

BRIEF SUMMARY

[0008] The present disclosure relates to antibodies that bind human Dectin-1, multispecific (*e.g.*, bispecific) binding molecules, and methods of use and production related thereto. Described herein are methods of targeted phagocytosis to remove disease-causing agents, including host cells/host cell products, microbes or their products, etc., upon administration of multispecific (*e.g.*, bispecific) binding molecules comprising a Dectin-1 binding arm and a second arm that specifically binds to the agent. The multispecific (*e.g.*, bispecific) binding molecules allow the phagocyte to engage the target agent and form a synapse between it and promote clustering of Dectin-1 on the phagocyte. This stimulates phagocytosis of the target agent and at the same time cytokine secretion via the Dectin-1/Syk/NfκB pathway by the phagocyte. Moreover, antigens from the engulfed material are presented on the surface of dendritic cells/macrophages to boost an adaptive immune response against the disease-causing agent. Overall, it is thought that the Dectin-1 agonistic, multispecific (*e.g.*, bispecific) binding molecules promote immune stimulation, targeted phagocytosis, and neo-antigen presentation/activation of the adaptive immune system to eliminate the disease-causing agent.

[0009] As such, the present disclosure describes, *inter alia*, the generation and functional characterization of an agonistic anti-human Dectin-1 antibody that exhibits high affinity binding to Dectin-1 and can promote immune stimulation. Further described is the generation of bispecific antibody formats including the anti-human Dectin-1 antibody with antibodies targeting antigens on disease-causing agents, with data supporting target engagement, immune stimulation, phagocytosis, and antigen presentation.

[0010] In ~~one aspect~~~~some embodiments~~, provided herein is 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). In some ~~embodiment~~~~examples~~, provided herein is 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 QVQLVQSGAEVKKPGASVKVSCKSSGYTFTDYYIHWVRQAPGQGLEWMGWINPNSGD

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

DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPSRFSGSGSGTDFTLTVSSSLQPEDFATYYCQQAYSFPFTFGPGTKVDIE (SEQ ID NO:8). In

some [embodiment examples](#), provided herein is 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 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 GASSLQSS (SEQ ID NO:92), and a CDR-L3 comprising the sequence QQAYSFPFT (SEQ ID NO:6). In

some [embodiment examples](#), the VH domain comprises a sequence with at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to the amino acid sequence

QVQLVQSGAEVKKPGASVKVSCKSSGYTFTDYYIHWVRQAPGQGLEWMGWINPNSGDTNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYWGQGLVTVSS (SEQ ID NO:7); and/or the VL domain comprises a sequence with at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to the amino acid sequence

DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPSRFSGSGSGTDFTLTVSSSLQPEDFATYYCQQAYSFPFTFGPGTKVDIE (SEQ ID NO:8). In

some [embodiment examples](#), the VH domain comprises the sequence

QVQLVQSGAEVKKPGASVKVSCKSSGYTFTDYYIHWVRQAPGQGLEWMGWINPNSGDTNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYWGQGLVTVSS (SEQ ID NO:7); and/or the VL domain comprises the sequence

DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPSRFSGSGSGTDFTLTVSSSLQPEDFATYYCQQAYSFPFTFGPGTKVDIE (SEQ ID NO:8). In

some [embodiment examples](#), provided herein is 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, less than 1nM, or less than 0.5nM. In some [embodiment examples](#), provided herein is 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. In some [embodiment examples](#), provided herein is an antibody or antigen-binding fragment thereof that binds to human Dectin-1, wherein the antibody or fragment does not compete (*e.g.*, for binding to human Dectin-1) with a native ligand of Dectin-1, *e.g.*, human Dectin-1. In some [embodiment examples](#), 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

QVQLVQSGAEVKKPGASVKVCKSSGYTFTDYYIHVVRQAPGQGLEWMGWINPNSGD
TNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYWGQGTLLVTV
SS (SEQ ID NO:7) and a light chain variable (VL) domain comprising the sequence

DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPS
RFGSGSGTDFTLTSSLQPEDFATYYCQQAYSFPFTFGPGTKVDIE (SEQ ID NO:8). In

some [embodiment examples](#), 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 QQAYSFPFT (SEQ ID NO:6); or (c) a heavy chain variable (VH) domain comprising the sequence

QVQLVQSGAEVKKPGASVKVSCKSSGYTFTDYYIHWVRQAPGQGLEWMGWINPNSGD
TNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSSGYSFGYWGGTLVTV
SS (SEQ ID NO:7) and a light chain variable (VL) domain comprising the sequence
DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPS
RFGSGSGTDFTLTVSSSLQPEDFATYYCQQAYSFPFTFGPGTKVDIE (SEQ ID NO:8). In

some [embodimentexamples](#), the antibody or fragment is a human, humanized, or chimeric antibody or fragment. In some [embodimentexamples](#), the antibody or fragment binds to human Dectin-1 expressed on the surface of a macrophage, monocyte, dendritic cell, and/or granulocyte. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), the antibody further comprises an Fc region. In some [embodimentexamples](#), the antibody or fragment is a multispecific antibody or fragment. In some [embodimentexamples](#), 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 that binds to a target of interest or comprising a first antigen binding domain that binds to a target of interest and a second antigen binding domain comprising the VH and VL domains that bind to human Dectin-1. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), the first Fc region comprises a T366W substitution, and the second Fc region comprises T366S, L368A, and Y407V substitutions, according to EU numbering. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), the first linker comprises one or more repeats of the sequence GGGGS (SEQ ID NO:26). In some [embodimentexamples](#), the first linker comprises the sequence GGGGSGGGGSGGGGS (SEQ ID NO:27) or GGGGSGGGGSGGGGSGGGGS (SEQ ID NO:28). In some [embodimentexamples](#), the second linker comprises the sequence EPKRSDKTHTCPPC (SEQ ID NO:29) or SATHTCPPC (SEQ ID NO:30). In some [embodimentexamples](#), 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. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), the first Fc region comprises a T366W substitution, and the second Fc region comprises T366S, L368A, and Y407V substitutions, according to EU numbering. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), the first Fc region comprises T366S, L368A, and Y407V substitutions, and the second Fc region comprises a T366W substitution, according to EU numbering. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), the target of interest is a disease-causing agent. In some [embodimentexamples](#), the disease-causing agent is a bacterial cell, fungal cell, virus, senescent cell, tumor cell, protein aggregate (*e.g.*, amyloid beta, or lambda or kappa light chain amyloids), LDL particle, mast cell, eosinophil, ILC2 cell, or inflammatory immune cell. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), the target of interest is a surface antigen of the virus. In some [embodimentexamples](#), the target of interest is an antigen expressed on the surface of a cancer cell. In some [embodimentexamples](#), the target of interest is CD70, HER2, DLL3, NECTIN-4, TROP-2, Mesothelin, LIV-1, C-MET, FOLR1, CD20, CCR8, CD33, or EGFR. In some [embodimentexamples](#), the target of interest is CD20; the second antigen-binding domain comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; and the VH domain of the second antigen-binding domain comprises the sequence QVQLQQPGAELVKPGASVKMSCKASGYTFTSYNMHWVKQTPGRGLEWIGAIYPGNGDTSYNQKFKGKATLTADKSSSTAYMQLSSLTSEDSAVYYCARSTYYGGDWYFNVWGAGTTVTVSA (SEQ ID NO:24) and/or the VL domain of the second antigen-binding domain comprises the sequence QIVLSQSPAILSASPGEKVTMTCRASSSVSYIHWFQQKPGSSPKPWIYATSNLASGVPVRFSGSGSGTSYSLTISRVEAEDAATYYCQQWTSNPPTFGGGTKLEIK (SEQ ID NO:25). In some [embodimentexamples](#), 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. In some [embodimentexamples](#), each of the antibody heavy chains comprises L234A, L235E, and G237A substitutions, according to EU numbering. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), the antibody comprises two arms, and 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. In some [embodimentexamples](#), the bispecific antibody comprises a first and a second antibody heavy chain, 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. In some [embodimentexamples](#), the first and second antibody heavy chains further comprise L234A, L235E, and G237A substitutions, according to EU numbering. In some [embodimentexamples](#), the first and second antibody heavy chains comprise human IgG1 Fc domains. In some [embodimentexamples](#), the 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. In some [embodimentexamples](#), the antibody may be produced in a cell line having an alpha1,6-fucosyltransferase (Fut8) or alpha-1,3-mannosylglycoprotein 2-beta-N-acetylglucosaminyltransferase (MGAT1) knockout. In some [embodimentexamples](#), the antibody may be produced in a cell line overexpressing β 1,4-N-acetylglucosaminyltransferase III (GnT-III). In further [embodimentexamples](#), the cell line additionally overexpresses Golgi μ -mannosidase II (ManII). In some [embodimentexamples](#), the antibody may be produced in a cell line treated with an inhibitor of mannosidase I, *e.g.*, kifunensine.

[0011] In [one aspectsome-embodiments](#), provided herein is 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. In some [embodimentexamples](#), the target of interest is a disease-causing agent. In some [embodimentexamples](#), the disease-causing agent is a bacterial cell, fungal cell, virus, senescent cell, tumor cell, protein aggregate (*e.g.*, amyloid beta, or lambda or kappa light chain amyloids), LDL particle, mast cell, eosinophil, ILC2 cell, or inflammatory immune cell. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), the target of interest is a surface antigen of the virus. In some [embodimentexample](#)s, the target of interest is CD70, HER2, DLL3, NECTIN-4, TROP-2, Mesothelin, LIV-1, C-MET, FOLR1, CD20, CCR8, CD33, or EGFR. In some [embodimentexamples](#), 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). In some [embodimentexamples](#), 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
TNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYWGGTLVTV
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). In some [embodimentexamples](#), the VH domain comprises a sequence with at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to the amino acid sequence

QVQLVQSGAEVKKPGASVKVSKSSGYTFTDYYIHWVRQAPGQGLEWMGWINPNSGD
TNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYWGGTLVTV
SS (SEQ ID NO:7); and/or the VL domain comprises a sequence with at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to the amino acid sequence

DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPS
RFSGSGSGTDFTLTVSSLPEDFATYYCQQAYSFPFTFGPGTKVDIE (SEQ ID NO:8). In some [embodimentexamples](#), the VH domain comprises the sequence

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

DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPS
RFSGSGSGTDFTLTVSSLPEDFATYYCQQAYSFPFTFGPGTKVDIE (SEQ ID NO:8). In some [embodimentexamples](#), the first antigen-binding domain: binds to human Dectin-1

expressed on the surface of a macrophage, monocyte, dendritic cell, or granulocyte; binds to human Dectin-1 expressed on the surface of a cell with an EC₅₀ of less than 2nM; is capable of binding human or cynomolgus Dectin-1; and/or does not compete with a native ligand of human Dectin-1. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), one or both of the first and second antibodies or fragments are human or humanized antibodies or fragments. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), one or both of the first and second antibodies or fragments further comprise an Fc domain. In some [embodimentexamples](#), the first antibody or fragment is a Fab fragment, and wherein the second antibody or fragment is a full-length antibody, *e.g.*, that comprises an antibody heavy chain and an antibody light chain. In some [embodimentexamples](#), the first and the second antibodies or fragments are both full-length antibodies, *e.g.*, that each comprise an antibody heavy chain and an antibody light chain. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), the first Fc region comprises a T366W substitution, and the second Fc region comprises T366S, L368A, and Y407V substitutions, according to EU numbering. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), the first linker comprises one or more repeats of the sequence GGGGS (SEQ ID NO:26). In some [embodimentexamples](#), the first linker comprises the sequence GGGGSGGGGSGGGGS (SEQ ID NO:27) or GGGGSGGGGSGGGGSGGGGS (SEQ ID NO:28). In some [embodimentexamples](#), the second linker comprises the sequence EPKRSDKTHTCPPC (SEQ ID NO:29) or SATHTCPPC (SEQ ID NO:30). In some [embodimentexamples](#), 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. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), the first Fc region comprises a T366W substitution, and wherein the second Fc region comprises T366S, L368A, and Y407V substitutions, according to EU numbering. In some [embodimentexamples](#), the multispecific binding molecule comprises a first antibody arm comprising the VH domain of the first antigen binding domain and a first Fc region and a second antibody arm comprising 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. In some [embodimentexamples](#), the first Fc region comprises T366S, L368A, and Y407V substitutions, and wherein the second Fc region comprises a T366W substitution, according to EU numbering. In some [embodimentexamples](#), the multispecific binding molecule comprises two antibody Fc regions, 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. In some [embodimentexamples](#), each of the antibody Fc regions comprises L234A, L235E, and G237A substitutions, according to EU numbering. In some [embodimentexamples](#), the multispecific binding molecule comprises two antibody heavy chains, and wherein only one of

the antibody heavy chains comprises H435R and Y436F substitutions, according to EU numbering. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), the first and second antibody heavy chains further comprise L234A, L235E, and G237A substitutions, according to EU numbering. In some [embodimentexamples](#), the first and second antibody heavy chains comprise human IgG1 Fc domains. In some [embodimentexamples](#), at least one or two of the heavy chains of the antibody is non-fucosylated. In some [embodimentexamples](#), the antibody may be produced in a cell line having an alpha1,6-fucosyltransferase (Fut8) or alpha-1,3-mannosyl-glycoprotein 2-beta-N-acetylglucosaminyltransferase (MGAT1) knockout. In some [embodimentexamples](#), the antibody may be produced in a cell line overexpressing β 1,4-N-acetylglucosaminyltransferase III (GnT-III). In further [embodimentexamples](#), the cell line additionally overexpresses Golgi μ -mannosidase II (ManII). In some [embodimentexamples](#), the antibody may be produced in a cell line treated with an inhibitor of mannosidase I, *e.g.*, kifunensine.

[0012] In some [embodimentexamples](#), provided herein is 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. In some [embodimentexamples](#), the first target of interest is human Dectin-1. In some [embodimentexamples](#), 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). In some [embodimentexamples](#), 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
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

DIQMTQSPSSVSASVGDRVTITCRASQGISWLAWEYQQKPGKAPKLLIFGASSLQSGVPS
RFGSGSGTDFTLTLSLQPEDFATYYCQQAYSFPFTFGPGTKVDIE (SEQ ID NO:8). In some [embodimentexamples](#), 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 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). In some [embodimentexamples](#), the VH domain comprises a sequence with at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to the amino acid sequence

QVQLVQSGAEVKKPGASVKVCKSSGYTFTDYYIHWVRQAPGQGLEWMGWINPNSGD
TNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYWGQGTLLVTV
SS (SEQ ID NO:7); and/or the VL domain comprises a sequence with at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to the amino acid sequence

DIQMTQSPSSVSASVGDRVTITCRASQGISWLAWEYQQKPGKAPKLLIFGASSLQSGVPS

RFSGSGSGTDFTLTIVSSSLQPEDFATYYCQQAYSFPFTFGPGTKVDIE (SEQ ID NO:8). In some embodiment examples, the VH domain comprises the sequence QVQLVQSGAEVKKPGASVKVCKSSGYTFTDYYIHVVRQAPGQGLEWMGWINPNSGD TNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGYSYSGYWGQGTLVTVSS (SEQ ID NO:7); and/or wherein the VL domain comprises the sequence DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPS RFSGSGSGTDFTLTIVSSSLQPEDFATYYCQQAYSFPFTFGPGTKVDIE (SEQ ID NO:8). In one aspect some embodiments, provided herein is a multispecific binding molecule, comprising: (a) a first polypeptide chain comprising the sequence QVQLVQSGAEVKKPGASVKVCKSSGYTFTDYYIHVVRQAPGQGLEWMGWINPNSGD TNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGYSYSGYWGQGTLVTVSSSGGGGSGGGGSGGGGSGGGGSDIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPSRFSGSGSGTDFTLTIVSSSLQPEDFATYYCQQAYSFPFTFGPGTKVDIEEPKRSDKTHTCPPCPAPPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG (SEQ ID NO:31); (b) a second polypeptide chain comprising the sequence QVQLQQPGAELVKPGASVKMSCKASGYTFTSYNMHWVKQTPGRGLEWIGAIYPGNGDTSYNQKFQKFKATLTADKSSSTAYMQLSSLTSEDSAVYYCARSTYYGGDWYFNWVGAGTTVTVSAASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCSVMHEALHNRFYTKKSLSLSPG (SEQ ID NO:32); and (c) a third polypeptide chain comprising the sequence QIVLSQSPAILSASPGEKVTMTCRASSSVSYIHWFFQQKPGSSPKPWIYATSNLASGVPVRFSGSGSGTSYSLTISRVEAEDAATYYCQQWTSNPPTFGGGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSSTYSLSSTLTLSKADYEEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:33). In one aspect some embodiments, provided herein is 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

QVQLVQSGAEVKKPGASVKVSCKSSGYTFTDYYIHWVRQAPGQGLEWMGWINPNSGD
TNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYWGGTLVTV
SSGGGGSGGGGSGGGGSGGGGSDIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQ
QKPGKAPKLLIFGASSLQSGVPSRFSGSGSGTDFTLTSSLQPEDFATYYCQQAYSFPFTF
GPGTKVDIEEPKRSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS
HEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV
NKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVKGFYPSDIAVEWESN
GQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLS
LSPG (SEQ ID NO:31). In some [embodimentexamples](#), the first antigen-binding domain binds to human Dectin-1 expressed on the surface of a macrophage, monocyte, dendritic cell, or granulocyte. In some [embodimentexamples](#), one or both of the first and second antibodies or fragments are human or humanized antibodies or fragments. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), one or both of the first and second antibodies or fragments further comprise an Fc domain. In some [embodimentexamples](#), the first antibody or fragment is a Fab fragment, and wherein the second antibody comprises an antibody heavy chain and an antibody light chain. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), the second target of interest is a disease-causing agent. In some [embodimentexamples](#), the disease-causing agent is a bacterial cell, fungal cell, virus, senescent cell, tumor cell, protein aggregate (*e.g.*, amyloid beta, or lambda or kappa light chain amyloids), LDL particle, mast cell, eosinophil, ILC2 cell, or inflammatory immune cell. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), the target of interest is a surface antigen of the virus. In some [embodimentexamples](#), the target of interest is an antigen expressed on the surface of a cancer cell. In some [embodimentexamples](#), the target of interest is CD70, HER2, DLL3, NECTIN-4, TROP-2, Mesothelin, LIV-1, C-MET, FOLR1, CD20, CCR8, CD33, or EGFR. In some [embodimentexamples](#), the target of interest is CD20; the second antigen-binding domain comprises a

heavy chain variable (VH) domain and a light chain variable (VL) domain; and the VH domain of the second antigen-binding domain comprises the sequence QVQLQQPGAELVKPGASVKMSCKASGYTFTSYNMHWVKQTPGRGLEWIGAIYPGNGDTSYNQKFKGKATLTADKSSSTAYMQLSSLTSEDSAVYYCARSTYYGGDWYFNVWGAGTTVTVSA (SEQ ID NO:24) and/or the VL domain of the second antigen-binding domain comprises the sequence

QIVLSQSPAILSASPGEKVTMTCRASSSVSYIHWFQQKPGSSPKPWIYATSNLASGVPVRFSGSGSGTSYSLTISRVEAEDAATYYCQQWTSNPPTFGGGTKLEIK (SEQ ID NO:25). In some [embodimentexamples](#), 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. In some [embodimentexamples](#), 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.

[0013] In some [embodimentexamples](#), provided herein is a polynucleotide encoding the antibody or multispecific binding molecule of any one of the above [embodimentexamples](#). [In one aspect, provided herein is a polynucleotide encoding the antibody or multispecific binding molecule as disclosed herein.](#) In some [embodimentexamples](#), provided herein is a vector (e.g., an expression vector) comprising the polynucleotide of any one of the above [embodimentexamples](#). [In one aspect, provided herein is a vector comprising the polynucleotide as disclosed herein.](#) In some [embodimentexamples](#), provided herein is a host cell (e.g., an isolated host cell or cell line) comprising the polynucleotide or vector of any one of the above [embodimentexamples](#). [In one aspect, provided herein is an isolated host cell comprising the polynucleotide of as disclosed herein or the vector as disclosed herein.](#) In some [embodimentexamples](#), provided herein is a method of producing an antibody or multispecific binding molecule, comprising culturing the host cell of any one of the above [embodimentexamples](#) under conditions suitable for production of the antibody or multispecific binding molecule. [In one aspect, provided herein is a method of producing an antibody or multispecific binding molecule, comprising culturing the host cell as disclosed herein under conditions suitable for production of the antibody or multispecific binding molecule.](#) In some [embodimentexamples](#), the method further comprises recovering the antibody or multispecific binding molecule. [In one aspect, provided herein is an antibody or antigen-binding fragment thereof that binds to human Dectin-1 produced by the method as disclosed herein.](#) In some [embodimentexamples](#), provided herein is a pharmaceutical composition comprising the antibody or multispecific binding molecule of any one of the above [embodimentexamples](#) and a pharmaceutically acceptable carrier. [In one aspect, provided herein is a pharmaceutical composition comprising the antibody or multispecific binding molecule as disclosed herein and a pharmaceutically acceptable carrier.](#)

[0014] In some [embodimentexamples](#), provided herein is 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. In some [embodiment examples](#), provided herein is 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. In some [embodiment examples](#), the first target of interest is human Dectin-1. In some [embodiment examples](#), 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). In some [embodiment examples](#), 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
TNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYWGQGTLLTV

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
RFSGSGSGTDFTLTVSSSLQPEDFATYYCQQAYSFPFTFGPGTKVDIE (SEQ ID NO:8). In some [embodimentexamples](#), 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). In some [embodimentexamples](#), the VH domain comprises a sequence with at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to the amino acid sequence

QVQLVQSGAEVKKPGASVKVSCKSSGYTFTDYYIHWVRQAPGQGLEWMGWINPNSGD
TNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYWGQGTLLTVV
SS (SEQ ID NO:7); and/or the VL domain comprises a sequence with at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to the amino acid sequence

DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPS
RFSGSGSGTDFTLTVSSSLQPEDFATYYCQQAYSFPFTFGPGTKVDIE (SEQ ID NO:8). In some [embodimentexamples](#), the VH domain comprises the sequence

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

DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPS
RFSGSGSGTDFTLTVSSSLQPEDFATYYCQQAYSFPFTFGPGTKVDIE (SEQ ID NO:8). In

some [embodimentexamples](#), the first antigen-binding domain binds to human Dectin-1 expressed on the surface of a macrophage, monocyte, dendritic cell, or granulocyte. In some

[embodimentexamples](#), one or both of the first and second antibodies or fragments are human or humanized antibodies or fragments. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), one or both of the first and second antibodies or fragments further comprise an Fc domain. In some [embodimentexamples](#), the first antibody or fragment is a Fab fragment,

and wherein the second antibody or fragment is a full-length antibody, *e.g.*, that comprises an antibody heavy chain and an antibody light chain. In some [embodimentexamples](#), the first and the second antibodies or fragments are both full-length antibodies, *e.g.*, that each comprise an antibody heavy chain and an antibody light chain. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), the second target of interest is a disease-causing agent. In some [embodimentexamples](#), the disease-causing agent is a bacterial cell, fungal cell, virus, senescent cell, tumor cell, protein aggregate (*e.g.*, amyloid beta, or lambda or kappa light chain amyloids), LDL particle, mast cell, eosinophil, ILC2 cell, or inflammatory immune cell. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), the target of interest is a surface antigen of the virus. In some [embodimentexamples](#), the target of interest is an antigen expressed on the surface of a cancer cell. In some [embodimentexamples](#), the target of interest is CD70, HER2, DLL3, NECTIN-4, TROP-2, Mesothelin, LIV-1, C-MET, FOLR1, CD20, CCR8, CD33, or EGFR. In some [embodimentexamples](#), the target of interest is CD20, the second antigen-binding domain comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, and the VH domain of the second antigen-binding domain comprises the sequence

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

comprises the sequence

QIVLSQSPAILSASPGEKVTMTCRASSSVSYIHWFFQKPGSSPKPWYATSNLASGVPVRF
SGSGSGTSYSLTISRVEAEDAATYYCQQWTSNPPTFGGGTKLEIK (SEQ ID NO:25). In

some [embodimentexamples](#), the antibody comprises two antibody Fc regions, and wherein each of the antibody Fc regions comprises an amino acid substitution at one or more of positions 234, 235, and 237, according to EU numbering. In some [embodimentexamples](#), each of the antibody heavy chains comprises L234A, L235E, and G237A substitutions, according to EU numbering. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), the first and second antibody heavy chains further comprise L234A, L235E, and G237A substitutions, according to EU numbering. In some [embodimentexamples](#), the first and second antibody heavy chains comprise human IgG1 Fc domains. In some [embodimentexamples](#), at least one or two of the heavy chains of the antibody is non-fucosylated. In some [embodimentexamples](#), the antibody may be produced in a cell line having an alpha1,6-fucosyltransferase (Fut8) or alpha-1,3-mannosyl-glycoprotein 2-beta-N-acetylglucosaminyltransferase (MGAT1) knockout. In some [embodimentexamples](#), the antibody may be produced in a cell line overexpressing beta1,4-N-acetylglucosaminyltransferase III (GnT-III). In further [embodimentexamples](#), the cell line additionally overexpresses Golgi mu-mannosidase II (ManII). In some [embodimentexamples](#), the antibody may be produced in a cell line treated with an inhibitor of mannosidase I, *e.g.*, kifunensine.

[0015] In some [embodimentexamples](#), provided herein is a method of treating a disease or disorder, comprising administering an effective amount of the antibody, multispecific binding molecule, or composition of any one of the above [embodimentexamples](#) to an individual in need thereof. In one aspect, provided herein is use of the antibody as disclosed herein, the multispecific binding molecule as disclosed herein, or the composition as disclosed herein in the manufacture of a medicament for treating a disease or disorder in an individual in need thereof.

In some [embodimentexamples](#), the first target of interest is human Dectin-1, and wherein the second target of interest is a disease-causing agent. In some [embodimentexamples](#), the disease-causing agent is a bacterial cell, fungal cell, virus, senescent cell, tumor cell, protein aggregate (*e.g.*, amyloid beta, or lambda or kappa light chain amyloids), LDL particle, mast cell, eosinophil, ILC2 cell, or inflammatory immune cell. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), the target of interest is a surface antigen of the virus. In some [embodimentexamples](#), the disease or disorder is cancer, a bacterial infection, a fungal infection, a viral infection, a mast cell disease or disorder, systemic mastocytosis, amyloidosis (*e.g.*, light chain amyloidosis or Alzheimer's disease), or an aging-related disease or disorder. In some [embodimentexamples](#), the target of interest is CD70, HER2, DLL3, NECTIN-4, TROP-2,

Mesothelin, LIV-1, C-MET, FOLR1, CD20, CCR8, CD33, or EGFR. In some

embodimentexamples, the individual is a human.

[0016] In some embodimentexamples, provided herein is a method of treating cancer, comprising administering an effective amount of a composition comprising a multispecific binding molecule to 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. In one aspect, provided herein is use of a composition comprising a multispecific binding molecule in the manufacture of a medicament for treating cancer 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. In some embodimentexamples, the second antigen binding domain binds to human CD70, human HER2, human DLL3, human NECTIN-4, human TROP-2, human Mesothelin, human LIV-1, human C-MET, human FOLR1, human CD20, human CCR8, human CD33, or human EGFR, *e.g.*, as expressed on the surface of a cancer cell. In some embodimentexamples, 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). In some embodimentexamples, 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
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
DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPS
RFGSGSGTDFTLTVSSLQPEDFATYYCQQAYSFPFTFGPGTKVDIE (SEQ ID NO:8). In some embodimentexamples, 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). In some embodiment examples, the VH domain comprises a sequence with at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to the amino acid sequence

QVQLVQSGAEVKKPGASVKVSKSSGYTFTDYYIHWVRQAPGQGLEWMGWINPNSGD
TNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYWGQGTLLTVV
SS (SEQ ID NO:7); and/or the VL domain comprises a sequence with at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to the amino acid sequence

DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPS
RFSGSGSGTDFTLTIVSSLPEDFATYYCQQAYSFPFTFGPGTKVDIE (SEQ ID NO:8). In

some embodiment examples, the VH domain of the first antigen-binding domain comprises the sequence

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

DIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQQKPGKAPKLLIFGASSLQSGVPS
RFSGSGSGTDFTLTIVSSLPEDFATYYCQQAYSFPFTFGPGTKVDIE (SEQ ID NO:8). In

some embodiment examples, 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
TSYNQKFQKATLTADKSSSTAYMQLSSLTSEDSAVYYCARSTYYGGDWYFNVWGAG
TTVTVSA (SEQ ID NO:24) and/or wherein the VL domain of the second antigen-binding domain comprises the sequence

QIVLSQSPAILSASPGEKVTMTCRASSSVSYIHWVFQQKPGSSPKPWIYATSNLASGVPVRF
SGSGSGTSYSLTISRVEAEDAATYYCQQWTSNPPTFGGGTKLEIK (SEQ ID NO:25). In

some embodiment examples, the multispecific binding molecule 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. In some embodiment examples, the first Fc region comprises a

T366W substitution, and the second Fc region comprises T366S, L368A, and Y407V substitutions, according to EU numbering. In some [embodimentexamples](#), the multispecific binding molecule 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. In some [embodimentexamples](#), the first Fc region comprises T366S, L368A, and Y407V substitutions, and the second Fc region comprises a T366W substitution, according to EU numbering. In some [embodimentexamples](#), the antibody comprises two antibody Fc regions, and wherein each of the antibody Fc regions comprises an amino acid substitution at one or more of positions 234, 235, and 237, according to EU numbering. In some [embodimentexamples](#), each of the antibody heavy chains comprises L234A, L235E, and G237A substitutions, according to EU numbering. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), 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. In some [embodimentexamples](#), the first and second antibody heavy chains further comprise L234A, L235E, and G237A substitutions, according to EU numbering. In some [embodimentexamples](#), the first and second antibody heavy chains comprise human IgG1 Fc domains. In some [embodimentexamples](#) (e.g., wherein the second antigen binding domain binds to CD20), the antibody comprises three polypeptide chains: a first polypeptide chain comprising the sequence

QVQLVQSGAEVKKPGASVKVSCKSSGYTFTDYYIHWVRQAPGQGLEWMGWINPNSGD
TNYAQKFQGRITMTRDTSISTAYLELSRLRSDDTAVFYCARNSGSYSFGYWGQGTLLVTV
SSGGGGSGGGGSGGGGSGGGGSDIQMTQSPSSVSASVGDRVTITCRASQGISSWLAWYQ
QKPGKAPKLLIFGASSLQSGVPSRFSGSGSGTDFTLTSSLQPEDFATYYCQQAYSFPFTF
GPGTKVDIEPKRSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS

HEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG (SEQ ID NO:31), a second polypeptide chain comprising the sequence

QVQLQQPGAELVKPGASVKMSCKASGYTFTSYNMHWVKQTPGRGLEWIGAIYPGNGDTSYNQKFKGKATLTADKSSSTAYMQLSSLTSEDSAVYYCARSTYYGGDWYFNVWGAGTTVTVSAASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCSVMHEALHNRTQKSLSLSPG (SEQ ID NO:32), and a third polypeptide chain comprising the sequence

QIVLSQSPAILSASPGEKVTMTCRASSSVSYIHWFQQKPGSSPKPWIYATSNLASGVPVRFSGSGSGTSYSLTISRVEAEDAATYYCQQWTSNPPTFGGGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDESTYSLSSLTSLTKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:33). In some

[embodimentexamples](#), at least one or two of the heavy chains of the antibody is non-fucosylated. In some [embodimentexamples](#), the antibody may be produced in a cell line having an alpha1,6-fucosyltransferase (Fut8) or alpha-1,3-mannosyl-glycoprotein 2-beta-N-acetylglucosaminyltransferase (MGAT1) knockout. In some [embodimentexamples](#), the antibody may be produced in a cell line overexpressing β 1,4-N-acetylglucosaminyltransferase III (GnT-III). In further [embodimentexamples](#), the cell line additionally overexpresses Golgi μ -mannosidase II (ManII). In some [embodimentexamples](#), the antibody may be produced in a cell line treated with an inhibitor of mannosidase I, *e.g.*, kifunensine. In some [embodimentexamples](#), the individual is a human.

[0017] In some [embodimentexamples](#), provided herein is a kit or article of manufacture comprising the antibody, multispecific binding molecule, or composition of any one of the above [embodimentexamples](#) and instructions for using the antibody, multispecific binding molecule, or composition according to the method of any one of the above [embodimentexamples](#).

[0018] It is to be understood that one, some, or all of the properties of the various [embodimentexamples](#) described herein may be combined to form other [embodimentexamples](#) of the present disclosure. These and other aspects of the present disclosure will become apparent to one of skill in the art. These and other [embodimentexamples](#) of the present disclosure are further described by the detailed description that follows.