cell membranes in endosomes, allowing the release of the ribonucleoprotein complex into the cytoplasm.

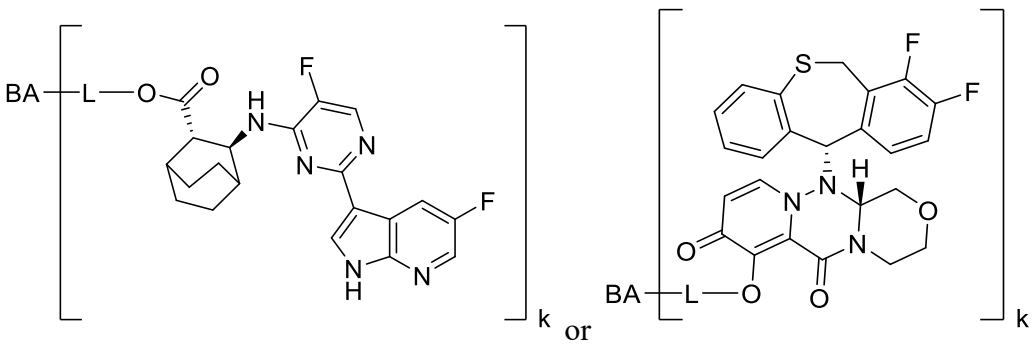
[0007] Currently, there are eighteen subtypes defined by their hemagglutinin proteins (H1 -H18). The eighteen HAs can be classified into two groups. Group 1 consists of H1, H2, H5, H6, H8, H9, H11, H12, H13, H16, H17, and H18 subtypes, and group 2 includes H3, H4, H7, H10, H14, and H15 subtypes.

[0008] Despite decades of research, there are no marketed antibodies or antibody-drug conjugates (ADCs) that broadly neutralize or inhibit influenza A virus infection or attenuate disease caused by influenza A virus. Therefore, there is a need to identify new antibodies and ADCs that neutralize multiple subtypes of influenza A virus and can be used as medicaments for prevention or therapy of influenza A infection.

SUMMARY

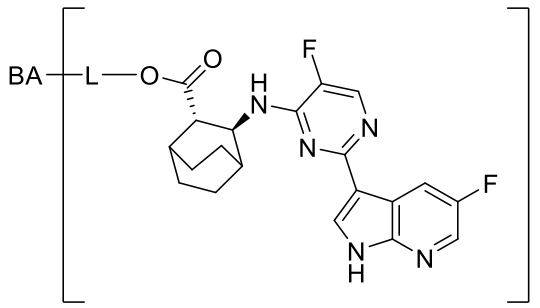
[0009] Provided herein are compounds useful, for example, in antiviral treatments. In certain examples, the compounds include VX-787 and derivatives thereof, baloxavir and derivatives thereof, and/or baloxavir marboxil and derivatives thereof. In one example, provided is an antibody-drug conjugate including an anti-influenza antibody or antigen-binding fragment thereof conjugated to a payload (e.g., an antiviral compound), linker-payload (e.g., linker-antiviral compound), and/or compound as described herein.

[0010] Provided herein are compounds having the following structure

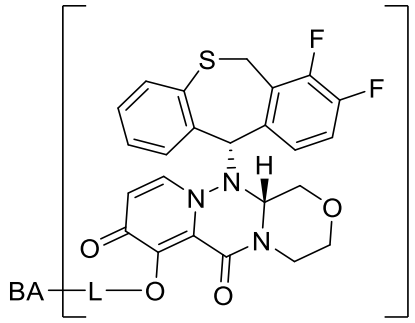


wherein **L** is a linker; **BA** is a binding agent; and **k** is an integer from one to thirty.

[0010a] In one aspect, provided herein is a compound selected from the group consisting of:



k and



k wherein

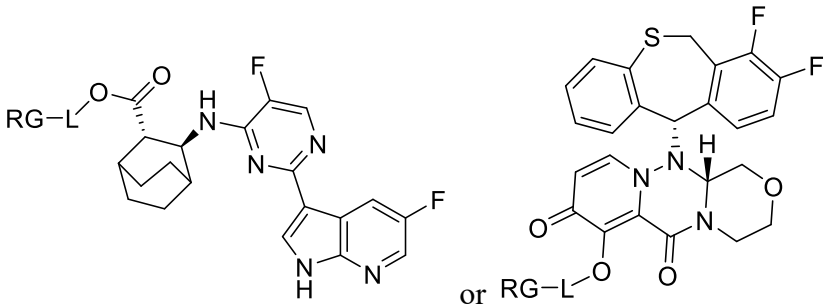
L is a linker;

BA is a binding agent,

wherein the binding agent is an antibody or an antigen binding fragment thereof; and

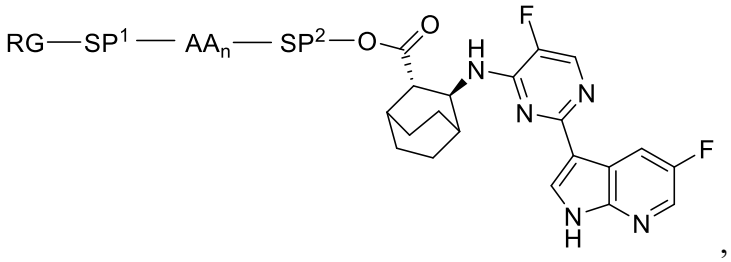
k is an integer from one to thirty.

[0011] There is also provided linker-payloads (e.g., linker-antiviral compounds) having the following structure

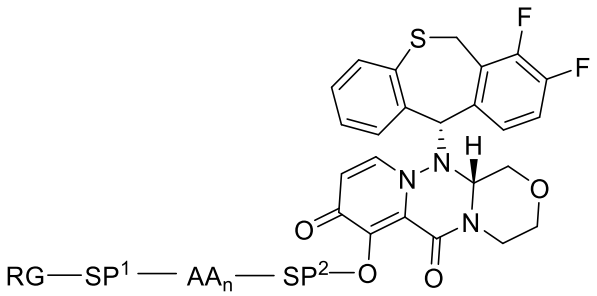


or a pharmaceutically acceptable salt thereof, wherein **L** is a linker; and **RG** is a reactive moiety.

[0011a] In another aspect, provided herein is **a** linker-payload compound selected from:



,



, or a pharmaceutically acceptable salt thereof, wherein

SP^1 and **SP^2**, when present, are spacer groups;

RG is a moiety reactive with an antibody or an antigen binding fragment thereof;

each **AA** is an amino acid; and

n is an integer from one to ten.

[0011b] In another aspect, provided herein is an antibody-drug conjugate comprising an antibody, or an antigen binding fragment thereof, where the antibody or antigen binding fragment thereof is conjugated to the linker-payload compound as defined herein.

[0012] In another example, set forth herein are methods for making the payloads or compounds, linker-payloads, or antibody-drug conjugates, and compositions described herein.

[0012a] In another aspect, provided herein is a method of preparing an antibody-drug conjugate comprising contacting a binding agent with a linker-payload compound as defined herein.

[0013] In another example, provided herein are methods for the treatment, prophylaxis, reduction, or inhibition of a disease, disorder, or condition associated with an infection, as described herein, in a subject including administering to the subject an effective amount of a payload (e.g., antiviral compound), linker-payload (e.g., linker-antiviral compound), antibody-drug conjugate, or pharmaceutical composition as described herein.

[0013a] In another aspect, provided herein is a pharmaceutical composition comprising the compound as defined herein, and a pharmaceutically acceptable excipient, carrier, or diluent.

[0013b] In another aspect, provided herein is the compound as defined herein, or the pharmaceutical composition as defined herein for use in the treatment, prophylaxis, reduction, or inhibition of a disease, disorder, or condition associated with an infection.

[0013a] In another aspect, provided herein is a pharmaceutical composition comprising the compound as defined herein, and a pharmaceutically acceptable excipient, carrier, or diluent.

[0013b] In another aspect, provided herein is the compound as defined herein, or the pharmaceutical composition as defined herein for use in the treatment, prophylaxis, reduction, or inhibition of a disease, disorder, or condition associated with an infection.

[0013c] In another aspect, provided herein is use of the compound as defined herein, or the pharmaceutical composition as defined herein in the manufacture of a medicament for the treatment, prophylaxis, reduction, or inhibition of an influenza infection.

BRIEF DESCRIPTIONS OF THE DRAWINGS

[0014] FIG. 1A shows the intensity-weighted average linker-payload (e.g., linker-antiviral compound) loadings as measured by LC-MS for 11729-Q295-**11**. FIG. 1B shows the intensity-weighted average linker-payload (e.g., linker-antiviral compound) loadings as measured by LC-MS for Isotype Control-Q295-**11**.

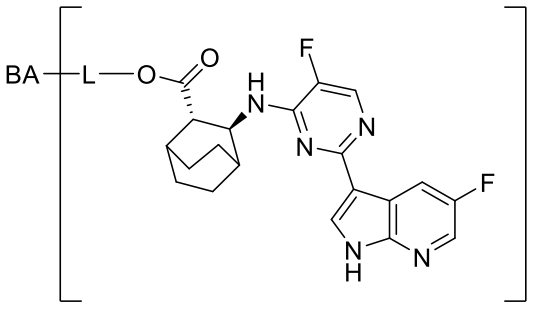
[0015] FIG. 2A shows the intensity-weighted average linker-payload (e.g., linker-antiviral compound) loadings as measured by LC-MS for 11729-HC-Cterm-**11**. FIG. 2B shows the intensity-weighted average linker-payload (e.g., linker-antiviral compound) loadings as measured by LC-MS for Isotype Control-HC-Cterm-**11**.

[0016] FIG. 3 shows ELISA sub-nanomolar specific binding of 11729-HC-Cterm-**11,** 11729-HC-Nterm-**11,** 11729-LC-Cterm-**11**, and 11729-LC-Nterm-**11** to influenza A-infected cells.

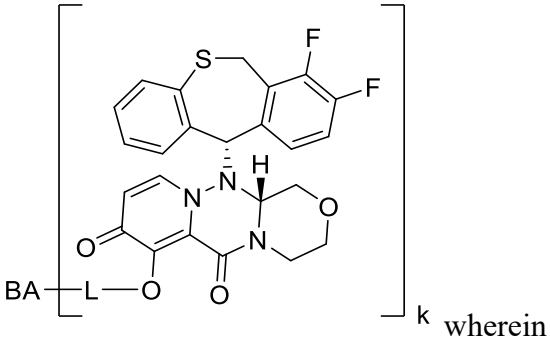
[0017] FIG. 4 shows comparative antiviral efficacy against influenza A infection between 11729-HC-Cterm-**11**, 11729-LC-Cterm-**11**, 11729-LC-Nterm-**11**, mAb11729, and an isotype control antibody and Isotype Control-HC-Cterm-**11**.

WHAT IS CLAIMED IS:

1. A compound selected from the group consisting of:



and



wherein

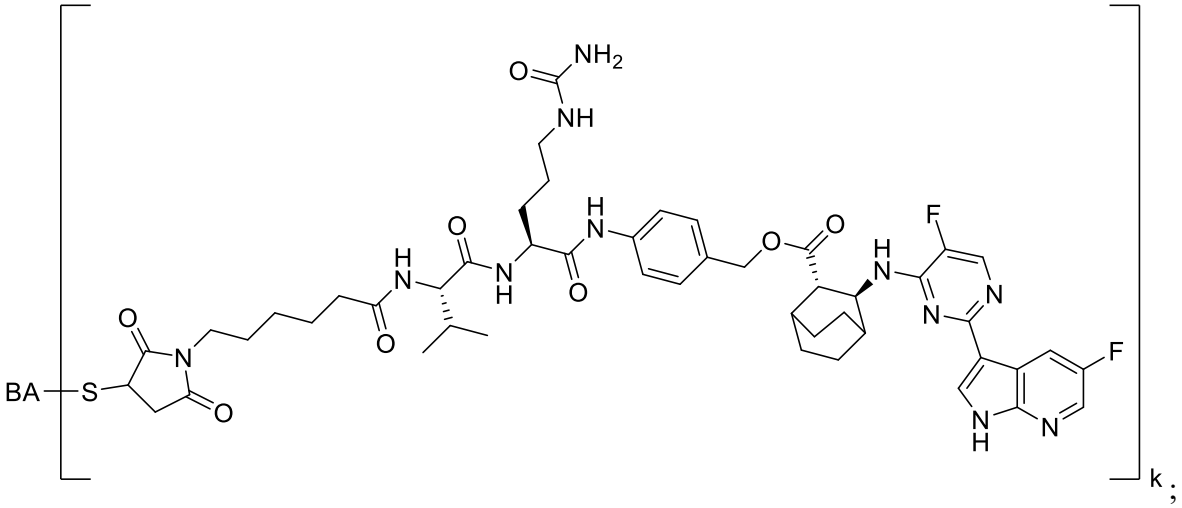
L is a linker;

BA is a binding agent,

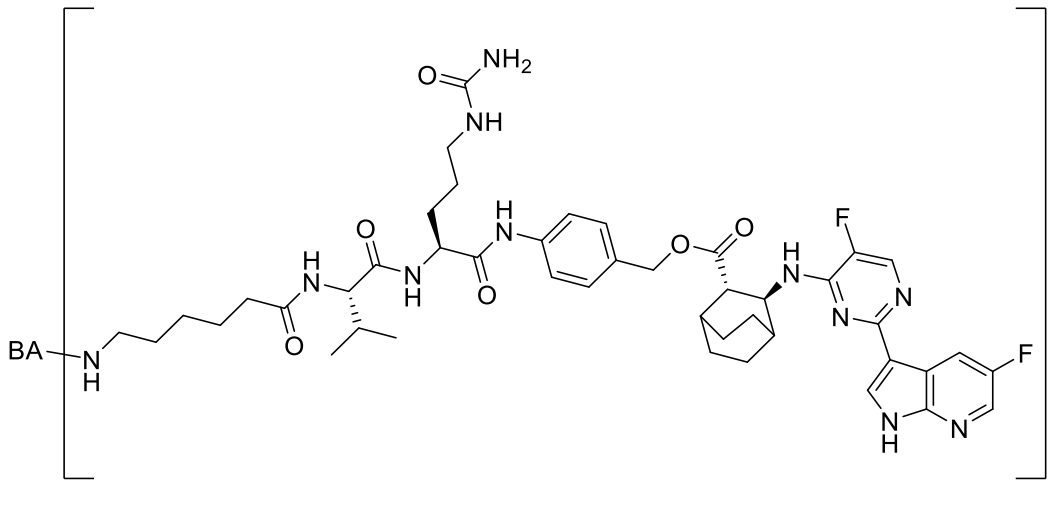
wherein the binding agent is an antibody or an antigen binding fragment thereof; and

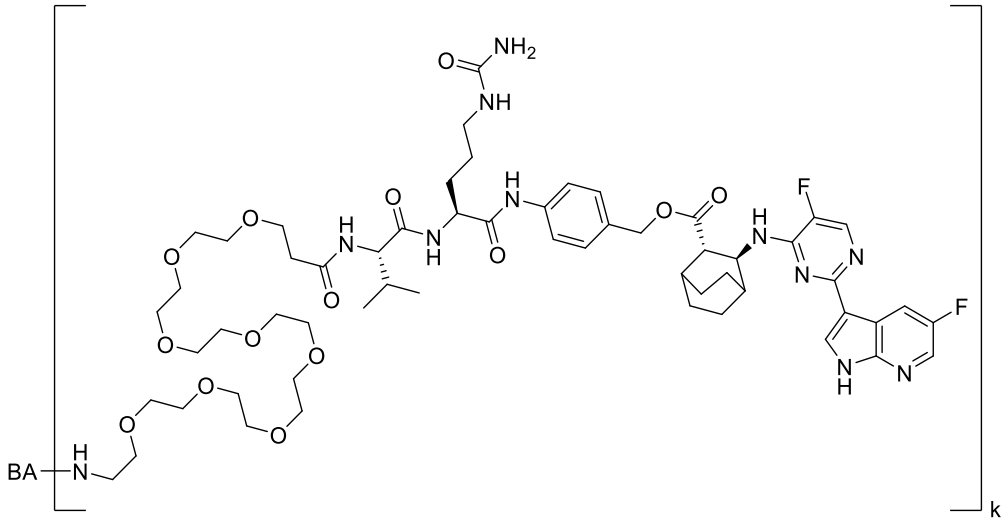
k is an integer from one to thirty.

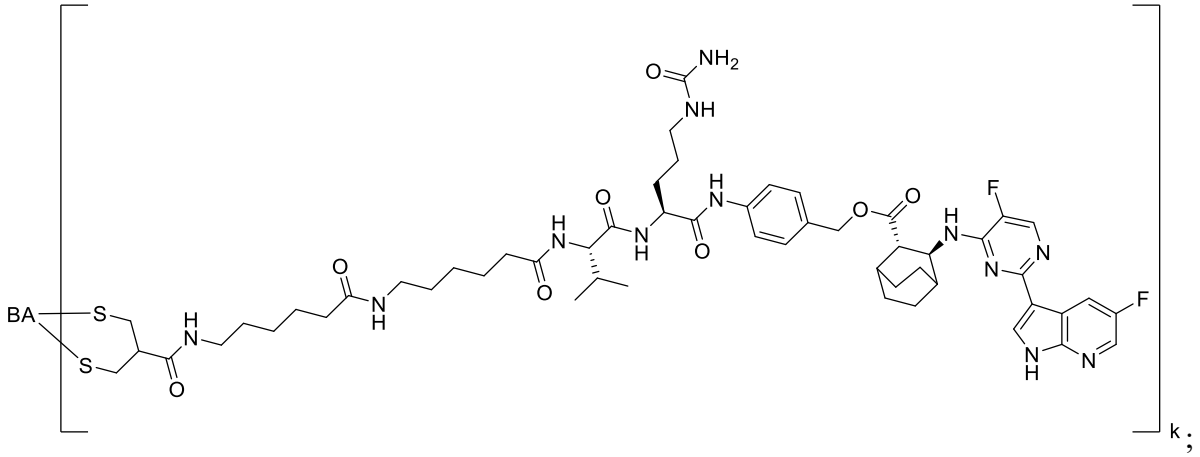
2. The compound of claim 1, selected from the group consisting of



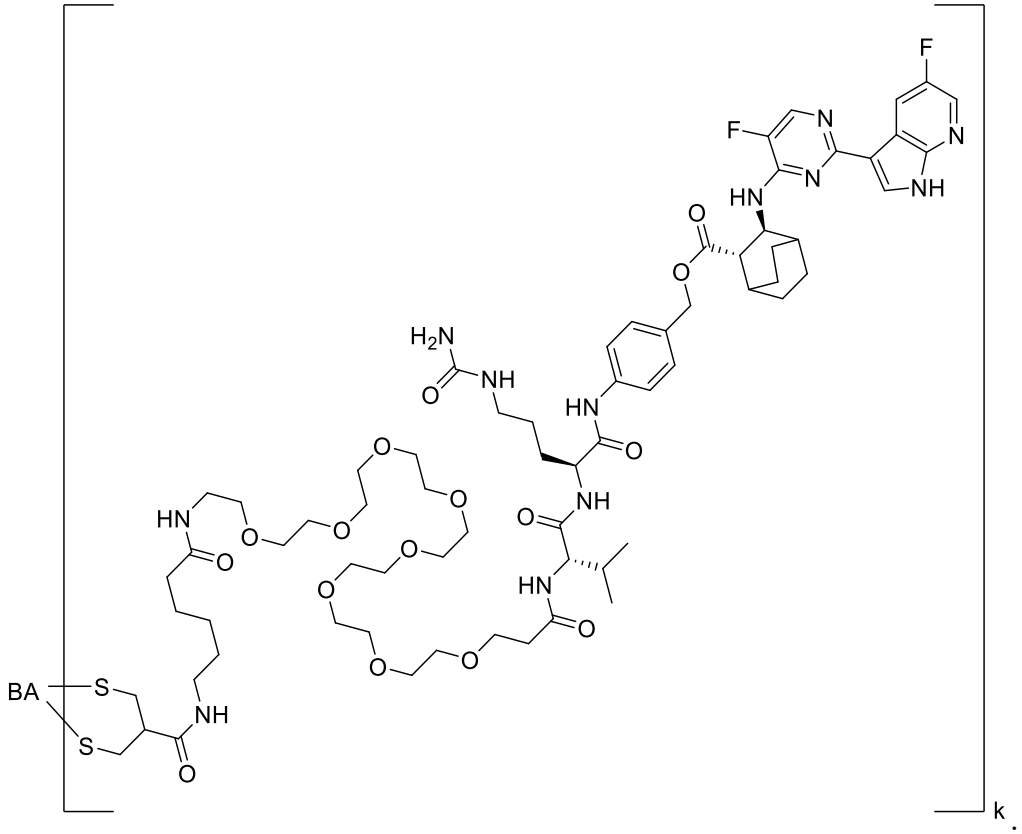
;







and



3. The compound of any of the preceding claims, wherein **BA** is a transglutaminase-modified antibody or antigen-binding fragment thereof comprising at least one glutamine residue used for conjugation.

4. The compound of any of the preceding claims, wherein **BA** is a transglutaminase-modified antibody or antigen-binding fragment thereof comprising at least two glutamine residues used for conjugation.

5. The compound of any of the preceding claims, wherein **BA** is a transglutaminase-modified antibody or antigen-binding fragment thereof comprising at least three glutamine residues used for conjugation.

6. The compound of any of the preceding claims, wherein **BA** is a transglutaminase-modified antibody or antigen-binding fragment thereof comprising at least four glutamine residues available for conjugation.

7. The compound of claim 6, wherein **BA** is a transglutaminase-modified antibody or antigen-binding fragment thereof, wherein conjugation is at two Q295 residues in the EU numbering system; and **k** is two.

8. The compound of claim 6, wherein **BA** is a transglutaminase-modified antibody or antigen-binding fragment thereof comprising an antibody heavy chain, wherein conjugation is at the C-terminus of the heavy chain; and **k** is two.

9. The compound of claim 8, wherein the conjugation is via a glutamine.

10. The compound of claim 8, wherein conjugation is via a glutamine in a LLQGA (SEQ ID NO: 297) sequence at the C-terminus of the antibody heavy chain.

11. The compound of claim 6, wherein conjugation is at two Q295 residues and two N297Q residues; and **k** is 4.

12. The compound of any of the preceding claims, wherein **BA** is mAb11729.

13. A pharmaceutical composition comprising the compound of any preceding claim, and a pharmaceutically acceptable excipient, carrier, or diluent.

14. The pharmaceutical composition of claim 13, wherein the pharmaceutical composition is formulated for an administration selected from the group consisting of oral, intravenous, intraperitoneal, inhalation, and intranasal.

15. The compound of any one of claims 1 to 12 or the pharmaceutical composition of claim 13 or 14 for use in the treatment, prophylaxis, reduction, or inhibition of a disease, disorder, or condition associated with an infection.

16. The compound or pharmaceutical composition for use of claim 15, wherein the infection is a viral infection.

17. The compound or pharmaceutical composition for use of claim 16, wherein the infection is influenza virus infection.

18. The compound or pharmaceutical composition for use of claim 16, wherein the infection is influenza A virus infection.

19. The compound or pharmaceutical composition for use of claim 16, wherein the infection is influenza B virus.

20. The compound or pharmaceutical composition for use of claim 16, wherein the infection is influenza A virus infection and influenza B virus infection.

21. The compound or pharmaceutical composition for use of any one of claims 15-20, wherein side effects of the compound or pharmaceutical composition are reduced when compared to administration of the unconjugated antiviral compound to a comparable subject.

22. Use of the compound of any one of claims 1 to 12 or the pharmaceutical composition of claim 13 or 14 in the manufacture of a medicament for the treatment, prophylaxis, reduction, or inhibition of an influenza infection.

23. The use of claim 22, wherein the influenza infection is caused by influenza A virus infection.

24. The use of claim 22, wherein the influenza infection is caused by an influenza A Group 1 virus.

25. The use of claim 22, wherein the influenza infection is caused by an influenza A H1 virus.

26. The use of claim 22, wherein the influenza infection is caused by an influenza A Group 2 virus.

27. The use of claim 22, wherein the influenza infection is caused by an influenza A H3 virus.

28. The use of claim 22, wherein the influenza infection is caused by an unknown or undetermined influenza virus.

29. The use of claim 22, wherein the influenza infection is caused by influenza B virus infection.

30. The use of claim 22, wherein the influenza infection is caused by influenza A virus infection and influenza B virus infection.

31. The use of any one of claims 22-30, wherein the compound or pharmaceutical composition is to be administered in combination with a supplementary therapeutic agent.

32. The use of claim 31, wherein the supplementary therapeutic is selected from the group consisting of an anti-viral drug, an anti-inflammatory drug, an antibody that binds specifically to influenza HA, a vaccine for influenza, a dietary supplement, and a palliative therapy to treat an influenza infection.

33. The use of claim 32, wherein the anti-inflammatory drug is selected from the group consisting of corticosteroids and non-steroidal anti-inflammatory drugs.

34. The use of claim 33, wherein the dietary supplement is an anti-oxidant.

35. The use of any one of claims 31-34, wherein the supplementary therapeutic agent is to be administered via a different route of administration as the compound or pharmaceutical composition.

36. The use of any one of claims 31-35, wherein the supplementary therapeutic agent is to be administered orally.

37. The use of claim 32, wherein the anti-viral drug is oseltamivir.

38. The use of claim 37, wherein the oseltamivir is to be administered prior to administration of the compound or pharmaceutical composition.

39. The use of claim 37, wherein the oseltamivir is to be administered concurrently with the compound or pharmaceutical composition.

40. The use of claim 37, wherein the oseltamivir is to be administered after administration of the compound or pharmaceutical composition.

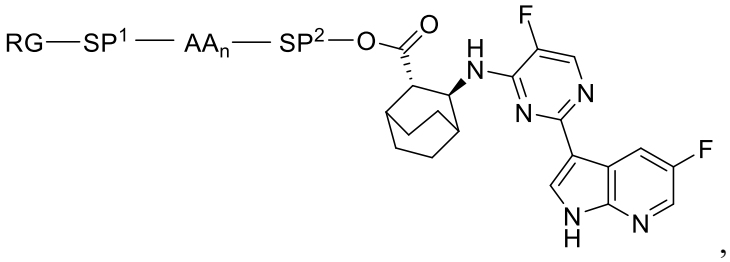
41. The use of claim 32, wherein the anti-viral drug is an anti-influenza A drug or an anti-influenza B drug.

42. The use of claim 41, wherein the anti-influenza A drug or the anti-influenza B drug is an antibody or antigen-binding portion thereof.

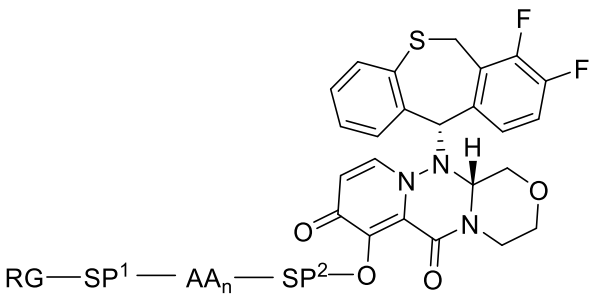
43. The use of claim 42, wherein the antibody binds specifically to influenza A HA or to influenza B HA.

44. The use of any one of claims 15-43, wherein the compound or pharmaceutical composition is to be administered subcutaneously, intravenously, intradermally, intramuscularly, intranasally, or orally.

45. A linker-payload compound selected from:



,

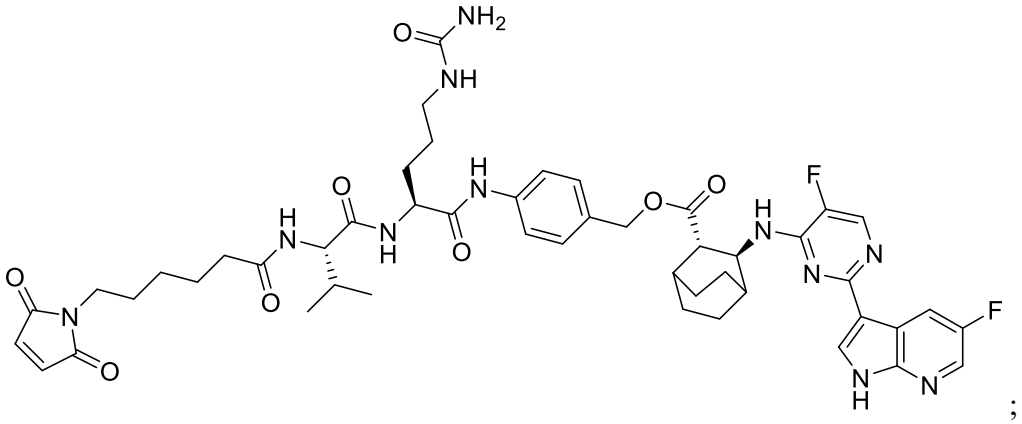


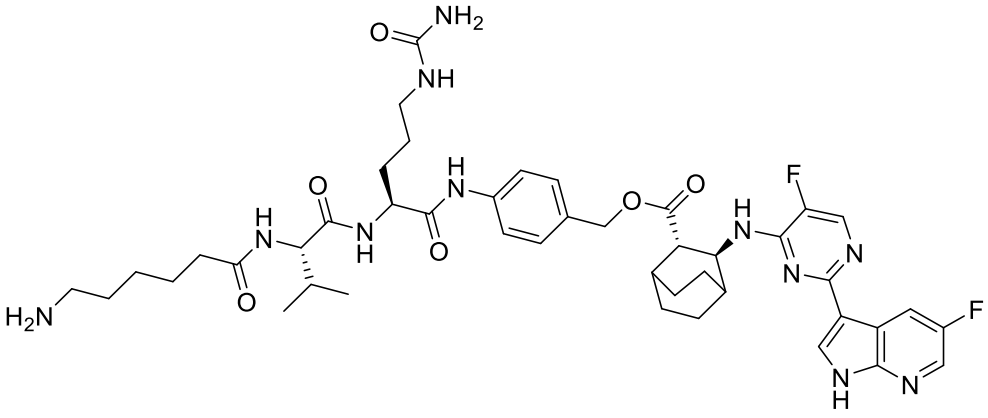
, or a pharmaceutically acceptable salt thereof, wherein

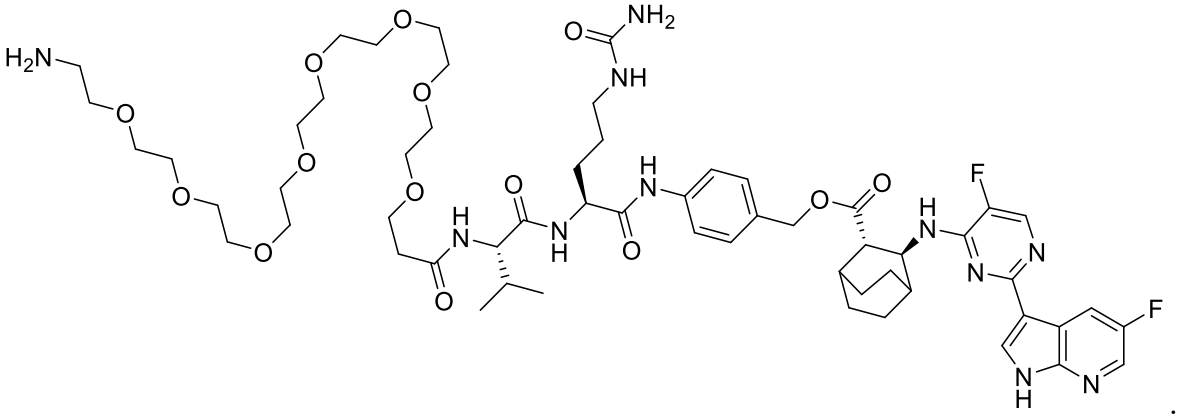
SP1 and **SP2**, when present, are spacer groups;

RG is a moiety reactive with an antibody or an antigen binding fragment thereof;
each **AA** is an amino acid; and
n is an integer from one to ten.

46. The linker-payload of claim 45, selected from the group consisting of

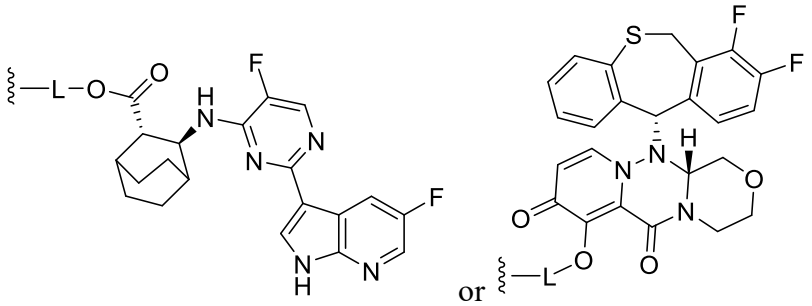

;


; and


.

47. An antibody-drug conjugate comprising an antibody, or an antigen binding fragment thereof, where the antibody or antigen binding fragment thereof is conjugated to the linker-payload compound of claim 45.

48. The antibody-drug conjugate of claim 47, wherein the conjugated compound is selected from



or

wherein **L** is a linker.

49. A method of preparing an antibody-drug conjugate comprising contacting a binding agent with a linker-payload compound of claim 45.

50. The compound of any one of claims 1-12, wherein **BA** is an anti-influenza A antibody or an antigen binding fragment thereof.

51. The compound of any one of claims 1-12, wherein **BA** is an anti-influenza A Group 1 antibody or an antigen binding fragment thereof.

52. The compound of any one of claims 1-12, wherein **BA** is an anti-influenza H1 antibody or an antigen binding fragment thereof.

53. The compound of any one of claims 1-12, wherein **BA** is an anti-influenza A Group 2 antibody or an antigen binding fragment thereof.

54. The compound of any one of claims 1-12, wherein **BA** is an anti-influenza H3 antibody or an antigen binding fragment thereof.

55. The compound of any one of claims 1-12, wherein **BA** is an anti-influenza B antibody or an antigen binding fragment thereof.

56. The compound of any one of claims 1-12, wherein the compound comprises an antibody heavy chain and further comprises a pentapeptide at the C-terminus of the antibody heavy chain.

57. The compound of claim 56, wherein the pentapeptide comprises the amino acid sequence LLQGA (SEQ ID NO: 297).

58. The compound of any one of claims 1-12, wherein the antibody or antigen binding fragment thereof comprises a LCVR further comprising an amino acid sequence set forth in SEQ ID NO: 26; and a HCVR further comprising an amino acid sequence set forth in SEQ ID NO: 18 .

59. The compound of any one of claims 1-12, wherein BA is an antibody or antigen binding fragment thereof comprising:

(a) a HCDR1 that comprises an amino acid sequence set forth in SEQ ID NO: 20;

(b) a HCDR2 that comprises an amino acid sequence set forth in SEQ ID NO: 22;

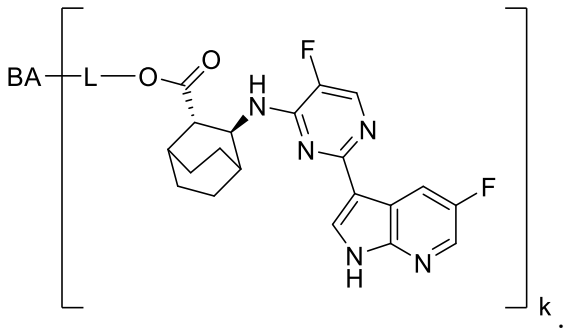
(c) a HCDR3 that comprises an amino acid sequence set forth in SEQ ID NO: 24;

(d) a LCDR1 that comprises an amino acid sequence set forth in SEQ ID NO: 28;

(e) a LCDR2 that comprises an amino acid sequence set forth in SEQ ID NO: 30; and

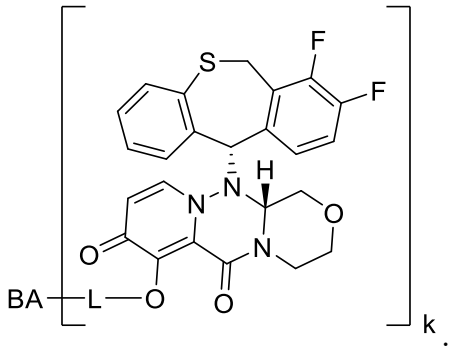
(f) a LCDR3 that comprises an amino acid sequence set forth in SEQ ID NO: 32 .

60. The compound of claim 1, that is:



.

61. The compound of claim 1, that is:



62. The compound of claim 1, wherein **BA** is an antiviral antibody or antigen binding fragment thereof.

63. The compound of claim 1, wherein **BA** is an anti-influenza antibody or antigen binding fragment thereof.

64. The compound of claim 1, wherein the antibody or antigen-binding fragment thereof is a transglutaminase-modified antibody or antigen-binding fragment thereof.

65. The compound of claim 1, wherein the antibody or antigen-binding fragment thereof is an anti-influenza antibody or antigen-binding fragment thereof.