WHAT IS CLAIMED IS:

1. A compound comprising the structure of Formula I, or a pharmaceutically acceptable salt thereof:

$$A\text{-}L^1\text{-}(L^2)_n\text{-}B$$

Formula I

wherein

A is a chelating moiety or a metal complex thereof;

B is an antibody or antigen-binding fragment thereof;

L^1 is a bond, C=O, C=S, optionally substituted C_1-C_6 alkyl, optionally substituted C_1-C_6 heteroalkyl, optionally substituted aryl, or optionally substituted heteroaryl;

n is an integer between 1 and 5 (inclusive); and

L^2 each independently has the structure of Formula II:

$$-X^1\text{-}L^3\text{-}Z^1-$$

Formula II

wherein

X^1 is $–C(O)NR^1–*$, $–NR^1C(O)–*$, $–C(S)NR^1–*$, $–NR^1C(S)–*$, $–OC(O)NR^1–*$, $–NR^1C(O)O–*$, $–NR^1C(O)NR^1–$, $–CH_2–Ph–C(O)NR^1–*$, $–NR^1C(O)–Ph–CH_2–*$, $–CH_2–Ph–NH–C(S)NR^1–*$, $–NR^1C(S)–NH–Ph–CH_2–*$, –O–, or $–NR^1–$, wherein "*" indicates the attachment point to L^3, and R^1 is hydrogen, optionally substituted C_1-C_6 alkyl, optionally substituted C_1-C_6 heteroalkyl, optionally substituted aryl, or optionally substituted heteroaryl;

L^3 is optionally substituted C_1-C_{50} alkyl or optionally substituted C_1-C_{50} heteroalkyl; and

Z^1 is $–CH_2–\#$, $–C(O)–\#$, $–C(S)–\#$, $–OC(O)–\#$, $–C(O)O–\#$, $–NR^2C(O)–\#$, $–C(O)NR^2–\#$, or $–NR^2–\#$, wherein "#" indicates the attachment point to B, and R^2 is hydrogen, optionally substituted C_1-C_6 alkyl, optionally substituted C_1-C_6 heteroalkyl, optionally substituted aryl, or optionally substituted heteroaryl, and

wherein the antibody or antigen-binding fragment thereof comprises a first antigen-binding domain that is capable of binding epidermal growth factor receptor (EGFR) and a second antigen-binding domain that is capable of binding c-mesenchymal-epithelial transition factor (cMET),

wherein the first antigen-binding domain comprises:

i. a heavy chain variable (VH) region comprising the following complementarity determining regions (CDRs):

HCDR1 having the amino acid sequence of SEQ ID NO: 1

HCDR2 having the amino acid sequence of SEQ ID NO: 2

HCDR3 having the amino acid sequence of SEQ ID NO: 3,

or a variant thereof in which one or two or three amino acids in one or more of HCDR1, HCDR2, and HCDR3 are substituted with another amino acid; and

ii. a light chain variable (VL) region comprising the following CDRs:

LCDR1 having the amino acid sequence of SEQ ID NO: 4

LCDR2 having the amino acid sequence of SEQ ID NO: 5

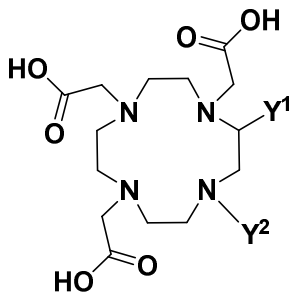
LCDR3 having the amino acid sequence of SEQ ID NO: 6,

or a variant thereof in which one or two or three amino acids in one or more of LCDR1, LCDR2, and LCDR3 are substituted with another amino acid.

2. The compound of claim 1, wherein said chelating moiety is selected from the group consisting of DOTA (1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid), DOTMA (1R,4R,7R,10R)-α, α', α", α'"-tetramethyl-1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid, DOTAM (1,4,7,10-tetrakis(carbamoylmethyl)-1,4,7,10-tetraazacyclododecane), DOTPA (1,4,7,10-tetraazacyclododecane-1,4,7,10-tetra propionic acid), DO3AM-acetic acid (2-(4,7,10-tris(2-amino-2-oxoethyl)-1,4,7,10-tetraazacyclododecan-1-yl)acetic acid), DOTA-GA anhydride (2,2',2"-(10-(2,6-dioxotetrahydro-2H-pyran-3-yl)-1,4,7,10-tetraazacyclododecane-1,4,7-triyl)triacetic acid, DOTP (1,4,7,10-tetraazacyclododecane-1,4,7,10-tetra(methylene phosphonic acid)), DOTMP (1,4,6,10-tetraazacyclodecane-1,4,7,10-tetramethylene phosphonic acid, DOTA-4AMP (1,4,7,10-tetraazacyclododecane-1,4,7,10-tetrakis(acetamido-methylenephosphonic acid), CB-TE2A (1,4,8,11-tetraazabicyclo[6.6.2]hexadecane-4,11-diacetic acid), NOTA (1,4,7-triazacyclononane-1,4,7-triacetic acid), NOTP (1,4,7-triazacyclononane-1,4,7-tri(methylene phosphonic acid), TETPA (1,4,8,11-tetraazacyclotetradecane-1,4,8,11-tetrapropionic acid), TETA (1,4,8,11-tetraazacyclotetradecane-1,4,8,11-tetra acetic acid), HEHA (1,4,7,10,13,16-hexaazacyclohexadecane-1,4,7,10,13,16-hexaacetic acid), PEPA (1,4,7,10,13-

pentaazacyclopentadecane-N,N',N",N''',N''''-pentaacetic acid), H_4octapa (N,N'-bis(6-carboxy-2-pyridylmethyl)-ethylenediamine-N,N'-diacetic acid), H_2dedpa (1,2-[[6-(carboxy)-pyridin-2-yl]-methylamino]ethane), H_6phospa (N,N'-(methylenephosphonate)-N,N'-[6-(methoxycarbonyl)pyridin-2-yl]-methyl-1,2-diaminoethane), TTHA (triethylenetetramine-N,N,N',N",N''',N'''-hexaacetic acid), DO2P (tetraazacyclododecane dimethanephosphonic acid), HP-DO3A (hydroxypropyltetraazacyclododecanetriacetic acid), EDTA (ethylenediaminetetraacetic acid), Deferoxamine, DTPA (diethylenetriaminepentaacetic acid), DTPA-BMA (diethylenetriaminepentaacetic acid-bismethylamide), and porphyrin.

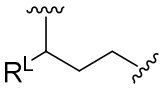
3. The compound of claim 2, wherein the compound is represented by Formula I-a, or a metal complex thereof:



Formula I-a

wherein Y^1 is $–CH_2OCH_2(L^2)_n$-B, $–C(O)(L^2)_n$-B, or $–C(S)(L^2)_n$-B and Y^2 is $–CH_2CO_2H$; or

wherein Y^1 is H and Y^2 is L^1-$(L^2)_n$-B.

4. The compound of any one of claims 1-3, wherein L^1 is 

, wherein R^L is hydrogen or $–CO_2H$.

5. The compound of any one of claims 1-4,

wherein the metal complex comprises a metal selected from the group consisting of Bi, Pb, Y, Mn, Cr, Fe, Co, Zn, Ni, Tc, In, Ga, Cu, Re, a lanthanide, and an actinide; or

wherein the metal complex comprises a radionuclide selected from the group consisting of ^{44}Sc, ^{47}Sc, ^{55}Co, ^{60}Cu, ^{61}Cu, ^{62}Cu, ^{64}Cu, ^{67}Cu, ^{66}Ga, ^{67}Ga, ^{68}Ga, ^{82}Rb, ^{86}Y, ^{87}Y, ^{89}Zr, ^{90}Y, ^{97}Ru, ^{99}Tc, ^{99m}Tc, ^{105}Rh, ^{109}Pd, ^{111}In, ^{117m}Sn, ^{149}Pm, ^{149}Tb, ^{153}Sm, ^{166}Ho, ^{177}Lu, ^{186}Re, ^{188}Re, ^{198}Au, ^{199}Au, ^{201}Tl, ^{203}Pb, ^{211}At, ^{212}Pb, ^{212}Bi, ^{213}Bi, ^{223}Ra, ^{225}Ac, ^{227}Th, and ^{229}Th.

6. The compound of any one of claims 3-5, wherein Y^1 is H.

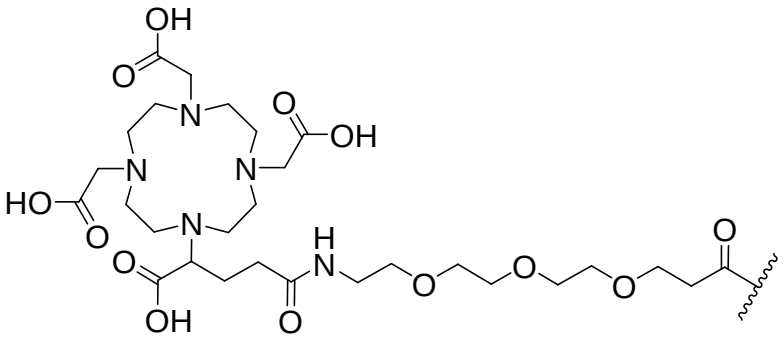
7. The compound of any one of claims 1-6, wherein X^1 is $–C(O)NR^1–*$ or $–NR^1C(O)–*$, "*" indicating the attachment point to L^3, and R^1 is H.

8. The compound of any one of claims 1-7, wherein Z^1 is $–CH_2–$.

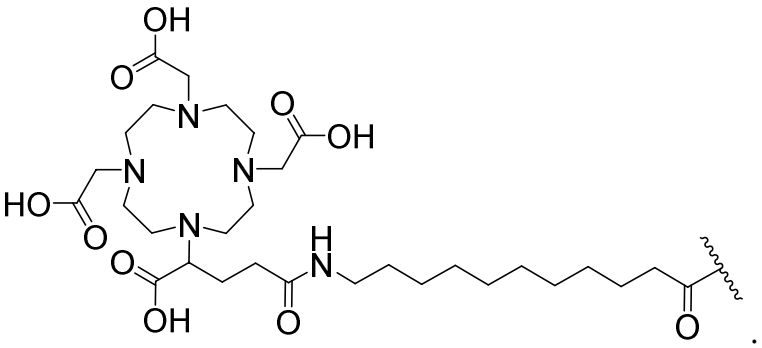
9. The compound of any one of claims 1-8, wherein n is 1, and L^3 comprises $(CH_2CH_2O)_{2\text{-}20}$.

10. The compound of any one of claims 1-8, wherein n is 1, and L^3 is $(CH_2CH_2O)_m(CH_2)_w$, wherein m and w are each independently an integer between 0 and 10 (inclusive), and at least one of m and w is not 0.

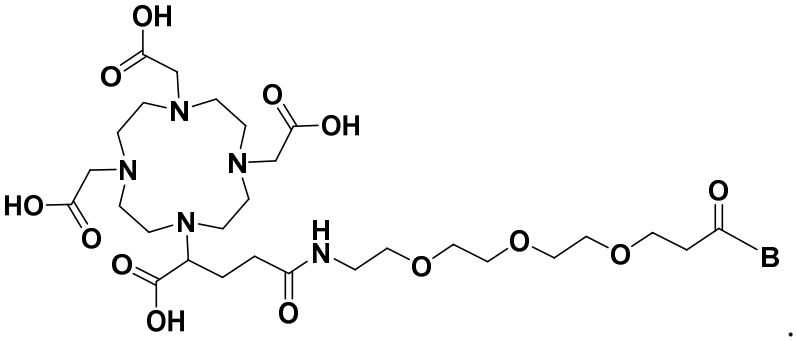
11. The compound of claim 1, wherein the compound comprises one of the following structures, or a metal complex thereof:



, and



12. The compound of claim 1, wherein the compound comprises the following structure, or a metal complex thereof:



13. The compound of any one of claims 1-12, wherein A is a metal complex of the chelating moiety, and the metal complex comprises a radionuclide.

14. The compound of claim 13, wherein the radionuclide is ^{68}Ga, ^{111}In, ^{177}Lu, or ^{225}Ac.

15. The compound of claim 13, wherein the radionuclide is ^{225}Ac.

16. The compound of claim 13, wherein the radionuclide is an alpha emitter selected from the group consisting of Astatine-211 (^{211}At), Bismuth-212 (^{212}Bi), Bismuth-213 (^{213}Bi), Actinium-225 (^{225}Ac), Radium-223 (^{223}Ra), Lead-212 (^{212}Pb), Thorium-227 (^{227}Th), and Terbium-149 (^{149}Tb), or a progeny thereof.

17. The compound of claim 16, wherein the alpha emitter is ^{225}Ac or a progeny thereof.

18. The compound of any one of the preceding claims, wherein the first antigen binding domain comprises:

i. a heavy chain variable (VH) region comprising the following complementarity determining regions (CDRs):

HCDR1 having the amino acid sequence of SEQ ID NO: 1

HCDR2 having the amino acid sequence of SEQ ID NO: 2

HCDR3 having the amino acid sequence of SEQ ID NO: 3; and

ii. a light chain variable (VL) region comprising the following CDRs:

LCDR1 having the amino acid sequence of SEQ ID NO: 4

LCDR2 having the amino acid sequence of SEQ ID NO: 5

LCDR3 having the amino acid sequence of SEQ ID NO: 6.

19. The compound of any one of the preceding claims, wherein the first antigen-binding domain is capable of binding to human EGFR with an affinity that is lower than the affinity with which an antigen-binding domain comprising the variable heavy region sequence and variable light region sequence of antibody QD6, the sequences set forth in SEQ ID NOs: 47 and 48, respectively is capable of binding to human EGFR.

20. The compound of any one of the preceding claims, wherein the first antigen binding domain comprises:

a. a VH region comprising an amino acid sequence having at least 70%, at least 80%, at least 90%, or at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 15; and

b. a VL region comprising an amino acid sequence having at least 70%, at least 80%, at least 90%, or at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 16.

21. The compound of any one of the preceding claims, wherein the second antigen binding domain comprises:

i. a VH region comprising the following CDRs:

HCDR1 having the amino acid sequence of SEQ ID NO: 17

HCDR2 having the amino acid sequence of SEQ ID NO: 18

HCDR3 having the amino acid sequence of SEQ ID NO: 19,

or a variant thereof in which one or two or three amino acids in one or more of HCDR1, HCDR2, and HCDR3 are substituted with another amino acid; and

ii. a VL region comprising the following CDRs:

LCDR1 having the amino acid sequence of SEQ ID NO: 20

LCDR2 having the amino acid sequence of SEQ ID NO: 21

LCDR3 having the amino acid sequence of SEQ ID NO: 22,

or a variant thereof in which one or two or three amino acids in one or more of LCDR1, LCDR2, and LCDR3 are substituted with another amino acid.

22. The compound of claim 21, wherein the second antigen binding domain comprises:

i. a VH region comprising the following CDRs:

HCDR1 having the amino acid sequence of SEQ ID NO: 17

HCDR2 having the amino acid sequence of SEQ ID NO: 18

HCDR3 having the amino acid sequence of SEQ ID NO: 19; and

ii. a VL region comprising the following CDRs:

LCDR1 having the amino acid sequence of SEQ ID NO: 20

LCDR2 having the amino acid sequence of SEQ ID NO: 21

LCDR3 having the amino acid sequence of SEQ ID NO: 22.

23. The compound of claim 21 or 22, wherein the second antigen binding domain comprises:

a. a VH region comprising an amino acid sequence having at least 70%, at least 80%, at least 90%, or at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 31; and

b. a VL region comprising an amino acid sequence having at least 70%, at least 80%, at least 90%, or at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 32.

24. The compound of any one of the preceding claims, wherein the antibody or antigen-binding fragment thereof comprises:

a. a first heavy chain, wherein the first heavy chain comprises the VH region of the first antigen-binding domain, and a first heavy chain constant (CH) region or a fragment thereof;
b. a first light chain, wherein the first light chain comprises the VL region of the first antigen-binding domain, and a first light chain constant (CL) region or a fragment thereof;
c. a second heavy chain, wherein the second heavy chain comprises the VH region of the second antigen-binding domain, and a second heavy chain constant (CH) region or a fragment thereof; and
d. a second light chain, wherein the second light chain comprises the VL region of the second antigen-binding domain, and a second light chain constant (CL) region or a fragment thereof.

25. The compound of claim 24, wherein the first and second CH region each comprise an amino acid sequence having at least 70%, at least 80%, at least 90%, or at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 33.

26. The compound of claim 24 or 25, wherein the first and second heavy chain form a heterodimer, optionally wherein one of the first and second heavy chains comprises a cysteine (C) residue at position 354 and a tryptophan (W) residue at position 366 and the other heavy chain comprises a cysteine (C) residue at position 349, a valine (V) residue at position 407, a serine (S) at position 366 and an alanine (A) at position 368, wherein the numbering of the constant region is as per the EU index.

27. The compound of any one of claims 24-26, wherein the antibody or antigen-binding fragment thereof comprises:

a. a modified CH region, wherein the modified CH region comprises a substitution of a native non-cysteine amino acid to a cysteine amino acid; and
b. a modified corresponding CL region, wherein the modified CL comprises a substitution of a native non-cysteine amino acid to a cysteine amino acid,

wherein either:

i. the first heavy chain comprises the modified CH region and the first light chain comprises the modified corresponding CL region; or

ii. the second heavy chain comprises the modified CH region and the second light chain comprises the modified corresponding CL region, and

wherein the substituted cysteine of the modified CH region and the substituted cysteine of the modified corresponding light chain can form a disulfide bond.

28. The compound of claim 27, wherein the modified CH region comprises a substitution of a native non-cysteine amino acid to a cysteine amino acid at position 126; and the modified corresponding CL region comprises a substitution of a native non-cysteine amino acid to a cysteine amino acid at position 121, wherein the numbering of the constant region is as per the EU index.

29. The compound of any one of claims 24-28, wherein the first and/or second CH region comprise a mutation to reduce or abrogate binding of the antibody or antigen-binding fragment thereof to one of more Fcγ receptors.

30. The compound of any one of claims 24-29, wherein the first and/or second CH region comprise a phenylalanine at position 234, glutamic acid at position 235, and serine at position 331, wherein the numbering of the constant region is as per the EU index.

31. The compound of any one of claims 24-30, wherein:

a. the first CH region comprises an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the sequence set forth in SEQ ID NO: 39;

b. the second CH region comprises an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the sequence set forth in SEQ ID NO: 40,

c. the first CL region comprises an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the sequence set forth in SEQ ID NO: 41; and
d. the second CL region comprises an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the sequence set forth in SEQ ID NO: 34.

32. The compound of any one of the preceding claims, wherein the antibody or antigen-binding fragment thereof comprises:
a. a first heavy chain comprising an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the sequence set forth in SEQ ID NO: 35;
b. a second heavy chain comprising an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the sequence set forth in SEQ ID NO: 36;
c. a first light chain comprising an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the sequence set forth in SEQ ID NO: 37; and
d. a second light chain comprising an amino acid sequence having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity to the sequence set forth in SEQ ID NO: 38.

33. The compound of claim 32, wherein:
a. the first heavy chain comprises an amino acid sequence having the sequence set forth in SEQ ID NO: 35;
b. the second heavy chain comprises an amino acid sequence having the sequence set forth in SEQ ID NO: 36;
c. the first light chain comprises an amino acid sequence having the sequence set forth in SEQ ID NO: 37; and
d. the second light chain comprises an amino acid sequence having the sequence set forth in SEQ ID NO: 38.

34. The compound of any one of the preceding claims, wherein:

a. the first antigen-binding domain that is capable of binding EGFR is capable of binding cynomologus EGFR;

b. the first antigen-binding domain that is capable of binding EGFR is capable of binding mouse EGFR;

c. the second antigen-binding domain that is capable of binding cMET is capable of binding cynomologus cMET;

d. the first antigen-binding domain is specific for EGFR;

e. the second antigen-binding domain is specific for cMET;

f. the antibody or antigen-binding fragment thereof is capable of concurrently engaging EGFR and cMET;

g. the antibody or antigen-binding fragment thereof is capable of being internalised into a cell;

h. the antibody or antigen-binding fragment thereof has cytotoxic activity when measured in an in vitro cell viability assay; and/or

i. the antibody or antigen-binding fragment thereof is capable of blocking ligand dependent signalling of EGFR and/or cMET.

35. The compound of claim 1, wherein:

(a) the first antigen-binding domain comprises:

i. a heavy chain variable (VH) region comprising the following complementarity determining regions (CDRs):

HCDR1 having the amino acid sequence of SEQ ID NO: 1

HCDR2 having the amino acid sequence of SEQ ID NO: 2

HCDR3 having the amino acid sequence of SEQ ID NO: 3; and

ii. a light chain variable (VL) region comprising the following CDRs:

LCDR1 having the amino acid sequence of SEQ ID NO: 4

LCDR2 having the amino acid sequence of SEQ ID NO: 5

LCDR3 having the amino acid sequence of SEQ ID NO: 6; and

(b) the second antigen-binding domain comprises:

i. a VH region comprising the following CDRs:

HCDR1 having the amino acid sequence of SEQ ID NO: 17

HCDR2 having the amino acid sequence of SEQ ID NO: 18

HCDR3 having the amino acid sequence of SEQ ID NO: 19; and

ii. a VL region comprising the following CDRs:

LCDR1 having the amino acid sequence of SEQ ID NO: 20

LCDR2 having the amino acid sequence of SEQ ID NO: 21

LCDR3 having the amino acid sequence of SEQ ID NO: 22.

36. The compound of any one of the preceding claims, wherein the first antigen-binding domain is capable of binding human EGFR with an affinity having a Kd that is:

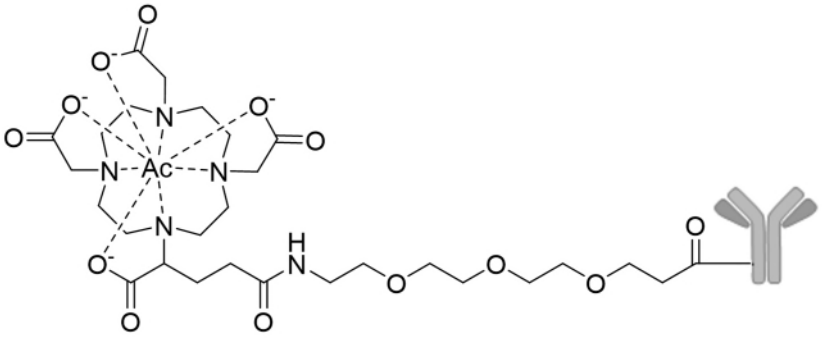
a. between 10 nM and 100 nM;
b. between 20 nM and 80 nM;
c. between 30 nM and 75 nM; or
d. between 35 nM and 50 nM.

37. The compound of any one of the preceding claims, wherein the second antigen-binding domain is capable of binding human cMET with an affinity having a Kd that is:

a. lower than 10 nM; or
b. lower than 5 nM.

38. The compound of any one of claims 19, 36, and 37, wherein the affinity is measured by surface plasmon resonance.

39. The compound of claim 1, wherein the compound comprises the following structure:



,

wherein  is an antibody or antigen-binding fragment thereof as defined in claim 1.

40. The compound of claim 39, wherein the antibody or antigen-binding fragment thereof is linked to A-L^1-$(L^2)_n$- via the side-chain amino group of a lysine residue.

41. A pharmaceutical composition comprising a compound of any one of claims 1-40 and a pharmaceutically acceptable carrier, diluent, or excipient.

42. A compound of any one of claims 1-40, or the pharmaceutical composition of claim 41, for use in a method of treatment of cancer.

43. Use of a compound of any one of claims 1-40, or the pharmaceutical composition of claim 41, in the manufacture of a medicament for the treatment of cancer.

44. The compound for use of claim 42, or the use of claim 43, wherein the cancer is a solid tumor cancer selected from the group consisting of adrenocortical carcinoma, bladder cancer, breast cancer, cervical cancer, colorectal cancer, endometrial adenocarcinoma, Ewing's sarcoma, gallbladder carcinoma, glioma, head and neck cancer, liver cancer, lung cancer, neuroblastoma, neuroendocrine cancer, ovarian cancer, pancreatic cancer, prostate cancer, renal cell carcinoma, salivary adenoid cystic cancer, spermatocytic seminoma, and uveal melanoma.

45. The compound for use or the use of claim 44, wherein the cancer is lung cancer, colorectal cancer, pancreatic cancer, or head and neck cancer.

46. The compound for use of any one of claims 42, 44, and 45, or the use of any one of claims 43-45, wherein an antiproliferative agent, a radiation sensitizer, or an immunomodulatory agent is to be furthered administered in the treatment of cancer.