WHAT IS CLAIMED IS:

1. An antibody or antigen-binding fragment thereof that binds to transferrin receptor 1 (TFR1), comprising:

a heavy chain single variable domain (VHH) comprising complementarity determining regions (CDRs) 1, 2, and 3, wherein the VHH CDR1 region comprises an amino acid sequence that is at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to a selected VHH CDR1 amino acid sequence, the VHH CDR2 region comprises an amino acid sequence that is at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to a selected VHH CDR2 amino acid sequence, and the VHH CDR3 region comprises an amino acid sequence that is at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to a selected VHH CDR3 amino acid sequence;

wherein the selected VHH CDRs 1, 2, and 3 amino acid sequences are one of the following:

(1) the selected VHH CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 10-12; or SEQ ID NOs: 22-24; respectively;
(2) the selected VHH CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 1-3; or SEQ ID NOs: 13-15; respectively;
(3) the selected VHH CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 4-6; or SEQ ID NOs: 16-18; respectively; and
(4) the selected VHH CDRs 1, 2, 3 amino acid sequences are set forth in SEQ ID NOs: 7-9; or SEQ ID NOs: 19-21; respectively.

2. The antibody or antigen-binding fragment thereof of claim 1, wherein:
(1) the VHH comprises CDRs 1, 2, 3 with the amino acid sequences set forth in SEQ ID NOs: 10-12; or SEQ ID NOs: 22-24; respectively;
(2) the VHH comprises CDRs 1, 2, 3 with the amino acid sequences set forth in SEQ ID NOs: 1-3; or SEQ ID NOs: 13-15; respectively;
(3) the VHH comprises CDRs 1, 2, 3 with the amino acid sequences set forth in SEQ ID NOs: 4-6; or SEQ ID NOs: 16-18; respectively; or
(4) the VHH comprises CDRs 1, 2, 3 with the amino acid sequences set forth in SEQ ID NOs: 7-9; or SEQ ID NOs: 19-21; respectively.

3. An antibody or antigen-binding fragment thereof that binds to TFR1 comprising a heavy chain single variable region (VHH) comprising an amino acid sequence that is at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to a selected VHH sequence, wherein the selected VHH sequence is selected from the group consisting of SEQ ID NOs: 28, 25, 26, and 27.

4. The antibody or antigen-binding fragment thereof of claim 3, wherein the VHH comprises the sequence of any one of SEQ ID NO: 28, and 25-27.

5. The antibody or antigen-binding fragment thereof of any one of claims 1-4, which has one or more features selected from the following:

(1) the antibody or antigen-binding fragment specifically binds to a human TFR1, a monkey TFR1, a mouse TFR1, or a chimeric TFR1;
(2) the antibody or antigen-binding fragment is a human or humanized antibody or antigen-binding fragment thereof;
(3) the antibody or antigen-binding fragment is a multi-specific antibody;
(4) the antibody or antigen-binding fragment is a bispecific antibody.

6. An antibody or antigen-binding fragment thereof comprising the VHH CDRs 1, 2, 3, of the antibody or antigen-binding fragment thereof of any one of claims 1-5.

7. The antibody or antigen-binding fragment thereof of any one of claims 1-6, which has one or more features selected from the following:
(1) the antibody or antigen-binding fragment comprises a human IgG Fc (e.g., a human IgG1 Fc);
(2) the antibody or antigen-binding fragment comprises a human IgG Fc (e.g., a human IgG1 Fc), which comprises a non-asparagine residue (e.g., alanine) at position 297 according to EU numbering;
(3) the antibody or antigen-binding fragment comprises two or more heavy chain single variable domains.

8. A nucleic acid comprising a polynucleotide encoding the antibody or antigen-binding fragment thereof any one of claims 1-7.

9. A vector comprising one or more of the nucleic acids of claim 8.

10. An isolated cell comprising (i) the vector of claim 9, or (ii) one or more of the nucleic acids of claim 8; wherein optionally, the cell is a CHO cell.

11. A method of producing an antibody or an antigen-binding fragment thereof, the method comprising
(a) culturing the isolated cell of claim 10 under conditions sufficient for the cell to produce the antibody or the antigen-binding fragment thereof; and
(b) collecting the antibody or the antigen-binding fragment thereof produced by the cell.

12. An antibody-drug conjugate comprising the antibody or antigen-binding fragment thereof of any one of claims 1-7 covalently bound to a therapeutic agent; wherein optionally the therapeutic agent is a cytotoxic or cytostatic agent.

13. Use of a composition comprising the antibody or antigen-binding fragment thereof of any one of claims 1-7, or the antibody-drug conjugate of claim 12, in manufacture of a medicament, wherein the medicament is used for:
(1) treating a subject having a brain disease (e.g., a brain cancer); and/or
(2) treating a subject having a cancer.

14. The use of claim 13, which has one or more features selected from the following:

(1) the antibody or antigen-binding fragment thereof, or the antibody-drug conjugate can pass across the blood-brain barrier (BBB) of the subject;
(2) the cancer is brain cancer, lung cancer, gastric cancer, colorectal cancer, liver cancer, ovarian cancer, prostate cancer, leukemia, or breast cancer.

15. A method of identifying a subject as having a brain disease (e.g., a brain cancer), the method comprising
detecting a sample collected from the subject as having the brain disease by the antibody or antigen-binding fragment thereof of any one of claims 1-7,
thereby identifying the subject as having the brain disease;
wherein optionally the sample is a brain parenchyma sample from the subject.

16. Use of an agent covalently linked to the antibody or antigen-binding fragment thereof of any one of claims 1-7, in manufacture of a medicament, wherein the medicament is used for delivering the agent to cross blood brain barrier in a subject;
optionally wherein the agent is an antibody or an antibody drug conjugate; and/or, the agent is anti-amyloid antibody.

17. A pharmaceutical composition comprising (i) the antibody or antigen-binding fragment thereof of any one of claims 1-7, or (ii) the antibody drug conjugate of claim 12, and a pharmaceutically acceptable carrier.