Claims

1. A conjugate compound or a pharmaceutically acceptable salt thereof, comprising a payload and two or more kinds of cell-interacting molecules, wherein the payload is conjugated with at least one of the cell-interacting molecules, wherein the two or more kinds of cell-interacting molecules comprise

   (a) a first ligand capable of specifically binding to a first cell surface receptor and a second ligand capable of specifically binding to a second cell surface receptor, wherein the first and second cell surface receptors are different from one another; or

   (b) a first ligand capable of specifically binding to a first cell surface receptor and an endocytosis molecule capable of mediating endocytosis,

   wherein the first and second surface receptors are selected from the group consisting of a transferrin receptor (TFR), a low-density lipoprotein receptor (LDLR), a uric acid kinase receptor, a tumor necrosis factor receptor (TNFR), a somatostatin-14 (SST-14) receptor, a luteinizing hormone releasing hormone (LHRH) receptor, a transient receptor potential cation channel subfamily V member 6 (TRPV6) receptor, and a protease surface antigen receptor; and

   the endocytosis molecule is selected from the group consisting of folate and analogs thereof, a peptide capable of mediating endocytosis, and a cell-penetrating peptide.

2. The conjugate compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the payload is conjugated with at least one of the cell-interacting molecules via a linker.

3. The conjugate compound of any one of claims 1 or 2, or a pharmaceutically acceptable salt thereof, wherein at least two of the cell-interacting molecules are ligands

capable of specifically binding to a cell surface receptor.

4. The conjugate compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the payload is conjugated with the first ligand, and the first ligand is conjugated with the second ligand.

5. The conjugate compound of claim 4, or a pharmaceutically acceptable salt thereof, wherein the first ligand is conjugated with the second ligand via a spacer.

6. The conjugate compound of claim 5, or a pharmaceutically acceptable salt thereof, wherein the spacer comprises the amino acid sequence selected from the group consisting of SEQ ID NOs: 1-14, Arg-Arg, Ala-Ser-Asn, Ala-Ala-Ala, Ser-Ser-Arg, Pro- Arg, and Pro-Leu-Gly.

7. The conjugate compound of claim 4, or a pharmaceutically acceptable salt thereof, wherein the payload is conjugated directly with each of the first ligand and the second ligand.

8. The conjugate compound of claim 4, or a pharmaceutically acceptable salt thereof, wherein the payload is conjugated with the first ligand via a first linker, and the payload is conjugated with the second ligand via a second linker.

9. The conjugate compound of any one of claims 1-8, or a pharmaceutically acceptable salt thereof, further comprising a third ligand capable of specifically binding to a third cell surface receptor.

10. The conjugate compound of claim 9, or a pharmaceutically acceptable salt thereof,

wherein the first, second and third cell surface receptors are different from one another.

11. The conjugate compound of any one of claims 1-10, or a pharmaceutically acceptable salt thereof, comprising one, two, three, four or more payloads.

12. The conjugate compound of any one of claims 1-11, or a pharmaceutically acceptable salt thereof, wherein the payload is selected from the group consisting of a small molecule compound, a nucleotide, a peptide, a protein, and a nanoparticle.

13. The conjugate compound of claim 12, or a pharmaceutically acceptable salt thereof, wherein the payload is a small molecule compound.

14. The conjugate compound of claim 13, or a pharmaceutically acceptable salt thereof, wherein the small molecule compound is selected from the group consisting of maytansine and any derivatives thereof, taxinol and any derivatives thereof, auristatins and any derivatives thereof, epothilones and any derivatives thereof, bleomycin and any derivatives thereof, dactinomycin and any derivatives thereof, plicamycin and any derivatives thereof, and miromycin C.

15. The conjugate compound of claim 12, or a pharmaceutically acceptable salt thereof, wherein the small molecule compound is auristatins or any derivatives thereof.

16. The conjugate compound of any one of claims 1-15, or a pharmaceutically acceptable salt thereof, wherein the endocytosis molecule is selected from the group consisting of folate and analogs thereof, a peptide capable of mediating endocytosis, and a cell-penetrating peptide.

17. The conjugate compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the cell-penetrating peptide is selected from the group consisting of a tumor-

homing peptide, a mitochondrial penetrating peptide, an activatable cell-penetrating peptide, and an antibacterial peptide.

18. The conjugate compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the cell-penetrating peptide comprises the amino acid sequence of SEQ ID NO: 19 or SEQ ID NO: 20.

19. The conjugate compound of claim 16, or a pharmaceutically acceptable salt thereof, wherein the peptide capable of mediating endocytosis comprises the amino acid sequence selected from the group consisting of SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, Arg-Gly-Asp, a homologous peptide having at least 70% amino acid sequence homology to any of SEQ ID NOs: 16-18, wherein the homologous peptide is a functional equivalent of any one of the peptides of SEQ ID NOs: 16-18.

20. The conjugate compound of claim 9, or a pharmaceutically acceptable salt thereof, wherein the first, second and the third ligand is independently selected from the group consisting of a peptide, folate and analogs thereof.

21. The conjugate compound of claim 20, or a pharmaceutically acceptable salt thereof, wherein the peptide comprises the amino acid sequence selected from the group consisting of SEQ ID NO: 15, and a homologous peptide having at least 70% amino acid sequence homology to SEQ ID NO: 15, wherein the homologous peptide is a functional equivalent of the peptide of SEQ ID NO: 15.

22. The conjugate compound of claim 20, or a pharmaceutically acceptable salt thereof, wherein the peptide comprises the amino acid sequence selected from the group consisting of SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, Arg-Gly-Asp, a homologous peptide having at least 70% amino acid sequence homology to any of SEQ ID NOs: 16-18,

wherein the homologous peptide is a functional equivalent of any one of the peptides of SEQ ID NOs: 16-18.

23. The conjugate compound of claim 2 or 8, or a pharmaceutically acceptable salt thereof, wherein the linker is a peptide linker, a disulfide linker, or a pH-dependent linker.

24. The conjugate compound of claim 23, or a pharmaceutically acceptable salt thereof, wherein the peptide linker is cleavable under certain physiological environment by protease cleavage or reduction.

25. The conjugate compound of claim 23 or 24, or a pharmaceutically acceptable salt thereof, wherein the peptide linker is selected from the group consisting of valine-citruline, phenylalanine-lysine, and valine-lysine.

26. The conjugate compound of claim 23, or a pharmaceutically acceptable salt thereof, wherein the disulfide linker is selected from the group consisting of DMDS, MDS, DSDM, and NDMDS.

27. The conjugate compound of claim 23, or a pharmaceutically acceptable salt thereof, wherein the pH-dependent linker is *cis*-aconitic anhydride.

28. The conjugate compound of any one of claims 1-27, or a pharmaceutically acceptable salt thereof, wherein the conjugate compound is selected from the group consisting of the following compounds: LDC10B, LDC10BR, LDC10BX, LDC11B, LDC12B, LDC13B, LDC1013, LDC10H, LDC11H, LDC12H, and LDC13H.

29. The conjugate compound of claim 1, or a pharmaceutically acceptable salt thereof, comprising the payload, a first endocytosis molecule and a second endocytosis molecule,

wherein the first endocytosis molecule is the same as the second endocytosis molecule.

30. The conjugate compound of claim 1, or a pharmaceutically acceptable salt thereof, comprising the payload, a first endocytosis molecule and a second endocytosis molecule, wherein the first endocytosis molecule is different from the second endocytosis molecule.

31. The conjugate compound of claim 30, or a pharmaceutically acceptable salt thereof, wherein the first endocytosis molecule is a cell-penetrating molecule.

32 The conjugate compound of claim 1, or a pharmaceutically acceptable salt thereof, comprising the payload, the first ligand capable of specifically binding to a cell surface receptor and the endocytosis molecule.

33. The conjugate compound of any one of claims 29-32, or a pharmaceutically acceptable salt thereof, further comprising a third cell-interacting molecule, wherein the third cell-interacting molecule is an endocytosis molecule.

34. The conjugate compound of any one of claims 1-33, or a pharmaceutically acceptable salt thereof, wherein the analogs of folate is selected from the group consisting of 5-methyltetrahydrofolate, 5-formyltetrahydrofolate, methotrexate, and 5, 10-methylenetetrahydrofolate.

35. A pharmaceutical composition comprising the conjugate compound of any one of claims 1-34, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

36. The pharmaceutical composition of claim 35, wherein the composition is

administered intravenously, subcutaneously, orally, intramuscularly or intraventricularly.

37. Use of the conjugate compound of any one of claims 1-34, or a pharmaceutically acceptable salt thereof, or the pharmaceutical composition of claim 35 or 36 in the manufacture of a medicament for treating a disease.

38. The use of claim 37, wherein the disease is selected from the group consisting of a cancer, an immunological disease, a cardiovascular disease, a metabolic disease, and a neurological disease.