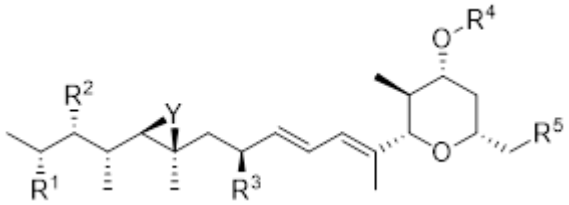
CLAIMS

1. A splicing modulator which is a compound of the following formula:



, or a pharmaceutically acceptable salt thereof, wherein:

Y is O;

R^1, R^2, and R^3 are each independently chosen from hydrogen, hydroxyl, -O-(C_1-C_6 alkyl) groups, -O-C(=O)-(C_1-C_6 alkyl) groups, -C(=O)-O-(C_1-C_6 alkyl) groups, and C_1-C_6 alkyl groups;

R^4 is chosen from C_1-C_6 alkyl groups, -C(=O)-(C_1-C_6 alkyl) groups, -C(=O)-(C_3-C_8 carbocyclyl) groups, -C(=O)-(C_3-C_8 heterocyclyl) groups, and -C(=O)-NR^6R^7;

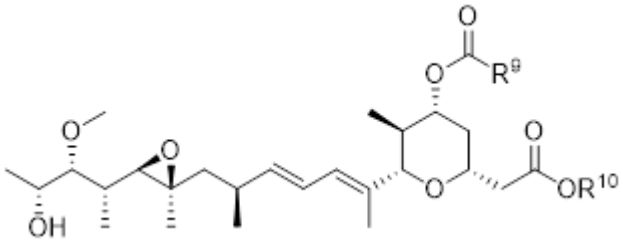
R^5 is chosen from hydrogen, hydroxyl, -CH_2-OH, -CO_2H, -C(=O)-O-(C_1-C_6 alkyl) groups, -C(=O)-NR^6R^7, -NR^6-C(=O)-R^8, -O-C(=O)-NR^6R^7, -NR^6-C(=O)-R^8, and -NR^6-C(=O)-NR^6R^7;

R^6 and R^7 are each independently chosen from hydrogen, -R^8, -C(=O)-R^8, and -C(=O)-O-R^8; and

R^8 is chosen from C_1-C_6 alkyl groups, C_3-C_8 carbocyclyl groups, and C_3-C_8 heterocyclyl groups,

wherein R^1, R^2, R^3, R^4, R^5, R^6, R^7, and R^8 are each independently substituted with 0 to 3 groups independently chosen from halogens, hydroxyl, C_1-C_6 alkyl groups, -O-(C_1-C_6 alkyl) groups, -CO_2H, -C(=O)-(C_1-C_6 alkyl) groups, -C(=O)-(C_3-C_8 carbocyclyl) groups, -C(=O)-(C_3-C_8 heterocyclyl) groups, -NR^6R^7, C_3-C_8 carbocyclyl groups, C_1-C_6 alkylhydroxy groups, C_1-C_6 alkylalkoxy groups, benzyl groups, and C_3-C_8 heterocyclyl groups, each of which may be independently substituted with 0 or 1 group chosen from halogens, hydroxyl, C_1-C_3 alkyl groups, C_1-C_3 alkoxy groups, C_1-C_3 haloalkyl groups, -NH-C(=O)(C_1-C_3 alkyl), and -NH-C(=O)-O-(C_1-C_3 alkyl).

2. The splicing modulator of claim 1, wherein the compound is of the following formula:



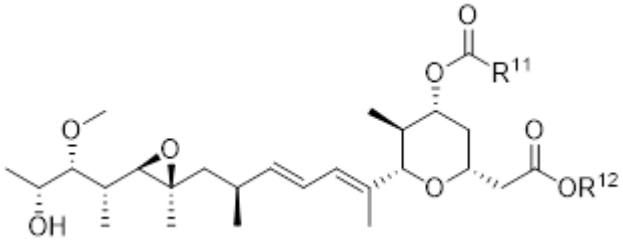
, or a pharmaceutically acceptable salt thereof, wherein:

R^9 is chosen from C_3-C_8 heterocyclyl groups; and

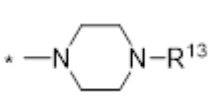
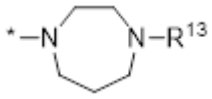
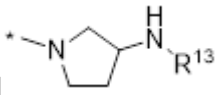
R^{10} is chosen from H and C_1-C_6 alkyl groups,

wherein R^9 and R^{10} are each independently substituted with 0 to 3 groups independently chosen from halogens, hydroxyl, C_1-C_3 alkyl groups, C_1-C_3 alkoxy groups, $-NH_2$, -NH-(C_1-C_3 alkyl), and -N-(C_1-C_3 alkyl)$_2$.

3. The splicing modulator of claim 1 or 2, wherein the compound is of the following formula:

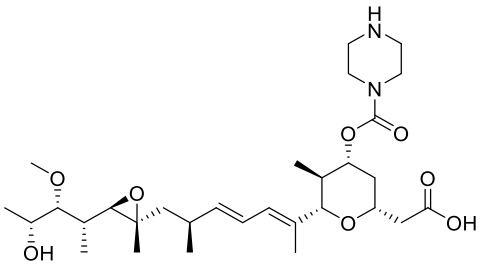
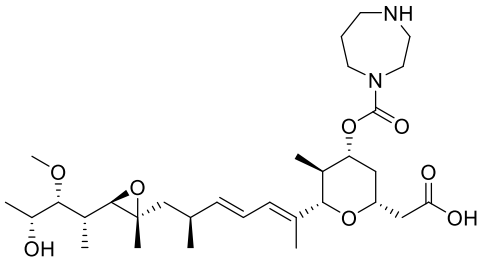


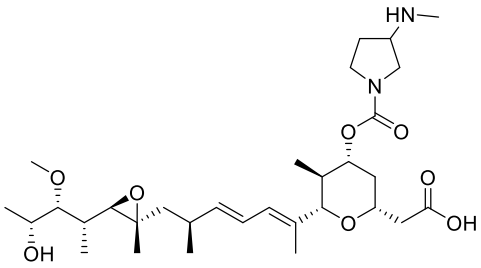
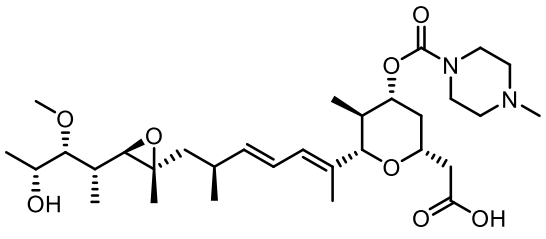
, or a pharmaceutically acceptable salt thereof, wherein:

R^{11} is chosen from , , and ,

wherein * denotes the point of connectivity of R^{11} to the remainder of the compound; and R^{12} and R^{13} are each independently chosen from H and methyl.

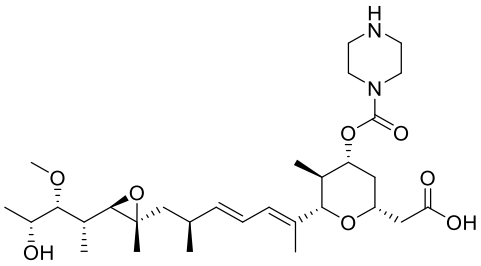
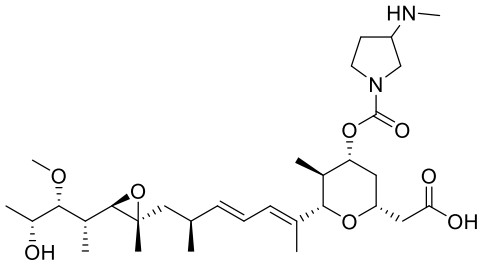
4. The splicing modulator of any one of claims 1 to 3, wherein the compound is selected from

 (H1),  (H2),

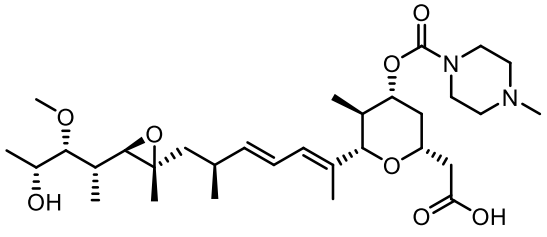
 (H3),  (H12),

and pharmaceutically acceptable salts thereof.

5. The splicing modulator of any one of claims 1 to 3, wherein the compound is

 (H1),  (H3), or a pharmaceutically acceptable salt thereof.

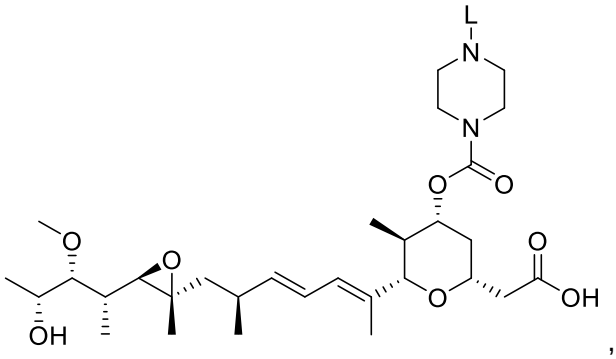
6. The splicing modulator of any one of claims 1 to 3, wherein the compound is

 (H12) or a pharmaceutically acceptable salt thereof.

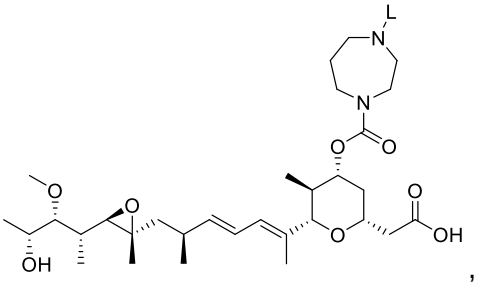
7. A compound which is a linker-payload of formula L-H, wherein L is a linker, and wherein H is a splicing modulator of any one of claims 1-6 or a pharmaceutically acceptable salt thereof.

8. The compound of claim 7, wherein H is covalently attached through any atom to L and the valency of the atom that is covalently attached to L is not exceeded.

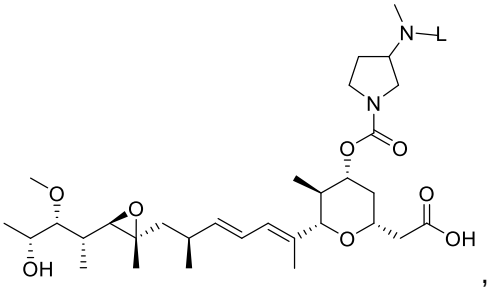
9. The compound of claim 7 or claim 8, wherein the linker-payload of formula L-H is selected from:



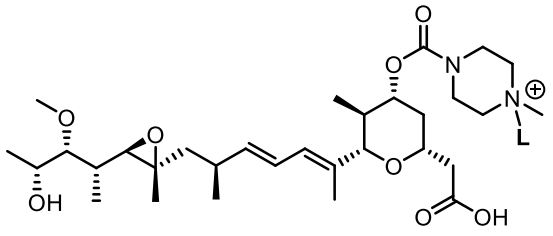
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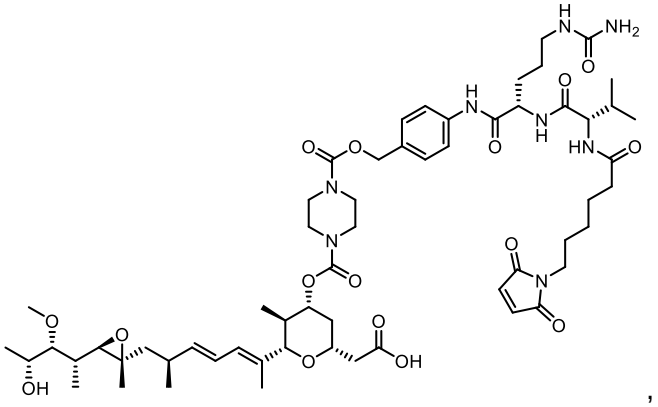


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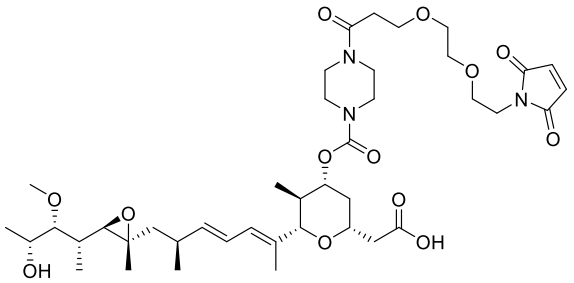


, and pharmaceutically acceptable salts thereof.

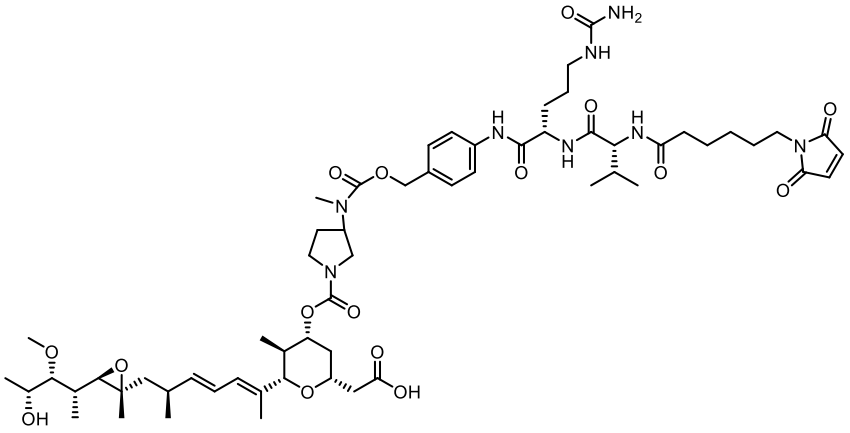
10. The compound of claim 7, wherein the linker-payload of formula L-H is selected from:



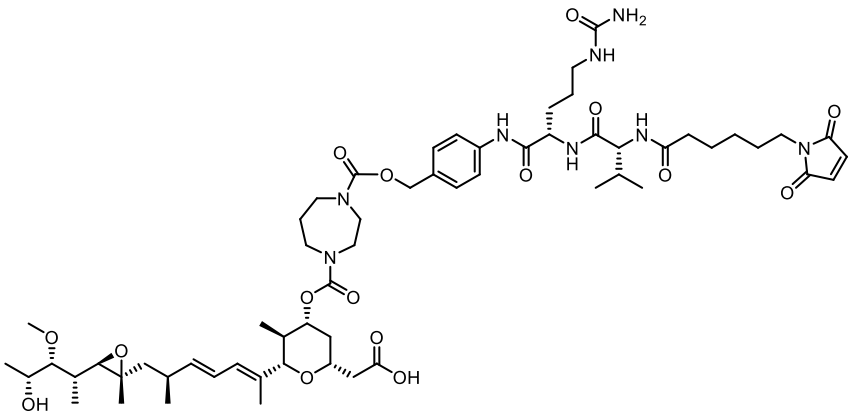
,



,



,



,

and pharmaceutically acceptable salts thereof.

11. The compound of any one of claims 7-10, wherein the linker is a cleavable linker comprising a cleavable moiety; and wherein the cleavable moiety comprises:
(i) a cleavable peptide; optionally wherein the cleavable peptide comprises valine-citrulline (Val-Cit), valine-alanine (Val-Ala), glutamic acid-valine-citrulline (Glu-Val-Cit), or alanine-alanine-asparagine (Ala-Ala-Asn); or
(ii) a cleavable glucuronide moiety; optionally wherein the cleavable glucuronide moiety is cleavable by an enzyme; optionally wherein the cleavable glucuronide moiety is cleavable by a glucuronidase; optionally wherein the cleavable glucuronide moiety is cleavable by β-glucuronidase.

12. The compound of claim 11, wherein the linker comprises a maleimide (Mal) moiety.

13. The compound of claim 12, wherein the Mal moiety comprises a maleimidocaproyl (MC).

14. The compound of claim 13, wherein the linker comprises MC-Val-Cit, MC-Val-Ala, MC-Glu-Val-Cit, or MC-Ala-Ala-Asn.

15. The compound of any one of claims 11-14, wherein the linker comprises at least one spacer unit, wherein either:

(i) the spacer unit comprises a polyethylene glycol (PEG) moiety, optionally wherein the PEG moiety comprises -$(PEG)_m$- and *m* is an integer from 1 to 10, optionally wherein *m* is 2; or

(ii) the spacer unit comprises an alkyl moiety, optionally wherein the alkyl moiety comprises -$(CH_2)_n$- and *n* is an integer from 1 to 10, optionally wherein *n* is 2, 5 or 6.

16. The compound of any one of claims 11-15, wherein the cleavable moiety in the linker is directly attached to the splicing modulator.

17. The compound of any one of claims 11-15, wherein a spacer unit attaches the cleavable moiety in the linker to the splicing modulator.

18. The compound of claim 17, wherein the spacer unit attaching the cleavable moiety to the splicing modulator is self-immolative.

19. The compound of claim 17, wherein the spacer unit attaching the cleavable moiety in the linker to the splicing modulator comprises a p-aminobenzyl (pAB) or a p-aminobenzyloxycarbonyl (pABC).

20. The compound of claim 19, wherein the linker comprises Val-Cit-pAB, Val-Ala-pAB, Glu-Val-Cit-pAB, Ala-Ala-Asn-pAB, Val-Cit-pABC, Val-Ala-pABC, Glu-Val-Cit-pABC, or Ala-Ala-Asn-pABC.

21. The compound of claim 20, wherein the linker comprises MC-Val-Cit-pAB, MC-Val-Ala-pAB, MC-Glu-Val-Cit-pAB, MC-Ala-Ala-Asn-pAB, MC-Val-Cit-pABC, MC-Val-Ala-pABC, MC-Glu-Val-Cit-pABC, or MC-Ala-Ala-Asn-pABC.

22. An antibody-drug conjugate of Formula (I):

$Ab-(L-H)_p$ (I)

wherein:

Ab is an antibody or antigen binding fragment which targets a neoplastic cell;

L-H is the linker-payload defined in any one of claims 7-21; and

p is an integer from 1 to 15.

23. The antibody-drug conjugate of claim 22, wherein the neoplastic cell is derived from:

(i) a hematological malignancy; optionally wherein the hematological malignancy is selected from a B-cell malignancy, a leukemia, a lymphoma, a myeloma, acute myeloid leukemia, and multiple myeloma; or

(ii) a solid tumor; optionally wherein the solid tumor is selected from breast cancer, gastric cancer, prostate cancer, ovarian cancer, lung cancer, uterine cancer, salivary duct carcinoma, melanoma, colon cancer, cervical cancer, pancreatic cancer, kidney cancer, colorectal cancer, and esophageal cancer.

24. The antibody-drug conjugate of claim 22 or claim 23, wherein the neoplastic cell is:

(i) a HER2-expressing cell, optionally wherein the antibody or antigen binding fragment is an anti-HER2 antibody or antigen binding fragment; and/or wherein the antibody or antigen binding fragment comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) comprising amino acid sequences of SEQ ID NO:1 (HCDR1), SEQ ID NO:2 (HCDR2), and SEQ ID NO:3 (HCDR3); and three light chain complementarity determining regions (LCDR1,

LCDR2, and LCDR3) comprising amino acid sequences of SEQ ID NO:4 (LCDR1), SEQ ID NO:5 (LCDR2), and SEQ ID NO:6 (LCDR3); and/or wherein the antibody or antigen binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:19, and a light chain variable region comprising an amino acid sequence of SEQ ID NO:20, optionally wherein the antibody or antigen binding fragment comprises a human IgG1 heavy chain constant region and/or wherein the antibody or antigen binding fragment comprises a human Ig kappa light chain constant region;

(ii) a CD138-expressing cell; optionally wherein the antibody or antigen binding fragment is an anti-CD138 antibody or antigen binding fragment; and/or wherein the antibody or antigen binding fragment comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) comprising amino acid sequences of SEQ ID NO:7 (HCDR1), SEQ ID NO:8 (HCDR2), and SEQ ID NO:9 (HCDR3); and three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3) comprising amino acid sequences of SEQ ID NO:10 (LCDR1), SEQ ID NO:11 (LCDR2), and SEQ ID NO:12 (LCDR3); and/or wherein the antibody or antigen binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:21, and a light chain variable region comprising an amino acid sequence of SEQ ID NO:22, optionally wherein the antibody or antigen binding fragment comprises a human IgG2a heavy chain constant region and/or wherein the antibody or antigen binding fragment comprises a human Ig kappa light chain constant region; or

(iii) an EPHA2-expressing cell; optionally wherein the antibody or antigen binding fragment is an anti-EPHA2 antibody or antigen binding fragment; and/or wherein the antibody or antigen binding fragment comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) comprising amino acid sequences of SEQ ID NO:13 (HCDR1), SEQ ID NO:14 (HCDR2), and SEQ ID NO:15 (HCDR3); and three light chain complementarity determining regions

(LCDR1, LCDR2, and LCDR3) comprising amino acid sequences of SEQ ID NO:16 (LCDR1), SEQ ID NO:17 (LCDR2), and SEQ ID NO:18 (LCDR3); and/or wherein the antibody or antigen binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:23, and a light chain variable region comprising an amino acid sequence of SEQ ID NO:24, optionally wherein the antibody or antigen binding fragment comprises a human IgG1 heavy chain constant region and/or wherein the antibody or antigen binding fragment comprises a human Ig kappa light chain constant region.

25. A pharmaceutical composition comprising: (i) the splicing modulator of any one of claims 1-6, or a pharmaceutically acceptable salt thereof; (ii) the compound of any one of claims 7-21, or (iii) the antibody-drug conjugate of any one of claims 22-24; and a pharmaceutically acceptable carrier.

26. A splicing modulator of any one of claims 1-6, or a pharmaceutically acceptable salt thereof, a compound of any one of claims 7-21, or an antibody-drug conjugate of any one of claims 22-24, for use in the treatment of a neoplastic disorder.

27. A splicing modulator of any one of claims 1-6, or a pharmaceutically acceptable salt thereof, a compound of any one of claims 7-21, or an antibody-drug conjugate of any one of claims 22-24, for use in manufacturing a medicament for the treatment of a neoplastic disorder.

28. The splicing modulator, compound, or antibody-drug conjugate for use of claim 26 or claim 27, wherein the neoplastic disorder is

(i) a HER2-expressing breast cancer, ovarian cancer, gastric cancer, lung cancer, uterine cancer, osteosarcoma, or salivary duct carcinoma; optionally wherein

the HER2-expressing lung cancer is lung adenocarcinoma and/or the HER2-expressing uterine cancer is uterine serous endometrial carcinoma;

(ii) a CD138-expressing multiple myeloma; or

(iii) an EPHA2-expressing breast cancer, prostate cancer, ovarian cancer, lung cancer, melanoma, colon cancer, or esophageal cancer.

29. The splicing modulator, compound, or antibody-drug conjugate for use of any one of claims 26-28, wherein the splicing modulator, compound, or antibody-drug conjugate is for use in the treatment of a neoplastic disorder in combination with a checkpoint inhibitor which targets CTLA4, PD1, PDL1, OX40, CD40, GITR, LAG3, TIM3, KIR, or a combination thereof.

30. A neoantigen vaccine comprising at least one neoantigen peptide or at least one neoantigen mRNA, wherein the at least one neoantigen peptide or at least one neoantigen mRNA comprises a neoantigen sequence induced by contacting a neoplastic cell with an effective amount of the splicing modulator of any one of claims 1-6 or pharmaceutically acceptable salt thereof, the compound of any one of claims 7-21, or the antibody-drug conjugate of any one of claims 22-24.