody of claim 217, wherein the antibody binds to an epitope on human KLK5 comprising one or more amino acid residues selected from Ser131, Ala132, Gly133, Leu163, Ser164, Gln165, Lys166, Arg167, Glu169, Asp170, Ala171, Pro173, Arg174, Gly184, Asp185, Lys186, Ala186A, Arg188, Asn223, Arg224, and Pro225 according to standard protease numbering.~~

~~221.—The isolated antibody of any one of claims 213–220, wherein the antibody binds an epitope within amino acids R71–N82, K152–S158, and/or Q211–K222 of KLK7 (SEQ ID NO: 4).~~

~~222.—The isolated antibody of any one of claims 213–221, wherein the antibody binds an epitope comprising one or more of amino acids H72, P73, G74, S76, Q78, N82, N157, K211, and/or T213 of KLK7 (SEQ ID NO: 4).~~

~~223.—A bispecific antibody comprising a first binding domain and a second binding domain, wherein the first binding domain binds human KLK7 and the second binding domain binds human KLK5, wherein when bound to human KLK7 results in a conformational change of human KLK7, wherein the conformational change allosterically results in the disruption of the substrate binding site and/or the active site of human KLK7.~~

~~224.—The bispecific antibody of claim 223, wherein when bound to human KLK5 results in a conformational change of human KLK5, wherein the conformational change allosterically results in the disruption of the substrate binding site and/or the active site of human KLK5.~~

~~225.—A bispecific antibody comprising a first binding domain and a second binding domain, wherein the first binding domain binds human KLK7 and the second binding domain binds human KLK5, wherein when bound to human KLK5 results in a conformational change of human KLK5, wherein the conformational change allosterically results in the disruption of the substrate binding site and/or the active site of human KLK5.~~

~~226.—The bispecific antibody of claim 224 or claim 225, wherein the antibody binds to an epitope on human KLK5 comprising one or more amino acid residues selected from Pro130, Ser131, Ala132, Gly133, Val162, Leu163, Ser164, Gln165, Lys166, Arg167, Glu169, Asp170, Ala171, Tyr172, Pro173, Arg174, Gln174A, Ile176, Asp177, Asp178, Gly184, Asp185, Lys186, Ala186A, Arg188, Asn223, Arg224, Pro225, and Lys233 according to standard protease numbering.~~

~~227.—The isolated antibody of claim 226, wherein the antibody binds to an epitope on human KLK5 comprising one or more amino acid residues selected from the group consisting of Pro130, Ser131, Ala132, Val162, Leu163, Ser164, Gln165, Lys166, Arg167, Glu169, Asp170, Ala171, Tyr172, Pro173, Arg174, Gln174A, Ile176, Asp177, Asp178, Arg224, and Lys233 according to standard protease numbering.~~

~~228.—The isolated antibody of claim 226, wherein the antibody binds to an epitope on human KLK5 comprising one or more amino acid residues selected from Pro130, Ser131, Ala132, Gly133, Val162, Leu163, Ser164, Gln165, Lys166, Arg167, Glu169, Asp170, Ala171, Tyr172, Pro173, Arg174, Gln174A, Ile176, Asp177, and Lys233 according to standard protease numbering.~~

~~229.—The isolated antibody of claim 226, wherein the antibody binds to an epitope on human KLK5 comprising one or more amino acid residues selected from Ser131, Ala132, Gly133, Leu163, Ser164, Gln165, Lys166, Arg167, Glu169, Asp170, Ala171, Pro173, Arg174, Gly184, Asp185, Lys186, Ala186A, Arg188, Asn223, Arg224, and Pro225 according to standard protease numbering.~~

~~230.—The bispecific antibody of any one of claims 223 to 229, wherein the antibody binds an epitope within amino acids R71-N82, K152-S158, and/or Q211-K222 of KLK7 (SEQ ID NO: 4).~~

~~231.—The bispecific antibody of any one of claims 223 to 230, wherein the antibody binds an epitope comprising one or more of amino acids H72, P73, G74, S76, Q78, N82, N157, K211, and/or T213 of KLK7 (SEQ ID NO: 4).~~

~~232.—A pharmaceutical composition comprising the antibody of any one of claims 213 to 222 and a pharmaceutically acceptable carrier.~~

~~233.—A pharmaceutical composition comprising the bispecific antibody of any one of claims 223 to 231 and a pharmaceutically acceptable carrier.~~

~~234.—The antibody of any one of claims 213 to 222, the bispecific antibody of any one of claims 223 to 231, or the pharmaceutical composition of claim 232 or claim 233 for use as a medicament.~~

~~235.—The antibody of any one of claims 213 to 222, the bispecific antibody of any one of claims 223 to 231, or the pharmaceutical composition of claim 232 or claim 233 for use in treating disease selected from Netherton Syndrome, asthma, atopic dermatitis, psoriasis, eosinophilic esophagitis, and rosacea.~~

~~236.—The antibody, bispecific antibody, or pharmaceutical composition for use of claim 235, wherein the asthma is selected from atopic asthma, allergic asthma, non-allergic asthma, exercise-induced asthma, aspirin-sensitive/exacerbated asthma, mild asthma, moderate to severe asthma, corticosteroid naïve asthma, chronic asthma, corticosteroid-resistant asthma, corticosteroid-refractory asthma, newly diagnosed and untreated asthma, asthma due to smoking, asthma uncontrolled on corticosteroids, T helper lymphocyte type 2 (Th2) or type 2 (Th2) high, or Type 2 (T2)-driven asthma, eosinophilic asthma, periostin-high asthma, eosinophil-high asthma, Th2-low asthma or non-Th2-driven asthma, periostin-low asthma, and eosinophil-low asthma.~~

~~237.—The antibody of any one of claims 213 to 222, the bispecific antibody of any one of claims 223 to 231, or the pharmaceutical composition of claim 232 or claim 233 for use in reducing epithelium inflammation, reducing epithelium permeability, reducing transepidermal water loss, reducing dermal infiltrates, reducing parakeratosis, restoring the epithelial barrier, and/or reducing skin inflammatory cytokines.~~

~~238.—Use of the antibody of any one of claims 213 to 222, the bispecific antibody of any one of claims 223 to 231, or the pharmaceutical composition of claim 232 or claim 233 in the manufacture of a medicament for treating disease selected from Netherton Syndrome, asthma, atopic dermatitis, psoriasis, eosinophilic esophagitis, and rosacea.~~

~~239.—The use of claim 238, wherein the asthma is selected from atopic asthma, allergic asthma, non-allergic asthma, exercise-induced asthma, aspirin-sensitive/exacerbated asthma, mild asthma, moderate to severe asthma, corticosteroid-naïve asthma, chronic asthma, corticosteroid-resistant asthma, corticosteroid-refractory asthma, newly diagnosed and untreated asthma, asthma due to smoking, asthma-uncontrolled on corticosteroids, T-helper lymphocyte type 2 (Th2) or type 2 (Th2) high, or Type 2 (T2)-driven asthma, eosinophilic asthma, periostin-high asthma, eosinophil-high asthma, Th2-low asthma or nonTh2-driven asthma, periostin-low asthma, and eosinophil-low asthma.~~

~~240.—Use of the antibody of any one of claims 213 to 222, the bispecific antibody of any one of claims 223 to 231, or the pharmaceutical composition of claim 232 or claim 233 in the manufacture of a medicament for reducing epithelium inflammation, reducing epithelium permeability, reducing transepidermal water loss, reducing dermal infiltrates, reducing parakeratosis, restoring the epithelial barrier, and/or reducing skin inflammatory cytokines.~~

~~241.—A method of treating an individual having a disease selected from Netherton Syndrome, asthma, atopic dermatitis, psoriasis, eosinophilic esophagitis, and rosacea, comprising administering to the individual an effective amount of the antibody of any one of 213 to 222, the bispecific antibody of any one of claims 223 to 231, or the pharmaceutical composition of claim 232 or claim 233.~~

~~242.—The method of claim 241, wherein the asthma is selected from atopic asthma, allergic asthma, non-allergic asthma, exercise-induced asthma, aspirin-sensitive/exacerbated asthma, mild asthma, moderate to severe asthma, corticosteroid-naïve asthma, chronic asthma, corticosteroid-resistant asthma, corticosteroid-refractory asthma, newly diagnosed and untreated asthma, asthma due to smoking, asthma-uncontrolled on corticosteroids, T-helper lymphocyte type 2 (Th2) or type 2 (Th2) high, or Type 2 (T2)-driven asthma, eosinophilic asthma, periostin-high asthma, eosinophil-high asthma, Th2-low asthma or nonTh2-driven asthma, periostin-low asthma, and eosinophil-low asthma.~~

~~243.—A method of reducing epithelium inflammation, reducing epithelium permeability, reducing transepidermal water loss, reducing dermal infiltrates, reducing parakeratosis, restoring the epithelial barrier, and/or reducing skin inflammatory cytokines in an individual comprising administering to the individual an effective amount of the antibody of any one of 213 to 222, the bispecific antibody of any one of claims 223 to 231, or the pharmaceutical composition of claim 232 or claim 233 to reduce epithelium inflammation, reduce epithelium~~

permeability, reduce transepidermal water loss, reduce dermal infiltrates, reduce parakeratosis, and/or restore the epithelial barrier.

244.—The antibody, bispecific antibody, or pharmaceutical composition for use of claim 179 or claim 235, wherein the disease is Netherton Syndrome.

245.—The combination for use of claim 183, wherein the disease is Netherton Syndrome.

246.—The use of any one of claims 186, 189, and 238, wherein the disease is Netherton Syndrome.

247.—The use of any one of claims 192, 193, and 240, wherein the medicament is for reducing epithelium inflammation, reducing epithelium permeability, reducing transepidermal water loss, reducing dermal infiltrates, reducing parakeratosis, restoring the epithelial barrier, and/or reducing skin inflammatory cytokines in an individual with Netherton Syndrome.

248.—A bispecific antibody for use in treating Netherton Syndrome, wherein the bispecific antibody comprises a first binding domain and a second binding domain, wherein the first binding domain binds human KLK7 and the second binding domain binds human KLK5, wherein the first binding domain comprises a heavy chain amino acid sequence of SEQ ID NO: 112 or 194, and a light chain amino acid sequence of SEQ ID NO: 113, and the second binding domain comprises a heavy chain amino acid sequence of SEQ ID NO: 114 or 195, and a light chain amino acid sequence of SEQ ID NO: 115.

249.—An anti-KLK5 antibody for use in treating Netherton Syndrome, wherein the anti-KLK5 antibody comprises (a) a VH sequence of SEQ ID NO: 52 and a VL sequence of SEQ ID NO: 55; or (b) a VH sequence of SEQ ID NO: 53 and a VL sequence of SEQ ID NO: 62.

250.—An anti-KLK7 antibody for use in treating Netherton Syndrome, wherein the anti-KLK7 antibody comprises (a) a VH sequence of SEQ ID NO: 29 and a VL sequence of SEQ ID NO: 32; or (b) a VH sequence of SEQ ID NO: 30 and a VL sequence of SEQ ID NO: 38.

251.—An antibody combination for use in treating Netherton Syndrome, wherein the antibody combination comprises an anti-KLK5 antibody and an anti-KLK7 antibody, wherein the anti-KLK5 antibody comprises a VH sequence of SEQ ID NO: 52 and a VL sequence of SEQ ID NO: 55, or a VH sequence of SEQ ID NO: 53 and a VL sequence of SEQ ID NO: 62; and wherein the anti-KLK7 antibody comprises a VH sequence of SEQ ID NO: 29 and a VL

sequence of SEQ ID NO: 32, or a VH sequence of SEQ ID NO: 30 and a VL sequence of SEQ ID NO: 38.

252.—A method of treating an individual having a disease selected from Netherton Syndrome, asthma, atopic dermatitis, psoriasis, eosinophilic esophagitis, and rosacea, comprising administering to the individual an effective amount of the bispecific antibody, wherein the bispecific antibody comprises a first binding domain and second binding domain, wherein the first binding domain binds human KLK7 and inhibits KLK7 protease activity and the second binding domain binds human KLK5 and inhibits KLK5 protease activity.

253.—A method of treating an individual having a disease selected from Netherton Syndrome, asthma, atopic dermatitis, psoriasis, eosinophilic esophagitis, and rosacea, comprising administering to the individual an anti-KLK5 antibody and an anti-KLK7 antibody, wherein the anti-KLK5 antibody inhibits KLK5 protease activity, and wherein the anti-KLK7 antibody inhibits KLK7 protease activity.

254.—A method of reducing epithelium inflammation, reducing epithelium permeability, reducing transepidermal water loss, reducing dermal infiltrates, reducing parakeratosis, restoring the epithelial barrier and/or reducing skin inflammatory cytokines in an individual comprising administering to the individual a KLK5 antagonist and a KLK7 antagonist.

255.—The method of claim 254, wherein the KLK5 antagonist is an anti-KLK5 antibody and/or the KLK7 antagonist is an anti-KLK7 antibody.

256.—A method of reducing epithelium inflammation, reducing epithelium permeability, reducing transepidermal water loss, reducing dermal infiltrates, reducing parakeratosis, restoring the epithelial barrier and/or reducing skin inflammatory cytokines in an individual comprising administering to the individual an effective amount of the bispecific antibody, wherein the bispecific antibody comprises a first binding domain and second binding domain, wherein the first binding domain binds human KLK7 and inhibits KLK7 protease activity and the second binding domain binds human KLK5 and inhibits KLK5 protease activity.

257.—A method of reducing epithelium inflammation, reducing epithelium permeability, reducing transepidermal water loss, reducing dermal infiltrates, reducing parakeratosis, restoring the epithelial barrier and/or reducing skin inflammatory cytokines in an individual comprising administering to the individual an anti-KLK5 antibody and an anti-KLK7 antibody, wherein the anti-KLK5 antibody inhibits KLK5 protease activity, and wherein the anti-KLK7 antibody inhibits KLK7 protease activity.

~~258-60. A method of ameliorating skin rash and/or scaling in an individual with Netherton Syndrome comprising administering to the individual an effective amount~~Use of (a) ~~the a~~ bispecific antibody, wherein the bispecific antibody comprises a first binding domain and second binding domain, wherein the first binding domain binds human KLK7 and inhibits KLK7 protease activity and the second binding domain binds human KLK5 and inhibits KLK5 protease activity; or (b) ~~an anti-KLK5 antibody and an anti-KLK7 antibody, wherein the anti-KLK5 antibody inhibits KLK5 protease activity, and wherein the anti-KLK7 antibody inhibits KLK7 protease activity, in the manufacture of a medicament for ameliorating skin rash and/or scaling in an individual with Netherton Syndrome.~~

~~259. A method of ameliorating skin rash and/or scaling in an individual with Netherton Syndrome comprising administering to the individual an anti-KLK5 antibody and an anti-KLK7 antibody, wherein the anti-KLK5 antibody inhibits KLK5 protease activity, and wherein the anti-KLK7 antibody inhibits KLK7 protease activity.~~

~~260. The use of any one of claims 192, 193, 240, or 247 or the method of any one of claims 205, 206, 209, 243, or 254-257, or the antibody, bispecific antibody, or pharmaceutical composition for use of claim 237, wherein the skin inflammatory cytokines are one or more of IL-8, TNF α , IL-6, IL-4, and/or G-CSF.~~