CLAIMS

1. An antibody or antigen-binding fragment thereof that specifically binds to an epitope of human EPH Receptor A5, wherein the antibody or antigen-binding fragment comprises:
   a. a heavy chain variable region comprising three heavy chain complementarity-determining regions (HCDRs), wherein
      HCDR1 comprises the amino acid sequence set forth in SEQ ID NO:16,
      HCDR2 comprises the amino acid sequence selected from the group consisting of SEQ ID NOs:17-19, and
      HCDR3 comprises the amino acid sequence set forth in SEQ ID NO:20; and
   b. a light chain variable region comprises three light chain complementarity-determining regions (LCDRs), wherein
      LCDR1 comprises the amino acid sequence selected from the group consisting of SEQ ID NOs:21 and 22,
      LCDR2 comprises the amino acid sequence set forth in SEQ ID NO:23, and
      LCDR3 comprises the amino acid sequence set forth in SEQ ID NO:24.

2. The antibody or antigen-binding fragment of claim 1, wherein the antibody or antigen-binding fragment further comprises:
   a. a heavy chain comprising a heavy chain variable region comprising an amino acid sequence having at least 85% sequence identity to SEQ ID NO:1; and
   b. a light chain comprising a light chain variable region comprising an amino acid sequence having at least 85% sequence identity to SEQ ID NO:8;

3. The antibody or antigen-binding fragment of claim 1 or 2, wherein:
   a. the heavy chain variable region comprises a HCDR1 comprising the amino acid sequence set forth in SEQ ID NO:16, a HCDR2 comprising the amino acid sequence set forth in SEQ ID NO:17, and a HCDR3 comprising the amino acid sequence set forth in SEQ ID NO:20; and the light chain variable region comprises a LCDR1 comprising the amino acid sequence set forth in SEQ ID NO:21, a LCDR2 comprising the amino acid sequence set forth in SEQ ID NO:23, and a LCDR3

comprising the amino acid sequence set forth in SEQ ID NO:24;

b. the heavy chain variable region comprises a HCDR1 comprising the amino acid sequence set forth in SEQ ID NO:16, a HCDR2 comprising the amino acid sequence set forth in SEQ ID NO:18, and a HCDR3 comprising the amino acid sequence set forth in SEQ ID NO:20; and the light chain variable region comprises a LCDR1 comprising the amino acid sequence set forth in SEQ ID NO:21, a LCDR2 comprising the amino acid sequence set forth in SEQ ID NO:23, and a LCDR3 comprising the amino acid sequence set forth in SEQ ID NO:24;

c. the heavy chain variable region comprises a HCDR1 comprising the amino acid sequence set forth in SEQ ID NO:16, a HCDR2 comprising the amino acid sequence set forth in SEQ ID NO:19, and a HCDR3 comprising the amino acid sequence set forth in SEQ ID NO:20; and the light chain variable region comprises a LCDR1 comprising the amino acid sequence set forth in SEQ ID NO:21, a LCDR2 comprising the amino acid sequence set forth in SEQ ID NO:23, and a LCDR3 comprising the amino acid sequence set forth in SEQ ID NO:24;

d. the heavy chain variable region comprises a HCDR1 comprising the amino acid sequence set forth in SEQ ID NO:16, a HCDR2 comprising the amino acid sequence set forth in SEQ ID NO:17, and a HCDR3 comprising the amino acid sequence set forth in SEQ ID NO:20; and the light chain variable region comprises a LCDR1 comprising the amino acid sequence set forth in SEQ ID NO:22, a LCDR2 comprising the amino acid sequence set forth in SEQ ID NO:23, and a LCDR3 comprising the amino acid sequence set forth in SEQ ID NO:24;

e. the heavy chain variable region comprises a HCDR1 comprising the amino acid sequence set forth in SEQ ID NO:16, a HCDR2 comprising the amino acid sequence set forth in SEQ ID NO:18, and a HCDR3 comprising the amino acid sequence set forth in SEQ ID NO:20; and the light chain variable region comprises a LCDR1 comprising the amino acid sequence set forth in SEQ ID NO:22, a LCDR2 comprising the amino acid sequence set forth in SEQ ID NO:23, and a LCDR3 comprising the amino acid sequence set forth in SEQ ID NO:24; or

f. the heavy chain variable region comprises a HCDR1 comprising the amino acid sequence set forth in SEQ ID NO:16, a HCDR2 comprising the amino acid sequence

set forth in SEQ ID NO:19, and a HCDR3 comprising the amino acid sequence set forth in SEQ ID NO:20; and the light chain variable region comprises a LCDR1 comprising the amino acid sequence set forth in SEQ ID NO:22, a LCDR2 comprising the amino acid sequence set forth in SEQ ID NO:23, and a LCDR3 comprising the amino acid sequence set forth in SEQ ID NO:24.

4. The antibody or antigen-binding fragment thereof of any one of claims 1-3, wherein the amino acid sequence of the heavy chain variable region has at least 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence selected from the group consisting of SEQ ID NOs:2-7.

5. The antibody or antigen-binding fragment thereof of any one of claims 1-4, wherein the heavy chain variable region comprises the amino acid sequence selected from the group consisting of SEQ ID NOs:2-7.

6. The antibody or antigen-binding fragment thereof of any one of claims 1-5, wherein the heavy chain variable region consists of the amino acid sequence selected from the group consisting of SEQ ID NOs:2-7.

7. The antibody or antigen-binding fragment thereof of any one of claims 1-6, wherein the heavy chain variable region is encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NOs:26-31.

8. The antibody or antigen-binding fragment thereof of any one of claims 1-7, wherein the amino acid sequence of the light chain variable region has at least85%, 90%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence selected from the group consisting of SEQ ID NOs:9-13.

9. The antibody or antigen-binding fragment thereof of any one of claims 1-3 and 8, wherein the light chain variable region comprises the amino acid sequence selected from the group consisting of SEQ ID NOs:9-13.

10. The antibody or antigen-binding fragment thereof of any one of claims 1-3 and 8-9, wherein the light chain variable region consists of the amino acid sequence selected from the group consisting of SEQ ID NOs:9-13.

11. The antibody or antigen-binding fragment thereof of any one of claims 1-3 and 8-9, wherein the light chain variable region is encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NOs:33-37.

12. The antibody or antigen binding fragment thereof of any one of claims 1-11, wherein:
    a. the heavy chain variable region is set forth in SEQ ID NO:2 and the light chain variable region is set forth in SEQ ID NO:9;
    b. the heavy chain variable region is set forth in SEQ ID NO:2 and the light chain variable region is set forth in SEQ ID NO:10;
    c. the heavy chain variable region is set forth in SEQ ID NO:2 and the light chain variable region is set forth in SEQ ID NO:11;
    d. the heavy chain variable region is set forth in SEQ ID NO:2 and the light chain variable region is set forth in SEQ ID NO:12;
    e. the heavy chain variable region is set forth in SEQ ID NO:2 and the light chain variable region is set forth in SEQ ID NO:13;
    f. the heavy chain variable region is set forth in SEQ ID NO:3 and the light chain variable region is set forth in SEQ ID NO:9;
    g. the heavy chain variable region is set forth in SEQ ID NO:3 and the light chain variable region is set forth in SEQ ID NO:10;
    h. the heavy chain variable region is set forth in SEQ ID NO:3 and the light chain variable region is set forth in SEQ ID NO:11;
    i. the heavy chain variable region is set forth in SEQ ID NO:3 and the light chain variable region is set forth in SEQ ID NO:12;
    j. the heavy chain variable region is set forth in SEQ ID NO:3 and the light chain variable region is set forth in SEQ ID NO:13;
    k. the heavy chain variable region is set forth in SEQ ID NO:4 and the light chain

variable region is set forth in SEQ ID NO:9;

l. the heavy chain variable region is set forth in SEQ ID NO:4 and the light chain variable region is set forth in SEQ ID NO:10;

m. the heavy chain variable region is set forth in SEQ ID NO:4 and the light chain variable region is set forth in SEQ ID NO:11;

n. the heavy chain variable region is set forth in SEQ ID NO:4 and the light chain variable region is set forth in SEQ ID NO:12;

o. the heavy chain variable region is set forth in SEQ ID NO:4 and the light chain variable region is set forth in SEQ ID NO:13;

p. the heavy chain variable region is set forth in SEQ ID NO:5 and the light chain variable region is set forth in SEQ ID NO:9;

q. the heavy chain variable region is set forth in SEQ ID NO:5 and the light chain variable region is set forth in SEQ ID NO:10;

r. the heavy chain variable region is set forth in SEQ ID NO:5 and the light chain variable region is set forth in SEQ ID NO:11;

s. the heavy chain variable region is set forth in SEQ ID NO:5 and the light chain variable region is set forth in SEQ ID NO:12;

t. the heavy chain variable region is set forth in SEQ ID NO:5 and the light chain variable region is set forth in SEQ ID NO:13;

u. the heavy chain variable region is set forth in SEQ ID NO:6 and the light chain variable region is set forth in SEQ ID NO:9;

v. the heavy chain variable region is set forth in SEQ ID NO:6 and the light chain variable region is set forth in SEQ ID NO:10;

w. the heavy chain variable region is set forth in SEQ ID NO:6 and the light chain variable region is set forth in SEQ ID NO:11;

x. the heavy chain variable region is set forth in SEQ ID NO:6 and the light chain variable region is set forth in SEQ ID NO:12;

y. the heavy chain variable region is set forth in SEQ ID NO:6 and the light chain variable region is set forth in SEQ ID NO:13;

z. the heavy chain variable region is set forth in SEQ ID NO:7 and the light chain variable region is set forth in SEQ ID NO:9;

aa. the heavy chain variable region is set forth in SEQ ID NO:7 and the light chain variable region is set forth in SEQ ID NO:10;

bb. the heavy chain variable region is set forth in SEQ ID NO:7 and the light chain variable region is set forth in SEQ ID NO:11;

cc. the heavy chain variable region is set forth in SEQ ID NO:7 and the light chain variable region is set forth in SEQ ID NO:12; or

dd. the heavy chain variable region is set forth in SEQ ID NO:7 and the light chain variable region is set forth in SEQ ID NO:13.

13. The antibody or antigen binding fragment thereof of any one of claims 1-11, wherein:

a. the heavy chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:2 and the light chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:9;

b. the heavy chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:2 and the light chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:10;

c. the heavy chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:2 and the light chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:11;

d. the heavy chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:2 and the light chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:12;

e. the heavy chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:2 and the light chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:13;

f. the heavy chain variable region comprises a sequence that has at least 90% sequence

identity to the sequence set forth in SEQ ID NO:3 and the light chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:9;

g. the heavy chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:3 and the light chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:10;

h. the heavy chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:3 and the light chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:11;

i. the heavy chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:3 and the light chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:12;

j. the heavy chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:3 and the light chain variable region comprises a sequence that has at least 90% sequence identity to the sequence forth in SEQ ID NO:13;

k. the heavy chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:4 and the light chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:9;

l. the heavy chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:4 and the light chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:10;

m. the heavy chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:4 and the light chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:11;

n. the heavy chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:4 and the light chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:12;
o. the heavy chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:4 and the light chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:13;
p. the heavy chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:5 and the light chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:9;
q. the heavy chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:5 and the light chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:10;
r. the heavy chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:5 and the light chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:11;
s. the heavy chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:5 and the light chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:12;
t. the heavy chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:5 and the light chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:13;
u. the heavy chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:6 and the light chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth

in SEQ ID NO:9;

v. the heavy chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:6 and the light chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:10;

w. the heavy chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:6 and the light chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:11;

x. the heavy chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:6 and the light chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:12;

y. the heavy chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:6 and the light chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:13;

z. the heavy chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:7 and the light chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:9;

aa. the heavy chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:7 and the light chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:10;

bb. the heavy chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:7 and the light chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:11;

cc. the heavy chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:7 and the light chain variable region

comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:12; or

dd. the heavy chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:7 and the light chain variable region comprises a sequence that has at least 90% sequence identity to the sequence set forth in SEQ ID NO:13.

14. An antibody or antigen-binding fragment thereof that specifically binds to an epitope of human EPH Receptor A5, wherein the antibody or antigen-binding fragment comprises:

a. a heavy chain comprising a heavy chain variable region comprising a heavy chain complementarity-determining region 1 (HCDR1) comprising the sequence set forth in SEQ ID NO:16, a HCDR2 comprising the sequence set forth in SEQ ID NO:18, a HCDR3 set forth in SEQ ID NO:20; and

b. a light chain comprising a light chain variable region comprising a light chain complementarity determining region 1 (LCDR1) comprising the sequence set forth in SEQ ID NO:21, a LCDR2 comprising the sequence set forth in SEQ ID NO:23a, and an LCDR3 comprising the sequence set forth in SEQ ID NO:24.

15. An antibody or antigen-binding fragment thereof that specifically binds to an epitope of human EPH Receptor A5, wherein the antibody or antigen-binding fragment comprises:

a. a heavy chain comprising a heavy chain variable region comprising a heavy chain complementarity-determining region 1 (HCDR1) comprising the sequence set forth in SEQ ID NO:16, a HCDR2 comprising the sequence set forth in SEQ ID NO:19, a HCDR3 set forth in SEQ ID NO:20; and

b. a light chain comprising a light chain variable region comprising a light chain complementarity determining region 1 (LCDR1) comprising the sequence set forth in SEQ ID NO:21, an LCDR2 comprising the sequence set forth in SEQ ID NO:23, and an LCDR3 comprising the sequence set forth in SEQ ID NO:24.

16. An antibody or antigen-binding fragment thereof that specifically binds to an epitope of human EPH Receptor A5, wherein the antibody or antigen-binding fragment comprises:

a. a heavy chain comprising a heavy chain variable region comprising a heavy chain complementarity-determining region 1 (HCDR1) comprising the sequence set forth in SEQ ID NO:16, a HCDR2 comprising the sequence set forth in SEQ ID NO:17, a HCDR3 set forth in SEQ ID NO:20; and

b. a light chain comprising a light chain variable region comprising a complementarity determining region 1 (LCDR1) comprising the sequence set forth in SEQ ID NO:22, an LCDR2 comprising the sequence set forth in SEQ ID NO:23, and an LCDR3 comprising the sequence set forth in SEQ ID NO:24.

17. An antibody or antigen-binding fragment thereof that specifically binds to an epitope of human EPH Receptor A5, wherein the antibody or antigen-binding fragment comprises:

a. a heavy chain comprising a heavy chain variable region comprising a heavy chain complementarity-determining region 1 (HCDR1) comprising the sequence set forth in SEQ ID NO:16, a HCDR2 comprising the sequence set forth in SEQ ID NO:18, a HCDR3 set forth in SEQ ID NO:20; and

b. a light chain comprising a light chain variable region comprising a light chain complementarity determining region 1 (LCDR1) comprising the sequence set forth in SEQ ID NO:22, LCDR2 comprising the sequence set forth in SEQ ID NO:23, and an LCDR3 comprising the sequence set forth in SEQ ID NO:24.

18. An antibody or antigen-binding fragment thereof comprising:

a. a heavy chain comprising a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO:5; and

b. a light chain comprising a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO:11.

19. An antibody or antigen-binding fragment thereof comprising:

a. a heavy chain comprising a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO:6; and

b. a light chain comprising a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO:11.

20. The antibody or antigen-binding fragment thereof of any one of claims 1-19, wherein the antibody or antigen-binding fragment thereof is selected from the group consisting of a full-length antibody, a Fab, and a single-chain variable fragment (scFv).

21. The antibody or antigen-binding fragment thereof of any one of claims 1-20, wherein the antibody or antigen-binding fragment thereof is a full-length antibody.

22. The antibody or antigen-binding fragment thereof of any one of claims 1-21, wherein the antibody is humanized.

23. The antibody or antigen-binding fragment thereof of any one of claims 1-22, wherein the heavy chain further comprises a constant domain of a human immunoglobulin heavy chain and the light chain further comprises a constant domain of a human light chain.

24. The antibody or antigen-binding fragment thereof of claim 23, wherein the constant domain of a human immunoglobulin heavy chain is from a IgG1 heavy chain.

25. The antibody or antigen-binding fragment thereof of claim 23 or 224 wherein the constant domain of a human immunoglobulin heavy chain comprises the amino acid sequence set forth in SEQ ID NO:14.

26. The antibody of claim 23, wherein the constant domain of a human light chain is from a human kappa light chain.

27. The antibody or antigen-binding fragment thereof of claim 23 or claim 26, wherein the constant domain of a human light chain comprises the amino acid sequence set forth in SEQ ID NO:15.

28. An antibody or antigen-binding fragment thereof that specifically binds to an epitope of human EPH Receptor A5, wherein the antibody or antigen-binding fragment comprises:

a. a heavy chain comprising at least 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence set forth in SEQ ID NO:38; and
b. a light chain comprising at least 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence set forth in SEQ ID NOs:40.

29. The antibody or antigen-binding fragment of claim 28, wherein:
a. the variable region of the heavy chain comprises a HCDR1 comprising the amino acid sequence set forth in SEQ ID NO:16, a HCDR2 comprising the amino acid sequence set forth in SEQ ID NO:17, and a HCDR3 comprising the amino acid sequence set forth in SEQ ID NO:20; and
b. the variable region of the light chain comprises a LCDR1 comprising the amino acid sequence set forth in SEQ ID NO:21, a LCDR2 comprising the amino acid sequence set forth in SEQ ID NO:23, and a LCDR3 comprising the amino acid sequence set forth in SEQ ID NO:24.

30. The antibody or antigen-binding fragment thereof of any of claims 1-29, wherein the heavy chain is set forth in SEQ ID NO:38 and the light chain is set forth in SEQ ID NO:40.

31. An antibody or antigen-binding fragment thereof that specifically binds to an epitope of human EPH Receptor A5, wherein the antibody or antigen-binding fragment comprises:
a. a heavy chain comprising at least 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence set forth in SEQ ID NO:39; and
b. a light chain comprising at least 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence set forth in SEQ ID NO:40.

32. The antibody or antigen-binding fragment of claim 31, wherein:

a. the variable region of the heavy chain comprises a HCDR1 comprising the amino acid sequence set forth in SEQ ID NO:16, a HCDR2 comprising the amino acid sequence set forth in SEQ ID NO:18, and a HCDR3 comprising the amino acid sequence set forth in SEQ ID NO:20; and
b. the variable region of the light chain comprises a LCDR1 comprising the amino acid sequence set forth in SEQ ID NO:21, a LCDR2 comprising the amino acid sequence set forth in SEQ ID NO:23, and a LCDR3 comprising the amino acid sequence set forth in SEQ ID NO:24.

33. The antibody or antigen-binding fragment thereof of any of claims 1-27, 31, and 32, wherein the heavy chain is set forth in SEQ ID NO:39 and the light chain is set forth in SEQ ID NO:40.

34. The antibody or antigen-binding fragment thereof of any one of claims 1-33, wherein the dissociation constant (K_D) for binding to human EpHA5 is less than 1.25×10^{-9} M.

35. The antibody or antigen-binding fragment thereof of any one of claims 1-34, wherein the dissociation constant (K_D) for binding to human EpHA5 is between 8×10^{-10} M and 1.1×10^{-9} M.

36. The antibody or antigen-binding fragment thereof of any one of claims 1-35, wherein the antibody or antigen-binding fragment has a dissociation constant (K_D) for binding to human EpHA5 that is within 2-fold better than a reference antibody, wherein the reference antibody is 11C12 or an antibody comprising a variable heavy chain set forth in SEQ ID NO:1 and a variable light chain set forth in SEQ ID NO:8, optionally wherein the reference antibody is of the same form.

37. The antibody or antigen-binding fragment thereof of any one of claims 1-36, wherein the dissociation constant (K_D) for binding to human EpHA5 is more than 1.2 fold better than a reference antibody, wherein the reference antibody is 11C12 or an antibody comprising a variable heavy chain set forth in SEQ ID NO:1 and a variable light chain set forth in

SEQ ID NO:8, optionally wherein the reference antibody is of the same form.

38. The antibody or antigen-binding fragment thereof of any one of claims 34-37, wherein the dissociation constant (K_D) is determined by Biacore.

39. The antibody or antigen-binding fragment thereof of any one of claims 1-38, which exhibits increased thermal stability compared to a reference antibody, wherein the reference antibody is 11C12 or an antibody comprising a variable heavy chain set forth in SEQ ID NO:1 and a variable light chain set forth in SEQ ID NO:8, optionally wherein the reference antibody is of the same form.

40. The antibody or antigen-binding fragment thereof of any one of claims 1-39, wherein the antibody or antigen-binding fragment has a melting temperature profile with a Tm1 that is increased greater than or about 5ºC compared to a reference antibody, wherein the reference antibody is 11C12 or an antibody comprising a variable heavy chain set forth in SEQ ID NO:1 and a variable light chain set forth in SEQ ID NO:8, optionally wherein the reference antibody is of the same form.

41. The antibody or antigen-binding fragment thereof of any one of claims 1-40, wherein the antibody or antigen-binding fragment has a melting temperature profile with a Tm1 that is increased greater than or about 10ºC compared to a reference antibody, wherein the reference antibody is 11C12 or an antibody comprising a variable heavy chain set forth in SEQ ID NO:1 and a variable light chain set forth in SEQ ID NO:8, optionally wherein the reference antibody is of the same form.

42. The antibody or antigen-binding fragment of claim 40 or 41, wherein the Tm1 of the thermal unfolding curve of the antibody or antigen-binding fragment is greater than 60 ºC.

43. The antibody or antigen-binding fragment thereof of any one of claims 40-42, wherein Tm1 of the antibody or antigen-binding fragment is between about 60 ºC and about 70

ºC.

44. The antibody or antigen-binding fragment thereof of any one of claims 40-43, wherein the Tm1 of the antibody or antigen-binding fragment is about 64 ºC, about 65 ºC, about 66 ºC, about 67 ºC, about 68 ºC, or about 69 ºC.

45. The antibody or antigen-binding fragment thereof of any one of claims 40-44, wherein the melting temperature profile is monophasic.

46. The antibody or antigen-binding fragment thereof of any one of claims 1-45, wherein onset temperature of aggregation (Tagg) of the antibody or antigen-binding fragment is increased greater than about 1ºC, greater than about 2ºC, greater than about 3ºC, greater than about 4ºC or greater than about 5ºC compared to a reference antibody, wherein the reference antibody is 11C12 or an antibody comprising a variable heavy chain set forth in SEQ ID NO:1 and a variable light chain set forth in SEQ ID NO:8.

47. The antibody or antigen-binding fragment thereof of any of claims 1-46, wherein onset temperature of aggregation (Tagg) of the antibody or antigen-binding fragment is greater than about 67 ºC.

48. The antibody or antigen-binding fragment thereof of any of claims 1-47, wherein onset temperature of aggregation (Tagg) of the antibody or antigen-binding fragment is between about 67 ºC and about 71 ºC.

49. The antibody or antigen-binding fragment thereof of any of claims 1-48, wherein the Tagg of the antibody or antigen-binding fragment is about 67 ºC, about 68 ºC, about 69 ºC, about 70 ºC, or about 71 ºC.

50. The antibody or antigen-binding fragment thereof of any one of claims 1-49, wherein the antibody or antigen-binding fragment binds to cell surface human EphA5.

51. The antibody or antigen-binding fragment thereof of any one of claims 1-50, wherein the antibody or fragment binds human EphA5 expressed on the surface of cells, optionally an H460 cell line, with an EC50 that is increased compared to a reference antibody, wherein the reference antibody is 11C12 or an antibody comprising a variable heavy chain set forth in SEQ ID NO:1 and a variable light chain set forth in SEQ ID NO:8, optionally wherein the reference antibody is of the same form.

52. The antibody or antigen-binding fragment thereof of any one of claims 1-51, wherein the antibody or fragment binds human EphA5 expressed on the surface of cells, optionally an H460 cell line, with an EC50 of less than or equal to 0.020 μg/mL optionally wherein the EC50 is determined by flow cytometry.

53. The antibody or antigen-binding fragment thereof of any one of claims 1-52, wherein the antibody or fragment binds human EphA5 expressed on the surface of cells, optionally an H460 cell line, with an EC50 of between about 0.010 μg/mL and 0.020 μg/mL, optionally wherein the EC50 is determined by flow cytometry.

54. The antibody or antigen-binding fragment thereof of any one of claims 1-53, wherein the antibody or fragment binds human EphA5 expressed on the surface of cells, optionally an H460 cell line, with an EC50 of about 0.015 μg/mL, about 0.016 μg/mL, about 0.017 μg/mL, about 0.018 μg/mL, about 0.019 μg/mL, or about 0.020μg/mL, optionally wherein the EC50 is determined by flow cytometry.

55. The antibody or antigen-binding fragment thereof of any one of claims 1-54, wherein the antibody or antigen-binding fragment is internalized by human EphA5-expressing cells.

56. A nucleic acid encoding the heavy chain of the antibody or antigen-binding fragment thereof of any one of claims 1-55.

57. A nucleic acid encoding the light chain of the antibody or antigen-binding fragment thereof of any one of claims 1-55.

58. A nucleic acid encoding the heavy chain and the light chain of the antibody or antigen-binding fragment thereof of any one of claims 1-55.

59. A vector comprising the nucleic acid of any one of claims 56-58.

60. The vector of claim 59, wherein the vector is an expression vector.

61. A vector comprising a nucleic acid encoding the heavy chain and a nucleic acid encoding the light chain, wherein the heavy chain and light chain is of the antibody or antigen-binding fragment thereof of any one of claims 1-58.

62. The vector of claim 61, which is a bicistronic vector.

63. A vector system comprising a first vector comprising a first nucleic acid encoding a heavy chain and a second vector comprising a second nucleic acid encoding a light chain, wherein the heavy chain and the light chain is of the antibody or antigen-binding fragment thereof of any one of claims 1-58.

64. The vector system of claim 63, wherein the first vector and the second vector are each an expression vector.

65. A host cell comprising the vector of any one of claims 61-62 or the vector system of any one of claims 63-64.

66. The host cell of claim 65, which is a mammalian cell.

67. A method of producing an antibody, the method comprising introducing a vector of any one of claims 61-62 and/or a vector system of any one of claims 63-64 into a host cell, culturing the host cell under conditions for expression of an antibody or antigen binding fragment from the host cell, and isolating or purifying the antibody or antigen-binding

fragment.

68. The method of claim 67, wherein the host cell is a mammalian cell.

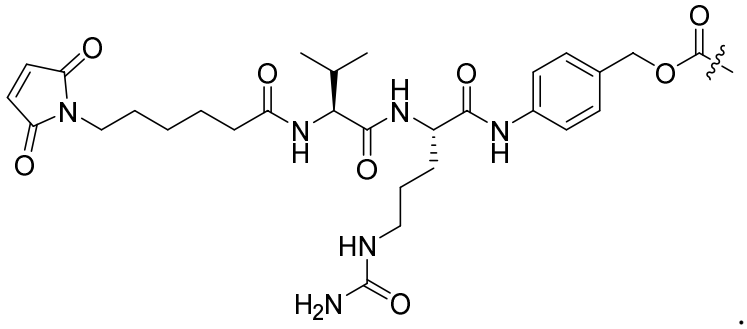
69. An immunoconjugate having the formula Ab-(L-D), wherein:
    a. Ab is the antibody or antigen-binding fragment thereof of any one of claims 1-55;
    b. L is a linker; and
    c. D is a cytotoxic drug.

70. The immunoconjugate of claim 69, wherein the linker is a cleavable linker.

71. The immunoconjugate of claim 69 or claim 70, wherein the linker is a cathepsin-cleavable linker.

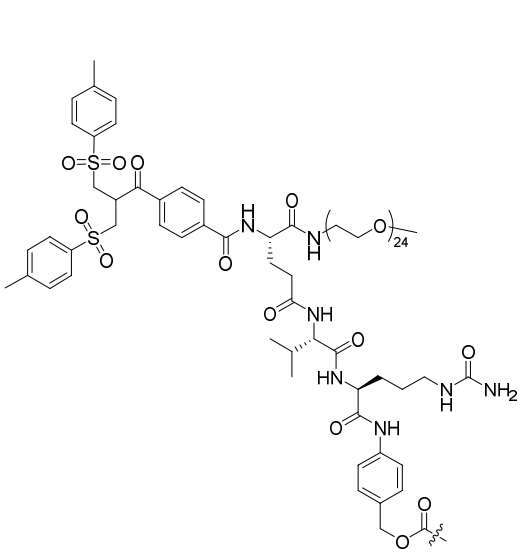
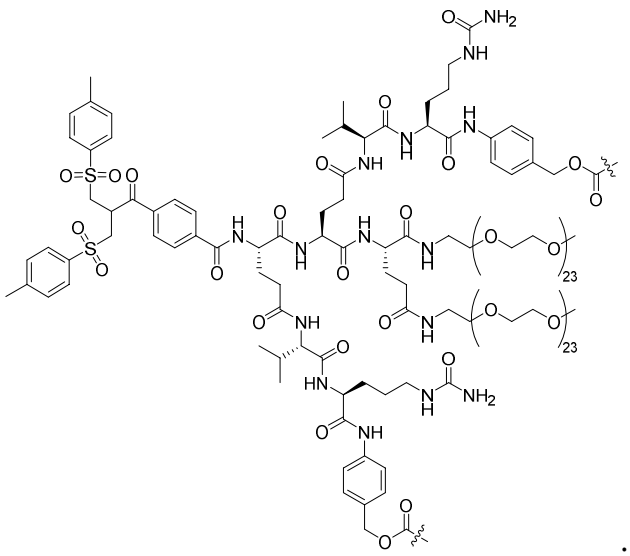
72. The immunoconjugate of claim 71, wherein the cathepsin-cleavable linker comprises a valine-citruline (Val-Cit).

73. The immunoconjugate of any one of claims 68-72, wherein the linker is MC-VCP, having the structure:



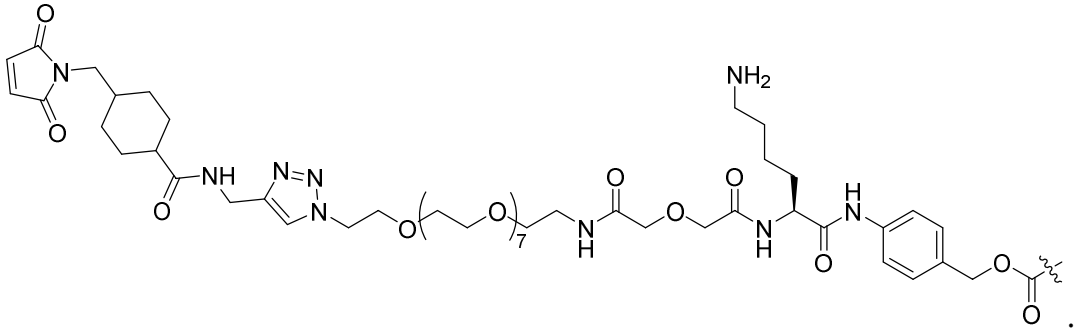
.

74. The immunoconjugate of any one of claims 69-72, wherein the linker comprises the structure:


or

.

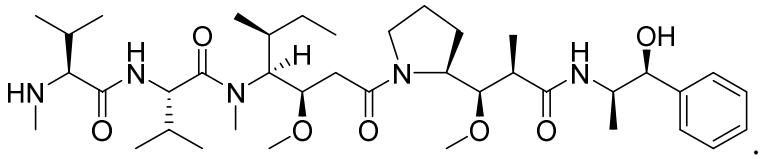
75. The immunoconjugate of any one of claims 68-74, wherein the linker is a pH cleavable linker.

76. The immunoconjugate of any one of claims 69-79 and 75, wherein the linker is CL2A, having the structure:

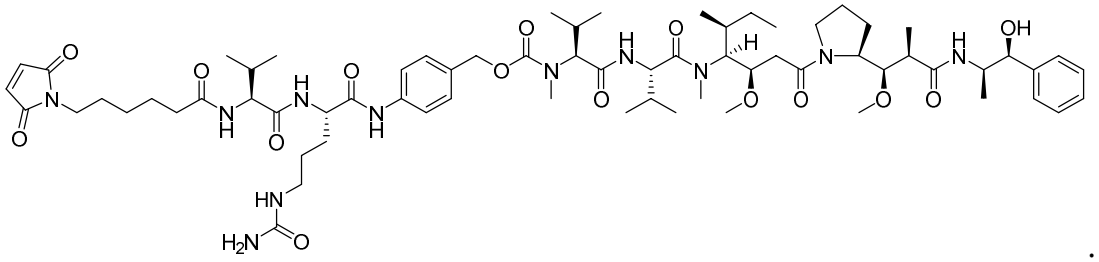

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77. The immunoconjugate of any one of claims 69-76, wherein the cytotoxic drug is an auristatin.

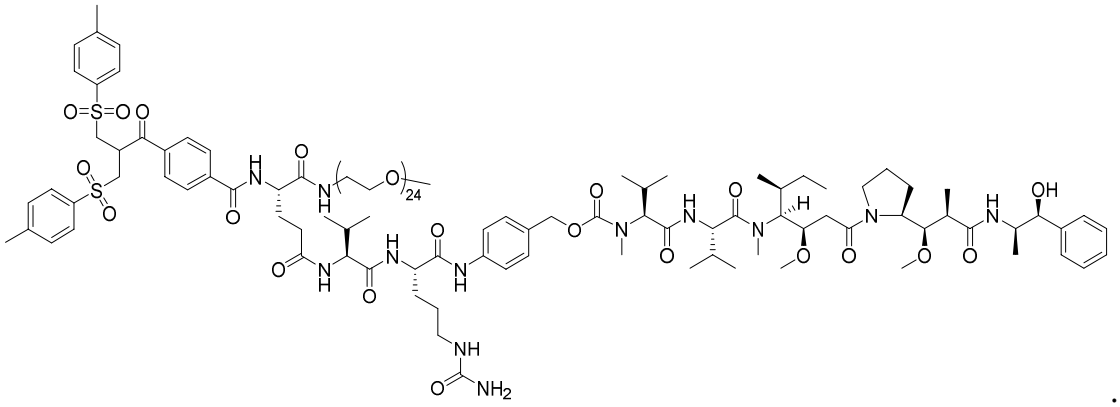
78. The immunoconjugate of claim 77, wherein the auristatin is monomethyl auristatin E (MMAE) having the structure:



79. The immunoconjugate of any one of claims 69-73, 77, and 78, wherein the L-D comprises the structure:



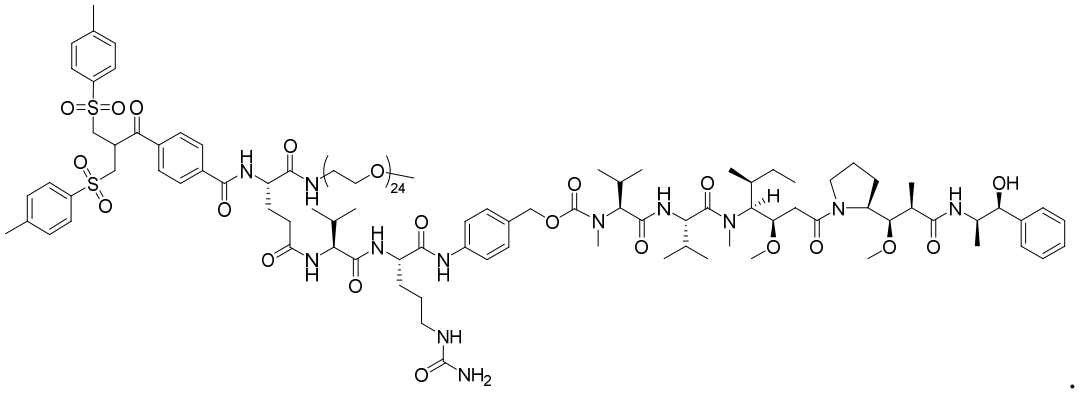
80. The immunoconjugate of any one of claims 69-72, 74, 77, and 78, wherein the L-D comprises the structure:



81. An immunoconjugate having the formula Ab-(L-D), wherein:

a. Ab is an antibody that specifically binds to an epitope of human EPH Receptor A5 (EphA5) comprising the heavy chain set forth in SEQ ID NO:38 and the light chain set forth in SEQ ID NO:40; and

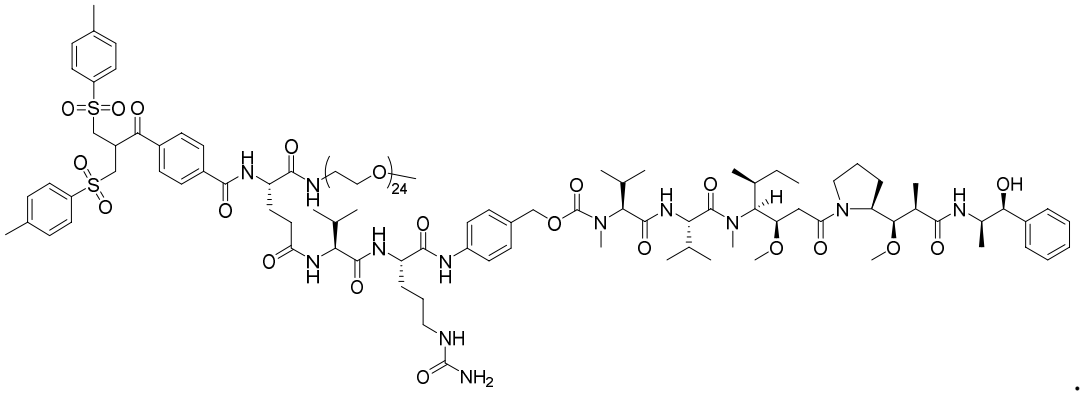
b. the L-D comprises the structure:



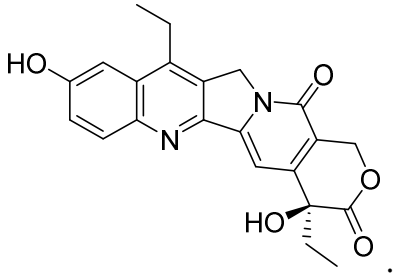
82. An immunoconjugate having the formula Ab-(L-D), wherein:

a. Ab is an antibody that specifically binds to an epitope of human EPH Receptor A5 (EphA5) comprising the heavy chain set forth in SEQ ID NO:39 and the light chain set forth in SEQ ID NO:40; and

b. the L-D comprises the structure:

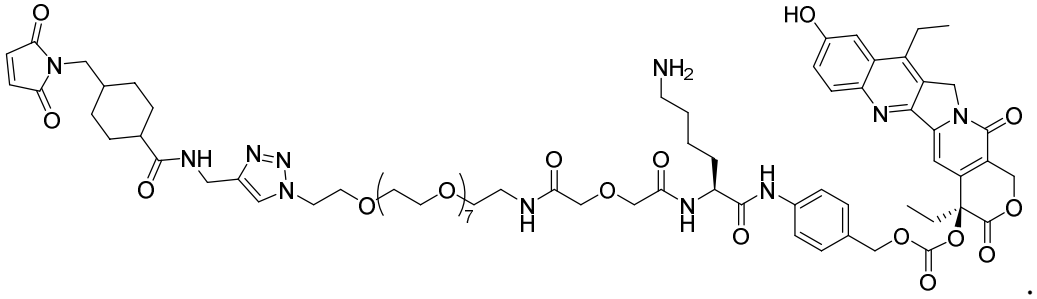


83. The immunoconjugate of any one of claims 69-76, wherein the cytotoxic drug is SN38, having the structure:

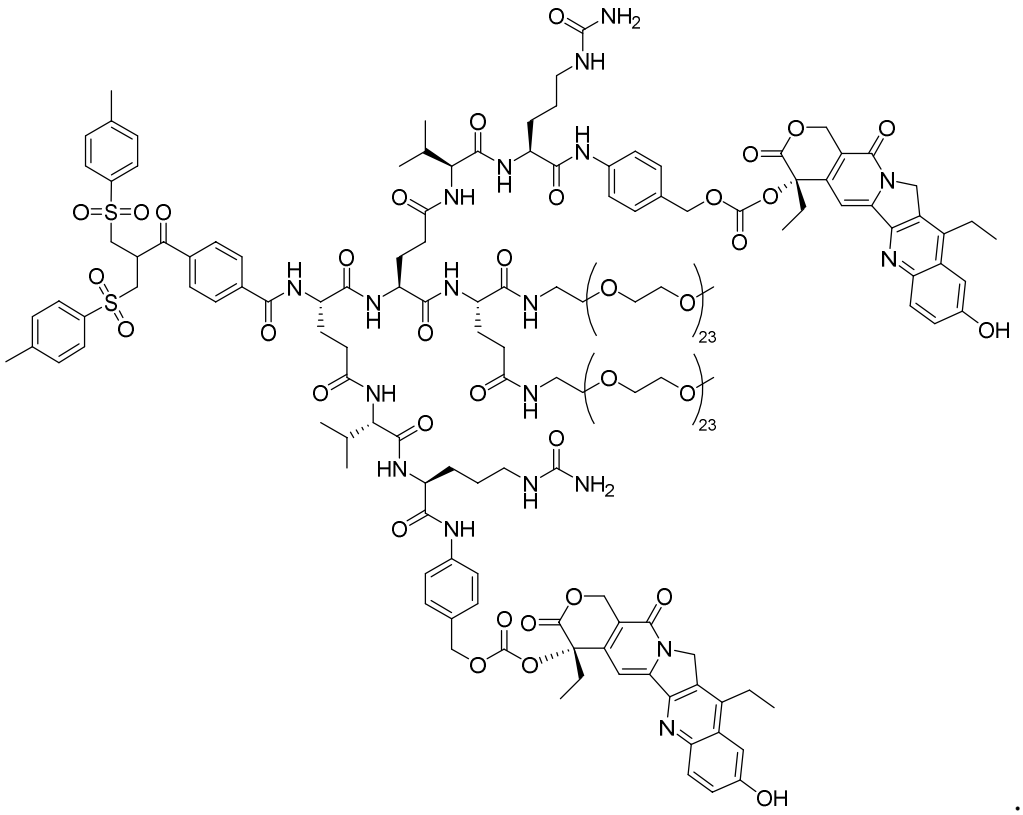


84. The immunoconjugate of any one of claims 69, 70, 75, 76, and 83 wherein the L-D

comprises the structure:



85. The immunoconjugate of any one of claims 69-72, 74 and 83, wherein the L-D comprises the structure:



86. The immunoconjugate of any one of claims 69-85, wherein the drug to antibody ratio is about 4.

87. The immunoconjugate of any one of claims 69-85, wherein the drug to antibody ratio is about 8.

88. A pharmaceutical composition comprising the antibody or antigen-binding fragment thereof of any one of claims 1-55 and a pharmaceutically acceptable carrier.

89. A pharmaceutical composition comprising the immunoconjugate of any one of claims 69-87 and a pharmaceutically acceptable carrier.

90. The antibody or antigen-binding fragment thereof of any one of claims 1-55 for use in the treatment, amelioration, and/or prevention of cancer in a subject in need thereof, wherein the cancer is associated with expression of EPH Receptor A5, wherein the EPH Receptor A5 is expressed on the cancer cells, and wherein the cancer is selected from the group consisting of lung cancer, breast cancer, esophageal cancer, gastric cancer, and ovarian cancer.

91. The immunoconjugate of any one of claims 69-87 for use in the treatment, amelioration, and/or prevention of cancer in a subject in need thereof, wherein the cancer is associated with expression of EPH Receptor A5, wherein the EPH Receptor A5 is expressed on the cancer cells, and wherein the cancer is selected from the group consisting of lung cancer, breast cancer, esophageal cancer, gastric cancer, and ovarian cancer.

92. The pharmaceutical composition of claim 88 for the use in treating, ameliorating, and/or preventing cancer in a subject in need thereof, wherein the cancer is associated with expression of EPH Receptor A5, wherein the EPH Receptor A5 is expressed on the cancer cells, and wherein the cancer is selected from the group consisting of lung cancer, breast cancer, esophageal cancer, gastric cancer, and ovarian cancer.

93. The pharmaceutical composition of claim 89 for use in treating, ameliorating, and/or preventing cancer in a subject in need thereof, wherein the cancer is associated with expression of EPH Receptor A5, wherein the EPH Receptor A5 is expressed on the cancer cells, and wherein the cancer is selected from the group consisting of lung cancer, breast cancer, esophageal cancer, gastric cancer, and ovarian cancer.

94. The antibody or antigen-binding fragment thereof of any one of claims 1-55 for use in inducing tumor regression in a subject, wherein the tumor is a cancer, wherein the tumor is associated with expression of EPH Receptor A5, wherein the EPH Receptor A5 is expressed on the cancer cells, and wherein the cancer is selected from the group consisting of lung cancer, breast cancer, esophageal cancer, gastric cancer, and ovarian cancer.

95. The immunoconjugate of any one of claim 69-87 for use in inducing tumor regression in a subject in need thereof, wherein the tumor is a cancer, wherein the tumor is associated with expression of EPH Receptor A5, wherein the EPH Receptor A5 is expressed on the cancer cells, and wherein the cancer is selected from the group consisting of lung cancer, breast cancer, esophageal cancer, gastric cancer, and ovarian cancer.

96. The pharmaceutical composition of claim 88 for use in inducing tumor regression in a subject in need thereof, wherein the tumor is a cancer, wherein the tumor is associated with expression of EPH Receptor A5, wherein the EPH Receptor A5 is expressed on the cancer cells, and wherein the cancer is selected from the group consisting of lung cancer, breast cancer, esophageal cancer, gastric cancer, and ovarian cancer.

97. The pharmaceutical composition of claim 89 for use in inducing tumor regression in a subject in need thereof, wherein the tumor is a cancer, wherein the tumor is associated with expression of EPH Receptor A5, wherein the EPH Receptor A5 is expressed on the cancer cells, and wherein the cancer is selected from the group consisting of lung cancer, breast cancer, esophageal cancer, gastric cancer, and ovarian cancer.

98. Use of the antibody or antigen-binding fragment thereof of any one of claims 1-55 in the manufacture of a medicament for the treatment, amelioration, and/or prevention of cancer in a subject in need thereof, wherein a therapeutically effective amount of the medicament is to be administered to the subject, wherein the cancer is associated with expression of EPH Receptor A5, wherein the EPH Receptor A5 is expressed on the

cancer cells, and wherein the cancer is selected from the group consisting of lung cancer, breast cancer, esophageal cancer, gastric cancer, and ovarian cancer.

99. Use of the immunoconjugate of any one of claims 69-87 in the manufacture of a medicament for the treatment, amelioration, and/or prevention of cancer in a subject in need thereof, wherein a therapeutically effective amount of the medicament is to be administered to the subject, wherein the cancer is associated with expression of EPH Receptor A5, wherein the EPH Receptor A5 is expressed on the cancer cells, and wherein the cancer is selected from the group consisting of lung cancer, breast cancer, esophageal cancer, gastric cancer, and ovarian cancer.

100. Use of the pharmaceutical composition of claim 88 in the manufacture of a medicament for the treatment, amelioration, and/or prevention of cancer in a subject in need thereof, wherein a therapeutically effective amount of the medicament is to be administered to the subject, wherein the cancer is associated with expression of EPH Receptor A5, wherein the EPH Receptor A5 is expressed on the cancer cells, and wherein the cancer is selected from the group consisting of lung cancer, breast cancer, esophageal cancer, gastric cancer, and ovarian cancer.

101. Use of the pharmaceutical composition of claim 89 in the manufacture of a medicament for the treatment, amelioration, and/or prevention of cancer in a subject in need thereof, wherein a therapeutically effective amount of the medicament is to be administered to the subject, wherein the cancer is associated with expression of EPH Receptor A5, wherein the EPH Receptor A5 is expressed on the cancer cells, and wherein the cancer is selected from the group consisting of lung cancer, breast cancer, esophageal cancer, gastric cancer, and ovarian cancer.

102. Use of the antibody or antigen-binding fragment thereof of any one of claims 1-55 in the manufacture of a medicament for use in a method of inducing tumor regression in a subject in need thereof, wherein a therapeutically effective amount of the medicament is to be administered to the subject, wherein the tumor is a cancer, wherein the tumor is

associated with expression of EPH Receptor A5, wherein the EPH Receptor A5 is expressed on the cancer cells, and wherein the cancer is selected from the group consisting of lung cancer, breast cancer, esophageal cancer, gastric cancer, and ovarian cancer.

103. Use of the immunoconjugate of any one of claim 69-87 in the manufacture of a medicament for use in a method of inducing tumor regression in a subject in need thereof, wherein a therapeutically effective amount of the medicament is to be administered to the subject, wherein the tumor is a cancer, wherein the tumor is associated with expression of EPH Receptor A5, wherein the EPH Receptor A5 is expressed on the cancer cells, and wherein the cancer is selected from the group consisting of lung cancer, breast cancer, esophageal cancer, gastric cancer, and ovarian cancer.

104. Use of the pharmaceutical composition of claim 88 in the manufacture of a medicament for use in a method of inducing tumor regression in a subject in need thereof, wherein a therapeutically effective amount of the medicament is to be administered to the subject, wherein the tumor is a cancer, wherein the tumor is associated with expression of EPH Receptor A5, wherein the EPH Receptor A5 is expressed on the cancer cells, and wherein the cancer is selected from the group consisting of lung cancer, breast cancer, esophageal cancer, gastric cancer, and ovarian cancer.

105. Use of the pharmaceutical composition of claim 89 in the manufacture of a medicament for use in a method of inducing tumor regression in a subject in need thereof, wherein a therapeutically effective amount of the medicament is to be administered to the subject, wherein the tumor is a cancer, wherein the tumor is associated with expression of EPH Receptor A5, wherein the EPH Receptor A5 is expressed on the cancer cells, and wherein the cancer is selected from the group consisting of lung cancer, breast cancer, esophageal cancer, gastric cancer, and ovarian cancer.