

CLAIMS

What is claimed is:

1. An antibody or antigen-binding fragment thereof that binds to human Dectin-1, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the sequence GYTFTDYY (SEQ ID NO:1), a CDR-H2 comprising the sequence INPNSGDT (SEQ ID NO:2), and a CDR-H3 comprising the sequence ARNSGSYSFGY (SEQ ID NO:3), and wherein the VL domain comprises a CDR-L1 comprising the sequence QGISSW (SEQ ID NO:4), a CDR-L2 comprising the sequence GAS (SEQ ID NO:5), and a CDR-L3 comprising the sequence QQAYSFPFT (SEQ ID NO:6).

~~2. An antibody or antigen-binding fragment thereof that binds to human Dectin-1, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1, CDR-H2, and CDR-H3 from the VH domain sequence~~
~~QVQLVQSGAEVKKPGASVKVCKSSGYTFTDYYIHVVRQAPGQGLEWMGWINPNSGD~~
~~TNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYWGQGTLLVTV~~
~~SS (SEQ ID NO:7), and wherein the VL domain comprises a CDR-L1, CDR-L2, and CDR-L3 from the VL domain sequence~~
~~DIQMTQSPSSVSASVGDRVTITCRASQGISWLAWYQQKPGKAPKLLIFGASSLQSGVPS~~
~~RFSGSGSGTDFTLTLSLQPEDFATYYCQQAYSFPFTFGPGTKVDIE (SEQ ID NO:8).~~

~~3. The antibody of claim 2, wherein the VH domain comprises a CDR-H1 comprising the sequence DYYI (SEQ ID NO:88), a CDR-H2 comprising the sequence~~
~~WINPNSGDTNYAQKFQG (SEQ ID NO:89), and a CDR-H3 comprising the sequence~~
~~NSGSYSFGY (SEQ ID NO:90), and wherein the VL domain comprises a CDR-L1 comprising~~
~~the sequence RASQGISWLA (SEQ ID NO:91), a CDR-L2 comprising the sequence GASSLQS~~
~~(SEQ ID NO:92), and a CDR-L3 comprising the sequence QQAYSFPFT (SEQ ID NO:6).~~

4.2. The antibody of claim 1~~any one of claims 1-3~~, wherein the antibody or fragment is a
human antibody or fragment that comprises a VH domain comprising~~comprises~~ a sequence with
at least 90% identity to the sequence

QVQLVQSGAEVKKPGASVKVCKSSGYTFTDYYIHVVRQAPGQGLEWMGWINPNSGD
TNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYWGQGTLLVTV

SS (SEQ ID NO:7); and/or ~~awherein the~~ VL domain ~~comprising~~~~comprises~~ a sequence with at least 90% identity to the sequence

DIQMTQSPSSVSASVGDRVITTCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPS
RFSGSGSGTDFTLTVSSSLQPEDFATYYCQQAYSFPFTFGPGTKVDIE (SEQ ID NO:8);~~;~~

~~wherein optionally the VH domain comprises the sequence~~

~~QVQLVQSGAEVKKPGASVKVCKSSGYTFTDYYIHWRQAPGQGLEWMGWINPNSGD
TNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYWGQGTLLTVV
SS (SEQ ID NO:7) and/or the VL domain comprises the sequence~~

~~DIQMTQSPSSVSASVGDRVITTCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPS
RFSGSGSGTDFTLTVSSSLQPEDFATYYCQQAYSFPFTFGPGTKVDIE (SEQ ID NO:8).~~

~~5. The antibody of claim 4, wherein the VH domain comprises the sequence~~

~~QVQLVQSGAEVKKPGASVKVCKSSGYTFTDYYIHWRQAPGQGLEWMGWINPNSGD
TNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYWGQGTLLTVV
SS (SEQ ID NO:7); and/or wherein the VL domain comprises the sequence~~

~~DIQMTQSPSSVSASVGDRVITTCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPS
RFSGSGSGTDFTLTVSSSLQPEDFATYYCQQAYSFPFTFGPGTKVDIE (SEQ ID NO:8).~~

~~6. The antibody of any one of claims 1-3, wherein the antibody or fragment is a human,
humanized, or chimeric antibody or fragment.~~

~~7. An antibody or antigen-binding fragment thereof that binds to human Dectin-1, wherein
the antibody or fragment binds to human Dectin-1 expressed on the surface of a cell with an
EC50 of less than 2nM.~~

~~8. An antibody or antigen-binding fragment thereof that binds to human Dectin-1, wherein
the antibody or fragment is capable of binding human or cynomolgus Dectin-1.~~

~~9. An antibody or antigen-binding fragment thereof that binds to human Dectin-1, wherein
the antibody or fragment does not compete with a native ligand of human Dectin-1.~~

~~10. The antibody of any one of claims 7-9, wherein the antibody or fragment is a human or
humanized antibody or fragment.~~

~~11. The antibody of any one of claims 7-10, wherein the antibody or fragment competes for
binding to human Dectin-1 with a reference antibody that comprises:~~

(a) a heavy chain variable (VH) domain comprising a CDR-H1 comprising the sequence GYTFTDYY (SEQ ID NO:1), a CDR-H2 comprising the sequence INPNSGDT (SEQ ID NO:2), and a CDR-H3 comprising the sequence ARNSGSYSFGY (SEQ ID NO:3), and a light chain variable (VL) domain comprising a CDR-L1 comprising the sequence QGISSW (SEQ ID NO:4), a CDR-L2 comprising the sequence GAS (SEQ ID NO:5), and a CDR-L3 comprising the sequence QQAYSFPFT (SEQ ID NO:6);

(b) a heavy chain variable (VH) domain comprising a CDR-H1 comprising the sequence DYYI (SEQ ID NO:88), a CDR-H2 comprising the sequence WINPNSGDTNYAQKFQG (SEQ ID NO:89), and a CDR-H3 comprising the sequence NSGSYSFGY (SEQ ID NO:90), and a light chain variable (VL) domain comprising a CDR-L1 comprising the sequence RASQGISSWLA (SEQ ID NO:91), a CDR-L2 comprising the sequence GASSLQS (SEQ ID NO:92), and a CDR-L3 comprising the sequence QQAYSFPFT (SEQ ID NO:6); or

(c) a heavy chain variable (VH) domain comprising the sequence QVQLVQSGAEVKKPGASVKVCKSSGYTFTDYYIHWVRQAPGQGLEWMGWINPNSGDTNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYWGGQGLTLVTVSS (SEQ ID NO:7) and a light chain variable (VL) domain comprising the sequence DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPSRFSGSGSGTDFTLTSSLQPEDFATYYCQQAYSFPFTFGPGTKVDIE (SEQ ID NO:8).

12.—The antibody of any one of claims 7-11, wherein the antibody or fragment binds the same epitope of human Dectin-1 as a reference antibody that comprises:

(a) a heavy chain variable (VH) domain comprising a CDR-H1 comprising the sequence GYTFTDYY (SEQ ID NO:1), a CDR-H2 comprising the sequence INPNSGDT (SEQ ID NO:2), and a CDR-H3 comprising the sequence ARNSGSYSFGY (SEQ ID NO:3), and a light chain variable (VL) domain comprising a CDR-L1 comprising the sequence QGISSW (SEQ ID NO:4), a CDR-L2 comprising the sequence GAS (SEQ ID NO:5), and a CDR-L3 comprising the sequence QQAYSFPFT (SEQ ID NO:6);

(b) a heavy chain variable (VH) domain comprising a CDR-H1 comprising the sequence DYYI (SEQ ID NO:88), a CDR-H2 comprising the sequence WINPNSGDTNYAQKFQG (SEQ ID NO:89), and a CDR-H3 comprising the sequence NSGSYSFGY (SEQ ID NO:90), and a light chain variable (VL) domain comprising a CDR-L1 comprising the sequence RASQGISSWLA

(SEQ ID NO:91), a CDR-L2 comprising the sequence GASSLQS (SEQ ID NO:92), and a CDR-L3 comprising the sequence QQAYSFPT (SEQ ID NO:6); or

(c) a heavy chain variable (VH) domain comprising the sequence QVQLVQSGAEVKKPGASVKVCKSSGYTFTDYYIHWRQAPGQGLEWMGWNPNSGD TNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYWGQGTLLVTV SS (SEQ ID NO:7) and a light chain variable (VL) domain comprising the sequence DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPS RFGSGSGTDFTLTLSLQPEDFATYYCQQAYSFPTFGPGTKVDIE (SEQ ID NO:8).

13.3. The antibody of claim 1 or claim 2~~any one of claims 1-12~~, wherein the antibody or fragment binds to human Dectin-1 expressed on the surface of a macrophage, monocyte, dendritic cell, and/or granulocyte.

14.4. The antibody of any one of claims 1-31-13, wherein the antigen-binding antibody fragment is a Fab, Fab', F(ab')₂, Fv, Fab'-SH, F(ab')₂, single chain antibody, nanobody, or scFv fragment and/or further comprises an Fc region.

~~15. The antibody of any one of claims 1-13, wherein the antibody further comprises an Fc region.~~

16.5. The antibody of any one of claims 1-41-15, wherein the antibody or fragment is a multispecific antibody or fragment; wherein optionally the antibody or fragment is a bispecific antibody, fragment, or diabody comprising a first antigen binding domain comprising the VH and VL domains that bind to human Dectin-1 and a second antigen binding domain comprising second VH and VL domains that bind to a target of interest.

~~17. The antibody of claim 16, wherein the antibody or fragment is a bispecific antibody, fragment, or diabody comprising a first antigen binding domain comprising the VH and VL domains that bind to human Dectin-1 and a second antigen binding domain comprising second VH and VL domains that bind to a target of interest.~~

18.6. The antibody of claim 5-17, wherein:

(a) the bispecific antibody comprises a first IgG antibody comprising the first antigen binding domain covalently linked to a second IgG antibody comprising the second antigen binding domain;

(b) the bispecific antibody comprises a first antibody arm comprising a first antibody heavy chain that comprises the VH domain of the first antigen binding domain and a first Fc region, and a second antibody arm comprising a second antibody heavy chain that comprises the VH domain of the second antigen binding domain and a second Fc region, wherein the first Fc region comprises one or more knob-forming mutations, and the second Fc region comprises one or more cognate hole-forming mutations, wherein optionally the first Fc region comprises a T366W substitution, and wherein the second Fc region comprises T366S, L368A, and Y407V substitutions, according to EU numbering;

(c) the bispecific antibody comprises a first antibody arm comprising a first antibody heavy chain that comprises the VH domain of the first antigen binding domain and a first Fc region, and a second antibody arm comprising a second antibody heavy chain that comprises the VH domain of the second antigen binding domain and a second Fc region, wherein the first Fc region comprises one or more hole-forming mutations, and the second Fc region comprises one or more cognate knob-forming mutations; wherein optionally the first Fc region comprises T366S, L368A, and Y407V substitutions, and wherein the second Fc region comprises a T366W substitution, according to EU numbering;

(d) the bispecific antibody comprises a first antibody arm comprising a single chain variable fragment (scFv) comprising the VH and VL domains that bind to human Dectin-1 and a first Fc region, and a second antibody arm comprising an antibody heavy chain that comprises the VH domain of the second antigen binding domain in association with an antibody light chain that comprises the VL domain of the second antigen binding domain and a second Fc region connected to the VH domain of the second antigen binding domain; wherein optionally the first Fc region comprises one or more knob-forming mutations, and the second Fc region comprises one or more cognate hole-forming mutations, or wherein the second Fc region comprises one or more knob-forming mutations, and the first Fc region comprises one or more cognate hole-forming mutations, wherein optionally the first antibody arm comprises a first linker between the VH and VL domains, and a second linker between the VL domain and the first Fc region, wherein optionally the first linker comprises one or more repeats of the sequence GGGGS (SEQ ID NO:26), wherein optionally the first linker comprises the sequence GGGSGGGSGGGGS (SEQ ID NO:27) or GGGSGGGSGGGSGGGGS (SEQ ID NO:28), wherein optionally the second linker comprises the sequence EPKRSDKTHTCPPC (SEQ ID NO:29) or SATHTCPPC (SEQ ID NO:30);

(e) the bispecific antibody comprises a first IgG antibody comprising the first antigen binding domain coupled to biotin or an avidin-binding derivative thereof, and a second IgG antibody comprising the second antigen binding domain coupled to avidin, streptavidin, neutravidin, or a biotin-binding derivative thereof, wherein the biotin or avidin-binding derivative thereof is bound to the avidin, streptavidin, neutravidin, or biotin-binding derivative thereof; or

(f) the bispecific antibody comprises a first IgG antibody comprising the first antigen binding domain coupled to avidin, streptavidin, neutravidin, or a biotin-binding derivative thereof, and a second IgG antibody comprising the second antigen binding domain coupled to biotin or an avidin-binding derivative thereof, wherein the biotin or avidin-binding derivative thereof is bound to the avidin, streptavidin, neutravidin, or biotin-binding derivative thereof.

~~19.—The antibody of claim 17, wherein the bispecific antibody comprises a first antibody arm comprising a first antibody heavy chain that comprises the VH domain of the first antigen binding domain and a first Fc region, and a second antibody arm comprising a second antibody heavy chain that comprises the VH domain of the second antigen binding domain and a second Fc region, wherein the first Fc region comprises one or more knob-forming mutations, and the second Fc region comprises one or more cognate hole-forming mutations.~~

~~20.—The antibody of claim 19, wherein the first Fc region comprises a T366W substitution, and wherein the second Fc region comprises T366S, L368A, and Y407V substitutions, according to EU numbering.~~

~~21.—The antibody of claim 17, wherein the bispecific antibody comprises a first antibody arm comprising a first antibody heavy chain that comprises the VH domain of the first antigen binding domain and a first Fc region, and a second antibody arm comprising a second antibody heavy chain that comprises the VH domain of the second antigen binding domain and a second Fc region, wherein the first Fc region comprises one or more hole-forming mutations, and the second Fc region comprises one or more cognate knob-forming mutations.~~

~~22.—The antibody of claim 21, wherein the first Fc region comprises T366S, L368A, and Y407V substitutions, and wherein the second Fc region comprises a T366W substitution, according to EU numbering.~~

~~23.—The antibody of claim 17, wherein the bispecific antibody comprises a first antibody arm comprising a single chain variable fragment (scFv) comprising the VH and VL domains that bind~~

to human Dectin-1 and a first Fc region, and a second antibody arm comprising an antibody heavy chain that comprises the VH domain of the second antigen binding domain in association with an antibody light chain that comprises the VL domain of the second antigen binding domain and a second Fc region connected to the VH domain of the second antigen binding domain.

24.—The antibody of claim 23, wherein the first Fc region comprises one or more knob-forming mutations, and the second Fc region comprises one or more cognate hole-forming mutations, or wherein the second Fc region comprises one or more knob-forming mutations, and the first Fc region comprises one or more cognate hole-forming mutations.

25.—The antibody of claim 23 or claim 24, wherein the first antibody arm comprises a first linker between the VH and VL domains, and a second linker between the VL domain and the first Fc region.

26.—The antibody of claim 25, wherein the first linker comprises one or more repeats of the sequence GGGGS (SEQ ID NO:26).

27.—The antibody of claim 26, wherein the first linker comprises the sequence GGGSGGGSGGGGS (SEQ ID NO:27) or GGGSGGGSGGGSGGGGS (SEQ ID NO:28).

28.—The antibody of any one of claims 25-27, wherein the second linker comprises the sequence EPKRSDKTHTCPPC (SEQ ID NO:29) or SATHTCPPC (SEQ ID NO:30).

29.—The antibody of claim 17, wherein the bispecific antibody comprises a first IgG antibody comprising the first antigen binding domain coupled to biotin or an avidin-binding derivative thereof, and a second IgG antibody comprising the second antigen binding domain coupled to avidin, streptavidin, neutravidin, or a biotin-binding derivative thereof, wherein the biotin or avidin-binding derivative thereof is bound to the avidin, streptavidin, neutravidin, or biotin-binding derivative thereof.

30.—The antibody of claim 17, wherein the bispecific antibody comprises a first IgG antibody comprising the first antigen binding domain coupled to avidin, streptavidin, neutravidin, or a biotin-binding derivative thereof, and a second IgG antibody comprising the second antigen binding domain coupled to biotin or an avidin-binding derivative thereof, wherein the biotin or avidin-binding derivative thereof is bound to the avidin, streptavidin, neutravidin, or biotin-binding derivative thereof.

~~31.7.~~ The antibody of claim 5 or claim 6~~any one of claims claim 17-30~~, wherein the target of interest is a disease-causing agent; wherein optionally the disease-causing agent is a bacterial cell, fungal cell, virus, senescent cell, tumor cell, protein aggregate, LDL particle, mast cell, eosinophil, ILC2 cell, or inflammatory immune cell.

~~32.~~—The antibody of claim 31, wherein the disease-causing agent is a bacterial cell, fungal cell, virus, senescent cell, tumor cell, protein aggregate, LDL particle, mast cell, eosinophil, ILC2 cell, or inflammatory immune cell.

~~33.8.~~ The antibody of claim 7-32, wherein the target of interest is:

(a) an antigen expressed on the surface of the bacterial cell, fungal cell, senescent cell, tumor cell, mast cell, eosinophil, ILC2 cell, or inflammatory immune cell;

(b) a surface antigen of the virus;

(c) an antigen expressed on the surface of a cancer cell, wherein optionally the target of interest is CD70, HER2, DLL3, NECTIN-4, TROP-2, Mesothelin, LIV-1, C-MET, FOLR1, CD20, CCR8, CD33, or EGFR; or

(d) amyloid beta, lambda light chain amyloid, or kappa light chain amyloid.

~~34.~~—The antibody of claim 32, wherein the target of interest is a surface antigen of the virus.

~~35.~~—The antibody of claim 31 or claim 32, wherein the target of interest is an antigen expressed on the surface of a cancer cell.

~~36.~~—The antibody of claim 35, wherein the target of interest is CD70, HER2, DLL3, NECTIN-4, TROP-2, Mesothelin, LIV-1, C-MET, FOLR1, CD20, CCR8, CD33, or EGFR.

~~37.~~—The antibody of claim 32, wherein the target of interest is amyloid beta, lambda light chain amyloid, or kappa light chain amyloid.

~~38.9.~~ The antibody of any one of claims 5-815-37, wherein:

(a) the antibody comprises two antibody heavy chains, and wherein each of the antibody heavy chains comprises an amino acid substitution at one or more of positions 234, 235, and 237, according to EU numbering, wherein optionally each of the antibody heavy chains comprises L234A, L235E, and G237A substitutions, according to EU numbering;

(b) the antibody comprises two antibody heavy chains, and wherein only one of the antibody heavy chains comprises H435R and Y436F substitutions, according to EU numbering; and/or

(c) the antibody comprises two arms, wherein only one of the two antibody arms comprises a heavy chain comprising F126C and C220V substitutions and a light chain comprising S121C and C214V substitutions, according to EU numbering.

~~39. The antibody of claim 38, wherein each of the antibody heavy chains comprises L234A, L235E, and G237A substitutions, according to EU numbering.~~

~~40. The antibody of any one of claims 17-39, wherein the antibody comprises two antibody heavy chains, and wherein only one of the antibody heavy chains comprises H435R and Y436F substitutions, according to EU numbering.~~

~~41. The antibody of any one of claims 17-40, wherein the antibody comprises two arms, wherein only one of the two antibody arms comprises a heavy chain comprising F126C and C220V substitutions and a light chain comprising S121C and C214V substitutions, according to EU numbering.~~

42.10. The antibody of claim 5-17, wherein the bispecific antibody comprises two antibody heavy chains and two antibody light chains, wherein the VH domain of the first antibody heavy chain forms an antigen binding domain with the VL domain of the first antibody light chain, wherein the VH domain of the second antibody heavy chain forms an antigen binding domain with the VL domain of the second antibody light chain, wherein the first antibody heavy chain comprises F126C, C220V, and T366W substitutions, wherein the first antibody light chain comprises S121C and C214V substitutions, and wherein the second antibody heavy chain comprises T366S, L368A, Y407V, H435R, and Y436F substitutions, according to EU numbering; wherein optionally the first and second antibody heavy chains further comprise L234A, L235E, and G237A substitutions, according to EU numbering.

~~43. The antibody of claim 42, wherein the first and second antibody heavy chains further comprise L234A, L235E, and G237A substitutions, according to EU numbering.~~

44.11. The antibody of any one of claims 5-1017-43, wherein the bispecific antibody comprises a first and a second antibody heavy chain, wherein the first and second antibody heavy chains

comprise human IgG1 Fc domains; and/or wherein at least one or two of the first and second antibody heavy chains is/are non-fucosylated.

~~45. The antibody of any one of claims 17-44, wherein the bispecific antibody comprises a first and a second antibody heavy chain, wherein at least one or two of the first and second antibody heavy chains is/are non-fucosylated.~~

~~46-12.~~ A multispecific binding molecule, comprising:

(a) a first antibody or antigen-binding fragment thereof comprising a first antigen-binding domain, wherein the first antigen-binding domain binds to human Dectin-1; and

(b) a second antibody or antigen-binding fragment thereof comprising a second antigen-binding domain, wherein the second antigen binding domain binds to a target of interest.

~~47-13.~~ The multispecific binding molecule of claim ~~12-46~~, wherein the target of interest is a disease-causing agent;

wherein optionally the disease-causing agent is a bacterial cell, fungal cell, virus, senescent cell, tumor cell, protein aggregate, LDL particle, mast cell, eosinophil, ILC2 cell, or inflammatory immune cell;

wherein optionally the target of interest is an antigen expressed on the surface of the bacterial cell, fungal cell, senescent cell, tumor cell, cancer cell, mast cell, eosinophil, ILC2 cell, or inflammatory immune cell or the target of interest is a surface antigen of the virus or the target of interest is amyloid beta, lambda light chain amyloid, or kappa light chain amyloid; and

wherein optionally the target of interest is CD70, HER2, DLL3, NECTIN-4, TROP-2, Mesothelin, LIV-1, C-MET, FOLR1, CD20, CCR8, CD33, or EGFR.

~~48. The multispecific binding molecule of claim 47, wherein the disease-causing agent is a bacterial cell, fungal cell, virus, senescent cell, tumor cell, protein aggregate, LDL particle, mast cell, eosinophil, ILC2 cell, or inflammatory immune cell.~~

~~49. The multispecific binding molecule of claim 48, wherein the target of interest is an antigen expressed on the surface of the bacterial cell, fungal cell, senescent cell, tumor cell, mast cell, eosinophil, ILC2 cell, or inflammatory immune cell.~~

~~50.—The multispecific binding molecule of claim 48, wherein the target of interest is a surface antigen of the virus.~~

~~51.—The multispecific binding molecule of claim 47 or claim 48, wherein the target of interest is an antigen expressed on the surface of a cancer cell.~~

~~52.—The multispecific binding molecule of claim 51, wherein the target of interest is CD70, HER2, DLL3, NECTIN 4, TROP 2, Mesothelin, LIV 1, C-MET, FOLR1, CD20, CCR8, CD33, or EGFR.~~

~~53.—The multispecific binding molecule of claim 48, wherein the target of interest is amyloid beta, lambda light chain amyloid, or kappa light chain amyloid.~~

~~54.14.~~ The multispecific binding molecule of claim 12 or claim 13~~any one of claims 46-53~~, wherein:

(a) the first antigen-binding domain comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the sequence GYTFTDYY (SEQ ID NO:1), a CDR-H2 comprising the sequence INPNSGDT (SEQ ID NO:2), and a CDR-H3 comprising the sequence ARNSGSYSFGY (SEQ ID NO:3), and wherein the VL domain comprises a CDR-L1 comprising the sequence QGISSW (SEQ ID NO:4), a CDR-L2 comprising the sequence GAS (SEQ ID NO:5), and a CDR-L3 comprising the sequence QQAYSFPFT (SEQ ID NO:6); or

(b) the first antigen-binding domain comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the sequence DYYI (SEQ ID NO:88), a CDR-H2 comprising the sequence WINPNSGDTNYAQKFQG (SEQ ID NO:89), and a CDR-H3 comprising the sequence NSGSYSFGY (SEQ ID NO:90), and wherein the VL domain comprises a CDR-L1 comprising the sequence RASQGISSWLA (SEQ ID NO:91), a CDR-L2 comprising the sequence GASLQS (SEQ ID NO:92), and a CDR-L3 comprising the sequence QQAYSFPFT (SEQ ID NO:6);

wherein optionally the VH domain comprises a sequence with at least 90% identity to the sequence

QVQLVQSGAEVKKPGASVKVCKSSGYTFTDYYIHWVRQAPGQGLEWMGWINPNSGD
TNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYWGQGTLVTV
SS (SEQ ID NO:7); and/or wherein the VL domain comprises a sequence with at least 90%

identity to the sequence

DIQMTQSPSSVSASVGDRVITTCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPS
RFSGSGSGTDFTLTVSSSLQPEDFATYYCQQAYSFPFTFGPGTKVDIE (SEQ ID NO:8); and

wherein optionally the VH domain comprises the sequence

QVQLVQSGAEVKKPGASVKVSCKSSGYTFTDYYIHWVRQAPGQGLEWMGWINPNSGD
TNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYWGQGTLLVTV
SS (SEQ ID NO:7); and/or wherein the VL domain comprises the sequence

DIQMTQSPSSVSASVGDRVITTCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPS
RFSGSGSGTDFTLTVSSSLQPEDFATYYCQQAYSFPFTFGPGTKVDIE (SEQ ID NO:8).

~~55.—The multispecific binding molecule of any one of claims 46-53, wherein the first antigen-binding domain comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1, CDR-H2, and CDR-H3 from the VH domain sequence~~

~~QVQLVQSGAEVKKPGASVKVSCKSSGYTFTDYYIHWVRQAPGQGLEWMGWINPNSGD
TNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYWGQGTLLVTV
SS (SEQ ID NO:7), and wherein the VL domain comprises a CDR-L1, CDR-L2, and CDR-L3
from the VL domain sequence~~

~~DIQMTQSPSSVSASVGDRVITTCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPS
RFSGSGSGTDFTLTVSSSLQPEDFATYYCQQAYSFPFTFGPGTKVDIE (SEQ ID NO:8).~~

~~56.—The multispecific binding molecule of any one of claims 46-53, wherein the first antigen-binding domain comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the sequence DYYI (SEQ ID NO:88), a CDR-H2 comprising the sequence WINPNSGDTNYAQKFQG (SEQ ID NO:89), and a CDR-H3 comprising the sequence NSGSYSFGY (SEQ ID NO:90), and wherein the VL domain comprises a CDR-L1 comprising the sequence RASQGISSWLA (SEQ ID NO:91), a CDR-L2 comprising the sequence GASSLQS (SEQ ID NO:92), and a CDR-L3 comprising the sequence QQAYSFPFT (SEQ ID NO:6).~~

~~57.—The multispecific binding molecule of any one of claims 54-56, wherein the VH domain comprises a sequence with at least 90% identity to the sequence~~

~~QVQLVQSGAEVKKPGASVKVSCKSSGYTFTDYYIHWVRQAPGQGLEWMGWINPNSGD
TNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYWGQGTLLVTV
SS (SEQ ID NO:7); and/or wherein the VL domain comprises a sequence with at least 90%~~

~~identity to the sequence~~

~~DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPS
RFGSGSGTDFTLTVSSLQPEDFATYYCQQAYSFPFTFGPGTKVDIE (SEQ ID NO:8).~~

~~58. The multispecific binding molecule of claim 57, wherein the VH domain comprises the sequence~~

~~QVQLVQSGAEVKKPGASVKVSCKSSGYTFTDYYIHWRQAPGQGLEWMGWNPNSGD
TNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYWGQGTLLTVV
SS (SEQ ID NO:7); and/or wherein the VL domain comprises the sequence~~

~~DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPS
RFGSGSGTDFTLTVSSLQPEDFATYYCQQAYSFPFTFGPGTKVDIE (SEQ ID NO:8).~~

~~59.15.~~ The multispecific binding molecule of any one of claims ~~12-14~~46-58, wherein the first antigen-binding domain:

(a) binds to human Dectin-1 expressed on the surface of a macrophage, monocyte, dendritic cell, or granulocyte;

(b) binds to human Dectin-1 expressed on the surface of a cell with an EC₅₀ of less than 2nM;

(c) is capable of binding human or cynomolgus Dectin-1; and/or

(d) does not compete with a native ligand of human Dectin-1.

~~60.16.~~ The multispecific binding molecule of any one of claims ~~12-15~~46-59, wherein:

(a) the second antigen-binding domain binds to CD20 and comprises a VH domain comprising the sequence of SEQ ID NO:24 and a VL domain comprising the sequence of SEQ ID NO:25;

(b) the second antigen-binding domain binds to Trop-2 and comprises a VH domain comprising the sequence of SEQ ID NO:42 and a VL domain comprising the sequence of SEQ ID NO:43;

(c) the second antigen-binding domain binds to light chain amyloid and comprises a VH domain comprising the sequence of SEQ ID NO:44 and a VL domain comprising the sequence of SEQ ID NO:45; or

(d) one or both of the first and second antibodies or fragments are human or humanized antibodies or fragments.

~~61. The multispecific binding molecule of any one of claims 46-59, wherein the second antigen-binding domain binds to Trop-2 and comprises a VH domain comprising the sequence of SEQ ID NO:42 and a VL domain comprising the sequence of SEQ ID NO:43.~~

~~62. The multispecific binding molecule of any one of claims 46-59, wherein the second antigen-binding domain binds to light chain amyloid and comprises a VH domain comprising the sequence of SEQ ID NO:44 and a VL domain comprising the sequence of SEQ ID NO:45.~~

~~63. The multispecific binding molecule of any one of claims 46-59, wherein one or both of the first and second antibodies or fragments are human or humanized antibodies or fragments.~~

~~64.~~17. The multispecific binding molecule of any one of claims ~~12-16~~46-63, wherein:

(a) one or both of the first and second antibodies or fragments are Fab, Fab', F(ab')₂, Fv, Fab'-SH, F(ab')₂, single chain antibodies, nanobodies, or scFv fragments;

(b) one or both of the first and second antibodies or fragments further comprise an Fc domain;

(c) the first antibody or fragment is a Fab fragment, and wherein the second antibody comprises an antibody heavy chain and an antibody light chain; or

(d) the first and the second antibodies both comprise an antibody heavy chain and an antibody light chain.

~~65. The multispecific binding molecule of any one of claims 46-63, wherein one or both of the first and second antibodies or fragments further comprise an Fc domain.~~

~~66. The multispecific binding molecule of any one of claims 46-63, wherein the first antibody or fragment is a Fab fragment, and wherein the second antibody comprises an antibody heavy chain and an antibody light chain.~~

~~67. The multispecific binding molecule of any one of claims 46-63, wherein the first and the second antibodies both comprise an antibody heavy chain and an antibody light chain.~~

~~68.—The multispecific binding molecule of any one of claims 46-67, wherein the first antibody or fragment is coupled to avidin, streptavidin, neutravidin, or a biotin-binding derivative thereof, and the second antibody or fragment is coupled to biotin or an avidin-binding derivative thereof; or wherein the second antibody or fragment is coupled to avidin, streptavidin, neutravidin, or a biotin-binding derivative thereof, and the first antibody or fragment is coupled to biotin or an avidin-binding derivative thereof; and wherein the first antibody or fragment is bound to the second antibody or fragment via an interaction between the avidin, streptavidin, neutravidin, or biotin-binding derivative thereof and the biotin or avidin-binding derivative thereof.~~

~~69.—The multispecific binding molecule of claim 68, wherein the first antibody or fragment is a Fab fragment coupled to monomeric streptavidin (mSA), and wherein the second antibody is a biotinylated antibody that comprises an antibody heavy chain and an antibody light chain.~~

~~70.—The multispecific binding molecule of claim 68, wherein the first antibody or fragment is a full-length antibody coupled to monomeric streptavidin (mSA), and wherein the second antibody is a biotinylated antibody that comprises an antibody heavy chain and an antibody light chain.~~

71.18. The multispecific binding molecule of any one of claims ~~12-17~~46-63, wherein:

(a) the multispecific binding molecule comprises a first IgG antibody comprising the first antigen binding domain covalently linked to a second IgG antibody comprising the second antigen binding domain;

(b) the multispecific binding molecule comprises a first antibody arm comprising a single chain variable fragment (scFv) comprising the VH and VL domains that bind to human Dectin-1 and a first Fc region, and a second antibody arm comprising an antibody heavy chain that comprises the VH domain of the second antigen binding domain in association with an antibody light chain that comprises the VL domain of the second antigen binding domain and a second Fc region connected to the VH domain of the second antigen binding domain;

(c) the multispecific binding molecule comprises a first antibody arm comprising a first antibody heavy chain that comprises the VH domain of the first antigen binding domain and a first Fc region and a first antibody light chain comprising the VL domain of the first antigen binding domain, and a second antibody arm comprising a second antibody heavy chain that comprises the VH domain of the second antigen binding domain and a second Fc region and a second antibody light chain comprising the VL domain of the second antigen binding domain,

wherein the first Fc region comprises one or more knob-forming mutations, and the second Fc region comprises one or more cognate hole-forming mutations; or

(d) the multispecific binding molecule comprises a first antibody arm comprising a first antibody heavy chain that comprises the VH domain of the first antigen binding domain and a first Fc region, and a second antibody arm comprising a second antibody heavy chain that comprises the VH domain of the second antigen binding domain and a second Fc region, wherein the first Fc region comprises one or more hole-forming mutations, and the second Fc region comprises one or more cognate knob-forming mutations.

~~72. The multispecific binding molecule of any one of claims 46-63, wherein the multispecific binding molecule comprises a first antibody arm comprising a single chain variable fragment (scFv) comprising the VH and VL domains that bind to human Dectin-1 and a first Fc region, and a second antibody arm comprising an antibody heavy chain that comprises the VH domain of the second antigen binding domain in association with an antibody light chain that comprises the VL domain of the second antigen binding domain and a second Fc region connected to the VH domain of the second antigen binding domain.~~

73.19. The multispecific binding molecule of claim 18(b)-72, wherein the first Fc region comprises one or more knob-forming mutations, and the second Fc region comprises one or more cognate hole-forming mutations, or wherein the second Fc region comprises one or more knob-forming mutations, and the first Fc region comprises one or more cognate hole-forming mutations; and/or wherein the first antibody arm comprises a first linker between the VH and VL domains, and a second linker between the VL domain and the first Fc region, wherein optionally the first linker comprises one or more repeats of the sequence GGGGS (SEQ ID NO:26), the sequence GGGSGGGSGGGGS (SEQ ID NO:27), or the sequence GGGSGGGSGGGSGGGGS (SEQ ID NO:28); wherein optionally the second linker comprises the sequence EPKRSDKTHTCPPC (SEQ ID NO:29) or SATHTCPPC (SEQ ID NO:30).

~~74. The multispecific binding molecule of claim 72 or claim 73, wherein the first antibody arm comprises a first linker between the VH and VL domains, and a second linker between the VL domain and the first Fc region.~~

~~75. The multispecific binding molecule of claim 74, wherein the first linker comprises one or more repeats of the sequence GGGGS (SEQ ID NO:26).~~

~~76.—The multispecific binding molecule of claim 75, wherein the first linker comprises the sequence GGGGSGGGGSGGGGS (SEQ ID NO:27) or GGGGSGGGGSGGGGSGGGGS (SEQ ID NO:28).~~

~~77.—The multispecific binding molecule of any one of claims 74-76, wherein the second linker comprises the sequence EPKRSDKTHTCPPC (SEQ ID NO:29) or SATHTCPPC (SEQ ID NO:30).~~

~~78.—The multispecific binding molecule of any one of claims 46-63, wherein the multispecific binding molecule comprises a first antibody arm comprising a first antibody heavy chain that comprises the VH domain of the first antigen binding domain and a first Fc region and a first antibody light chain comprising the VL domain of the first antigen binding domain, and a second antibody arm comprising a second antibody heavy chain that comprises the VH domain of the second antigen binding domain and a second Fc region and a second antibody light chain comprising the VL domain of the second antigen binding domain, wherein the first Fc region comprises one or more knob-forming mutations, and the second Fc region comprises one or more cognate hole-forming mutations.~~

79.20. The multispecific binding molecule of claim ~~1973 or claim 78~~, wherein the first Fc region comprises a T366W substitution, and wherein the second Fc region comprises T366S, L368A, and Y407V substitutions, according to EU numbering; or wherein the first Fc region comprises T366S, L368A, and Y407V substitutions, and wherein the second Fc region comprises a T366W substitution, according to EU numbering.

~~80.—The multispecific binding molecule of any one of claims 46-63, wherein the multispecific binding molecule comprises a first antibody arm comprising a first antibody heavy chain that comprises the VH domain of the first antigen binding domain and a first Fc region, and a second antibody arm comprising a second antibody heavy chain that comprises the VH domain of the second antigen binding domain and a second Fc region, wherein the first Fc region comprises one or more hole-forming mutations, and the second Fc region comprises one or more cognate knob-forming mutations.~~

~~81.—The multispecific binding molecule of claim 73 or claim 80, wherein the first Fc region comprises T366S, L368A, and Y407V substitutions, and wherein the second Fc region comprises a T366W substitution, according to EU numbering.~~

82.21. The multispecific binding molecule of any one of claims ~~18-2072-81~~, wherein:

(a) the first and/or the second Fc region comprises an amino acid substitution at one or more of positions 234, 235, and 237, according to EU numbering, wherein optionally each of the first and second Fc regions comprises L234A, L235E, and G237A substitutions, according to EU numbering;

(b) only one of the Fc regions comprises H435R and Y436F substitutions, according to EU numbering; and/or

(c) only one of the antibody arms comprises a heavy chain comprising F126C and C220V substitutions and a light chain comprising S121C and C214V substitutions, according to EU numbering.

~~83.—The multispecific binding molecule of claim 82, wherein each of the first and second Fc regions comprises L234A, L235E, and G237A substitutions, according to EU numbering.~~

~~84.—The multispecific binding molecule of any one of claims 78–83, wherein only one of the Fc regions comprises H435R and Y436F substitutions, according to EU numbering.~~

~~85.—The multispecific binding molecule of any one of claims 78–84, wherein only one of the antibody arms comprises a heavy chain comprising F126C and C220V substitutions and a light chain comprising S121C and C214V substitutions, according to EU numbering.~~

86.22. The multispecific binding molecule of claim 12–46, wherein the multispecific binding molecule comprises a first antibody heavy chain and a first antibody light chain and a second antibody heavy chain and a second antibody light chain, wherein the VH domain of the first antibody heavy chain forms a first antigen binding domain with the VL domain of the first antibody light chain, wherein the VH domain of the second antibody heavy chain forms a second antigen binding domain with the VL domain of the second antibody light chain, wherein the first antibody heavy chain comprises F126C, C220V, and T366W substitutions, wherein the first antibody light chain comprises S121C and C214V substitutions, and wherein the second antibody heavy chain comprises T366S, L368A, Y407V, H435R, and Y436F substitutions, according to EU numbering; wherein optionally the first and second antibody heavy chains further comprise L234A, L235E, and G237A substitutions, according to EU numbering.

~~87.—The multispecific binding molecule of claim 86, wherein the first and second antibody heavy chains further comprise L234A, L235E, and G237A substitutions, according to EU numbering.~~

~~88.23.~~ The multispecific binding molecule of any one of claims ~~18-2278-87~~, wherein the first and second antibody heavy chains comprise human IgG1 Fc domains; and/or wherein at least one or two of the first and second antibody heavy chains is/are non-fucosylated.

~~89.—The multispecific binding molecule of any one of claims 78-88, wherein at least one or two of the first and second antibody heavy chains is/are non-fucosylated.~~

~~90.—A multispecific binding molecule, comprising:~~

~~(a) a first antibody or antigen-binding fragment thereof comprising a first antigen-binding domain, wherein the first antigen-binding domain binds to a first target of interest; and~~

~~(b) a second antibody or antigen-binding fragment thereof comprising a second antigen-binding domain, wherein the second antigen-binding domain binds to a second target of interest;~~

~~wherein:~~

~~——(i) the first antibody or fragment is coupled to avidin, streptavidin, neutravidin, or a biotin-binding derivative thereof, and the second antibody or fragment is coupled to biotin or an avidin-binding derivative thereof; or~~

~~——(ii) the second antibody or fragment is coupled to avidin, streptavidin, neutravidin, or a biotin-binding derivative thereof, and the first antibody or fragment is coupled to biotin or an avidin-binding derivative thereof; and~~

~~wherein the first antibody or fragment is bound to the second antibody or fragment via an interaction between the avidin, streptavidin, neutravidin, or biotin-binding derivative thereof and the biotin or avidin-binding derivative thereof.~~

~~91.—The multispecific binding molecule of claim 90, wherein the first target of interest is human Dectin-1.~~

~~92.—The multispecific binding molecule of claim 91, wherein the first antigen-binding domain comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the sequence GYTFTDYY (SEQ ID NO:1), a CDR-H2 comprising the sequence INPNSGDT (SEQ ID NO:2), and a CDR-H3 comprising the sequence ARNSGSYSFGY (SEQ ID NO:3), and wherein the VL domain comprises a CDR-L1~~

comprising the sequence QGISSW (SEQ ID NO:4), a CDR-L2 comprising the sequence GAS (SEQ ID NO:5), and a CDR-L3 comprising the sequence QQAYSPFT (SEQ ID NO:6).

93.—The multispecific binding molecule of claim 91, wherein the first antigen-binding domain comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1, CDR-H2, and CDR-H3 from the VH domain sequence QVQLVQSGAEVKKPGASVKVSKSSGYTFTDYYIHVVRQAPGQGLEWMGWINPNSGD TNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYWGQGTLLVTVSS (SEQ ID NO:7), and wherein the VL domain comprises a CDR-L1, CDR-L2, and CDR-L3 from the VL domain sequence DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPS RFSGSGSGTDFTLTLSLQPEDFATYYCQQAYSPFTFGPGTKVDIE (SEQ ID NO:8).

94.—The multispecific binding molecule of claim 92 or claim 93, wherein the VH domain comprises a sequence with at least 90% identity to the sequence QVQLVQSGAEVKKPGASVKVSKSSGYTFTDYYIHVVRQAPGQGLEWMGWINPNSGD TNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYWGQGTLLVTVSS (SEQ ID NO:7); and/or wherein the VL domain comprises a sequence with at least 90% identity to the sequence DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPS RFSGSGSGTDFTLTLSLQPEDFATYYCQQAYSPFTFGPGTKVDIE (SEQ ID NO:8).

95.—The multispecific binding molecule of claim 94, wherein the VH domain comprises the sequence QVQLVQSGAEVKKPGASVKVSKSSGYTFTDYYIHVVRQAPGQGLEWMGWINPNSGD TNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYWGQGTLLVTVSS (SEQ ID NO:7); and/or wherein the VL domain comprises the sequence DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPS RFSGSGSGTDFTLTLSLQPEDFATYYCQQAYSPFTFGPGTKVDIE (SEQ ID NO:8).

96.—The multispecific binding molecule of any one of claims 91-95, wherein the first antigen-binding domain binds to human Dectin-1 expressed on the surface of a macrophage, monocyte, dendritic cell, or granulocyte.

97.—The multispecific binding molecule of any one of claims 46-96, wherein one or both of the first and second antibodies or fragments are humanized antibodies or fragments.

~~98-24.~~ The multispecific binding molecule of any one of claims ~~12-2346-97~~, wherein:

~~(a) one or both of the first and second antibodies or fragments are Fab, Fab', F(ab')₂, Fv, Fab'-SH, F(ab')₂, single chain antibodies, nanobodies, or scFv fragments;~~

~~(b) one or both of the first and second antibodies or fragments further comprise an Fc domain;~~

~~(c) the first antibody or fragment is a Fab fragment, and wherein the second antibody or fragment comprises an antibody heavy chain and an antibody light chain;~~

~~(d) the first and the second antibodies or fragments are both full-length antibodies;~~

~~(e) the first antibody or fragment is a Fab fragment coupled to monomeric streptavidin (mSA), and wherein the second antibody is a biotinylated antibody that comprises an antibody heavy chain and an antibody light chain; or~~

~~(f) the first antibody or fragment is a full-length antibody coupled to monomeric streptavidin (mSA), and wherein the second antibody or fragment is a biotinylated full-length antibody.~~

~~99.—The multispecific binding molecule of any one of claims 46-97, wherein one or both of the first and second antibodies or fragments further comprise an Fc domain.~~

~~100.—The multispecific binding molecule of any one of claims 46-97, wherein the first antibody or fragment is a Fab fragment, and wherein the second antibody or fragment comprises an antibody heavy chain and an antibody light chain.~~

~~101.—The multispecific binding molecule of any one of claims 46-97, wherein the first and the second antibodies or fragments are both full-length antibodies.~~

~~102.—The multispecific binding molecule of any one of claims 46-97, wherein the first antibody or fragment is a Fab fragment coupled to monomeric streptavidin (mSA), and wherein the second antibody is a biotinylated antibody that comprises an antibody heavy chain and an antibody light chain.~~

~~103.—The multispecific binding molecule of any one of claims 46-97, wherein the first antibody or fragment is a full-length antibody coupled to monomeric streptavidin (mSA), and wherein the second antibody or fragment is a biotinylated full-length antibody.~~

~~104.25.~~ The multispecific binding molecule of any one of claims ~~12-2446-103~~, wherein the first target of interest is human Dectin-1, and wherein the second target of interest is a disease-causing agent; wherein optionally the disease-causing agent is a bacterial cell, fungal cell, virus, senescent cell, tumor cell, protein aggregate, LDL particle, mast cell, eosinophil, ILC2 cell, or inflammatory immune cell.

~~105.—The multispecific binding molecule of claim 104, wherein the disease-causing agent is a bacterial cell, fungal cell, virus, senescent cell, tumor cell, protein aggregate, LDL particle, mast cell, eosinophil, ILC2 cell, or inflammatory immune cell.~~

~~106.26.~~ The multispecific binding molecule of claim ~~25-105~~, wherein:

(a) the target of interest is an antigen expressed on the surface of the bacterial cell, fungal cell, senescent cell, tumor cell, mast cell, eosinophil, ILC2 cell, or inflammatory immune cell;

(b) the target of interest is a surface antigen of the virus;

(c) the target of interest is an antigen expressed on the surface of a cancer cell, wherein optionally the target of interest is CD70, HER2, DLL3, NECTIN-4, TROP-2, Mesothelin, LIV-1, C-MET, FOLR1, CD20, CCR8, CD33, or EGFR; or

(d) the target of interest is amyloid beta, lambda light chain amyloid, or kappa light chain amyloid.

~~107.—The multispecific binding molecule of claim 105, wherein the target of interest is a surface antigen of the virus.~~

~~108.—The multispecific binding molecule of claim 104 or claim 105, wherein the target of interest is an antigen expressed on the surface of a cancer cell.~~

~~109.—The multispecific binding molecule of claim 108, wherein the target of interest is CD70, HER2, DLL3, NECTIN-4, TROP-2, Mesothelin, LIV-1, C-MET, FOLR1, CD20, CCR8, CD33, or EGFR.~~

~~110.27.~~ The multispecific binding molecule of claim ~~26-109~~, wherein:

(a) the second antigen binding domain binds to CD20; wherein the second antigen-binding domain comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; and wherein the VH domain of the second antigen-binding domain comprises the

sequence

QVQLQQPGAELVKPGASVKMSCKASGYTFTSYNMHWVKQTPGRGLEWIGAIYPGNGD
TSYNQKFKGKATLTADKSSSTAYMQLSSLTSEDSAVYYCARSTYYGGDWYFNVWGAG
TTVTVSA (SEQ ID NO:24) and/or wherein the VL domain of the second antigen-binding domain comprises the sequence

QIVLSQSPAILSASPGEKVTMTCRASSSVSYIHWFQQKPGSSPKPWIYATSNLASGVPVRF
SGSGSGTSYSLTISRVEAEDAATYYCQQWTSNPPTFGGGTKLEIK (SEQ ID NO:25);

(b) the second antigen binding domain binds to Trop-2; wherein the second antigen-binding domain comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; and wherein the VH domain of the second antigen-binding domain comprises the sequence of SEQ ID NO:42 and/or wherein the VL domain of the second antigen-binding domain comprises the sequence of SEQ ID NO:43; or

(c) the second antigen binding domain binds to light chain amyloid; wherein the second antigen-binding domain comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; and wherein the VH domain of the second antigen-binding domain comprises the sequence of SEQ ID NO:44 and/or wherein the VL domain of the second antigen-binding domain comprises the sequence of SEQ ID NO:45.

~~111.—The multispecific binding molecule of claim 109, wherein the second antigen binding domain binds to Trop-2; wherein the second antigen-binding domain comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; and wherein the VH domain of the second antigen-binding domain comprises the sequence of SEQ ID NO:42 and/or wherein the VL domain of the second antigen-binding domain comprises the sequence of SEQ ID NO:43.~~

~~112.—The multispecific binding molecule of claim 109, wherein the second antigen binding domain binds to light chain amyloid; wherein the second antigen-binding domain comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; and wherein the VH domain of the second antigen-binding domain comprises the sequence of SEQ ID NO:44 and/or wherein the VL domain of the second antigen-binding domain comprises the sequence of SEQ ID NO:45.~~

~~113.—The multispecific binding molecule of claim 105, wherein the target of interest is amyloid beta, lambda light chain amyloid, or kappa light chain amyloid.~~

~~114~~.28. A multispecific binding molecule comprising a first arm comprising a first antigen-binding domain and a second arm comprising a second antigen-binding domain; wherein the first antigen-binding domain binds to human Dectin-1 and the second antigen-binding domain binds to a target of interest; and wherein the first arm comprises a polypeptide chain comprising the sequence

QVQLVQSGAEVKKPGASVKVSKSSGYTFTDYYIHWVRQAPGQGLEWMGWINPNSGD
TNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYWGGTLVTV
SSGGGGSGGGGSGGGGSGGGGSDIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQ
QKPGKAPKLLIFGASSLQSGVPSRFSGSGSGTDFTLTSSLQPEDFATYYCQQAYSFPFTF
GPGTKVDIEEPKRSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS
HEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSN
KALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVKGFYPSDIAVEWESN
GQPENNYKTTTPVLDSGDSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLS
LSPG (SEQ ID NO:31).

~~115~~.29. A multispecific binding molecule, comprising:

(a) a first polypeptide chain comprising the sequence

QVQLVQSGAEVKKPGASVKVSKSSGYTFTDYYIHWVRQAPGQGLEWMGWINP
NSGDTNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYW
GGTLVTVSSGGGGSGGGGSGGGGSGGGGSDIQMTQSPSSVSASVGDRVTITCR
ASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPSRFSGSGSGTDFTLTSSLQP
EDFATYYCQQAYSFPFTFGPGTKVDIEEPKRSDKTHTCPPCPAPELLGGPSVFLFPP
KPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNS
TYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPP
PSREEMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGDSFFLY
YSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG (SEQ ID NO:31);

(b) a second polypeptide chain comprising the sequence

QVQLQQPGAELVKPGASVKMSCKASGYTFTSYNMHWVKQTPGRGLEWIGAIYP
GNGDTSYNQKFKGKATLTADKSSSTAYMQLSSLTSEDSAVYYCARSTYYGGDW
YFNVWGAGTTVTVSAASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVD
KKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYK

CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPS
DIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVDFSCSVMH
EALHNRFTQKSLSLSPG (SEQ ID NO:32); and

(c) a third polypeptide chain comprising the sequence

QIVLSQSPAILSASPGEKVTMTCRASSSVSYIHWFFQKPGSSPKPWIYATSNLASG
VPVRFSGSGSGTSYSLTISRVEAEDAATYYCQQWTSNPPTFGGGTKLEIKRTVAA
PSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQD
SKDSTYLSSTLTLSKADYEEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID
NO:33).

~~116-30.~~ 30. A polynucleotide encoding the antibody or multispecific binding molecule of any one of claims ~~1-291-115~~.

~~117-31.~~ 31. A vector comprising the polynucleotide of claim ~~30-116~~.

~~118-32.~~ 32. An isolated host cell comprising the polynucleotide of claim ~~30-116~~ or the vector of claim ~~31-117~~.

~~119-33.~~ 33. The isolated host cell of claim ~~32-118~~, wherein:

(a) the host cell is a yeast, insect, plant, or prokaryotic cell; or

(b) the host cell is a mammalian cell.

~~120.—The isolated host cell of claim 118, wherein the host cell is a mammalian cell.~~

~~121-34.~~ 34. The isolated host cell of claim ~~33(b)-120~~, wherein the mammalian cell is a Chinese hamster ovary (CHO) cell; and wherein optionally:

(a) the host cell comprises an alpha1,6-fucosyltransferase (Fut8) or alpha-1,3-mannosyl-glycoprotein 2-beta-N-acetylglucosaminyltransferase (MGAT1) knockout; or

(b) the host cell overexpresses β 1,4-N-acetylglucosaminyltransferase III (GnT-III) and optionally further overexpresses Golgi μ -mannosidase II (ManII).

~~122.—The isolated host cell of claim 120 or claim 121, wherein the host cell comprises an alpha1,6-fucosyltransferase (Fut8) or alpha-1,3-mannosyl-glycoprotein 2-beta-N-acetylglucosaminyltransferase (MGAT1) knockout.~~

~~123.—The isolated host cell of claim 120 or claim 121, wherein the host cell overexpresses β 1,4 N-acetylglucosaminyltransferase III (GnT-III).~~

~~124.—The isolated host cell of claim 123, wherein the host cell further overexpresses Golgi μ -mannosidase II (ManII).~~

125.35. A method of producing an antibody or multispecific binding molecule, comprising culturing the host cell of any one of claims ~~32-34~~~~118-124~~ under conditions suitable for production of the antibody or multispecific binding molecule.

126.36. The method of claim ~~34~~~~125~~, further comprising recovering the antibody or multispecific binding molecule; and/or wherein, prior to production of the antibody or multispecific binding molecule, the host cell is treated with kifunensine.

~~127.—The method of claim 125 or claim 126, wherein, prior to production of the antibody or multispecific binding molecule, the host cell is treated with kifunensine.~~

128.37. An antibody or antigen-binding fragment thereof that binds to human Dectin-1 produced by the method of claim 35 or claim 36~~any one of claims 125-127~~.

129.38. A pharmaceutical composition comprising the antibody or multispecific binding molecule of any one of claims ~~1-29~~~~115~~ and ~~37~~~~128~~ and a pharmaceutically acceptable carrier.

~~130.—A method of generating a multispecific binding molecule, comprising:~~

~~(a) providing a first antibody or antigen-binding fragment thereof comprising a first antigen-binding domain, wherein the first antigen-binding domain binds to a first target of interest;~~

~~(b) providing a second antibody or antigen-binding fragment thereof comprising a second antigen-binding domain, wherein the second antigen-binding domain binds to a second target of interest;~~

~~wherein:~~

~~——(i) the first antibody or fragment is coupled to avidin, streptavidin, neutravidin, or a biotin-binding derivative thereof, and the second antibody or fragment is coupled to biotin or an avidin-binding derivative thereof; or~~

~~——(ii) the second antibody or fragment is coupled to avidin, streptavidin, neutravidin, or a biotin-binding derivative thereof, and the first antibody or fragment is coupled to biotin or an avidin-binding derivative thereof; and~~

~~(c) contacting the first antibody or fragment with the second antibody or fragment under conditions suitable for binding between the first antibody or fragment and the second antibody or fragment via an interaction between the avidin, streptavidin, neutravidin, or biotin-binding derivative thereof and the biotin or avidin-binding derivative thereof, thereby generating a multispecific binding molecule.~~

131. ~~A method of identifying a multispecific binding molecule that binds a first and a second target of interest, comprising:~~

~~(a) providing a first antibody or antigen-binding fragment thereof comprising a first antigen-binding domain, wherein the first antigen-binding domain binds to a first target of interest;~~

~~(b) providing a second antibody or antigen-binding fragment thereof comprising a second antigen-binding domain, wherein the second antigen-binding domain binds to a second target of interest;~~

~~wherein:~~

~~——(i) the first antibody or fragment is coupled to avidin, streptavidin, neutravidin, or a biotin-binding derivative thereof, and the second antibody or fragment is coupled to biotin or an avidin-binding derivative thereof; or~~

~~——(ii) the second antibody or fragment is coupled to avidin, streptavidin, neutravidin, or a biotin-binding derivative thereof, and the first antibody or fragment is coupled to biotin or an avidin-binding derivative thereof;~~

~~(c) contacting the first antibody or fragment with the second antibody or fragment under conditions suitable for binding between the first antibody or fragment and the second antibody or fragment via an interaction between the avidin, streptavidin, neutravidin, or biotin-binding derivative thereof and the biotin or avidin-binding derivative thereof, thereby generating a multispecific binding molecule; and~~

(d) measuring binding between the multispecific binding molecule and at least one of the first and the second target of interest.

132.—The method of claim 130 or claim 131, wherein the first target of interest is human Dectin-1.

133.—The method of claim 132, wherein the first antigen-binding domain comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the sequence GYTFTDYY (SEQ ID NO:1), a CDR-H2 comprising the sequence INPNSGDT (SEQ ID NO:2), and a CDR-H3 comprising the sequence ARNSGSYSFGY (SEQ ID NO:3), and wherein the VL domain comprises a CDR-L1 comprising the sequence QGISSW (SEQ ID NO:4), a CDR-L2 comprising the sequence GAS (SEQ ID NO:5), and a CDR-L3 comprising the sequence QQAYSFPFT (SEQ ID NO:6).

134.—The method of claim 132, wherein the first antigen-binding domain comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1, CDR-H2, and CDR-H3 from the VH domain sequence QVQLVQSGAEVKKPGASVKVSKSSGYTFTDYYIHWVRQAPGQGLEWMGWINPNSGD TNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYWGQGTLLVTVSS (SEQ ID NO:7), and wherein the VL domain comprises a CDR-L1, CDR-L2, and CDR-L3 from the VL domain sequence DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPS RFSGSGSGTDFTLTLSLQPEDFATYYCQQAYSFPFTFGPGTKVDIE (SEQ ID NO:8).

135.—The method of claim 133 or claim 134, wherein the VH domain comprises a sequence with at least 90% identity to the sequence QVQLVQSGAEVKKPGASVKVSKSSGYTFTDYYIHWVRQAPGQGLEWMGWINPNSGD TNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYWGQGTLLVTVSS (SEQ ID NO:7); and/or wherein the VL domain comprises a sequence with at least 90% identity to the sequence DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPS RFSGSGSGTDFTLTLSLQPEDFATYYCQQAYSFPFTFGPGTKVDIE (SEQ ID NO:8).

136.—The method of claim 135, wherein the VH domain comprises the sequence QVQLVQSGAEVKKPGASVKVSKSSGYTFTDYYIHWVRQAPGQGLEWMGWINPNSGD TNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYWGQGTLLVTV

SS (SEQ ID NO:7); and/or wherein the VL domain comprises the sequence
DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPS
RFGSGSGTDFTLTVSSLQPEDFATYYCQAYSPFTFGPGTKVDIE (SEQ ID NO:8).

137. — The method of any one of claims 132–136, wherein the first antigen-binding domain binds to human Dectin-1 expressed on the surface of a macrophage, monocyte, dendritic cell, or granulocyte.

138. — The method of any one of claims 130–137, wherein one or both of the first and second antibodies or fragments are humanized antibodies or fragments.

139. — The method of any one of claims 130–138, wherein one or both of the first and second antibodies or fragments are Fab, Fab', F(ab')₂, Fv, Fab'-SH, F(ab')₂, single-chain antibodies, nanobodies, or scFv fragments.

140. — The method of any one of claims 130–138, wherein one or both of the first and second antibodies or fragments further comprise an Fc domain.

141. — The method of any one of claims 130–138, wherein the first antibody or fragment is a Fab fragment, and wherein the second antibody comprises an antibody heavy chain and an antibody light chain.

142. — The method of any one of claims 130–138, wherein the first and the second antibodies both comprise an antibody heavy chain and an antibody light chain.

143. — The method of any one of claims 130–138, wherein the first antibody or fragment is a Fab fragment coupled to monomeric streptavidin (mSA), and wherein the second antibody or fragment is a biotinylated antibody that comprises an antibody heavy chain and an antibody light chain.

144. — The method of any one of claims 130–138, wherein the first antibody or fragment is a full-length antibody coupled to monomeric streptavidin (mSA), and wherein the second antibody is a biotinylated antibody that comprises an antibody heavy chain and an antibody light chain.

145. — The method of any one of claims 130–144, wherein the second target of interest is a disease-causing agent.

~~146.—The method of claim 145, wherein the disease-causing agent is a bacterial cell, fungal cell, virus, senescent cell, tumor cell, protein aggregate, LDL particle, mast cell, eosinophil, ILC2 cell, or inflammatory immune cell.~~

~~147.—The method of claim 146, wherein the target of interest is an antigen expressed on the surface of the bacterial cell, fungal cell, senescent cell, tumor cell, mast cell, eosinophil, ILC2 cell, or inflammatory immune cell.~~

~~148.—The method of claim 146, wherein the target of interest is a surface antigen of the virus.~~

~~149.—The method of claim 145 or claim 146, wherein the target of interest is an antigen expressed on the surface of a cancer cell.~~

~~150.—The method of claim 149, wherein the target of interest is CD70, HER2, DLL3, NECTIN-4, TROP-2, Mesothelin, LIV-1, C-MET, FOLR1, CD20, CCR8, CD33, or EGFR.~~

~~151.—The method of claim 146, wherein the target of interest is amyloid beta, lambda light chain amyloid, or kappa light chain amyloid.~~

~~152.39. Use of the antibody of any one of claims 1-11, the multispecific binding molecule of any one of claims 12-23 and 25-29, or the composition of claim 38 in the manufacture of a medicament for~~A method of treating a disease or disorder, ~~comprising administering an effective amount of the antibody of any one of claims 1-44, the multispecific binding molecule of any one of claims 46-88 and 104-115, or the composition of claim 129 to~~ in an individual in need thereof.

~~153.40. The use~~method of claim ~~39-152~~, wherein the first target of interest is human Dectin-1, and wherein the second target of interest is a disease-causing agent.

~~154.41. The use~~method of claim ~~40-153~~, wherein the disease-causing agent is a bacterial cell, fungal cell, virus, senescent cell, tumor cell, protein aggregate, LDL particle, mast cell, eosinophil, ILC2 cell, or inflammatory immune cell.; wherein optionally:

(a) the target of interest is an antigen expressed on the surface of the bacterial cell, fungal cell, senescent cell, tumor cell, mast cell, eosinophil, ILC2 cell, or inflammatory immune cell;

(b) the target of interest is a surface antigen of the virus; or

(c) the target of interest is amyloid beta, lambda light chain amyloid, or kappa light chain amyloid.

~~155.—The method of claim 154, wherein the target of interest is an antigen expressed on the surface of the bacterial cell, fungal cell, senescent cell, tumor cell, mast cell, eosinophil, ILC2 cell, or inflammatory immune cell.~~

~~156.—The method of claim 154, wherein the target of interest is a surface antigen of the virus.~~

~~157.42.~~ The ~~use method~~ of any one of claims ~~39-41~~~~151-156~~, wherein the disease or disorder is cancer, a bacterial infection, a fungal infection, a viral infection, a mast cell disease or disorder, systemic mastocytosis, amyloidosis, or an aging-related disease or disorder; and/or wherein the target of interest is an antigen expressed on the surface of a cancer cell, wherein optionally the second target of interest is CD70, HER2, DLL3, NECTIN-4, TROP-2, Mesothelin, LIV-1, C-MET, FOLR1, CD20, CCR8, CD33, or EGFR.

~~158.—The method of any one of claims 151-157, wherein the target of interest is an antigen expressed on the surface of a cancer cell.~~

~~159.—The method of claim 158, wherein the second target of interest is CD70, HER2, DLL3, NECTIN-4, TROP-2, Mesothelin, LIV-1, C-MET, FOLR1, CD20, CCR8, CD33, or EGFR.~~

~~160.43.~~ Use of a composition comprising a multispecific binding molecule in the manufacture of a medicament for~~A method of treating cancer, comprising administering an effective amount of a composition comprising a multispecific binding molecule to~~ in an individual in need thereof, wherein the multispecific binding molecule comprises:

(a) a first antibody or antigen-binding fragment thereof comprising a first antigen-binding domain, wherein the first antigen-binding domain binds to human Dectin-1; and

(b) a second antibody or antigen-binding fragment thereof comprising a second antigen-binding domain, wherein the second antigen binding domain binds to CD70, HER2, DLL3, NECTIN-4, TROP-2, Mesothelin, LIV-1, C-MET, FOLR1, CD20, CCR8, CD33, or EGFR.

~~161.44.~~ The ~~use method~~ of claim ~~43-160~~, wherein the first antigen-binding domain comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the sequence GYTFTDYY (SEQ ID NO:1), a CDR-H2 comprising the sequence INPNSGDT (SEQ ID NO:2), and a CDR-H3 comprising the sequence ARNSGSYSFGY (SEQ ID NO:3), and wherein the VL domain comprises a CDR-L1 comprising the sequence QGISSW (SEQ ID NO:4), a CDR-L2 comprising the sequence GAS (SEQ ID NO:5), and a CDR-L3 comprising the sequence QQAYSFPFT (SEQ ID NO:6);~~;~~

wherein optionally the VH domain comprises a sequence with at least 90% identity to the sequence

QVQLVQSGAEVKKPGASVKVCKSSGYTFTDYYIHWVRQAPGQGLEWMGWINPNSGD
TNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYWGQGTLLTVV
SS (SEQ ID NO:7); and/or wherein the VL domain comprises a sequence with at least 90%
identity to the sequence

DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPS
RFSGSGSGTDFTLTVSSLPEDFATYYCQQAYSFPFTFGPGTKVDIE (SEQ ID NO:8); and

wherein optionally the VH domain of the first antigen-binding domain comprises the sequence
QVQLVQSGAEVKKPGASVKVCKSSGYTFTDYYIHWVRQAPGQGLEWMGWINPNSGD
TNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYWGQGTLLTVV
SS (SEQ ID NO:7); and/or wherein the VL domain of the first antigen-binding domain comprises
the sequence

DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPS
RFSGSGSGTDFTLTVSSLPEDFATYYCQQAYSFPFTFGPGTKVDIE (SEQ ID NO:8).

162. — The method of claim 160, wherein the first antigen-binding domain comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1, CDR-H2, and CDR-H3 from the VH domain sequence

~~QVQLVQSGAEVKKPGASVKVCKSSGYTFTDYYIHWVRQAPGQGLEWMGWINPNSGD
TNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYWGQGTLLTVV
SS (SEQ ID NO:7), and wherein the VL domain comprises a CDR-L1, CDR-L2, and CDR-L3
from the VL domain sequence~~

~~DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPS
RFSGSGSGTDFTLTVSSLPEDFATYYCQQAYSFPFTFGPGTKVDIE (SEQ ID NO:8).~~

163. — The method of claim 161 or claim 162, wherein the VH domain comprises a sequence with at least 90% identity to the sequence

~~QVQLVQSGAEVKKPGASVKVCKSSGYTFTDYYIHWVRQAPGQGLEWMGWINPNSGD
TNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYWGQGTLLTVV
SS (SEQ ID NO:7); and/or wherein the VL domain comprises a sequence with at least 90%
identity to the sequence~~

~~DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPS
RFSGSGSGTDFTLTVSSLPEDFATYYCQQAYSFPFTFGPGTKVDIE (SEQ ID NO:8).~~

~~164.—The method of claim 163, wherein the VH domain of the first antigen-binding domain comprises the sequence
QVQLVQSGAEVKKPGASVKVSCKSSGYTFTDYYIHVVRQAPGQGLEWMGWINPNSGD
TNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSEGYWGQGTLLVTV
SS (SEQ ID NO:7); and/or wherein the VL domain of the first antigen-binding domain comprises the sequence
DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPS
RFSGSGSGTDFTLTLSLQPEDFATYYCQQAYSFPFTFGPGTKVDIE (SEQ ID NO:8).~~

~~165.45.~~ The ~~use~~method of ~~claim 43 or claim 44~~any one of claims 160-164, wherein:

~~(a) the second antigen binding domain binds to CD20; wherein the second antigen-binding domain comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; and wherein the VH domain of the second antigen-binding domain comprises the sequence~~

~~QVQLQQPGAELVKPGASVKMSCKASGYTFTSYNMHWVKQTPGRGLEWIGAIYPGNGD
TSYNQKFKGKATLTADKSSSTAYMQLSSLTSEDSAVYYCARSTYYGGDWYFNVWGAG
TTVTVSA (SEQ ID NO:24) and/or wherein the VL domain of the second antigen-binding domain comprises the sequence
QIVLSQSPAILSASPGEKVTMTCRASSSVSYIHWFFQQKPGSSPKPWIYATSNLASGVPVRF
SGSGSGTSSYSLTISRVEAEDAATYYCQQWTSNPPTFGGGTKLEIK (SEQ ID NO:25);~~

~~(b) the second antigen binding domain binds to Trop-2; wherein the second antigen-binding domain comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; and wherein the VH domain of the second antigen-binding domain comprises the sequence of SEQ ID NO:42 and/or wherein the VL domain of the second antigen-binding domain comprises the sequence of SEQ ID NO:43; or~~

~~(c) the second antigen binding domain binds to light chain amyloid; wherein the second antigen-binding domain comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; and wherein the VH domain of the second antigen-binding domain comprises the sequence of SEQ ID NO:44 and/or wherein the VL domain of the second antigen-binding domain comprises the sequence of SEQ ID NO:45.~~

~~166.—The method of any one of claims 160-164, wherein the second antigen-binding domain binds to Trop-2; wherein the second antigen-binding domain comprises a heavy chain variable~~

~~(VH) domain and a light chain variable (VL) domain; and wherein the VH domain of the second antigen-binding domain comprises the sequence of SEQ ID NO:42 and/or wherein the VL domain of the second antigen-binding domain comprises the sequence of SEQ ID NO:43.~~

~~167. The method of any one of claims 160-164, wherein the second antigen-binding domain binds to light chain amyloid; wherein the second antigen-binding domain comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; and wherein the VH domain of the second antigen-binding domain comprises the sequence of SEQ ID NO:44 and/or wherein the VL domain of the second antigen-binding domain comprises the sequence of (SEQ ID NO:45.~~

~~168-46.~~ 46. The ~~use method~~ of any one of claims ~~43-45~~160-167, wherein:

(a) the multispecific antibody comprises a first antibody arm comprising the first antigen binding domain and a first Fc region and a second antibody arm comprising the second antigen binding domain and a second Fc region, wherein the first Fc region comprises one or more knob-forming mutations, and the second Fc region comprises one or more cognate hole-forming mutations; or

(b) the multispecific antibody comprises a first antibody arm comprising the first antigen binding domain and a first Fc region and a second antibody arm comprising the second antigen binding domain and a second Fc region, wherein the first Fc region comprises one or more hole-forming mutations, and the second Fc region comprises one or more cognate knob-forming mutations;

wherein optionally the first Fc region comprises a T366W substitution, and wherein the second Fc region comprises T366S, L368A, and Y407V substitutions, according to EU numbering; or the first Fc region comprises T366S, L368A, and Y407V substitutions, and wherein the second Fc region comprises a T366W substitution, according to EU numbering.

~~169. The method of claim 168, wherein:~~

~~(a) wherein the first Fc region comprises a T366W substitution, and wherein the second Fc region comprises T366S, L368A, and Y407V substitutions, according to EU numbering; or~~

~~(b) the first Fc region comprises T366S, L368A, and Y407V substitutions, and wherein the second Fc region comprises a T366W substitution, according to EU numbering.~~

~~170-47.~~ The ~~use~~method of any one of claims ~~43-46~~~~160-169~~, wherein:

(a) the antibody comprises two antibody heavy chains, and wherein only one of the antibody heavy chains comprises H435R and Y436F substitutions, according to EU numbering;

(b) only one of the antibody arms comprises a heavy chain comprising F126C and C220V substitutions and a light chain comprising S121C and C214V substitutions, according to EU numbering; and/or

(c) the first and second antibody heavy chains comprise human IgG1 Fc domains.

~~171. The method of any one of claims 160-170, wherein only one of the antibody arms comprises a heavy chain comprising F126C and C220V substitutions and a light chain comprising S121C and C214V substitutions, according to EU numbering.~~

~~172. The method of any one of claims 160-171, wherein the first and second antibody heavy chains comprise human IgG1 Fc domains.~~

~~173-48.~~ The ~~use~~method of ~~claim 43 or claim 44~~any one of claims ~~160-164~~, wherein the second antigen binding domain binds to CD20; and wherein the multispecific binding molecule comprises three polypeptide chains:

(a) a first polypeptide chain comprising the sequence

QVQLVQSGAEVKKPGASVKVSKSSGYTFTDYYIHWVRQAPGQGLEWMGWINP
NSGDTNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYW
GQGTLLTVSSGGGGSGGGGSGGGGSGGGGSDIQMTQSPSSVSASVGDRVITTCR
ASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPSRFSGSGSGTDFTLTVSSLQP
EDFATYYCQAYSFPTFGPGTKVDIEPKRSDKTHTCPPELGGPSVFLFPP
KPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNS
TYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL
PSREEMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFL
YSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG (SEQ ID NO:31);

(b) a second polypeptide chain comprising the sequence

QVQLQQPGAELVKPGASVKMSCKASGYTFTSYNMHWVKQTPGRGLEWIGAIYP
GNGDTSYNQKFKGKATLTADKSSSTAYMQLSSLTSEDSAVYYCARSTYYGGDW
YFNVWGAGTTVTVSAASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVD

KKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYK
CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPS
DIAVEWESNGQPENNYKTTTPVLDSGSSFLVSKLTVDKSRWQQGNVFSCSVMH
EALHNRFTQKSLSLSPG (SEQ ID NO:32); and

(c) a third polypeptide chain comprising the sequence

QIVLSQSPAILSASPGEKVTMTCRASSSVSYIHWFQQKPGSSPKPWIYATSNLASG
VPVRFSGSGSGTSYSLTISRVEAEDAATYYCQQWTSNPPTFGGGTKLEIKRTVAA
PSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQD
SKDSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID
NO:33).

174.49. The usemethod of any one of claims 43-48~~160-173~~, wherein at least one or two of the first and second antibody heavy chains is/are non-fucosylated.

175.50. The usemethod of any one of claims 39-49~~151-174~~, wherein the individual is a human.