HtrA1 promoter region, which results in increased HtrA1 transcript levels (Dewan, A., et al., *Science* 314:989-92 (2006); Yang, Z., et al., *Science* 314:992-3 (2006)). Therefore, inhibition of HtrA1 enzymatic function is an attractive therapeutic approach, e.g. in age-related macular degeneration and in arthritic disease.

SUMMARY

The ~~invention~~disclosure provides anti-HtrA1 antibodies and methods of using the same for diagnostic and therapeutic purposes.

In one aspect, the invention provides an isolated antibody that binds to HtrA1 competitively with antibody comprising a VH sequence of SEQ ID NO:8 and a VL sequence of SEQ ID NO:7. Competitive binding may be determined, for example, using an ELISA assay.

In one ~~aspect~~embodiment, the ~~invention~~disclosure provides an isolated antibody that bind to HtrA1 having one or more of the following properties: (i) an IC_{50} of less than 50 nM, 30 nM, 25 nM, 20 nM, 15 nM, 10 nM, 5 nM, 3 nM, 2.5 nM, 2 nM, 1 nM, or less for one or more HtrA1 substrates; (ii) binds to HtrA1 with a ratio of 1 variable domain to one subunit of an HtrA1 trimer (e.g., a Fab binds to an HtrA1 trimer with a ratio of 3 Fab to 1 HtrA1 trimer, and an IgG binds to an HtrA1 trimer with a ratio of 3 IgG to 2 HtrA1 trimers), (iii) for antibodies comprising two variable domains, binds to HtrA1 in a manner that results in the forming a "cage" similar to that shown in Fig. 9, (iv) does not prevent trimer formation of HtrA1, (v) binds to one or more residues in Loop C of the HtrA1 protein, (vi) binds to the protease domain of HtrA1, (vii) binds to an epitope comprising one or both of amino acids N224 or K248 of SEQ ID NO:13, or amino acids equivalent thereto in a different HtrA1 sequence (e.g., amino acids N224 and K248 of SEQ ID NO:14, see Figs. 10A and B); (viii) binds to an epitope comprising one or more of the following residues of N224, K248, V201, T223, K243, K225, E247 and H220 of SEQ ID NO:13, or amino acids equivalent thereto in a different HtrA1 sequence; (ix) cross-reacts with murine HtrA1; (x) does not cross-react with HtrA2, HtrA3 and/or HtrA4; (xi) binds to HtrA1 competitively with an antibody comprising a VH sequence of SEQ ID NO:8 and a VL sequence of SEQ ID NO:7, (xii) binds to HtrA1 with a dissociation constant of $\leq$500 nM, or (xiii) inhibits complex formation between HtrA1 and α1-antitrypsin (A1AT).

In another aspect, the invention provides an isolated antibody that binds to HtrA1, wherein the antibody (i) binds to an epitope that includes N224, K248, or both of HtrA1, and (ii) inhibits HtrA1 with an IC_{50} of $\leq$ 30 nM. In certain embodiments, the epitope further includes one or more of the following residues of HtrA1: V201, T223, K243, K225, E247 and H220. In certain embodiments, the antibody may further comprise one or more of the

In certain embodiments, an antibody described herein comprises (a) HVR-L1 comprising the amino acid sequence of SEQ ID NO:18; (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (c) HVR-L3 comprising the amino acid sequence of SEQ ID NO:19.

In certain embodiments, an antibody described herein comprises (a) HVR-L1 comprising the amino acid sequence of SEQ ID NO:21; (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (c) HVR-L3 comprising the amino acid sequence of SEQ ID NO:22.

In certain embodiments, an antibody described herein further comprises a heavy chain variable domain framework (FR2) sequence of SEQ ID NO:17.

~~In certain embodiments, an antibody described herein comprises~~In one aspect, there is provided an antibody that binds to HtrA1 comprising (a) a VH sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:8; (b) a VL sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:7; or (c) a ~~VH~~ sequence as in (a) and a VL sequence as in (b).

In certain embodiments, an antibody described herein comprises (a) a VH sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:29; (b) a VL sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:7; or (c) a VH sequence as in (a) and a VL sequence as in (b).

In certain embodiments, an antibody described herein comprises (a) a VH sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:29; (b) a VL sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:28; or (c) a VH sequence as in (a) and a VL sequence as in (b).

In certain embodiments, an antibody described herein comprises (a) a VH sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:29; (b) a VL sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:30; or (c) a VH sequence as in (a) and a VL sequence as in (b).

~~In certain embodiments, an antibody described herein comprises~~In one aspect, there is provided an antibody that binds to HtrA1 comprising (a) a VH sequence comprising SEQ ID NO: 32; (b) a VL sequence comprising SEQ ID NO: 31; or (c) a VH sequence comprising SEQ ID NO: 32 and a VL sequence comprising SEQ ID NO: 31.

In certain embodiments, an antibody described herein comprises a VH sequence of SEQ ID NO:8.

In certain embodiments, an antibody described herein comprises a VL sequence of SEQ ID NO:7.

In certain embodiments, an antibody described herein comprises a VH sequence of SEQ ID NO:30.

In certain embodiments, an antibody described herein comprises a VL sequence of SEQ ID NO:28.

In certain embodiments, an antibody described herein comprises a VL sequence of SEQ ID NO:29.

In ~~certain embodiments~~one aspect, an antibody described herein comprises a VH sequence of SEQ ID NO:8 and a VL sequence of SEQ ID NO:7.

In one aspect, there is provided an antibody comprising a VH sequence of SEQ ID NO:29 and a VL sequence of SEQ ID NO:28.

In certain embodiments, an antibody described herein comprises a VH sequence of SEQ ID NO:30 and a VL sequence of SEQ ID NO:28.

In ~~certain embodiments~~one aspect, an antibody described herein comprises a VH sequence of SEQ ID NO:30 and a VL sequence of SEQ ID NO:29.

~~In certain embodiments, an antibody described herein comprises~~In one aspect, there is provided an antibody comprising (a) HVR-H1 comprising the amino acid sequence $GFX_lIX_mX_nYYIH$, wherein X_l is N, S or T; X_m is S, D, Y or A; and X_n is G or D (SEQ ID NO: 25); (b) HVR-H2 comprising the amino acid sequence $WIDPYGGDTX_oYADSVKG$, wherein X_o is N or D (SEQ ID NO:26); (c) HVR-H3 comprising the amino acid sequence $GTFLTX_pWGHYFDY$, wherein X_p is S or T (SEQ ID NO: 27); (d) HVR-L1 comprising the amino acid sequence $RASQX_aX_bX_cX_dX_eX_fA$, wherein X_a is D, S or V; X_b is V or I; X_c is S, N or G; X_d is T or N; X_e is A or Y; and X_f is V or L (SEQ ID NO: 23); (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (f) HVR-L3 comprising the amino acid sequence $QQX_gX_hX_iX_jPX_kT$, wherein X_g is S, V or D; X_h is Y, D or S; X_i is T, S, A, D or N; X_j is T, H, N, S, A, L or R; and X_k is P, T, A or S (SEQ ID NO: 24).

In certain embodiments, an antibody described herein comprises (a) HVR-H1 comprising an amino acid sequence selected from: SEQ ID NO:4, 20,and 47-51; (b) HVR-H2 comprising an amino acid sequence selected from: SEQ ID NO:5 and 52; (c) HVR-H3 comprising an amino acid sequence selected from: SEQ ID NO:6 and 53; (d) HVR-L1 comprising an amino acid sequence selected from: SEQ ID NO:1, 18, 21 and 33; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (f) HVR-L3 comprising an amino acid sequence selected from: SEQ ID NO:3, 19, 22, and 34-46.

In certain embodiments, an antibody described herein comprises (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:4; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:5; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:6; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:1; (e) HVR-L2 comprising

the amino acid sequence of SEQ ID NO:2; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:3.

In certain embodiments, an antibody described herein comprises (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:20; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:5; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:6; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:18; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:19.

In certain embodiments, an antibody described herein comprises (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:20; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:5; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:6; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:21; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:22.

In certain embodiments, an antibody described herein comprises (a) HVR-H3 comprising the amino acid sequence GTFLTX$_p$WGHY, wherein X$_p$ is S or T (SEQ ID NO: 89); (b) HVR-L3 comprising the amino acid sequence X$_g$X$_h$X$_i$X$_j$PX$_k$, wherein X$_g$ is S, V or D; X$_h$ is Y, D or S; X$_i$ is T, S, A, D or N; X$_j$ is T, H, N, S, A, L or R; and X$_k$ is P, T, A or S (SEQ ID NO: 86); and (c) HVR-H2 comprising the amino acid sequence WIDPYGGDTX$_o$, wherein X$_o$ is N or D (SEQ ID NO:88).

In one aspect, there is provided an antibody comprising (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 87; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:88; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:89; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:85; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:58; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 86.

In certain embodiments, an antibody described herein comprises (a) HVR-H1 comprising the amino acid sequence GFX$_l$IX$_m$X$_n$YY, wherein X$_l$ is N, S or T; X$_m$ is S, D, Y or A; and X$_n$ is G or D (SEQ ID NO:87); (b) HVR-H2 comprising the amino acid sequence WIDPYGGDTX$_o$, wherein X$_o$ is N or D (SEQ ID NO:88); and (c) HVR-H3 comprising the amino acid sequence GTFLTX$_p$WGHY, wherein X$_p$ is S or T (SEQ ID NO: 89).

In certain embodiments, an antibody described herein further comprises (a) HVR-L1 comprising the amino acid sequence X$_a$X$_b$X$_c$X$_d$X$_e$X$_f$, wherein X$_a$ is D, S or V; X$_b$ is V or I; X$_c$ is S, N or G; X$_d$ is T or N; X$_e$ is A or Y; and X$_f$ is V or L (SEQ ID NO: 85); (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO:58; and (c) HVR-L3 comprising the amino acid sequence X$_g$X$_h$X$_i$X$_j$PX$_k$, wherein X$_g$ is S, V or D; X$_h$ is Y, D or S; X$_i$ is T, S, A, D or N; X$_j$ is T, H, N, S, A, L or R; and X$_k$ is P, T, A or S (SEQ ID NO: 86).

In certain embodiments, an antibody described herein comprises (a) HVR-H1 comprising the amino acid sequence GFX$_l$IX$_m$X$_n$YY, wherein X$_l$ is N, S or T; X$_m$ is S, D, Y or A; and X$_n$ is G or D (SEQ ID NO:87); (b) HVR-H2 comprising the amino acid sequence

WIDPYGGDTX$_o$, wherein X$_o$ is N or D (SEQ ID NO:88); (c) HVR-H3 comprising the amino acid sequence GTFLTX$_p$WGHY, wherein X$_p$ is S or T (SEQ ID NO: 89); (d) HVR-L1 comprising the amino acid sequence X$_a$X$_b$X$_c$X$_d$X$_e$X$_f$, wherein X$_a$ is D, S or V; X$_b$ is V or I; X$_c$ is S, N or G; X$_d$ is T or N; X$_e$ is A or Y; and X$_f$ is V or L (SEQ ID NO: 85); (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:58; and (f) HVR-L3 comprising the amino acid sequence X$_g$X$_h$X$_i$X$_j$PX$_k$, wherein X$_g$ is S, V or D; X$_h$ is Y, D or S; X$_i$ is T, S, A, D or N; X$_j$ is T, H, N, S, A, L or R; and X$_k$ is P, T, A or S (SEQ ID NO:86).

In certain embodiments, an antibody described herein comprises (a) HVR-H1 comprising an amino acid sequence selected from: SEQ ID NO:4, 20,47-51, and 75-80; (b) HVR-H2 comprising an amino acid sequence selected from: SEQ ID NO:5, 52, and 81-82; (c) HVR-H3 comprising an amino acid sequence selected from: SEQ ID NO:6, 53 and 83-84; (d) HVR-L1 comprising an amino acid sequence selected from: SEQ ID NO:1, 18, 21, 33, and 54-57; (e) HVR-L2 comprising an amino acid sequence selected from: SEQ ID NO:2 and 58; and (f) HVR-L3 comprising an amino acid sequence selected from: SEQ ID NO:3, 19, 22, 34-46, and 59-74.

In certain embodiments, an antibody described herein is a full length IgG1 or IgG4 antibody.

In one aspect, there is provided an isolated nucleic acid encoding the antibody as defined herein.

In ~~another aspect~~an embodiment, an isolated nucleic acid encoding an anti-HtrA1 antibody described herein is provided.

In one aspect, there is provided a host cell comprising the nucleic acid as defined herein.

In ~~another aspect~~an embodiment, a host cell comprising an isolated nucleic acid encoding an anti-HtrA1 antibody described herein is provided.

In one aspect, there is provided a method of producing an antibody comprising culturing the host cell as defined herein under conditions suitable for expression of the nucleic acid encoding the anti-HtrA1 antibody.

In ~~another aspect~~an embodiment, a method of producing an antibody is provided. The method may comprise culturing a host cell comprising an isolated nucleic acid encoding an anti-HtrA1 antibody under conditions suitable for expression of the nucleic acid encoding the anti-HtrA1 antibody. The method may further comprise recovering the anti-HtrA1 antibody from the host cell culture, purifying the anti-HtrA1 antibody, or formulating the anti-HtrA1 antibody with a pharmaceutically acceptable excipient.

In one aspect, there is provided an immunoconjugate comprising the antibody as defined herein and a cytotoxic agent.

In ~~another aspect~~an embodiment, an immunoconjugate comprising an anti-HtrA1 antibody and a cytotoxic agent is provided.

In one aspect, there is provided a pharmaceutical formulation comprising the antibody as defined herein and a pharmaceutically acceptable carrier.

In ~~another aspect~~an embodiment, a pharmaceutical formulation comprising an anti-HtrA1 antibody and a pharmaceutically acceptable carrier is provided.

In one aspect, there is provided the antibody as defined herein for use as a medicament.

In ~~another aspect~~an embodiment, the application provides an anti-HtrA1 antibody for use as a medicament, e.g., for use in treating age-related macular degeneration (wet or dry), geographic atrophy, diabetic retinopathy, retinopathy of prematurity, or polypoidal choroidal vasculopathy,

for inhibiting degeneration of retinal or photoreceptor cells, or for inhibiting HtrA1 protease activity in an eye.

In one aspect, there is provided a use of the antibody as defined herein in the manufacture of a medicament.

In ~~another aspect~~an embodiment, the application provides use of an anti-HtrA1 antibody for the manufacture of a medicament, e.g., a medicament for the treatment of age-related macular degeneration (AMD, wet or dry), geographic atrophy (GA), diabetic retinopathy (DR), retinopathy of prematurity (ROP), or polypoidal choroidal vasculopathy (PCV), for inhibiting degeneration of retinal or photoreceptor cells, or for inhibiting HtrA1 protease activity in an eye.

In another ~~aspect~~embodiment, the application provides a method of treating an individual having age-related macular degeneration (wet or dry), geographic atrophy, diabetic retinopathy, retinopathy of prematurity, or polypoidal choroidal vasculopathy, comprising administering to the individual an effective amount of an anti-HtrA1 antibody as described herein.

In another ~~aspect~~embodiment, the application provides a method for inhibiting retinal or photoreceptor cell degeneration in an individual comprising administering to the individual an effective amount of an anti-HtrA1 antibody as described herein to inhibit retinal or photoreceptor cell degeneration.

In another embodiment~~aspect~~, the application provides a method of inhibiting HtrA1 serine protease activityin an eye of an individual comprising administering to the individual an effective amount of an anti-HtrA1 antibody as described herein to inhibit HtrA1 serine protease activity in the eye.

BRIEF DESCRIPTION OF THE FIGURES

The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

Figs. 1A-B. Fig. 1A shows the light chain variable domain sequence of anti-HtrA1 antibody94 (YW505.94) (SEQ ID NO:7). Fig. 1B shows the heavy chain variable domain sequence of anti-HtrA1 antibody94 (YW505.94) (SEQ ID NO:8). The residues are numbered according to the Kabat numbering system (Kabat, E.A., et al., 1991, In: Sequences of proteins of immunological interest, fifth edition. National Institutes of Health, Bethesda, MD). The YW505.94 light chain variable domain sequence is aligned with human Kappa1 light chain consensus sequence (SEQ ID NO: 9) and the YW505.94 heavy chain variable domain sequence is aligned with the human subgroup III heavy chain sequence (SEQ ID NO: 10). The boxed

WHAT IS CLAIMED IS:

1. An isolated antibody that binds to HtrA1 competitively with an antibody comprising a VH sequence of SEQ ID NO:8 and a VL sequence of SEQ ID NO:7.

2. The antibody of claim 1, wherein competitive binding is determined using an ELISA assay.

3. An isolated antibody that binds to HtrA1, wherein the antibody (i) binds to an epitope that includes N224, K248, or both of HtrA1, and (ii) inhibits HtrA1 with an IC_{50} of ≤ 30 nM.

4. The antibody of claim 3, wherein the antibody further comprises one or more of the following properties: (i) binds to HtrA1 with a ratio of 1 variable domain to one subunit of an HtrA1 trimer, or (ii) does not prevent trimer formation of HtrA1.

5. The antibody of claim 3, wherein the IC_{50} is determined using a serine protease assay with a substrate having SEQ ID NO:12.

6. The antibody of any one of claims 1-5, wherein the antibody does not cross-react with one or more of HtrA2, HtrA3 and HtrA4.

7. The antibody of any one of claims 1-6, wherein the antibody has a dissociation constant of ≤500 nM.

8. The antibody of claim 6, wherein the dissociation constant is determined by BIAcore using a Fab at 25 °C.

9. The antibody of any one of claims 1-8, which is a monoclonal antibody.

10. The antibody of any one of claims 1-8, which is a human, humanized, or chimeric antibody.

11. The antibody of any one of claims 1-8, which is an antibody fragment that binds HtrA1.

12. The antibody of any one of claims 1-11, wherein the antibody comprises (a) HVR-H3 comprising the amino acid sequence $GTFLTX_pWGHYFDY$, wherein X_p is S or T (SEQ ID NO: 27); (b) HVR-L3 comprising the amino acid sequence $QQX_gX_hX_iX_jPX_kT$, wherein X_g is S, V or D; X_h is Y, D or S; X_i is T, S, A, D or N; X_j is T, H, N, S, A, L or R; and X_k is P, T, A or S (SEQ ID NO: 24); and (c) HVR-H2 comprising the amino acid sequence $WIDPYGGDTX_oYADSVKG$, wherein X_o is N or D (SEQ ID NO: 26).

13. The antibody of any one of claims 1-12, wherein the antibody comprises (a) HVR-H3 comprising the amino acid sequence of SEQ ID NO:6; (b) HVR-L3 comprising the amino acid sequence of SEQ ID NO:3; and (c) HVR-H2 comprising the amino acid sequence of SEQ ID NO:5.

14. The antibody of any one of claims 1-12, wherein the antibody comprises (a) HVR-H3 comprising the amino acid sequence of SEQ ID NO:6; (b) HVR-L3 comprising the amino acid sequence of SEQ ID NO:19; and (c) HVR-H2 comprising the amino acid sequence of SEQ ID NO:5.

15. The antibody of any one of claims 1-12, wherein the antibody comprises (a) HVR-H3 comprising the amino acid sequence of SEQ ID NO:6; (b) HVR-L3 comprising the amino acid sequence of SEQ ID NO:22; and (c) HVR-H2 comprising the amino acid sequence of SEQ ID NO:5.

16. The antibody of any one of claims 1-12, wherein the antibody comprises (a) HVR-H1 comprising the amino acid sequence $GFX_lIX_mX_nYYIH$, wherein X_l is N, S or T; X_m is S, D, Y or A; and X_n is G or D (SEQ ID NO: 25); (b) HVR-H2 comprising the amino acid sequence $WIDPYGGDTX_oYADSVKG$, wherein X_o is N or D (SEQ ID NO:26); and (c) HVR-H3 comprising the amino acid sequence $GTFLTX_pWGHYFDY$, wherein X_p is S or T (SEQ ID NO: 27).

17. The antibody of any one of claims 1-12 or 16, further comprising (a) HVR-L1 comprising the amino acid sequence $RASQX_aX_bX_cX_dX_eX_fA$, wherein X_a is D, S or V; X_b is V or I; X_c is S, N or G; X_d is T or N; X_e is A or Y; and X_f is V or L (SEQ ID NO: 23); (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (c) HVR-L3 comprising the amino acid sequence $QQX_gX_hX_iX_jPX_kT$, wherein X_g is S, V or D; X_h is Y, D or S; X_i is T, S, A, D or N; X_j is T, H, N, S, A, L or R; and X_k is P, T, A or S (SEQ ID NO: 24).

18. The antibody of any one of claims 1-12, 16 or 17, wherein the antibody comprises (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:4; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:5; and (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:6.

19. The antibody of claim 18, further comprising (a) HVR-L1 comprising the amino acid sequence of SEQ ID NO:1; (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (c) HVR-L3 comprising the amino acid sequence of SEQ ID NO:3.

20. The antibody of any one of claims 1-12, 16 or 17, wherein the antibody comprises (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:20; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:5; and (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:6.

21. The antibody of claim 20, further comprising (a) HVR-L1 comprising the amino acid sequence of SEQ ID NO:18; (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (c) HVR-L3 comprising the amino acid sequence of SEQ ID NO:19.

22. The antibody of claim 20, further comprising (a) HVR-L1 comprising the amino acid sequence of SEQ ID NO:21; (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (c) HVR-L3 comprising the amino acid sequence of SEQ ID NO:22.

23. The antibody of any one of claims 1-12, 16 or 17, comprising (a) HVR-L1 comprising the amino acid sequence of SEQ ID NO:1; (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (c) HVR-L3 comprising the amino acid sequence of SEQ ID NO:3.

24. The antibody of any one of claims 1-12, 16 or 17, comprising (a) HVR-L1 comprising the amino acid sequence of SEQ ID NO:18; (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (c) HVR-L3 comprising the amino acid sequence of SEQ ID NO:19.

25. The antibody of any one of claims 1-2, 16 or 17, comprising (a) HVR-L1 comprising the amino acid sequence of SEQ ID NO:21; (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (c) HVR-L3 comprising the amino acid sequence of SEQ ID NO:22.

26. The antibody of any one of claims 1-25, further comprising a heavy chain variable domain framework (FR2) sequence of SEQ ID NO:17.

27. The antibody of any one of claims 1-26, comprising (a) a VH sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:8; (b) a VL sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:7; or (c) a VH sequence as in (a) and a VL sequence as in (b).

28. The antibody of any one of claims 1-27, comprising (a) a VH sequence comprising SEQ ID NO: 32; (b) a VL sequence comprising SEQ ID NO: 31; or (c) a VH sequence comprising SEQ ID NO: 32 and a VL sequence comprising SEQ ID NO: 31.

29. The antibody of claim 27 or 28, comprising a VH sequence of SEQ ID NO:8.

30. The antibody of claim 27 or 28, comprising a VL sequence of SEQ ID NO:7.

31. The antibody of claim 27 or 28, comprising a VH sequence of SEQ ID NO:30.

32. The antibody of claim 27 or 28, comprising a VL sequence of SEQ ID NO:28.

33. The antibody of claim 27 or 28, comprising a VL sequence of SEQ ID NO:29.

34. An antibody comprising a VH sequence of SEQ ID NO:8 and a VL sequence of SEQ ID NO:7.

35. An antibody comprising a VH sequence of SEQ ID NO:30 and a VL sequence of SEQ ID NO:28.

36. An antibody comprising a VH sequence of SEQ ID NO:30 and a VL sequence of SEQ ID NO:29.

37. An antibody that binds to HtrA1 comprising (a) a VH sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:8; (b) a VL sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:7; or (c) a VH sequence as in (a) and a VL sequence as in (b).

38. An antibody that binds to HtrA1 comprising (a) a VH sequence comprising SEQ ID NO: 32; (b) a VL sequence comprising SEQ ID NO: 31; or (c) a VH sequence comprising SEQ ID NO: 32 and a VL sequence comprising SEQ ID NO: 31.

39. An antibody comprising (a) HVR-H1 comprising the amino acid sequence $GFX_lIX_mX_nYYIH$, wherein X_l is N, S or T; X_m is S, D, Y or A; and X_n is G or D (SEQ ID NO: 25); (b) HVR-H2 comprising the amino acid sequence $WIDPYGGDTX_oYADSVKG$, wherein X_o is N or D (SEQ ID NO:26); (c) HVR-H3 comprising the amino acid sequence $GTFLTX_pWGHYFDY$, wherein X_p is S or T (SEQ ID NO: 27); (d) HVR-L1 comprising the amino acid sequence $RASQX_aX_bX_cX_dX_eX_fA$, wherein X_a is D, S or V; X_b is V or I; X_c is S, N or G; X_d is T or N; X_e is A or Y; and X_f is V or L (SEQ ID NO: 23); (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (f) HVR-L3 comprising the amino acid sequence $QQX_gX_hX_iX_jPX_kT$, wherein X_g is S, V or D; X_h is Y, D or S; X_i is T, S, A, D or N; X_j is T, H, N, S, A, L or R; and X_k is P, T, A or S (SEQ ID NO: 24).

40. The antibody of claim 39, wherein the antibody comprises (a) HVR-H1 comprising an amino acid sequence selected from: SEQ ID NO:4, 20,and 47-51; (b) HVR-H2 comprising an amino acid sequence selected from: SEQ ID NO:5 and 52; (c) HVR-H3 comprising an amino acid sequence selected from: SEQ ID NO:6 and 53; (d) HVR-L1 comprising an amino acid sequence selected from: SEQ ID NO:1, 18, 21 and 33; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (f) HVR-L3 comprising an amino acid sequence selected from: SEQ ID NO:3, 19, 22, and 34-46.

41. The antibody of claim 40, wherein the antibody comprises (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:4; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:5; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:6; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:1; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:3.

42. The antibody of claim 40, wherein the antibody comprises (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:20; (b) HVR-H2 comprising the amino

acid sequence of SEQ ID NO:5; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:6; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:18; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:19.

43. The antibody of claim 40, wherein the antibody comprises (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:20; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:5; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:6; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:21; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:22.

44. The antibody of any one of claims 1-43, which is a full length IgG1 or IgG4 antibody.

45. An isolated nucleic acid encoding the antibody of any one of claims 1-44.

46. A host cell comprising the nucleic acid of claim 45.

47. A method of producing an antibody comprising culturing the host cell of claim 46 under conditions suitable for expression of the nucleic acid encoding the anti-HtrA1 antibody.

48. The method of claim 47, further comprising recovering the anti-HtrA1 antibody from the host cell culture.

49. An immunoconjugate comprising the antibody of any one of claims 1-44 and a cytotoxic agent.

50. A pharmaceutical formulation comprising the antibody of any one of claims 1-44 and a pharmaceutically acceptable carrier.

51. The antibody of any one of claims 1-44 for use as a medicament.

52. The antibody of any one of claims 1-44 for use in treating age-related macular degeneration, geographic atrophy, diabetic retinopathy, retinopathy of prematurity, or polypoidal choroidal vasculopathy.

53. The antibody of claim 52, for use in treating dry age-related macular degeneration.

54. The antibody of any one of claims 1-44 for use in inhibiting degeneration of retinal or photoreceptor cells.

55. The antibody of any one of claims 1-44 for use in inhibiting HtrA1 protease activity in an eye.

56. Use of the antibody of any one of claims 1-44 in the manufacture of a medicament.

57. The use of claim 56, wherein the medicament is for treatment of treating age-related macular degeneration, geographic atrophy, diabetic retinopathy, retinopathy of prematurity, or polypoidal choroidal vasculopathy.

58. The use of claim 57, wherein the age-related macular degeneration is dry age-related macular degeneration.

59. The use of claim 56, wherein the medicament is for inhibiting degeneration of retinal or photoreceptor cells.

60. The use of claim 56, wherein the medicament is for inhibiting HtrA1 protease activity in an eye.

61. A method of treating an individual having age-related macular degeneration, geographic atrophy, diabetic retinopathy, retinopathy of prematurity, or polypoidal choroidal vasculopathy comprising administering to the individual an effective amount of the antibody of any one of claims 1-44.

62. The method of claim 61, wherein the age-related macular degeneration is dry age-related macular degeneration.

63. A method of inhibiting retinal or photoreceptor cell degeneration in an individual comprising administering to the individual an effective amount of the antibody of any one of claims 1-44 to inhibit retinal or photoreceptor cell degeneration.

64. A method of inhibiting HtrA1 activity in an eye of an individual comprising administering to the individual an effective amount of the antibody of any one of claims 1-44 to inhibit HtrA1 activity in the eye.

65. The antibody of any one of claims 1-12, wherein the antibody comprises (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 87; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:88; and (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 89.

66. The antibody of any one of claims 1-12 or 65, further comprising (a) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 85; (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO:58; and (c) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 86.

67. An antibody comprising (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 87; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:88; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:89; (d) HVR-L1 comprising the

amino acid sequence of SEQ ID NO:85; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:58; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 86.

68. The antibody of claim 67, wherein the antibody comprises (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 25; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:26; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:27; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:23; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:24.

69. The antibody of claim 67 or 68, wherein the antibody comprises (a) HVR-H1 comprising an amino acid sequence selected from: SEQ ID NO:4, 20, 47-51 and 75-80; (b) HVR-H2 comprising an amino acid sequence selected from: SEQ ID NO:5, 52 and 81-82; (c) HVR-H3 comprising an amino acid sequence selected from: SEQ ID NO:6, 53 and 83-84; (d) HVR-L1 comprising an amino acid sequence selected from: SEQ ID NO:1, 18, 21, 33 and 54-57; (e) HVR-L2 comprising an amino acid sequence selected from: SEQ ID NO:2 and 58; and (f) HVR-L3 comprising an amino acid sequence selected from: SEQ ID NO:3, 19, 22, 34-46 and 59-74.

70. The antibody of any one of claims 65-69, which is a full length IgG1 or IgG4 antibody.

71. An isolated nucleic acid encoding the antibody of any one of claims 65-70.

72. A host cell comprising the nucleic acid of claim 71.

73. A method of producing an antibody comprising culturing the host cell of claim 72 under conditions suitable for expression of the nucleic acid encoding the anti-HtrA1 antibody.

74. The method of claim 73, further comprising recovering the anti-HtrA1 antibody from the host cell culture.

75. An immunoconjugate comprising the antibody of any one of claims 65-70 and a cytotoxic agent.

76. A pharmaceutical formulation comprising the antibody of any one of claims 65-70 and a pharmaceutically acceptable carrier.

77. The antibody of any one of claims 65-70 for use as a medicament.

78. The antibody of any one of claims 65-70 for use in treating age-related macular degeneration, geographic atrophy, diabetic retinopathy, retinopathy of prematurity, or polypoidal choroidal vasculopathy.

79. The antibody of claim 78, for use in treating dry age-related macular degeneration.

80. The antibody of any one of claims 65-70 for use in inhibiting degeneration of retinal or photoreceptor cells.

81. The antibody of any one of claims 65-70 for use in inhibiting HtrA1 protease activity in an eye.

82. Use of the antibody of any one of claims 65-70 in the manufacture of a medicament.

83. The use of claim 82, wherein the medicament is for treatment of treating age-related macular degeneration, geographic atrophy, diabetic retinopathy, retinopathy of prematurity, or polypoidal choroidal vasculopathy.

84. The use of claim 83, wherein the age-related macular degeneration is dry age-related macular degeneration.

85. The use of claim 82, wherein the medicament is for inhibiting degeneration of retinal or photoreceptor cells.

86. The use of claim 82, wherein the medicament is for inhibiting HtrA1 protease activity in an eye.

87. A method of treating an individual having age-related macular degeneration, geographic atrophy, diabetic retinopathy, retinopathy of prematurity, or polypoidal choroidal vasculopathy comprising administering to the individual an effective amount of the antibody of any one of claims 65-70.

88. The method of claim 87, wherein the age-related macular degeneration is dry age-related macular degeneration.

89. A method of inhibiting retinal or photoreceptor cell degeneration in an individual comprising administering to the individual an effective amount of the antibody of any one of claims 65-70 to inhibit retinal or photoreceptor cell degeneration.

90. A method of inhibiting HtrA1 activity in an eye of an individual comprising administering to the individual an effective amount of the antibody of any one of claims 65-70 to inhibit HtrA1 activity in the eye.

AMENDED CLAIMS
received by the International Bureau on 11 February 2013 (11.02.2013)

1. An isolated antibody that binds to HtrA1 competitively with an antibody comprising a VH sequence of SEQ ID NO:8 and a VL sequence of SEQ ID NO:7.

2. The antibody of claim 1, wherein competitive binding is determined using an ELISA assay.

3. An isolated antibody that binds to HtrA1, wherein the antibody (i) binds to an epitope that includes N224, K248, or both of HtrA1, and (ii) inhibits HtrA1 with an IC_{50} of ≤ 30 nM.

4. The antibody of claim 3, wherein the antibody further comprises one or more of the following properties: (i) binds to HtrA1 with a ratio of 1 variable domain to one subunit of an HtrA1 trimer, or (ii) does not prevent trimer formation of HtrA1.

5. The antibody of claim 3, wherein the IC_{50} is determined using a serine protease assay with a substrate having SEQ ID NO:12.

6. The antibody of any one of claims 1-5, wherein the antibody does not cross-react with one or more of HtrA2, HtrA3 and HtrA4.

7. The antibody of any one of claims 1-6, wherein the antibody has a dissociation constant of ≤500 nM.

8. The antibody of claim 6, wherein the dissociation constant is determined by BIAcore using a Fab at 25 °C.

9. The antibody of any one of claims 1-8, which is a monoclonal antibody.

10. The antibody of any one of claims 1-8, which is a human, humanized, or chimeric antibody.

11. The antibody of any one of claims 1-8, which is an antibody fragment that binds HtrA1.

12. The antibody of any one of claims 1-11, wherein the antibody comprises (a) HVR-H3 comprising the amino acid sequence $GTFLTX_pWGHYFDY$, wherein X_p is S or T (SEQ ID NO: 27); (b) HVR-L3 comprising the amino acid sequence $QQX_gX_hX_iX_jPX_kT$, wherein X_g is S, V or D; X_h is Y, D or S; X_i is T, S, A, D or N; X_j is T, H, N, S, A, L or R; and X_k is P, T, A or S (SEQ ID NO: 24); and (c) HVR-H2 comprising the amino acid sequence $WIDPYGGDTX_oYADSVKG$, wherein X_o is N or D (SEQ ID NO: 26).

13. The antibody of any one of claims 1-12, wherein the antibody comprises (a) HVR-H3 comprising the amino acid sequence of SEQ ID NO:6; (b) HVR-L3 comprising the amino acid sequence of SEQ ID NO:3; and (c) HVR-H2 comprising the amino acid sequence of SEQ ID NO:5.

14. The antibody of any one of claims 1-12, wherein the antibody comprises (a) HVR-H3 comprising the amino acid sequence of SEQ ID NO:6; (b) HVR-L3 comprising the amino acid sequence of SEQ ID NO:19; and (c) HVR-H2 comprising the amino acid sequence of SEQ ID NO:5.

15. The antibody of any one of claims 1-12, wherein the antibody comprises (a) HVR-H3 comprising the amino acid sequence of SEQ ID NO:6; (b) HVR-L3 comprising the amino acid sequence of SEQ ID NO:22; and (c) HVR-H2 comprising the amino acid sequence of SEQ ID NO:5.

16. The antibody of any one of claims 1-12, wherein the antibody comprises (a) HVR-H1 comprising the amino acid sequence $GFX_lIX_mX_nYYIH$, wherein X_l is N, S or T; X_m is S, D, Y or A; and X_n is G or D (SEQ ID NO: 25); (b) HVR-H2 comprising the amino acid sequence $WIDPYGGDTX_oYADSVKG$, wherein X_o is N or D (SEQ ID NO:26); and (c) HVR-H3 comprising the amino acid sequence $GTFLTX_pWGHYFDY$, wherein X_p is S or T (SEQ ID NO: 27).

17. The antibody of any one of claims 1-12 or 16, further comprising (a) HVR-L1 comprising the amino acid sequence $RASQX_aX_bX_cX_dX_eX_fA$, wherein X_a is D, S or V; X_b is V or I; X_c is S, N or G; X_d is T or N; X_e is A or Y; and X_f is V or L (SEQ ID NO: 23); (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (c) HVR-L3 comprising the amino acid sequence $QQX_gX_hX_iX_jPX_kT$, wherein X_g is S, V or D; X_h is Y, D or S; X_i is T, S, A, D or N; X_j is T, H, N, S, A, L or R; and X_k is P, T, A or S (SEQ ID NO: 24).

18. The antibody of any one of claims 1-12, 16 or 17, wherein the antibody comprises (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:4; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:5; and (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:6.

19. The antibody of claim 18, further comprising (a) HVR-L1 comprising the amino acid sequence of SEQ ID NO:1; (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (c) HVR-L3 comprising the amino acid sequence of SEQ ID NO:3.

20. The antibody of any one of claims 1-12, 16 or 17, wherein the antibody comprises (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:20; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:5; and (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:6.

21. The antibody of claim 20, further comprising (a) HVR-L1 comprising the amino acid sequence of SEQ ID NO:18; (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (c) HVR-L3 comprising the amino acid sequence of SEQ ID NO:19.

22. The antibody of claim 20, further comprising (a) HVR-L1 comprising the amino acid sequence of SEQ ID NO:21; (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (c) HVR-L3 comprising the amino acid sequence of SEQ ID NO:22.

23. The antibody of any one of claims 1-12, 16 or 17, comprising (a) HVR-L1 comprising the amino acid sequence of SEQ ID NO:1; (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (c) HVR-L3 comprising the amino acid sequence of SEQ ID NO:3.

24. The antibody of any one of claims 1-12, 16 or 17, comprising (a) HVR-L1 comprising the amino acid sequence of SEQ ID NO:18; (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (c) HVR-L3 comprising the amino acid sequence of SEQ ID NO:19.

25. The antibody of any one of claims 1-2, 16 or 17, comprising (a) HVR-L1 comprising the amino acid sequence of SEQ ID NO:21; (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (c) HVR-L3 comprising the amino acid sequence of SEQ ID NO:22.

26. The antibody of any one of claims 1-25, further comprising a heavy chain variable domain framework (FR2) sequence of SEQ ID NO:17.

27. The antibody of any one of claims 1-26, comprising (a) a VH sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:8; (b) a VL sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:7; or (c) a VH sequence as in (a) and a VL sequence as in (b).

28. The antibody of any one of claims 1-27, comprising (a) a VH sequence comprising SEQ ID NO: 32; (b) a VL sequence comprising SEQ ID NO: 31; or (c) a VH sequence comprising SEQ ID NO: 32 and a VL sequence comprising SEQ ID NO: 31.

29. The antibody of claim 27 or 28, comprising a VH sequence of SEQ ID NO:8.

30. The antibody of claim 27 or 28, comprising a VL sequence of SEQ ID NO:7.

31. The antibody of claim 27 or 28, comprising a VL sequence of SEQ ID NO:30.

32. The antibody of claim 27 or 28, comprising a VL sequence of SEQ ID NO:28.

33. The antibody of claim 27 or 28, comprising a VH sequence of SEQ ID NO:29.

34. An antibody comprising a VH sequence of SEQ ID NO:8 and a VL sequence of SEQ ID NO:7.

35. An antibody comprising a VH sequence of SEQ ID NO:29 and a VL sequence of SEQ ID NO:28.

36. An antibody comprising a VL sequence of SEQ ID NO:30 and a VH sequence of SEQ ID NO:29.

37. An antibody that binds to HtrA1 comprising (a) a VH sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:8; (b) a VL sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:7; or (c) a VH sequence as in (a) and a VL sequence as in (b).

38. An antibody that binds to HtrA1 comprising (a) a VH sequence comprising SEQ ID NO: 32; (b) a VL sequence comprising SEQ ID NO: 31; or (c) a VH sequence comprising SEQ ID NO: 32 and a VL sequence comprising SEQ ID NO: 31.

39. An antibody comprising (a) HVR-H1 comprising the amino acid sequence $GFX_iIX_mX_nYYIH$, wherein X_i is N, S or T; X_m is S, D, Y or A; and X_n is G or D (SEQ ID NO: 25); (b) HVR-H2 comprising the amino acid sequence $WIDPYGGDTX_oYADSVKG$, wherein X_o is N or D (SEQ ID NO:26); (c) HVR-H3 comprising the amino acid sequence $GTFLTX_pWGHYFDY$, wherein X_p is S or T (SEQ ID NO: 27); (d) HVR-L1 comprising the amino acid sequence $RASQX_aX_bX_cX_dX_eX_fA$, wherein X_a is D, S or V; X_b is V or I; X_c is S, N or G; X_d is T or N; X_e is A or Y; and X_f is V or L (SEQ ID NO: 23); (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (f) HVR-L3 comprising the amino acid sequence $QQX_gX_hX_iX_jPX_kT$, wherein X_g is S, V or D; X_h is Y, D or S; X_i is T, S, A, D or N; X_j is T, H, N, S, A, L or R; and X_k is P, T, A or S (SEQ ID NO: 24).

40. The antibody of claim 39, wherein the antibody comprises (a) HVR-H1 comprising an amino acid sequence selected from: SEQ ID NO:4, 20,and 47-51; (b) HVR-H2 comprising an amino acid sequence selected from: SEQ ID NO:5 and 52; (c) HVR-H3 comprising an amino acid sequence selected from: SEQ ID NO:6 and 53; (d) HVR-L1 comprising an amino acid sequence selected from: SEQ ID NO:1, 18, 21 and 33; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (f) HVR-L3 comprising an amino acid sequence selected from: SEQ ID NO:3, 19, 22, and 34-46.

41. The antibody of claim 40, wherein the antibody comprises (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:4; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:5; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:6; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:1; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:3.

42. The antibody of claim 40, wherein the antibody comprises (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:20; (b) HVR-H2 comprising the amino

acid sequence of SEQ ID NO:5; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:6; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:18; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:19.

43. The antibody of claim 40, wherein the antibody comprises (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:20; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:5; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:6; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:21; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:22.

44. The antibody of any one of claims 1-43, which is a full length IgG1 or IgG4 antibody.

45. An isolated nucleic acid encoding the antibody of any one of claims 1-44.

46. A host cell comprising the nucleic acid of claim 45.

47. A method of producing an antibody comprising culturing the host cell of claim 46 under conditions suitable for expression of the nucleic acid encoding the anti-HtrA1 antibody.

48. The method of claim 47, further comprising recovering the anti-HtrA1 antibody from the host cell culture.

49. An immunoconjugate comprising the antibody of any one of claims 1-44 and a cytotoxic agent.

50. A pharmaceutical formulation comprising the antibody of any one of claims 1-44 and a pharmaceutically acceptable carrier.

51. The antibody of any one of claims 1-44 for use as a medicament.

52. The antibody of any one of claims 1-44 for use in treating age-related macular degeneration, geographic atrophy, diabetic retinopathy, retinopathy of prematurity, or polypoidal choroidal vasculopathy.

53. The antibody of claim 52, for use in treating dry age-related macular degeneration.

54. The antibody of any one of claims 1-44 for use in inhibiting degeneration of retinal or photoreceptor cells.

55. The antibody of any one of claims 1-44 for use in inhibiting HtrA1 protease activity in an eye.

56. Use of the antibody of any one of claims 1-44 in the manufacture of a medicament.

57. The use of claim 56, wherein the medicament is for treatment of treating age-related macular degeneration, geographic atrophy, diabetic retinopathy, retinopathy of prematurity, or polypoidal choroidal vasculopathy.

58. The use of claim 57, wherein the age-related macular degeneration is dry age-related macular degeneration.

59. The use of claim 56, wherein the medicament is for inhibiting degeneration of retinal or photoreceptor cells.

60. The use of claim 56, wherein the medicament is for inhibiting HtrA1 protease activity in an eye.

61. A method of treating an individual having age-related macular degeneration, geographic atrophy, diabetic retinopathy, retinopathy of prematurity, or polypoidal choroidal vasculopathy comprising administering to the individual an effective amount of the antibody of any one of claims 1-44.

62. The method of claim 61, wherein the age-related macular degeneration is dry age-related macular degeneration.

63. A method of inhibiting retinal or photoreceptor cell degeneration in an individual comprising administering to the individual an effective amount of the antibody of any one of claims 1-44 to inhibit retinal or photoreceptor cell degeneration.

64. A method of inhibiting HtrA1 activity in an eye of an individual comprising administering to the individual an effective amount of the antibody of any one of claims 1-44 to inhibit HtrA1 activity in the eye.

65. The antibody of any one of claims 1-12, wherein the antibody comprises (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 87; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:88; and (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 89.

66. The antibody of any one of claims 1-12 or 65, further comprising (a) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 85; (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO:58; and (c) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 86.

67. An antibody comprising (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 87; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:88; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:89; (d) HVR-L1 comprising the

amino acid sequence of SEQ ID NO:85; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:58; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 86.

68. The antibody of claim 67, wherein the antibody comprises (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 25; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:26; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:27; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:23; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:24.

69. The antibody of claim 67 or 68, wherein the antibody comprises (a) HVR-H1 comprising an amino acid sequence selected from: SEQ ID NO:4, 20, 47-51 and 75-80; (b) HVR-H2 comprising an amino acid sequence selected from: SEQ ID NO:5, 52 and 81-82; (c) HVR-H3 comprising an amino acid sequence selected from: SEQ ID NO:6, 53 and 83-84; (d) HVR-L1 comprising an amino acid sequence selected from: SEQ ID NO:1, 18, 21, 33 and 54-57; (e) HVR-L2 comprising an amino acid sequence selected from: SEQ ID NO:2 and 58; and (f) HVR-L3 comprising an amino acid sequence selected from: SEQ ID NO:3, 19, 22, 34-46 and 59-74.

70. The antibody of any one of claims 65-69, which is a full length IgG1 or IgG4 antibody.

71. An isolated nucleic acid encoding the antibody of any one of claims 65-70.

72. A host cell comprising the nucleic acid of claim 71.

73. A method of producing an antibody comprising culturing the host cell of claim 72 under conditions suitable for expression of the nucleic acid encoding the anti-HtrA1 antibody.

74. The method of claim 73, further comprising recovering the anti-HtrA1 antibody from the host cell culture.

75. An immunoconjugate comprising the antibody of any one of claims 65-70 and a cytotoxic agent.

76. A pharmaceutical formulation comprising the antibody of any one of claims 65-70 and a pharmaceutically acceptable carrier.

77. The antibody of any one of claims 65-70 for use as a medicament.

78. The antibody of any one of claims 65-70 for use in treating age-related macular degeneration, geographic atrophy, diabetic retinopathy, retinopathy of prematurity, or polypoidal choroidal vasculopathy.

79. The antibody of claim 78, for use in treating dry age-related macular degeneration.

80. The antibody of any one of claims 65-70 for use in inhibiting degeneration of retinal or photoreceptor cells.

81. The antibody of any one of claims 65-70 for use in inhibiting HtrA1 protease activity in an eye.

82. Use of the antibody of any one of claims 65-70 in the manufacture of a medicament.

83. The use of claim 82, wherein the medicament is for treatment of treating age-related macular degeneration, geographic atrophy, diabetic retinopathy, retinopathy of prematurity, or polypoidal choroidal vasculopathy.

84. The use of claim 83, wherein the age-related macular degeneration is dry age-related macular degeneration.

85. The use of claim 82, wherein the medicament is for inhibiting degeneration of retinal or photoreceptor cells.

86. The use of claim 82, wherein the medicament is for inhibiting HtrA1 protease activity in an eye.

87. A method of treating an individual having age-related macular degeneration, geographic atrophy, diabetic retinopathy, retinopathy of prematurity, or polypoidal choroidal vasculopathy comprising administering to the individual an effective amount of the antibody of any one of claims 65-70.

88. The method of claim 87, wherein the age-related macular degeneration is dry age-related macular degeneration.

89. A method of inhibiting retinal or photoreceptor cell degeneration in an individual comprising administering to the individual an effective amount of the antibody of any one of claims 65-70 to inhibit retinal or photoreceptor cell degeneration.

90. A method of inhibiting HtrA1 activity in an eye of an individual comprising administering to the individual an effective amount of the antibody of any one of claims 65-70 to inhibit HtrA1 activity in the eye.

WHAT IS CLAIMED IS:

1. An isolated antibody that binds to HtrA1 competitively with an antibody comprising a VH sequence of SEQ ID NO:8 and a VL sequence of SEQ ID NO:7.

2. The antibody of claim 1, wherein competitive binding is determined using an ELISA assay.

3. An isolated antibody that binds to HtrA1, wherein the antibody (i) binds to an epitope that includes N224, K248, or both of HtrA1, and (ii) inhibits HtrA1 with an IC_{50} of $\leq$ 30 nM.

4. The antibody of claim 3, wherein the antibody further comprises one or more of the following properties: (i) binds to HtrA1 with a ratio of 1 variable domain to one subunit of an HtrA1 trimer, or (ii) does not prevent trimer formation of HtrA1.

5. The antibody of claim 3, wherein the IC_{50} is determined using a serine protease assay with a substrate having SEQ ID NO:12.

6. The antibody of any one of claims 1-5, wherein the antibody does not cross-react with one or more of HtrA2, HtrA3 and HtrA4.

7. The antibody of any one of claims 1-6, wherein the antibody has a dissociation constant of $\leq$500 nM.

8. The antibody of claim 6, wherein the dissociation constant is determined by BIAcore using a Fab at 25 °C.

9. The antibody of any one of claims 1-8, selected from a group consisting of:

i) an antibody which is a monoclonal antibody,

ii) an antibody which is a human, humanized, or chimeric antibody, and

iii) an antibody which is an antibody fragment that binds HtrA1.

10. The antibody of any one of claims 1-9, wherein the antibody comprises (a) HVR-H3 comprising the amino acid sequence $GTFLTX_pWGHYFDY$, wherein X_p is S or T (SEQ ID NO: 27); (b) HVR-L3 comprising the amino acid sequence $QQX_gX_hX_iX_jPX_kT$, wherein X_g is S, V or D; X_h is Y, D or S; X_i is T, S, A, D or N; X_j is T, H, N, S, A, L or R; and X_k is P, T, A or S (SEQ ID NO: 24); and (c) HVR-H2 comprising the amino acid sequence $WIDPYGGDTX_oYADSVKG$, wherein X_o is N or D (SEQ ID NO: 26).

11. The antibody of any one of claims 1-10, selected from a group consisting of:

(i) an antibody which comprises (a) HVR-H3 comprising the amino acid sequence of SEQ ID NO:6; (b) HVR-L3 comprising the amino acid sequence of SEQ ID NO:3; and (c) HVR-H2 comprising the amino acid sequence of SEQ ID NO:5,

(ii) an antibody which comprises (a) HVR-H3 comprising the amino acid sequence of SEQ ID NO:6; (b) HVR-L3 comprising the amino acid sequence of SEQ ID NO:19; and (c) HVR-H2 comprising the amino acid sequence of SEQ ID NO:5,

(iii) an antibody which comprises (a) HVR-H3 comprising the amino acid sequence of SEQ ID NO:6; (b) HVR-L3 comprising the amino acid sequence of SEQ ID NO:22; and (c) HVR-H2 comprising the amino acid sequence of SEQ ID NO:5, and

(iv) an antibody which comprises (a) HVR-H1 comprising the amino acid sequence $GFX_lIX_mX_nYYIH$, wherein X_l is N, S or T; X_m is S, D, Y or A; and X_n is G or D (SEQ ID NO: 25); (b) HVR-H2 comprising the amino acid sequence $WIDPYGGDTX_oYADSVKG$, wherein X_o is N or D (SEQ ID NO:26); and (c) HVR-H3 comprising the amino acid sequence $GTFLTX_pWGHYFDY$, wherein X_p is S or T (SEQ ID NO: 27).

12. The antibody of any one of claims 1-10 or 11(iv), further comprising (a) HVR-L1 comprising the amino acid sequence $RASQX_aX_bX_cX_dX_eX_fA$, wherein X_a is D, S or V; X_b is V or I; X_c is S, N or G; X_d is T or N; X_e is A or Y; and X_f is V or L (SEQ ID NO: 23); (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (c) HVR-L3 comprising the amino acid sequence $QQX_gX_hX_iX_jPX_kT$, wherein X_g is S, V or D; X_h is Y, D or S; X_i is T, S, A, D or N; X_j is T, H, N, S, A, L or R; and X_k is P, T, A or S (SEQ ID NO: 24).

13. The antibody of any one of claims 1-10, 11(iv) or 12, selected from a group consisting of:

(i) an antibody which comprises (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:4; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:5; and (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:6,

(ii) an antibody which comprises (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:20; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:5; and (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:6,

(iii) an antibody which comprises (a) HVR-L1 comprising the amino acid sequence of SEQ ID NO:1; (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (c) HVR-L3 comprising the amino acid sequence of SEQ ID NO:3,

(iv) an antibody which comprises (a) HVR-L1 comprising the amino acid sequence of SEQ ID NO:18; (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (c) HVR-L3 comprising the amino acid sequence of SEQ ID NO:19, and

(v) an antibody which comprises (a) HVR-L1 comprising the amino acid sequence of SEQ ID NO:21; (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (c) HVR-L3 comprising the amino acid sequence of SEQ ID NO:22.

14. The antibody of claim 13(i), further comprising (a) HVR-L1 comprising the amino acid sequence of SEQ ID NO:1; (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (c) HVR-L3 comprising the amino acid sequence of SEQ ID NO:3.

15. The antibody of claim 13(ii), selected from a group consisting of:

an antibody that further comprises (a) HVR-L1 comprising the amino acid sequence of SEQ ID NO:18; (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (c) HVR-L3 comprising the amino acid sequence of SEQ ID NO:19; and

an antibody that further comprises (a) HVR-L1 comprising the amino acid sequence of SEQ ID NO:21; (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (c) HVR-L3 comprising the amino acid sequence of SEQ ID NO:22.

16. The antibody of any one of claims 1-15, further comprising a heavy chain variable domain framework (FR2) sequence of SEQ ID NO:17.

17. The antibody of any one of claims 1-16 comprising (a) a VH sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:8; (b) a VL sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:7; or (c) a VH sequence as in (a) and a VL sequence as in (b).

18. The antibody of any one of claims 1-17, comprising (a) a VH sequence comprising SEQ ID NO: 32; (b) a VL sequence comprising SEQ ID NO: 31; or (c) a VH sequence comprising SEQ ID NO: 32 and a VL sequence comprising SEQ ID NO: 31.

19. The antibody of claim 17 or 18, selected from a group consisting of:

(i) an antibody comprising a VH sequence of SEQ ID NO:8,

(ii) an antibody comprising a VL sequence of SEQ ID NO:7,

(iii) an antibody comprising a VL sequence of SEQ ID NO:30,

(iv) an antibody comprising a VL sequence of SEQ ID NO:28; and

(v) an antibody comprising a VH sequence of SEQ ID NO:29.

20. An antibody comprising a VH sequence of SEQ ID NO:8 and a VL sequence of SEQ ID NO:7.

21. An antibody comprising a VH sequence of SEQ ID NO:29 and a VL sequence of SEQ ID NO:28.

22. An antibody comprising a VL sequence of SEQ ID NO:30 and a VH sequence of SEQ ID NO:29.

23. An antibody that binds to HtrA1 comprising (a) a VH sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:8; (b) a VL sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:7; or (c) a VH sequence as in (a) and a VL sequence as in (b).

24. An antibody that binds to HtrA1 comprising (a) a VH sequence comprising SEQ ID NO: 32; (b) a VL sequence comprising SEQ ID NO: 31; or (c) a VH sequence comprising SEQ ID NO: 32 and a VL sequence comprising SEQ ID NO: 31.

25. An antibody comprising (a) HVR-H1 comprising the amino acid sequence $GFX_lIX_mX_nYYIH$, wherein X_l is N, S or T; X_m is S, D, Y or A; and X_n is G or D (SEQ ID NO: 25); (b) HVR-H2 comprising the amino acid sequence $WIDPYGGDTX_oYADSVKG$, wherein X_o is N or D (SEQ ID NO:26); (c) HVR-H3 comprising the amino acid sequence $GTFLTX_pWGHYFDY$, wherein X_p is S or T (SEQ ID NO: 27); (d) HVR-L1 comprising the amino acid sequence $RASQX_aX_bX_cX_dX_eX_fA$, wherein X_a is D, S or V; X_b is V or I; X_c is S, N or G; X_d is T or N; X_e is A or Y; and X_f is V or L (SEQ ID NO: 23); (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (f) HVR-L3 comprising the amino acid sequence $QQX_gX_hX_iX_jPX_kT$, wherein X_g is S, V or D; X_h is Y, D or S; X_i is T, S, A, D or N; X_j is T, H, N, S, A, L or R; and X_k is P, T, A or S (SEQ ID NO: 24).

26. The antibody of claim 25, wherein the antibody comprises (a) HVR-H1 comprising an amino acid sequence selected from: SEQ ID NO:4, 20,and 47-51; (b) HVR-H2 comprising an amino acid sequence selected from: SEQ ID NO:5 and 52; (c) HVR-H3 comprising an amino acid sequence selected from: SEQ ID NO:6 and 53; (d) HVR-L1 comprising an amino acid sequence selected from: SEQ ID NO:1, 18, 21 and 33; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (f) HVR-L3 comprising an amino acid sequence selected from: SEQ ID NO:3, 19, 22, and 34-46.

27. The antibody of claim 26, selected from a group consisting of:

(i)an antibody which comprises (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:4; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:5; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:6; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:1; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:3,

(ii) an antibody which comprises (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:20; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:5; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:6; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:18; (e) HVR-L2 comprising the

amino acid sequence of SEQ ID NO:2; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:19, and

(iii)an antibody which comprises (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO:20; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:5; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:6; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:21; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:22.

28. The antibody of any one of claims 1-27, which is a full length IgG1 or IgG4 antibody.

29. An isolated nucleic acid encoding the antibody of any one of claims 1-28.

30. A host cell comprising the nucleic acid of claim 29.

31. A method of producing an antibody comprising culturing the host cell of claim 30 under conditions suitable for expression of the nucleic acid encoding the anti-HtrA1 antibody.

32. The method of claim 31, further comprising recovering the anti-HtrA1 antibody from the host cell culture.

33. An immunoconjugate comprising the antibody of any one of claims 1-28 and a cytotoxic agent.

34. A pharmaceutical formulation comprising the antibody of any one of claims 1-28 and a pharmaceutically acceptable carrier.

35. The antibody of any one of claims 1-28 for use as a medicament.

36. Use of the antibody of any one of claims 1-28 in the manufacture of a medicament.

37. The use of claim 36, selected from a group consisting of:

(i) a use wherein the medicament is for treatment of treating age-related macular degeneration, geographic atrophy, diabetic retinopathy, retinopathy of prematurity, or polypoidal choroidal vasculopathy,

(ii) a use wherein the medicament is for inhibiting degeneration of retinal or photoreceptor cells, and

(iii) a use wherein the medicament is for inhibiting HtrA1 protease activity in an eye.

38. The use of claim 37(i), wherein the age-related macular degeneration is dry age-related macular degeneration.

39. The antibody of any one of claims 1-10, wherein the antibody comprises (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 87; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:88; and (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO: 89.

40. The antibody of any one of claims 1-10 or 39, further comprising (a) HVR-L1 comprising the amino acid sequence of SEQ ID NO: 85; (b) HVR-L2 comprising the amino acid sequence of SEQ ID NO:58; and (c) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 86.

41. An antibody comprising (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 87; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:88; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:89; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:85; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:58; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO: 86.

42. The antibody of claim 41, wherein the antibody comprises (a) HVR-H1 comprising the amino acid sequence of SEQ ID NO: 25; (b) HVR-H2 comprising the amino acid sequence of SEQ ID NO:26; (c) HVR-H3 comprising the amino acid sequence of SEQ ID NO:27; (d) HVR-L1 comprising the amino acid sequence of SEQ ID NO:23; (e) HVR-L2 comprising the amino acid sequence of SEQ ID NO:2; and (f) HVR-L3 comprising the amino acid sequence of SEQ ID NO:24.

43. The antibody of claim 41 or 42, wherein the antibody comprises (a) HVR-H1 comprising an amino acid sequence selected from: SEQ ID NO:4, 20, 47-51 and 75-80; (b) HVR-H2 comprising an amino acid sequence selected from: SEQ ID NO:5, 52 and 81-82; (c) HVR-H3 comprising an amino acid sequence selected from: SEQ ID NO:6, 53 and 83-84; (d) HVR-L1 comprising an amino acid sequence selected from: SEQ ID NO:1, 18, 21, 33 and 54-57; (e) HVR-L2 comprising an amino acid sequence selected from: SEQ ID NO:2 and 58; and (f) HVR-L3 comprising an amino acid sequence selected from: SEQ ID NO:3, 19, 22, 34-46 and 59-74.

44. The antibody of any one of claims 39-43, which is a full length IgG1 or IgG4 antibody.

45. An isolated nucleic acid encoding the antibody of any one of claims 39-44.

46. A host cell comprising the nucleic acid of claim 45.

47. A method of producing an antibody comprising culturing the host cell of claim 46 under conditions suitable for expression of the nucleic acid encoding the anti-HtrA1 antibody.

48. The method of claim 47, further comprising recovering the anti-HtrA1 antibody from the host cell culture.

49. An immunoconjugate comprising the antibody of any one of claims 39-44 and a cytotoxic agent.

50. A pharmaceutical formulation comprising the antibody of any one of claims 39-44 and a pharmaceutically acceptable carrier.

51. The antibody of any one of claims 39-44 for use as a medicament.

52. Use of the antibody of any one of claims 39-44 in the manufacture of a medicament.

53. The use of claim 52, selected from a group consisting of:

(i) a use wherein the medicament is for treatment of treating age-related macular degeneration, geographic atrophy, diabetic retinopathy, retinopathy of prematurity, or polypoidal choroidal vasculopathy,

(ii) a use wherein the medicament is for inhibiting degeneration of retinal or photoreceptor cells, and

(iii) a use wherein the medicament is for inhibiting HtrA1 protease activity in an eye.

54. The use of claim 53(i), wherein the age-related macular degeneration is dry age-related macular degeneration.

55. An isolated antibody that binds to HtrA1 and inhibits its serine protease activity for one or more HtrA1 substrates.

56. The antibody of claim 55, wherein the antibody inhibits HtrA1 with an IC_{50} of less than 50 nM.