

CLAIMS

1. An anti- Chemerin Like Receptor 1 (CMKLR1) antibody or antigen-binding fragment thereof which binds to CMKLR1, in particular human CMKLR1, said antibody of antigen-binding fragment thereof comprising:
- 5 a. an antibody heavy chain variable (VH) domain comprising the three CDRs VHCDR1, VHCDR2 and VHCDR3, wherein:
- VHCDR1 is selected from the group consisting of SEQ ID No.3, SEQ ID No. 4, SEQ ID No. 5, SEQ ID No. 6 and SEQ ID No. 7; and
 - 10 - VHCDR2 is selected from the group consisting of SEQ ID No. 9, SEQ ID No. 10, SEQ ID No. 11, SEQ ID NO: 12 and SEQ ID No. 61; and
 - VHCDR3 is selected from the group consisting of SEQ ID No. 13, SEQ ID No. 14, SEQ ID No. 15 and SEQ ID No. 16; and
- 15 b. an antibody light chain variable (VL) domain comprising the three CDRs VLCDR1, VLCDR2 and VLCDR3, wherein:
- VLCDR1 is selected from the group consisting of SEQ ID No. 17, SEQ ID No. 18, SEQ ID No. 19, SEQ ID No. 20, SEQ ID No. 21, SEQ ID No. 22 and SEQ ID No. 23; and
 - VLCDR2 is selected from the group consisting of SEQ ID No. 24, SEQ ID No. 25, SEQ ID No. 26, SEQ ID No. 27, SEQ ID No. 28, SEQ ID No. 29, SEQ ID No. 30, SEQ ID No. 31, SEQ ID No. 32 and SEQ ID No. 33; and
 - 20 - VLCDR3 is selected from the group consisting of SEQ ID No. 34, SEQ ID No. 35 and SEQ ID No. 36.
- 25 2. The anti-CMKLR1 antibody or antigen-binding fragment thereof according to claim 1 wherein the antibody or antigen-binding fragment thereof binds specifically to the third extra-cellular loop (EL3) of CMKLR1, in particular to an epitope located within third extra-cellular loop (EL3) of CMKLR1, or within the polypeptide comprising amino acid sequence SEQ ID No: 2 or SEQ ID No. 59 or to an epitope located within amino acid
- 30 sequence SEQ ID No. 60.
3. The anti-CMKLR1 antibody or antigen-binding fragment thereof according to claim 1 or 2, which is a Resolvin E1-like agonist of CMKLR1, in particular wherein the anti-CMKLR1 antibody or antigen-binding fragment thereof has an effect of a pro-resolution
- 35 factor of inflammation, in particular has such an effect by interacting with myeloid cell.

4. The anti-CMKLR1 antibody or antigen-binding fragment thereof according to any one of claims 1 to 3, wherein:
- VHCDR1 is selected from the group consisting of SEQ ID No. 3 and SEQ ID No. 4; and/or
 - 5 - VHCDR2 is selected from the group consisting of SEQ ID No. 9, SEQ ID No. 10, SEQ ID No. 11 and SEQ ID No. 61; and/or
 - VHCDR3 is selected from the group consisting of SEQ ID No. 13, SEQ ID No. 14 and SEQ ID No. 15.
- 10 5. The anti-CMKLR1 antibody or antigen-binding fragment thereof according to any one of claims 1 to 4, wherein:
- VLCDR1 is selected from the group consisting of SEQ ID No. 17, SEQ ID No. 18, SEQ ID No. 19 and SEQ ID No. 23, and/or
 - VLCDR2 is selected from the group consisting of SEQ ID No. 24, SEQ ID No. 25, 15 SEQ ID No. 26, SEQ ID No. 27 and SEQ ID No. 33; and/or
 - VLCDR3 is selected from the group consisting of SEQ ID No. 34, SEQ ID No. 35 and SEQ ID No. 36.
- 20 6. The anti-CMKLR1 antibody or antigen-binding fragment thereof according to any one of claims 1 to 5 which comprises a heavy chain variable domain comprising or consisting of an amino acid sequence selected from the group consisting of SEQ ID No. 38, SEQ ID No. 39, SEQ ID No. 40 and SEQ ID No. 62.
- 25 7. The anti-CMKLR1 antibody or antigen-binding fragment thereof according to any one of claims 1 to 6, which comprises a light chain variable domain comprising or consisting of an amino acid sequence selected from the group consisting of SEQ ID No. 49, SEQ ID No. 50, SEQ ID No. 51, SEQ ID No. 52, SEQ ID No. 53, SEQ ID No. 54, SEQ ID No. 55, SEQ ID No. 56, SEQ ID No. 57 and, SEQ ID No. 58.
- 30 8. The anti-CMKLR1 antibody or antigen-binding fragment thereof according to any one of claims 1 to 7, which comprises a heavy chain variable domain comprising or consisting of the amino acid sequence selected from the group consisting of SEQ ID No. 38, SEQ ID No. 39, SEQ ID No. 40 and, SEQ ID No. 62; and a light chain variable domain comprising or consisting of an amino acid sequence selected from the group 35 consisting of SEQ ID No. 54, SEQ ID No. 55 and SEQ ID No. 56.

9. The anti-CMKLR1 antibody or antigen-binding fragment thereof according to any one of claims 1 to 3, which comprises the following CDRs: VHCDR1 of SEQ ID No. 4; VHCDR2 of SEQ ID No. 12; VHCDR3 of SEQ ID No. 13, VLCDR1 of SEQ ID No. 19, VLCDR2 of SEQ ID No. 26, and VLCDR3 of SEQ ID No. 35.
10. The anti-CMKLR1 antibody or antigen-binding fragment thereof according to any one of claims 1 to 9, which comprises the following frameworks: VHFR1 of SEQ ID No. 65, VHFR2 of SEQ ID No. 67, VHFR3 of SEQ ID No. 69, VHFR4 of SEQ ID No. 71, VLFR1 of SEQ ID No. 72, VLFR2 of SEQ ID No. 73, VLFR3 of SEQ ID No. 76 and VLFR4 of SEQ ID No. 77.
11. The anti-CMKLR1 antibody or antigen-binding fragment thereof according to claim 9 or 10, which comprises a heavy chain variable domain comprising or consisting of the amino acid sequence SEQ ID No. 91 and a light chain variable domain comprising or consisting of the amino acid sequence SEQ ID No. 93.
12. The anti-CMKLR1 antibody or antigen-binding fragment thereof according to any one of claims 1 to 11, which does not activate the beta-arrestin signaling pathway in CMKLR1-positive cells *in vitro* and/or *in vivo*.
13. The anti-CMKLR1 antibody or antigen-binding fragment thereof according to any one of claims 1 to 12, which does not exhibit a significant depletion of CMKLR1-positive cells *in vitro* and/or *in vivo*.
14. The anti-CMKLR1 antibody or antigen-binding fragment thereof according to any one of claims 1 to 13, which does not compete with Chemerin for the binding to CMKLR1, and/or which does not interfere with the binding of Chemerin to CMKLR1.
15. The anti-CMKLR1 antibody or antigen-binding fragment according to any one of claims 1 to 14 which is a humanized monoclonal antibody or antigen-binding fragment thereof, in particular wherein the antibody light chain constant domain is derived from a human kappa light chain constant domain, in particular wherein the light chain constant domain comprises or consists of the sequence of SEQ ID No: 79, and wherein the antibody heavy chain constant domain is derived from a human IgG1, IgG2, IgG3, or IgG4 heavy chain constant domain, in particular wherein the antibody heavy chain constant domain comprises or consists of the amino acid sequence of SEQ ID 80, SEQ ID No. 81, SEQ ID No. 82, SEQ ID No. 83 or SEQ ID No. 84, in particular from a human IgG1 heavy

chain constant domain, in particular wherein the antibody heavy chain constant domain comprises or consists of the amino acid sequence of SEQ ID No:80 or SEQ ID No. 83.

- 5 **16.** An antibody or antigen-binding fragment thereof, in particular selected from the group consisting of a chimeric, a modified and a humanized antibody, which specifically binds to CMKLR1, in particular human CMKLR1, which comprises an antibody heavy chain variable domain comprising (i) VHCDR2 comprising or consisting of an amino acid sequence set forth in SEQ ID No: 9, SEQ ID No. 10, SEQ ID No. 11, SEQ ID No. 12 and SEQ ID No. 61, and (ii) VHCDR3 comprising or consisting of an amino acid
10 sequence set forth in SEQ ID No: 13, SEQ ID No. 14, SEQ ID No. 15 and SEQ ID No. 16 or a mutated sequence thereof wherein amino acid residue(s) is(are) substituted provided that amino acid residues at positions 1 and 2 of the mutated sequence are respectively L and I; and
15 wherein the anti-CMKLR1 compound binds specifically to an epitope located within the third extra-cellular loop (EL3) of CMKLR1, in particular wherein the compound binds specifically to a polypeptide comprising or consisting of amino acid sequence SEQ ID No: 2 or SEQ ID No. 59 or to an epitope located within amino acid sequence SEQ ID No. 60 ; and
20 wherein said compound competes with an antibody comprising the heavy chain variable domain corresponding to SEQ ID No: 37 and the light chain variable domain corresponding to SEQ ID No: 49, for the binding to a polypeptide comprising or consisting of amino acid sequence of sequence SEQ ID No: 2 or SEQ ID No. 59 or of SEQ ID No. 60 or to a polypeptide comprising or consisting of the third loop (EL3) of the extracellular domain of CMKLR1.
25 **17.** The anti-CMKLR1 antibody or antigen-binding fragment thereof according to claim 16, which comprises the following CDRs:
- VHCDR1 of SEQ ID No. 4;
- VHCDR2 of SEQ ID No. 12;
30 - VHCDR3 of SEQ ID No. 13,
- VLCDR1 of SEQ ID No. 19,
- VLCDR2 of SEQ ID No. 26, and
- VLCDR3 of SEQ ID No. 35.
35 **18.** The anti-CMKLR1 antibody or antigen-binding fragment thereof according to any one of claims 16 or 17, which comprises the following frameworks: VHFR1 of SEQ ID No. 65, VHFR2 of SEQ ID No. 67, VHFR3 of SEQ ID No. 69, VHFR4 of SEQ ID No. 71,

VLFR1 of SEQ ID No. 72, VLFR2 of SEQ ID No. 73, VLFR3 of SEQ ID No. 76, and VLFR4 of SEQ ID No. 77.

19. The anti-CMKLR1 antibody or antigen-binding fragment thereof according to claim 18,
5 which comprises a heavy chain variable domain comprising or consisting of the amino acid sequence SEQ ID No. 91 and a light chain variable domain comprising or consisting of the amino acid sequence SEQ ID No. 93.
20. The anti-CMKLR1 antibody or antigen-binding fragment thereof according to any one
10 of claims 1 to 19 for use in the preventive or the therapeutic treatment of:
- an inflammatory disease, in particular acute inflammatory diseases, chronic inflammatory diseases such as chronic inflammatory pulmonary diseases, keratoconjunctivitis, periodontal disease, eczema, inflammatory bowel disease, in particular Crohn's disease or colitis, in particular ulcerative colitis or spontaneous
15 colitis, cystic fibrosis, NASH (Nonalcoholic steatohepatitis), scleroderma, anti-neutrophil cytoplasm antibodies-related disease ANCA associated disease, in particular wherein, as a result of the administration of the treatment, the resolution of inflammation is enhanced;
 - an autoimmune disease such as diabetes, in particular type I diabetes, psoriasis,
20 lupus, rheumatoid arthritis, multiple sclerosis, Sjögren's syndrome, celiac disease, vasculitis, myasthenia gravis, or an infection disease such as sepsis, peritonitis, degenerative diseases, wound healing disorders or dry eye syndrome, in particular wherein, as a result of the administration of the treatment, the resolution of inflammation is enhanced;
 - a cancer, in particular metastatic cancers, solid or liquid cancers such as carcinoma, more particularly hepatocarcinoma, in particular mammary carcinoma or colon carcinoma, colorectal cancer or lung cancer or mesothelioma or myeloid cancer such as leukemia, in particular a cancer wherein cancer cells express
25 CMKLR1 or where the microenvironment of the tumor is invaded by cells expressing or overexpressing CMKLR1, in particular wherein, as a result of the
30 administration of the treatment, the resolution of inflammation is enhanced.
21. The anti-CMKLR1 antibody or antigen-binding fragment thereof according to any one
35 of claims 1 to 20 for use in the preventive or the therapeutic treatment NASH (Nonalcoholic steatohepatitis), scleroderma, cystic fibrosis or anti-neutrophil cytoplasm antibodies-related disease (ANCA).