

What is claimed is:

1. An antibody that binds to a TREM2 protein, wherein the antibody comprises a heavy chain variable region comprising an HVR-H1, HVR-H2, and HVR-H3, and a light chain variable region comprising an HVR-L1, HVR-L2, and HVR-L3, wherein:

the HVR-H1 comprises the sequence of SEQ ID NO: 124, the HVR-H2 comprises the sequence of SEQ ID NO: 162, the HVR-H3 comprises the sequence of SEQ ID NO: 126, the HVR-L1 comprises the sequence of SEQ ID NO: 130, the HVR-L2 comprises the sequence of SEQ ID NO: 131, and the HVR-L3 comprises the sequence of SEQ ID NO: 129;

the HVR-H1 comprises the sequence of SEQ ID NO: 124, the HVR-H2 comprises the sequence of SEQ ID NO: 163, the HVR-H3 comprises the sequence of SEQ ID NO: 126, the HVR-L1 comprises the sequence of SEQ ID NO: 130, the HVR-L2 comprises the sequence of SEQ ID NO: 131, and the HVR-L3 comprises the sequence of SEQ ID NO: 129;

the HVR-H1 comprises the sequence of SEQ ID NO: 124, the HVR-H2 comprises the sequence of SEQ ID NO: 164, the HVR-H3 comprises the sequence of SEQ ID NO: 126, the HVR-L1 comprises the sequence of SEQ ID NO: 130, the HVR-L2 comprises the sequence of SEQ ID NO: 131, and the HVR-L3 comprises the sequence of SEQ ID NO: 129;

the HVR-H1 comprises the sequence of SEQ ID NO: 124, the HVR-H2 comprises the sequence of SEQ ID NO: 125, the HVR-H3 comprises the sequence of SEQ ID NO: 126, the HVR-L1 comprises the sequence of SEQ ID NO: 144, the HVR-L2 comprises the sequence of SEQ ID NO: 131, and the HVR-L3 comprises the sequence of SEQ ID NO: 129;

the HVR-H1 comprises the sequence of SEQ ID NO: 124, the HVR-H2 comprises the sequence of SEQ ID NO: 125, the HVR-H3 comprises the sequence of SEQ ID NO: 126, the HVR-L1 comprises the sequence of SEQ ID NO: 184, the HVR-L2 comprises the sequence of SEQ ID NO: 131, and the HVR-L3 comprises the sequence of SEQ ID NO: 129;

the HVR-H1 comprises the sequence of SEQ ID NO: 157, the HVR-H2 comprises the sequence of SEQ ID NO: 165, the HVR-H3 comprises the sequence of SEQ ID NO: 126, the HVR-L1 comprises the sequence of SEQ ID NO: 185, the HVR-L2 comprises the sequence of SEQ ID NO: 134, and the HVR-L3 comprises the sequence of SEQ ID NO: 129;

the HVR-H1 comprises the sequence of SEQ ID NO: 157, the HVR-H2 comprises the sequence of SEQ ID NO: 166, the HVR-H3 comprises the sequence of SEQ ID NO: 181, the HVR-L1 comprises

the HVR-H1 comprises the sequence of SEQ ID NO: 132, the HVR-H2 comprises the sequence of SEQ ID NO: 143, the HVR-H3 comprises the sequence of SEQ ID NO: 126, the HVR-L1 comprises the sequence of SEQ ID NO: 142, the HVR-L2 comprises the sequence of SEQ ID NO: 131, and the HVR-L3 comprises the sequence of SEQ ID NO: 129.

2. The antibody of claim 1, wherein the heavy chain variable region comprises one, two, three or four framework regions selected from VH FR1, VH FR2, VH FR3, and VH FR4, wherein:

the VH FR1 comprises a sequence selected from the group consisting of SEQ ID NOs: 9-11,

the VH FR2 comprises a sequence selected from the group consisting of SEQ ID NOs: 12 and 13,

the VH FR3 comprises a sequence selected from the group consisting of SEQ ID NOs: 14 and 15, and

the VH FR4 comprises the sequence of SEQ ID NO: 16; and/or

the light chain variable region comprises one, two, three or four framework regions selected from VL FR1, VL FR2, VL FR3, and VL FR4, wherein:

the VL FR1 comprises a sequence selected from the group consisting of SEQ ID NOs: 17-20,

the VL FR2 comprises a sequence selected from the group consisting of SEQ ID NOs: 21 and 22,

the VL FR3 comprises a sequence selected from the group consisting of SEQ ID NOs: 23 and 24, and

the VL FR4 comprises a sequence selected from the group consisting of SEQ ID NOs: 25 and 26.

3. The antibody of claim 1 or 2, wherein:

(a) the HVR-H1 comprises the amino acid sequence YAFSSQWMN (SEQ ID NO: 132), the HVR-H2 comprises the amino acid sequence RIYPGGGDTNYARKFQG (SEQ ID NO: 133), the HVR-H3 comprises the amino acid sequence ARLLRNQPGESYAMDY (SEQ ID NO: 126), the HVR-L1 comprises the amino acid sequence RSSQSLVHSNGYTYLH (SEQ ID NO: 130), the HVR-L2 comprises the amino acid sequence KVSNNRRS (SEQ ID NO: 134), and the HVR-L3 comprises the amino acid sequence SQSTRVPYT (SEQ ID NO: 129);

(b) the HVR-H1 comprises the amino acid sequence YAFSSQWMN (SEQ ID NO: 132), the HVR-H2 comprises the amino acid sequence RIYPGGGDTNYAGKFQG (SEQ ID NO: 135), the HVR-H3 comprises the amino acid sequence ARLLRNQPGESYAMDY (SEQ ID NO: 126), the HVR-L1 comprises the amino acid sequence RSSQSLVHSNGYTYLH (SEQ ID NO: 130), the HVR-L2 comprises the amino acid sequence KVSNNRFS (SEQ ID NO: 131), and the HVR-L3 comprises the amino acid sequence SQSTRVPYT (SEQ ID NO: 129);

(c) the HVR-H1 comprises the amino acid sequence YAFSSDWMN (SEQ ID NO: 136), the HVR-H2 comprises the amino acid sequence RIYPGEGDTNYARKFHG (SEQ ID NO:

- 137), the HVR-H3 comprises the amino acid sequence ARLLRNKPGESYAMDY (SEQ ID NO: 138), the HVR-L1 comprises the amino acid sequence RTSQSLVHSNAYTYLH (SEQ ID NO: 139), the HVR-L2 comprises the amino acid sequence KVSNNRVS (SEQ ID NO: 140), and the HVR-L3 comprises the amino acid sequence SQSTRVPYT (SEQ ID NO: 129);
- (d) the HVR-H1 comprises the amino acid sequence YAFSSQWMN (SEQ ID NO: 132), the HVR-H2 comprises the amino acid sequence RIYPGEGDTNYARKFQG (SEQ ID NO: 141), the HVR-H3 comprises the amino acid sequence ARLLRNQPGESYAMDY (SEQ ID NO: 126), the HVR-L1 comprises the amino acid sequence RSSQSLVHSNQYTYLH (SEQ ID NO: 142), the HVR-L2 comprises the amino acid sequence KVSNNRRS (SEQ ID NO: 134), and the HVR-L3 comprises the amino acid sequence SQSTRVPYT (SEQ ID NO: 129);
- (e) the HVR-H1 comprises the amino acid sequence YAFSSQWMN (SEQ ID NO: 132), the HVR-H2 comprises the amino acid sequence RIYPGEGDTNYAGKFQG (SEQ ID NO: 143), the HVR-H3 comprises the amino acid sequence ARLLRNQPGESYAMDY (SEQ ID NO: 126), the HVR-L1 comprises the amino acid sequence RSSQSLVHSNQYTYLH (SEQ ID NO: 142), the HVR-L2 comprises the amino acid sequence KVSNNRFS (SEQ ID NO: 131), and the HVR-L3 comprises the amino acid sequence SQSTRVPYT (SEQ ID NO: 129);
- (f) the HVR-H1 comprises the amino acid sequence YAFSSQWMN (SEQ ID NO: 132), the HVR-H2 comprises the amino acid sequence RIYPGGGDTNYAGKFQG (SEQ ID NO: 135), the HVR-H3 comprises the amino acid sequence ARLLRNQPGESYAMDY (SEQ ID NO: 126), the HVR-L1 comprises the amino acid sequence RSSQSLVHSNNRYTYLH (SEQ ID NO: 144), the HVR-L2 comprises the amino acid sequence KVSNNRFS (SEQ ID NO: 131), and the HVR-L3 comprises the amino acid sequence SQSTRVPYT (SEQ ID NO: 129); or
- (g) the HVR-H1 comprises the amino acid sequence YAFSSQWMN (SEQ ID NO: 132), the HVR-H2 comprises the amino acid sequence RIYPGGGDTNYARKFQG (SEQ ID NO: 133), the HVR-H3 comprises the amino acid sequence ARLLRNQPGESYAMDY (SEQ ID NO: 126), the HVR-L1 comprises the amino acid sequence RSSQSLVHSNNRYTYLH (SEQ ID NO: 144), the HVR-L2 comprises the amino acid sequence KVSNNRRS (SEQ ID NO: 134), and the HVR-L3 comprises the amino acid sequence SQSTRVPYT (SEQ ID NO: 129).

4. An antibody that binds to a TREM2 protein, wherein the antibody comprises a heavy chain variable region comprising an HVR-H1, HVR-H2, and HVR-H3, and a light chain variable region comprising an HVR-L1, HVR-L2, and HVR-L3, wherein the HVR-H1 comprises the amino acid sequence YAFSSDWMN (SEQ ID NO: 136), the HVR-H2 comprises the amino acid sequence RIYPGEGDTNYARKFHG (SEQ ID NO: 137), the HVR-H3 comprises the amino acid sequence ARLLRNKPGESYAMDY (SEQ ID NO: 138), the HVR-L1 comprises the amino acid sequence RTSQSLVHSNAYTYLH (SEQ ID NO: 139), the HVR-L2 comprises the amino acid sequence KVSNRVS (SEQ ID NO: 140), and the HVR-L3 comprises the amino acid sequence SQSTRVPYT (SEQ ID NO: 129).

5. An antibody that binds to a TREM2 protein, wherein the antibody comprises a heavy chain variable region comprising an HVR-H1, HVR-H2, and HVR-H3, and a light chain variable region comprising an HVR-L1, HVR-L2, and HVR-L3, wherein the HVR-H1 comprises the amino acid sequence YAFSSQWMN (SEQ ID NO: 132), the HVR-H2 comprises the amino acid sequence RIYPGEGDTNYARKFQG (SEQ ID NO: 141), the HVR-H3 comprises the amino acid sequence ARLLRNQPGESYAMDY (SEQ ID NO: 126), the HVR-L1 comprises the amino acid sequence RSSQSLVHSNQYTYLH (SEQ ID NO: 142), the HVR-L2 comprises the amino acid sequence KVSNRRS (SEQ ID NO: 134), and the HVR-L3 comprises the amino acid sequence SQSTRVPYT (SEQ ID NO: 129).

6. An antibody that binds to a TREM2 protein, wherein the antibody comprises a heavy chain variable region comprising an HVR-H1, HVR-H2, and HVR-H3, and a light chain variable region comprising an HVR-L1, HVR-L2, and HVR-L3, wherein the HVR-H1 comprises the amino acid sequence YAFSSQWMN (SEQ ID NO: 132), the HVR-H2 comprises the amino acid sequence RIYPGGGDTNYAGKFQG (SEQ ID NO: 135), the HVR-H3 comprises the amino acid sequence ARLLRNQPGESYAMDY (SEQ ID NO: 126), the HVR-L1 comprises the amino acid sequence RSSQSLVHSNRYTYLH (SEQ ID NO: 144), the HVR-L2 comprises the amino acid sequence KVSNRFS (SEQ ID NO: 131), and the HVR-L3 comprises the amino acid sequence SQSTRVPYT (SEQ ID NO: 129).

7. An antibody that binds to a TREM2 protein, wherein the antibody comprises:
a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 27 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 92;
a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 28 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 92;

a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 68 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 109;

a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 69 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 108;

a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 69 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 109;

a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 59 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 112;

a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 91 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 118;

a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 53 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 113;

a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 70 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 110; or

a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 71 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 111.

8. The antibody of claim 7, wherein:

- (a) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 53, and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 97;
- (b) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 59; and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 104;
- (c) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 64; and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 108;
- (d) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 70; and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 110;
- (e) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 71; and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 111;

- (f) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 59; and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 112; or
 - (g) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 53; and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 113.
9. An antibody that binds to a TREM2 protein, wherein the antibody comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 64 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 108.
10. An antibody that binds to a TREM2 protein, wherein the antibody comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 70 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 110.
11. An antibody that binds to a TREM2 protein, wherein the antibody comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 59 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 112.
12. The antibody of any one of claims 1-11, wherein the antibody comprises:
- a heavy chain comprising the amino acid sequence of SEQ ID NO: 198, and a light chain comprising the amino acid sequence of SEQ ID NO: 214;
 - a heavy chain comprising the amino acid sequence of SEQ ID NO: 199, and a light chain comprising the amino acid sequence of SEQ ID NO: 214;
 - a heavy chain comprising the amino acid sequence of SEQ ID NO: 200, and a light chain comprising the amino acid sequence of SEQ ID NO: 214;
 - a heavy chain comprising the amino acid sequence of SEQ ID NO: 201, and a light chain comprising the amino acid sequence of SEQ ID NO: 214;
 - a heavy chain comprising the amino acid sequence of SEQ ID NO: 202, and a light chain comprising the amino acid sequence of SEQ ID NO: 215;
 - a heavy chain comprising the amino acid sequence of SEQ ID NO: 203, and a light chain comprising the amino acid sequence of SEQ ID NO: 215;
 - a heavy chain comprising the amino acid sequence of SEQ ID NO: 204, and a light chain comprising the amino acid sequence of SEQ ID NO: 215;
 - a heavy chain comprising the amino acid sequence of SEQ ID NO: 205, and a light chain comprising the amino acid sequence of SEQ ID NO: 215;

a heavy chain comprising the amino acid sequence of SEQ ID NO: 206, and a light chain comprising the amino acid sequence of SEQ ID NO: 216;

a heavy chain comprising the amino acid sequence of SEQ ID NO: 207, and a light chain comprising the amino acid sequence of SEQ ID NO: 216;

a heavy chain comprising the amino acid sequence of SEQ ID NO: 208, and a light chain comprising the amino acid sequence of SEQ ID NO: 218;

a heavy chain comprising the amino acid sequence of SEQ ID NO: 209, and a light chain comprising the amino acid sequence of SEQ ID NO: 218;

a heavy chain comprising the amino acid sequence of SEQ ID NO: 210, and a light chain comprising the amino acid sequence of SEQ ID NO: 218;

a heavy chain comprising the amino acid sequence of SEQ ID NO: 211, and a light chain comprising the amino acid sequence of SEQ ID NO: 218;

a heavy chain comprising the amino acid sequence of SEQ ID NO: 212, and a light chain comprising the amino acid sequence of SEQ ID NO: 217; or

a heavy chain comprising the amino acid sequence of SEQ ID NO: 213, and a light chain comprising the amino acid sequence of SEQ ID NO: 217.

13. An antibody that binds to a TREM2 protein, wherein the antibody comprises:

(a) a heavy chain comprising the amino acid sequence of SEQ ID NO: 202, and a light chain comprising the amino acid sequence of SEQ ID NO: 215; or

(b) a heavy chain comprising the amino acid sequence of SEQ ID NO: 203, and a light chain comprising the amino acid sequence of SEQ ID NO: 215.

14. An antibody that binds to a TREM2 protein, wherein the antibody comprises:

(a) a heavy chain comprising the amino acid sequence of SEQ ID NO: 206, and a light chain comprising the amino acid sequence of SEQ ID NO: 216; or

(b) a heavy chain comprising the amino acid sequence of SEQ ID NO: 207, and a light chain comprising the amino acid sequence of SEQ ID NO: 216.

15. An antibody that binds to a TREM2 protein, wherein the antibody comprises:

(a) a heavy chain comprising the amino acid sequence of SEQ ID NO: 200, and a light chain comprising the amino acid sequence of SEQ ID NO: 214; or

(b) a heavy chain comprising the amino acid sequence of SEQ ID NO: 201, and a light chain comprising the amino acid sequence of SEQ ID NO: 214.

16. An antibody that binds to a TREM2 protein, wherein the antibody comprises:
- a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 53, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 115;
 - a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 27, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 92;
 - a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 56, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 104;
 - a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 56, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 117;
 - a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 56, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 115;
 - a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 72, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 114;
 - a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 72, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 115;
 - a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 73, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 115;
 - a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 74, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 115;
 - a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 75, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 115;
 - a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 76, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 115;
 - a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 77, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 115;
 - a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 78, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 115;
 - a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 79, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 115;
 - a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 80, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 115;
 - a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 81, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 115;

a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 82, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 115;

a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 83, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 115;

a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 84, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 115;

a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 85, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 115;

a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 86, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 92;

a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 86, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 116;

a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 87, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 92;

a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 88, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 92;

a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 89, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 92; or

a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 90, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 104.

17. The antibody of any one of claims 1-11 or 16, wherein the antibody is of the IgG class, the IgM class, or the IgA class.

18. The antibody of claim 17, wherein the antibody is of the IgG class and has an IgG1, IgG2, IgG3, or IgG4 isotype.

19. The antibody of claim 18, wherein the antibody comprises one or more amino acid substitutions in the Fc region at a residue position selected from the group consisting of: C127S, L234A, L234F, L235A, L235E, S267E, K322A, L328F, A330S, P331S, E345R, E430G, S440Y, and any combination thereof, wherein the numbering of the residues is according to EU or Kabat numbering.

20. The antibody of claim 19, wherein:

- (a) the Fc region comprises an amino acid substitution at positions E430G, L23443A, L235A, and P331S, wherein the numbering of the residue position is according to EU numbering;

- (b) the Fc region comprises an amino acid substitution at positions E430G and P331S, wherein the numbering of the residue position is according to EU numbering;
 - (c) the Fc region comprises an amino acid substitution at positions E430G and K322A , wherein the numbering of the residue position is according to EU numbering;
 - (d) the Fc region comprises an amino acid substitution at positions E430G, A330S, and P331S, wherein the numbering of the residue position is according to EU numbering;
 - (e) the Fc region comprises an amino acid substitution at positions E430G, K322A, A330S, and P331S, wherein the numbering of the residue position is according to EU numbering;
 - (f) the Fc region comprises an amino acid substitution at positions E430G, K322A, and A330S, wherein the numbering of the residue position is according to EU numbering;
 - (g) the Fc region comprises an amino acid substitution at positions E430G, K322A, and P331S, wherein the numbering of the residue position is according to EU numbering;
 - (h) the Fc region comprises an amino acid substitution at positions S267E and L328F, wherein the numbering of the residue position is according to EU numbering;
 - (i) the Fc region comprises an amino acid substitution at position C127S, wherein the numbering of the residue position is according to EU numbering;
 - (j) the Fc region comprises an amino acid substitution at positions E345R, E430G and S440Y, wherein the numbering of the residue position is according to EU numbering; or
 - (k) the Fc region comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 146-156.
21. An antibody that binds to a TREM2 protein, wherein the antibody comprises:
- (a) a heavy chain variable region comprising an HVR-H1, HVR-H2, and HVR-H3, and a light chain variable region comprising an HVR-L1, HVR-L2, and HVR-L3, wherein the HVR-H1 comprises the amino acid sequence YAFSSDWMN (SEQ ID NO: 136), the HVR-H2 comprises the amino acid sequence RIYPGEGDTNYARKFHG (SEQ ID NO: 137), the HVR-H3 comprises the amino acid sequence ARLLRNKPGESYAMDY (SEQ ID NO: 138), the HVR-L1 comprises the amino acid sequence RTSQSLVHSNAYTYLH (SEQ ID NO: 139), the HVR-L2 comprises the amino acid sequence KVSNRVS (SEQ ID NO: 140), and the HVR-L3 comprises the amino acid sequence SQSTRVPYT (SEQ ID NO: 129), wherein the antibody has an IgG1 isotype;
 - (b) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 64 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 108, wherein the antibody has an IgG1 isotype;

- (c) a heavy chain comprising the amino acid sequence of SEQ ID NO: 202, and a light chain comprising the amino acid sequence of SEQ ID NO: 215; or
 - (d) a heavy chain comprising the amino acid sequence of SEQ ID NO: 203, and a light chain comprising the amino acid sequence of SEQ ID NO: 215.
22. An antibody that binds to a TREM2 protein, wherein the antibody comprises:
- (a) a heavy chain variable region comprising an HVR-H1, HVR-H2, and HVR-H3, and a light chain variable region comprising an HVR-L1, HVR-L2, and HVR-L3, wherein the HVR-H1 comprises the amino acid sequence YAFSSQWMN (SEQ ID NO: 132), the HVR-H2 comprises the amino acid sequence RIYPGEGDTNYARKFQG (SEQ ID NO: 141), the HVR-H3 comprises the amino acid sequence ARLLRNQPGESYAMDY (SEQ ID NO: 126), the HVR-L1 comprises the amino acid sequence RSSQSLVHSNQYTYLH (SEQ ID NO: 142), the HVR-L2 comprises the amino acid sequence KVSNNRRS (SEQ ID NO: 134), and the HVR-L3 comprises the amino acid sequence SQSTRVPYT (SEQ ID NO: 129), wherein the antibody has an IgG1 isotype;
 - (b) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 70 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 110, wherein the antibody has an IgG1 isotype;
 - (c) a heavy chain comprising the amino acid sequence of SEQ ID NO: 206, and a light chain comprising the amino acid sequence of SEQ ID NO: 216; or
 - (d) a heavy chain comprising the amino acid sequence of SEQ ID NO: 207, and a light chain comprising the amino acid sequence of SEQ ID NO: 216.
23. An antibody that binds to a TREM2 protein, wherein the antibody comprises:
- (a) a heavy chain variable region comprising an HVR-H1, HVR-H2, and HVR-H3, and a light chain variable region comprising an HVR-L1, HVR-L2, and HVR-L3, wherein the HVR-H1 comprises the amino acid sequence YAFSSQWMN (SEQ ID NO: 132), the HVR-H2 comprises the amino acid sequence RIYPGGGDTNYAGKFQG (SEQ ID NO: 135), the HVR-H3 comprises the amino acid sequence ARLLRNQPGESYAMDY (SEQ ID NO: 126), the HVR-L1 comprises the amino acid sequence RSSQSLVHSNRYTYLH (SEQ ID NO: 144), the HVR-L2 comprises the amino acid sequence KVSNNRFS (SEQ ID NO: 131), and the HVR-L3 comprises the amino acid sequence SQSTRVPYT (SEQ ID NO: 129), wherein the antibody has an IgG1 isotype comprising an Fc region that comprises an amino acid substitution at positions E430G and P331S, wherein the numbering of the residue position is according to EU numbering;
 - (b) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 59 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 112, wherein the

antibody has an IgG1 isotype comprising an Fc region that comprises an amino acid substitution at positions E430G and P331S, wherein the numbering of the residue position is according to EU numbering;

(c) a heavy chain comprising the amino acid sequence of SEQ ID NO: 200, and a light chain comprising the amino acid sequence of SEQ ID NO: 214; or

(d) a heavy chain comprising the amino acid sequence of SEQ ID NO: 201, and a light chain comprising the amino acid sequence of SEQ ID NO: 214.

24. The antibody of any one of claims 1-23, wherein the TREM2 protein is a human protein.

25. The antibody of claim 24, wherein the TREM2 protein is a wild-type protein.

26. The antibody of claim 24, wherein the TREM2 protein is a naturally occurring variant.

27. The antibody of any one of claims 1-11 or 16-26, wherein the antibody is an antibody fragment that binds to one or more human proteins selected from the group consisting of human TREM2, a naturally occurring variant of human TREM2, and a disease variant of human TREM2, and optionally wherein the antibody fragment is cross-linked to a second antibody fragment that binds to one or more human proteins selected from the group consisting of human TREM2, a naturally occurring variant of human TREM2, and a disease variant of human TREM2.

28. The antibody of claim 27, wherein the fragment is an Fab, Fab', Fab'-SH, F(ab')₂, Fv or scFv fragment.

29. The antibody of any one of claims 1-28, wherein the antibody is a monoclonal antibody.

30. The antibody of any one of claims 1-11 and 16-28, wherein the antibody is a humanized antibody.

31. The antibody of any one of claims 1-30, wherein the antibody is a bispecific antibody recognizing a first antigen and a second antigen, wherein the first antigen is human TREM2 or a naturally occurring variant thereof, and the second antigen is:

- (a) an antigen facilitating transport across the blood-brain-barrier;
- (b) an antigen facilitating transport across the blood-brain-barrier selected from the group consisting of transferrin receptor (TR), insulin receptor (HIR), insulin-like growth factor receptor (IGFR), low-density lipoprotein receptor related proteins 1 and 2 (LPR-1 and 2), diphtheria toxin receptor, CRM197, a llama single domain antibody, TMEM 30(A), a protein transduction domain, TAT, Syn-B, penetratin, a poly-arginine peptide, an angiopeptide, and ANG1005;

- (c) a disease-causing agent selected from the group consisting of disease-causing peptides or proteins, and disease-causing nucleic acids, wherein the disease-causing nucleic acids are antisense GGCCCC (G2C4) repeat-expansion RNA, and the disease-causing proteins are selected from the group consisting of amyloid beta, oligomeric amyloid beta, amyloid beta plaques, amyloid precursor protein or fragments thereof, Tau, IAPP, alpha-synuclein, TDP-43, FUS protein, C9orf72 (chromosome 9 open reading frame 72), c9RAN protein, prion protein, PrPSc, huntingtin, calcitonin, superoxide dismutase, ataxin, ataxin 1, ataxin 2, ataxin 3, ataxin 7, ataxin 8, ataxin 10, Lewy body, atrial natriuretic factor, islet amyloid polypeptide, insulin, apolipoprotein AI, serum amyloid A, medin, prolactin, transthyretin, lysozyme, beta 2 microglobulin, gelsolin, keratoepithelin, cystatin, immunoglobulin light chain AL, S-IBM protein, Repeat-associated non-ATG (RAN) translation products, DiPeptide repeat (DPR) peptides, glycine-alanine (GA) repeat peptides, glycine-proline (GP) repeat peptides, glycine-arginine (GR) repeat peptides, proline-alanine (PA) repeat peptides, ubiquitin, and proline-arginine (PR) repeat peptides;
 - (d) ligands and/or proteins expressed on immune cells, wherein the ligands and/or proteins are selected from the group consisting of CD40, OX40, ICOS, CD28, CD137/4-1BB, CD27, GITR, PD-L1, CTLA-4, PD-L2, PD-1, B7-H3, B7-H4, HVEM, BTLA, KIR, GAL9, TIM3, A2AR, LAG-3, and phosphatidylserine; or
 - (e) a protein, lipid, polysaccharide, or glycolipid expressed on one or more tumor cells.
32. The antibody of any one of the preceding claims, wherein the antibody binds specifically to both human TREM2 and cynomolgus monkey TREM2.
33. The antibody of claim 32, wherein the antibody has a dissociation constant (K_D) for cynomolgus monkey TREM2 that ranges from 50 nM to 100 pM, or less than 100 pM, wherein the K_D is determined at a temperature of approximately 25°C.
34. The antibody of any one of the preceding claims, wherein the antibody binds to primary human immune cells with an affinity that is at least 10 times higher than that of an anti-TREM2 antibody comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 27 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 92; or at least 10 times higher than an anti-TREM2 antibody comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 56 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 104.

35. The antibody of any one of the preceding claims, wherein the antibody clusters and activates TREM2 signaling in an amount that is greater than that of a human control IgG1 antibody.
36. The antibody of any one of the preceding claims, wherein the antibody increases immune cell survival *in vitro* to an extent that is greater than a human control IgG1 antibody.
37. The antibody of any one of the preceding claims, wherein the antibody has an *in vivo* half-life that is lower than a human control IgG1 antibody.
38. The antibody of any one of the preceding claims, wherein the antibody decreases plasma levels of soluble TREM2 *in vivo* by at least 20%.
39. The antibody of claim 38, wherein the antibody decreases plasma levels of soluble TREM2 *in vivo* by blocking cleavage and/or by inducing internalization.
40. An isolated nucleic acid comprising a nucleic acid sequence encoding the antibody of any one of the preceding claims.
41. A vector comprising the nucleic acid of claim 40.
42. An isolated host cell comprising the vector of claim 41.
43. A method of producing an antibody that binds to TREM2, comprising culturing the cell of claim 42 so that the antibody is produced.
44. The method of claim 43, further comprising recovering the antibody produced by the cell.
45. A pharmaceutical composition comprising the antibody of any one of claims 1-39 and a pharmaceutically acceptable carrier.
46. Use of a therapeutically effective amount of the antibody of any one of claims 1-39 in the manufacture of a medicament for preventing, reducing risk, or treating an individual in need thereof having a disease, disorder, or injury selected from the group consisting of dementia, frontotemporal dementia, Alzheimer's disease, cognitive deficit, memory loss, spinal cord injury, traumatic brain injury, multiple sclerosis, chronic colitis, ulcerative colitis, and cancer.
47. The use of claim 46, wherein the disease, disorder, or injury is Alzheimer's disease.