Claims:

1. A dual transporter comprising:

(A) a first binding region that specifically binds to a blood brain barrier (BBB) transport protein, wherein the BBB transport protein is the transferrin receptor (TfR) or CD98hc; and

(B) a second binding region that specifically binds to a second protein wherein the second protein is expressed on the luminal surface of the BBB or is a brain retention protein, and wherein the second protein is different from the BBB transport protein.

2. The dual transporter of claim 1, wherein the second protein is:

(a) selected from the group consisting of: TfR, CD98hc, Large neutral amino acids transporter small subunit 1 (CD98 light chain), glucose transporter 1 (GLUT1), major facilitator superfamily domain-containing protein 2A (MFSD2A), carbonic anhydrase IV (CA-IV), Low density lipoprotein receptor, Insulin-like growth factor 1 receptor (IGF1R), Insulin-like growth factor 2 receptor, IgG receptor FcRn large subunit p51, Low density lipoprotein receptor-related protein 1, Low density lipoprotein receptor-related protein 2, Insulin receptor, Cell cycle control protein 50A, Transmembrane protein 50A, Basigin, Leptin Receptor, Claudin-5, P-selectin, Lactoferrin receptor, Folate receptor, Sodium-dependent lysophosphatidylcholine symporter 1, Solute carrier organic anion transporter family member 1C1, Sodium-coupled neutral amino acid transporter 5, LDL receptor-related protein 8, High affinity cationic amino acid transporter 1, Sodium- and chloride-dependent taurine transporter, Insulin-like growth factor-binding protein 7, Solute carrier family 40 member 1, Zinc transporter 6, heparin-binding epidermal growth factor-like growth factor, and Myelin-oligodendrocyte glycoprotein (MOG); or

(b) a brain retention protein and/or undergoes receptor-mediated transcytosis, optionally wherein the brain retention protein is CD98hc, MOG, GLUT1, IGF1R, or CA-IV, or MFSD2A.

3. The dual transporter of claim 1 or 2, wherein:

(a) the transferrin receptor is human TfR1; and/or

(b) the CD98hc is human CD98hc.

4. The dual transporter of claim 2, wherein:

(a) the BBB transport protein is human TfR1 and the second protein is human CD98hc;

(b) the BBB transport protein is human TfR1 and the second protein is human MOG;

(c) the BBB transport protein is human TfR1 and the second protein is human GLUT1;

(d) the BBB transport protein is human TfR1 and the second protein is human IGF1R;

(d) the BBB transport protein is human TfR1 and the second protein is human CA-IV;

(d) the BBB transport protein is human TfR1 and the second protein is human MFSD2A; or

(e) the first binding region specifically binds TfR and the second binding region specifically binds CD98hc.

5. The dual transporter of any one of claims 1-4, wherein:

(1) the first binding region comprises:

(a) a first peptide that specifically binds the BBB transport protein;

(b) a first antibody antigen binding domain that specifically binds the BBB transport protein,

optionally wherein the first antibody antigen binding domain comprises: an antibody, a single chain antibody, a F(ab′)2 fragment, a Fab fragment, a single chain Fab (scFab), a Fv fragment, a single chain variable fragment (scFv), or a heavy chain only antibody variable domain (nanobody);

(c) a first Fc polypeptide modified to specifically bind the BBB transport protein;

(d) a first CH3 peptide modified to specifically bind the BBB transport protein;

(e) a first fibronectin type III domain peptide modified to specifically bind the BBB transport protein; or

(f) a first bicyclic peptide that specifically binds the BBB transport protein; and/or

(2) the second binding region comprises:

(a) a second peptide that specifically binds the second protein;

(b) a second antibody antigen binding domain that specifically binds the second protein;

(c) a second Fc polypeptide modified to specifically bind the second protein,

optionally wherein the second antibody antigen binding domain comprises: an antibody, a single chain antibody, a F(ab′)2 fragment, a Fab fragment, a single chain Fab (scFab), a Fv fragment, a single chain variable fragment (scFv), or a heavy chain only antibody variable domain (nanobody);

(d) a second CH3 peptide modified to specifically bind the second protein;

(e) a second fibronectin type III domain peptide modified to specifically bind the second protein; or

(f) a second bicyclic peptide that specifically binds the second protein; or

(3) the first binding region comprises a first antibody antigen binding domain that specifically binds the BBB transport protein and the second binding region comprises a second antibody antigen binding domain that specifically binds the second protein,

optionally wherein the dual transporter comprises a bispecific antibody selected from the group consisting of a full-length IgG bispecific antibody, a bispecific heavy chain antibody, and a bispecific F(ab′)2 comprising the first antibody antigen binding domain and the second antibody antigen binding domain;

optionally wherein the first binding region comprises a Fab fragment, a scFab, a Fv fragment, a scFv, or a nanobody and the second binding region comprises a Fab fragment, scFab, a Fv fragment, a scFv, or a nanobody.

6. The dual transporter of claim 5, wherein:

(a) the first binding region comprises the first antibody antigen binding domain and the second binding region comprises the second peptide, the second Fc

polypeptide, the second CH3 peptide, the second fibronectin type III domain peptide, or the second bicyclic peptide;

(b) the first binding region comprises the first peptide, the first Fc polypeptide, the first CH3 peptide, the first fibronectin type III domain peptide, or the first bicyclic peptide and the second binding region comprises the second antibody antigen binding domain;

(c) the first binding region comprises the first Fc polypeptide and the second binding region comprises the second peptide, the second antibody antigen binding domain, the second Fc polypeptide, the second CH3 peptide, the second fibronectin type III domain peptide, or the second bicyclic peptide;

(d) the first binding region comprises the first CH3 peptide and the second binding region comprises the second peptide, the second antibody antigen binding domain, the second Fc polypeptide, the second CH3 peptide, the second fibronectin type III domain peptide, or the second bicyclic peptide;

(e) the first binding region comprises the first peptide, the first antibody antigen binding domain, the first Fc polypeptide, the first CH3 peptide, the first fibronectin type III domain peptide, or the first bicyclic peptide and the second binding region comprises the second Fc polypeptide;

(f) the first binding region comprises the first peptide, the first antibody antigen binding domain, the first Fc polypeptide, the first CH3 peptide, the first fibronectin type III domain peptide, or the first bicyclic peptide and the second binding region comprises the second CH3 peptide;

(g) the first binding region comprises the first Fc polypeptide and the second binding region comprises the second Fc polypeptide, optionally wherein the first Fc polypeptide and the second Fc polypeptide form a Fc dimer;

(h) the first binding region comprises a first Fc polypeptide and the second binding region comprises a second Fc polypeptide, wherein the first Fc polypeptide and the second Fc polypeptide form a Fc dimer, and wherein the Fc dimer is linked to one or more Fabs, one or more F(ab′)2s, one or more scFabs, one or more scFvs, or one or more nanobodies, optionally wherein the Fab, $F(ab')_2$, scFab, scFv, or nanobody comprises a therapeutic Fab, $F(ab')_2$, scFab, scFv, or nanobody;

(i) the first binding region comprises the first CH3 peptide and the second binding region comprises the second CH3 polypeptide;

(j) the first binding region comprises the first fibronectin type III domain peptide and the second binding region comprises the second fibronectin type III domain peptide;

(k) the first binding region comprises the first bicyclic peptide and the second binding region comprises the second bicyclic peptide;

(l) the first binding region forms a dimer with the second binding region;

(m) the first binding region is linked to a polypeptide that forms a dimer with the second binding region;

(n) the second binding region is linked to a polypeptide that forms a dimer with the first binding region; or

(o) the first binding region is linked to a first polypeptide and the second binding region is linked to a second polypeptide, wherein the first polypeptide and the second polypeptide form a dimer.

7. The dual transporter of any one of claims 1-6, wherein the first binding region, the second binding region, or both the first binding region and the second binding region are linked to a scaffold;

optionally wherein the scaffold comprises an antibody or a fragment thereof;

optionally wherein:

(a) the first binding region is linked to a heavy chain of the antibody, the second binding region is linked to a heavy chain of the antibody, or the first and the second binding regions are both linked to a heavy chain of the antibody, optionally wherein the first binding region is linked to the C terminal end of a heavy chain of the antibody and/or the second binding region is linked to the C terminal end a heavy chain of the antibody;

(b) the first binding region is linked to a Fc region of the antibody, the second binding region is linked to a Fc region of the antibody, or the first and the second binding regions are both linked to a Fc region of the antibody, optionally wherein the first binding region is linked to the C terminal end of a Fc region of the antibody and/or the second binding region is linked to the C terminal end a Fc region of the antibody;

(c) the first binding region is linked to a light chain of the antibody, the second binding region is linked to a light chain of the antibody, or the first and the second binding regions are both linked to a light chain of the antibody, optionally wherein the first

binding region is linked to the C terminal end of a light chain of the antibody and/or the second binding region is linked to the C terminal end of a light chain of the antibody;

(d) the first binding region is linked to a light chain of the antibody and the second binding region is linked to a heavy chain of the antibody or the first binding region is linked to a heavy chain of the antibody and the second binding region is linked to a light chain of the antibody;

(e) the first binding region comprises an anti-TfR antibody antigen binding domain linked to the C terminal end of a first light chain of an antibody and the second binding region comprises an anti-CD98hc antibody antigen binding domain linked to the C terminal end of a second light chain of the antibody;

(f) first binding region comprises an anti-TfR antibody antigen binding domain linked to the C terminal end of a first heavy chain of an antibody and the second binding region comprises an anti-CD98hc antibody antigen binding domain linked to the C terminal end of a second heavy chain of the antibody; or

(g) the scaffold is a full-length IgG antibody that binds to a therapeutic brain target, and the first and the second binding regions are each attached to a respective C-terminal end of a heavy chain of the full-length IgG antibody,

optionally wherein the first and second binding regions are each an antibody antigen binding domain.

8. The dual transporter of any one of claims 1-7, wherein:

(a) the dual transport binds to the BBB transport protein with greater affinity than the dual transporter binds to the second protein, optionally wherein the dual transporter binds to the BBB transport protein with an affinity of 50 nM to 1000 nM and binds to the second protein with an affinity of 5- to 10-fold less than the affinity to the BBB transport protein;

(b) the dual transport binds to the BBB transport protein with lesser affinity than the dual transporter binds to the second protein, optionally wherein the dual transporter binds to the BBB transport protein with an affinity of 50 nM to 6000 nM and binds to second protein with an affinity of 5- to 10-fold greater than the affinity to BBB transport protein;

(c) the first binding region has moderate or weak affinity to the BBB transport protein and the second binding region has strong affinity to the second protein;

(d) the first binding region binds to TfR with an affinity of 1000 nM to 6000 nM and the second binding region binds to CD98hc with an affinity of 1000 nM to 6000 nM;

(e) the first binding region binds to TfR with an affinity of 900 nM to 6000 nM and the second binding region binds to CD98hc with an affinity of 900 nM to 6000 nM;

(f) the first binding region binds to TfR with an affinity of 1000 nM to 6000 nM and the second binding region binds to CD98hc with an affinity of300 nM to 900 nM;

(g) the first binding region binds to TfR with an affinity of 900 nM to 6000 nM and the second binding region binds to CD98hc with an affinity of 300 nM to 900 nM;

(h) the first binding region binds to TfR with an affinity of 1000 nM to 6000 nM and the second binding region binds to CD98hc with an affinity of less than 250 nM;

(i) the first binding region binds to TfR with an affinity of 900 nM to 6000 nM and the second binding region binds to CD98hc with an affinity of 50 nM to 250 nM;

(j) the first binding region binds to TfR with an affinity of 300 nM to 900 nM and the second binding region binds to CD98hc with an affinity of 1000 nM to 6000 nM;

(k) the first binding region binds to TfR with an affinity of 300 nM to 900 nM and the second binding region binds to CD98hc with an affinity of 300 nM to 900 nM;

(l) the first binding region binds to TfR with an affinity of 300 nM to 900 nM and the second binding region binds to CD98hc with an affinity of less than 250 nM;

(m) the first binding region binds to TfR with an affinity of 300 nM to 900 nM and the second binding region binds to CD98hc with an affinity of 50 nM to 250 nM;

(n) the first binding region binds to TfR with an affinity of less than 250 nM and the second binding region binds to CD98hc with an affinity of 1000 nM to 6000 nM;

(o) the first binding region binds to TfR with an affinity of less than 250 nM and the second binding region binds to CD98hc with an affinity of 300 nM to 900 nM;

(p) the first binding region binds to TfR with an affinity of 50 nM to 250 nM and the second binding region binds to CD98hc with an affinity of 300 nM to 900 nM;

(q) the first binding region binds to TfR with an affinity of less than 250 nM and the second binding region binds to CD98hc with an affinity of less than 250 nM;

(r) the first binding region binds to TfR with an affinity of 50 nM to 250 nM and the second binding region binds to CD98hc with an affinity of 50 nM to 250 nM;

(s) the first binding region binds to TfR with an affinity of 300 nM to 6000 nM and the second binding region binds to CD98hc with an affinity of 1000 nM to 6000 nM;

(t) the first binding region binds to TfR with an affinity of 300 nM to 6000 nM and the second binding region binds to CD98hc with an affinity of 900 nM to 6000 nM;

(u) the first binding region binds to TfR with an affinity of 300 nM to 6000 nM and the second binding region binds to CD98hc with an affinity of 300 nM to 900 nM;

(v) the first binding region binds to TfR with an affinity of 300 nM to 6000 nM and the second binding region binds to CD98hc with an affinity of less than 250 nM;

(w) the first binding region binds to TfR with an affinity of 300 nM to 6000 nM and the second binding region binds to CD98hc with an affinity of 50 nM to 250 nM;

(x) the first binding region binds to TfR with an affinity of 300 nM to 6000 nM and the second binding region binds to CD98hc with an affinity of 50 nM to 900 nM;

(y) the first binding region binds to TfR with an affinity of 50 nM to 1000 nM and the second binding region binds to CD98hc with an affinity of 1 nM to 500 nM;

(z) the first binding region binds to TfR with an affinity of 100 nM to 600 nM and the second binding region binds to CD98hc with an affinity of 50 nM to 300 nM;

(aa) the first binding region binds to TfR with an affinity of 100 nM to 400 nM and the second binding region binds to CD98hc with an affinity of 50 nM to 200 nM

(ab) the first binding region binds to TfR with an affinity of 250 nM to 6000 nM and the second binding region binds to CD98hc with an affinity of 1 nM to 250 nM;

(ac) the first binding region binds to TfR with an affinity of 250 nM to 1000 nM and the second binding region binds to CD98hc with an affinity of 1 nM to 100 nM;

(ad) the first binding region binds to TfR with an affinity of 50 nM to 250 nM and the second binding region binds to CD98hc with an affinity of 1 nM to 100 nM;

(ae) the first binding region binds to TfR with an affinity of 1000 nM to 6000 nM and the second binding region binds to CD98hc with an affinity of 1 nM to 500 nM;

(af) the first binding region binds to TfR with an affinity of 250 nM to 1000 nM and the second binding region binds to CD98hc with an affinity of 250 nM to 1000 nM; or

(ag) the first binding region binds to TfR with an affinity of 50 nM to 250 nM and the second binding region binds to CD98hc with an affinity of 500 nM to 6000 nM.

9. The dual transporter of claim 4, wherein:

(a) the first binding region comprises the CDRs or the variable chain regions of a Brain shuttle anti-TfR antibody, a TfR12 anti-TfR antibody, a TfR13 anti-TfR scFv, a

13E4v2ii anti-TfR antibody, a JC-141 anti-TfR antibody, a JC-171 anti-TfR antibody, a 17H10 anti-TfR Fab or scFv, or a 17H10.1 anti-TfR Fab or scFv; and/or

(b) the second binding region comprises the CDRs or the variable chain regions of: 1C03-4 anti-CD98hc VHH, a 1C03-5 anti-CD98hc VHH, a CD98hc2 anti-CD98hc nanobody, a CD98hc4 anti-CD98hc scFv, or a CD98hc5 anti-CD98hc scFv.

10. The dual transporter of claim 7, wherein:

(a) the scaffold comprises a full-length antibody directed to a therapeutic brain target and the first and second binding regions are each respectively linked to a C-terminal end of a light chain of the full-length antibody;

(b) the scaffold comprises a bispecific antibody;

(c) the scaffold comprises an antibody that specifically binds to a therapeutic target;

(d) the scaffold comprises a bispecific antibody that specifically binds to the BBB transport protein and specifically binds to a therapeutic target and wherein the second binding region is linked to the bispecific antibody; or

(e) the scaffold comprises a bispecific antibody that specifically binds to the second protein and specifically binds to a therapeutic target and wherein the first binding region is linked to the bispecific antibody.

11. The dual transporter of any one of claims 1-9, wherein the dual transport molecule comprises:

(a) a tri-specific antibody;

(b) a tri-specific antibody-like molecule;

(c) a tetra-specific antibody;

(d) tetra-specific antibody-like molecule; or

(e) a DVD-Ig, wherein a first Fab arm of the DVD-Ig comprises a first Fv fragment that specifically binds to a first target protein and a second Fv fragment that specifically binds to the BBB transport protein, and a second Fab arm of the DVD-Ig comprises a third Fv fragment that specifically binds to a second target protein and a fourth Fv fragment that specifically binds to the second protein.

12. The dual transporter of any one of claims 1-11, wherein the dual transport molecule is linked to a therapeutic agent.

13. The dual transporter of claim 6, wherein the dual transport molecule comprises a therapeutic antibody comprising the first Fc polypeptide or CH3 peptide modified to specifically bind the BBB transport protein and the second Fc polypeptide or CH3 peptide modified to specifically bind a second protein.

14. The dual transporter of any one of claims 1-13, wherein:

(a) the first binding region binds to the apical domain of TfR; or

(b) the first binding region binds TfR without inhibiting binding of transferrin to the TfR.

15. The dual transporter of any one of claims 1-4, wherein:

(a) the first binding region comprises a first antibody antigen binding domain that specifically binds TfR;

optionally wherein the first antibody antigen binding domain comprises:

(i) the CDR sequences of a JC-141 anti-TfR antibody, a JC-171 anti-TfR antibody, a Brain shuttle anti-TfR antibody, a 13E4v2ii anti-TfR antibody, a TfR12 anti-TfR antibody, a TfR13 anti-TfR antibody, a 17H10 anti-TfR Fab or scFv, or a 17H10.1 anti-TfR Fab or scFv; or

(ii) an antibody antigen binding domain from the JC-141 anti-TfR antibody, the JC-171 anti-TfR antibody, the Brain shuttle anti-TfR antibody, the 13E4v2ii anti-TfR antibody, the TfR12 anti-TfR antibody, the TfR13 anti-TfR antibody, the 17H10 anti-TfR Fab or scFv, or the 17H10.1 anti-TfR Fab or scFv; or

(b) the first binding region comprises a first Fc polypeptide or a first CH3 peptide modified to specifically bind TfR.

16. The dual transporter of any one of claims 1-7 and 10-14, wherein the first binding region specifically binds TfR with an affinity of:

(a) less than100 nM;

(b) 100 nM to 1000 nM;

(c) 100 nM to 600 nM;

(d) 600 nM to 6000 nM; or

(e) 600 nM to 1000 nM.

17. The dual transporter of claim 5, wherein the first CH3 peptide is modified to specifically bind TfR and comprises:

(a) five, six, seven, eight, nine, ten, eleven, twelve, thirteen, fourteen, fifteen, or sixteen substitutions in a set of amino acid positions consisting of: 380, 384, 386, 387, 388, 389, 390, 391, 392, 413, 414, 415, 416, 421, 424, and 426;

(b) a L, Q, S, V, W, or Y at position 380; a F, L, M, P, V, W, Y, or I at position 384; a F, H, I, L, N, P, T, or V at position 386; a D, E, I, or V at position 387; a W, F, or Y at position 388; an A, G, I, S, T, or V at position 389; an A, D, E, F, G, H, K, L, Q, R, S, T, V, or Y at position 390; a F, Q, S, T, or V at position 391; a Q, F, or H at position 392; an A, E, H, I, L, P, S, or T at position 413; a R, G, or P at position 414; a D, E, G, T, P, Q, or R at position 415; a D, E, N, or T at position 416; a F, H, K, W, or Y at position 421; a T, W, E, or K at position 424; and a C, P, M, W, or G at position 426;

(c) a F, L, M, P, V, W, Y, or I at position 384; a F, H, I, L, N, P, T, or V at position 386; a W, F, or Y at position 388; an A, G, I, S, T, or V at position 389; and; a F, H, K, W, or Y at position 421;

(d) a F, L, M, P, V, W, Y, or I at position 384; a F, H, I, L, N, P, T, or V at position 386; a W, F, or Y at position 388; an A, G, I, S, T, or V at position 389; and; a F, H, K, W, or Y at position 421 and one, two, three, four, five, six, seven, eight, nine, ten, or eleven substitutions selected from: a L, Q, S, V, W, or Y at position 380; a D, E, I, or V at position 387; an A, D, E, F, G, H, K, L, Q, R, S, T, V, or Y at position 390; a F, Q, S, T, or V at position 391; a Q, F, or H at position 392; an A, E, H, I, L, P, S, or T at position 413; a R, G, or P at position 414; a D, E, G, T, P, Q, or R at position 415; a D, E, N, or T at position 416; a T, W, E, or K at position 424; and a C, P, M, W, or G at position 426;

(e) four, five, six, seven, eight, or nine substitutions in a set of amino acid positions consisting of: 384, 386, 387, 388, 389, 413, 415, 416, and 421;

(f) a Y at position 384; a T at position 386; an E at position 387; a W at position 388; a V, S, or A at position 389; a T or S at position 413; an E at position 415; an E at position 416; and a F at position 421,

wherein the positions are determined with reference to EU numbering.

optionally wherein the first CH3 peptide further comprises Y at position 391, a K at position 392, a S at position 424; and S at position 426.

18. The dual transporter of claim 17, wherein the first CH3 peptide modified to specifically bind TfR comprises: (a) a polypeptide having at least 85%, at least 90%, at least 95%, or 100% identity to the amino acid sequence of any of SEQ ID NOs:6-14 and 124-125;

or (b) a polypeptide having at least 85%, at least 90%, at least 95%, or 100% identity to the amino acids 111-217 of any of SEQ ID NOs:6-14 and 124-125.

19. The dual transporter of claim 5, wherein the first CH3 peptide is modified to specifically bind TfR and comprises:

(a) six, seven, eight, nine, ten, eleven, twelve, thirteen, fourteen, fifteen, sixteen, seventeen, eighteen, nineteen, twenty, twenty-one, twenty-two, twenty-three, twenty-four, twenty-five, twenty-six, twenty-seven, twenty-eight, twenty-nine, thirty, or thirty-one amino acid substitutions in a set of amino acid positions consisting of: 378, 380, 382, 383, 384, 385, 386, 387, 388, 389, 390, 391, 414, 417, 419, 420, 421, 422, 424, 426, 427, 428, 429, 433, 434, 437, 438, 439, 440, 442, and 443, and 426;

(b) an E, L, or I at position 378; a N, R, Y, I, S, or F at position 380; a F at position 382; a Y, A, G, T, or a deletion at position 383; an A, D, E, F, G, or T at position 384; an A, D, or N at position 385; an A, G, K, N, S, or Y at position 386; a G, I, K, N, R, S, or T at position 387; a L, Q, or D at position 388; an I, P, Q, R, S, or T at position 389; a G, T, Y, or L at position 390; a S, T, I, L, or P at position 391; a P at position 414; a K at position 417; a P at position 419; a R or Q at position 420; an A, F, G, S, or Y at position 421; a L at position 422; an A at position 424; an E at position 426; an E at position 427; an E at position 428; a G at position 429; an E at position 433; a G at position 434; a D at position 437; a Y at position 438; a D, E, or S at position 439; a L at position 440; a G or W at position 442; and an E or Y at position 443;

(c) a F at position 382, a L at position 422, an A at position 424, an E at position 426, a Y at position 438, and a L at position 440;

(d) a F at position 382, a L at position 422, an A at position 424, an E at position 426, a Y at position 438, and a L at position 440 and one or more of: an E, L, or I at position 378; a N, R, Y, I, S, or F at position 380; a Y, A, G, T, or a deletion at position 383; an A, D, E, F, G, or T at position 384; an A, D, or N at position 385; an A, G, K, N, S, or Y at position 386; a G, I, K, N, R, S, or T at position 387; a L, Q, or D at position 388; an I, P, Q, R, S, or T at position 389; a G, T, Y, or L at position 390; a S, T, I, L, or P at position 391; a P at position 414; a K at position 417; a P at position 419; a R or Q at position 420; an A, F, G, S, or Y at position 421; an E at position 427; an E at position 428; a G at position 429; an E at position 433; a G at position 434; a D at position 437; a D, E, or S at position 439; a G or W at position 442; and an E or Y at position 443;

(e) four, five, six, seven, eight, nine, ten, eleven, twelve, thirteen, fourteen, fifteen, or sixteen substitutions in a set of amino acid positions consisting of: 378, 380, 382, 383, 384, 385, 386, 421, 422, 424, 426, 428, 434, 438, 440, and 442;

(f) a D, E, F, H, N, Q, S, V, or Y at position 378; an A, D, F, H, I, K, L, M, Q, S, T, or Y at position 380; a G at position 382; a T at position 383; an A, E, F, H, I, K, L, Q, S, V, or Y at position 384; an I, T, or V at position 385; an A, H, N, S, T, or V at position 386; an A, F, H, K, L, M, Q, S, T, V, or Y at position 421; an A, F, H, I, K, L, R, T, or Y at position 422; an A, G, or P at position 424; an A, I, L, T, or V at position 426; an A or L at position 428; a S at position 434; an I, F, L, V, or Y at position 438; an A, G, I, M, N, P, T, or V at position 440; and an A, K, M, R, T, or V at position 442;

(g) a G at position 382; an A, E, F, H, I, K, L, Q, S, V, or Y at position 384; an I, T, or V at position 385; and an I, F, L, V, or Y at position 438; or

(h) a G at position 382; an A, E, F, H, I, K, L, Q, S, V, or Y at position 384; an I, T, or V at position 385; and an I, F, L, V, or Y at position 438, and one, two, three, four, five, six, seven, eight, nine, ten, eleven, twelve, thirteen, fourteen, fifteen, or sixteen substitutions selected from: a D, E, F, H, N, Q, S, V, or Y at position 378; an A, D, F, H, I, K, L, M, Q, S, T, or Y at position 380; a T at position 383; an A, H, N, S, T, or V at position 386; an A, F, H, K, L, M, Q, S, T, V, or Y at position 421; an A, F, H, I, K, L, R, T, or Y at position 422; an A, G, or P at position 424; an A, I, L, T, or V at position 426; an A or L at position 428; a S at position 434; an A, G, I, M, N, P, T, or V at position 440; and an A, K, M, R, T, or V at position 442,

wherein the positions are determined with reference to EU numbering.

20. The dual transporter of claim 19, wherein the first CH3 peptide modified to specifically bind TfR comprises (a) a polypeptide having at least 85%, at least 90%, at least 95%, or 100% identity to the amino acid sequence of any of SEQ ID NOs:57-64 and 126; or (b) a polypeptide having at least 85%, at least 90%, at least 95%, or 100% identity to the amino acids 111-217 of any of SEQ ID NOs:57-64 and 126.

21. The dual transporter of any one of claims 1-20, wherein the second binding region comprises:

(a) a second antibody antigen binding domain that specifically binds CD98hc;

optionally wherein the second antibody antigen binding domain comprises:

(i) the CDR sequences of: a 1C03-4 anti-CD98hc VHH, a 1C03-5 anti-CD98hc VHH, a CD98hc2 anti-CD98hc nanobody, a CD98hc4 anti-CD98hc scFv, or a CD98hc5 anti-CD98hc scFv; or

(ii) a 1C03-4 anti-CD98hc VHH, a 1C03-5 anti-CD98hc VHH, a CD98hc2 anti-CD98hc nanobody, a CD98hc4 anti-CD98hc scFv, or a CD98hc5 anti-CD98hc scFv; or

(d) a second Fc polypeptide or a second CH3 peptide modified to specifically bind CD98hc.

22. The dual transporter of claim 21, wherein the second binding region specifically binds CD98hc with an affinity of:

(a) 15 nM to 5000 nM; or

(b) 100 nM to 500 nM.

23. The dual transporter of claim 21 or 22, wherein the second CH3 peptide modified to specifically bind CD98hc comprises:

(a) five, six, seven, eight, or nine substitutions in a set of amino acid positions consisting of 382, 384, 385, 387, 422, 424, 426, 438, and 440;

(b) a R, Y, F, S, W, Y, K, or N at position 382; a L, Y, A, S, or F at position 384; a F, K, D, M, I, N, Y, L, or H at position 385; a N, L, Y, R, F, G, S, D, or T at position 387; an I, K, L, R, T, F, or H at position 422; a V, W, G, L, I, P, or Y at position 424; a D, A, Q, W, L, or P at position 426; an I, V, F, N, P, or S at position 438; and a K, T, P, I, or F at position 440;

(c) at least five, six, seven, eight, or nine substitutions in a set of amino acid positions consisting of 382, 383, 384, 385, 386, 387, 389, 421, 422, 424, 426, 428, 434, 436, 438, 440, and 442;

(d) a S or V at position 378; a D, M, N, P, F, or H at position 380; a R, Y, F, S, W, Y, K, or N at position 382; a T at position 383; a L, Y, A, S, or F at position 384; a F, K, D, M, I, N, Y, L, or H at position 385; a T, P, E, K, A, V, D, T, or F at position 386; a N, L, Y, R, F, G, S, D, or T at position 387; a T , Y, or F at position 389; a D, E, or Q at position 421; an I, K, L, R, T, F, or H at position 422; a V, W, G, L, I, P, or Y at position 424; a D, A, Q, W, L, or P at position 426; a L or Y at position 428; a S at position 434; a F at position

436; an I, V, F, N, P, or S at position 438; a K, T, P, I, or F at position 440; and Q or M at position 442;

(e) at least eleven, twelve, thirteen, fourteen, or fifteen substitutions in a set of amino acid positions consisting of 378, 380, 382, 383, 384, 385, 386, 387, 389, 391, 421, 422, 424, 426, 428, 434, 436, 438, 440, 441, and 442;

(f) a S, V, D, E, or Y at position 378; a L, I, M, A, Q, V, or K at position 380; a N, S, L, M, P, Y, K, A, or T at position 382; a T, F, N, P, D, L, H, or Q at position 383; a K, R, H, I, L, F, Y, V, or Q at position 384; a F or Y at position 385; a V, L, A, I, F, Y, S, T, H, R, or E at position 386; a L or I at position 387; a D, Q, A, T, H, or V at position 389; a T, V, or A at position 391; an E, Q, or A at position 421; a L, M, I, T, or P at position 422; an A at position 424; a N at position 426; a L, T, P, Y F, I, A, K, H, or W at position 428; a S at position 434; a L, V, H, F, P, R or W at position 436; a F or W at position 438; a L, P, E, N, V, A, I, or D at position 440; a P at position 441; and an A, V, M, Q, F, P, L, Y, K, R, H, or M at position 442;

(g) eleven, twelve, thirteen, fourteen, or fifteen substitutions in a set of amino acid positions consisting of: 380, 382, 384, 385, 386, 387, 421, 422, 424, 426, 428, 436, 438, 440, and 442;

(h) a L at position 380; a N at position 382; a R, H, or Q at position 384; a F or Y at position 385; a V, L, I, F, Y, or E at position 386; a L at position 387; an E, Q or A at position 421; an I, T, or P at position 422; an A at position 424; a N at position 426; a Y or W at position 428; a R or W at position 436; a F or W at position 438; a N at position 440; and an A, Q, K, R, H, or M at position 442;

(i) eight, nine, ten, eleven, twelve, thirteen, fourteen, fifteen, sixteen, seventeen, eighteen, or nineteen substitutions in a set of amino acid positions consisting of: 378, 380, 382, 383, 384, 385, 386, 387, 389, 421, 422, 424, 426, 428, 434, 436, 438, 440, and 442;

(j) a S or V at position 378; a D, M, N, P, F, or H at position 380; a R, Y, F, S, W, Y, K, or N at position 382; a T at position 383; a L, Y, A, S, or F at position 384; a F, K, D, M, I, N, Y, L, or H at position 385; a T, P, E, K, A, V, D, T, or F at position 386; a N, L, Y, R, F, G, S, D, or T at position 387; a T , Y, or F at position 389; a D, E, or Q at position 421; a I, K, L, R, T, F, or H at position 422; a V, W, G, L, I, P, or Y at position 424; a D, A, Q, W, L, or P at position 426; a L or Y at position 428; a S at position 434; a F at position

436; a I, V, F, N, P, or S at position 438; a K, T, P, I, or F at position 440; and a Q or M at position 442;

(k) eight, nine, ten, eleven, twelve, or thirteen substitutions in a set of amino acid positions consisting of 380, 382, 384, 385, 386, 387, 422, 424, 426, 428, 434, 438, and 440;

(l) a D, M, N, P, F, or H at position 380; a R, Y, F, S, W, Y, K, or N at position 382; a L, Y, A, S, or F at position 384; a F, K, D, M, I, N, Y, L, or H at position 385; a T, P, E, K, A, V, D, T, or F at position 386; a N, L, Y, R, G, S, D, or T at position 387; an I, K, R, T, F, or H at position 422; a V, W, G, L, I, P, or Y at position 424; a D, A, Q, W, L, or P at position 426; a L at position 428; a S at position 434; an I, F, N, P, or S at position 438; and a K, T, I, or F at position 440;

(m) eight, nine, ten, eleven, twelve, thirteen, fourteen, fifteen, sixteen, seventeen, eighteen, or nineteen substitutions in a set of amino acid positions consisting of 378, 380, 382, 383, 384, 385, 386, 387, 389, 421, 422, 424, 426, 428, 434, 436, 438, 440, and 442; or

(n) a S or V at position 378; a D at position 380; a R at position 382; a T at position 383; a Y at position 384; a K at position 385; a P at position 386; a Y at position 387; a T, Y, or F at position 389; a D, E, or Q at position 421; an I at position 422; a V at position 424; a D at position 426; a L or Y at position 428; a S at position 434; a F at position 436; an I or V at position 438; a K at position 440; and a Q or M at position 442,

wherein the positions are determined according to EU numbering.

24. The dual transporter of claim 23, wherein the second CH3 peptide modified to specifically bind CD98hc comprises:

(a) a polypeptide having at least 85%, at least 90%, at least 95%, or 100% identity to the amino acid sequence of any of SEQ ID NOs:15-30;

(b) a polypeptide having at least 85%, at least 90%, at least 95%, or 100% identity to the amino acids 111-217 of any of SEQ ID NOs:15-30;

(c) a polypeptide having at least 85%, at least 90%, at least 95%, or 100% identity to the amino acid sequence of SEQ ID NOs:34 or 35; or

(d) a polypeptide having at least 85%, at least 90%, at least 95%, or 100% identity to the amino acids 111-217 of SEQ ID NOs: 34 or 35.

25. The dual transporter of any one of claims 1-24, wherein the dual transporter comprises an Fc polypeptide having one or more mutations that (a) promote heterodimer formation; (b) modulate effector function; or (c) extend serum half-life.

26. The dual transporter of claim7, wherein the antibody comprises:

(a) a monospecific antibody;

(b) a bispecific antibody;

(c) a monospecific therapeutic antibody,

(d) a bispecific therapeutic antibody;

(e) bispecific antibody wherein one Fab arm of the antibody specifically binds TfR and the other Fab arm of the antibody specifically binds CD98hc; or

(f) a bispecific antibody wherein one Fab arm of the antibody specifically binds TfR or CD98hc and the other Fab arm of the antibody specifically binds a target protein.

27. The dual transporter of any one of claims 1-5 and 8, wherein:

(a) the first binding region comprises a first fibronectin type III domain peptide modified to specifically bind TfR and the second binding region comprises a second fibronectin type III domain peptide modified to specifically bind CD98hc, wherein the first and second binding regions are linked to an antibody; or

(b) the first binding region comprises a first bicyclic peptide that specifically binds TfR and the second binding region comprises a second bicyclic peptide that specifically binds CD98hc, wherein the first and second binding regions are linked to an antibody.

28. The dual transporter of any one of claims 1-9, 15, and 21, wherein the dual transporter comprises:

(a) an anti-TfR monospecific or bispecific antibody linked to the second binding region; or

(b) an anti-CD98hc monospecific or bispecific antibody linked to the first binding region.

29. The dual transporter of any one of claims 1-28, wherein the dual transporter is capable of being actively transported across the blood brain barrier or facilitating transport of a therapeutic agent across the blood brain barrier.

30. A nucleic acid encoding the dual transporter of any one of claims 1-29.

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

32. A pharmaceutical composition comprising the dual transporter of any one of claims 1-29 and a pharmaceutically acceptable excipient.

33. The dual transporter of any one of claims 1-29 or the pharmaceutical composition of claim 32 for use in improving delivery of a molecule to the central nervous system, delivering a molecule to the brain of a subject, or treating disease or condition of the central nervous system (CNS) in a subject, wherein the dual transporter is linked to the molecule.

34. The dual transporter for use as in claim 33, wherein the molecule comprises a therapeutic agent,

optionally wherein the therapeutic agent targets: ABCA1, ABCA7, ADAM17, ALK, alpha-synuclein or a derivative or fragment thereof, an amyloid-beta peptide or a derivative or fragment thereof, AXL, B7H3, BCMA, CD125, CD166, CD19, CD20, CD205, CD22, CD25, CD25, CD30, CD33, CD37, CD39, CD44v6, CD46, CD56 (NCAM), CD73, CD79b, CDH6 (cadherin 6), CEACAM 5 (CD66E), CR1, EGFR viii, EGFR, ETBR, FGFR (1-4), Folate Receptor alpha, GAL-3BP (galectin binding protein), GD2, GD3, GloboH (globohexasylceramide), gp100, gpNMB, HER2, HER3, HER4, HLA-DR1, HLA-DR5, huntingtin, IGFR1, IL1RAP, IL-34, KIT, LIV1A, LRRC15 (leucine rich repeat containing 15), MET, MS4A4A, MS4A4E, MS4A6A, NaPi2B, TAR DNA-binding protein 43 (TDP-43) or a derivative or fragment thereof, PDL1, PILRA, PMEL17, PRAME, PSMA, pTau, PTK7 (CCK4; colon carcinoma kinase), RON, ROR1, Siglec11, SORL1, Tau or a derivative or fragment thereof, TF (tissue factor), transthyretin, TREM2, TREML2, TROP2, or a tumor cell.

35. The dual transporter or the pharmaceutical composition for use as in claim 33, wherein the disease or condition of the CNS comprises: a neurological disease or condition, a neurodegenerative disease or condition, cancer, or an infection.

36. A method of manufacturing a dual transporter comprising:

(a) providing (i) a first polypeptide comprising a first binding region known to specifically binds to a BBB transport protein and (ii) a second polypeptide comprising a second binding region known to specifically binds a second protein, wherein the second protein is expressed on the luminal surface of the BBB or is a brain retention protein, and wherein the second protein is different from the BBB transport protein; and

(b) forming a single molecule that incorporates the first polypeptide and the second polypeptide, thereby forming the dual transporter;

wherein the dual transporter has increased and/or prolonged brain exposure in an animal as compared to a corresponding control molecule that binds to only the BBB transport protein or only the second protein.

37. A method of identifying a dual transporter comprising:

(a) providing (i) a first polypeptide comprising a first binding region known to specifically binds to a BBB transport protein and (ii) a second polypeptide comprising a second binding region known to specifically binds a second protein, wherein the second protein is expressed on the luminal surface of the BBB or is a brain retention protein, and wherein the second protein is different from the BBB transport protein;

(b) forming a single molecule that incorporates the first polypeptide and the second polypeptide; and

(c) measuring the brain concentration of the single molecule at a predetermined time and identifying the single molecule as a dual transporter if the single molecule is present in the brain at a higher concentration than a corresponding control molecule that binds only to the BBB transport protein or the second protein.

38. A method for improving delivery to the central nervous system of a therapeutic agent linked to a delivery vehicle having a first binding region that specially binds to a BBB transport protein, the method comprising linking the delivery vehicle to a second binding region that specifically binds to a second protein wherein the second protein is expressed on the luminal surface of the BBB or is a brain retention protein, and wherein the second protein is different from the BBB transport protein.