CLAIMS

1. ~~An~~ A human-derived antibody or antigen-binding fragment thereof that binds to a chromosome 9 open reading frame 72 (C9orf72) dipeptide repeat protein (DPR) with a poly-Glycine-Alanine $(GA)_{15}$ repeat, wherein the human-derived antibody or antigen-binding fragment thereof comprises:

a heavy chain variable region (VH) comprising VH complementarity determining regions (CDRs) 1, 2, and 3, wherein the VH CDRs 1, 2, and 3 comprise the amino acid sequences set forth in amino acid positions 32-36 of SEQ ID NO:8, amino acid positions 51-67 of SEQ ID NO:8, and amino acid positions 100-113 of SEQ ID NO:8, respectively; and

a light chain variable region (VL) comprising VL CDRs 1, 2, and 3, wherein the VL CDRs 1, 2, and 3 comprise the amino acid sequences set forth in amino acid positions 25-35 of SEQ ID NO:10, amino acid positions 51-57 of SEQ ID NO:10, and amino acid positions 90-98 of SEQ ID NO:10, respectively; and

wherein the human-derived antibody or antigen-binding fragment thereof is detectably labeled, comprises a heterologous sequence that is heterologous to the VH CDRs 1, 2, and 3 and the VL CDRs 1, 2, and 3, or a combination thereof.

2. The human-derived antibody or antigen-binding fragment thereof of claim 1, wherein the VH comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:8.

3. The human-derived antibody or antigen-binding fragment thereof of claim 1, wherein the VH comprises the amino acid sequence set forth in SEQ ID NO:8 or a variant of the amino acid sequence set forth in SEQ ID NO:8 with one amino acid deletion.

4. The human-derived antibody or antigen-binding fragment thereof of claim 1, wherein the VL comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:10.

5. The human-derived antibody or antigen-binding fragment thereof of claim 1, wherein the VL comprises the amino acid sequence set forth in SEQ ID NO:10 or a variant of the amino acid sequence set forth in SEQ ID NO:10 with one amino acid deletion.

6. The human-derived antibody or antigen-binding fragment thereof of claim 1, wherein the VH comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:8, and wherein the VL comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:10.

7. The human-derived antibody or antigen-binding fragment thereof of claim 1, wherein the VH comprises the amino acid sequence set forth in SEQ ID NO:8 or a variant of the amino acid sequence set forth in SEQ ID NO:8 with one amino acid deletion, and wherein the VL comprises the amino acid sequence set forth in SEQ ID NO:10 or a variant of the amino acid sequence set forth in SEQ ID NO:10 with one amino acid deletion.

8. The human-derived antibody or antigen-binding fragment thereof of any one of claims 1 to 7, wherein the human-derived antibody comprises an immunoglobulin heavy chain and an immunoglobulin light chain, wherein the immunoglobulin heavy chain comprises a human IgG1 constant region, and wherein the immunoglobulin light chain comprises a human kappa constant region.

9. The human-derived antibody or antigen-binding fragment thereof of any one of claims 1 to 7, wherein the heterologous sequence is an immunoglobulin heavy chain constant region, an immunoglobulin light chain constant region, or a mammalian secretory signal peptide.

~~9. The antibody or antigen-binding fragment thereof of any one of claims 1 to 8, which is detectably labeled.~~

10. The human-derived antibody of any one of claims 1 to 9, wherein the detectable label is selected from the group consisting of an enzyme, a radioisotope, a fluorophore, and a heavy metal.

11. A pharmaceutical composition comprising the human-derived antibody or antigen-binding fragment thereof of any one of claims 1 to 10 and a pharmaceutically acceptable carrier.

12. A pharmaceutical composition comprising a human-derived antibody or antigen-binding fragment thereof that binds to a chromosome 9 open reading frame 72 (C9orf72) dipeptide repeat protein (DPR) with a poly-Glycine-Alanine $(GA)_{15}$ repeat, and a pharmaceutically acceptable carrier;

wherein the human-derived antibody or antigen-binding fragment thereof comprises:

a heavy chain variable region (VH) comprising VH complementarity determining regions (CDRs) 1, 2, and 3, wherein the VH CDRs 1, 2, and 3 comprise the amino acid sequences set forth in amino acid positions 32-36 of SEQ ID NO:8, amino acid positions 51-67 of SEQ ID NO:8, and amino acid positions 100-113 of SEQ ID NO:8, respectively; and

a light chain variable region (VL) comprising VL CDRs 1, 2, and 3, wherein the VL CDRs 1, 2, and 3 comprise the amino acid sequences set forth in amino acid positions 25-35 of SEQ ID NO:10, amino acid positions 51-57 of SEQ ID NO:10, and amino acid positions 90-98 of SEQ ID NO:10, respectively.

13. The pharmaceutical composition of claim 12, wherein the VH comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:8.

14. The pharmaceutical composition of claim 12, wherein the VH comprises the amino acid sequence set forth in SEQ ID NO:8 or a variant of the amino acid sequence set forth in SEQ ID NO:8 with one amino acid deletion.

15. The pharmaceutical composition of claim 12, wherein the VL comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:10.

16. The pharmaceutical composition of claim 12, wherein the VL comprises the amino acid sequence set forth in SEQ ID NO:10 or a variant of the amino acid sequence set forth in SEQ ID NO:10 with one amino acid deletion.

17. The pharmaceutical composition of claim 12, wherein the VH comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:8, and wherein the VL comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:10.

18. The pharmaceutical composition of claim 12, wherein the VH comprises the amino acid sequence set forth in SEQ ID NO:8 or a variant of the amino acid sequence set forth in SEQ ID NO:8 with one amino acid deletion, and wherein the VL comprises the amino acid sequence set forth in SEQ ID NO:10 or a variant of the amino acid sequence set forth in SEQ ID NO:10 with one amino acid deletion.

19. The pharmaceutical composition of any one of claims 12 to 18, wherein the human-derived antibody comprises an immunoglobulin heavy chain and an immunoglobulin light chain, wherein the immunoglobulin heavy chain comprises a human IgG1 constant region, and wherein the immunoglobulin light chain comprises a human kappa constant region.

~~12~~20. A combination of polynucleotides for expressing the human-derived antibody or antigen-binding fragment thereof of any one of claims 1 to ~~8~~ 9, comprising: (i) a polynucleotide encoding a polypeptide comprising the VH of the human-derived antibody or antigen-binding fragment thereof of any one of claims 1 to ~~8~~ 9; and (ii) a polynucleotide encoding a polypeptide comprising the VL of the human-derived antibody or antigen-binding fragment thereof of any one of claims 1 to ~~8~~ 9; and wherein the human-derived antibody or antigen-binding fragment thereof comprises the heterologous sequence.

~~13~~21. The combination of polynucleotides of claim ~~12~~ 20, wherein each polynucleotide further comprises a heterologous nucleic acid encoding a secretory signal peptide.

22. A combination of polynucleotides for expressing a human-derived antibody or antigen-binding fragment thereof,

wherein the human-derived antibody or antigen-binding fragment thereof binds to a chromosome 9 open reading frame 72 (C9orf72) dipeptide repeat protein (DPR) with a poly-Glycine-Alanine $(GA)_{15}$ repeat, and a pharmaceutically acceptable carrier;

wherein the human-derived antibody or antigen-binding fragment thereof comprises:

a heavy chain variable region (VH) comprising VH complementarity determining regions (CDRs) 1, 2, and 3, wherein the VH CDRs 1, 2, and 3 comprise the amino acid sequences set forth in amino acid positions 32-36 of SEQ ID NO:8, amino acid positions 51-67 of SEQ ID NO:8, and amino acid positions 100-113 of SEQ ID NO:8, respectively; and

a light chain variable region (VL) comprising VL CDRs 1, 2, and 3, wherein the VL CDRs 1, 2, and 3 comprise the amino acid sequences set forth in amino acid positions 25-35 of SEQ ID NO:10, amino acid positions 51-57 of SEQ ID NO:10, and amino acid positions 90-98 of SEQ ID NO:10, respectively;

wherein the combination of polynucleotides comprises (i) a first polynucleotide encoding a polypeptide comprising the VH of the human-derived antibody or antigen-binding fragment thereof; and (ii) a second polynucleotide encoding a polypeptide comprising the VL of the human-derived antibody or antigen-binding fragment thereof; and

wherein each polynucleotide further comprises a heterologous nucleic acid encoding a secretory signal peptide.

23. The combination of polynucleotides of claim 22, wherein the VH comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:8.

24. The combination of polynucleotides of claim 22, wherein the VH comprises the amino acid sequence set forth in SEQ ID NO:8 or a variant of the amino acid sequence set forth in SEQ ID NO:8 with one amino acid deletion.

25. The combination of polynucleotides of claim 22, wherein the VL comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:10.

26. The combination of polynucleotides of claim 22, wherein the VL comprises the amino acid sequence set forth in SEQ ID NO:10 or a variant of the amino acid sequence set forth in SEQ ID NO:10 with one amino acid deletion.

27. The combination of polynucleotides of claim 22, wherein the VH comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:8, and wherein the VL comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:10.

28. The combination of polynucleotides of claim 22, wherein the VH comprises the amino acid sequence set forth in SEQ ID NO:8 or a variant of the amino acid sequence set forth in SEQ ID NO:8 with one amino acid deletion, and wherein the VL comprises the amino acid sequence set forth in SEQ ID NO:10 or a variant of the amino acid sequence set forth in SEQ ID NO:10 with one amino acid deletion.

29. The combination of polynucleotides of any one of claims 22 to 28, wherein the human-derived antibody comprises an immunoglobulin heavy chain and an immunoglobulin light chain, wherein the immunoglobulin heavy chain comprises a human IgG1 constant region, and wherein the immunoglobulin light chain comprises a human kappa constant region.

~~14~~30. An expression vector for expressing the human-derived antibody or antigen-binding fragment thereof of any one of claims 1 to ~~8~~ 9 comprising (i) a promoter operably linked to a polynucleotide encoding a polypeptide comprising the VH of the human-derived antibody or antigen-binding fragment thereof of any one of claims 1 to ~~8~~ 9; and (ii) a promoter operably linked to a polynucleotide encoding a polypeptide comprising the VL of the human-derived antibody or antigen-binding fragment thereof of any one of claims 1 to ~~8~~ 9; and wherein the human-derived antibody or antigen-binding fragment thereof comprises the heterologous sequence.

31. An expression vector for expressing a human-derived antibody or antigen-binding fragment thereof, wherein the expression vector comprises the combination of polynucleotides of any one of claims 22 to 29, wherein the first polynucleotide is operably linked to a promoter, and wherein the second polynucleotide is operably linked to a promoter.

~~15~~32. An expression vector for expressing the human-derived antibody or antigen-binding fragment thereof of any one of claims 1 to ~~8~~ 9 comprising:

a first polynucleotide encoding a first polypeptide comprising a VH of the human-derived antibody or antigen binding fragment thereof of any one of claims 1 to ~~8~~ 9; and

a second polynucleotide encoding a second polypeptide comprising a VL of the human-derived antibody or antigen binding fragment thereof of any one of claims 1 to ~~8~~ 9; and wherein the human-derived antibody or antigen-binding fragment thereof comprises the heterologous sequence.

~~16~~33. A host cell comprising the combination of polynucleotides of ~~claim 12 or 13~~ any one of claims 20 to 29 or the expression vector of ~~claim 14 or 15~~ any one of claims 30 to 32.

~~17~~34. A method for preparing ~~the~~ a human-derived antibody or antigen-binding fragment thereof ~~of any one of claims 1 to 8~~, the method comprising:

(a) culturing the host cell of claim ~~16~~ 33; and

(b) isolating the human-derived antibody or antigen-binding fragment thereof from the culture.

~~18~~35. Use of ~~the~~ a human-derived antibody or antigen-binding fragment thereof ~~of any one of claims 1 to 10~~ in the manufacture of a diagnostic agent for use in detecting ~~medicament for diagnosing a disorder associated with DPR protein in a human subject, wherein the diagnosing comprises obtaining a sample from the subject, determining~~ the presence of poly-GA DPR protein species, or fragments thereof, in ~~the~~ a sample obtained from ~~the~~ a subject, ~~wherein the presence of the DPR protein species, or fragments thereof, in the sample is determined using the antibody or antigen-binding fragment thereof of any one of claims 1 to 10,~~ wherein the presence of the poly-GA

DPR protein species, or fragments thereof, is indicative for amyotrophic lateral sclerosis (ALS) and/or frontotemporal lobar degeneration (FTLD); and

wherein the human-derived antibody or antigen-binding fragment thereof binds to a chromosome 9 open reading frame 72 (C9orf72) dipeptide repeat protein (DPR) with a poly-Glycine-Alanine $(GA)_{15}$ repeat and comprises:

a heavy chain variable region (VH) comprising VH complementarity determining regions (CDRs) 1, 2, and 3, wherein the VH CDRs 1, 2, and 3 comprise the amino acid sequences set forth in amino acid positions 32-36 of SEQ ID NO:8, amino acid positions 51-67 of SEQ ID NO:8, and amino acid positions 100-113 of SEQ ID NO:8, respectively; and

a light chain variable region (VL) comprising VL CDRs 1, 2, and 3, wherein the VL CDRs 1, 2, and 3 comprise the amino acid sequences set forth in amino acid positions 25-35 of SEQ ID NO:10, amino acid positions 51-57 of SEQ ID NO:10, and amino acid positions 90-98 of SEQ ID NO:10, respectively.

36. The use of claim 35, wherein the VH comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:8.

37. The use of claim 35, wherein the VH comprises the amino acid sequence set forth in SEQ ID NO:8 or a variant of the amino acid sequence set forth in SEQ ID NO:8 with one amino acid deletion.

38. The use of claim 35, wherein the VL comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:10.

39. The use of claim 35, wherein the VL comprises the amino acid sequence set forth in SEQ ID NO:10 or a variant of the amino acid sequence set forth in SEQ ID NO:10 with one amino acid deletion.

40. The use of claim 35, wherein the VH comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:8, and wherein the VL comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:10.

41. The use of claim 35, wherein the VH comprises the amino acid sequence set forth in SEQ ID NO:8 or a variant of the amino acid sequence set forth in SEQ ID NO:8 with one amino acid deletion, and wherein the VL comprises the amino acid sequence set forth in SEQ ID NO:10 or a variant of the amino acid sequence set forth in SEQ ID NO:10 with one amino acid deletion.

42. The use of claim 35, wherein the human-derived antibody comprises an immunoglobulin heavy chain and an immunoglobulin light chain, wherein the immunoglobulin heavy chain comprises a human IgG1 constant region, and wherein the immunoglobulin light chain comprises a human kappa constant region.

43. The use of any one of claims 35 to 42, wherein the human-derived antibody or antigen-binding fragment thereof is detectably labeled.

44. The use of claim 43, wherein the detectable label is selected from the group consisting of an enzyme, a radioisotope, a fluorophore, and a heavy metal.

~~19~~45. Use of the human-derived antibody or antigen-binding fragment thereof of any one of claims 1 to 10 in the manufacture of a ~~medicament~~ diagnostic agent for *in vivo* detection of a poly-GA DPR protein in a human subject, wherein the human-derived antibody or antigen-binding fragment thereof is ~~attached to a detectable label~~ detectably labeled.

~~20~~46. Use of the pharmaceutical composition of any one of claims 11 to 19 ~~antibody or antigen-binding fragment thereof of any one of claims 1 to 8~~ in the manufacture of a medicament for prophylactic and/or therapeutic treatment of a disease associated with poly-GA DPR protein or aggregated forms thereof in a human subject, wherein the disease is selected from the group consisting of amyotrophic lateral sclerosis (ALS), Frontotemporal lobar degeneration (FTLD), and FTLD-ALS.

~~21. The use of claim 20, wherein the disease is selected from the group consisting of amyotrophic lateral sclerosis (ALS), Frontotemporal lobar degeneration (FTLD), and FTLD-ALS.~~

~~22~~47. The use of claim ~~20 or 21~~ 46, wherein the human-derived antibody or antigen-binding fragment thereof is formulated for intrathecal, intravenous, or subcutaneous delivery.

~~23. An antibody or antigen-binding fragment thereof that binds to a chromosome 9 open reading frame 72 (C9orf72) dipeptide repeat (DPR) protein with a poly-glycine-alanine (GA)15 repeat, wherein the antibody or antigen-binding fragment thereof comprises:~~

~~(a) (i) a heavy chain variable region (VH) comprising VH complementarity determining regions (CDRs) 1, 2, and 3, wherein the VH CDRs 1, 2, and 3 comprise the amino acid sequences set forth in amino acid positions 32-36 of SEQ ID NO:2, amino acid positions 51-66 of SEQ ID NO:2, and amino acid positions 99-112 of SEQ ID NO:2, respectively; and (ii) a light chain variable region (VL) comprising VL CDRs 1, 2, and 3, wherein the VL CDRs 1, 2, and 3 comprise the amino acid sequences set forth in amino acid positions 25-40 of SEQ ID NO:4, amino acid positions 56-62 of SEQ ID NO:4, and amino acid positions 95-102 of SEQ ID NO:4, respectively;~~

~~(b) (i) a VH comprising VH CDRs 1, 2, and 3, wherein the VH CDRs 1, 2, and 3 comprise the amino acid sequences set forth in amino acid positions 32-36 of SEQ ID NO:22, amino acid positions 51-66 of SEQ ID NO:22, and amino acid positions 99-112 of SEQ ID NO:22, respectively; and (ii) a VL comprising VL CDRs 1, 2, and 3, wherein the VL CDRs 1, 2, and 3 comprise the amino acid sequences set forth in amino acid positions 25-40 of SEQ ID NO:24, amino acid positions 56-62 of SEQ ID NO:24, and amino acid positions 95-103 of SEQ ID NO:24, respectively; or~~

~~(c) (i) a VH comprising VH CDRs 1, 2, and 3, wherein the VH CDRs 1, 2, and 3 comprise the amino acid sequences set forth in amino acid positions 32-38 of SEQ ID NO:30, amino acid positions 53-70 of SEQ ID NO:30, and amino acid positions 103-118 of SEQ ID NO:30, respectively; and (ii) a VL comprising VL CDRs 1, 2, and 3, wherein the VL CDRs 1, 2, and 3 comprise the amino acid sequences set forth in amino acid positions 25-40 of SEQ ID NO:32, amino acid positions 56-62 of SEQ ID NO:32, and amino acid positions 95-103 of SEQ ID NO:32, respectively.~~

~~24. An antibody or antigen-binding fragment thereof that binds to a chromosome 9 open reading frame 72 (C9orf72) dipeptide repeat (DPR) protein with a poly-proline-arginine (PR)15 repeat, wherein the antibody or antigen-binding fragment thereof comprises:~~

(a) (i) a heavy chain variable region (VH) comprising VH complementarity determining regions (CDRs) 1, 2, and 3, wherein the VH CDRs 1, 2, and 3 comprise the amino acid sequences set forth in amino acid positions 32-36 of SEQ ID NO:38, amino acid positions 51-66 of SEQ ID NO:38, and amino acid positions 99-116 of SEQ ID NO:38, respectively; and (ii) a light chain variable region (VL) comprising VL CDRs 1, 2, and 3, wherein the VL CDRs 1, 2, and 3 comprise the amino acid sequences set forth in amino acid positions 25-35 of SEQ ID NO:40, amino acid positions 51-57 of SEQ ID NO:40, and amino acid positions 90-98 of SEQ ID NO:40, respectively; or

(b) (i) a VH comprising VH CDRs 1, 2, and 3, wherein the VH CDRs 1, 2, and 3 comprise the amino acid sequences set forth in amino acid positions 32-36 of SEQ ID NO:80, amino acid positions 51-67 of SEQ ID NO:80, and amino acid positions 100-114 of SEQ ID NO:80, respectively; and (ii) a VL comprising VL CDRs 1, 2, and 3, wherein the VL CDRs 1, 2, and 3 comprise the amino acid sequences set forth in amino acid positions 25-36 of SEQ IDNO:82, amino acid positions 52-58 of SEQ ID NO:82, and amino acid positions 91-95 of SEQ ID NO:82, respectively.

25. An antibody or antigen-binding fragment thereof that binds to a chromosome 9 open reading frame 72 (C9orf72) dipeptide repeat (DPR) protein with a poly-glycine-proline (GP)15 repeat, wherein the antibody or antigen-binding fragment thereof comprises:

(a) (i) a heavy chain variable region (VH) comprising VH complementarity determining regions (CDRs) 1, 2, and 3, wherein the VH CDRs 1, 2, and 3 comprise the amino acid sequences set forth in amino acid positions 32-36 of SEQ ID NO:14, amino acid positions 51-67 of SEQ ID NO:14, and amino acid positions 100-113 of SEQ ID NO:14, respectively; and (ii) a light chain variable region (VL) comprising VL CDRs 1, 2, and 3, wherein the VL CDRs 1, 2, and 3 comprise the amino acid sequences set forth in amino acid positions 25-41 of SEQ ID NO:16, amino acid positions 57-63 of SEQ ID NO:16, and amino acid positions 96-104 of SEQ ID NO:16, respectively;

(b) (i) a VH comprising VH CDRs 1, 2, and 3, wherein the VH CDRs 1, 2, and 3 comprise the amino acid sequences set forth in amino acid positions 32-36 of SEQ ID NO:44, amino acid positions 53-68 of SEQ ID NO:44, and amino acid positions 101-113 of SEQ ID NO:44, respectively; and (ii) a VL comprising VL CDRs 1, 2, and 3, wherein the VL CDRs 1, 2, and 3 comprise the amino acid sequences set forth in amino

~~acid positions 25-35 of SEQ ID NO:46, amino acid positions 51-57 of SEQ ID NO:46, and amino acid positions 90-98 of SEQ ID NO:46, respectively; or~~

~~(c) (i) a VH comprising VH CDRs 1, 2, and 3, wherein the VH CDRs 1, 2, and 3 comprise the amino acid sequences set forth in amino acid positions 31-36 of SEQ ID NO:72, amino acid positions 51-67 of SEQ ID NO:72, and amino acid positions 100-116 of SEQ ID NO:72, respectively; and (ii) a VL comprising VL CDRs 1, 2, and 3, wherein the VL CDRs 1, 2, and 3 comprise the amino acid sequences set forth in amino acid positions 25-41 of SEQ ID NO:74, amino acid positions 57-63 of SEQ ID NO:74, and amino acid positions 96-104 of SEQ ID NO:74, respectively.~~

~~26. An antibody or antigen-binding fragment thereof that binds to a chromosome 9 open reading frame 72 (C9orf72) dipeptide repeat (DPR) protein with a poly-glycine-arginine (GR)15 repeat, wherein the antibody or antigen-binding fragment thereof comprises:~~

~~(a) (i) a heavy chain variable region (VH) comprising VH complementarity determining regions (CDRs) 1, 2, and 3, wherein the VH CDRs 1, 2, and 3 comprise the amino acid sequences set forth in amino acid positions 32-36 of SEQ ID NO:52, amino acid positions 51-67 of SEQ ID NO:52, and amino acid positions 100-118 of SEQ ID NO:52, respectively; and (ii) a light chain variable region (VL) comprising VL CDRs 1, 2, and 3, wherein the VL CDRs 1, 2, and 3 comprise the amino acid sequences set forth in amino acid positions 25-35 of SEQ ID NO:54, amino acid positions 51-57 of SEQ ID NO:54, and amino acid positions 90-98 of SEQ ID NO:54, respectively; or~~

~~(b) (i) a VH comprising VH CDRs 1, 2, and 3, wherein the VH CDRs 1, 2, and 3 comprise the amino acid sequences set forth in amino acid positions 32-36 of SEQ ID NO:58, amino acid positions 51-67 of SEQ ID NO:58, and amino acid positions 100-115 of SEQ ID NO:58, respectively; and (ii) a VL comprising VL CDRs 1, 2, and 3, wherein the VL CDRs 1, 2, and 3 comprise the amino acid sequences set forth in amino acid positions 24-36 of SEQ ID NO:60, amino acid positions 52-58 of SEQ ID NO:60, and amino acid positions 91-101 of SEQ ID NO:60, respectively.~~

~~27. An antibody or antigen-binding fragment thereof that binds to a chromosome 9 open reading frame 72 (C9orf72) dipeptide repeat (DPR) protein with a poly-proline-alanine (PA)15 repeat, wherein the antibody or antigen-binding fragment thereof comprises:~~

(i) a heavy chain variable region (VH) comprising VH complementarity determining regions (CDRs) 1, 2, and 3, wherein the VH CDRs 1, 2, and 3 comprise the amino acid sequences set forth in amino acid positions 32-36 of SEQ ID NO:64, amino acid positions 51-67 of SEQ ID NO:64, and amino acid positions 100-116 of SEQ ID NO:64, respectively; and (ii) a light chain variable region (VL) comprising VL CDRs 1, 2, and 3, wherein the VL CDRs 1, 2, and 3 comprise the amino acid sequences set forth in amino acid positions 25-35 of SEQ ID NO:66, amino acid positions 51-57 of SEQ ID NO:66, and amino acid positions 90-99 of SEQ ID NO:66, respectively.

28. The antibody or antigen-binding fragment thereof of any one of claims 23 to 27, wherein the antibody comprises an immunoglobulin heavy chain and an immunoglobulin light chain, wherein the immunoglobulin heavy chain comprises a human IgG1 constant region, and wherein the immunoglobulin light chain comprises a human kappa constant region.

29. The antibody or antigen-binding fragment thereof of any one of claims 23 to 28, which is detectably labeled.

30. The antibody or antigen-binding fragment thereof of claim 29, wherein the detectable label is selected from the group consisting of an enzyme, a radioisotope, a fluorophore and a heavy metal.

31. A pharmaceutical composition comprising the antibody or antigen-binding fragment thereof of any one of claims 23 to 30 and a pharmaceutically acceptable carrier.

32. A combination for expressing the antibody or antigen-binding fragment thereof of any one of claims 23 to 28 comprising:

(i) a polynucleotide encoding a polypeptide comprising the VH of the antibody or antigen-binding fragment thereof of any one of claims 23 to 28; and

(ii) a polynucleotide encoding a polypeptide comprising the VL of the antibody or antigen-binding fragment thereof of any one of claims 23 to 28.

33. The combination of claim 32, wherein each polynucleotide further comprises a heterologous nucleic acid encoding a secretory signal peptide.

34. An expression vector for expressing the antibody or antigen-binding fragment thereof of any one of claims 23 to 28 comprising (i) a promoter operably linked to a polynucleotide encoding a polypeptide comprising the VH of the antibody or antigen-binding fragment thereof of any one of claims 23 to 28; and (ii) a promoter operably linked to a polynucleotide encoding a polypeptide comprising the VL of the antibody or antigen-binding fragment thereof of any one of claims 23 to 28.

35. An expression vector for expressing the antibody or antigen-binding fragment thereof of any one of claims 23 to 28 comprising:

a first polynucleotide encoding a first polypeptide comprising a VH of the antibody or antigen binding fragment thereof of any one of claims 23 to 28; and

a second polynucleotide encoding a second polypeptide comprising a VL of the antibody or antigen binding fragment thereof of any one of claims 23 to 28.

36. A host cell comprising the combination of claim 32 or 33 or the expression vector of claim 34 or 35.

37. A method for preparing the antibody or antigen-binding fragment thereof of any one of claims 23 to 28, the method comprising:

(a) culturing the cell of claim 36; and

(b) isolating the antibody or antigen-binding fragment thereof from the culture.

38. Use of the antibody or antigen-binding fragment thereof of any one of claims 1 to 10 in the manufacture of a medicament for diagnosing a disorder associated with DPR protein in a human subject, wherein the diagnosing comprises obtaining a sample from the subject, determining the presence of DPR protein species, or fragments thereof, in the sample from the subject, wherein the presence of the DPR protein species, or fragments thereof, in the sample is determined using the antibody or antigen-binding fragment thereof of any one of claims 23 to 30, wherein the presence of DPR protein species, or fragments thereof, is indicative for amyotrophic lateral sclerosis (ALS) and/or frontotemporal lobar degeneration (FTLD).

~~39. Use of the antibody or antigen-binding fragment thereof of claim 23 in the manufacture of a medicament for in vivo detection of a poly-GA DPR protein in a human subject, wherein the antibody or antigen-binding fragment thereof is attached to a detectable label.~~

~~40. Use of the antibody or antigen-binding fragment thereof of claim 24 in the manufacture of a medicament for in vivo detection of a poly-proline-arginine (PR) DPR protein in a human subject, wherein the antibody or antigen-binding fragment thereof is attached to a detectable label.~~

~~41. Use of the antibody or antigen-binding fragment thereof of claim 25 in the manufacture of a medicament for in vivo detection of a poly-glycine-proline (GP) DPR protein in a human subject, wherein the antibody or antigen-binding fragment thereof is attached to a detectable label.~~

~~42. Use of the antibody or antigen-binding fragment thereof of claim 26 in the manufacture of a medicament for in vivo detection of a poly-glycine-arginine (GR) DPR protein in a human subject, wherein the antibody or antigen-binding fragment thereof is attached to a detectable label.~~

~~43. Use of the antibody or antigen-binding fragment thereof of claim 27 in the manufacture of a medicament for in vivo detection of a poly-proline-alanine (PA) DPR protein in a human subject, wherein the antibody or antigen-binding fragment thereof is attached to a detectable label.~~

~~44. Use of the antibody or antigen-binding fragment thereof of any one of claims 23 to 30 in the manufacture of a medicament for prophylactic and/or therapeutic treatment of a disease associated with DPR protein or aggregated forms thereof in a human subject.~~

~~45. The use of claim 44, wherein the disease is selected from the group consisting of amyotrophic lateral sclerosis (ALS), frontotemporal lobar degeneration (FTLD), and FTLD-ALS.~~

~~46. The use of claim 44 or 45, wherein the antibody or antigen-binding fragment thereof is formulated for intrathecal, intravenous, or subcutaneous delivery.~~