WHAT IS CLAIMED:

1. An anti-CD63 antibody or antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment thereof comprises three heavy chain complementarity determining regions (HCDRs) with the heavy chain variable region (HCVR) amino acid sequence and three light chain complementarity determining regions (LCDRs) with the light chain variable region (LCVR) amino acid sequence of the HCVR/LCVR pair set forth as SEQ ID NOs:34/42,

wherein the antibody or antigen-binding fragment thereof comprises an HCDR1, HCDR2, and HCDR3 of the HCVR set forth as SEQ ID NO: 34, and an LCDR1, LCDR2, and LCDR3 of the LCVR set forth as SEQ ID NO: 42, and wherein the method used to identify the HCDRs and LCDRs is selected from: the Kabat definition, the Chothia definition, and the AbM definition; or

wherein:

(i) the HCDR1 comprising the amino acid sequence of SEQ ID NO:36,

(ii) the HCDR2 comprising the amino acid sequence of SEQ ID NO:38,

(iii) the HCDR3 comprising the amino acid sequence of SEQ ID NO:40,

(iv) the LCDR1 comprising the amino acid sequence of SEQ ID NO:44,

(v) the LCDR2 comprising the amino acid sequence of SEQ ID NO:46, and

(vi) the LCDR3 comprising the amino acid sequence of SEQ ID NO:48.

2. The anti-CD63 antibody or antigen-binding fragment of claim 1, comprising an HCVR/LCVR amino acid sequence pair set forth as SEQ ID NOs:34/42.

3. A bispecific antigen-binding molecule comprising:

(i) a first antigen-binding domain comprising the anti-CD63 antibody or antigen-binding fragment thereof of any one of claim 1 or claim 2, and

(ii) a second antigen-binding domain that binds a target antigen.

4. The bispecific antigen-binding molecule of claim 3, wherein the target antigen is a tumor associated antigen.

5. The bispecific antigen-binding molecule of claim 3 or claim 4, wherein complexation of the bispecific antigen-binding molecule to CD63 mediates internalization of the antigen-binding molecule/CD63 complex.

6. The bispecific antigen-binding molecule of any one of claims 3-5, wherein each of the first antigen-binding domain and the second antigen-binding domain is fully humanized.

7. The bispecific antigen-binding molecule of any one of claims 3-6, wherein the bispecific antigen-binding molecule is not internalized by cells that express human CD63 but do not express the target antigen.

8. The bispecific antigen-binding molecule of any one of claims 3-7, wherein the bispecific antigen-binding molecule is fully humanized.

9. A multidomain therapeutic protein comprising:
(i) the anti-CD63 antibody or antigen-binding fragment thereof of claim 1 or claim 2, and
(ii) an enzyme domain.

10. The multidomain therapeutic protein of claim 9, wherein the enzyme domain comprises GAA.

11. The multidomain therapeutic protein of claim 9 or claim 10, comprising an amino acid sequence set forth as SEQ ID NO:364.

12. A polynucleotide comprising a nucleotide sequence encoding the anti-CD63 antibody or antigen-binding fragment thereof of claim 1 or claim 2, the bispecific antigen-binding molecule of any one of claims 3-8, or the multidomain therapeutic protein of any one of claims 9-11.

13. The polynucleotide of claim 12, wherein the nucleotide sequence encodes the multidomain therapeutic protein of any one of claims 9-11 and further comprises 5’ and 3’ AAV inverted terminal repeat (ITR) sequences.

14. The polynucleotide of claim 13, wherein the 5’ and 3’ AAV ITR sequences comprise the sequences set forth as SEQ ID NO:365 and SEQ ID NO:366, respectively.

15. The polynucleotide of any one of claims 12-14, wherein the nucleotide sequence further comprises a liver-specific enhancer and/or a liver-specific promoter.

16. The polynucleotide of claim 15, wherein the liver-specific enhancer comprises a sequence set forth as SEQ ID NO:367 and the liver-specific promoter comprises the sequence set forth as SEQ ID NO:368.

17. A pharmaceutical composition comprising:

(i) the anti-CD63 antibody or antigen-binding fragment thereof of claim 1 or claim 2, the bispecific antigen-binding molecule of any one of claims 3-8, the multidomain therapeutic protein of any one of claims 9-11, or the polynucleotide of any one of claims 12-16, and

(ii) a pharmaceutically acceptable carrier.

18. Use of the anti-CD63 antibody or antigen-binding fragment thereof of claim 1 or claim 2, the bispecific antigen-binding molecule of any one of claims 3-8, the multidomain therapeutic protein of any one of claims 9-11, or the polynucleotide of any one of claims 12-16 in the manufacture of a medicament for:

(i) treating rheumatoid arthritis, IgE-dependent allergic reactions and Fc-ER1-mediated allergic reactions, asthma, cancer and/or metastases, or

(ii) identifying and/or isolating exosomes.