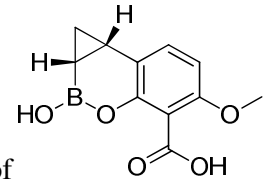
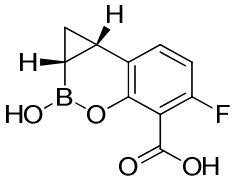
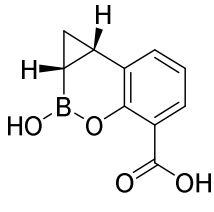
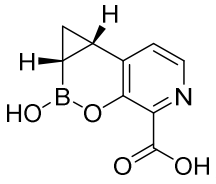
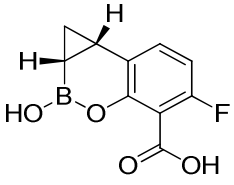
carbocyclyl optionally substituted with 0-2 substituents selected from the group consisting of C_{1-4} alkyl, C_{1-4} alkoxy, amino, halogen, C-amido, and N-amido; 5-10 membered heteroaryl optionally substituted with 0-2 substituents selected from the group consisting of C_{1-4} alkyl, C_{1-4} alkoxy, amino, halogen, C-amido, and N-amido; and 3-10 membered heterocyclyl optionally substituted with 0-2 substituents selected from the group consisting of C_{1-4} alkyl, C_{1-4} alkoxy, amino, halogen, C-amido, and N-amido;

each R^c, R^d, R^e, R^f, and R^g are independently selected from the group consisting of H, halogen, optionally substituted C_{1-4}alkyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10}aryl, and optionally substituted 5-10 membered heteroaryl; and

each p and q is independently 0 or 1.

[0010b] In another aspect, the present disclosure refers to a compound selected from the group consisting of , , , and , and pharmaceutically acceptable salts thereof.

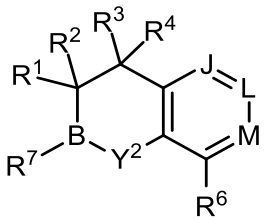
[0010c] In another aspect, the present disclosure relates to a compound having the structure , or a pharmaceutically acceptable salt thereof.

[0010d] In another aspect, the present disclosure refers to a pharmaceutical composition comprising a therapeutically effective amount of a compound as described herein, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

[0010e] In yet another aspect, the present disclosure refers to the compound as described herein, or a pharmaceutically acceptable salt thereof, for use in therapy.

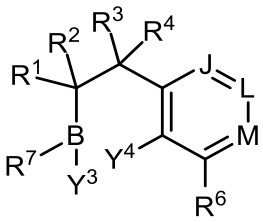
What is claimed is:

1. A compound having the structure of the Formula Ic or IIc, or a pharmaceutically acceptable salt thereof:



Ic

,



IIc

wherein

R^2 and R^3 together with the atoms to which they are attached form a fused ring or ring system selected from the group consisting of C_{3-7} cycloalkyl and 3-10 membered heterocyclyl, each optionally substituted with one or more R^5, and

each of $R^1$and R^4 is independently selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} haloalkyl, optionally substituted C_{1-6} alkoxy, optionally substituted C_{1-6} haloalkoxy, optionally substituted (C_{1-6} alkoxy)C_{1-6} alkyl, optionally substituted C_{2-10} alkenyl, optionally substituted C_{2-10}alkynyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10}aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted (C_{3-7}carbocyclyl)C_{1-6}alkyl, optionally substituted (3-10 membered heterocyclyl)C_{1-6}alkyl, optionally substituted (C_{6-10}aryl)C_{1-6}alkyl, (C_{6-10}aryl)C_{1-6}alkoxy, optionally substituted (5-10 membered heteroaryl)C_{1-6}alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, $-SR^c$, $-C(O)(CH_2)_{0-3}SR^c$, $-C(O)(CH_2)_{1-3}R^d$, $-NR^fC(O)NR^fR^g$, $-NR^fS(O)_2NR^fR^g$, $-C(=NR^e)R^c$, $-C(=NR^e)NR^fR^g$, $-NR^fCR^c(=NR^e)$, $-NR^fC(=NR^e)NR^fR^g$, $-S(O)(CH_2)_{1-3}R^c$, and $-NR^fS(O)_2NR^fOR^d$; or

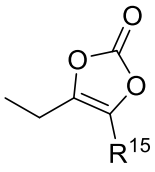
R^5 is $-Y^5-(CH_2)_t-G$;

t is an integer of 0 or 1;

G is selected from the group consisting of H, amino, halogen, cyano, hydroxy, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} haloalkyl, optionally substituted C_{1-6} alkoxy, optionally substituted C_{1-6} haloalkoxy, optionally substituted (C_{1-6} alkoxy)C_{1-6} alkyl, optionally substituted C_{2-10}alkenyl, optionally substituted C_{2-10}alkynyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10}aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted (C_{3-7}carbocyclyl)C_{1-6}alkyl, optionally substituted (3-10 membered heterocyclyl)C_{1-6}alkyl, optionally substituted (C_{6-10}aryl)C_{1-6}alkyl, (C_{6-10}aryl)C_{1-6}alkoxy, optionally substituted (5-10 membered heteroaryl)C_{1-6}alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, $-SR^c$, $-C(O)(CH_2)_{0-3}SR^c$, $-C(O)(CH_2)_{1-3}R^d$, $-NR^fC(O)NR^fR^g$, $-NR^fS(O)_2NR^fR^g$, $-C(=NR^e)R^c$, $-C(=NR^e)NR^fR^g$, $-NR^fCR^c(=NR^e)$, $-NR^fC(=NR^e)NR^fR^g$, $-S(O)(CH_2)_{1-3}R^c$, and $-NR^fS(O)_2NR^fOR^d$;

each J, L, M is independently CR^{12} or N (nitrogen);

R^6 is selected from the group consisting of -C(O)OR, and a carboxylic acid isostere;

R is selected from the group consisting of H, C_{1-9} alkyl, $-CR^{10}R^{11}OC(O)C_{1-9}$alkyl, $-CR^{10}R^{11}OC(O)C_{3-7}$carbocyclyl, $-CR^{10}R^{11}OC(O)$(3 to 7 membered heterocyclyl), $-CR^{10}R^{11}OC(O)C_{2-8}$alkoxyalkyl, $-CR^{10}R^{11}OC(O)OC_{1-9}$alkyl, $-CR^{10}R^{11}OC(O)OC_{3-7}$carbocyclyl, $-CR^{10}R^{11}OC(O)O$(3 to 7 membered heterocyclyl), $-CR^{10}R^{11}OC(O)OC_{2-8}$alkoxyalkyl, $-CR^{10}R^{11}OC(O)C_{6-10}$aryl, $-CR^{10}R^{11}OC(O)OC_{6-10}$aryl, $-CR^{10}R^{11}C(O)NR^{13}R^{14}$, $-CR^{10}R^{11}OC(O)O(CH_2)_{1-3}C(O)NR^{13}R^{14}$, $-CR^{10}R^{11}OC(O)O(CH_2)_{2-3}OC(O)C_{1-4}$ alkyl, $-CR^{10}R^{11}OC(O)O(CH_2)_{1-3}C(O)OC_{1-4}$ alkyl, $-CR^{10}R^{11}OC(O)(CH_2)_{1-3}OC(O)C_{1-4}$ alkyl, and 

;

R^7 is selected from the group consisting of –OH and optionally substituted C_{1-6} alkoxy;

each R^{10} and R^{11} is independently selected from the group consisting of H, optionally substituted C_{1-4}alkyl, optionally substituted C_{3-7} carbocyclyl, optionally

substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10}aryl, and optionally substituted 5-10 membered heteroaryl;

R^{12} is selected from the group consisting of hydrogen, amino, halogen, cyano, hydroxy, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} haloalkyl, optionally substituted C_{1-6} alkoxy, optionally substituted C_{1-6} haloalkoxy, optionally substituted (C_{1-6} alkoxy)C_{1-6} alkyl, optionally substituted C_{2-10}alkenyl, optionally substituted C_{2-10}alkynyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10}aryl, optionally substituted 5-10 membered heteroaryl, optionally substituted (C_{3-7}carbocyclyl)C_{1-6}alkyl, optionally substituted (3-10 membered heterocyclyl)C_{1-6}alkyl, optionally substituted (C_{6-10}aryl)C_{1-6}alkyl, (C_{6-10}aryl)C_{1-6}alkoxy, optionally substituted (5-10 membered heteroaryl)C_{1-6}alkyl, acyl, C-carboxy, O-carboxy, C-amido, N-amido, S-sulfonamido, N-sulfonamido, sulfhydryl, $-C(O)(CH_2)_{0-3}SR^c$, $-C(O)(CH_2)_{1-3}R^d$, $-NR^fC(O)NR^fR^g$, $-NR^fS(O)_2NR^fR^g$, $-C(=NR^e)R^c$, $-C(=NR^e)NR^fR^g$, $-NR^fCR^c(=NR^e)$, $-NR^fC(=NR^e)NR^fR^g$, $-S(O)(CH_2)_{1-3}R^c$, $-NR^fS(O)_2NR^fOR^d$, and $-(CH_2)_p-Y^6-(CH_2)_qK$;

each R^{13} and R^{14} is independently selected from the group consisting of H, optionally substituted C_{1-6}alkyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10}aryl, and optionally substituted 5-10 membered heteroaryl;

R^{15} is optionally substituted C_{1-6} alkyl;

Y^2 is -O- or -S- ;

Y^3 is -OHor -SH;

Y^4 is selected from the group consisting of -OH, and optionally substituted C_{1-6} alkoxy;

Y^5 is absent;

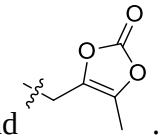
Y^6 is selected from the group consisting of -S-, -S(O)-, $-S(O)_2-$, -O-, $-CR^fR^g-$, and $-NR^f-$;

K is selected from the group consisting of C-amido; N-amido; S-sulfonamido; N-sulfonamido; $-NR^fC(O)NR^fR^g$; $-NR^fS(O)_2NR^fR^g$; $-C(=NR^e)R^c$; $-C(=NR^e)NR^fR^g$; $-NR^fCR^c(=NR^e)$; $-NR^fC(=NR^e)NR^fR^g$; C_{1-4} alkyl optionally substituted with 0-2 substituents selected from the group consisting of C_{1-4} alkoxy, amino, halogen, C-amido,

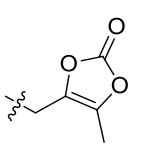
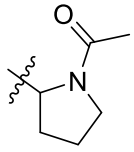
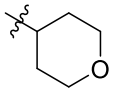
and N-amido; C_{6-10} aryl optionally substituted with 0-2 substituents selected from the group consisting of C_{1-4} alkyl, C_{1-4} alkoxy, amino, halogen, C-amido, and N-amido; C_{3-7} carbocyclyl optionally substituted with 0-2 substituents selected from the group consisting of C_{1-4} alkyl, C_{1-4} alkoxy, amino, halogen, C-amido, and N-amido; 5-10 membered heteroaryl optionally substituted with 0-2 substituents selected from the group consisting of C_{1-4} alkyl, C_{1-4} alkoxy, amino, halogen, C-amido, and N-amido; and 3-10 membered heterocyclyl optionally substituted with 0-2 substituents selected from the group consisting of C_{1-4} alkyl, C_{1-4} alkoxy, amino, halogen, C-amido, and N-amido;

each R^c, R^d, R^e, R^f, and R^g are independently selected from the group consisting of H, halogen, optionally substituted C_{1-4}alkyl, optionally substituted C_{3-7} carbocyclyl, optionally substituted 3-10 membered heterocyclyl, optionally substituted C_{6-10}aryl, and optionally substituted 5-10 membered heteroaryl; and

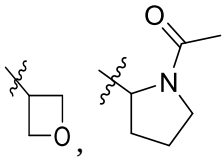
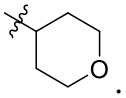
each p and q is independently 0 or 1.

2. The compound of claim 1, wherein R is selected from the group consisting of H, C_{1-9} alkyl, $-CR^{10}R^{11}OC(O)C_{1-9}$alkyl, $-CR^{10}R^{11}OC(O)OC_{1-9}$alkyl, $-CR^{10}R^{11}OC(O)C_{6-10}$aryl, $-CR^{10}R^{11}OC(O)OC_{6-10}$aryl and .

3. The compound of claim 1, wherein R is $-CR^{10}R^{11}OC(O)C_{1-9}$alkyl, $-CR^{10}R^{11}OC(O)C_{3-7}$carbocyclyl, $-CR^{10}R^{11}OC(O)$(3 to 7 membered heterocyclyl), or $-CR^{10}R^{11}OC(O)C_{2-8}$alkoxyalkyl.

4. The compound of claim 3, wherein the 3 to 7 membered heterocyclyl of R is , , or .

5. The compound of claim 1, wherein R is $-CR^{10}R^{11}OC(O)OC_{1-9}$alkyl, $-CR^{10}R^{11}OC(O)OC_{3-7}$carbocyclyl, $-CR^{10}R^{11}OC(O)O$(3 to 7 membered heterocyclyl), or $-CR^{10}R^{11}OC(O)OC_{2-8}$alkoxyalkyl.

6. The compound of claim 5, wherein the 3 to 7 membered heterocyclyl of R is , , or .

7. The compound of claim 1, wherein R is $-CR^{10}R^{11}C(O)NR^{13}R^{14}$.

8. The compound of claim 1, wherein R is $-CR^{10}R^{11}OC(O)O(CH_2)_{1-3}C(O)NR^{13}R^{14}$, $-CR^{10}R^{11}OC(O)O(CH_2)_{2-3}OC(O)C_{1-4}$ alkyl, $-CR^{10}R^{11}OC(O)(CH_2)_{1-3}OC(O)C_{1-4}$ alkyl, or $-CR^{10}R^{11}OC(O)O(CH_2)_{1-3}C(O)OC_{1-4}$ alkyl.

9. The compound of claim 1, wherein each J, L and M is CR^{12}.

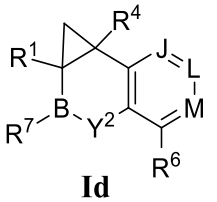
10. The compound of claim 9, wherein each R^{12} is independently hydrogen, halogen, C_{1-6} alkoxy, or C_{1-6} haloalkoxy.

11. The compound of claim 1, wherein at least one of J, L and M is N.

12. The compound of claim 11, wherein M is N.

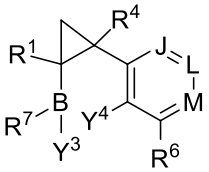
13. The compound of claim 1, wherein R^2 and R^3 together with the atoms to which they are attached form C_{3-7} cycloalkyl optionally substituted with one or more R^5.

14. The compound of claim 13, having the structure of Formula Id or IId, or a pharmaceutically acceptable salt thereof:

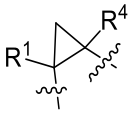


Id

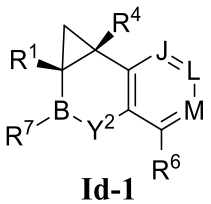
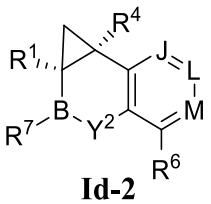
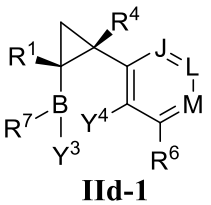
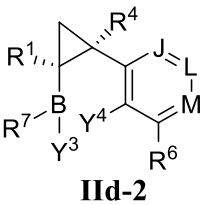
or



IId,

wherein the cyclopropyl moiety  is optionally substituted with one or more R^5.

15. The compound of claim 14, having the structure of Formula Id-1, Id-2, IId-1 or IId-2, or a pharmaceutically acceptable salt thereof:


Id-1, 
Id-2, 
IId-1, or 
IId-2.

16. The compound of claim 15 , wherein each J, L and M is CR^{12}.

17. The compound of claim 16, wherein each R^{12} is independently hydrogen, halogen, C_{1-6} alkoxy, or C_{1-6} haloalkoxy.

18. The compound of claim 17, wherein R^6 is -C(O)OR.

19. The compound of claim 1, wherein R^1 is hydrogen or C_{1-6} hydroxyalkyl.

20. The compound of claim 1, wherein R^4 is hydrogen.

21. The compound of claim 1, wherein R^6 is -C(O)OR.

22. The compound of claim 21, wherein R is H.

23. The compound of claim 1, wherein R^7 is -OH.

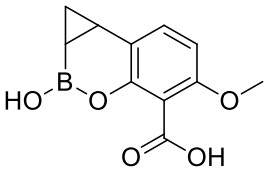
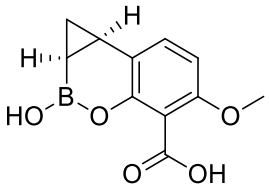
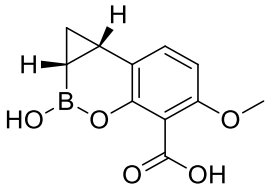
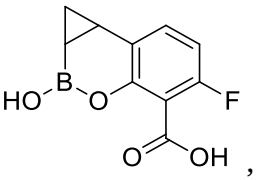
24. The compound of claim 1, wherein Y^2 is -O-.

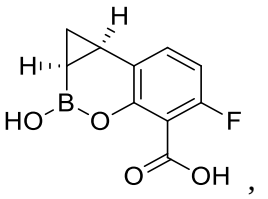
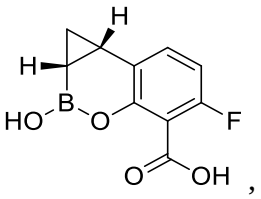
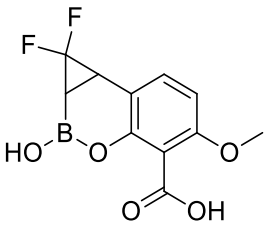
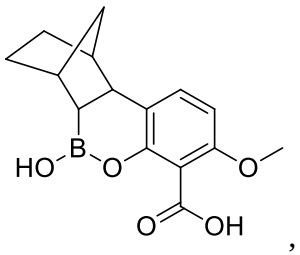
25. The compound of claim 1, wherein Y^3 is -OH.

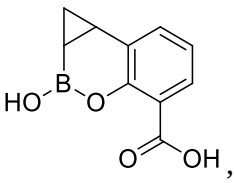
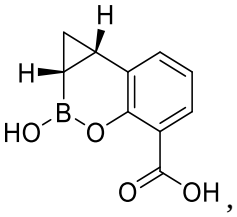
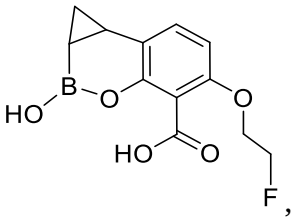
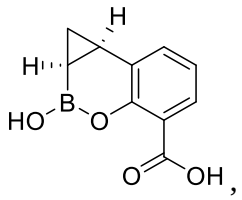
26. The compound of claim 1, wherein Y^4 is -OH.

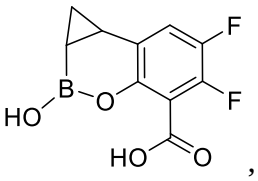
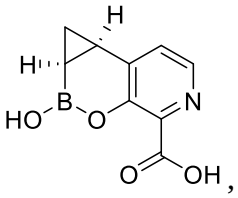
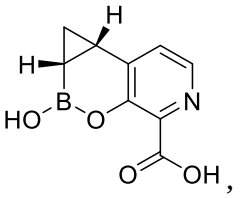
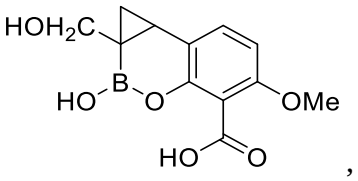
27. The compound of claim 1, wherein t is 0, and R^5 is selected from the group consisting of amino, halogen, cyano, hydroxy, optionally substituted C_{1-6} alkoxy, acyl, C-carboxy, C-amido, N-amido, N-sulfonamido, $-SR^c$, $-C(O)(CH_2)_{0-3}SR^c$, $-C(O)(CH_2)_{1-3}R^d$, $-NR^fC(O)NR^fR^g$, $-NR^fS(O)_2NR^fR^g$, $-C(=NR^e)R^c$, $-C(=NR^e)NR^fR^g$, $-NR^fCR^c(=NR^e)$, $-NR^fC(=NR^e)NR^fR^g$, $-S(O)(CH_2)_{1-3}R^c$, and $-NR^fS(O)_2NR^fOR^d$.

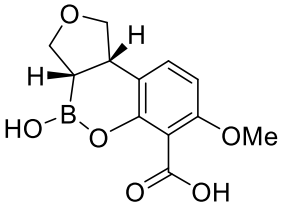
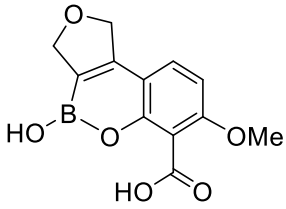
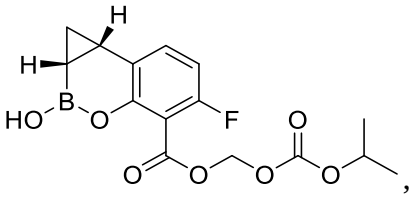
28. The compound of claim 1, selected from the group consisting of

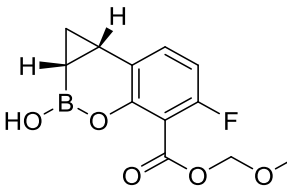
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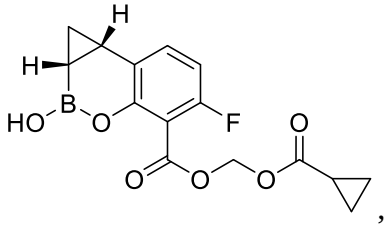
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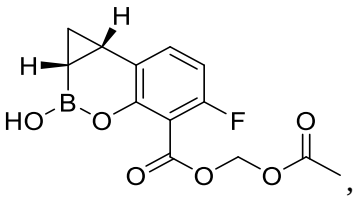
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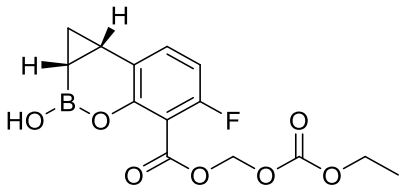
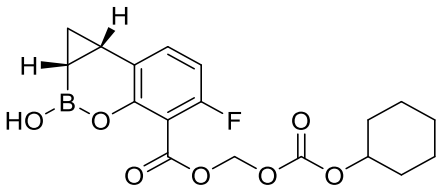
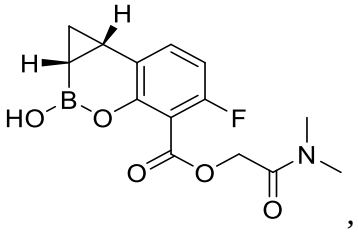
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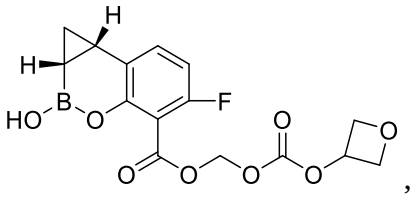
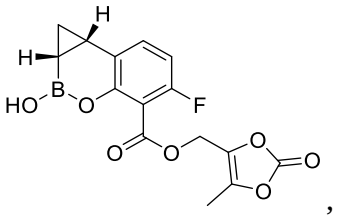
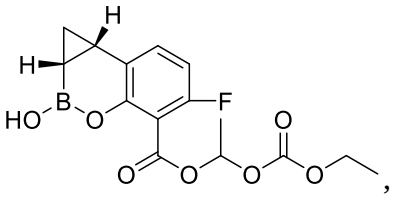
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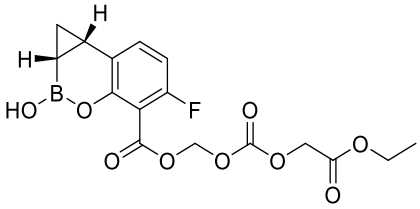
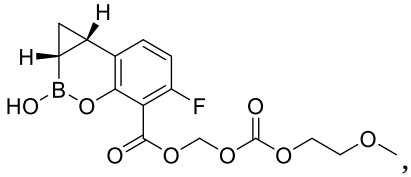
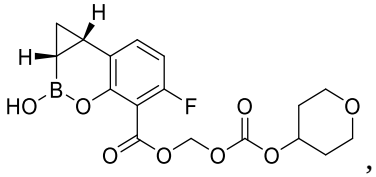
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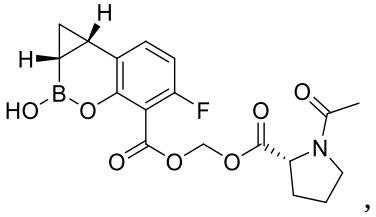
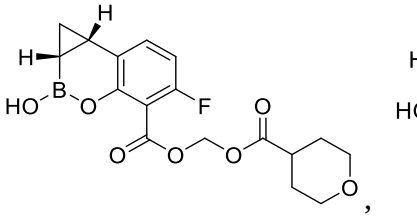
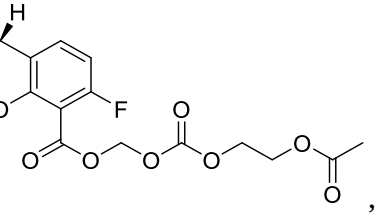
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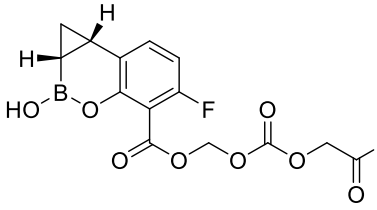
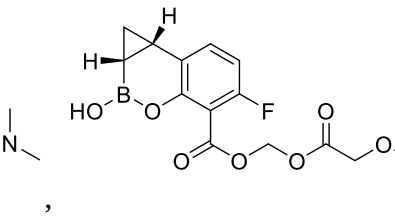
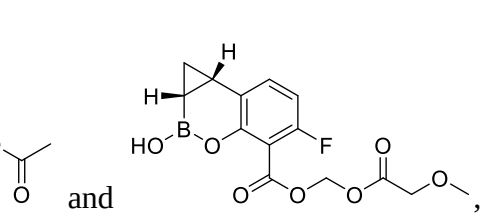
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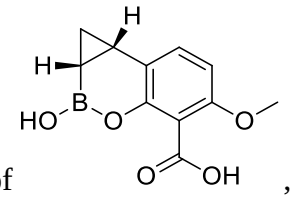
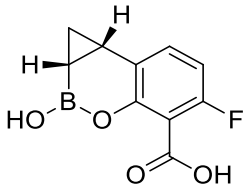
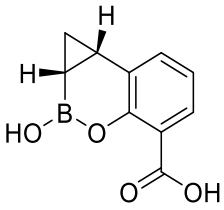
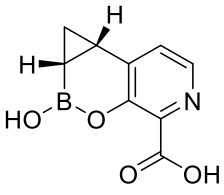
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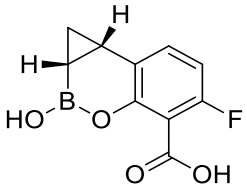
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and pharmaceutically acceptable salts thereof.

29. A compound selected from the group consisting of , , , and , and pharmaceutically acceptable salts thereof.

30. A compound having the structure , or a pharmaceutically acceptable salt thereof.

31. The compound of any one of claims 28 to 30, wherein the pharmaceutically acceptable salt is a sodium salt.

32. A pharmaceutical composition comprising a therapeutically effective amount of a compound of any one of claims 1 to 31, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

33. The pharmaceutical composition of claim 32, further comprising an additional medicament.

34. The compound of any one of claims 1 to 31, or a pharmaceutically acceptable salt thereof, for use in therapy.