

The IL-33 pathway has been suggested to be involved in various diseases, including ocular diseases (e.g, GA) for which there remains a need to develop improved compositions, and methods for treatment.

5

SUMMARY

The present ~~invention~~disclosure relates, *inter alia*, to anti-IL-33 antibodies and methods of making and using the same.

In one aspect, provided herein is an isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, the binding domain comprising the following
10 six complementarity-determining regions (CDRs): (a) a CDR-H1 comprising the amino acid sequence of NYWMT (SEQ ID NO: 1); (b) a CDR-H2 comprising the amino acid sequence of SITYTGGGTYPDSVKG (SEQ ID NO: 2); (c) a CDR-H3 comprising the amino acid sequence of ANYYYNTYGGFPY (SEQ ID NO: 3); (d) a CDR-L1 comprising the amino acid sequence of
15 LASEGFSNDLA (SEQ ID NO: 4); (e) a CDR-L2 comprising the amino acid sequence of AASRLQD (SEQ ID NO: 5); and (f) a CDR-L3 comprising the amino acid sequence of QQGSKYPLT (SEQ ID NO: 6).

In another aspect, provided herein is an isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid
20 sequence of SEQ ID NO: 7; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 8; or (c) a VH domain as in (a) and a VL domain as in (b).

In some ~~aspect~~examples, the VH domain comprises: (a) an FR-H1 comprising the amino acid sequence of EVQLVX₁SGX₂X₃X₄X₅X₆PGX₇SX₈X₉X₁₀SCX₁₁ASGFTFN (SEQ ID NO: 9), wherein X₁ is E or
25 Q; X₂ is G or A; X₃ is G or E; X₄ is L or V; X₅ is V or K; X₆ is Q or K; X₇ is G, A, or T; X₈ is L or V; X₉ is R or K; X₁₀ is L or V; and X₁₁ is A, K, or L; (b) an FR-H2 comprising the amino acid sequence of WX₁RQAPGX₂GLEWX₃X₄ (SEQ ID NO: 10), wherein X₁ is I or V; X₂ is K or Q; X₃ is V, M, or I; and X₄ is A or G; (c) an FR-H3 comprising the amino acid sequence of
RX₁TX₂X₃RDX₄X₅X₆X₇X₈X₉YX₁₀X₁₁X₁₂X₁₃SLRX₁₄EDTAX₁₅YYCTR (SEQ ID NO: 11), wherein X₁ is F or V;
30 X₂ is I or M; X₃ is S or T; X₄ is D, N, or T; X₅ is A or S; X₆ is K or T; X₇ is S or N; X₈ is S or T; X₉ is L or V; X₁₀ is L or M; X₁₁ is Q or E; X₁₂ is M or L; X₁₃ is N or S; X₁₄ is A or S; and X₁₅ is V or T; and (d) an FR-H4 comprising the amino acid sequence of WGQGTLVTVSS (SEQ ID NO: 12).

In some ~~aspect~~examples, the VH domain comprises: (a) an FR-H1 comprising the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFN (SEQ ID NO: 17); (b) an FR-H2 comprising
35 the amino acid sequence of WIRQAPGKGLEWVA (SEQ ID NO: 18); (c) an FR-H3 comprising the amino acid sequence of RFTISRDDAKSSLYLQMNSLRAEDTAVYYCTR (SEQ ID NO: 19); and (d) an FR-H4 comprising the amino acid sequence of WGQGTLVTVSS (SEQ ID NO: 12).

In some ~~aspect~~examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 7.

In some ~~aspect~~examples, the VH domain comprises: (a) an FR-H1 comprising the amino acid
40 sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFN (SEQ ID NO: 17); (b) an FR-H2 comprising the amino

acid sequence of WVRQAPGKGLEWVA (SEQ ID NO: 39); (c) an FR-H3 comprising the amino acid sequence of RFTISRDNKNSLYLQMNSLRAEDTAVYYCTR (SEQ ID NO: 40); and (d) an FR-H4 comprising the amino acid sequence of WGQGTSLTVSS (SEQ ID NO: 12).

5 In some aspectexamples, the VH domain comprises the amino acid sequence of SEQ ID NO: 41.

In some aspectexamples, the VH domain comprises: (a) an FR-H1 comprising the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFN (SEQ ID NO: 17); (b) an FR-H2 comprising the amino acid sequence of WVRQAPGKGLEWIA (SEQ ID NO: 42); (c) an FR-H3 comprising the amino acid sequence of RFTISRDDAKSSLYLQMNSLRAEDTAVYYCTR (SEQ ID NO: 19); and (d) an FR-H4 comprising the amino acid sequence of WGQGTSLTVSS (SEQ ID NO: 12).

10 In some aspectexamples, the VH domain comprises the amino acid sequence of SEQ ID NO: 43.

In some aspectexamples, the VH domain comprises: (a) an FR-H1 comprising the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFN (SEQ ID NO: 17); (b) an FR-H2 comprising the amino acid sequence of WVRQAPGKGLEWVA (SEQ ID NO: 39); (c) an FR-H3 comprising the amino acid sequence of RFTISRDDAKSSLYLQMNSLRAEDTAVYYCTR (SEQ ID NO: 19); and (d) an FR-H4 comprising the amino acid sequence of WGQGTSLTVSS (SEQ ID NO: 12).

15 In some aspectexamples, the VH domain comprises the amino acid sequence of SEQ ID NO: 44.

In some aspectexamples, the VH domain comprises: (a) an FR-H1 comprising the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFN (SEQ ID NO: 17); (b) an FR-H2 comprising the amino acid sequence of WVRQAPGKGLEWVA (SEQ ID NO: 39); (c) an FR-H3 comprising the amino acid sequence of RFTISRDDAKNSLYLQMNSLRAEDTAVYYCTR (SEQ ID NO: 45); and (d) an FR-H4 comprising the amino acid sequence of WGQGTSLTVSS (SEQ ID NO: 12).

20 In some aspectexamples, the VH domain comprises the amino acid sequence of SEQ ID NO: 46.

In some aspectexamples, the VH domain comprises: (a) an FR-H1 comprising the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFN (SEQ ID NO: 17); (b) an FR-H2 comprising the amino acid sequence of WVRQAPGKGLEWVA (SEQ ID NO: 39); (c) an FR-H3 comprising the amino acid sequence of RFTISRDNKSSLYLQMNSLRAEDTAVYYCTR (SEQ ID NO: 47); and (d) an FR-H4 comprising the amino acid sequence of WGQGTSLTVSS (SEQ ID NO: 12).

25 In some aspectexamples, the VH domain comprises the amino acid sequence of SEQ ID NO: 48.

In some aspectexamples, the VH domain comprises: (a) an FR-H1 comprising the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFN (SEQ ID NO: 17); (b) an FR-H2 comprising the amino acid sequence of WVRQAPGKGLEWIA (SEQ ID NO: 49); (c) an FR-H3 comprising the amino acid sequence of RFTISRDDAKSSLYLQMNSLRAEDTAVYYCTR (SEQ ID NO: 19); and (d) an FR-H4 comprising the amino acid sequence of WGQGTSLTVSS (SEQ ID NO: 12).

30 In some aspectexamples, the VH domain comprises the amino acid sequence of SEQ ID NO: 50.

In some aspectexamples, the VH domain comprises: (a) an FR-H1 comprising the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFN (SEQ ID NO: 17); (b) an FR-H2 comprising the amino acid sequence of WVRQAPGKGLEWIA (SEQ ID NO: 49); (c) an FR-H3 comprising the amino acid sequence of RFTISRDDSKSTLYLQMNSLRAEDTAVYYCTR (SEQ ID NO: 51); and (d) an FR-H4 comprising the amino acid sequence of WGQGTSLTVSS (SEQ ID NO: 12).

35 In some aspectexamples, the VH domain comprises the amino acid sequence of SEQ ID NO: 52.

In some [aspectexamples](#), the VL domain comprises: (a) an FR-L1 comprising the amino acid sequence of X₁IX₂X₃TQSPX₄X₅LSX₆SX₇GX₈X₉X₁₀X₁₁X₁₂X₁₃C (SEQ ID NO: 13), wherein X₁ is D or E; X₂ is Q or V; X₃ is M or L; X₄ is S or A; X₅ is S or T; X₆ is A or L; X₇ is V, P, or L; X₈ is D or E; X₉ is R or T; X₁₀ is V or A; X₁₁ is T or S; X₁₂ is I or L; and X₁₃ is T, S, or E; (b) an FR-L2 comprising the amino acid sequence of WX₁QQKX₂GX₃X₄PX₅X₆LIY (SEQ ID NO: 14), wherein X₁ is Y or F; X₂ is P or S; X₃ is K or Q; X₄ is S or A; X₅ is K, R, or Q; and X₆ is L or S; (c) an FR-L3 comprising the amino acid sequence of GX₁PX₂RFSGSGSGTX₃FX₄LX₅ISX₆X₇X₈PEDX₉AX₁₀YX₁₁C (SEQ ID NO: 15), wherein X₁ is V or I; X₂ is S or A; X₃ is D or R; X₄ is T or S; X₅ is T or K; X₆ is S or G; X₇ is L or M; X₈ is Q or E; X₉ is F, V, or E; X₁₀ is T, V, or D; and X₁₁ is F or Y; and (d) an FR-L4 comprising the amino acid sequence of FGX₁GTX₂EIK (SEQ ID NO: 16), wherein X₁ is G or S and X₂ is V or L.

In some [aspectexamples](#), the VL domain comprises: (a) an FR-L1 comprising the amino acid sequence of DIQMTQSPSSLSASVGDRVTITC (SEQ ID NO: 21); (b) an FR-L2 comprising the amino acid sequence of WYQQKPGKSPKLLIY (SEQ ID NO: 22); (c) an FR-L3 comprising the amino acid sequence of GVPSRFSGSGSGTDFTLTISLQPEDFATYFC (SEQ ID NO: 23); and (d) an FR-L4 comprising the amino acid sequence of FGGGTKVEIK (SEQ ID NO: 24).

In some [aspectexamples](#), the VL domain comprises the amino acid sequence of SEQ ID NO: 8.

In one aspect, provided herein is an isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising the amino acid sequence of SEQ ID NO: 7 and (b) a VL domain comprising the amino acid sequence of SEQ ID NO: 8. In another [aspectexample](#), provided herein is an isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 7 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 8.

In another aspect, provided herein is an isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a heavy chain (HC) comprising the amino acid sequence of SEQ ID NO: 25 and (b) a light chain (LC) comprising the amino acid sequence of SEQ ID NO: 26. In another [aspectexample](#), provided herein is an isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a heavy chain (HC) comprising an amino acid sequence of SEQ ID NO: 25 and (b) a light chain (LC) comprising an amino acid sequence of SEQ ID NO: 26.

In some [aspectexamples](#), the VL domain comprises: (a) an FR-L1 comprising the amino acid sequence of DIQMTQSPSSLSASVGDRVTITC (SEQ ID NO: 21); (b) an FR-L2 comprising the amino acid sequence of WFQQKPGKAPKSLIY (SEQ ID NO: 53); (c) an FR-L3 comprising the amino acid sequence of GVPSRFSGSGSGTDFTLTISLQPEDFATYYC (SEQ ID NO: 54); and (d) an FR-L4 comprising the amino acid sequence of FGGGTKVEIK (SEQ ID NO: 24).

In some [aspectexamples](#), the VL domain comprises the amino acid sequence of SEQ ID NO: 55.

In some [aspectexamples](#), the VL domain comprises: (a) an FR-L1 comprising the amino acid sequence of DIQMTQSPSSLSASVGDRVTITC (SEQ ID NO: 21); (b) an FR-L2 comprising the amino acid sequence of WYQQKPGKAPKSLIY (SEQ ID NO: 56); (c) an FR-L3 comprising the amino acid sequence of GVPSRFSGSGSGTDFTLTISLQPEDFATYFC (SEQ ID NO: 23); and (d) an FR-L4 comprising the amino acid sequence of FGGGTKVEIK (SEQ ID NO: 24).

In some [aspectexamples](#), the VL domain comprises the amino acid sequence of SEQ ID NO: 57.

In some [aspectexamples](#), the VL domain comprises: (a) an FR-L1 comprising the amino acid sequence of DIQMTQSPSSLSASVGDRVTITC (SEQ ID NO: 21); (b) an FR-L2 comprising the amino acid sequence of WFQQKPGKAPKSLIY (SEQ ID NO: 53); (c) an FR-L3 comprising the amino acid sequence of

GVPSRFSGSGSGTDFLTISLQPEDFATYFC (SEQ ID NO: 23); and (d) an FR-L4 comprising the amino acid sequence of FGGGTKVEIK (SEQ ID NO: 24).

In some aspectexamples, the VL domain comprises the amino acid sequence of SEQ ID NO: 58.

5 In some aspectexamples, the VL domain comprises: (a) an FR-L1 comprising the amino acid sequence of DIQMTQSPSSLSASVGDRVTITC (SEQ ID NO: 21); (b) an FR-L2 comprising the amino acid sequence of WYQQKPGKAPKSLIY (SEQ ID NO: 56); (c) an FR-L3 comprising the amino acid sequence of GVPSRFSGSGSGTDFLTISLQPEDFATYYC (SEQ ID NO: 54); and (d) an FR-L4 comprising the amino acid sequence of FGGGTKVEIK (SEQ ID NO: 24).

10 In some aspectexamples, the VL domain comprises the amino acid sequence of SEQ ID NO: 59.

In some aspectexamples, the VL domain comprises: (a) an FR-L1 comprising the amino acid sequence of DIQMTQSPSSLSASVGDRVTITC (SEQ ID NO: 21); (b) an FR-L2 comprising the amino acid sequence of WYQQKPGKSPKLLIY (SEQ ID NO: 22); (c) an FR-L3 comprising the amino acid sequence of GVPSRFSGSGSGTDFLTISLQPEDVATYYC (SEQ ID NO: 60); and (d) an FR-L4 comprising the amino acid sequence of FGGGTKVEIK (SEQ ID NO: 24).

15 In some aspectexamples, the VL domain comprises the amino acid sequence of SEQ ID NO: 61.

In one aspect, provided herein is an isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises:

(i) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 41 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 55;

(ii) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 43 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 55;

(iii) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 41 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 8;

(iv) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 43 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 8;

(v) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 44 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 8;

(vi) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 46 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 8;

(vii) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 48 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 8;

(viii) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 43 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 57;

(ix) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 44 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 57;

(x) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 46 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 57;

(xi) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 48 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 57;

(xii) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 50 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 57;

(xiii) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 43 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 58;

(xiv) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 44 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 58;

(xv) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 46 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 58;
(xvi) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 48 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 58;
(xvii) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 50 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 58;
(xviii) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 43 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 59;
(xix) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 44 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 59;
(xx) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 46 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 59;
(xxi) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 48 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 59;
(xxii) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 50 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 59; or
(xxiii) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 52 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 61. In another aspectexample, provided herein is an isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 41 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 55.

In another aspectexample, provided herein is an isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 43 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 55.

In another aspectexample, provided herein is an isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 41 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 8.

In another aspectexample, provided herein is an isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 43 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 8.

In another aspectexample, provided herein is an isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 44 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 8.

In another aspectexample, provided herein is an isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 46 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 8.

In another [aspectexample](#), provided herein is an isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 50 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 58.

In another [aspectexample](#), provided herein is an isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 43 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 59.

In another [aspectexample](#), provided herein is an isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 44 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 59.

In another [aspectexample](#), provided herein is an isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 46 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 59.

In another [aspectexample](#), provided herein is an isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 48 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 59.

In another [aspectexample](#), provided herein is an isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 50 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 59.

In another [aspectexample](#), provided herein is an isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 52 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 61.

In one aspect, provided herein is an isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises:

(i) a binding domain comprising (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 35; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 36; or (c) a VH domain as in (a) and a VL domain as in (b);

(ii) a binding domain comprising (a) a heavy chain (HC) comprising an amino acid sequence of SEQ ID NO: 37 and (b) a light chain (LC) comprising an amino acid sequence of SEQ ID NO: 38; or

(iii) a binding domain comprising (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 65; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 69; or (c) a VH domain as in (a) and a VL domain as in (b). In another [aspectexample](#), provided

herein is an isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 35; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 36; or (c) a VH domain as in (a) and a VL domain as in (b).

In some [aspectexamples](#), the VH domain comprises: (a) an FR-H1 comprising the amino acid sequence of EVQLVESGGGLVQPGTSLKLSCLASGFTFN (SEQ ID NO: 27); (b) an FR-H2 comprising the amino acid sequence of WIRQAPGKGLEWIA (SEQ ID NO: 28); (c) an FR-H3 comprising the amino acid sequence of RFTISRDDAKSTLYLQMNSLRSEDATYYCTR (SEQ ID NO: 29); and (d) an FR-H4 comprising the amino acid sequence of WGQGTLTVSS (SEQ ID NO: 12).

In some [aspectexamples](#), the VH domain comprises the amino acid sequence of SEQ ID NO: 35.

In some [aspectexample](#)s, the VL domain comprises: (a) an FR-L1 comprising the amino acid sequence of DIQMTQSPASLSASLGSETVSIEC (SEQ ID NO: 31); (b) an FR-L2 comprising the amino acid sequence of WYQQKSGKSPQLLIY (SEQ ID NO: 32); (a) an FR-L3 comprising the amino acid sequence of GVPSRFSGSGSGTRFSLKISGMQPEDEADYFC (SEQ ID NO: 33); and (d) an FR-L4 comprising the amino acid sequence of FGSGTKLEIK (SEQ ID NO: 34).

In some [aspectexample](#)s, the VL domain comprises the amino acid sequence of SEQ ID NO: 36.

In another [aspectexample](#), provided herein is an isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 35 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 36.

In another [aspectexample](#), provided herein is an isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising (a) a heavy chain (HC) comprising an amino acid sequence of SEQ ID NO: 37 and (b) a light chain (LC) comprising an amino acid sequence of SEQ ID NO: 38.

In another [aspectexample](#), provided herein is an isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 65; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 69; or (c) a VH domain as in (a) and a VL domain as in (b).

In some [aspectexample](#)s, the VH domain comprises: (a) an FR-H1 comprising the amino acid sequence of EVQLVQSGAEVKKPGASVKVSCKASGFTFN (SEQ ID NO: 62); (b) an FR-H2 comprising the amino acid sequence of WVRQAPGQGLEWMG (SEQ ID NO: 63); (c) an FR-H3 comprising the amino acid sequence of RVTMTRDTSTSTVYMELSSLRSEDTAVYYCTR (SEQ ID NO: 64); and (d) an FR-H4 comprising the amino acid sequence of WGQGTLVTVSS (SEQ ID NO: 12).

In some [aspectexample](#)s, the VH domain comprises the amino acid sequence of SEQ ID NO: 65.

In some [aspectexample](#)s, the VL domain comprises: (a) an FR-L1 comprising the amino acid sequence of EIVLTQSPATLSLSPGERATLSC (SEQ ID NO: 66); (b) an FR-L2 comprising the amino acid sequence of WYQQKPGQAPRLIY (SEQ ID NO: 67); (c) an FR-L3 comprising the amino acid sequence of GIPARFSGSGSGTDFTLTISSLEPEDFAVYYC (SEQ ID NO: 68); and (d) an FR-L4 comprising the amino acid sequence of FGGGTKVEIK (SEQ ID NO: 24).

In some [aspectexample](#)s, the VL domain comprises the amino acid sequence of SEQ ID NO: 69.

In another [aspectexample](#), provided herein is an isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 65 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 69.

In some [aspectexample](#)s, the antibody specifically binds human or cyno IL-33.

In some [aspectexample](#)s, the antibody specifically binds both human and cyno IL-33.

In some [aspectexample](#)s, the antibody specifically binds both human and cyno IL-33 with a K_D of about 1 nM or lower.

In some [aspectexample](#)s, the antibody specifically binds human IL-33 with a K_D between about 100 fM and about 1 nM.

In some [aspectexample](#)s, the antibody specifically binds human IL-33 with a K_D between about 750 fM and about 300 pM.

5 In some [aspectexample](#)s, the antibody specifically binds human IL-33 with a K_D between about 1 pM and about 200 pM.

In some [aspectexample](#)s, the antibody specifically binds human IL-33 with a K_D of about 118 pM.

In some [aspectexample](#)s, the antibody specifically binds human IL-33 with a K_D of about 15 pM.

10 In some [aspectexample](#)s, the antibody specifically binds cyno IL-33 with a K_D between about 100 fM and about 1 nM.

In some [aspectexample](#)s, the antibody specifically binds cyno IL-33 with a K_D between about 1 pM and about 500 pM.

In some [aspectexample](#)s, the antibody specifically binds cyno IL-33 with a K_D between about 20 pM and about 50 pM.

15 In some [aspectexample](#)s, the antibody specifically binds cyno IL-33 with a K_D of about 35 pM.

In some [aspectexample](#)s, the antibody specifically binds both human and cyno IL-33 with a K_D of between about 1 pM and about 500 pM.

In some [aspectexample](#)s, the antibody specifically binds both human and cyno IL-33 with a K_D of between about 10 pM and about 40 pM.

20 In some [aspectexample](#)s, the antibody is capable of inhibiting the binding of IL-33 to an IL-33 receptor.

In some [aspectexample](#)s, the inhibiting is measured using a cell-based blocking assay.

In some [aspectexample](#)s, the antibody inhibits binding of human IL-33 to an IL-33 receptor with an IC50 of between about 800 fM and about 100 pM.

25 In some [aspectexample](#)s, the IC50 is between about 1 pM and about 50 pM.

In some [aspectexample](#)s, the IC50 is about 31 pM.

In some [aspectexample](#)s, the antibody has a viscosity of less than about 5 centipoise (cP) at a concentration of about 180 mg/mL.

30 In some [aspectexample](#)s, the antibody has a viscosity of between about 3 cP and about 5 cP at a concentration of about 180 mg/mL.

In some [aspectexample](#)s, the antibody has a viscosity of about 4.6 cP at a concentration of about 180 mg/mL.

In some [aspectexample](#)s, the antibody has a turbidity (optical density (OD)) of about 0.5 or lower at a concentration of about 150 mg/ml or higher in phosphate-buffered saline (PBS) pH 7.4.

35 In some [aspectexample](#)s, the antibody has a turbidity (OD) of between about 0.25 and about 0.5 at a concentration of about 150 mg/ml to about 250 mg/ml.

In some [aspectexample](#)s, the antibody has a turbidity (OD) of about 0.38 at a concentration of about 200 mg/ml.

In some [aspectexample](#)s, the antibody is monoclonal, human, humanized, or chimeric.

40 In some [aspectexample](#)s, the antibody is an antibody fragment that binds IL-33.

In some [aspectexample](#)s, the antibody fragment is an Fab, Fab'-SH, Fv, scFv, or (Fab')₂ fragment.

In some aspectexamples, the antibody fragment is an Fab.
 In some aspectexamples, the antibody is a full-length antibody.
 In some aspectexamples, the antibody is an IgG antibody.
 In some aspectexamples, the IgG antibody is an IgG1 antibody.
 In some aspectexamples, the IgG antibody is an IgG4 antibody.
 In some aspectexamples, the antibody is a monospecific antibody.
 In some aspectexamples, the antibody is a multispecific antibody.
 In some aspectexamples, the antibody is a bispecific antibody.
 In some aspectexamples, the bispecific antibody comprises a second binding domain that binds
 to a second biological molecule, wherein the second biological molecule is interleukin-13 (IL-13),
 interleukin-4 (IL-4), interleukin-5 (IL-5), interleukin-17 (IL-17), Factor D, HtrA1, VEGF, or a VEGF
 receptor.
In one aspect, provided herein is an isolated nucleic acid or a set of isolated nucleic acids
encoding the antibody as disclosed herein. In another aspectexample, provided herein is an isolated
 nucleic acid encoding any one of the antibodies disclosed herein or a set of isolated nucleic acids
 together encoding the antibody.
In another aspect, provided herein is a vector or a set of vectors comprising the isolated nucleic
acid or set of isolated nucleic acids as disclosed herein. In another aspectexample, provided herein is a
 vector or a set of vectors comprising any of the isolated nucleic acids or set of isolated nucleic acids
 disclosed herein.
In another aspect, provided herein is a host cell comprising the vector or the set of vectors as
disclosed herein. In another aspectexample, provided herein is a host cell comprising any one of the
 vectors or the set of vectors disclosed herein.
 In some aspectexamples, the host cell is a mammalian cell.
 In some aspectexamples, the mammalian cell is a Chinese hamster ovary (CHO) cell.
 In some aspectexamples, the host cell is a prokaryotic cell.
 In some aspectexamples, the prokaryotic cell is *E. coli*.
In one aspect, provided herein is a method of producing an antibody that specifically binds to IL-
33, the method comprising culturing the host cell as disclosed herein in a culture medium. In another
aspectexample, provided herein is a method of producing an antibody that specifically binds to IL-33, the
 method comprising culturing any one of the host cells disclosed herein in a culture medium.
 In some aspectexamples, the method further comprises recovering the antibody from the host cell
 or the culture medium.
In one aspect, provided herein is a pharmaceutical composition comprising the antibody as
disclosed herein, further comprising a pharmaceutically acceptable carrier, excipient, or diluent.
 In another aspectexample, provided herein is a composition comprising any one of the antibodies
 disclosed herein.
 In some aspectexamples, the composition further comprises a pharmaceutically acceptable
 carrier, excipient, or diluent.
 In some aspectexamples, the composition is a pharmaceutical composition.
 In some aspectexamples, the pharmaceutical composition further comprises an ST2 binding
 antagonist, a Factor D binding antagonist, an HtrA1 binding antagonist, a VEGF antagonist, a tryptase-
 beta binding antagonist, a chemoattractant receptor-homologous molecule expressed on Th2 cells
 (CRTH2) binding antagonist, an interleukin-13 (IL-13) binding antagonist, an interleukin-17 (IL-17) binding
 antagonist, a JAK1 antagonist, and/or an interleukin-5 (IL-5) binding antagonist.
 In some aspectexamples, the pharmaceutical composition comprises a Factor D binding
 antagonist.
 In some aspectexamples, the Factor D binding antagonist is an anti-Factor D antibody or an
 antigen-binding fragment thereof.
 In some aspectexamples, the pharmaceutical composition comprises an HtrA1 binding
 antagonist.

In some aspectexamples, the HtrA1 binding antagonist is an anti-HtrA1 antibody or an antigen-binding fragment thereof.

In some aspectexamples, the pharmaceutical composition comprises a VEGF antagonist.

In some aspectexamples, the VEGF antagonist is an anti-VEGF antibody or an antigen-binding
5 fragment thereof.

In some aspectexamples, the antibody concentration is about 1 mg/mL to about 400 mg/mL.

In some aspectexamples, the antibody concentration is about 150 mg/mL to about 250 mg/mL.

In some aspectexamples, the antibody concentration is about 175 mg/mL to about 225 mg/mL.

In some aspectexamples, the antibody concentration is about 200 mg/mL.

10 In another aspectexample, provided herein is any one of the antibodies disclosed herein or any one of the compositions disclosed herein for use as a medicament.

In another aspectexample, provided herein is any one of the antibodies disclosed herein or any one of the compositions disclosed herein for use in treating an IL-33-mediated disorder.

15 In some aspectexamples, the IL-33-mediated disorder is an ocular disorder, an inflammatory condition, an immune disorder, a fibrotic disorder, an eosinophilic disorder, an infection, pain, a central nervous system disorder, or a solid tumor.

In some aspectexamples, the ocular disorder is age-related macular degeneration (AMD), retinopathy of the eye, polypoidal choroidal vasculopathy (PCV), diabetic macular edema, dry eye disease, Behcet's disease, retina detachment, glaucoma, uveitis, retinitis pigmentosa, Leber Congenital
20 Amaurosis, Stargardt's disease, traumatic eye injury, or conjunctivitis.

In some aspectexamples, the AMD is geographic atrophy (GA), wet AMD, or dry AMD.

In some aspectexamples, the AMD is GA.

In some aspectexamples, the AMD is intermediate AMD or advanced AMD.

25 In some aspectexamples, the retinopathy of the eye is diabetic retinopathy (DR) or retinopathy of prematurity (ROP).

In some aspectexamples, the retinopathy of the eye is high-altitude DR.

In some aspectexamples, the conjunctivitis is infectious conjunctivitis or non-infectious conjunctivitis.

In some aspectexamples, the conjunctivitis is allergic conjunctivitis.

30 In some aspectexamples, the inflammatory condition is asthma, sepsis, septic shock, atopic dermatitis, allergic rhinitis, rheumatoid arthritis, or chronic obstructive pulmonary disease (COPD).

In some aspectexamples, the immune disorder is asthma, rheumatoid arthritis, allergy, anaphylaxis, anaphylactic shock, allergic rhinitis, psoriasis, inflammatory bowel disease (IBD), Crohn's disease, diabetes, or liver disease.

35 In some aspectexamples, the fibrotic disease is idiopathic pulmonary fibrosis (IPF).

In some aspectexamples, the eosinophilic disorder is an eosinophil-associated gastrointestinal disorder (EGID).

In some aspectexamples, the EGID is eosinophilic esophagitis.

40 In some aspectexamples, the infection is a helminth infection, a protozoan infection, or a viral infection.

In some aspectexamples, the protozoan infection is a *Leishmania major* infection.

In some aspectexamples, the viral infection is a respiratory syncytial virus (RSV) infection or an influenza infection.

In some aspectexamples, the pain is inflammatory pain.

In some aspectexamples, the central nervous system disorder is Alzheimer's disease.

In some aspectexamples, the solid tumor is a breast tumor, a colon tumor, a prostate tumor, a lung tumor, a kidney tumor, a liver tumor, a pancreas tumor, a stomach tumor, an intestinal tumor, a brain tumor, a bone tumor, and a skin tumor.

In some aspectexamples, the antibody or composition is used in combination with an ST2 binding antagonist, a Factor D binding antagonist, an HtrA1 binding antagonist, a VEGF antagonist, a tryptase-beta binding antagonist, a CRTH2 binding antagonist, an IL-13 binding antagonist, an IL-17 binding antagonist, a JAK1 antagonist, and/or an IL-5 binding antagonist.

In some aspectexamples, the antibody or composition is used in combination with a Factor D binding antagonist.

In some aspectexamples, the Factor D binding antagonist is an anti-Factor D antibody or an antigen-binding fragment thereof.

In some aspectexamples, the antibody or composition is used in combination with an HtrA1 binding antagonist.

In some aspectexamples, the HtrA1 binding antagonist is an anti-HtrA1 antibody or an antigen-binding fragment thereof.

In some aspectexamples, the antibody or composition is used in combination with a VEGF antagonist.

In some aspectexamples, the VEGF antagonist is an anti-VEGF antibody or an antigen-binding fragment thereof.

In another aspectexample, provided herein is the use of any one of the antibodies disclosed herein or any one of the compositions disclosed herein in the manufacture of a medicament for treating an IL-33-mediated disorder.

In some aspectexamples, the IL-33-mediated disorder is an ocular disorder, an inflammatory condition, an immune disorder, a fibrotic disorder, an eosinophilic disorder, an infection, pain, a central nervous system disorder, or a solid tumor.

In some aspectexamples, the ocular disorder is AMD, retinopathy of the eye, PCV, diabetic macular edema, dry eye disease, Behcet's disease, retina detachment, glaucoma, uveitis, retinitis pigmentosa, Leber Congenital Amaurosis, Stargardt's disease, traumatic eye injury, or conjunctivitis.

In some aspectexamples, the AMD is GA, wet AMD, or dry AMD.

In some aspectexamples, the AMD is GA.

In some aspectexamples, the AMD is intermediate AMD or advanced AMD.

In some aspectexamples, the retinopathy of the eye is DR or ROP.

In some aspectexamples, the retinopathy of the eye is high-altitude DR.

In some aspectexamples, the conjunctivitis is infectious conjunctivitis or non-infectious conjunctivitis.

In some aspectexamples, the conjunctivitis is allergic conjunctivitis.

In some aspectexamples, the inflammatory condition is asthma, sepsis, septic shock, atopic dermatitis, allergic rhinitis, rheumatoid arthritis, or COPD.

In some aspectexamples, the immune disorder is asthma, rheumatoid arthritis, allergy, anaphylaxis, anaphylactic shock, allergic rhinitis, psoriasis, IBD, Crohn's disease, diabetes, or liver disease.

In some aspectexamples, the fibrotic disease is IPF.

5 In some aspectexamples, the eosinophilic disorder is an EGID.

In some aspectexamples, the EGID is eosinophilic esophagitis.

In some aspectexamples, the infection is a helminth infection, a protozoan infection, or a viral infection.

10 In some aspectexamples, the protozoan infection is a *Leishmania major* infection.

In some aspectexamples, the viral infection is an RSV infection or an influenza infection.

In some aspectexamples, the pain is inflammatory pain.

In some aspectexamples, the central nervous system disorder is Alzheimer's disease.

15 In some aspectexamples, the solid tumor is a breast tumor, a colon tumor, a prostate tumor, a lung tumor, a kidney tumor, a liver tumor, a pancreas tumor, a stomach tumor, an intestinal tumor, a brain tumor, a bone tumor, and a skin tumor.

In some aspectexamples, the medicament is formulated for use in combination with an ST2 binding antagonist, a Factor D binding antagonist, an HtrA1 binding antagonist, a VEGF antagonist, a tryptase-beta binding antagonist, a CRTH2 binding antagonist, an IL-13 binding antagonist, an IL-17 binding antagonist, a JAK1 antagonist, and/or an IL-5 binding antagonist.

20 In some aspectexamples, the medicament is formulated for use in combination with a Factor D binding antagonist.

In some aspectexamples, the Factor D binding antagonist is an anti-Factor D antibody or an antigen-binding fragment thereof.

25 In some aspectexamples, the medicament is formulated for use in combination with an HtrA1 binding antagonist.

In some aspectexamples, the HtrA1 binding antagonist is an anti-HtrA1 antibody or an antigen-binding fragment thereof.

In some aspectexamples, the medicament is formulated for use in combination with a VEGF antagonist.

30 In some aspectexamples, the VEGF antagonist is an anti-VEGF antibody or an antigen-binding fragment thereof.

In one aspect, provided herein is use of the antibody as disclosed herein in the manufacture of a medicament for treating an IL-33-mediated disorder in a subject in need thereof. In another aspectexample, provided herein is a method of treating an IL-33-mediated disorder in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of any one of the antibodies disclosed herein or any one of the compositions disclosed herein.

35 In some aspectexamples, the IL-33-mediated disorder is an ocular disorder, an inflammatory condition, an immune disorder, a fibrotic disorder, an eosinophilic disorder, an infection, pain, a central nervous system disorder, or a solid tumor.

40 In some aspectexamples, the ocular disorder is AMD, retinopathy of the eye, PCV, diabetic macular edema, dry eye disease, Behcet's disease, retina detachment, glaucoma, uveitis, retinitis pigmentosa, Leber Congenital Amaurosis, Stargardt's disease, traumatic eye injury, or conjunctivitis.

In some aspectexamples, the AMD is GA, wet AMD, or dry AMD.

In some aspectexamples, the AMD is GA.

45 In some aspectexamples, the AMD is intermediate AMD or advanced AMD.

In some aspectexamples, the retinopathy of the eye is DR or ROP.

In some aspectexamples, the retinopathy of the eye is high-altitude DR.

In some aspectexamples, the conjunctivitis is infectious conjunctivitis or non-infectious conjunctivitis.

5 In some aspectexamples, the conjunctivitis is allergic conjunctivitis.

In some aspectexamples, the inflammatory condition is asthma, sepsis, septic shock, atopic dermatitis, allergic rhinitis, rheumatoid arthritis, or COPD.

In some aspectexamples, the immune disorder is asthma, rheumatoid arthritis, allergy, anaphylaxis, anaphylactic shock, allergic rhinitis, psoriasis, IBD, Crohn's disease, diabetes, and liver

10 disease.

In some aspectexamples, the fibrotic disease is IPF.

In some aspectexamples, the eosinophilic disorder is an EGID.

In some aspectexamples, the EGID is eosinophilic esophagitis.

In some aspectexamples, the infection is a helminth infection, a protozoan infection, or a viral

15 infection.

In some aspectexamples, the protozoan infection is a Leishmania major infection.

In some aspectexamples, the viral infection is an RSV infection or an influenza infection.

In some aspectexamples, the pain is inflammatory pain.

In some aspectexamples, the solid tumor is a breast tumor, a colon tumor, a prostate tumor, a

20 lung tumor, a kidney tumor, a liver tumor, a pancreas tumor, a stomach tumor, an intestinal tumor, a brain tumor, a bone tumor, and a skin tumor.

In some aspectexamples, the method further comprises administering to the subject an ST2 binding antagonist, a Factor D binding antagonist, an HtrA1 binding antagonist, a VEGF antagonist, a tryptase-beta binding antagonist, a CRTH2 binding antagonist, an IL-13 binding antagonist, an IL-17

25 binding antagonist, a JAK1 antagonist, and/or an IL-5 binding antagonist.

In some aspectexamples, the method further comprises administering to the subject a Factor D binding antagonist.

In some aspectexamples, the Factor D binding antagonist is anti-Factor D antibody or an antigen-binding fragment thereof.

30 In some aspectexamples, the method further comprises administering to the subject an HtrA1 binding antagonist.

In some aspectexamples, the HtrA1 binding antagonist is an anti-HtrA1 antibody or an antigen-binding fragment thereof.

In some aspectexamples, the method further comprises administering to the subject a VEGF

35 antagonist.

In some aspectexamples, the VEGF antagonist is an anti-VEGF antibody or an antigen-binding fragment thereof.

In another aspectexample, provided herein is a method of treating GA in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of any one

40 of the antibodies disclosed herein or any one of the compositions disclosed herein.

In some aspectexamples, the antibody is an Fab fragment.

In some aspectexamples, the antibody or the composition is administered intravitreally, ocularly, intraocularly, juxtasclerally, subtenonally, superchoroidally, topically, intravenously, intramuscularly, intradermally, percutaneously, intraarterially, intraperitoneally, intralesionally, intracranially, intraarticularly,

intraprostatically, intrapleurally, intratracheally, intrathecally, intranasally, intravaginally, intrarectally, topically, intratumorally, intraperitoneally, peritoneally, intraventricularly, subcutaneously, subconjunctivally, intravesicularly, mucosally, intrapericardially, intraumbilically, intraorbitally, orally, transdermally, by inhalation, by injection, by eye drop, by implantation, by infusion, by continuous
5 infusion, by localized perfusion bathing target cells directly, by catheter, by lavage, in cremes, or in lipid compositions.

In some aspectexamples, the antibody or the composition is administered intravitreally, ocularly, intraocularly, juxtasclerally, subtenonally, superchoroidally, or topically.

In some aspectexamples, the antibody or the composition is administered intravitreally by
10 injection.

In some aspectexamples, the antibody or the composition is administered topically by eye drop or ointment.

In some aspectexamples, the antibody or the composition is administered by a port delivery device.

15 In some aspectexamples, the subject is a human.

Brief Description of the Drawings

FIGS. 1A and 1B are sequence alignments of the heavy chain variable region (VH) and light chain variable region (VL) sequences of the 1E1 hybridoma and 1E1v8 anti-IL-33 antibody clones.

20 Complementarity-determining region (CDR) sequences according to Kabat definition are underlined.

FIGS. 2A and 2B are sequence alignments of the VH and VL sequences of the indicated anti-IL-33 antibody clones. CDR sequences according to Kabat definition are underlined.

FIG. 3A is a network plot showing relationships between clones or bins of anti-IL-33 antibody clones based on blocking activity.

25 **FIG. 3B** is a heatmap showing relationships between clones or bins of anti-IL-33 antibody clones based on blocking activity.

FIGS. 3C-3E are a series of graphs showing results of epitope binning using surface plasmon resonance (SPR). The graphs show normalized response as a function of time.

Detailed Description of Embodiments of the Invention

I. Definitions

The term “about” as used herein refers to the usual error range for the respective value readily known to the skilled person in this technical field. Reference to “about” a value or parameter herein includes (and describes) embodiments that are directed to that value or parameter *per se*.

35 An “acceptor human framework” for the purposes herein is a framework comprising the amino acid sequence of a light chain variable domain (VL) framework or a heavy chain variable domain (VH) framework derived from a human immunoglobulin framework or a human consensus framework, as defined below. An acceptor human framework “derived from” a human immunoglobulin framework or a human consensus framework may comprise the same amino acid sequence thereof, or it may contain
40 amino acid sequence changes. In some embodiments, the number of amino acid changes are 10 or less, 9 or less, 8 or less, 7 or less, 6 or less, 5 or less, 4 or less, 3 or less, or 2 or less. In some embodiments,

WHAT IS CLAIMED IS:

1. An isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, the binding domain comprising the following six complementarity-determining regions (CDRs):

- (a) a CDR-H1 comprising the amino acid sequence of NYWMT (SEQ ID NO: 1);
- (b) a CDR-H2 comprising the amino acid sequence of SITYTGGGTYPDSVKG (SEQ ID NO: 2);
- (c) a CDR-H3 comprising the amino acid sequence of ANYYYNTYGGFPY (SEQ ID NO: 3);
- (d) a CDR-L1 comprising the amino acid sequence of LASEGFSNDLA (SEQ ID NO: 4);
- (e) a CDR-L2 comprising the amino acid sequence of AASRLQD (SEQ ID NO: 5); and
- (f) a CDR-L3 comprising the amino acid sequence of QQGSKYPLT (SEQ ID NO: 6).

2. An isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 7; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 8; or (c) a VH domain as in (a) and a VL domain as in (b).

3. The antibody of claim 1 or 2, wherein the VH domain comprises:

- (a) an FR-H1 comprising the amino acid sequence of EVQLVX₁SGX₂X₃X₄X₅X₆PGX₇SX₈X₉X₁₀SCX₁₁ASGFTFN (SEQ ID NO: 9), wherein X₁ is E or Q; X₂ is G or A; X₃ is G or E; X₄ is L or V; X₅ is V or K; X₆ is Q or K; X₇ is G, A, or T; X₈ is L or V; X₉ is R or K; X₁₀ is L or V; and X₁₁ is A, K, or L;
- (b) an FR-H2 comprising the amino acid sequence of WX₁RQAPGX₂GLEWX₃X₄ (SEQ ID NO: 10), wherein X₁ is I or V; X₂ is K or Q; X₃ is V, M, or I; and X₄ is A or G;
- (c) an FR-H3 comprising the amino acid sequence of RX₁TX₂X₃RDX₄X₅X₆X₇X₈X₉YX₁₀X₁₁X₁₂X₁₃SLRX₁₄EDTAX₁₅YYCTR (SEQ ID NO: 11), wherein X₁ is F or V; X₂ is I or M; X₃ is S or T; X₄ is D, N, or T; X₅ is A or S; X₆ is K or T; X₇ is S or N; X₈ is S or T; X₉ is L or V; X₁₀ is L or M; X₁₁ is Q or E; X₁₂ is M or L; X₁₃ is N or S; X₁₄ is A or S; and X₁₅ is V or T; and
- (d) an FR-H4 comprising the amino acid sequence of WGQGTLTVSS (SEQ ID NO: 12).

4. The antibody of any one of claims 1-3, wherein the VH domain comprises:

- (a) an FR-H1 comprising the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFN (SEQ ID NO: 17);
- (b) an FR-H2 comprising the amino acid sequence of WIRQAPGKGLEWVA (SEQ ID NO: 18);
- (c) an FR-H3 comprising the amino acid sequence of RFTISRDDAKSSLYLQMNSLRAEDTAVYYCTR (SEQ ID NO: 19); and
- (d) an FR-H4 comprising the amino acid sequence of WGQGTLTVSS (SEQ ID NO: 12).

5. The antibody of any one of claims 1-3, wherein the VH domain comprises the amino acid sequence of SEQ ID NO: 7.

~~6. The antibody of any one of claims 1-3, wherein the VH domain comprises:~~

- ~~(a) an FR-H1 comprising the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFN (SEQ ID NO: 17);~~
- ~~(b) an FR-H2 comprising the amino acid sequence of WVRQAPGKGLEWVA (SEQ ID NO: 39);~~
- ~~(c) an FR-H3 comprising the amino acid sequence of RFTISRDNAKNSLYLQMNSLRAEDTAVYYCTR (SEQ ID NO: 40); and~~
- ~~(d) an FR-H4 comprising the amino acid sequence of WGQGTLTVSS (SEQ ID NO: 12).~~

~~7. The antibody of any one of claims 1-3, wherein the VH domain comprises the amino acid sequence of SEQ ID NO: 41.~~

~~8. The antibody of any one of claims 1-3, wherein the VH domain comprises:~~

- ~~(a) an FR-H1 comprising the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFN (SEQ ID NO: 17);~~
- ~~(b) an FR-H2 comprising the amino acid sequence of WIRQAPGKGLEWIA (SEQ ID NO: 42);~~
- ~~(c) an FR-H3 comprising the amino acid sequence of RFTISRDDAKSSLYLQMNSLRAEDTAVYYCTR (SEQ ID NO: 19); and~~
- ~~(d) an FR-H4 comprising the amino acid sequence of WGQGTLTVSS (SEQ ID NO: 12).~~

~~9. The antibody of any one of claims 1-3, wherein the VH domain comprises the amino acid sequence of SEQ ID NO: 43.~~

~~10. The antibody of any one of claims 1-3, wherein the VH domain comprises:~~

- ~~(a) an FR-H1 comprising the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFN (SEQ ID NO: 17);~~
- ~~(b) an FR-H2 comprising the amino acid sequence of WVRQAPGKGLEWVA (SEQ ID NO: 39);~~
- ~~(c) an FR-H3 comprising the amino acid sequence of RFTISRDDAKSSLYLQMNSLRAEDTAVYYCTR (SEQ ID NO: 19); and~~
- ~~(d) an FR-H4 comprising the amino acid sequence of WGQGTLTVSS (SEQ ID NO: 12).~~

~~11. The antibody of any one of claims 1-3, wherein the VH domain comprises the amino acid sequence of SEQ ID NO: 44.~~

~~12. The antibody of any one of claims 1-3, wherein the VH domain comprises:~~

- ~~(a) an FR-H1 comprising the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFN (SEQ ID NO: 17);~~
- ~~(b) an FR-H2 comprising the amino acid sequence of WVRQAPGKGLEWVA (SEQ ID NO: 39);~~

~~(c) an FR-H3 comprising the amino acid sequence of~~

~~RFTISRDDAKNSLYLQMNSLRAEDTAVYYCTR (SEQ ID NO: 45); and~~

~~(d) an FR-H4 comprising the amino acid sequence of WGQGTLTVSS (SEQ ID NO: 12).~~

~~13. The antibody of any one of claims 1-3, wherein the VH domain comprises the amino acid sequence of SEQ ID NO: 46.~~

~~14. The antibody of any one of claims 1-3, wherein the VH domain comprises:~~

~~(a) an FR-H1 comprising the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFN (SEQ ID NO: 17);~~

~~(b) an FR-H2 comprising the amino acid sequence of WVRQAPGKGLEWVA (SEQ ID NO: 39);~~

~~(c) an FR-H3 comprising the amino acid sequence of~~

~~RFTISRDNKSSLYLQMNSLRAEDTAVYYCTR (SEQ ID NO: 47); and~~

~~(d) an FR-H4 comprising the amino acid sequence of WGQGTLTVSS (SEQ ID NO: 12).~~

~~15. The antibody of any one of claims 1-3, wherein the VH domain comprises the amino acid sequence of SEQ ID NO: 48.~~

~~16. The antibody of any one of claims 1-3, wherein the VH domain comprises:~~

~~(a) an FR-H1 comprising the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFN (SEQ ID NO: 17);~~

~~(b) an FR-H2 comprising the amino acid sequence of WVRQAPGKGLEWIA (SEQ ID NO: 49);~~

~~(c) an FR-H3 comprising the amino acid sequence of~~

~~RFTISRDDAKSSLYLQMNSLRAEDTAVYYCTR (SEQ ID NO: 19); and~~

~~(d) an FR-H4 comprising the amino acid sequence of WGQGTLTVSS (SEQ ID NO: 12).~~

~~17. The antibody of any one of claims 1-3, wherein the VH domain comprises the amino acid sequence of SEQ ID NO: 50.~~

~~18. The antibody of any one of claims 1-3, wherein the VH domain comprises:~~

~~(a) an FR-H1 comprising the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFN (SEQ ID NO: 17);~~

~~(b) an FR-H2 comprising the amino acid sequence of WVRQAPGKGLEWIA (SEQ ID NO: 49);~~

~~(c) an FR-H3 comprising the amino acid sequence of~~

~~RFTISRDDSKSTLYLQMNSLRAEDTAVYYCTR (SEQ ID NO: 51); and~~

~~(d) an FR-H4 comprising the amino acid sequence of WGQGTLTVSS (SEQ ID NO: 12).~~

~~19. The antibody of any one of claims 1-3, wherein the VH domain comprises the amino acid sequence of SEQ ID NO: 52.~~

20-6. The antibody of any one of claims 1-~~195~~, wherein the VL domain comprises:

- (a) an FR-L1 comprising the amino acid sequence of X₁I X₂X₃TQSPX₄X₅LSX₆SX₇GX₈X₉X₁₀X₁₁X₁₂X₁₃C (SEQ ID NO: 13), wherein X₁ is D or E; X₂ is Q or V; X₃ is M or L; X₄ is S or A; X₅ is S or T; X₆ is A or L; X₇ is V, P, or L; X₈ is D or E; X₉ is R or T; X₁₀ is V or A; X₁₁ is T or S; X₁₂ is I or L; and X₁₃ is T, S, or E;
- (b) an FR-L2 comprising the amino acid sequence of WX₁QQKX₂GX₃X₄PX₅X₆LIY (SEQ ID NO: 14), wherein X₁ is Y or F; X₂ is P or S; X₃ is K or Q; X₄ is S or A; X₅ is K, R, or Q; and X₆ is L or S;
- (c) an FR-L3 comprising the amino acid sequence of GX₁PX₂RFSGSGSGTX₃FX₄LX₅ISX₆X₇X₈PEDX₉AX₁₀YX₁₁C (SEQ ID NO: 15), wherein X₁ is V or I; X₂ is S or A; X₃ is D or R; X₄ is T or S; X₅ is T or K; X₆ is S or G; X₇ is L or M; X₈ is Q or E; X₉ is F, V, or E; X₁₀ is T, V, or D; and X₁₁ is F or Y; and
- (d) an FR-L4 comprising the amino acid sequence of FGX₁GTX₂EIK (SEQ ID NO: 16), wherein X₁ is G or S and X₂ is V or L.

21.7. The antibody of any one of claims 1-~~20~~5, wherein the VL domain comprises:

- (a) an FR-L1 comprising the amino acid sequence of DIQMTQSPSSLSASVGDRVITC (SEQ ID NO: 21);
- (b) an FR-L2 comprising the amino acid sequence of WYQQKPGKSPKLLIY (SEQ ID NO: 22);
- (c) an FR-L3 comprising the amino acid sequence of GVPSRFSGSGSGTDFTLTISLQPEDFATYFC (SEQ ID NO: 23); and
- (d) an FR-L4 comprising the amino acid sequence of FGGGTKVEIK (SEQ ID NO: 24).

22.8. The antibody of any one of claims 1-~~20~~5, wherein the VL domain comprises the amino acid sequence of SEQ ID NO: 8.

23.9. An isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising ~~an~~the amino acid sequence of SEQ ID NO: 7 and (b) a VL domain comprising ~~an~~the amino acid sequence of SEQ ID NO: 8.

24.10. An isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a heavy chain (HC) comprising ~~an~~the amino acid sequence of SEQ ID NO: 25 and (b) a light chain (LC) comprising ~~an~~the amino acid sequence of SEQ ID NO: 26.

~~25. The antibody of any one of claims 1-20, wherein the VL domain comprises:~~

- ~~(a) an FR-L1 comprising the amino acid sequence of DIQMTQSPSSLSASVGDRVITC (SEQ ID NO: 21);~~
- ~~(b) an FR-L2 comprising the amino acid sequence of WFQQKPGKAPKSLIY (SEQ ID NO: 53);~~
- ~~(c) an FR-L3 comprising the amino acid sequence of GVPSRFSGSGSGTDFTLTISLQPEDFATYYC (SEQ ID NO: 54); and~~
- ~~(d) an FR-L4 comprising the amino acid sequence of FGGGTKVEIK (SEQ ID NO: 24).~~

~~26. The antibody of any one of claims 1-20, wherein the VL domain comprises the amino acid sequence of SEQ ID NO: 55.~~

~~27. The antibody of any one of claims 1-20, wherein the VL domain comprises:~~

- ~~(a) an FR-L1 comprising the amino acid sequence of DIQMTQSPSSLSASVGDRVITTC (SEQ ID NO: 21);~~
- ~~(b) an FR-L2 comprising the amino acid sequence of WYQQKPGKAPKSLIY (SEQ ID NO: 56);~~
- ~~(c) an FR-L3 comprising the amino acid sequence of GVPSRFSGSGSGTDFTLTISLQPEDFATYFC (SEQ ID NO: 23); and~~
- ~~(d) an FR-L4 comprising the amino acid sequence of FGGGTKVEIK (SEQ ID NO: 24).~~

~~28. The antibody of any one of claims 1-20, wherein the VL domain comprises the amino acid sequence of SEQ ID NO: 57.~~

~~29. The antibody of any one of claims 1-20, wherein the VL domain comprises:~~

- ~~(a) an FR-L1 comprising the amino acid sequence of DIQMTQSPSSLSASVGDRVITTC (SEQ ID NO: 21);~~
- ~~(b) an FR-L2 comprising the amino acid sequence of WFQQKPGKAPKSLIY (SEQ ID NO: 53);~~
- ~~(c) an FR-L3 comprising the amino acid sequence of GVPSRFSGSGSGTDFTLTISLQPEDFATYFC (SEQ ID NO: 23); and~~
- ~~(d) an FR-L4 comprising the amino acid sequence of FGGGTKVEIK (SEQ ID NO: 24).~~

~~30. The antibody of any one of claims 1-20, wherein the VL domain comprises the amino acid sequence of SEQ ID NO: 58.~~

~~31. The antibody of any one of claims 1-20, wherein the VL domain comprises:~~

- ~~(a) an FR-L1 comprising the amino acid sequence of DIQMTQSPSSLSASVGDRVITTC (SEQ ID NO: 21);~~
- ~~(b) an FR-L2 comprising the amino acid sequence of WYQQKPGKAPKSLIY (SEQ ID NO: 56);~~
- ~~(c) an FR-L3 comprising the amino acid sequence of GVPSRFSGSGSGTDFTLTISLQPEDFATYYC (SEQ ID NO: 54); and~~
- ~~(d) an FR-L4 comprising the amino acid sequence of FGGGTKVEIK (SEQ ID NO: 24).~~

~~32. The antibody of any one of claims 1-20, wherein the VL domain comprises the amino acid sequence of SEQ ID NO: 59.~~

~~33. The antibody of any one of claims 1-20, wherein the VL domain comprises:~~

- ~~(a) an FR-L1 comprising the amino acid sequence of DIQMTQSPSSLSASVGDRVITTC (SEQ ID NO: 21);~~
- ~~(b) an FR-L2 comprising the amino acid sequence of WYQQKPGKSPKLLIY (SEQ ID NO: 22);~~

~~(c) an FR-L3 comprising the amino acid sequence of~~

~~GVPSTRFSGSGSGTDFLTISLQPEDVATYYC (SEQ ID NO: 60); and~~

~~(d) an FR-L4 comprising the amino acid sequence of FGGGTKVEIK (SEQ ID NO: 24).~~

~~34. The antibody of any one of claims 1-20, wherein the VL domain comprises the amino acid sequence of SEQ ID NO: 61.~~

35.11. An isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises: ~~a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 41 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 55.~~

~~(i) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 41 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 55;~~

~~(ii) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 43 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 55;~~

~~(iii) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 41 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 8;~~

~~(iv) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 43 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 8;~~

~~(v) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 44 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 8;~~

~~(vi) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 46 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 8;~~

~~(vii) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 48 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 8;~~

~~(viii) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 43 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 57;~~

~~(ix) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 44 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 57;~~

~~(x) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 46 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 57;~~

~~(xi) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 48 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 57;~~

~~(xii) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 50 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 57;~~

~~(xiii) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 43 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 58;~~

~~(xiv) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 44 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 58;~~

~~(xv) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 46 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 58;~~

(xvi) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 48 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 58;

(xvii) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 50 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 58;

(xviii) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 43 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 59;

(xix) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 44 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 59;

(xx) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 46 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 59;

(xxi) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 48 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 59;

(xxii) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 50 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 59; or

(xxiii) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 52 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 61.

~~36. An isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 43 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 55.~~

~~37. An isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 41 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 8.~~

~~38. An isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 43 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 8.~~

~~39. An isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 44 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 8.~~

~~40. An isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 46 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 8.~~

~~41. An isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 48 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 8.~~

~~52. An isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 43 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 59.~~

~~53. An isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 44 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 59.~~

~~54. An isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 46 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 59.~~

~~55. An isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 48 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 59.~~

~~56. An isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 50 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 59.~~

~~57. An isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 52 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 61.~~

58.12. An isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises: ~~a binding domain comprising (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 35; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 36; or (c) a VH domain as in (a) and a VL domain as in (b).~~

~~(i) a binding domain comprising (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 35; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 36; or (c) a VH domain as in (a) and a VL domain as in (b);~~

~~(ii) a binding domain comprising (a) a heavy chain (HC) comprising an amino acid sequence of SEQ ID NO: 37 and (b) a light chain (LC) comprising an amino acid sequence of SEQ ID NO: 38; or~~

~~(iii) a binding domain comprising (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 65; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 69; or (c) a VH domain as in (a) and a VL domain as in (b).~~

59. The antibody of any one of claims 1, 3, 20, and 58, wherein the VH domain comprises:
(a) an FR-H1 comprising the amino acid sequence of EVQLVESGGGLVQPGTSLKLSCLASGFTFN (SEQ ID NO: 27);
(b) an FR-H2 comprising the amino acid sequence of WIRQAPGKGLEWIA (SEQ ID NO: 28);
(c) an FR-H3 comprising the amino acid sequence of RFTISRDDAKSTLYLQMNSLRSEDATYYCTR (SEQ ID NO: 29); and
(d) an FR-H4 comprising the amino acid sequence of WGQGTLTVSS (SEQ ID NO: 12).

60. The antibody of any one of claims 1, 3, 20, and 58, wherein the VH domain comprises the amino acid sequence of SEQ ID NO: 35.

61. The antibody of any one of claims 1, 3, 20, and 58-60, wherein the VL domain comprises:
(a) an FR-L1 comprising the amino acid sequence of DIQMTQSPASLSASLGTVSIEC (SEQ ID NO: 31);
(b) an FR-L2 comprising the amino acid sequence of WYQQKSGKSPQLLIY (SEQ ID NO: 32);
(c) an FR-L3 comprising the amino acid sequence of GVPSRFSGSGSGTRFSLKISGMQPEDEADYFC (SEQ ID NO: 33); and
(d) an FR-L4 comprising the amino acid sequence of FGSGTKLEIK (SEQ ID NO: 34).

62. The antibody of any one of claims 1, 3, 20, and 58-60, wherein the VL domain comprises the amino acid sequence of SEQ ID NO: 36.

63. An isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 35 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 36.

64. An isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising (a) a heavy chain (HC) comprising an amino acid sequence of SEQ ID NO: 37 and (b) a light chain (LC) comprising an amino acid sequence of SEQ ID NO: 38.

65. An isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 65; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 69; or (c) a VH domain as in (a) and a VL domain as in (b).

66. The antibody of any one of claims 1, 3, 20, and 65, wherein the VH domain comprises:
(a) an FR-H1 comprising the amino acid sequence of EVQLVQSGAEVKKPGASVKVSCASGFTFN (SEQ ID NO: 62);
(b) an FR-H2 comprising the amino acid sequence of WVRQAPGQGLEWMG (SEQ ID NO: 63);

~~(c) an FR-H3 comprising the amino acid sequence of~~

~~RVTMTRDTSTSTVYMESSLRSED TAVYYCTR (SEQ ID NO: 64); and~~

~~(d) an FR-H4 comprising the amino acid sequence of WGQGTLVTVSS (SEQ ID NO: 12).~~

~~67. The antibody of any one of claims 1, 3, 20, and 65, wherein the VH domain comprises the amino acid sequence of SEQ ID NO: 65.~~

~~68. The antibody of any one of claims 1, 3, 20, and 65-67, wherein the VL domain comprises:~~

~~(a) an FR-L1 comprising the amino acid sequence of EIVLTQSPATLSLSPGERATLSC (SEQ ID NO: 66);~~

~~(b) an FR-L2 comprising the amino acid sequence of WYQQKPGQAPRLLIY (SEQ ID NO: 67);~~

~~(c) an FR-L3 comprising the amino acid sequence of GIPARFSGSGSGTDFLTITSSLEPEDFAVYYC (SEQ ID NO: 68); and~~

~~(d) an FR-L4 comprising the amino acid sequence of FGGGTKVEIK (SEQ ID NO: 24).~~

~~69. The antibody of any one of claims 1, 3, 20, and 65-67, wherein the VL domain comprises the amino acid sequence of SEQ ID NO: 69.~~

~~70. An isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 65 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 69.~~

~~71. The antibody of any one of claims 1-70, wherein the antibody specifically binds human or cyno IL-33.~~

72.13. The antibody of ~~any one of claims 1-12~~claim 71, wherein the antibody specifically binds both human and ~~cyno IL-33~~ cynomolgus monkey (cyno) interleukin-33 (IL-33) with a K_D of about 1 nM or lower and/or inhibits the binding of human IL-33 to an IL-33 receptor with a 50% inhibitory concentration (IC50) of between about 800 fM and about 100 pM.

~~73. The antibody of claim 72, wherein the antibody specifically binds both human and cyno IL-33 with a K_D of about 1 nM or lower.~~

~~74. The antibody of any one of claims 71-73, wherein the antibody specifically binds human IL-33 with a K_D between about 100 fM and about 1 nM.~~

~~75. The antibody of claim 74, wherein the antibody specifically binds human IL-33 with a K_D between about 750 fM and about 300 pM.~~

~~76.—The antibody of claim 75, wherein the antibody specifically binds human IL-33 with a K_D between about 1 pM and about 200 pM.~~

~~77.—The antibody of claim 76, wherein the antibody specifically binds human IL-33 with a K_D of about 118 pM.~~

~~78.—The antibody of claim 76, wherein the antibody specifically binds human IL-33 with a K_D of about 15 pM.~~

~~79.—The antibody of any one of claims 71-78, wherein the antibody specifically binds cyno IL-33 with a K_D between about 100 fM and about 1 nM.~~

~~80.—The antibody of claim 79, wherein the antibody specifically binds cyno IL-33 with a K_D between about 1 pM and about 500 pM.~~

~~81.—The antibody of claim 80, wherein the antibody specifically binds cyno IL-33 with a K_D between about 20 pM and about 50 pM.~~

~~82.—The antibody of claim 81, wherein the antibody specifically binds cyno IL-33 with a K_D of about 35 pM.~~

~~83.—The antibody of claim 72 or 73, wherein the antibody specifically binds both human and cyno IL-33 with a K_D of between about 1 pM and about 500 pM.~~

~~84.—The antibody of claim 83, wherein the antibody specifically binds both human and cyno IL-33 with a K_D of between about 10 pM and about 40 pM.~~

~~85.—The antibody of any one of claims 1-84, wherein the antibody is capable of inhibiting the binding of IL-33 to an IL-33 receptor.~~

~~86.—The antibody of claim 85, wherein the inhibiting is measured using a cell-based blocking assay.~~

~~87.—The antibody of any one of claims 1-86, wherein the antibody inhibits binding of human IL-33 to an IL-33 receptor with an IC_{50} of between about 800 fM and about 100 pM.~~

~~88.—The antibody of claim 87, wherein the IC_{50} is between about 1 pM and about 50 pM.~~

~~89.—The antibody of claim 88, wherein the IC_{50} is about 31 pM.~~

90.14. The antibody of any one of claims 1-~~89~~13, wherein the antibody has a viscosity of less than about 5 centipoise (cP) at a concentration of about 180 mg/mL and/or a turbidity (optical density

(OD)) of about 0.5 or lower at a concentration of about 150 mg/mL or higher in phosphate-buffered saline (PBS) pH 7.4.

~~91.—The antibody of claim 90, wherein the antibody has a viscosity of between about 3 cP and about 5 cP at a concentration of about 180 mg/mL.~~

~~92.—The antibody of claim 91, wherein the antibody has a viscosity of about 4.6 cP at a concentration of about 180 mg/mL.~~

~~93.—The antibody of any one of claims 1-92, wherein the antibody has a turbidity (optical density (OD)) of about 0.5 or lower at a concentration of about 150 mg/ml or higher in phosphate-buffered saline (PBS) pH 7.4.~~

~~94.—The antibody of claim 93, wherein the antibody has a turbidity (OD) of between about 0.25 and about 0.5 at a concentration of about 150 mg/ml to about 250 mg/ml.~~

~~95.—The antibody of claim 94, wherein the antibody has a turbidity (OD) of about 0.38 at a concentration of about 200 mg/ml.~~

96-15. The antibody of any one of claims 1-~~95~~14, wherein the antibody is monoclonal, human, humanized, or chimeric.

97-16. The antibody of any one of claims 1-~~96~~15, wherein the antibody is an antibody fragment that binds IL-33.

98-17. The antibody of claim ~~97~~16, wherein the antibody fragment is an Fab, Fab'-SH, Fv, scFv, or (Fab')₂ fragment.

~~99.—The antibody of claim 98, wherein the antibody fragment is an Fab.~~

~~100.—The antibody of any one of claims 1-96, wherein the antibody is a full-length antibody.~~

~~101.—The antibody of claim 100, wherein the antibody is an IgG antibody.~~

~~102.—The antibody of claim 101, wherein the IgG antibody is an IgG1 antibody.~~

~~103.—The antibody of claim 101, wherein the IgG antibody is an IgG4 antibody.~~

104-18. The antibody of any one of claims 1-~~103~~17, wherein the antibody is a monospecific antibody.

~~105-19.~~ The antibody of any one of claims 1-~~10317~~, wherein the antibody is a multispecific antibody.

~~106-20.~~ The antibody of claim ~~10519~~, wherein the antibody is a bispecific antibody.

~~107. The antibody of claim 106, wherein the bispecific antibody comprises a second binding domain that binds to a second biological molecule, wherein the second biological molecule is interleukin-13 (IL-13), interleukin-4 (IL-4), interleukin-5 (IL-5), interleukin-17 (IL-17), Factor D, HtrA1, VEGF, or a VEGF receptor.~~

~~108-21.~~ An isolated nucleic acid or a set of isolated nucleic acids encoding the antibody of any one of claims 1-~~20107~~ or a set of isolated nucleic acids together encoding the antibody.

~~109-22.~~ A vector or a set of vectors comprising the isolated nucleic acid or set of isolated nucleic acids of claim ~~10821~~.

~~110-23.~~ A host cell comprising the vector or the set of vectors of claim ~~10922~~.

~~111. The host cell of claim 110, wherein the host cell is a mammalian cell.~~

~~112. The host cell of claim 111, wherein the mammalian cell is a Chinese hamster ovary (CHO) cell.~~

~~113. The host cell of claim 110, wherein the host cell is a prokaryotic cell.~~

~~114. The host cell of claim 113, wherein the prokaryotic cell is *E. coli*.~~

~~115-24.~~ A method of producing an antibody that specifically binds to IL-33, the method comprising culturing the host cell of ~~any one of claims 110-114~~ claim 23 in a culture medium.

~~116. The method of claim 115, wherein the method further comprises recovering the antibody from the host cell or the culture medium.~~

~~117-25.~~ A pharmaceutical composition comprising the antibody of any one of claims 1-~~10720~~, further comprising a pharmaceutically acceptable carrier, excipient, or diluent.

~~118. The composition of claim 117, further comprising a pharmaceutically acceptable carrier, excipient, or diluent.~~

~~119. The composition of claim 118, wherein the composition is a pharmaceutical composition.~~

~~120. The composition of claim 119, wherein the pharmaceutical composition further comprises an ST2 binding antagonist, a Factor D binding antagonist, an HtrA1 binding antagonist, a VEGF antagonist, a tryptase-beta binding antagonist, a chemoattractant receptor-homologous molecule-expressed on Th2 cells (CRTH2) binding antagonist, an interleukin-13 (IL-13) binding antagonist, an interleukin-17 (IL-17) binding antagonist, a JAK1 antagonist, and/or an interleukin-5 (IL-5) binding antagonist.~~

~~121. The composition of claim 120, wherein the pharmaceutical composition comprises a Factor D binding antagonist.~~

~~122. The composition of claim 121, wherein the Factor D binding antagonist is an anti-Factor D antibody or an antigen-binding fragment thereof.~~

~~123. The composition of claim 120, wherein the pharmaceutical composition comprises an HtrA1 binding antagonist.~~

~~124. The composition of claim 123, wherein the HtrA1 binding antagonist is an anti-HtrA1 antibody or an antigen-binding fragment thereof.~~

~~125. The composition of claim 120, wherein the pharmaceutical composition comprises a VEGF antagonist.~~

~~126. The composition of claim 125, wherein the VEGF antagonist is an anti-VEGF antibody or an antigen-binding fragment thereof.~~

~~127. The composition of any one of claims 117-126, wherein the antibody concentration is about 1 mg/mL to about 400 mg/mL.~~

~~128. The composition of claim 127, wherein the antibody concentration is about 150 mg/mL to about 250 mg/mL.~~

~~129. The composition of claim 128, wherein the antibody concentration is about 175 mg/mL to about 225 mg/mL.~~

~~130. The composition of claim 129, wherein the antibody concentration is about 200 mg/mL.~~

~~131. The antibody of any one of claims 1-107 or the composition of any one of claims 119-130 for use as a medicament.~~

~~132. The antibody of any one of claims 1-107 or the composition of any one of claims 119-130 for use in treating an IL-33-mediated disorder.~~

~~133. The antibody or composition for use of claim 132, wherein the IL-33-mediated disorder is an ocular disorder, an inflammatory condition, an immune disorder, a fibrotic disorder, an eosinophilic disorder, an infection, pain, a central nervous system disorder, or a solid tumor.~~

~~134. The antibody or composition for use of claim 133, wherein the ocular disorder is age-related macular degeneration (AMD), retinopathy of the eye, polypoidal choroidal vasculopathy (PCV), diabetic macular edema, dry eye disease, Behcet's disease, retina detachment, glaucoma, uveitis, retinitis pigmentosa, Leber Congenital Amaurosis, Stargardt's disease, traumatic eye injury, or conjunctivitis.~~

~~135. The antibody or composition for use of claim 134, wherein the AMD is geographic atrophy (GA), wet AMD, or dry AMD.~~

~~136. The antibody or composition for use of claim 135, wherein the AMD is GA.~~

~~137. The antibody or composition for use of claim 134, wherein the AMD is intermediate AMD or advanced AMD.~~

~~138. The antibody or composition for use of claim 134, wherein the retinopathy of the eye is diabetic retinopathy (DR) or retinopathy of prematurity (ROP).~~

~~139. The antibody or composition for use of claim 134, wherein the retinopathy of the eye is high-altitude DR.~~

~~140. The antibody or composition for use of claim 134, wherein the conjunctivitis is infectious conjunctivitis or non-infectious conjunctivitis.~~

~~141. The antibody or composition for use of claim 134, wherein the conjunctivitis is allergic conjunctivitis.~~

~~142. The antibody or composition for use of claim 133, wherein the inflammatory condition is asthma, sepsis, septic shock, atopic dermatitis, allergic rhinitis, rheumatoid arthritis, or chronic obstructive pulmonary disease (COPD).~~

~~143. The antibody or composition for use of claim 133, wherein the immune disorder is asthma, rheumatoid arthritis, allergy, anaphylaxis, anaphylactic shock, allergic rhinitis, psoriasis, inflammatory bowel disease (IBD), Crohn's disease, diabetes, or liver disease.~~

~~144. The antibody or composition for use of claim 133, wherein the fibrotic disease is idiopathic pulmonary fibrosis (IPF).~~

~~145. The antibody or composition for use of claim 133, wherein the eosinophilic disorder is an eosinophil-associated gastrointestinal disorder (EGID).~~

~~146. The antibody or composition for use of claim 145, wherein the EGID is eosinophilic esophagitis.~~

~~147. The antibody or composition for use of claim 133, wherein the infection is a helminth infection, a protozoan infection, or a viral infection.~~

~~148. The antibody or composition for use of claim 147, wherein the protozoan infection is a *Leishmania major* infection.~~

~~149. The antibody or composition for use of claim 147, wherein the viral infection is a respiratory syncytial virus (RSV) infection or an influenza infection.~~

~~150. The antibody or composition for use of claim 133, wherein the pain is inflammatory pain.~~

~~151. The antibody or composition for use of claim 133, wherein the central nervous system disorder is Alzheimer's disease.~~

~~152. The antibody or composition for use of claim 133, wherein the solid tumor is a breast tumor, a colon tumor, a prostate tumor, a lung tumor, a kidney tumor, a liver tumor, a pancreas tumor, a stomach tumor, an intestinal tumor, a brain tumor, a bone tumor, and a skin tumor.~~

~~153. The antibody or composition for use of any one of claims 131-152, wherein the antibody or composition is used in combination with an ST2-binding antagonist, a Factor D-binding antagonist, an HtrA1-binding antagonist, a VEGF antagonist, a tryptase-beta-binding antagonist, a CRTH2-binding antagonist, an IL-13-binding antagonist, an IL-17-binding antagonist, a JAK1 antagonist, and/or an IL-5 binding antagonist.~~

~~154. The antibody or composition for use of claim 153, wherein the antibody or composition is used in combination with a Factor D-binding antagonist.~~

~~155. The antibody or composition for use of claim 154, wherein the Factor D-binding antagonist is an anti-Factor D antibody or an antigen-binding fragment thereof.~~

~~156. The antibody or composition for use of claim 153, wherein the antibody or composition is used in combination with an HtrA1-binding antagonist.~~

~~157. The antibody or composition for use of claim 156, wherein the HtrA1 binding antagonist is an anti-HtrA1 antibody or an antigen-binding fragment thereof.~~

~~158. The antibody or composition for use of claim 153, wherein the antibody or composition is used in combination with a VEGF antagonist.~~

~~159. The antibody or composition for use of claim 158, wherein the VEGF antagonist is an anti-VEGF antibody or an antigen-binding fragment thereof.~~

~~160. Use of an antibody of any one of claims 1-107 or the composition of any one of claims 119-130 in the manufacture of a medicament for treating an IL-33-mediated disorder.~~

~~161. The use of claim 160, wherein the IL-33-mediated disorder is an ocular disorder, an inflammatory condition, an immune disorder, a fibrotic disorder, an eosinophilic disorder, an infection, pain, a central nervous system disorder, or a solid tumor.~~

~~162. The use of claim 161, wherein the ocular disorder is AMD, retinopathy of the eye, PCV, diabetic macular edema, dry eye disease, Behcet's disease, retina detachment, glaucoma, uveitis, retinitis pigmentosa, Leber Congenital Amaurosis, Stargardt's disease, traumatic eye injury, or conjunctivitis.~~

~~163. The use of claim 162, wherein the AMD is GA, wet AMD, or dry AMD.~~

~~164. The use of claim 163, wherein the AMD is GA.~~

~~165. The use of claim 162, wherein the AMD is intermediate AMD or advanced AMD.~~

~~166. The use of claim 162, wherein the retinopathy of the eye is DR or ROP.~~

~~167. The use of claim 162, wherein the retinopathy of the eye is high-altitude DR.~~

~~168. The use of claim 162, wherein the conjunctivitis is infectious conjunctivitis or non-infectious conjunctivitis.~~

~~169. The use of claim 162, wherein the conjunctivitis is allergic conjunctivitis.~~

~~170. The use of claim 161, wherein the inflammatory condition is asthma, sepsis, septic shock, atopic dermatitis, allergic rhinitis, rheumatoid arthritis, or COPD.~~

~~171. The use of claim 161, wherein the immune disorder is asthma, rheumatoid arthritis, allergy, anaphylaxis, anaphylactic shock, allergic rhinitis, psoriasis, IBD, Crohn's disease, diabetes, or liver disease.~~

- ~~172. The use of claim 161, wherein the fibrotic disease is IPF.~~
- ~~173. The use of claim 161, wherein the eosinophilic disorder is an EGID.~~
- ~~174. The use of claim 173, wherein the EGID is eosinophilic esophagitis.~~
- ~~175. The use of claim 161, wherein the infection is a helminth infection, a protozoan infection, or a viral infection.~~
- ~~176. The use of claim 175, wherein the protozoan infection is a *Leishmania major* infection.~~
- ~~177. The use of claim 175, wherein the viral infection is an RSV infection or an influenza infection.~~
- ~~178. The use of claim 161, wherein the pain is inflammatory pain.~~
- ~~179. The use of claim 161, wherein the central nervous system disorder is Alzheimer's disease.~~
- ~~180. The use of claim 161, wherein the solid tumor is a breast tumor, a colon tumor, a prostate tumor, a lung tumor, a kidney tumor, a liver tumor, a pancreas tumor, a stomach tumor, an intestinal tumor, a brain tumor, a bone tumor, and a skin tumor.~~
- ~~181. The use of any one of claims 160-180, wherein the medicament is formulated for use in combination with an ST2-binding antagonist, a Factor D-binding antagonist, an HtrA1-binding antagonist, a VEGF antagonist, a tryptase-beta-binding antagonist, a CRTH2-binding antagonist, an IL-13-binding antagonist, an IL-17-binding antagonist, a JAK1 antagonist, and/or an IL-5-binding antagonist.~~
- ~~182. The use of claim 181, wherein the medicament is formulated for use in combination with a Factor D-binding antagonist.~~
- ~~183. The use of claim 182, wherein the Factor D-binding antagonist is an anti-Factor D antibody or an antigen-binding fragment thereof.~~
- ~~184. The use of claim 181, wherein the medicament is formulated for use in combination with an HtrA1-binding antagonist.~~
- ~~185. The use of claim 184, wherein the HtrA1-binding antagonist is an anti-HtrA1 antibody or an antigen-binding fragment thereof.~~

~~186. The use of claim 181, wherein the medicament is formulated for use in combination with a VEGF antagonist.~~

~~187. The use of claim 186, wherein the VEGF antagonist is an anti-VEGF antibody or an antigen-binding fragment thereof.~~

~~188-26. Use of the antibody of any one of claims 1-20 in the manufacture of a medicament for a method of treating an IL-33-mediated disorder in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of the antibody of any one of claims 1-107 or the composition of any one of claims 119-130.~~

~~189-27. The method use of claim 18826, wherein the IL-33-mediated disorder is an ocular disorder, an inflammatory condition, an immune disorder, a fibrotic disorder, an eosinophilic disorder, an infection, pain, a central nervous system disorder, or a solid tumor.~~

~~190-28. The method use of claim 18927, wherein the ocular disorder is AMD, retinopathy of the eye, PCV, diabetic macular edema, dry eye disease, Behcet's disease, retina detachment, glaucoma, uveitis, retinitis pigmentosa, Leber Congenital Amaurosis, Stargardt's disease, traumatic eye injury, or conjunctivitis.~~

~~191-29. The method use of claim 19028, wherein the AMD is GA, wet AMD, or dry AMD.~~

~~192. The method of claim 191, wherein the AMD is GA.~~

~~193. The method of claim 190, wherein the AMD is intermediate AMD or advanced AMD.~~

~~194. The method of claim 190, wherein the retinopathy of the eye is DR or ROP.~~

~~195. The method of claim 190, wherein the retinopathy of the eye is high-altitude DR.~~

~~196. The method of claim 190, wherein the conjunctivitis is infectious conjunctivitis or non-infectious conjunctivitis.~~

~~197. The method of claim 190, wherein the conjunctivitis is allergic conjunctivitis.~~

~~198. The method of claim 189, wherein the inflammatory condition is asthma, sepsis, septic shock, atopic dermatitis, allergic rhinitis, rheumatoid arthritis, or COPD.~~

~~199. The method of claim 189, wherein the immune disorder is asthma, rheumatoid arthritis, allergy, anaphylaxis, anaphylactic shock, allergic rhinitis, psoriasis, IBD, Crohn's disease, diabetes, and liver disease.~~

~~200. The method of claim 189, wherein the fibrotic disease is IPF.~~

~~201. The method of claim 189, wherein the eosinophilic disorder is an EGID.~~

~~202. The method of claim 201, wherein the EGID is eosinophilic esophagitis.~~

~~203. The method of claim 189, wherein the infection is a helminth infection, a protozoan infection, or a viral infection.~~

~~204. The method of claim 203, wherein the protozoan infection is a Leishmania major infection.~~

~~205. The method of claim 203, wherein the viral infection is an RSV infection or an influenza infection.~~

~~206. The method of claim 189, wherein the pain is inflammatory pain.~~

~~207. The method of claim 189, wherein the solid tumor is a breast tumor, a colon tumor, a prostate tumor, a lung tumor, a kidney tumor, a liver tumor, a pancreas tumor, a stomach tumor, an intestinal tumor, a brain tumor, a bone tumor, and a skin tumor.~~

208-30. The ~~method use~~ of any one of claims ~~188-207~~26-29, wherein the medicament is for administration with ~~further comprising administering to the subject~~ an ST2 binding antagonist, a Factor D binding antagonist, an HtrA1 binding antagonist, a VEGF antagonist, a tryptase-beta binding antagonist, a CRTH2 binding antagonist, an IL-13 binding antagonist, an IL-17 binding antagonist, a JAK1 antagonist, and/or an IL-5 binding antagonist.

~~209. The method of claim 208, wherein the method further comprises administering to the subject a Factor D binding antagonist.~~

~~210. The method of claim 209, wherein the Factor D binding antagonist is anti-Factor D antibody or an antigen-binding fragment thereof.~~

~~211. The method of claim 208, wherein the method further comprises administering to the subject an HtrA1 binding antagonist.~~

~~212. The method of claim 211, wherein the HtrA1 binding antagonist is an anti-HtrA1 antibody or an antigen-binding fragment thereof.~~

~~213. The method of claim 208, wherein the method further comprises administering to the subject a VEGF antagonist.~~

~~214. The method of claim 213, wherein the VEGF antagonist is an anti-VEGF antibody or an antigen-binding fragment thereof.~~

~~215. A method of treating GA in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of the antibody of any one of claims 1-107.~~

~~216. The method of claim 215, wherein the antibody is an Fab fragment.~~

~~217-31.~~ The ~~method-use~~ of any one of claims ~~188-216~~26-30, wherein the antibody ~~or the composition~~ is to be administered intravitreally, ocularly, intraocularly, juxtasclerally, subtenonally, superchoroidally, topically, intravenously, intramuscularly, intradermally, percutaneously, intraarterially, intraperitoneally, intralesionally, intracranially, intraarticularly, intraprostatically, intrapleurally, intratracheally, intrathecally, intranasally, intravaginally, intrarectally, topically, intratumorally, intraperitoneally, peritoneally, intraventricularly, subcutaneously, subconjunctivally, intravesicularly, mucosally, intrapericardially, intraumbilically, intraorbitally, orally, transdermally, by inhalation, by injection, by eye drop, by implantation, by infusion, by continuous infusion, by localized perfusion bathing target cells directly, by catheter, by lavage, in cremes, or in lipid compositions.

~~218. The method of claim 217, wherein the antibody or the composition is administered intravitreally, ocularly, intraocularly, juxtasclerally, subtenonally, superchoroidally, or topically.~~

~~219. The method of claim 217 or 218, wherein the antibody or the composition is administered intravitreally by injection.~~

~~220. The method of claim 217 or 218, wherein the antibody or the composition is administered topically by eye drop or ointment.~~

~~221. The method of claim 217 or 218, wherein the antibody or the composition is administered by a port delivery device.~~

~~222. The method of any one of claims 188-221, wherein the subject is a human.~~