

or G, and (c) a CDR-H3 comprising the amino acid sequence YDAHYGELDF of SEQ ID NO: 59;

and

5 a VL domain comprising (d) a CDR-L1 comprising the amino acid sequence RASQHVSDAYLA of SEQ ID NO: 60; (e) a CDR-L2 comprising the amino acid sequence DASDRAE of SEQ ID NO: 61, and (f) a CDR-L3 comprising the amino acid sequence HQYIHLHSFT of SEQ ID NO: 62;

and

10 ii) said second antigen-binding site comprises a VH domain comprising (a) a CDR-H1 comprising the amino acid sequence HTYMH of SEQ ID NO: 76, (b) a CDR-H2 comprising the amino acid sequence RIDPXNHNTKFDPKFQG of SEQ ID NO: 77 wherein X is D or E, and (c) a CDR-H3 comprising the amino acid
15 sequences GVFGFFXH of SEQ ID NO: 78 wherein X is D or E; and a VL domain comprising (d) a CDR-L1 comprising the amino acid sequence KAX¹EDIYNRX²A of SEQ ID NO: 79 wherein X¹ is F or T and X² is R or L, (e) a CDR-L2 comprising the amino acid sequence
20 GATSLEH of SEQ ID NO: 80, and (f) a CDR-L3 comprising the amino acid sequence QQFXSAPYT of SEQ ID NO: 81 wherein X is W or R.

Thus, in one aspect, the present disclosure relates to a biparatopic antibody comprising a first antigen-binding site that binds to a first epitope on human
25 CCL2 and a second different antigen-binding site that binds a second different epitope on human CCL2, wherein the biparatopic antibody comprises a constant heavy chain domain of human IgG1 isotype

wherein

30 i) said first antigen-binding site comprises a VH domain comprising (a) a CDR-H1 comprising the amino acid sequence SHYGXS of SEQ ID NO: 57 wherein X is I or T, (b) a CDR-H2 comprising the amino acid sequence GX¹IX²IFX³TANYAQKFQG

of SEQ ID NO: 58 wherein X^1 is V, I, or H, X^2 is P or H, and X^3 is H or G, and (c) a CDR-H3 comprising the amino acid sequence YDAHYGELDF of SEQ ID NO: 59;

and

5 a VL domain comprising (d) a CDR-L1 comprising the amino acid sequence RASQHVSDAYLA of SEQ ID NO: 60; (e) a CDR-L2 comprising the amino acid sequence DASDRAE of SEQ ID NO: 61, and (f) a CDR-L3 comprising the amino acid sequence HQYIHLHSFT of SEQ ID NO: 62;

10 and

ii) said second antigen-binding site comprises

a VH domain comprising (a) a CDR-H1 comprising the amino acid sequence HTYMH of SEQ ID NO: 76, (b) a CDR-H2 comprising the amino acid sequence RIDPXNHNTKFDPKFQG of SEQ ID NO: 77

15 wherein X is D or E, and (c) a CDR-H3 comprising the amino acid sequence GVFGFFXH of SEQ ID NO: 78 wherein X is D or E;

and

a VL domain comprising (d) a CDR-L1 comprising the amino acid sequence $KAX^1EDIYNRX^2A$ of SEQ ID NO: 79 wherein X^1 is F or T

20 and X^2 is R or L, (e) a CDR-L2 comprising the amino acid sequence GATSLEH of SEQ ID NO: 80, and (f) a CDR-L3 comprising the amino acid sequence QQFXSAPYT of SEQ ID NO: 81 wherein X is W or R.

25 One example of the disclosure is an (isolated) bispecific antibody comprising a first antigen-binding site that (specifically) binds to a first epitope on human CCL2 and a second antigen-binding site that (specifically) binds a second epitope on human CCL2, wherein

30 i) said first antigen-binding site comprises

a VH domain comprising (a) a CDR-H1 comprising the amino acid sequence SHYGXS of SEQ ID NO: 57 wherein X is I or T, (b) a CDR-H2 comprising the amino acid sequence $GX^1IX^2IFX^3TANYAQKFQG$ of SEQ ID NO: 58 wherein X^1 is V, I, or H, X^2 is P or H, and X^3 is H

35 or G, (c) a CDR-H3 comprising the amino acid sequence YDAHYGELDF of SEQ ID NO: 59, (d) a FR-H1 comprising the amino acid sequence QVQLVQSGAEVKKPGSSVKV SCKASGGTF

In one example of the disclosure such method further comprises the step of recovering the antibody from the host cell.

5 In another example, the present disclosure relates to a pharmaceutical formulation comprising the bispecific antibody as described herein and a pharmaceutically acceptable carrier. In one aspect, the present disclosure refers to a pharmaceutical formulation comprising the biparatopic antibody as described herein and a pharmaceutically acceptable carrier.

10 In another example, the present disclosure relates to the bispecific antibody as described herein for use as a medicament. In one aspect, the present disclosure refers to a biparatopic antibody as described herein for use as a medicament.

15 In another example, the present disclosure relates to use of the bispecific antibody as described herein in the manufacture of a medicament. In one aspect, the present disclosure refers to use of the biparatopic antibody as described herein in the manufacture of a medicament for treating cancer.

In one example such medicament is for the treatment of cancer.

In one example such medicament is for the treatment of an inflammatory or autoimmune disease.

20 In another example, the present disclosure relates to the bispecific antibody as described herein for use in treating cancer.

In another example, the present disclosure relates to the bispecific antibody as described herein for use in treating an inflammatory or autoimmune disease.

25 One example of the disclosure is a method of treating an individual having cancer comprising administering to the individual an effective amount of the antibody as described herein.

One example of the disclosure is a method of treating an individual having an inflammatory or autoimmune disease comprising administering to the individual an effective amount of the antibody as described herein.

Description of the Figures

30 Figure 1: Surface plasmon resonance (Biacore®) sensorgrams showing binding of monospecific anti-CCL2 antibodies (CNTO888 (= CNTO), 1A5, 1G9 and humanized 11K2 (=11k2) to recombinant CCL2 and CCL2 homologs.

35 Figure 2a: Serum concentration of hCCL2 over time after i.v. injection of pre-formed immune complex consisting of a) solid line: 0.1mg/kg human