~~What is claimed is:~~

CLAIMS

1. ~~——~~ ____An antibody-drug conjugate of the formula:

Ab-(L-D),

wherein:

~~(a)~~ Ab is an antibody~~, or antigen-binding fragment thereof,~~ that binds to human protein tyrosine kinase 7 (PTK7~~); and~~

~~(b) L-D is a linker-drug moiety, wherein L is a linker, and D is an auristatin.~~

~~2. The antibody-drug conjugate of claim 1, wherein the Ab is a chimeric, CDR-grafted, humanized, or recombinant human antibody.~~

~~3. The antibody-drug conjugate of claim 1 or 2, wherein the Ab is an internalizing antibody.~~

~~4. The antibody-drug conjugate of claim 1 or 2, wherein the Ab is a neutralizing antibody.~~

~~5. The antibody-drug conjugate of any one of claims 1-4, wherein the Ab competes for binding to human PTK7 with, and/or binds the same epitope as, an antibody~~) comprising~~:~~

~~(a)~~ at least one of a heavy chain ~~variable region set forth as SEQ ID NO: 25 and a light chain variable region set forth as SEQ ID NO: 39;~~

~~(b) a heavy chain variable region set forth as SEQ ID NO: 1 and a light chain variable region set forth as SEQ ID NO: 15; or~~

~~(c) a heavy chain variable region set forth as SEQ ID NO: 49 and a light chain variable region set forth as SEQ ID NO: 63.~~

~~6. The antibody-drug conjugate of claim 5, wherein the Ab comprises at least one heavy chain variable region and at least one light chain variable region, wherein the at least one heavy chain variable region comprises three CDRs set forth as SEQ ID NOs: 27, 31, and 35.~~

~~7. The antibody-drug conjugate of claim 5, wherein the Ab comprises at least one heavy chain variable region and at least one light chain variable region, wherein the at least one light chain variable region comprises three CDRs set forth as SEQ ID NOs: 41, 43, and 45.~~

~~8. The antibody-drug conjugate of any of claims 5-7, wherein the Ab comprises:~~

~~(a) a heavy chain variable region~~ comprising ~~three CDRs set forth as SEQ ID NOs: 27, 31, and 35; and~~

~~(b) a light chain variable region comprising three CDRs set forth as SEQ ID NOs: 41, 43, and 45.~~

~~9. The antibody-drug conjugate of any of claims 5-8, wherein the Ab comprises a heavy chain variable region having~~ an amino acid sequence ~~that is at least 90% identical to SEQ ID NO: 25 and a light chain variable having an amino acid sequence that is at least 90% identical to SEQ ID NO: 39.~~

~~10. The antibody-drug conjugate of claim 9, wherein the Ab comprises a heavy chain variable region set forth as SEQ ID NO: 25 and a light chain variable region set forth as SEQ ID NO: 39.~~

~~11. The antibody-drug conjugate of claim 10, wherein the Ab comprises an IgG1 heavy chain constant region.~~

~~12. The antibody-drug conjugate of claim 11, wherein the Ab comprises a heavy chain~~ set forth as SEQ ID NO: 37~~.~~

~~13. The antibody-drug conjugate of any one of claims 10-12, wherein the Ab comprises a kappa light chain constant region.~~

~~14. The antibody-drug conjugate of claim 13, wherein the Ab comprises a light chain~~ and a light chain comprising an amino acid sequence set forth as SEQ ID NO: 47~~.~~; and

15. The antibody-drug conjugate of any of claims 10-14, wherein the Ab comprises a heavy chain set forth as SEQ ID NO: 37 and a light chain set forth as SEQ ID NO: 47.

16. The antibody-drug conjugate of claim 5, wherein the Ab comprises at least one heavy chain variable region and at least one light chain variable region, wherein the at least one heavy chain variable region comprises three CDRs set forth as SEQ ID NOs: 3, 7, and 11.

17. The antibody-drug conjugate of claim 5, wherein the Ab comprises at least one heavy chain variable region and at least one light chain variable region, wherein the at least one light chain variable region comprises three CDRs set forth as SEQ ID NOs: 17, 19, and 21.

18. The antibody-drug conjugate of any of claims 5, 16-17, wherein the Ab comprises:

(a) a heavy chain variable region comprising three CDRs set forth as SEQ ID NOs: 3, 7, and 11; and

(b) a light chain variable region comprising three CDRs set forth as SEQ ID NOs: 17, 19, and 21.

19. The antibody-drug conjugate of any of claims 5, 16-18, wherein the Ab comprises a heavy chain variable region having an amino acid sequence that is at least 90% identical to SEQ ID NO: 1 and a light chain variable having an amino acid sequence that is at least 90% identical to SEQ ID NO: 15.

20. The antibody-drug conjugate of claim 19, wherein the Ab comprises a heavy chain variable region set forth as SEQ ID NO: 1 and a light chain variable region set forth as SEQ ID NO: 15.

21. The antibody-drug conjugate of claim 20, wherein the Ab comprises an IgG1 heavy chain constant region.

~~22. The antibody-drug conjugate of claim 21, wherein the Ab comprises a heavy chain set forth as SEQ ID NO: 13.~~

~~23. The antibody-drug conjugate of any one of claims 20-22, wherein the Ab comprises a kappa light chain constant region.~~

~~24. The antibody-drug conjugate of claim 23 wherein the Ab comprises a light chain set forth as SEQ ID NO: 23.~~

~~25. The antibody-drug conjugate of any one of claims 20-24, wherein the Ab comprises a heavy chain set forth as SEQ ID NO: 13 and a light chain set forth as SEQ ID NO: 23.~~

~~26. The antibody-drug conjugate of claim 5, wherein the Ab comprises at least one heavy chain variable region and at least one light chain variable region, wherein the at least one heavy chain variable region comprises three CDRs set forth as SEQ ID NOs: 51, 55, and 59.~~

~~27. The antibody-drug conjugate of claim 5, wherein the Ab comprises at least one heavy chain variable region and at least one light chain variable region, wherein the at least one light chain variable region comprises three CDRs set forth as SEQ ID NOs: 65, 67, and 69.~~

~~28. The antibody-drug conjugate of any of claims 5, 26-27, wherein the Ab comprises:~~

~~(a) a heavy chain variable region comprising three CDRs set forth as SEQ ID NOs: 51, 55, and 59; and~~

~~(b) a light chain variable region comprising three CDRs set forth as SEQ ID NOs: 65, 67, and 69.~~

~~29. The antibody-drug conjugate of claim 5, wherein the Ab comprises a heavy chain variable region having an amino acid sequence that is at least 90% identical to SEQ ID NO: 49 and a light chain variable having an amino acid sequence that is at least 90% identical to SEQ ID NO: 63.~~

30. The antibody-drug conjugate of claim 29, wherein the Ab comprises a heavy chain variable region set forth as SEQ ID NO: 49 and a light chain variable region set forth as SEQ ID NO: 63.

31. The antibody-drug conjugate of claim 30, wherein the Ab comprises an IgG1 heavy chain constant region.

32. The antibody-drug conjugate of claim 31, wherein the Ab comprises a heavy chain set forth as SEQ ID NO: 61.

33. The antibody-drug conjugate of any one of claims 30-32, wherein the Ab comprises a kappa light chain constant region.

34. The antibody-drug conjugate of claim 33 wherein the Ab comprises a light chain set forth as SEQ ID NO: 71.

35. The antibody-drug conjugate of any one of claims 30-34, wherein the Ab comprises a heavy chain set forth as SEQ ID NO: 61 and a light chain set forth as SEQ ID NO: 71.

36. The antibody-drug conjugate of claim 5, wherein the Ab comprises a heavy chain variable region set forth as SEQ ID NO: 25, 1 or 49.

37. The antibody-drug conjugate of claim 5, wherein the Ab comprises a light chain variable region set forth as SEQ ID NO: 39, 15 or 63.

38. The antibody-drug conjugate of any of claims 1-37, wherein the a linker is selected from the group consisting of maleimidocapronic-valine-citruline-p-aminobenzyloxycarbonyl (vc) and maleimidocaproyl (mc).

39. The antibody-drug conjugate of any of claims 1-38, wherein the linker is maleimidocapronic-valine-citruline-p-aminobenzyloxycarbonyl (vc).

40. The antibody-drug conjugate of any of claims 1-38, wherein the linker is maleimidocaproyl (mc).

41. The antibody-drug conjugate of any of claims claim 1-40, wherein the , and D is an auristatin is 0101 (2-Methylalanyl-N-[(3R,4S,5S)-3-methoxy-1-{(2S)-2-[(1R,2R)-1-methoxy-2-methyl-3-oxo-3-{[(1S)-2-phenyl-1-(1,3-thiazol-2-yl)ethyl]amino}propyl]pyrrolidin-1-yl}-5-methyl-1-oxoheptan-4-yl]-N-methyl-L-valinamide).

42. The antibody-drug conjugate of claim 41 , wherein the linker and auristatin are is vc0101 (N-[6-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)hexanoyl]-L-valyl-N-{4-[(21S,24S,25R)-24-[(2S)-butan-2-yl]-25-(2-{(2S)-2-[(1R,2R)-1-methoxy-2-methyl-3-oxo-3-{[(1S)-2-phenyl-1-(1,3-thiazol-2-yl)ethyl]amino}propyl]pyrrolidin-1-yl}-2-oxoethyl)-18,18,23-trimethyl-3,16,19,22-tetraoxo-21-(propan-2-yl)-2,7,10,13,26-pentaoxa-4,17,20,23-tetraazaheptacos-1-yl]phenyl}-N~5~-carbamoyl-L-ornithinamide).

43. The antibody-drug conjugate of any of claims 1-40, wherein the auristatin is 8261 2-Methylalanyl-N-[(3R,4S,5S)-1-{(2S)-2-[(1R,2R)-3-{[(1S)-1-carboxy-2-phenylethyl]amino}-1-methoxy-2-methyl-3-oxopropyl]pyrrolidin-1-yl}-3-methoxy-5-methyl-1-oxoheptan-4-yl]-N-methyl-L-valinamide.

44. The antibody-drug conjugate ofclaim 43 , wherein the linker and auristatin are is mc8261 N-[6-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)hexanoyl]-2-methylalanyl-N-[(3R,4S,5S)-1-{(2S)-2-[(1R,2R)-3-{[(1S)-1-carboxy-2-phenylethyl]amino}-1-methoxy-2-methyl-3-oxopropyl]pyrrolidin-1-yl}-3-methoxy-5-methyl-1-oxoheptan-4-yl]-N-methyl-L-valinamide.

45. An antibody-drug conjugate ofhave the formula:

Ab-(L-D), wherein:

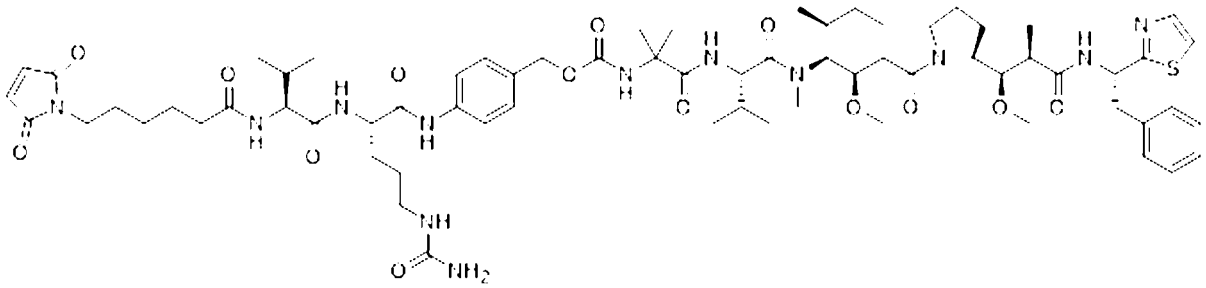
(a) Ab is an antibody or antigen-binding fragment thereof selected from the group consisting of:

(i) an antibody or antigen-binding fragment thereof comprising a heavy chain set forth as SEQ ID NO: 37 and a light chain set forth as SEQ ID NO: 47;

(ii) an antibody or antigen-binding fragment thereof comprising a heavy chain set forth as SEQ ID NO: 13 and a light chain set forth as SEQ ID NO: 23; and

(iii) an antibody or antigen-binding fragment thereof comprising a heavy chain set forth as SEQ ID NO: 61 and a light chain set forth as SEQ ID NO: 71; and

L-D is a



(b) 2. The linker drug moiety, wherein L is a linker, and D is an auristatin, wherein the linker is maleimidocapronic-valine-citruline-p-aminobenzyloxycarbonyl (vc), and the auristatin is 0101.

46. A pharmaceutical composition comprising of claim 1, wherein the antibody-drug conjugate of any one of claims 1-45 and a pharmaceutically acceptable carrier.

47. A composition comprising a plurality of an antibody-drug conjugate of any one of claims 1-45, and optionally a pharmaceutical carrier, wherein the composition has an average a drug-to antibody ratio (DAR within a range) of 1 to 8.

48. A process for producing an antibody-drug conjugate of any one of claims 1-45 comprising:

(a) linking the linker to the drug;

(b) conjugating the linker-drug moiety to the antibody; and

(c) purifying the antibody-drug conjugate.

~~49. A method of treating a PTK7 associated disorder comprising administering a therapeutically effective amount of a composition comprising an antibody-drug conjugate of any one of claims 1-45 to a subject in need thereof.~~

~~50. The method of claim 49, wherein the PTK7 associated disorder is a hyperproliferative disorder.~~

~~51. The method of claim 50, wherein the hyperproliferative disorder is a neoplastic disorder.~~

~~52. The method of claim 51, wherein the neoplastic disorder is a solid tumor.~~

~~53. The method of claim 52, wherein the neoplastic disorder is breast cancer, such as triple-negative breast cancer (TNBC), progesterone-receptor positive breast cancer (PR+), estrogen-receptor positive breast cancer (ER+) and double positive breast cancer; ovarian cancer; colorectal cancer; esophageal cancer; gastric cancer; melanoma; sarcoma; kidney cancer; pancreatic cancer; prostate cancer; liver cancer, such as hepatocellular carcinoma (HCC); and lung cancer such as non-small cell lung cancer (NSCLC).~~

~~54. The method of claim 53, wherein the neoplastic disorder is a hematologic malignancy.~~

~~55. The method of claim 54, wherein the hematologic malignancy is leukemia.~~

~~56. The method of claim 55, wherein the leukemia is adult myeloid leukemia (AML) or acute lymphoblastic leukemia (ALL).~~

~~57. Use of the antibody-drug conjugate of any one of claims 1-45, in the manufacture of a medicament for the treatment of a PTK7 associated disorder in a subject.~~

58. Use according to claim 57, wherein the PTK7 associated disorder is a hyperproliferative disorder.

59. Use according to claim 58, wherein the hyperproliferative disorder is a neoplastic disorder.

60. Use according to claim 59, wherein the neoplastic disorder is a solid tumor.

61. Use according to claim 60, wherein the solid tumor is breast cancer,such as triple-negative breast cancer (TNBC), progesterone-receptor positive breast cancer (PR+), estrogen-receptor positive breast cancer (ER+) and double positive breast cancer; ovarian cancer; colorectal cancer; esophageal cancer; gastric cancer; melanoma; sarcoma; kidney cancer; pancreatic cancer; prostate cancer; liver cancer, such as hepatocellular carcinoma (HCC); and lung cancer such as non-small cell lung cancer (NSCLC).

62. Use according to claim 59, wherein the neoplastic disorder is a hematologic malignancy.

63. Use according to claim 62, wherein the hematologic malignancy is leukemia.

64. Use according to claim 63, wherein the leukemia is adult myeloid leukemia (AML) or acute lymphoblastic leukemia (ALL).

65. The antibody-drug conjugate of any one of claims 1-45, for use in the treatment of a PTK7 associated disorder.

66. The antibody-drug conjugate for use of claim 65, wherein the PTK7 associated disorder is a hyperproliferative disorder.

67. The antibody-drug conjugate for use of claim 66, wherein the hyperproliferative disorder is a neoplastic disorder.

68. The antibody-drug conjugate for use of claim 67, wherein the neoplastic disorder is a solid tumor.

69. The antibody-drug conjugate for use of claim 68, wherein the solid tumor is breast cancer, such as triple-negative breast cancer (TNBC), progesterone-receptor positive breast cancer (PR+), estrogen-receptor positive breast cancer (ER+) and double positive breast cancer; ovarian cancer; colorectal cancer; esophageal cancer; gastric cancer; melanoma; sarcoma; kidney cancer; pancreatic cancer; prostate cancer; liver cancer, such as hepatocellular carcinoma (HCC); and lung cancer such as non-small cell lung cancer (NSCLC).

70. The antibody-drug conjugate for use of claim 69, wherein the neoplastic disorder is a hematologic malignancy.

71. The antibody-drug conjugate for use of claim 70, wherein the hematologic malignancy is leukemia.

72. The antibody-drug conjugate for use of claim 71, wherein the leukemia is adult myeloid leukemia (AML) or acute lymphoblastic leukemia (ALL).

73. A method of reducing tumor initiating cells in a tumor cell population, the method comprising contacting a tumor cell population, wherein the population comprises tumor initiating cells and tumor cells other than tumor initiating cells, with a PTK7 antibody-drug conjugate; whereby the frequency of tumor initiating cells in the tumor cell population is reduced.

74. The method of claim 73, wherein the contacting is performed in vivo.

75. The method of claim 73, wherein the contacting is performed in vitro.