

fusion proteins or conjugated to at least one diagnostic and/or therapeutic agent or in combination with other treatment modalities. Binding of human Clec12A with the anti-Clec12A antibodies or fragments thereof described herein may demonstrate Antibody-dependent cellular cytotoxicity (ADCC) activity, including for example induction of apoptosis and inhibition of cancer cell proliferation.

[0005a] In one aspect, the present disclosure provides an anti-Clec12A antibody or antigen-binding fragment thereof comprising:

(a) a heavy chain complementarity determining region (HCDR) 1 comprising an amino acid sequence of GGSISTYY (SEQ ID NO: 19), an HCDR2 comprising an amino acid sequence of IYYSGST (SEQ ID NO: 20), an HCDR3 comprising an amino acid sequence of AREDDYYGSGSPFDY (SEQ ID NO: 21); and a light chain complementarity determining region (LCDR) 1 comprising an amino acid sequence of QGIRYD (SEQ ID NO: 22), an LCDR2 comprising an amino acid sequence of AAS (SEQ ID NO:23), and an LCDR3 comprising an amino acid sequence of LQDYNFPRT (SEQ ID NO: 24);

(e) an HCDR1 comprising an amino acid sequence of GGSISTYY (SEQ ID NO: 19), an HCDR2 comprising an amino acid sequence of IYFSGST (SEQ ID NO: 38), and HCDR3 comprising an amino acid sequence of AREDDYYGSGSPFDY (SEQ ID NO:21); and an LCDR1 comprising an amino acid sequence of QGIRND (SEQ ID NO: 39), an LCDR2 comprising an amino acid sequence of AAS (SEQ ID NO: 23), an LCDR3 comprising an amino acid sequence of LQDYNYPRT (SEQ ID NO:40); or

(f) an HCDR1 comprising an amino acid sequence of GGSISTDY (SEQ ID NO:41), an HCDR2 comprising an amino acid sequence of IYFSGST (SEQ ID NO:38), and HCDR3 comprising an amino acid sequence of AREDDYYGSGSPFDY (SEQ ID NO:21); and an LCDR1 comprising an amino acid sequence of QDIRND (SEQ ID NO:42), an LCDR2 comprising an amino acid sequence of AAS (SEQ ID NO: 23), an LCDR3 comprising an amino acid sequence of LQDYNFPRT (SEQ ID NO: 24).

[0006] In one example, an anti-Clec12A antibody or an antigen-binding fragment thereof is provided comprising:

(a) an immunoglobulin heavy chain variable (VH) region comprising an amino acid sequence that is at least 80% identical to

QVQLQESGPGLVKPSETLSLTCTVSGGSISTYYWSWIRQPPGKGLEWIGYIYYSGSTK
YNPSLKSRVTISVDTSKNLFSCLKLSSVTAADTAVYYCAREDYYGSGSPFDYWGGTL
VTVSS (SEQ ID NO: 1), and

an immunoglobulin light chain variable (VL) region comprising an amino acid sequence that is at least about 80% identical to

IQMTQSPSSLSASVGDRVTITCRASQGIRYDLGWYQQKPGKAPKLLIYAASSLQSGVP
SRFSGSGSGTDFTLTISLQPEDFATYYCLQDYNFPRTFGQGTKVEIK (SEQ ID NO: 2);

(b) an immunoglobulin heavy chain variable (VH) region comprising an amino acid sequence that is at least about 80% identical to

QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDG
SDKYYVDSVKGRFTISRDN SKNTLYLHMNSLRAEDTAVYYCARDKGYFDYWGGQ
TLVTVSS (SEQ ID NO: 3), and

an immunoglobulin light chain variable (VL) region comprising an amino acid sequence that is at least about 80% identical to

EIVMTQSPATLSLSPGERATLSCRASQSVGNRYLSWYQQKPGQAPRLLIYGASTRAT
GIPARFSGSGSGTDFTLTISLQPEDFAVYYCQQDYNLPLTFGGGTKVEIK (SEQ ID
NO: 4);

(c) an immunoglobulin heavy chain variable (VH) region comprising an amino acid sequence that is at least about 80% identical to

QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDG
SDKYSADSVKGRFNISRDN SKNTLYLQMNSLRAEDTAVYYCARDGSRFYFDYWGGQ
TLVTVSS (SEQ ID NO: 5), and

an immunoglobulin light variable (VL) region comprising an amino acid sequence that is at least about 80% identical to

AIQLTQSPSSLSASVGDRVTTTCRTSQGISSALAWYQQKPGKTPKLLIYDASSLESGVP
SRFSGSGSGTDFTLTISLQPEDFATYYCQQFNYPRTFGQGKVEIK (SEQ ID NO:
18).

[0006a] In another aspect, the present disclosure provides a use of a composition comprising the anti-Clec12A antibody or antigen-binding fragment thereof of any one of the proceeding claims, in the manufacture of a medicament for treating a Clec12A expressing cancer in a subject.

[0007] In some examples, the anti-Clec12A antibody or antibody-binding fragment thereof comprises:

(a) an immunoglobulin heavy chain variable (VH) region comprising an amino acid sequence of

QVQLQESGPGLVKPSETLSLTCTVSGGSISTYYWSWIRQPPGKGLEWIGYIYYSGSTK
YNPSLKSRTISVDTSKNLFSKLSSVTAADTAVYYCAREDYYGSGSPFDYWGGTL
VTVSS (SEQ ID NO: 1), and

an immunoglobulin light chain variable (VL) region comprising an amino acid sequence of
IQMTQSPSSLSASVGDRVTTTCRASQGIRYDLGWYQQKPGKAPKLLIYAASSLQSGVP
SRFSGSGSGTDFTLTISLQPEDFATYYCLQDYNFPRTFGQGKVEIK (SEQ ID NO: 2);

(b) an immunoglobulin heavy chain variable (VH) region comprising an amino acid sequence of

QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDG
SDKYYVDSVKGRFTISRDNKNTLYLHMNSLRAEDTAVYYCARDKGYFFDYWGQG
TLVTVSS (SEQ ID NO: 3), and

an immunoglobulin light chain variable (VL) region comprising an amino acid sequence of
EIVMTQSPATLSLSPGERATLSCRASQSVGNRYLSWYQQKPGQAPRLLIYGASTRAT
GIPARFSGSGSGTDFTLTISLQPEDFAVYYCQQDYNLPLTFGGGKVEIK (SEQ ID
NO: 4);

(c) an immunoglobulin heavy chain variable (VH) region comprising an amino acid sequence

of QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYD

YLNWYQQKPGKAPKLLIYASSLQSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQ
SYSTPFTFGPGTKVDIK (SEQ ID NO: 59).

[0016] In some examples, the anti-Clec12A antibody or antigen-binding fragment thereof binds to Clec12A with a dissociation constant (K_D) of less than about 10^{-8} M, less than about 10^{-9} M, less than about 10^{-10} M, less than about 10^{-11} M, less than about 10^{-12} M, or less than about 10^{-13} M.

[0017] In some examples, the K_D is 0.1 pM or below.

[0018] In some examples, the K_D is between 0.05 and 0.5 pM.

[0019] In some examples, the K_D is between about 0.1 nM and 5.0 nM.

[0020] In some examples, the K_D is between about 0.3 nM and 3.5 nM.

[0021] In some examples, the EC_{50} is between about 1 and about 100 nM.

[0022] In some examples, a method of treating a cancer is provided, comprising administering the anti-Clec12A antibody or antigen-binding fragment thereof described herein.

[0023] In some examples, the cancer is selected from leukemia, lymphoma, and myeloma.

[0023a] In one aspect, the present disclosure provides a pharmaceutical composition comprising an anti-Clec12A antibody or an antigen-binding fragment thereof as described herein and a pharmaceutically acceptable carrier.

[0024] In another example, a pharmaceutical composition is provided comprising anti-Clec12A antibody or antigen-binding fragment thereof and a pharmaceutically acceptable carrier, wherein the anti-Clec12A antibody or antigen-binding fragment thereof comprises:

(a) an immunoglobulin heavy chain variable (VH) region comprising an amino acid sequence that is at least about 80% identical to

QVQLQESGPGLVKPSSETLSLTCTVSGGSISTYYWSWIRQPPGKGLEWIGYIYYSGSTKYN
PSLKSRVTISVDTSKNLFSLKLSSVTAADTAVYYCAREDYYGSGSPFDYWGQGTLVTVSS
(SEQ ID NO: 1), and

an immunoglobulin light chain variable (VL) region comprising an amino acid sequence that is at least about 80% identical to

IQMTQSPSSLSASVGDRVTITCRASQGIRYDLGWYQQKPGKAPKLLIYAASSLQSGVPSRF
SGSGSGTDFTLTISLQPEDFATYYCLQDYNFPRTEFGQGTKVEIK (SEQ ID NO: 2);

(b) an immunoglobulin heavy chain variable (VH) region comprising an amino acid sequence that is at least about 80% identical to

WGQGTLLTVSSASTGGGGSGGGGSGGGGSEIVMTQSPATLSLSPGERATLSCRASQSVG
NRYLSWYQQKPGQAPRLLIYGASTRATGIPARFSGSGSGTDFTLTISLQPEDFAVYYCQ
QDYNLPLTFGGGTKVEIK (SEQ ID NO: 57);

(c)

QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVI
SYDGSDDKYSADSVKGRFNISRDNSKNTLYLQMNSLRAEDTAVYYCARDGSRFYDY
WGQGTLLTVSSASTGGGGSGGGGSGGGGSEIFMTQSPATLSLSPGERATLSCRASQSV
HSKYLSWYQQKPGQAPSLLIYGASTRATGIPARFSGSGSGTDFTLTISLQPEDFAVY
YCQQDYNLPITFGQGTRLEIK (SEQ ID NO: 58); or

(d)

QLQLQESGPGLVKPSETLSLTCTVSGGSISSTYYWGWIRQPPRKGLEWIGSTH
YRGSTYYNPSLKSRTISVDTSKNQFSLKVSSVTAADTAVYYCARELTGEVFDYWG
QGTLLTVSSASTGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQSISS
YLNWYQQKPGKAPKLLIYASSLQSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQ
SYSTPFTFGPGTKVDIK (SEQ ID NO: 59).

[0034] In one aspect, the present disclosure provides a nucleic acid sequence encoding an amino acid sequence at least 90% identical to any one of the amino acid sequences as described herein. In another example, a nucleic acid sequence is provided encoding an amino acid sequence that is at least 90% identical to any one of SEQ ID NO: 1-59.

[0035] In one aspect, the present disclosure provides a vector comprising the nucleic acid sequence as described herein. In another example, a vector is provided comprising the nucleic acid encoding an amino acid sequence that is at least about 90% identical to any one of SEQ ID NO: 1-59.

[0036] In another aspect, a cell is provided comprising a vector as described herein.

[0037] In some examples, a method of treating cancer is provided comprising administering an anti-Clec12A antibody or antigen-binding fragment thereof to a subject in need thereof, the anti-Clec12A antibody or antigen-binding fragment thereof comprising:

(a) an immunoglobulin heavy chain variable (VH) region comprising an amino acid sequence of

QVQLQESGPGLVKPSETLSLTCTVSGGSISTYYWSWIRQPPGKGLEWIGYIYYSGSTKYN
PSLKSRTISVDTSKNLFSLKLSSVTAADTAVYYCAREDDYGGSGSPFDYWGQGTLLTVSS
(SEQ ID NO: 1), and

CLAIMS

1. An anti-Clec12A antibody or antigen-binding fragment thereof comprising:
 - (a) a heavy chain complementarity determining region (HCDR) 1 comprising an amino acid sequence of GGSISTYY (SEQ ID NO: 19), an HCDR2 comprising an amino acid sequence of IYYSGST (SEQ ID NO: 20), an HCDR3 comprising an amino acid sequence of AREYYGSGSPFDY (SEQ ID NO: 21); and
a light chain complementarity determining region (LCDR) 1 comprising an amino acid sequence of QGIRYD (SEQ ID NO: 22), an LCDR2 comprising an amino acid sequence of AAS (SEQ ID NO: 23), and an LCDR3 comprising an amino acid sequence of LQDYNFPRT (SEQ ID NO: 24);
 - (e) an HCDR1 comprising an amino acid sequence of GGSISTYY (SEQ ID NO: 19), an HCDR2 comprising an amino acid sequence of IYFSGST (SEQ ID NO: 38), and HCDR3 comprising an amino acid sequence of AREYYGSGSPFDY (SEQ ID NO: 21); and
an LCDR1 comprising an amino acid sequence of QGIRND (SEQ ID NO: 39), an LCDR2 comprising an amino acid sequence of AAS (SEQ ID NO: 23), an LCDR3 comprising an amino acid sequence of LQDYNFPRT (SEQ ID NO: 40); or
 - (f) an HCDR1 comprising an amino acid sequence of GGSISTDY (SEQ ID NO: 41), an HCDR2 comprising an amino acid sequence of IYFSGST (SEQ ID NO: 38), and HCDR3 comprising an amino acid sequence of AREYYGSGSPFDY (SEQ ID NO: 21); and
an LCDR1 comprising an amino acid sequence of QDIRND (SEQ ID NO: 42), an LCDR2 comprising an amino acid sequence of AAS (SEQ ID NO: 23), an LCDR3 comprising an amino acid sequence of LQDYNFPRT (SEQ ID NO: 24).
2. The anti-Clec12A antibody or antigen-binding fragment thereof of claim 1 comprising:
 - (a) an immunoglobulin heavy chain variable (V_H) region comprising an amino acid sequence that is at least 80% identical to
QVQLQESGPGLVKPSSETLSLTCTVSGGSISTYYWSWIRQPPGKGLEWIGYIYYSGS

TKYNPSLKS RVTISVDT SKNLFSLKLSSVTAADTAVYYCARE DYYGSGSPFDYW
GQGTLVTVSS (SEQ ID NO: 1), and

an immunoglobulin light chain variable (V_L) region comprising an amino acid
sequence that is at least 80% identical to

IQMTQSPSSLSASVGDRVTITCRASQGIRYDLGWYQQKPGKAPKLLIYAASSLQS
GVPSRFSGSGSGTDFTLTISLQPEDFATYYCLQDYNFPRTFGQGTKVEIK (SEQ
ID NO: 2);

(e) an immunoglobulin heavy chain variable (V_H) region comprising an amino acid
sequence that is at least 80% identical to

QVQLQESGPGLVKPSETLSLTCTVSGGSISTYYWSWIRQPPGKGLEWLGYYIF
SGSTNYPNPSLKSRLTISVAASKSQFSLKLSSVTAADTAVYYCARE DYYGSGSPFD
YWQGTLVTVSS (SEQ ID NO: 9), and

an immunoglobulin light variable (V_L) region comprising an amino acid sequence
that is at least 80% identical to

AIQMTQSPSSLSASVGDRVTITCRASQGIRNDLGWFQQKPGKAPKLLIYAASS
LQSGVPSRFSGSGSGTYFTLTISLQPEDSATYYCLQDYNPRTFGQGTKVEIK
(SEQ ID NO: 10); or

(f) an immunoglobulin heavy chain variable (V_H) region comprising an amino acid
sequence that is at least 80% identical to

QVQLQESGPGLVKPSETLSLTCTVSGGSISTDYWSWIRQPPGKGLEWIGYYIF
SGSTKYNPSLKS RVTISVDT SKNQFSLKLSSVTAADTAVYYCARE DYYGSGSPFD
YWQGTLVTVSS (SEQ ID NO: 11), and

an immunoglobulin light variable (V_L) region comprising an amino acid sequence
that is at least 80% identical to

AIQMTQSPSSLSASVGDRVTITCRASQDIRNDLGWFQQKPGKAPKLLIYAASS
LQSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCLQDYNFPRTFGQGTKVEIK
(SEQ ID NO: 12).

3. The anti-Clec12A antibody or antigen-binding fragment thereof of claim 1 or 2,
comprising:

(a) an immunoglobulin heavy chain variable (V_H) region comprising an amino acid sequence of

QVQLQESGPGLVKPSETLSLTCTVSGGSISTYYWSWIRQPPGKGLEWIGYIYYSGS
TKYNPSLKSRTISVDTSKNLFSKLSSVTAADTAVYYCAREDDYYGSGSPFDYW
GQGTLVTVSS (SEQ ID NO: 1), and

an immunoglobulin light chain variable (V_L) region comprising an amino acid sequence of

IQMTQSPSSLSASVGDRVTITCRASQGIRYDLGWYQQKPGKAPKLLIYAASSLQS
GVPSRFSGSGSGTDFTLTISLQPEDFATYYCLQDYNFPRTFGQGTKVEIK (SEQ
ID NO: 2);

(e) an immunoglobulin heavy chain variable (V_H) region comprising an amino acid sequence of

QVQLQESGPGLVKPSETLSLTCTVSGGSISTYYWSWIRQPPGKGLEWLGYIYFSG
STNYPNPSLKSRLTISVAASKSQFSLKLSSVTAADTAVYYCAREDDYYGSGSPFDYW
GQGTLVTVSS (SEQ ID NO: 9), and

an immunoglobulin light variable (V_L) region comprising an amino acid sequence of
AIQMTQSPSSLSASVGDRVTITCRASQGIRNDLGWFQQKPGKAPKLLIYAASS
LQSGVPSRFSGSGSGTYFTLTISLQPEDSATYYCLQDYNFPRTFGQGTKVEIK
(SEQ ID NO: 10); or

(f) an immunoglobulin heavy chain variable (V_H) region comprising an amino acid sequence of

QVQLQESGPGLVKPSETLSLTCTVSGGSISTDYWSWIRQPPGKGLEWIGYIYF
SGSTKYNPSLKSRTISVDTSKNQFSLKLSSVTAADTAVYYCAREDDYYGSGSP
FDYWGGQGTLVTVSS (SEQ ID NO: 11), and

an immunoglobulin light variable (V_L) region comprising an amino acid sequence of
AIQMTQSPSSLSASVGDRVTITCRASQDIRNDLGWFQQKPGKAPKLLIYAASS
LQSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCLQDYNFPRTFGQGTKVEIK
(SEQ ID NO: 12).

4. The anti-Clec12A antibody or antigen-binding fragment thereof of any one of the preceding claims, wherein the anti-Clec12A antibody or antigen-binding fragment thereof

is selected from the group consisting of an IgA antibody, IgG antibody, IgE antibody, IgM antibody, bi- or multi- specific antibody.

5. The anti-Clec12A antibody or antigen-binding fragment thereof of any one of the preceding claims, wherein the anti-Clec12A antibody or fragment thereof is a monoclonal antibody or a single-chain variable fragment (scFv).
6. The anti-Clec12A antibody or antigen-binding fragment thereof of any one of the preceding claims, wherein the anti-Clec12A antibody is an antibody comprising an IgG constant region.
7. The anti-Clec12A antibody or antibody-binding fragment thereof of any one of the preceding claims, wherein the anti-Clec12A antigen-binding fragment thereof is a single-chain variable fragment (scFv).
8. The anti-Clec12A antibody or antibody-binding fragment thereof of claim 7, wherein the scFv comprises a heavy chain variable sequence, a GS-Linker, and a light chain variable sequence.
9. The anti-Clec12A antibody or antigen-binding fragment of claim 8, wherein the scFv comprises a sequence having at least 80% identity to:
QVQLQESGPGLVKPSETLSLTCTVSGGSISTYYWSWIRQPPGKGLEWIGYIYY
SGSTKYNPSLKSRTISVDTSKNLFSKLSSVTAADTAVYYCAREDYYGSGSP
FDYWGGQGLTVTVSSASTGGGGSGGGGSGGGGSAIQMTQSPSSLSASVGDRV
TITCRASQGIRYDLGWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFT
LTISSLQPEDFATYYCLQDYNFPRTFGQGTKVEIK (SEQ ID NO: 56).
10. The anti-Clec12A antibody or antibody-binding fragment thereof of claim 9, wherein the scFv comprises a sequence of:
QVQLQESGPGLVKPSETLSLTCTVSGGSISTYYWSWIRQPPGKGLEWIGYIYY
SGSTKYNPSLKSRTISVDTSKNLFSKLSSVTAADTAVYYCAREDYYGSGSP
FDYWGGQGLTVTVSSASTGGGGSGGGGSGGGGSAIQMTQSPSSLSASVGDRV
TITCRASQGIRYDLGWYQQKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFT
LTISSLQPEDFATYYCLQDYNFPRTFGQGTKVEIK (SEQ ID NO: 56).
11. The anti-Clec12A antibody of any one of the preceding claims, wherein the anti-Clec12A antibody or fragment thereof binds to Clec12A with a disassociation constant (K_D) of less

than 10^{-8} M, less than 10^{-9} M, less than 10^{-10} M, less than 10^{-11} M, less than 10^{-12} M, or less than 10^{-13} M.

12. The anti-Clec12A antibody of claim 11, wherein the K_D is 0.1 pM or below.
13. The anti-Clec12A antibody of claim 11, wherein the K_D is between 0.05 and 0.5 pM.
14. The anti-Clec12A antibody of claim 11, wherein the K_D is between 0.1 nM and 5.0 nM.
15. The anti-Clec12A antibody of claim 14, wherein the K_D is between 0.3 nM and 3.5 nM.
16. The anti-Clec12A antibody of any one of the preceding claims, wherein the EC50 is between 1 and 100 nM.
17. Use of a composition comprising the anti-Clec12A antibody or antigen-binding fragment thereof of any one of the proceeding claims, in the manufacture of a medicament for treating a Clec12A expressing cancer in a subject.
18. The use according to claim 17, wherein the cancer is selected from leukemia, lymphoma, and myeloma.
19. A pharmaceutical composition comprising an anti-Clec12A antibody or an antigen-binding fragment thereof of any one of claims 1-16 and a pharmaceutically acceptable carrier.
20. A nucleic acid sequence encoding an amino acid sequence at least 90% identical to any one of the amino acid sequences in claims 1-16.
21. A vector comprising the nucleic acid sequence of claim 20.
22. A cell comprising the vector of claim 21.
23. The use according to claim 17, further comprising that one or more additional agents is to be administered.
24. The use according to claim 23, wherein the one or more additional agents is selected from an antibody, a chemotherapeutic, and radiation therapy.