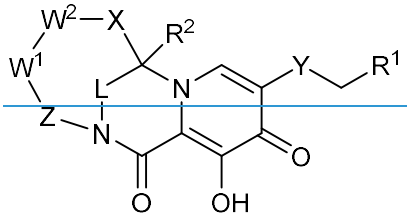
CLAIMS

We claim:

1. A compound of formula (I):



I

or a pharmaceutically acceptable salt thereof, wherein

R^1 is H or C_{6-10}aryl, wherein C_{6-10}aryl is optionally substituted with one to four R^{A1}, wherein each R^{A1} is independently halo, C_{1-6}alkyl, C_{1-4}haloalkyl, cyano, -O-C_{1-4}alkyl, or C_{1-4}alkyl-O-C_{1-4}alkyl;

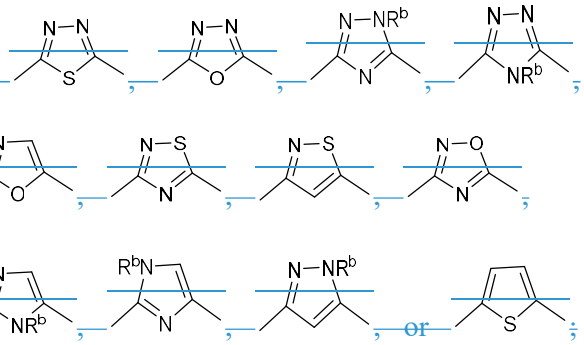
R^2 is H, C_{1-6}alkyl, or C_{1-4}haloalkyl;

L is $-CR^{3a}R^{3b}-$, -C(O)-, $-SO_2-$, $-CH_2-CH_2-$, or $-N(R^a)-$;

W^1 is a bond or $-CR^{4a}R^{4b}-$;

W^2 is $-CR^{5a}R^{5b}-$, $-CR^{5a}R^{5b}CR^{5c}R^{5d}-$, $-CR^{6a}=CR^{6b}-$, $-N(R^7)-$, -O-, $-S(O)_n-$, -C(O)-, -C(O)O-, -C(O)NH-, $-CR^{5a}R^{5b}-N(R^7)-$, $-CR^{5a}R^{5b}-O-$, $-CR^{5a}R^{5b}-S(O)_n-$, $-CR^{5a}R^{5b}-C(O)-$, $-CR^{5a}R^{5b}-C(O)O-$, $-CR^{5a}R^{5b}-OC(O)-$, $-CR^{5a}R^{5b}-C(O)NH-$, or $-CR^{5a}R^{5b}-NHC(O)-$;

X is a bond or $-CR^{8a}R^{8b}-$;

Y is –C(O)NH– or Q, wherein Q is 

Z is –$CR^{9a}R^{9b}$–, –$CR^{9a}R^{9b}CR^{9c}R^{9d}$–, or –$CR^{10a}$=$CR^{10b}$–;

R^{3a} and R^{3b} are independently H, C_{1-6}alkyl, C_{1-4}haloalkyl, or –O–C_{1-4}alkyl; or optionally:

R^{3a} and R^{3b} together with the carbon atom to which they are attached form a 3- to 7-membered saturated or partially unsaturated spiro ring containing 0 to 2 heteroatoms selected from N, O, and S, wherein the spiro ring is optionally substituted with one to three R^{A2}, wherein each R^{A2} is independently halo, C_{1-4}alkyl or C_{1-4}haloalkyl;

R^{4a} and R^{4b} are independently H, C_{1-6}alkyl, C_{1-4}haloalkyl, or halo;

R^{5a}, R^{5b}, R^{5c}, and R^{5d} are independently H, C_{1-6}alkyl, C_{1-4}haloalkyl, halo, hydroxyl, cyano, –O–C_{1-4}alkyl, or C_{1-4}alkylene–O–C_{1-4}alkyl; or optionally:

R^{5a} and R^{5b} or R^{5c} and R^{5d} together with the carbon atom to which they are attached form a 3- to 7-membered saturated or partially unsaturated spiro ring containing 0 to 2 heteroatoms selected from N, O, and S, wherein the spiro ring is optionally substituted with one to three R^{A3}, wherein each R^{A3} is independently halo, C_{1-4}alkyl or C_{1-4}haloalkyl; or

R^{5a} and R^{5c} or R^{5b} and R^{5d} together with the carbon atoms to which each is attached form a 3- to 7-membered saturated or partially unsaturated fused

ring containing 0 heteroatoms or 1 heteroatom selected from N, O, and S, wherein the fused ring is optionally substituted with one to three R^{A3}, wherein each R^{A3} is independently halo, C_{1-4}alkyl or C_{1-4}haloalkyl;

each R^{6a} and R^{6b} is independently H, halo, C_{1-4}haloalkyl, or C_{1-6}alkyl; optionally:

R^{6a} and R^{6b} together with the carbon atoms to which each is attached form a 5- to 10-membered partially unsaturated fused ring containing 0 heteroatoms or 1 heteroatom selected from N, O, and S, or a 5- to 10-membered fused aromatic ring, or a 5- to 10-membered fused heteroaromatic ring containing 1 to 2 heteroatoms selected from N, O and S, wherein the partially unsaturated fused ring, fused aromatic ring, or fused heteroaromatic ring is optionally substituted with one to four R^{A4}, wherein each R^{A4} is independently halo or C_{1-4}alkyl;

R^7 is H, C_{1-6}alkyl, C_{1-4}haloalkyl, $C(O)R^e$, or SO_2R^e;

R^{8a} and R^{8b} are each independently H, hydroxyl, –O–C_{1-4}alkyl, C_{1-4}alkylene–O–C_{1-4}alkyl, C_{1-6}alkyl, C_{1-4}haloalkyl, cyano, or halo; or optionally:

R^{8a} and R^{8b} together with the carbon atom to which they are attached form a 3- to 7-membered saturated or partially unsaturated spiro ring containing 0 to 2 heteroatoms selected from N, O, and S, wherein the spiro ring is optionally substituted with one to four R^{A5}, wherein each R^{A5} is independently halo, C_{1-4}alkyl or C_{1-4}haloalkyl; or optionally:

R^{8a} is H, hydroxyl, –O–C_{1-4}alkyl, C_{1-4}alkylene–O–C_{1-4}alkyl, C_{1-6}alkyl, C_{1-4}haloalkyl, cyano, or halo; and

R^{8b} and one of R^{5a}, R^{5b}, R^{5c}, R^{5d}, and R^{7} together with the atoms to which each is attached form a 3- to 7-membered saturated or partially unsaturated fused ring containing 0 to 2 heteroatoms selected from N, O and S, wherein the fused ring is optionally substituted with one to four R^{A5}, wherein each R^{A5} is independently halo or C_{1-4}alkyl; or

R^{8b} and R^{2} together with the carbon atoms to which each is attached form a 3- to 7-membered saturated or partially unsaturated fused ring containing 0 to 2 heteroatoms selected from N, O and S, wherein the fused ring is optionally substituted with one to four R^{A5}, wherein each R^{A5} is independently halo or C_{1-4}alkyl;

R^{9a}, R^{9b}, R^{9c}, and R^{9d} are each independently H, C_{1-6}alkyl, C_{1-4}haloalkyl, or halo; or optionally:

R^{9a} and R^{9b} or R^{9c} and R^{9d} together with the carbon atom to which they are attached form a 3- to 7-membered saturated or partially unsaturated spiro ring containing 0 to 2 heteroatoms selected from N, O, and S, wherein the spiro ring is optionally substituted with one to three R^{A6}, wherein each R^{A6} is independently halo, C_{1-4}alkyl or C_{1-4}haloalkyl; or

R^{9a} and R^{9c} or R^{9b} and R^{9d} together with the carbon atoms to which each is attached form a 3- to 7-membered saturated or partially unsaturated fused ring containing 0 heteroatoms or 1 heteroatom selected from N, O, and S, wherein the fused ring is optionally substituted with one to three R^{A6}, wherein each R^{A6} is independently halo, C_{1-4}alkyl, or C_{1-4}haloalkyl; or

one of R^{9a}, R^{9b}, R^{9c}, and R^{9d} and one of R^{4a}, R^{4b}, R^{5a}, R^{5b}, and R^{7} together with the atoms to which each is attached form a 3- to 7-membered saturated or

partially unsaturated fused ring containing 0 to 2 heteroatoms selected from N, O and S, wherein the fused ring is optionally substituted with one to four R^{A6}, wherein each R^{A6} is independently halo or C_{1-4}alkyl;

R^{10a} and R^{10b} are independently H, halo, C_{1-4}haloalkyl, or C_{1-6}alkyl; or optionally:

R^{10a} and R^{10b} together with the carbon atoms to which each is attached form a 5- to 10-membered partially unsaturated fused ring containing 0 heteroatoms or 1 heteroatom selected from N, O, and S, or a 5- to 10-membered fused aromatic ring, or a 5- to 10-membered fused heteroaromatic ring containing 1 to 2 heteroatoms selected from N, O and S, wherein the partially unsaturated fused ring, fused aromatic ring, or fused heteroaromatic ring is optionally substituted with one to four R^{A7}, wherein each R^{A7} is independently halo or C_{1-4}alkyl;

R^a is independently H, C_{1-6}alkyl, C_{1-6}haloalkyl, $C(O)R^e$, or SO_2R^e;

R^b is H or C_{1-4}alkyl;

R^e is C_{1-4}alkyl or –O–C_{1-4}alkyl; and

each n is 0, 1, or 2.

2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R^2 is selected from the group consisting of –H, –CH_3, –CH_2CH_3, and –CH_2F, or R^2 and R^{8b} together with the carbon to which they are attached form a 3-membered fused carbocyclic ring.

3. The compound of claim 1 or 2, or a pharmaceutically acceptable salt thereof, wherein R^2 is selected from the group consisting of H, –CH_3, –CH_2CH_3, and –CH_2F.

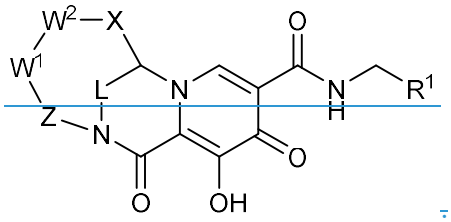
4. The compound of claim 1 or 2, or a pharmaceutically acceptable salt thereof, wherein R^2 and R^{8b} together with the carbon to which they are attached form a 3-membered fused carbocyclic ring.

5. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R^2 is H or C_{1-4}alkyl.

6. The compound of claim 1 or 5, or a pharmaceutically acceptable salt thereof, wherein R^2 is H or methyl.

7. The compound of any one of claims 1-6, or a pharmaceutically acceptable salt thereof, wherein Y is -C(O)NH-.

8. The compound of any one of claims 1-7, or a pharmaceutically acceptable salt thereof, having the formula (**II**):

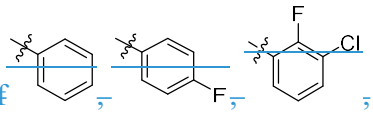
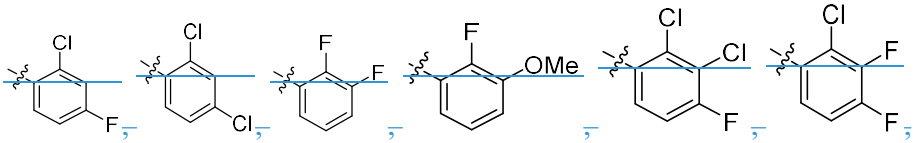
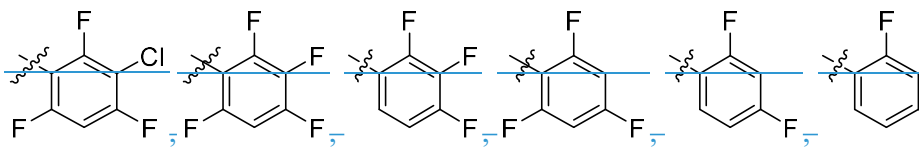


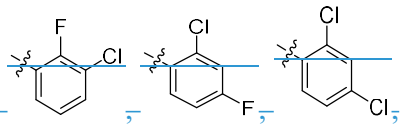
II

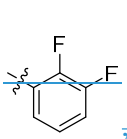
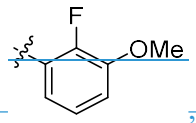
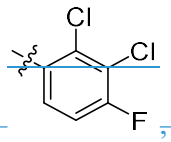
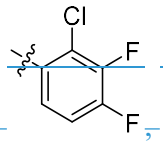
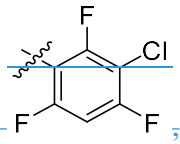
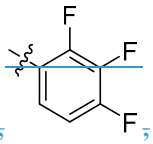
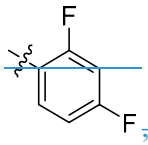
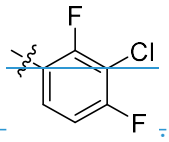
9. The compound of any one of claims 1-8, or a pharmaceutically acceptable salt thereof, wherein R^1 is phenyl, optionally substituted with one to four R^{A1}, wherein each R^{A1} is independently halo, C_{1-4}alkyl, C_{1-4}haloalkyl, cyano, -O-C_{1-4}alkyl, or C_{1-4}alkyl-O-C_{1-4}alkyl.

10. The compound of any one of claims 1-9, or a pharmaceutically acceptable salt thereof, wherein R^1 is phenyl, optionally substituted with one, two, three, or four R^{A1}, wherein each R^{A1} is independently halo, C_{1-4}alkyl, C_{1-4}haloalkyl, or -O-C_{1-4}alkyl.

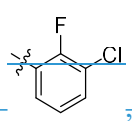
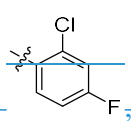
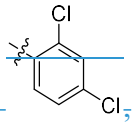
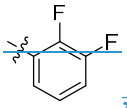
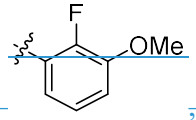
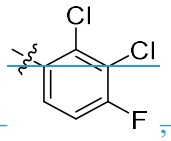
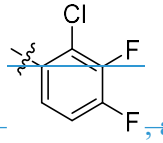
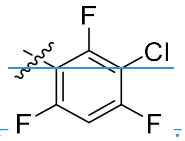
11. The compound of any one of claims 1-10, or a pharmaceutically acceptable salt thereof, wherein R^1 is phenyl substituted with one, two, three, or four R^{A1}, wherein each R^{A1} is independently halo or -O-C_{1-4}alkyl.

12. The compound of any one of claims 1-11, or a pharmaceutically acceptable salt thereof, wherein R^1 is selected from the group consisting of , , , , and .

13. The compound of any one of claims 1-12, or a pharmaceutically acceptable salt thereof, wherein R^1 is selected from the group consisting of .

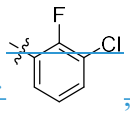
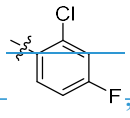
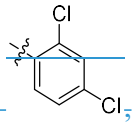
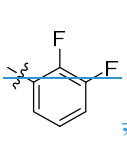
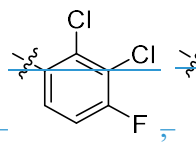
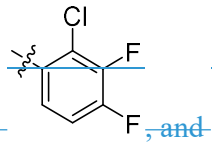
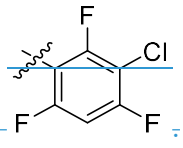
14. The compound of any one of claims 1-13, or a pharmaceutically acceptable salt thereof, wherein R^1 is selected from the group consisting of

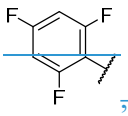
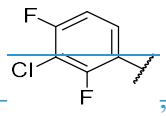
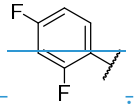
15. The compound of any one of claims 1-11, or a pharmaceutically acceptable salt thereof, wherein R^1 is phenyl substituted with one, two, three, or four halogens.

16. The compound of any one of claims 1-11 and 15, or a pharmaceutically acceptable salt thereof, wherein R^1 is phenyl substituted with two or three halogens selected from chloro and fluoro.

17. The compound of any one of claims 1-16, or a pharmaceutically acceptable salt thereof, wherein R^1 is selected from the group consisting of

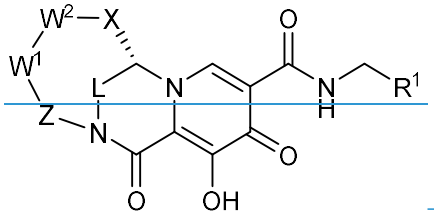
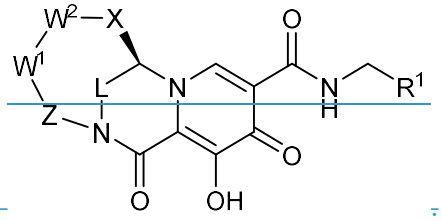








18. The compound of any one of claims 1-17, or a pharmaceutically acceptable salt thereof, wherein R^1 is

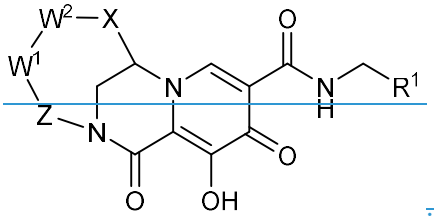
19. The compound of any one of claims 1-18, or a pharmaceutically acceptable salt thereof, wherein L is $-CH_2-$, $-CH(CH_3)-$, $-C(O)-$, or $-CH_2-CH_2-$.

20. The compound of any one of claims 1-19, or a pharmaceutically acceptable salt thereof, having the formula:

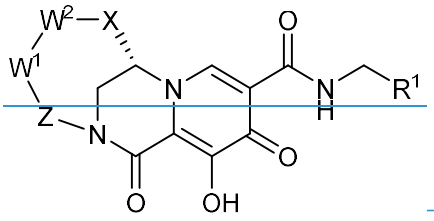
IIIa **IIIb**

21. The compound of any one of claims 1-19, or a pharmaceutically acceptable salt thereof, having the formula (**IV**):

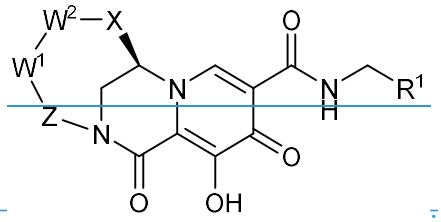


IV

22. The compound of any one of claims 1-21, or a pharmaceutically acceptable salt thereof, having the formula:

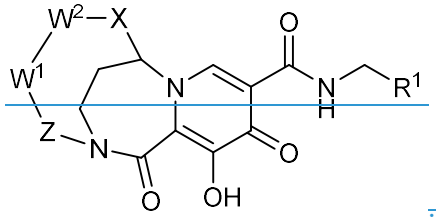


or



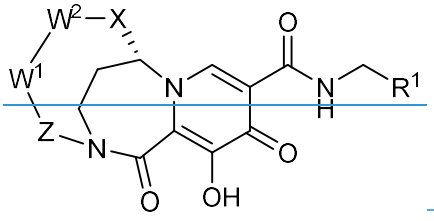
Va **Vb**

23. The compound of any one of claims 1-19, or a pharmaceutically acceptable salt thereof, having the formula (**VI**):

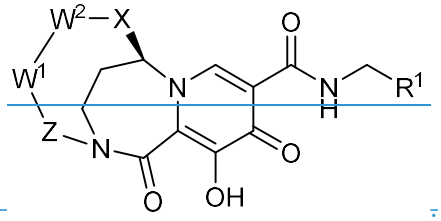


VI

24. The compound of any one of claims 1-19 and 23 or a pharmaceutically acceptable salt thereof, having the formula:



or



VIIa **VIIb**

25. The compound of any one of claims 1-24, or a pharmaceutically acceptable salt thereof, wherein W^1 is a bond or $-CR^{4a}R^{4b}-$; wherein R^{4a} and R^{4b} are independently H, C_{1-6}alkyl, or halo.

26. The compound of any one of claims 1-25, or a pharmaceutically acceptable salt thereof, wherein W^1 is a bond or $-CR^{4a}R^{4b}-$; wherein R^{4a} and R^{4b} are independently H, $-CH_3$, or halo.

27. The compound of any one of claims 1-26, or a pharmaceutically acceptable salt thereof, wherein W^1 is bond, $-CH_2-$, $-CF_2-$, $-CH(F)-$, $-CH(CH_3)-$, or $-CF(CH_3)-$.

28. The compound of any one of claims 1-25 and 27, or a pharmaceutically acceptable salt thereof, wherein W^1 is a bond, $-CH_2-$, $-CF_2-$ or $-CH(F)-$.

29. The compound of any one of claims 1-28, or a pharmaceutically acceptable salt thereof, wherein W^2 is selected from the group consisting of $-CR^{5a}R^{5b}-$, $-CR^{5a}R^{5b}CR^{5c}R^{5d}-$, $-CR^{6a}=CR^{6b}-$, $-N(R^7)-$, $-O-$, $-S(O)_n-$, $-C(O)-$, $-CR^{5a}R^{5b}-C(O)-$, and $-CR^{5a}R^{5b}-O-$; wherein

each R^{5a}, R^{5b}, R^{5c}, and R^{5d} are independently H, C_{1-4}alkyl, C_{1-4}haloalkyl, halo, hydroxyl, cyano, $-O-C_{1-4}$alkyl, or C_{1-4}alkylene$-O-C_{1-4}$alkyl; or

R^{5a} and R^{5b}, R^{5c} and R^{5d}, R^{5a} and R^{5c}, or R^{5b} and R^{5d} together with the carbon atoms to which each is attached form a 3 to 7 membered saturated or partially unsaturated carbocyclic ring, optionally substituted with one to three R^{A3}, wherein each R^{A3} is independently halo, C_{1-4}alkyl or C_{1-4}haloalkyl;

each R^{6a} and R^{6b} are independently H, halo, C_{1-4}haloalkyl, or C_{1-4}alkyl; or

R^{6a} and R^{6b} together with the atoms to which each is attached form (i) a 5 to 10 membered fused aromatic ring or (ii) a 5 to 10 membered fused heteroaromatic ring containing 1 to 2 heteroatoms selected from N, O and S, wherein the 5-10 membered fused aromatic ring or the 5-10 membered fused heteroaromatic ring is optionally substituted with one to four R^{A4}, wherein each R^{A4} is independently halo or C_{1-4}alkyl;

R^7 is H, C_{1-4}alkyl, C_{1-4}haloalkyl, $C(O)R^e$, or SO_2R^e;

R^e is a C_{1-4}alkyl; and

n is 0, 1, or 2.

30. The compound of any one of claims 1-29, or a pharmaceutically acceptable salt thereof, wherein W^2 is selected from the group consisting of $-CR^{5a}R^{5b}-$, $-CR^{5a}R^{5b}CR^{5c}R^{5d}-$, $-CR^{6a}=CR^{6b}-$, $-N(R^7)-$, $-O-$, $-S(O)_n-$, $-C(O)-$, $-CR^{5a}R^{5b}-C(O)-$, and $-CR^{5a}R^{5b}-O-$; wherein

each R^{5a}, R^{5b}, R^{5c}, and R^{5d} are independently H, C_{1-4}alkyl, C_{1-4}haloalkyl, halo, hydroxyl, cyano, $-O-C_{1-4}$alkyl, or C_{1-4}alkylene-$O-C_{1-4}$alkyl; or

R^{5a} and R^{5b}, R^{5c} and R^{5d}, R^{5a} and R^{5c}, or R^{5b} and R^{5d} together with the carbon atoms to which each is attached form a 3-membered carbocyclic ring, optionally substituted with one to three R^{A3}, wherein each R^{A3} is independently halo, C_{1-4}alkyl or C_{1-4}haloalkyl;

each R^{6a} and R^{6b} are independently H, halo, C_{1-4}haloalkyl, or C_{1-4}alkyl; or

R^{6a} and R^{6b} together with the atoms to which each is attached form (i) a fused phenyl ring or (ii) a 5-6 membered fused heteroaromatic ring containing 1 to 2 heteroatoms selected from N, O and S, wherein the fused phenyl ring or the 5-6 membered fused heteroaromatic ring is optionally substituted with one to four R^{A4}, wherein each R^{A4} is independently halo or C_{1-4}alkyl;

R^7 is H, C_{1-4}alkyl, C_{1-4}haloalkyl, $C(O)R^e$, or SO_2R^e;

Rc is a C_{1-4}alkyl; and

n is 0, 1, or 2.

31. The compound of any one of claims 1-30, or a pharmaceutically acceptable salt thereof, wherein W^2 is selected from the group consisting of $-CR^{5a}R^{5b}-$, $-CR^{5a}R^{5b}CR^{5c}R^{5d}-$, $-CR^{6a}=CR^{6b}-$, $-N(R^7)-$, $-O-$, $-S(O)_n-$, $-C(O)-$, $-CR^{5a}R^{5b}-C(O)-$, and $-CR^{5a}R^{5b}-O-$; wherein

each R^{5a}, R^{5b}, R^{5c}, and R^{5d} are independently H, C_{1-4}alkyl, halo, hydroxyl, or $-O-C_{1-4}$alkyl; or

R^{5a} and R^{5b}, R^{5c} and R^{5d}, R^{5a} and R^{5c}, or R^{5b} and R^{5d} together with the carbon atoms to which each is attached form a 3-membered carbocyclic ring;

each R^{6a} and R^{6b} are independently H, halo, or C_{1-4}alkyl; or

R^{6a} and R^{6b} together with the atoms to which each is attached form (i) a fused phenyl ring or (ii) a 5-6 membered fused heteroaromatic ring containing 1 to 2 heteroatoms selected from N and O, wherein the fused phenyl ring or the 5-6 membered fused heteroaromatic ring is optionally substituted with one or two R^{A4}, wherein each R^{A4} is independently halo or C_{1-4}alkyl;

R^7 is H, C_{1-4}alkyl, C_{1-4}haloalkyl, $C(O)R^e$, or SO_2R^e;

R^e is a C_{1-4}alkyl; and

n is 0 or 1.

32. The compound of any one of claims 1-31, or a pharmaceutically acceptable salt thereof, wherein W^2 is selected from the group consisting of $-CR^{5a}R^{5b}-$, $-CR^{5a}R^{5b}CR^{5c}R^{5d}-$, $-CR^{6a}=CR^{6b}-$, $-N(R^7)-$, $-O-$, $-S(O)_n-$, $-C(O)-$, $-CR^{5a}R^{5b}-C(O)-$, and $-CR^{5a}R^{5b}-O-$; wherein

each R^{5a}, R^{5b}, R^{5c}, and R^{5d} are independently H, $-CH_3$, halo, hydroxyl, or $-OCH_3$; or

R^{5a} and R^{5b}, R^{5c} and R^{5d}, R^{5a} and R^{5c}, or R^{5b} and R^{5d} together with the carbon atoms to which each is attached form a 3-membered carbocyclic ring;

each R^{6a} and R^{6b} are independently H, halo, or CH_3; or

R^{6a} and R^{6b} together with the atoms to which each is attached form (i) a fused phenyl ring or (ii) a 5-membered fused heteroaromatic ring containing 1 to 2 heteroatoms selected from N and O, wherein the fused phenyl ring or the 5-membered fused heteroaromatic ring is optionally substituted with one or two R^{A4}, wherein each R^{A4} is independently halo or CH_3;

R^7 is H, $-CH_3$, $-CH(CH_3)_2$, $-CF_3$, $-C(O)R^e$, or $-SO_2R^e$;

R^e is $-CH_3$; and

n is 0 or 1.

33. The compound of any one of claims 1-32, or a pharmaceutically acceptable salt thereof, wherein W^2 is selected from the group consisting of $-CR^{5a}R^{5b}-$, $-CR^{5a}R^{5b}CR^{5c}R^{5d}-$, $-CR^{6a}=CR^{6b}-$, $-N(R^7)-$, $-O-$, $-S(O)_n-$, $-C(O)-$, $-CR^{5a}R^{5b}-C(O)-$, and $-CR^{5a}R^{5b}-O-$; wherein

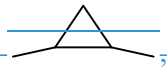
each R^{5a}, R^{5b}, R^{5c}, and R^{5d} are independently H, $-CH_3$, halo, hydroxyl, or $-OCH_3$;

each R^{6a} and R^{6b} are independently H, halo, or $-CH_3$;

R^7 is H, $-CH_3$, $-CH(CH_3)_2$, $-CF_3$, $-C(O)R^e$, or $-SO_2R^e$;

R^e is $-CH_3$; and

n is 0 or 1.

34. The compound of any one of claims 1-33, or a pharmaceutically acceptable salt thereof, wherein W^2 is $-CH_2-$, $-CH_2CH_2-$, $-CH=CH-$, , $-NH-$, $-N(CH_3)-$, $-N(CH(CH_3)_2)-$, $-N(C(O)CH_3)-$, $-N(SO_2CH_3)-$, $-O-$, or $-CH_2-O-$.

35. The compound of any one of claims 1-34, or a pharmaceutically acceptable salt thereof, wherein X is $-CH_2-$, $-CF_2-$, $-CH(F)-$, $-CH(OH)-$, $-CH(CH_3)-$, $-CH(CH_2F)-$ or $-CF(CH_3)-$.

36. The compound of any one of claims 1-34, or a pharmaceutically acceptable salt thereof, wherein X is $-CH_2-$, $-CF_2-$, $-CH(F)-$, $-CH(OH)-$, $-CH(CH_3)$ or $-CF(CH_3)-$.

37. The compound of any one of claims 1-34, or a pharmaceutically acceptable salt thereof, wherein X is a bond or $-CR^{8a}R^{8b}-$, wherein R^{8a} and R^{8b} are independently H, hydroxyl, -O-C_{1-4}alkyl, C_{1-4}alkyl, C_{1-4}haloalkyl, or halo; or

R^{8a} and R^{8b} together with the carbon to which they are attached form a 3- to 5-membered saturated spiro ring containing 0 to 2 heteroatoms selected from N, O, and S, wherein the spiro ring is optionally substituted with one to four R^{A5}, wherein each R^{A5} is independently halo, C_{1-4}alkyl or C_{1-4}haloalkyl.

38. The compound of any one of claims 1-37, or a pharmaceutically acceptable salt thereof, wherein X is a bond or $-CR^{8a}R^{8b}-$, wherein R^{8a} and R^{8b} are independently H, hydroxyl, -O-C_{1-4}alkyl, C_{1-4}alkyl, C_{1-4}haloalkyl, or halo; or

R^{8a} and R^{8b} together with the carbon to which they are attached form a 3-5 membered saturated spiro carbocyclic ring, wherein the a 3-5 membered saturated spiro carbocyclic ring is optionally substituted with one to four R^{A5}, wherein each R^{A5} is independently halo, C_{1-4}alkyl or C_{1-4}haloalkyl.

39. The compound of any one of claims 1-38, or a pharmaceutically acceptable salt thereof, wherein X is a bond or $-CR^{8a}R^{8b}-$, wherein R^{8a} and R^{8b} are independently H, hydroxyl, $-O-C_{1-4}$alkyl, C_{1-4}alkyl, C_{1-4}haloalkyl, or halo, or

R^{8a} and R^{8b} together with the carbon to which they are attached form a 3-membered saturated spiro carbocyclic ring.

40. The compound of any one of claims 1-39 or a pharmaceutically acceptable salt thereof, wherein X is a bond, $-CH_2-$, $-CF_2-$, $-CH(F)-$, $-CH(Cl)-$, $-CH(OH)-$, $-C(CH_2F)(H)-$, $-C(CH_2F)(OH)-$, $-C(CH_3)(OH)-$, $-CH(OCH_3)-$, $-C(CH_2CH_3)(OCH_3)-$, $-C(CH_2CH_3)(OH)-$, $-CH(CH_3)-$, $-CH(CH_2CH_3)-$, $-CF(CH_3)-$, $-CF(CH_2CH_3)-$, or $-CR^{8a}R^{8b}-$, wherein R^{8a} and R^{8b} together with the carbon to which they are attached form an spiro cyclopropane ring.

41. The compound of any one of claims 1-40, or a pharmaceutically acceptable salt thereof, wherein X is a bond, $-CH_2-$, $-CF_2-$, $-CH(F)-$, $-CH(Cl)-$, $-CH(OH)-$, $-C(CH_2F)(H)-$, $-C(CH_2F)(OH)-$, $-C(CH_3)(OH)-$, $-CH(OCH_3)-$, $-C(CH_2CH_3)(OCH_3)-$, $-C(CH_2CH_3)(OH)-$, $-CH(CH_3)-$, $-CH(CH_2CH_3)-$, $-CF(CH_3)-$, or $-CF(CH_2CH_3)-$.

42. The compound of any one of claims 1-41 or a pharmaceutically acceptable salt thereof, wherein X is a bond, $-CH_2-$, $-CF_2-$, $-CH(F)-$, $-CH(Cl)-$, $-CH(OH)-$, $-C(CH_2F)(OH)-$, $-C(CH_3)(OH)-$, $-CH(OCH_3)-$, $-C(CH_2CH_3)(OCH_3)-$, $-C(CH_2CH_3)(OH)-$, $-CH(CH_3)-$, $-CH(CH_2CH_3)-$, $-CF(CH_3)-$, $-CF(CH_2CH_3)-$, or $-CR^{8a}R^{8b}-$, wherein R^{8a} and R^{8b} together with the carbon to which they are attached form an spiro cyclopropane ring.

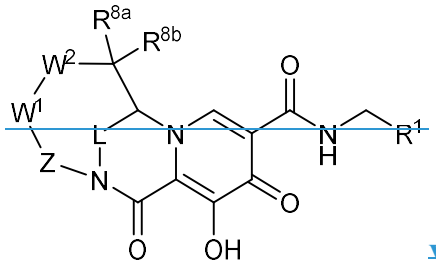
43. The compound of any one of claims 1-42, or a pharmaceutically acceptable salt thereof, wherein X is a bond, $-CH_2-$, $-CF_2-$, $-CH(F)-$, $-CH(Cl)-$, $-CH(OH)-$, $-C(CH_2F)(OH)-$, $-C(CH_3)(OH)-$, $-CH(OCH_3)-$, $-C(CH_2CH_3)(OCH_3)-$, $-C(CH_2CH_3)(OH)-$, $-CH(CH_3)-$, $-CH(CH_2CH_3)-$, $-CF(CH_3)-$, or $-CF(CH_2CH_3)-$.

44. The compound of any one of claims 1-37, or a pharmaceutically acceptable salt thereof, wherein X is –$CR^{8a}R^{8b}$–, wherein R^{8a} and R^{8b} together with the carbon to which they are attached form a 3 to 5 membered saturated spiro ring containing 0 to 2 heteroatoms selected from N, O, and S, wherein the spiro ring is optionally substituted with one to four R^{A5}, wherein each R^{A5} is independently halo, C_{1-4}alkyl or C_{1-4}haloalky.

45. The compound of any one of claims 1-38 and 44, or the pharmaceutically acceptable salt thereof, wherein X is –$CR^{8a}R^{8b}$–, wherein R^{8a} and R^{8b} together with the carbon to which they are attached form a 3-5 membered saturated spiro carbocyclic ring, wherein the a 3-5 membered saturated spiro carbocyclic ring optionally substituted with one to four R^{A5}, wherein each R^{A5} is independently halo, C_{1-4}alkyl or C_{1-4}haloalkyl.

46. The compound of any one of claims 1-39, 44, and 45, or the pharmaceutically acceptable salt thereof, wherein X is –$CR^{8a}R^{8b}$–, wherein R^{8a} and R^{8b} together with the carbon to which they are attached form a 3-membered spiro carbocyclic ring.

47. The compound of any one of claims 1-19 or a pharmaceutically acceptable salt thereof, having the formula (**VIII**):



VIII.

48. The compound of any one of claims 1-47, or a pharmaceutically acceptable salt thereof, wherein Z is –$CR^{9a}R^{9b}$–, –$CR^{9a}R^{9b}CR^{9e}R^{9d}$–, or –$CR^{10a}$=$CR^{10b}$–; wherein

R^{9a}, R^{9b}, R^{9e}, and R^{9d} are each independently H, C_{1-6}alkyl, C_{1-4}haloalkyl, or halo; or

R^{9a} and R^{9b} or R^{9c} and R^{9d} together with the carbon atom to which they are attached form a 3 to 7 membered saturated or partially unsaturated ring containing 0 to 2 heteroatoms selected from N, O, and S, wherein the spiro ring is optionally substituted with one to three R^{A6}, wherein each R^{A6} is independently halo, C_{1-4}alkyl or C_{1-4}haloalkyl;

R^{10a} and R^{10b} are independently H, halo, C_{1-4}haloalkyl, or C_{1-6}alkyl; or

R^{10a} and R^{10b} together with the carbon atoms to which each is attached form (i) a 5-10 membered partially unsaturated fused ring containing 0 heteroatoms or 1 heteroatom selected from N, O, and S, (ii) a 5-10 membered fused aromatic ring, or (iii) a 5-10 membered fused heteroaromatic ring containing 1 to 2 heteroatoms selected from N, O and S, wherein the 5-10 membered partially unsaturated fused ring, 5-10 membered fused aromatic ring, or 5-10 membered fused heteroaromatic ring is optionally substituted with one to four R^{A7}, wherein each R^{A7} is independently halo or C_{1-4}alkyl.

49. The compound of any one of claims 1-48, or a pharmaceutically acceptable salt thereof, wherein Z is $CR^{9a}R^{9b}$, $CR^{9a}R^{9b}CR^{9c}R^{9d}$, or $CR^{10a}=CR^{10b}$; wherein R^{9a}, R^{9b}, R^{9c}, and R^{9d} are each independently H, C_{1-6}alkyl, C_{1-4}haloalkyl, or halo; or

R^{9a} and R^{9b} or R^{9c} and R^{9d} together with the carbon atom to which they are attached form a 3-membered saturated spiro carbocyclic ring;

R^{10a} and R^{10b} are independently H, halo, C_{1-4}haloalkyl, or C_{1-6}alkyl; or

R^{10a} and R^{10b} together with the carbon atoms to which each is attached form (i) a fused phenyl ring or (ii) a 5-6 membered fused heteroaromatic ring containing 1 to 2 heteroatoms selected from N, O and S, wherein the fused phenyl ring or the fused heteroaromatic ring is optionally substituted with one to two R^{A7}, wherein each R^{A7} is independently halo or C_{1-4}alkyl.

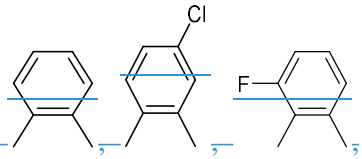
~~50. The compound of any one of claims 1-49, or a pharmaceutically acceptable salt thereof, wherein Z is $-CR^{9a}R^{9b}-$, $-CR^{9a}R^{9b}CR^{9c}R^{9d}-$, or $-CR^{10a}=CR^{10b}-$; wherein~~

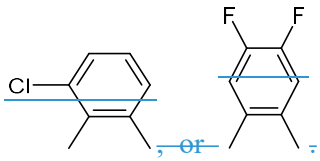
~~R^{9a}, R^{9b}, R^{9c}, and R^{9d} are each independently H, CH_3, CH_2CH_3, CHF_2, or halo; or~~

~~R^{9a} and R^{9b} or R^{9c} and R^{9d} together with the carbon atom to which they are attached form a 3-membered carbocyclic ring;~~

~~R^{10a} and R^{10b} are independently H, halo, or CH_3; or~~

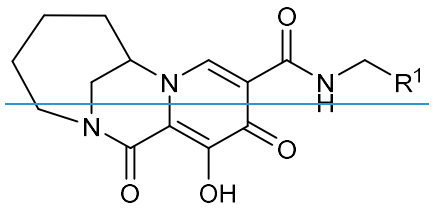
~~R^{10a} and R^{10b} together with the carbon atoms to which each is attached form (i) a fused phenyl ring or (ii) a 5-6 membered fused heteroaromatic ring containing 1 to 2 heteroatoms selected from N, O and S, wherein the fused phenyl ring or the fused heteroaromatic ring is optionally substituted with one to two R^{A7}, wherein each R^{A7} is independently halo or CH_3.~~

~~51. The compound of any one of claims 1-50 or a pharmaceutically acceptable salt thereof, wherein Z is $-CH_2-$, $-CH(CH_3)-$, $-CH_2-CH_2-$,~~ 

~~,~~ 

~~, or~~ .

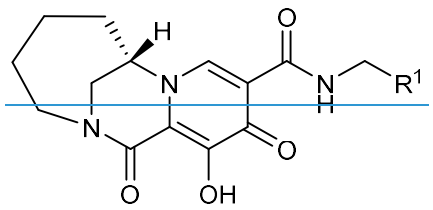
~~52. The compound of any one of claims 1-51, wherein the compound has a formula (**IX**):~~



~~IX~~

~~or a pharmaceutically acceptable salt thereof.~~

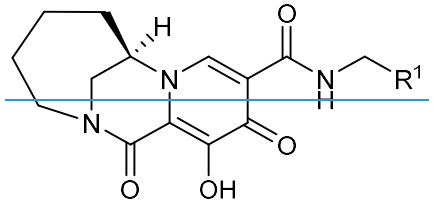
~~53. The compound of any one of claims 1-52, wherein the compound has a formula (**IXa**):~~



~~IXa~~

~~or a pharmaceutically acceptable salt thereof.~~

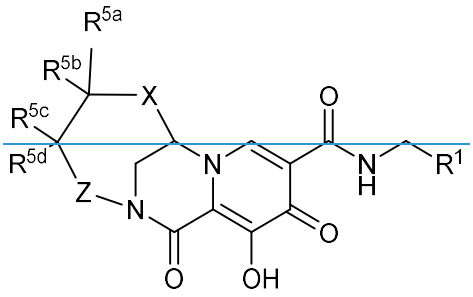
~~54. The compound of any one of claims 1-52, wherein the compound has a formula (**IXb**):~~



~~IXb~~

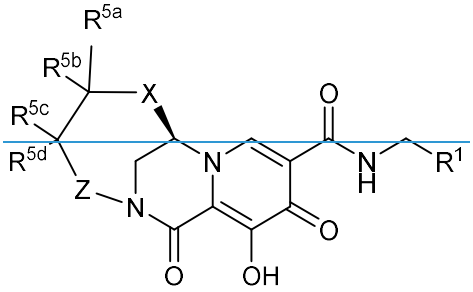
~~or a pharmaceutically acceptable salt thereof.~~

~~55. The compound of any one of claims 1-19 or a pharmaceutically acceptable salt thereof, wherein the compound has a Formula (**X**):~~



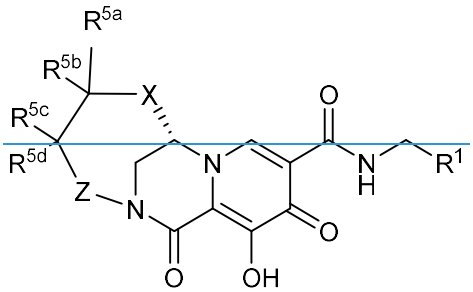
Formula (**X**).

56. The compound of any one of claims 1-19 and 55, or a pharmaceutically acceptable salt thereof, wherein the compound has a Formula (**Xa**):



Formula (**Xa**).

57. The compound of any one of claims 1-19 and 55, or a pharmaceutically acceptable salt thereof, wherein the compound has a Formula (**Xb**):



Formula (**Xb**).

58. The compound of any one of claims 55-57, wherein X is bond or $-CR^{8a}R^{8b}-$; wherein R^{8a} and R^{8b} are each independently H, hydroxyl, $-O-C_{1-4}$alkyl, C_{1-4}alkylene$-O-C_{1-4}$alkyl, C_{1-6}alkyl, C_{1-4}haloalkyl, cyano, or halo.

59. The compound of any one of claims 55-58, wherein X is bond.

60. The compound of any one of claims 55-58, wherein X is $-CR^{8a}R^{8b}-$; wherein R^{8a} and R^{8b} are each independently H, hydroxyl, $-O-C_{1-4}$alkyl, C_{1-4}alkylene$-O-C_{1-4}$alkyl, C_{1-6}alkyl, C_{1-4}haloalkyl, cyano, or halo.

61. The compound of any one of claims 55-58 and 60, wherein X is $-CR^{8a}R^{8b}-$; wherein R^{8a} and R^{8b} are each independently H, C_{1-6}alkyl, C_{1-4}haloalkyl, or halo.

62. The compound of any one of claims 55-58, 60, and 61, wherein R^{8a} and R^{8b} are each independently H, $-CH_3$, $-CHF_2$, $-CH_2F$, or halo.

63. The compound of any one of claims 55-62, wherein Z is $-CR^{9a}R^{9b}-$ or $-CR^{9a}R^{9b}CR^{9c}R^{9d}-$; wherein R^{9a}, R^{9b}, R^{9c}, and R^{9d} are each independently H, C_{1-6}alkyl, or C_{1-4}haloalkyl.

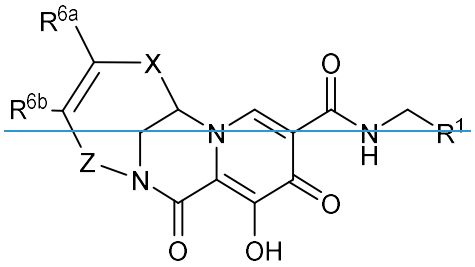
64. The compound of any one of claims 55-63, wherein Z is $-CR^{9a}R^{9b}-$.

65. The compound of any one of claims 55-63, wherein Z is $-CR^{9a}R^{9b}CR^{9c}R^{9d}-$.

66. The compound of any one of claims 55-65, wherein R^{9a}, R^{9b}, R^{9c}, and R^{9d} are each independently H, $-CH_3$, $-CHF_2$, or $-CH_2F$.

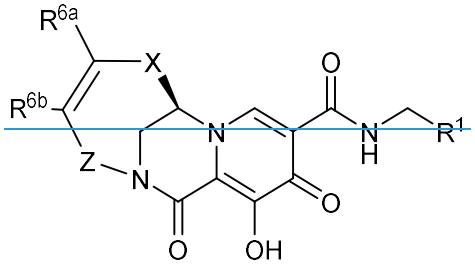
67. The compound of any one of claims 55-66, wherein each R^{5a}, R^{5b}, R^{5c}, and R^{5d} is independently H, halo, C_{1-4}haloalkyl, or C_{1-6}alkyl.

68. The compound of any one of claims 1-19 or a pharmaceutically acceptable salt thereof, wherein the compound has a Formula (**XI**):



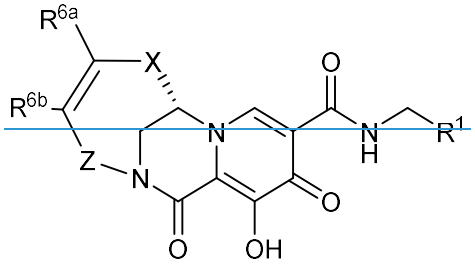
Formula (**XI**).

69. The compound of any one of claims 1-19 and 68, or a pharmaceutically acceptable salt thereof, wherein the compound has a Formula (**XIa**):



Formula (**XIa**).

70. The compound of any one of claims 1-19 and 68, or a pharmaceutically acceptable salt thereof, wherein the compound has a Formula (**XIb**):



Formula (**XIb**).

71. The compound of any one of claims 68-70, wherein X is bond or $-CR^{8a}R^{8b}-$; wherein R^{8a} and R^{8b} are each independently H, hydroxyl, $-O-C_{1-4}$alkyl, C_{1-4}alkylene$-O-C_{1-4}$alkyl, C_{1-6}alkyl, C_{1-4}haloalkyl, cyano, or halo.

72. The compound of any one of claims 68-71, wherein X is bond.

~~73. The compound of any one of claims 68-71, wherein X is $-CR^{8a}R^{8b}-$; wherein R^{8a} and R^{8b} are each independently H, hydroxyl, $-O-C_{1-4}$alkyl, C_{1-4}alkylene$-O-C_{1-4}$alkyl, C_{1-6}alkyl, C_{1-4}haloalkyl, cyano, or halo.~~

~~74. The compound of any one of claims 68-71 and 73, wherein X is $-CR^{8a}R^{8b}-$; wherein R^{8a} and R^{8b} are each independently H, C_{1-6}alkyl, C_{1-4}haloalkyl, or halo.~~

~~75. The compound of any one of claims 68-71, 73, and 74, wherein R^{8a} and R^{8b} are each independently H, $-CH_3$, $-CHF_2$, $-CH_2F$, or halo.~~

~~76. The compound of any one of claims 68-75, wherein Z is $-CR^{9a}R^{9b}-$ or $-CR^{9a}R^{9b}CR^{9c}R^{9d}-$; wherein R^{9a}, R^{9b}, R^{9c}, and R^{9d} are each independently H, C_{1-6}alkyl, or C_{1-4}haloalkyl.~~

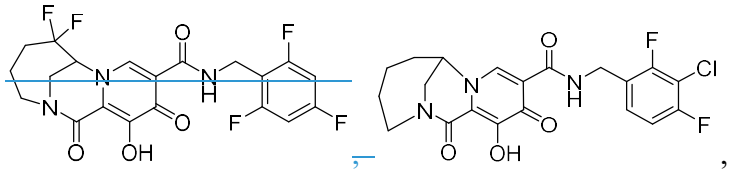
~~77. The compound of any one of claims 68-76, wherein Z is $-CR^{9a}R^{9b}-$.~~

~~78. The compound of any one of claims 68-76, wherein Z is $-CR^{9a}R^{9b}CR^{9c}R^{9d}-$.~~

~~79. The compound of any one of claims 68-78, wherein R^{9a}, R^{9b}, R^{9c}, and R^{9d} are each independently H, $-CH_3$, $-CHF_2$, or $-CH_2F$.~~

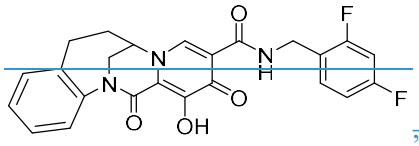
~~80. The compound of any one of claims 68-79, wherein each R^{6a} and R^{6b} is independently H, halo, C_{1-4}haloalkyl, or C_{1-6}alkyl.~~

~~81.~~1. A compound having the formula:

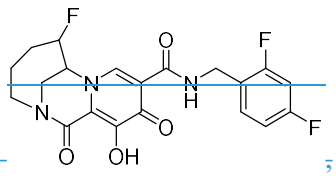


,

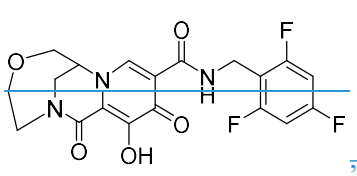
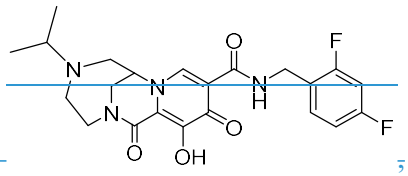
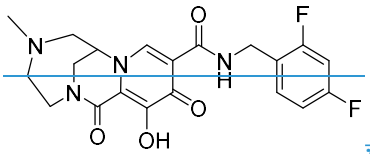
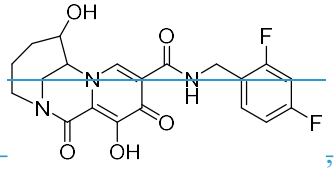
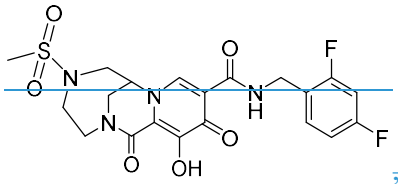
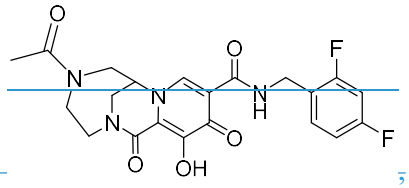
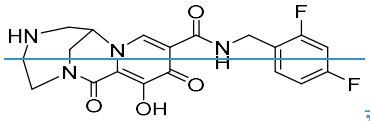
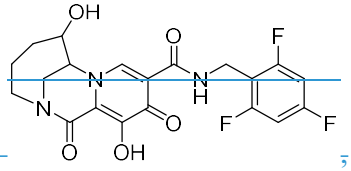
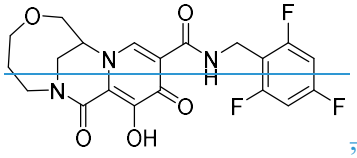
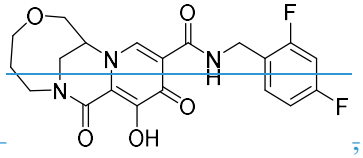
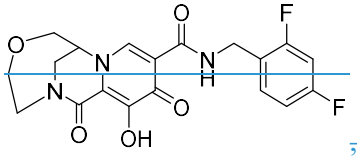
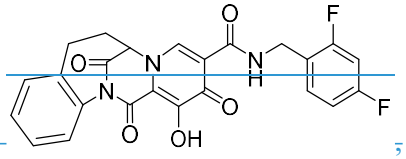
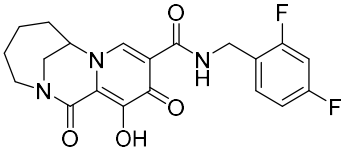
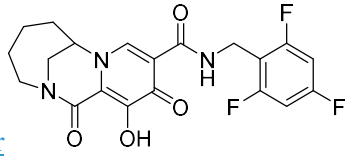
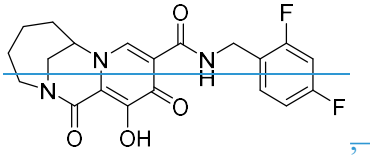
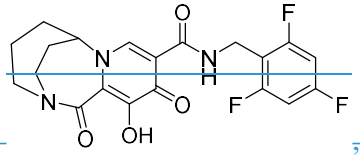
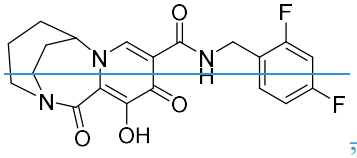
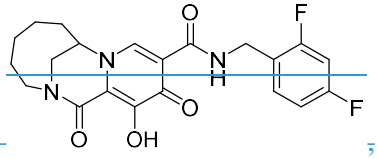
,

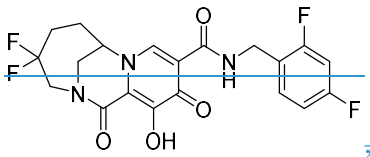
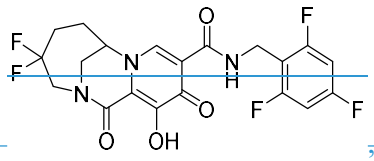
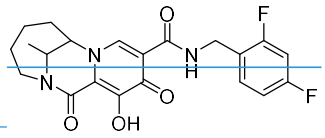
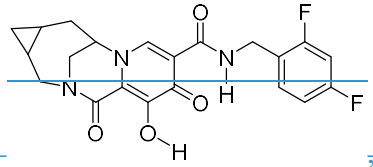


,



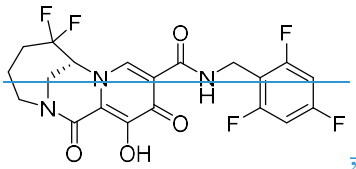
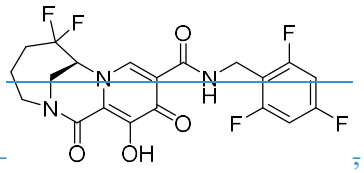
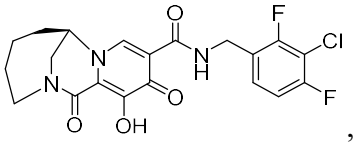
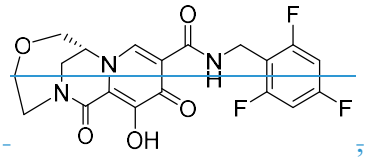
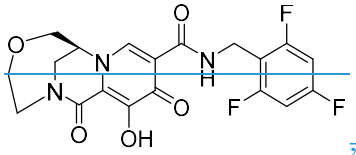
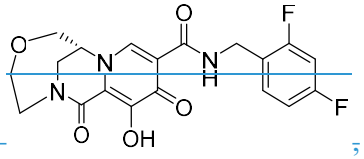
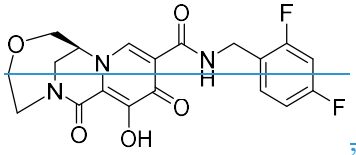
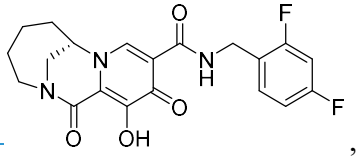
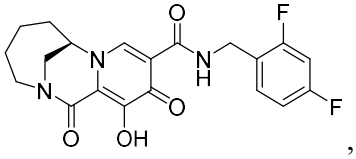
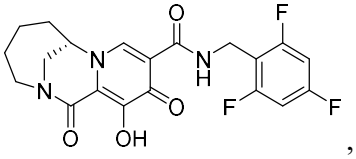
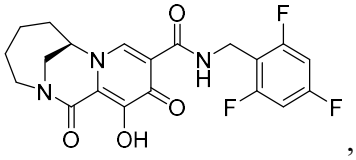
;


,

,

,

,

,

,

,

,

,

,

,

,

,

, or ,

,

,

,

,

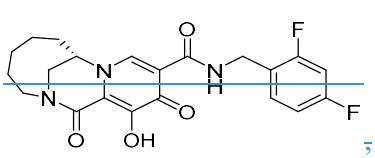





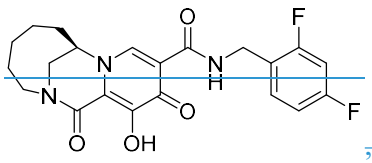
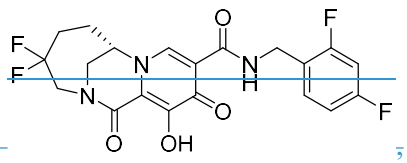
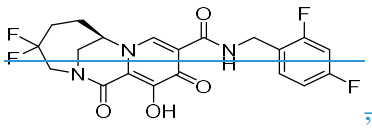
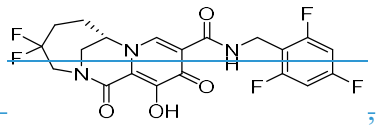
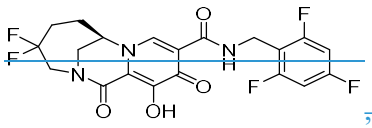
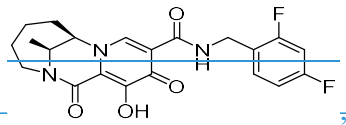
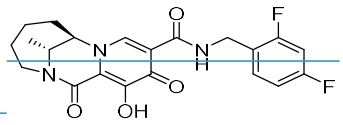
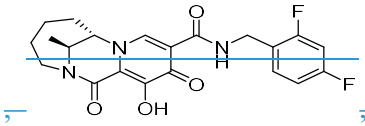
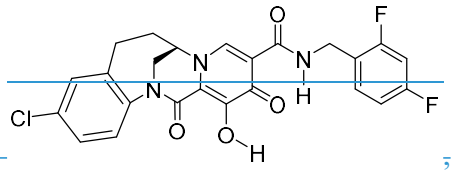
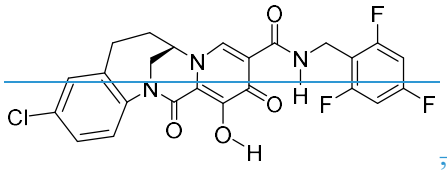
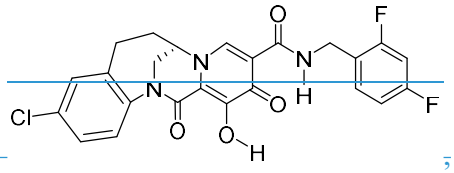
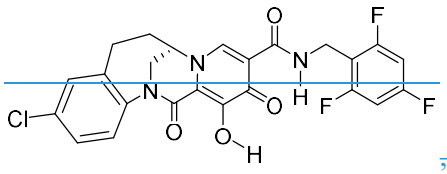
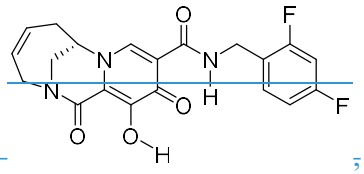
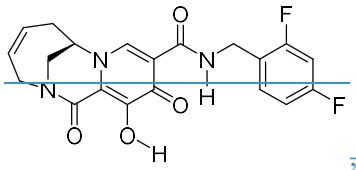
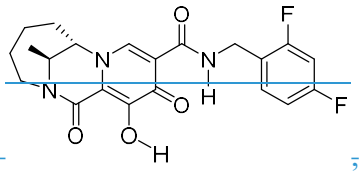
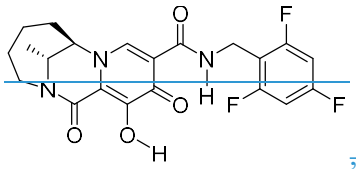
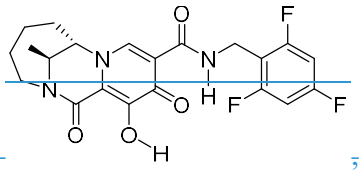
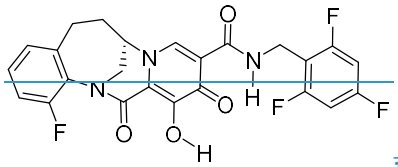
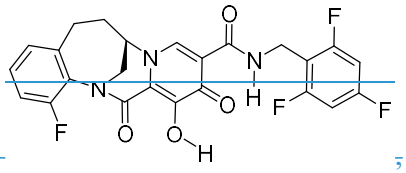
, or a pharmaceutically acceptable salt thereof.

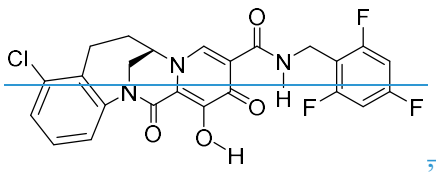
82. 2. A compound of claim 1 having the formula

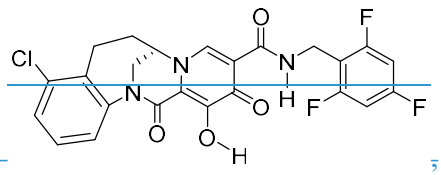












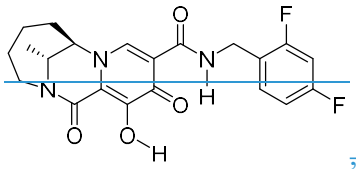
, or

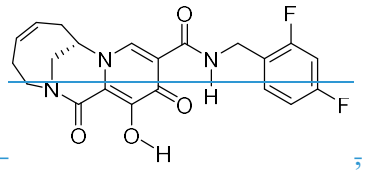


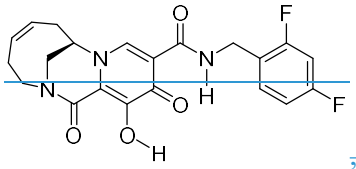




















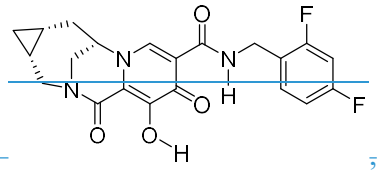

,

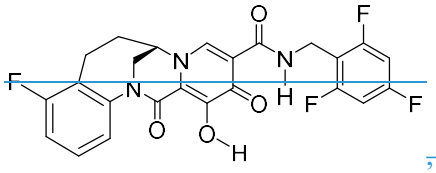

,

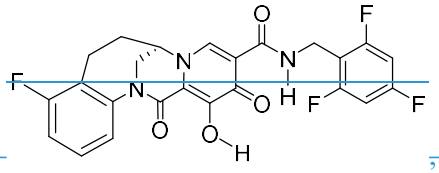

,

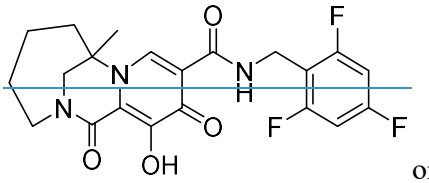

,


,


,

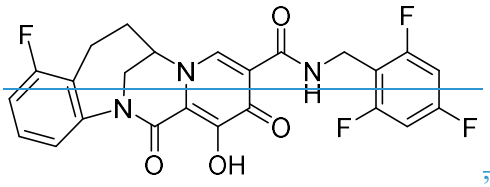

,

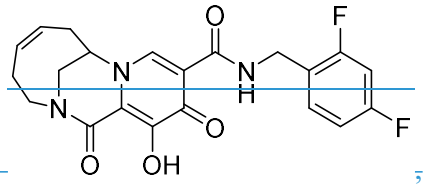

, and

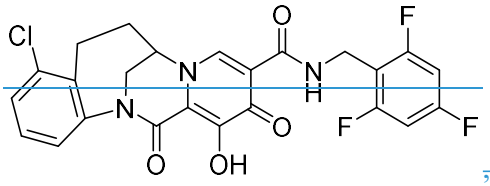


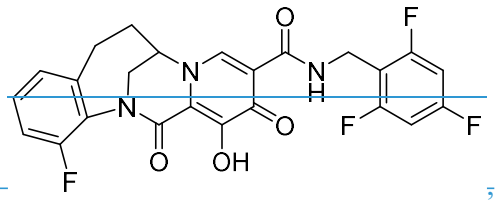
or a pharmaceutically acceptable salt thereof.

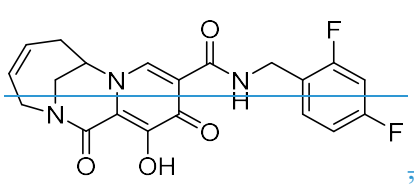
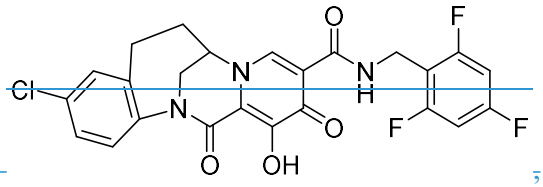
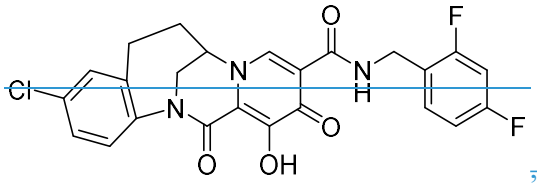
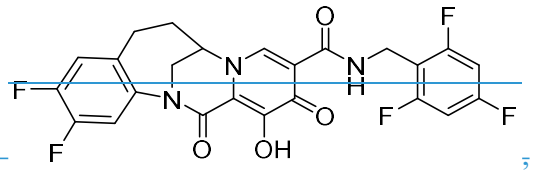
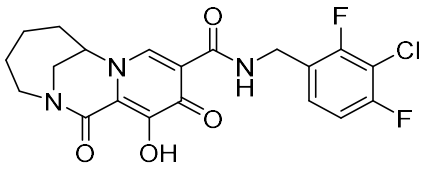
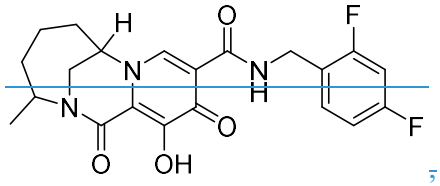
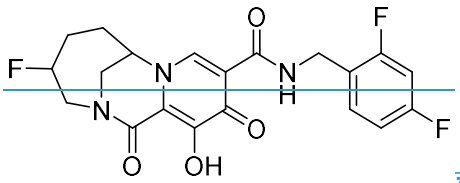
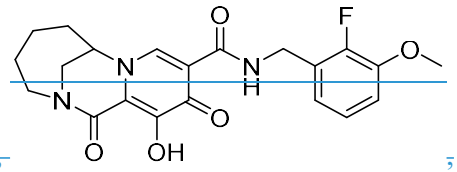
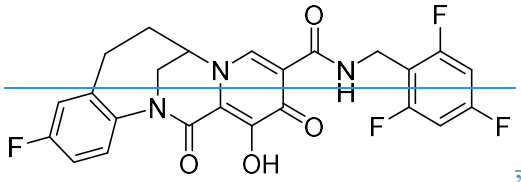
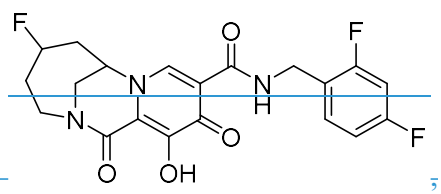
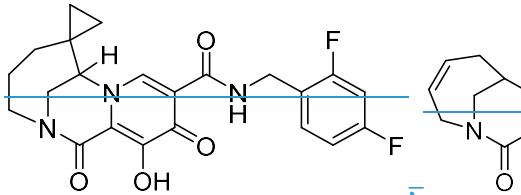
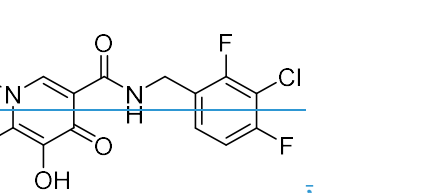
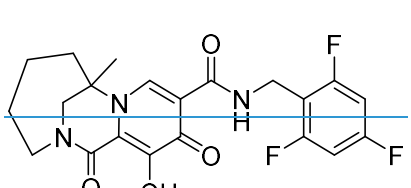
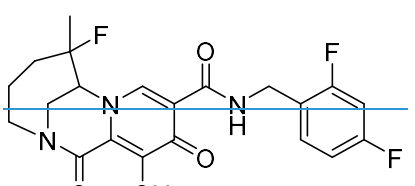
~~83.~~3. A compound of claim 1 having the formula~~selected from the group consisting of~~:

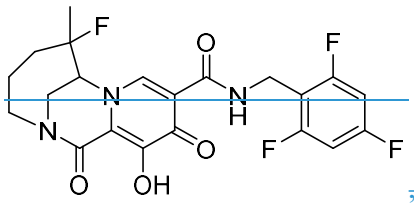
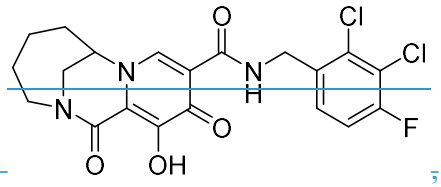

,

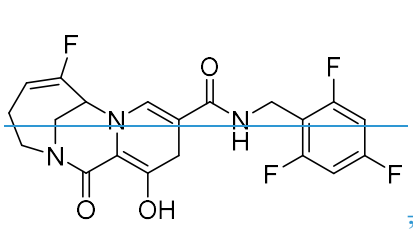
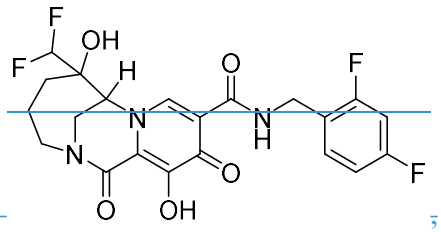
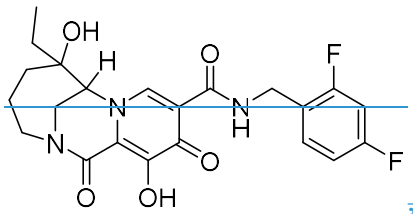
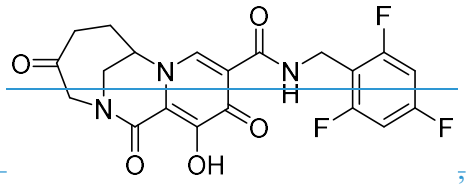
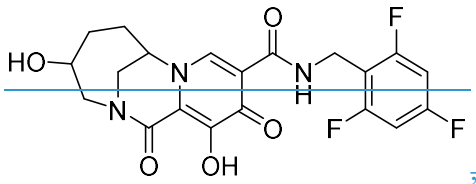
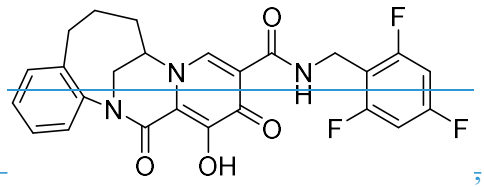
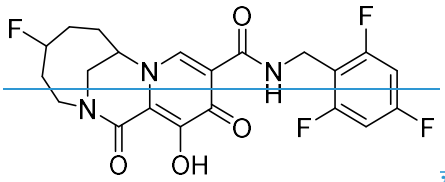
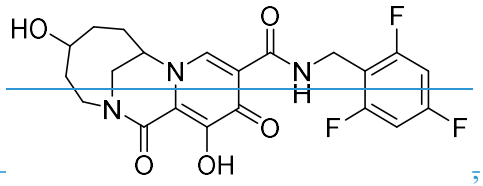
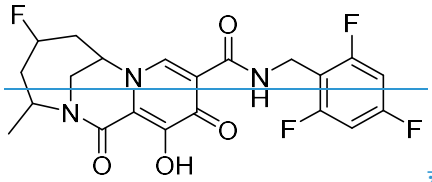
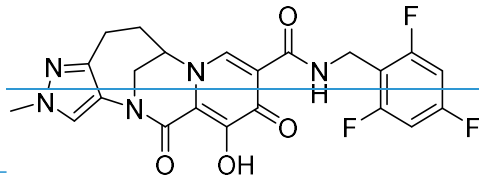
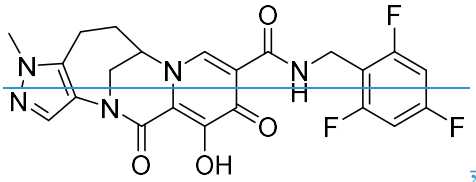
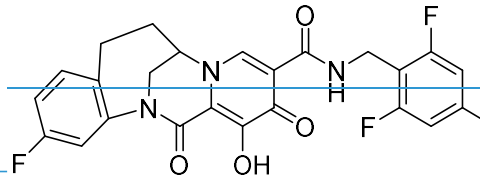
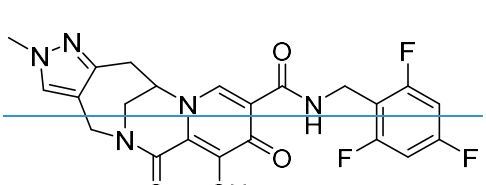
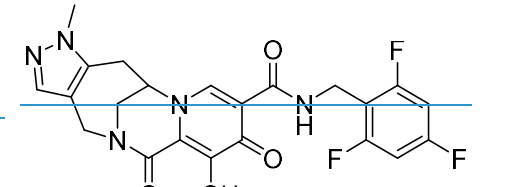

,


,

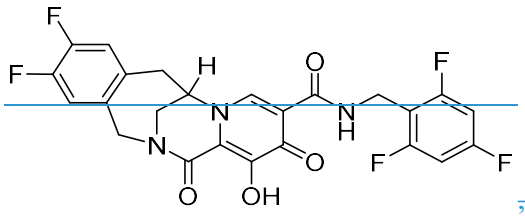

,

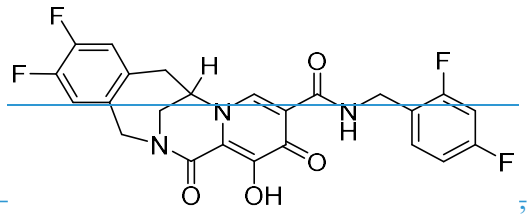















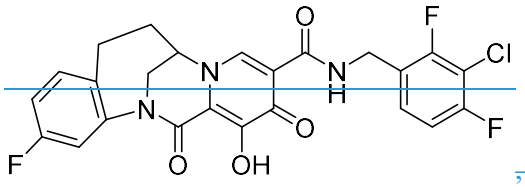



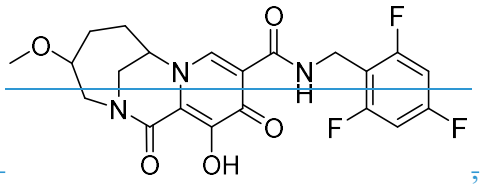















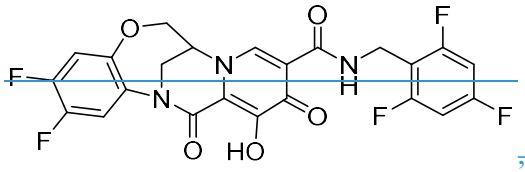


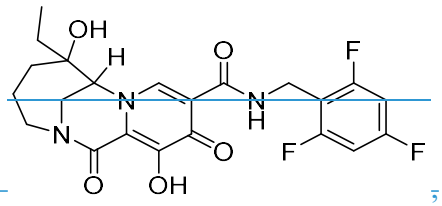


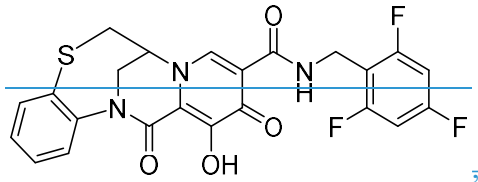


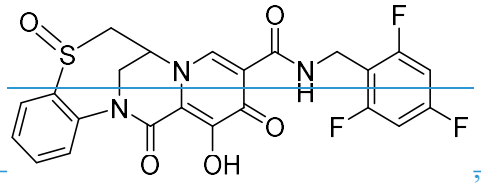


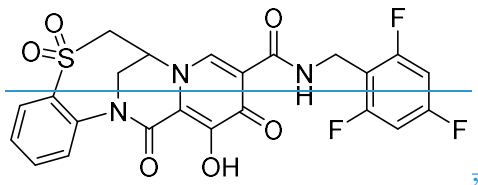


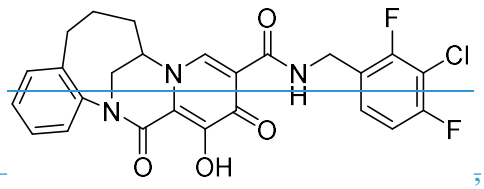


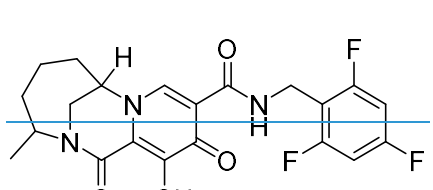


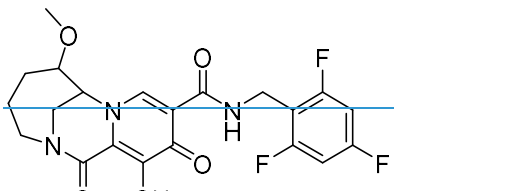


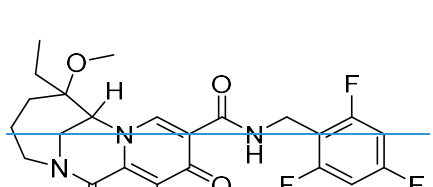


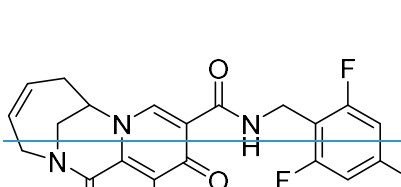


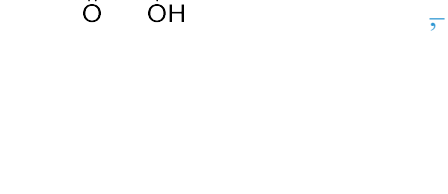


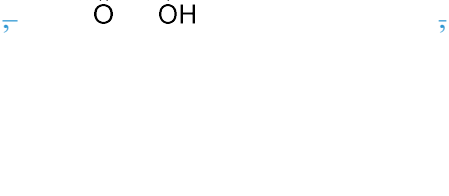


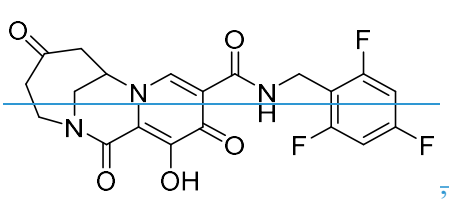
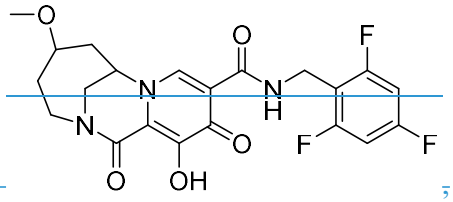
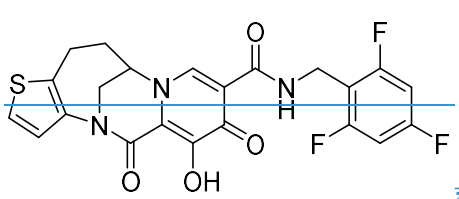
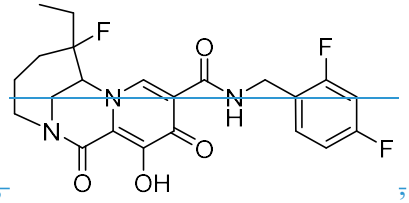
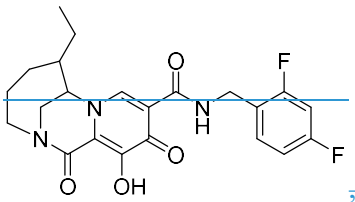
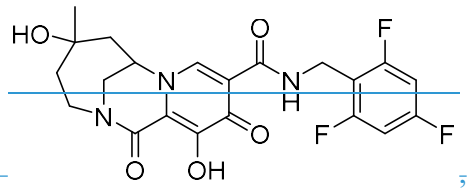
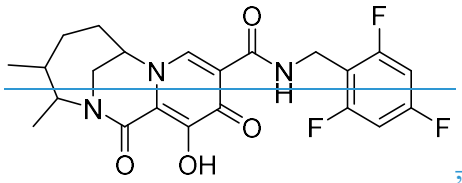
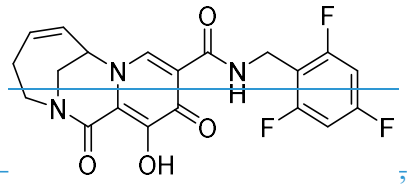
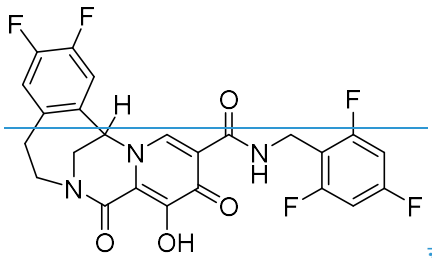
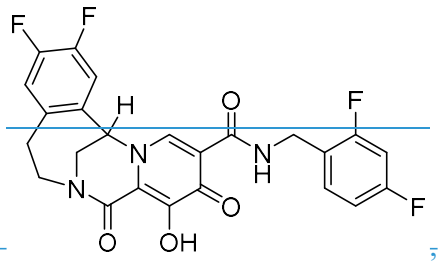
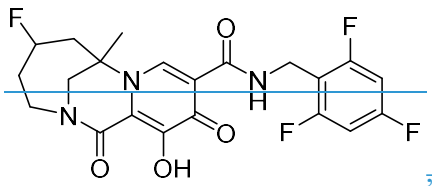
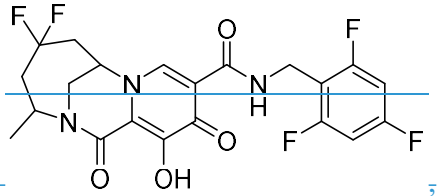
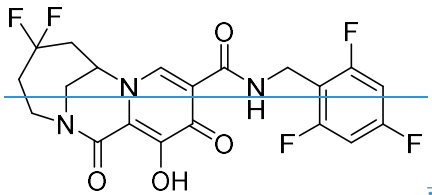
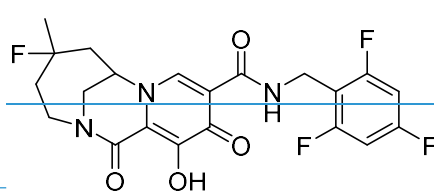


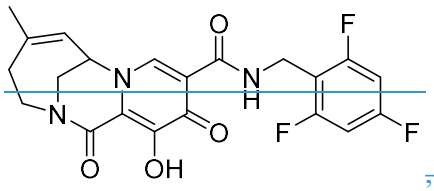
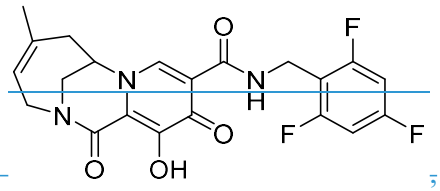
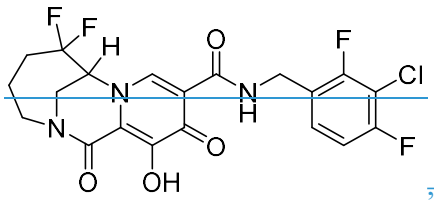
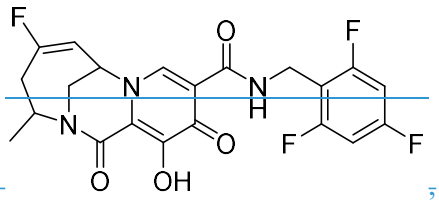
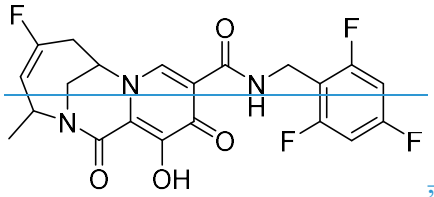
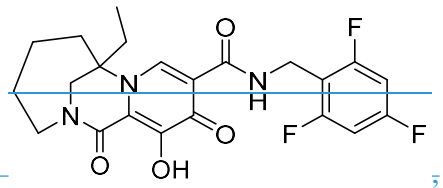
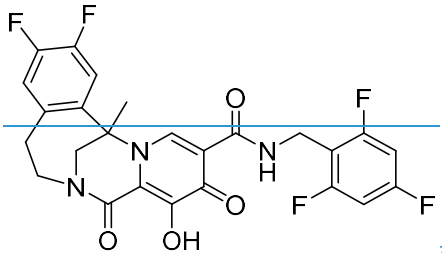
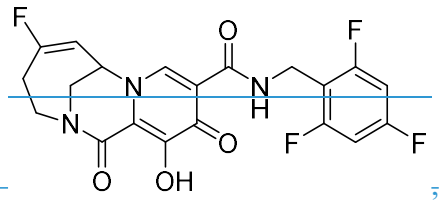
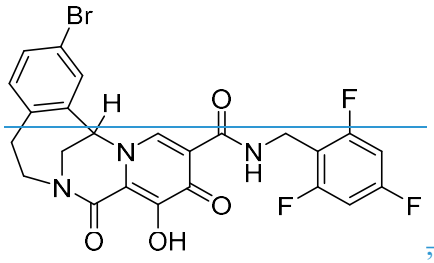
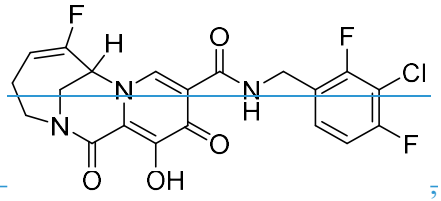
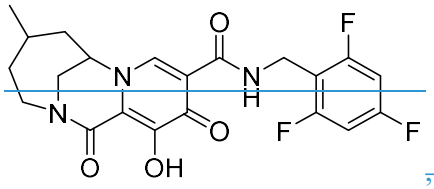
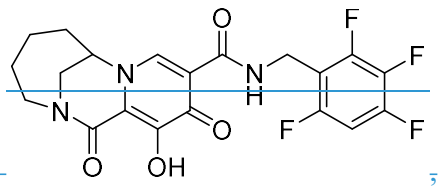
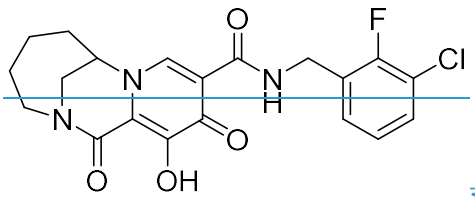
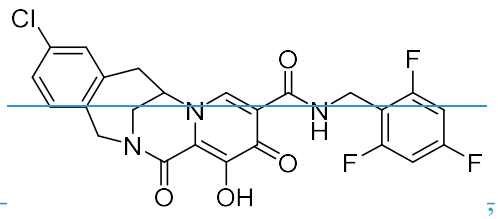


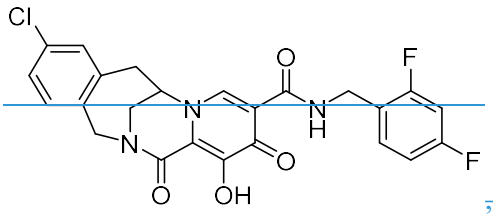
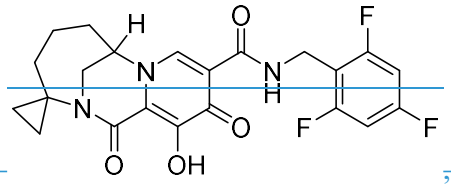
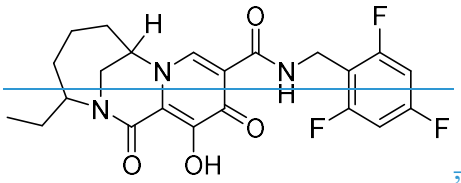
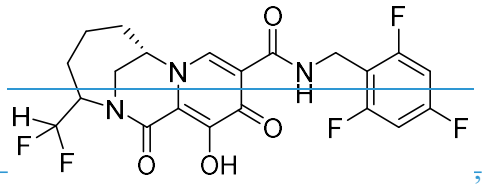
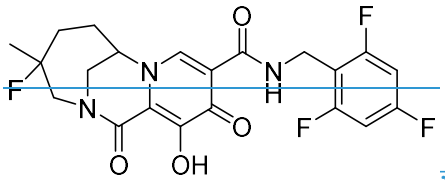
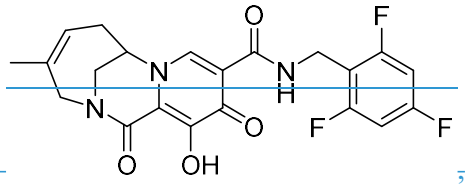
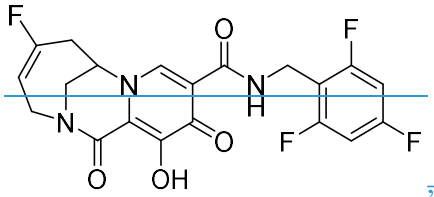
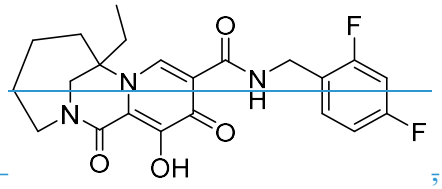
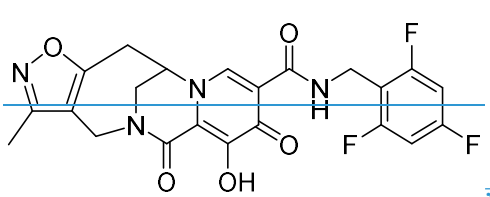
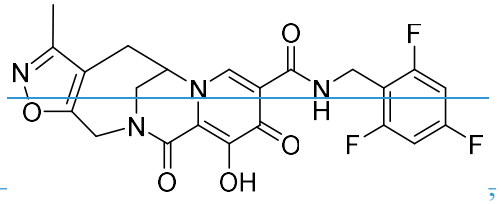
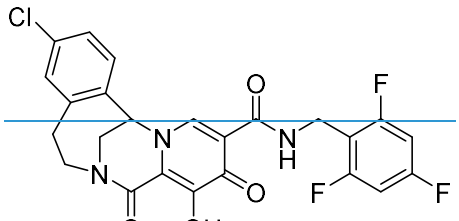
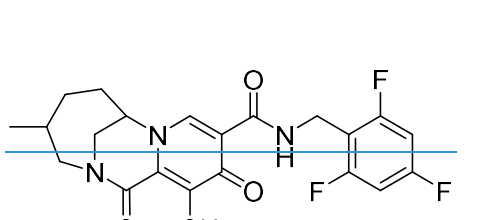
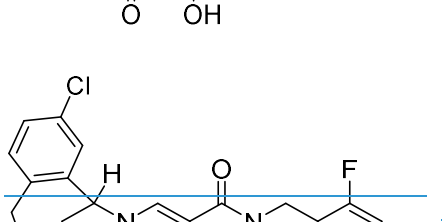
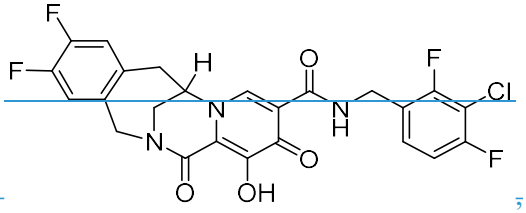


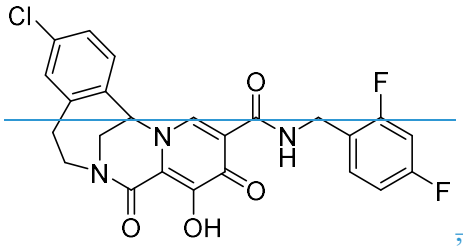


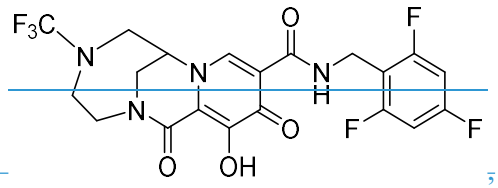


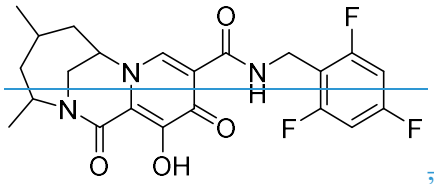















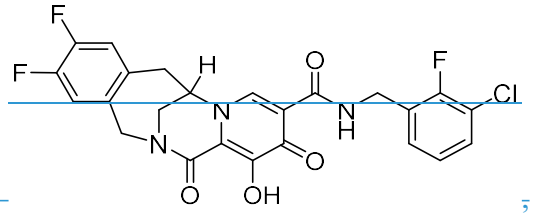















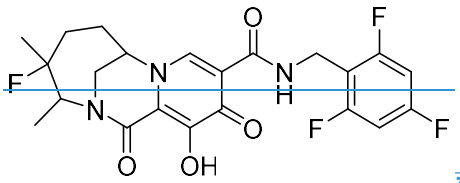















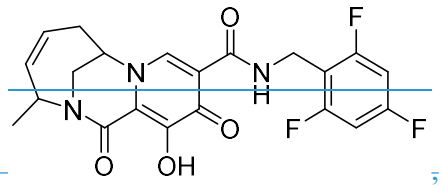


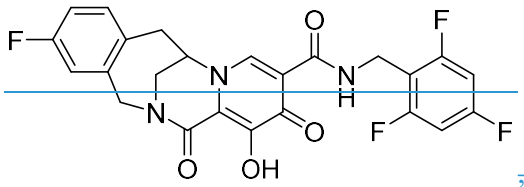


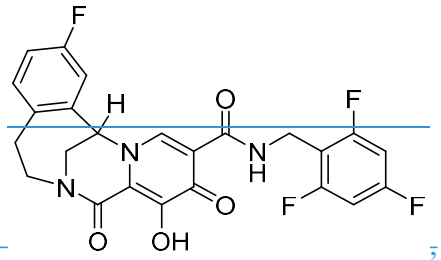


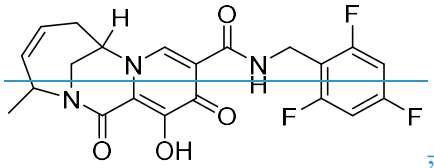


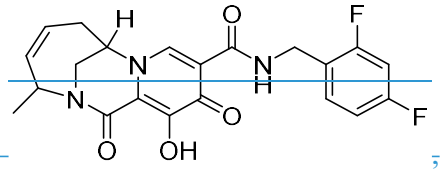


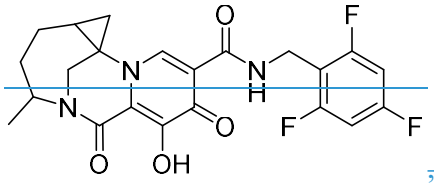


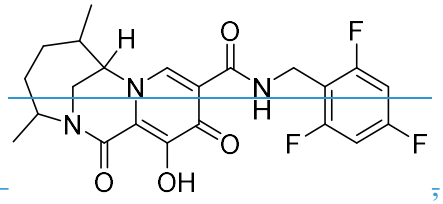


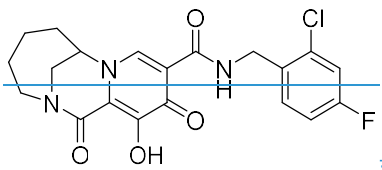


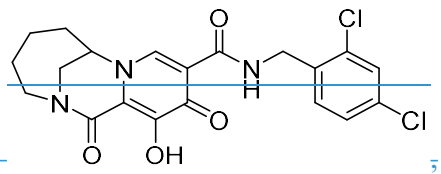


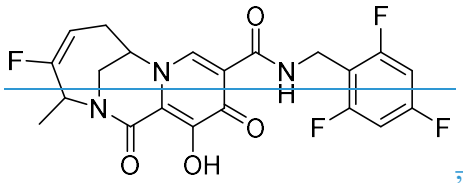


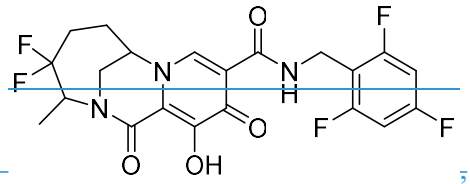


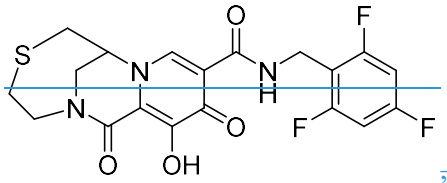


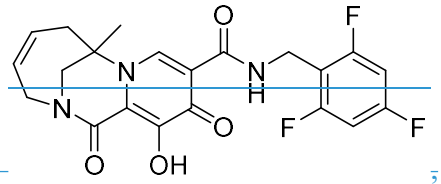


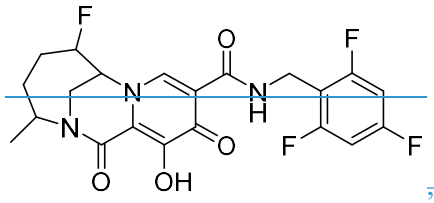


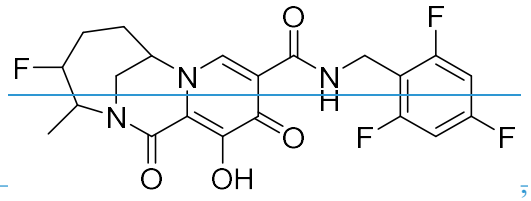

,

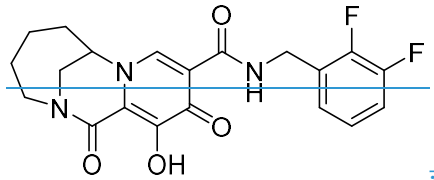

,

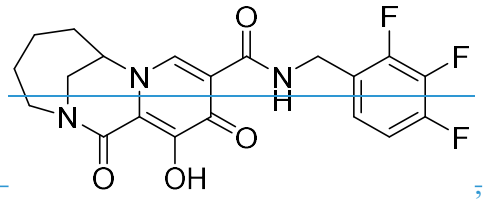

,

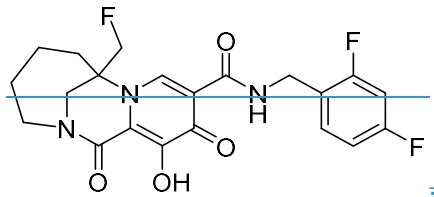

,

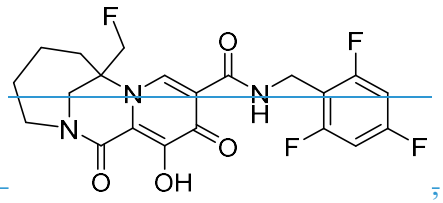

,

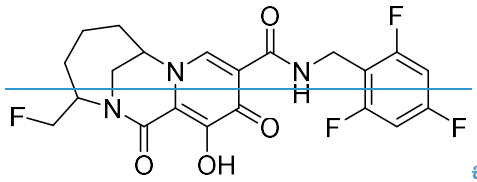

,

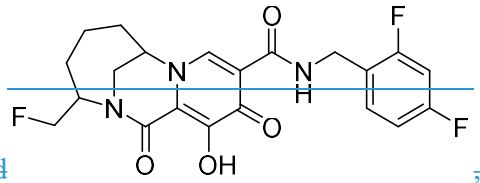

,


,

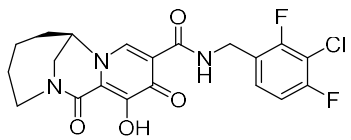

,


,

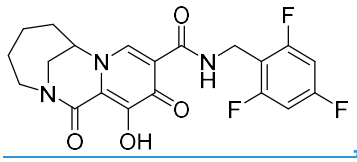

and


, or a pharmaceutically acceptable salt thereof.

4. A compound ~~selected from the group consisting of~~of claim 1 having the formula:

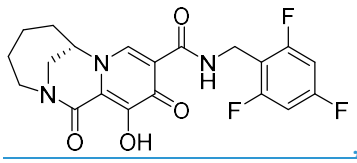

, or a pharmaceutically acceptable salt thereof.

5. A compound of claim 1 having the formula:



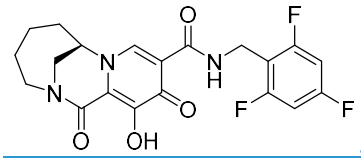
, or a pharmaceutically acceptable salt thereof.

6. A compound of claim 1 having the formula:



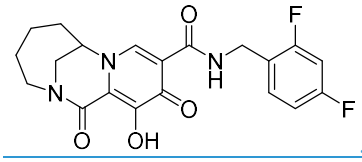
, or a pharmaceutically acceptable salt thereof.

7. A compound of claim 1 having the formula:



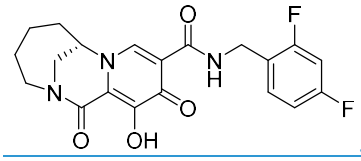
, or a pharmaceutically acceptable salt thereof.

8. A compound of claim 1 having the formula:



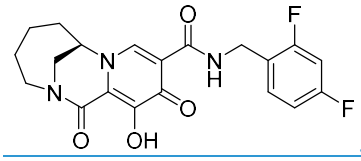
, or a pharmaceutically acceptable salt thereof.

9. A compound of claim 1 having the formula:

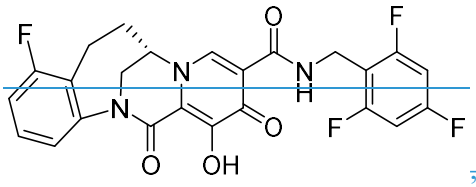
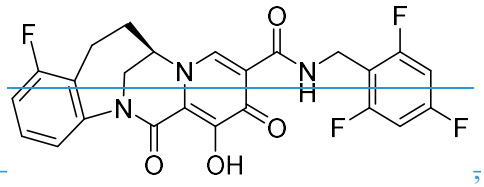
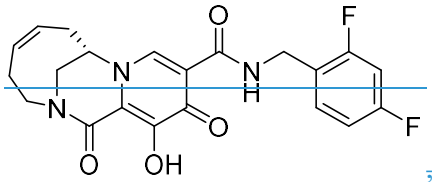
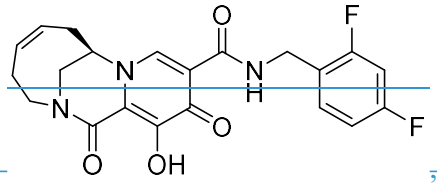
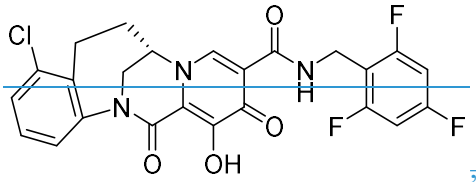
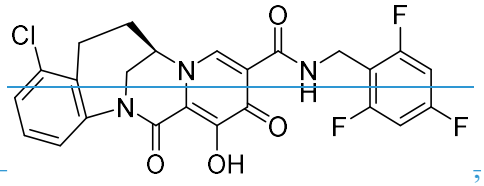
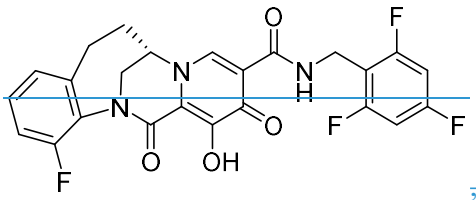
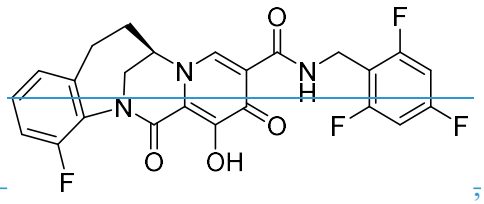
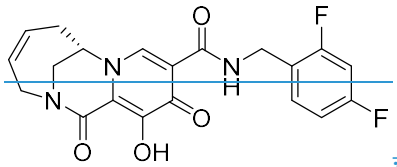
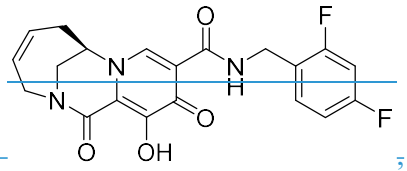
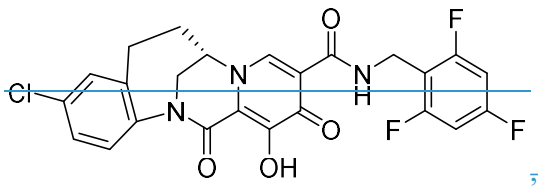
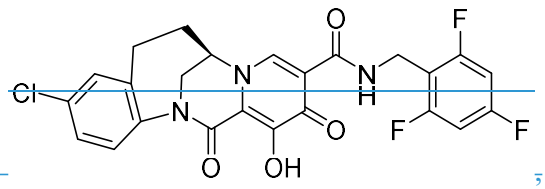
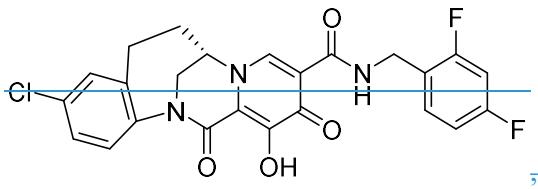
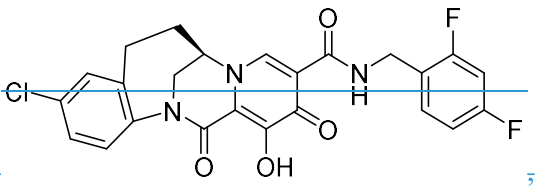
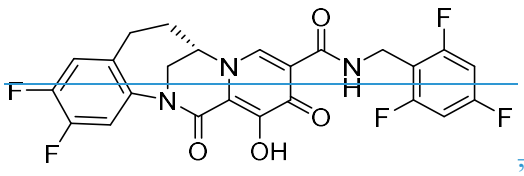
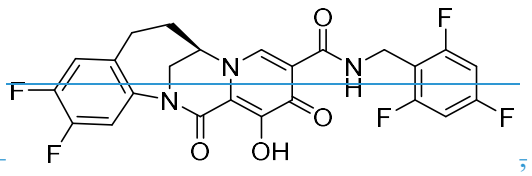


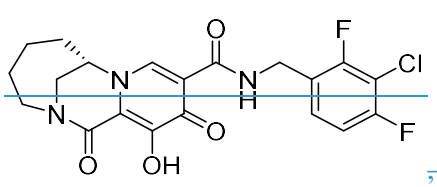
, or a pharmaceutically acceptable salt thereof.

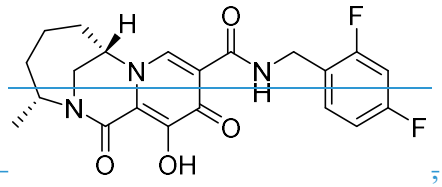
10. A compound of claim 1 having the formula:

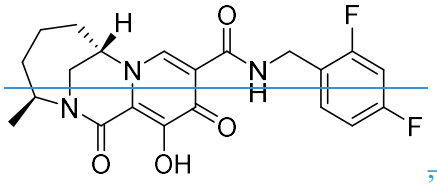


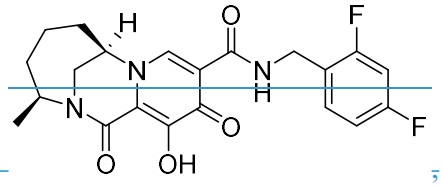
, or a pharmaceutically acceptable salt thereof.

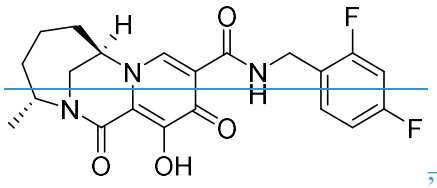

















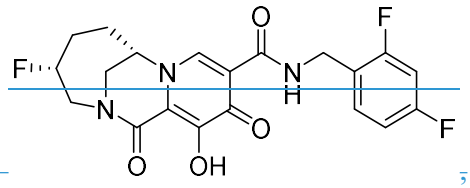


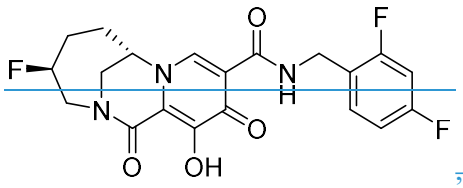


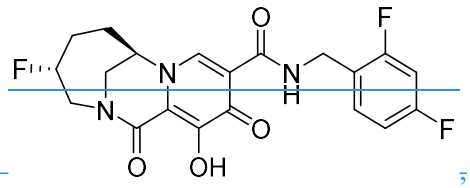


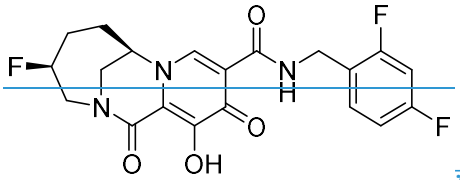


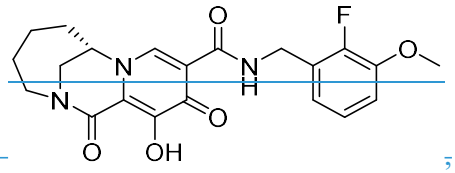


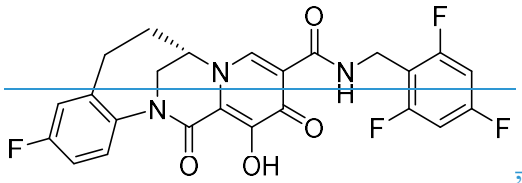


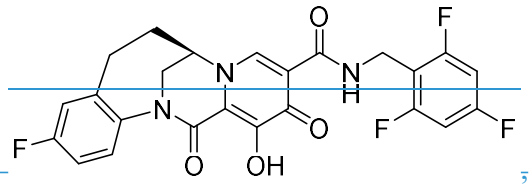


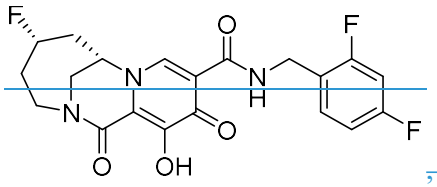


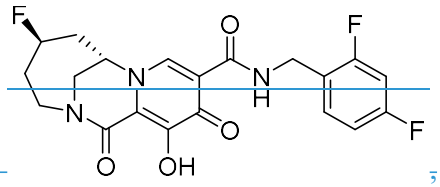


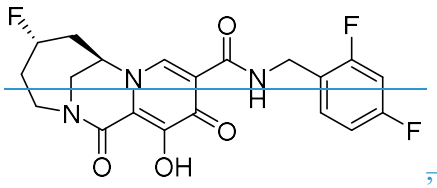


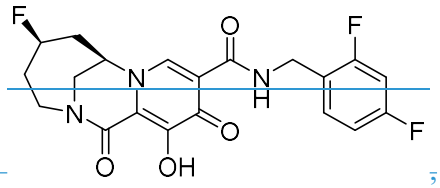


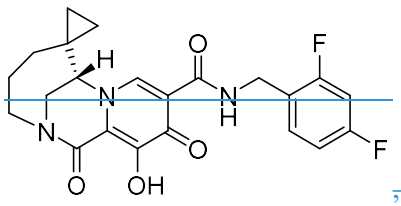
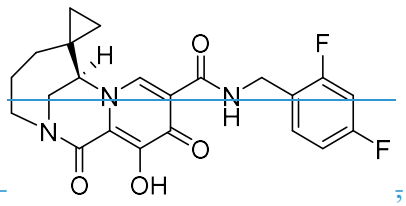
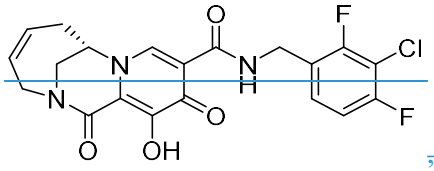
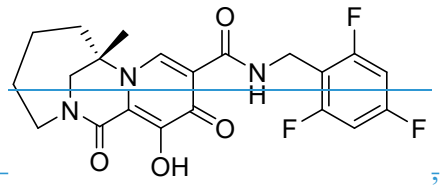
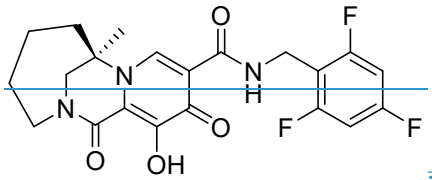
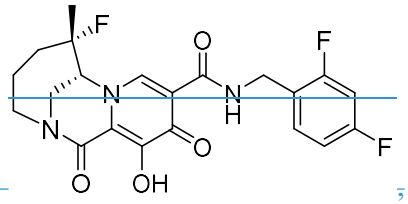
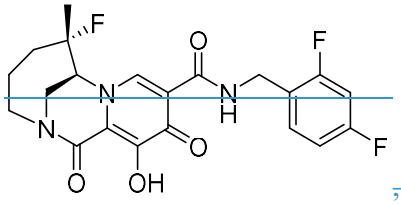
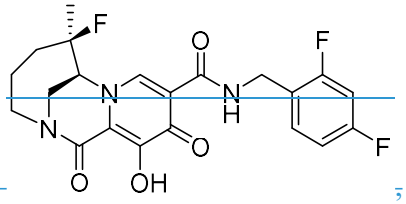
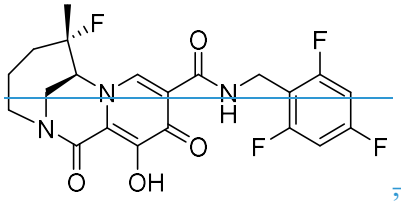
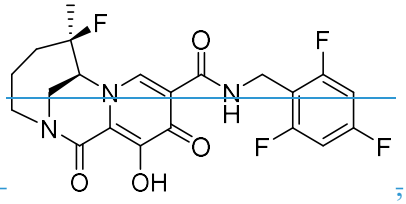
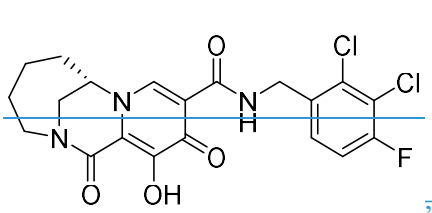
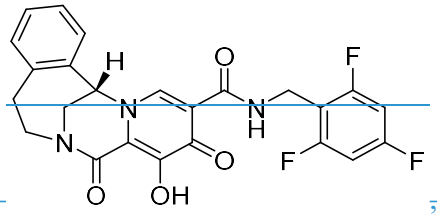
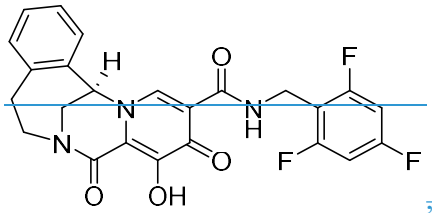
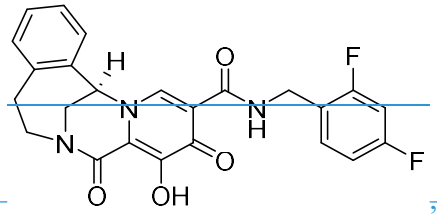


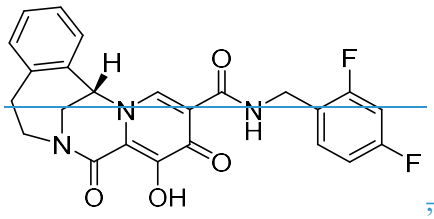


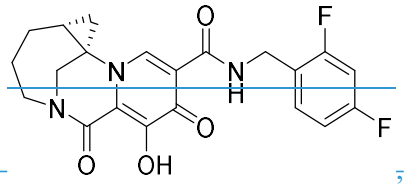


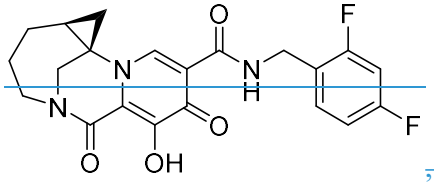


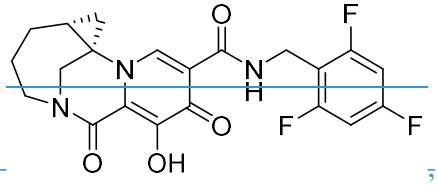


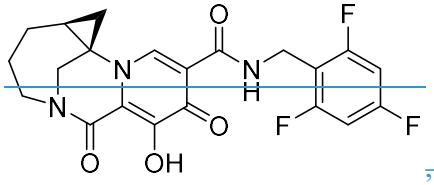

,

,

,

,

,

,

,

,

,

,

,

,

,

,

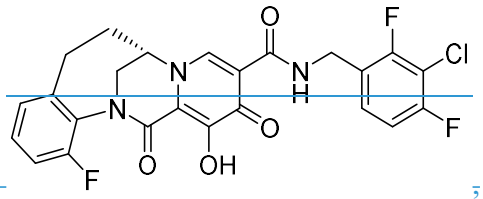


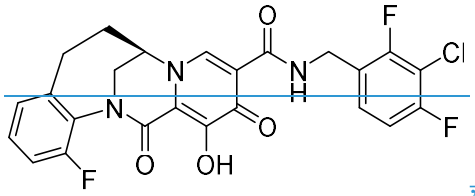


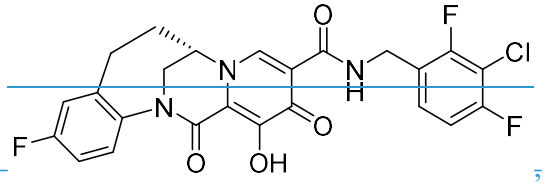


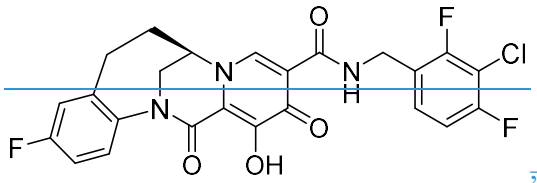


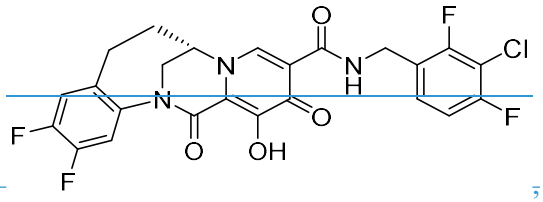


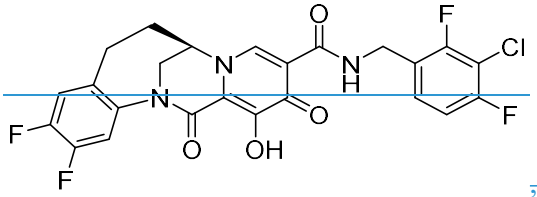


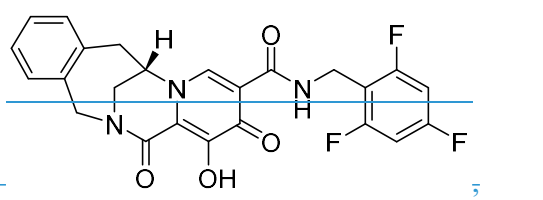


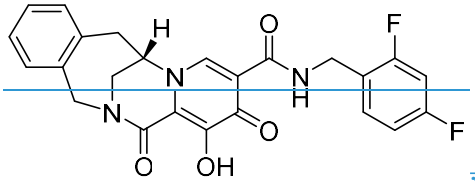


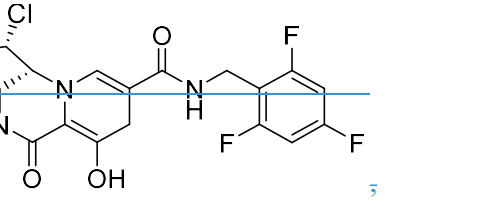




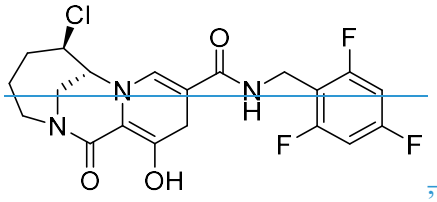
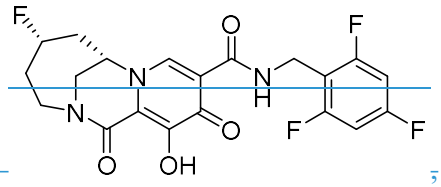
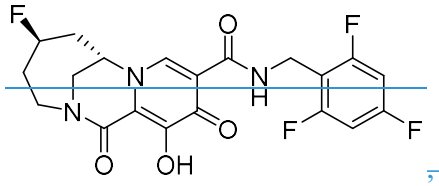
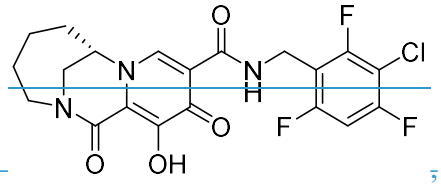
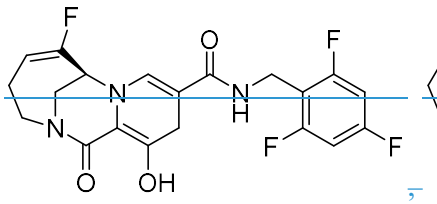
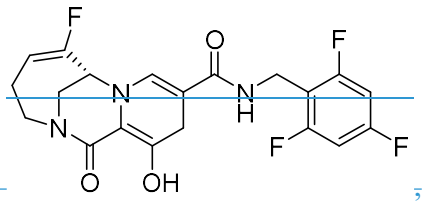
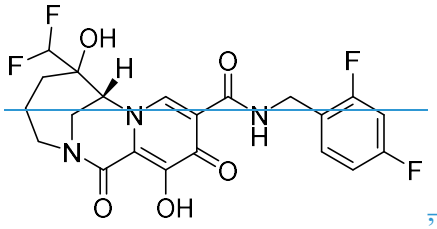
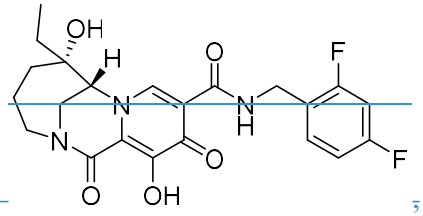
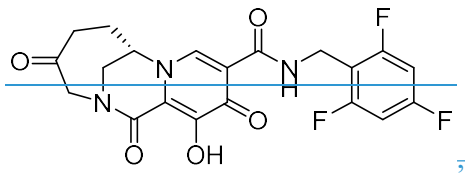
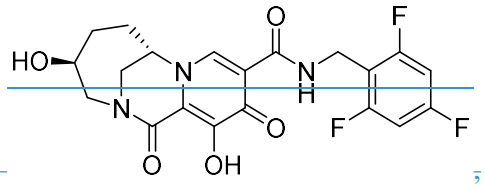
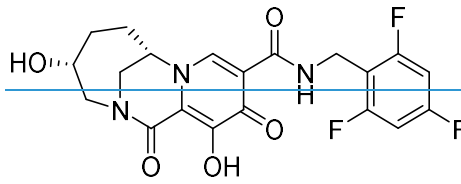


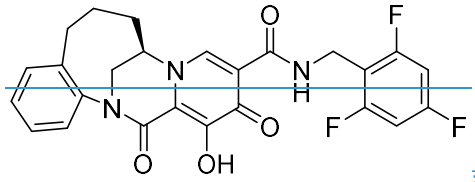
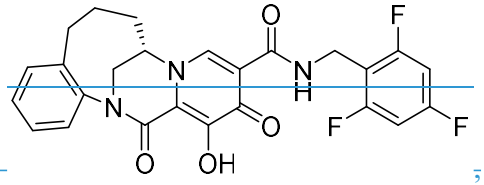


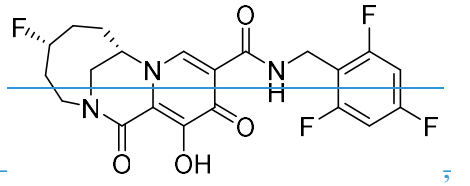


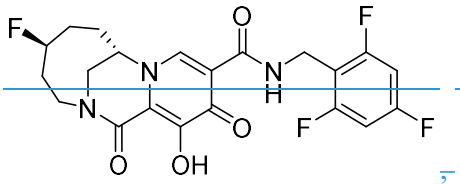


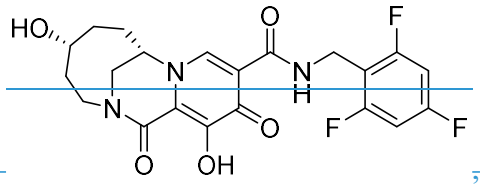


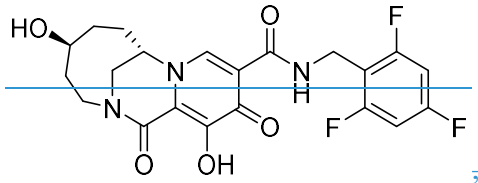












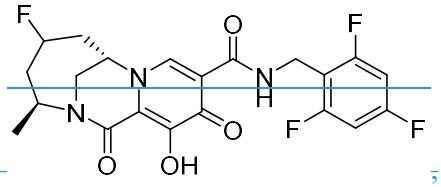



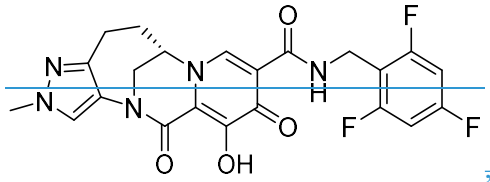



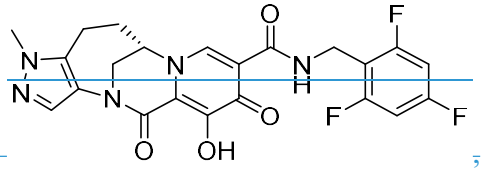


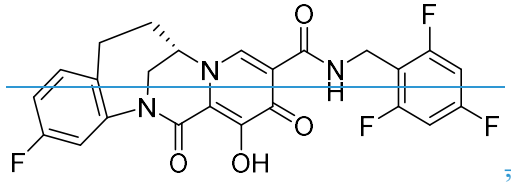


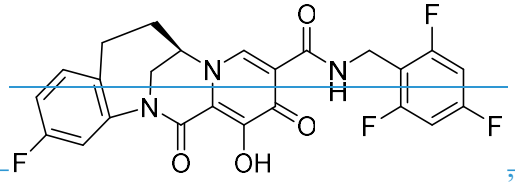


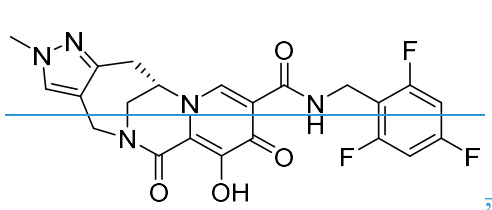


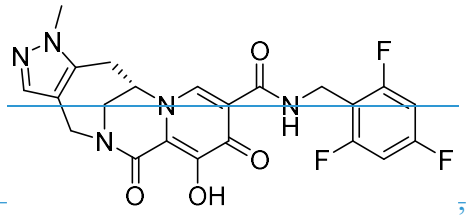


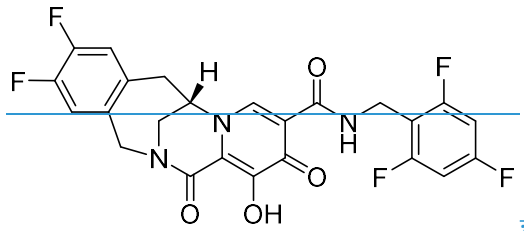


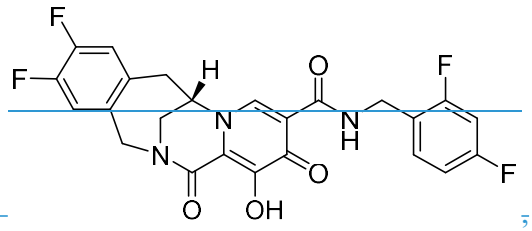


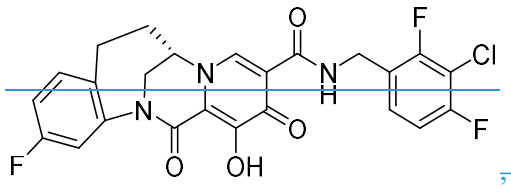


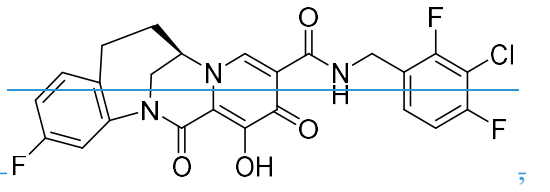


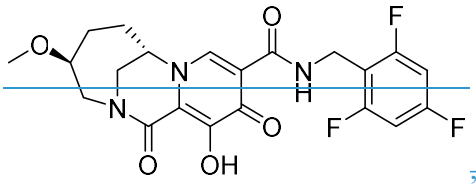
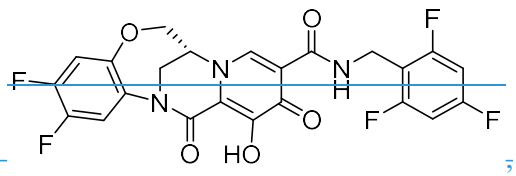
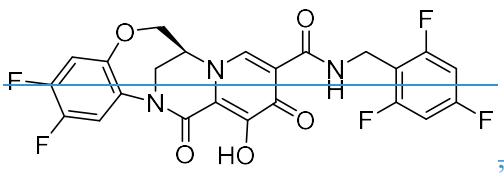
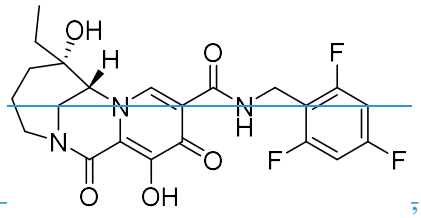
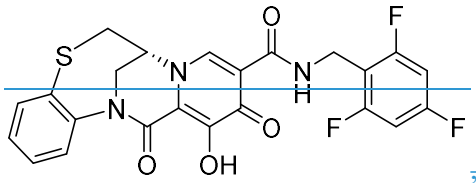
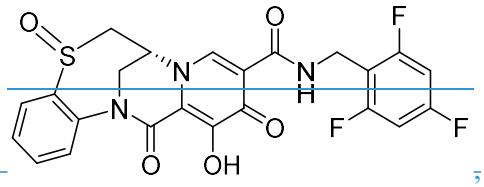
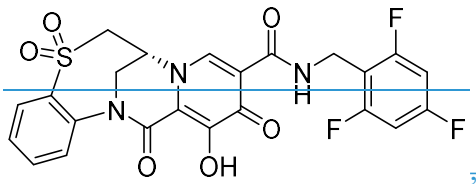
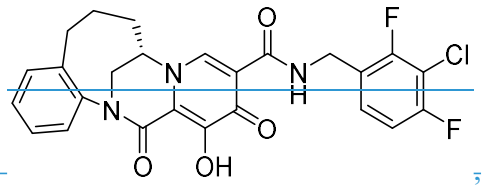
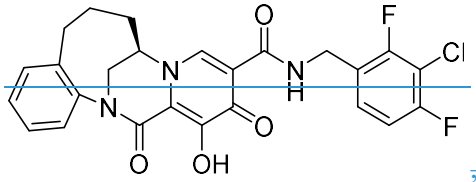


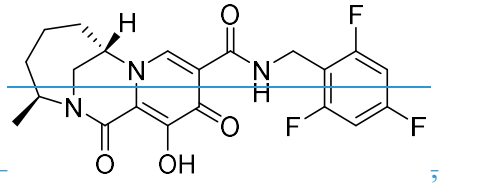
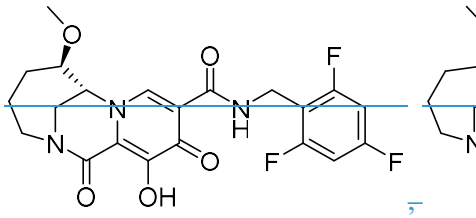
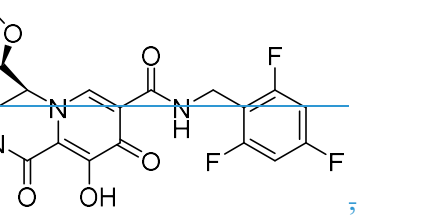


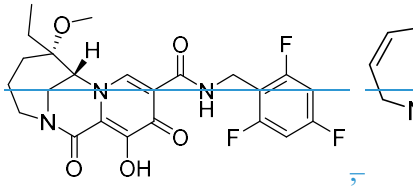
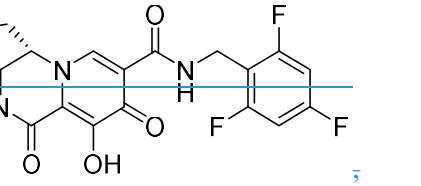


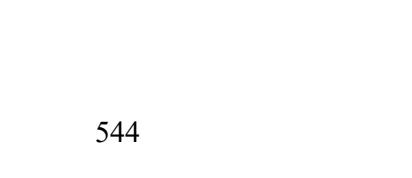


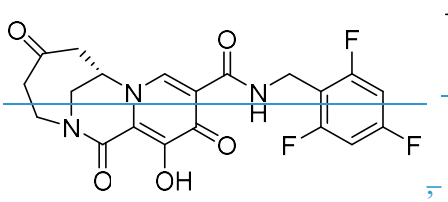


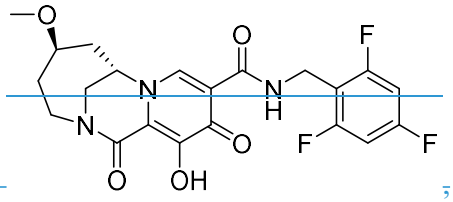










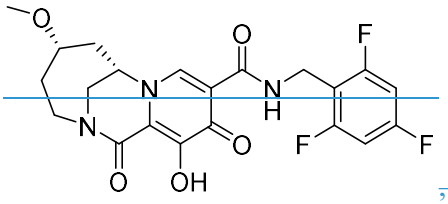




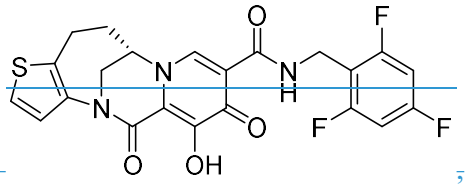



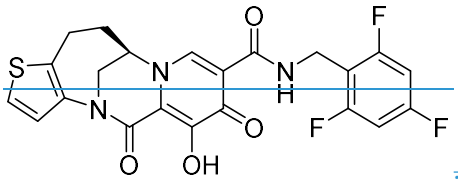


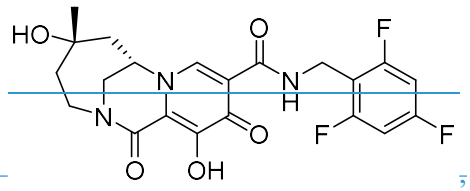


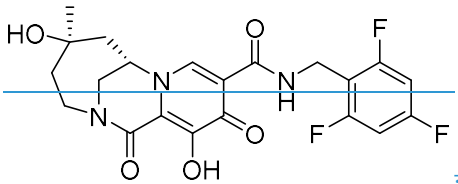


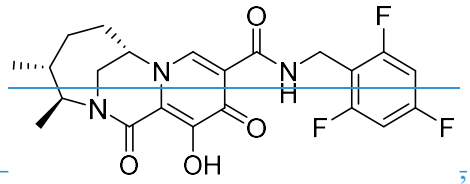


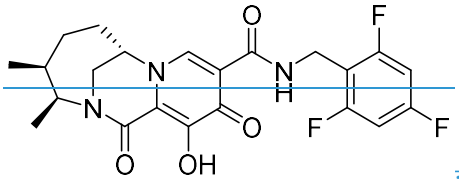


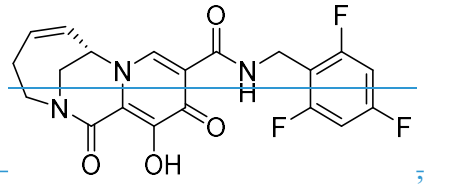


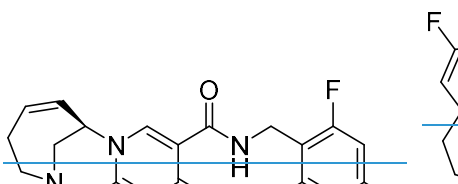


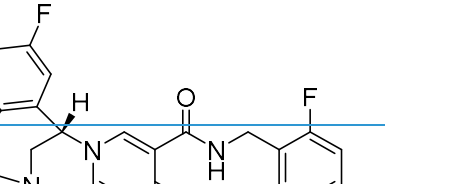


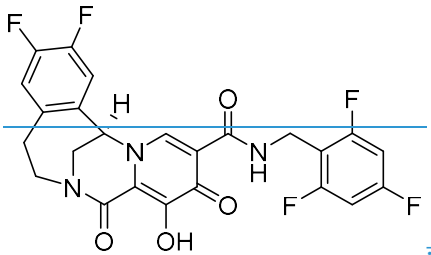


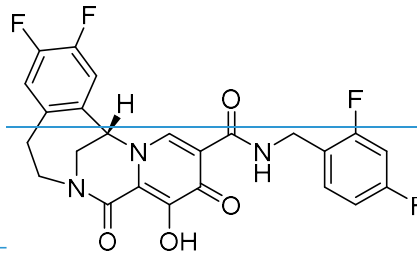


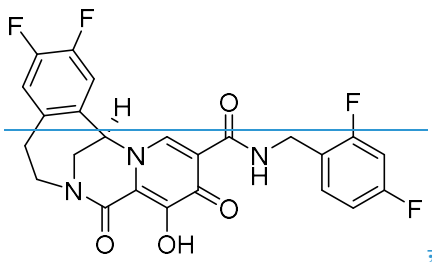


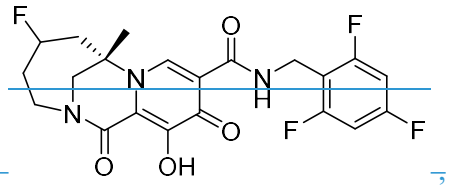


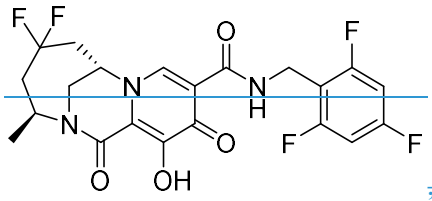


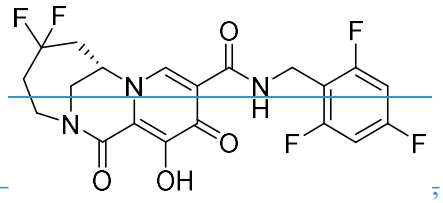


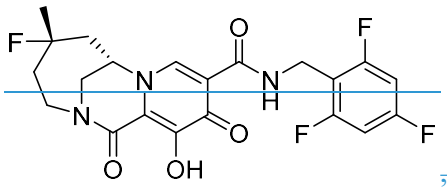


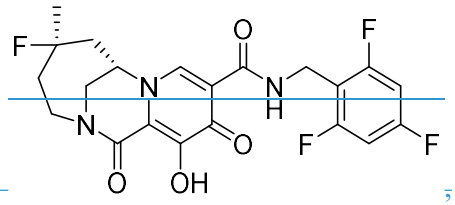


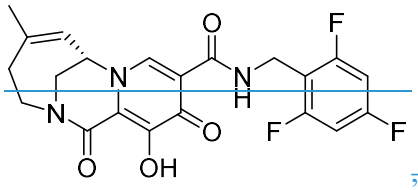


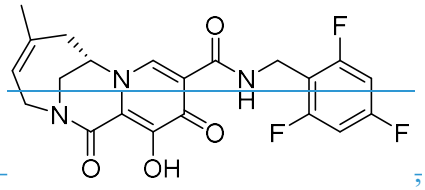


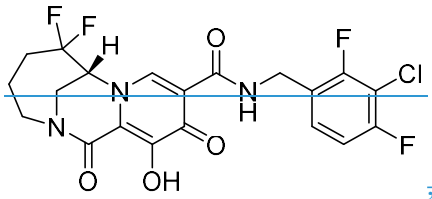


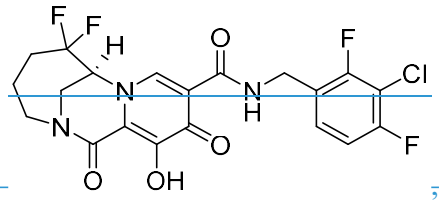


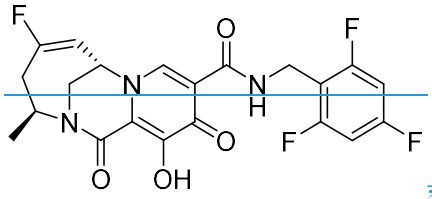


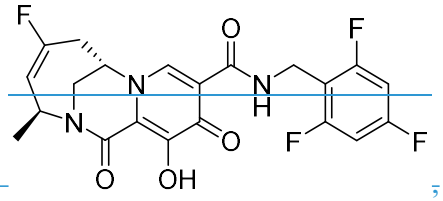


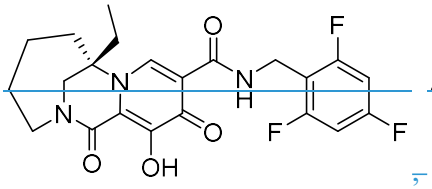


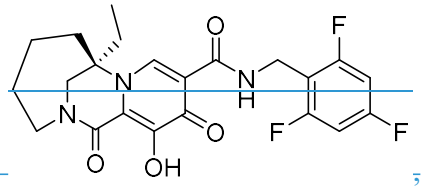


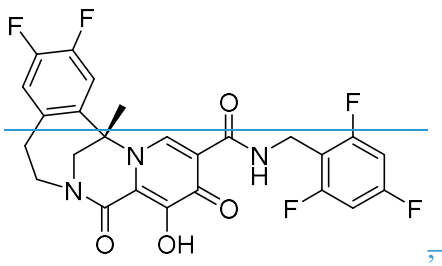


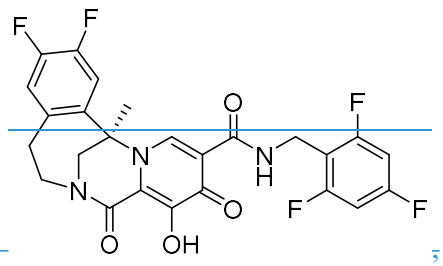


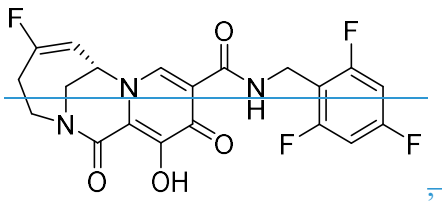


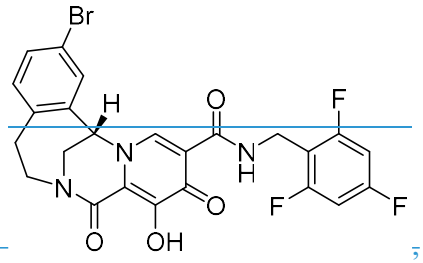


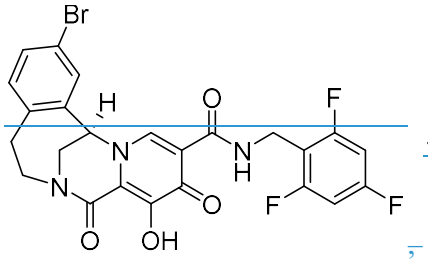


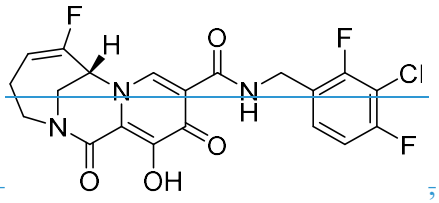


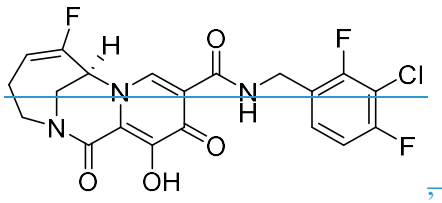


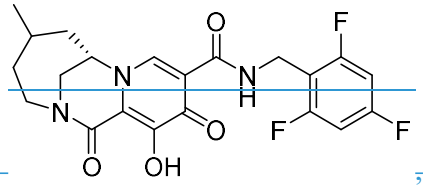


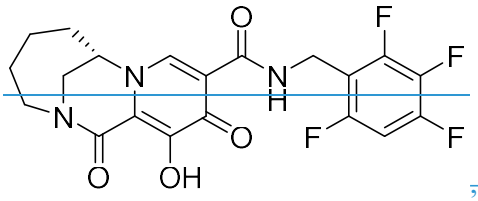


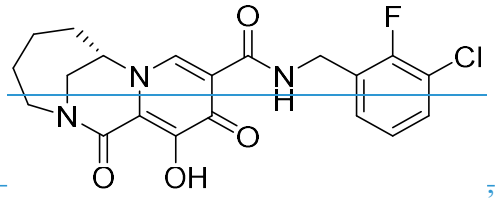


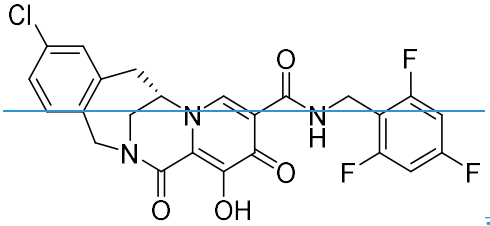


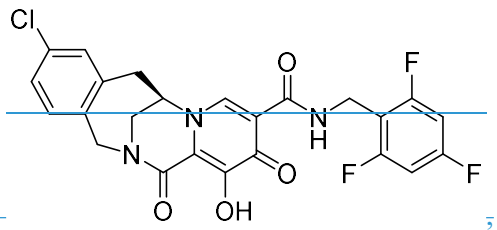


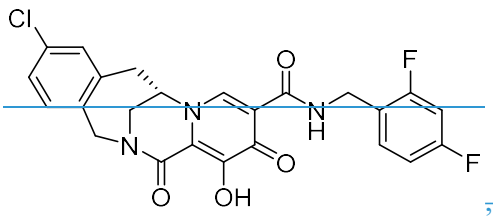
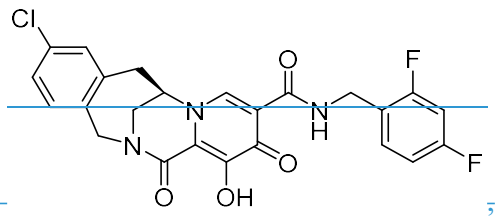
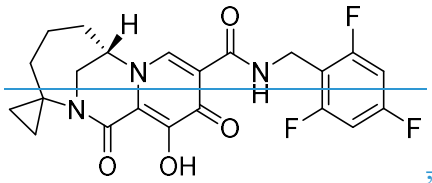
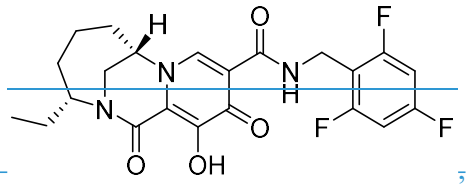
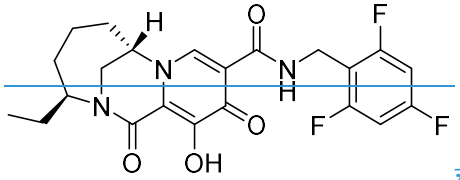
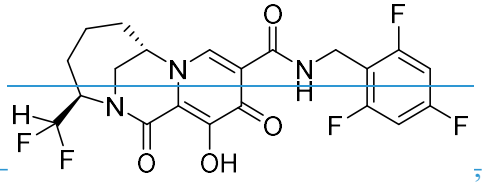
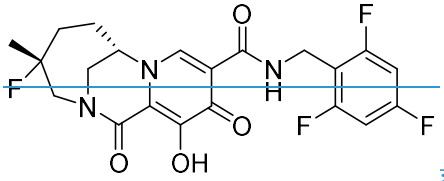
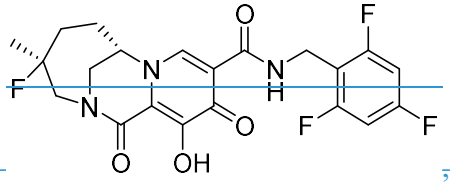
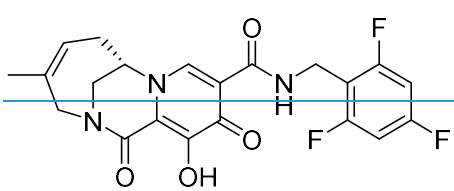
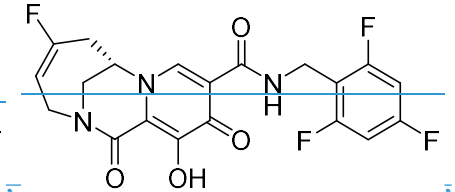


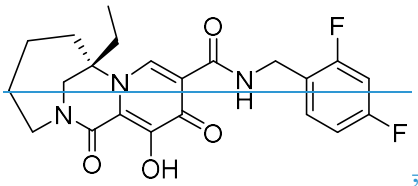
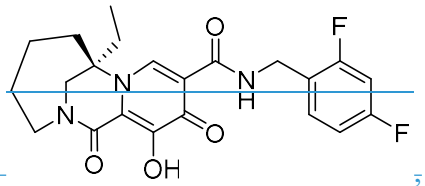
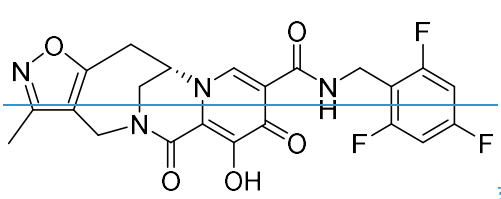
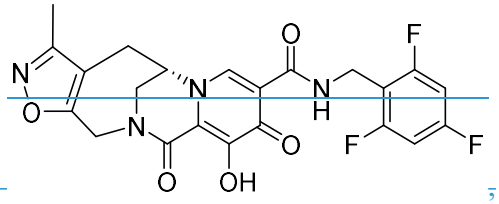


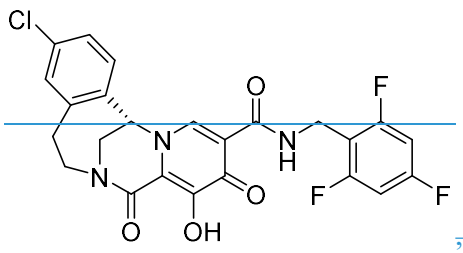


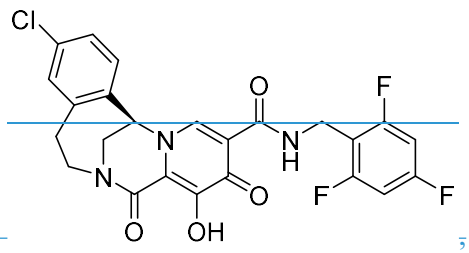


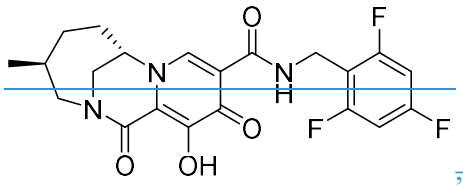


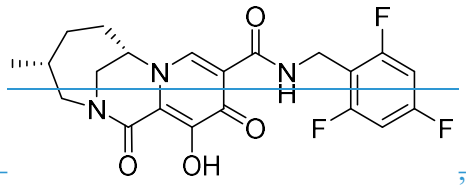











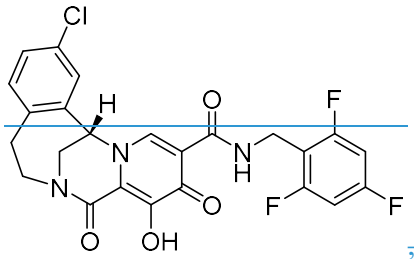





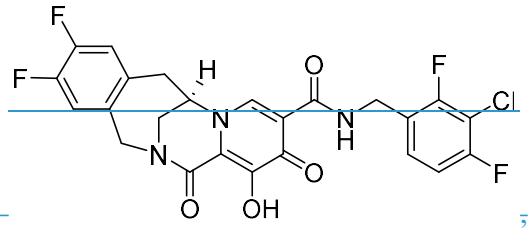


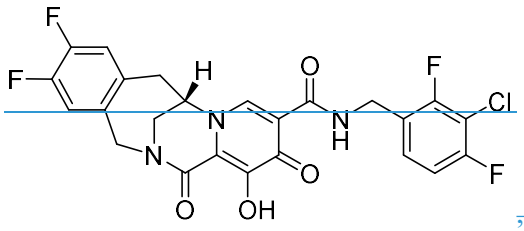


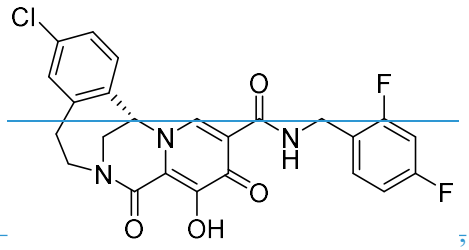


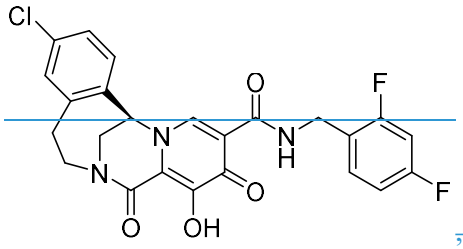


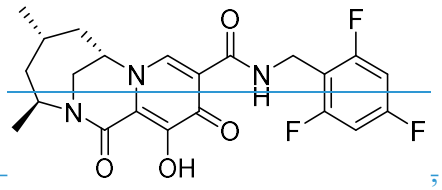


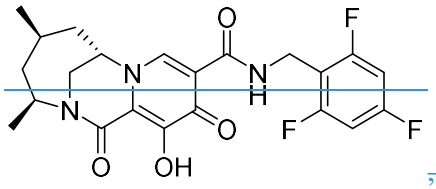


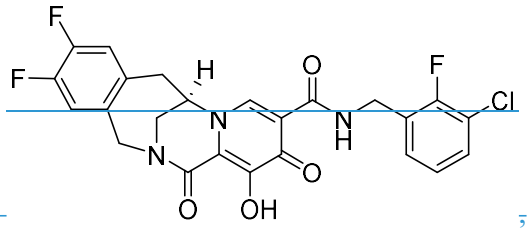


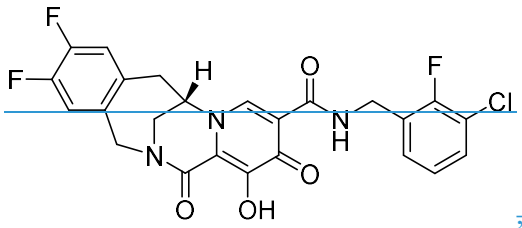
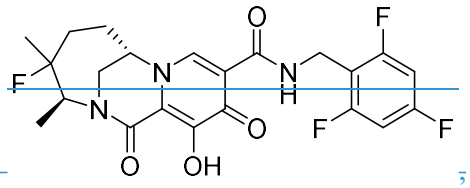
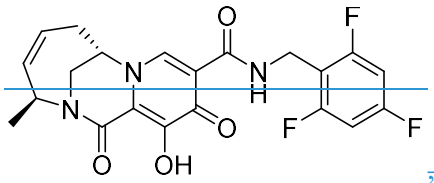
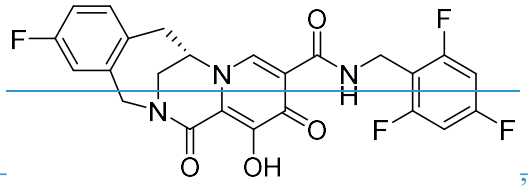
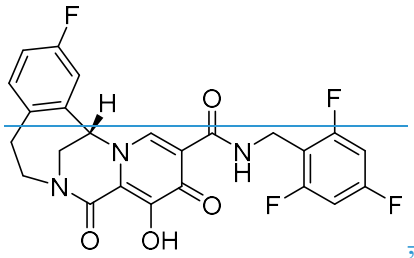
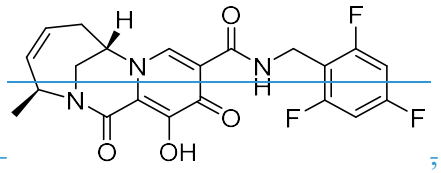
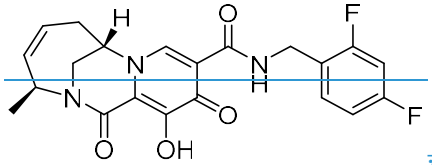
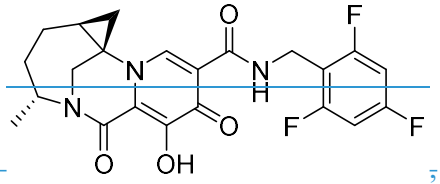
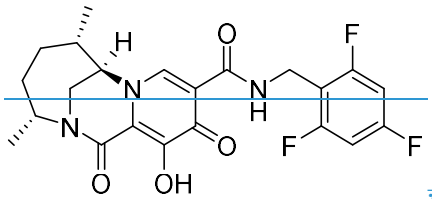
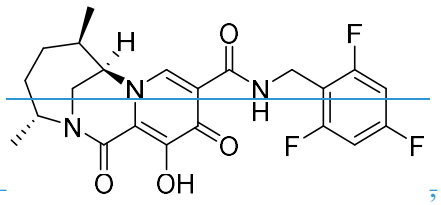
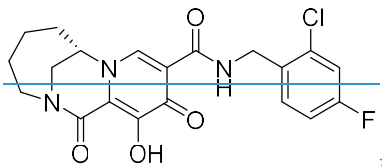
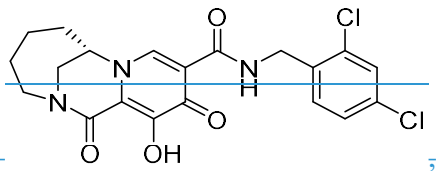
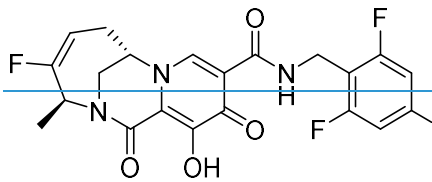
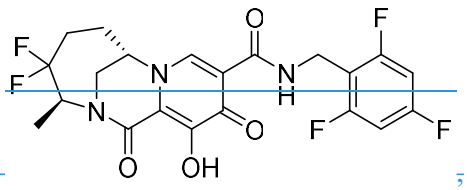




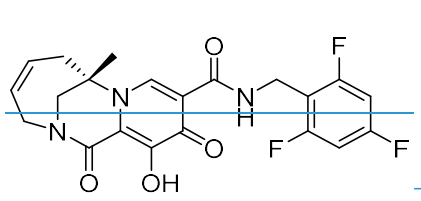


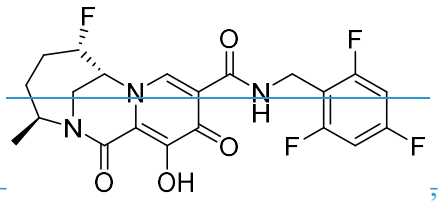


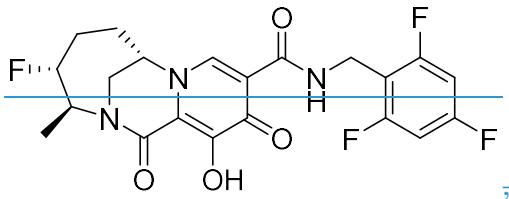


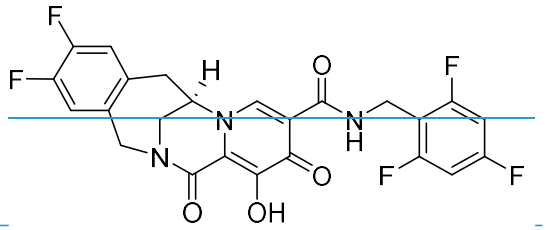















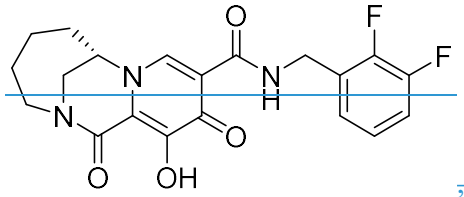


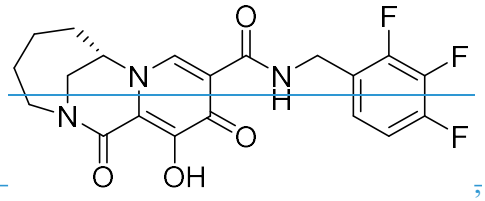

,

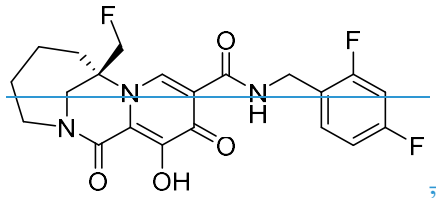

;

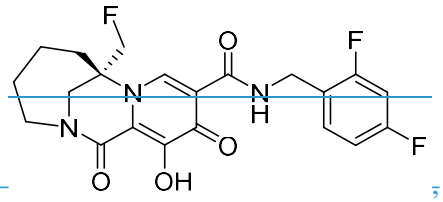

,

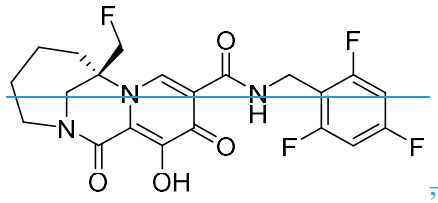

;

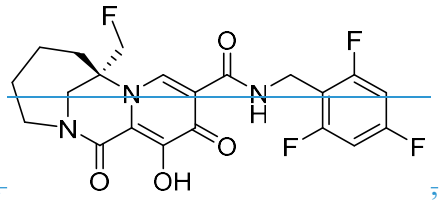

,

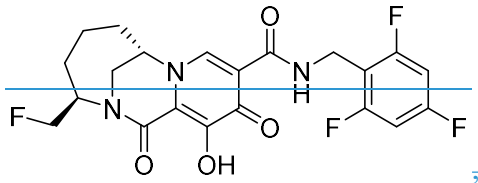

;

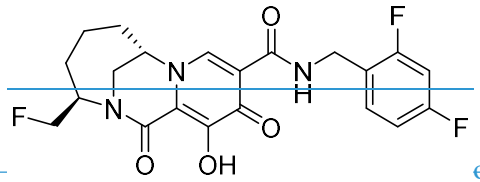

,


;

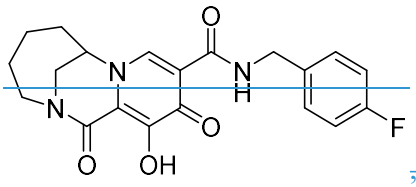
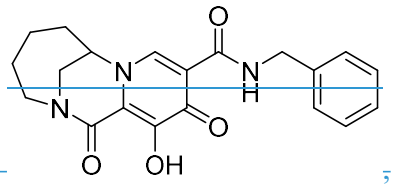

, and

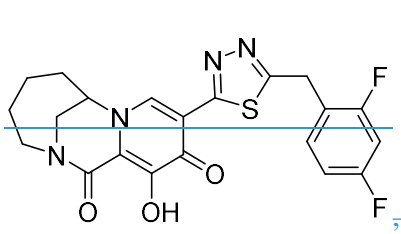

;

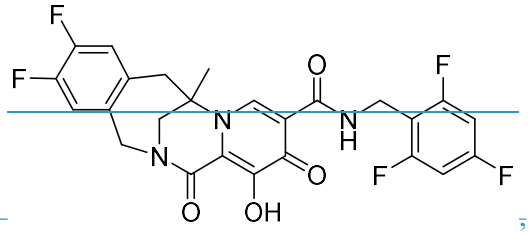

, and

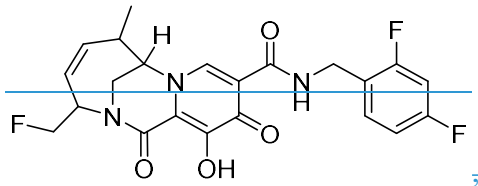

or a pharmaceutically acceptable salt thereof.

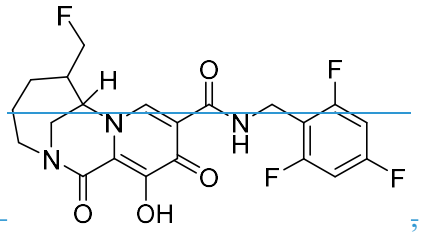
84. A compound selected from the group consisting of:

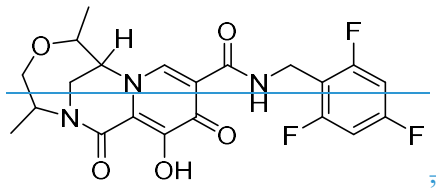



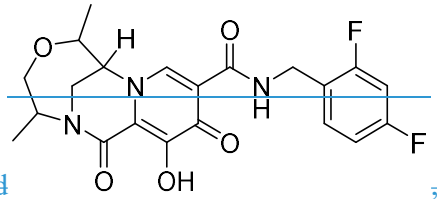

,


,

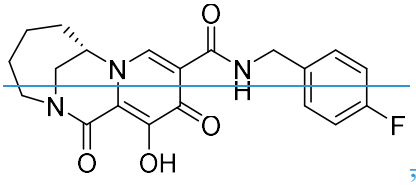

,

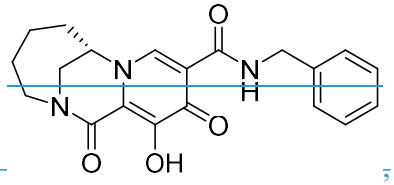

,

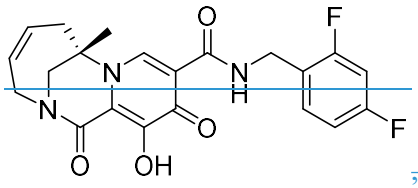

, and

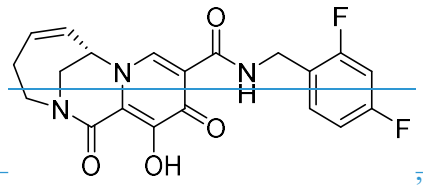

, or a pharmaceutically acceptable salt thereof.

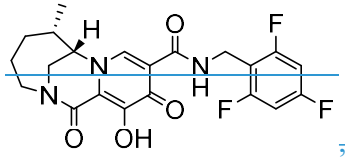
85. A compound selected from the group consisting of:

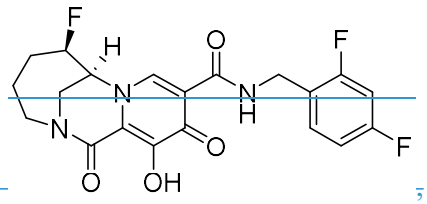

,

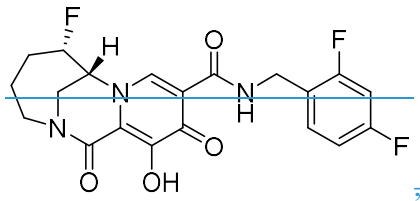
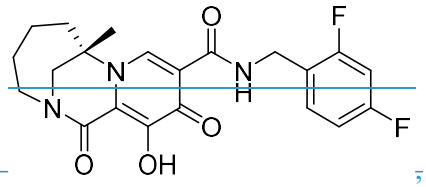
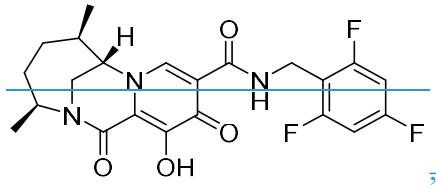
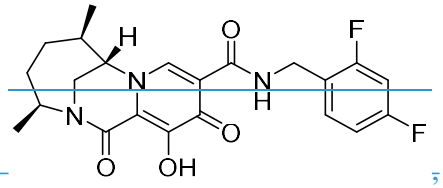
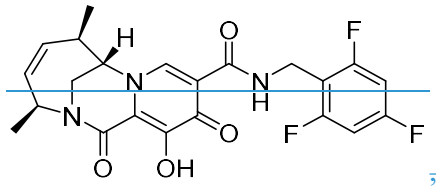
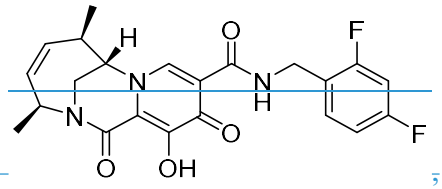
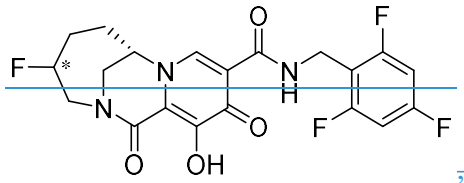
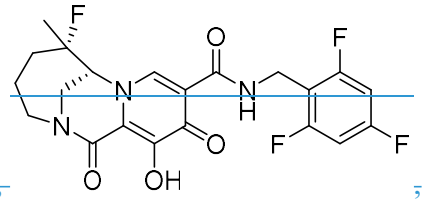
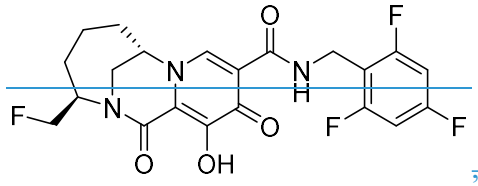
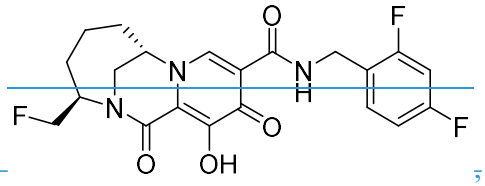
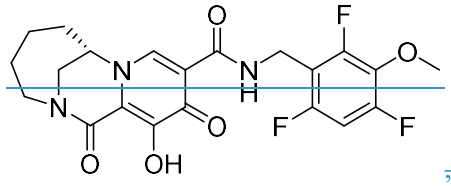
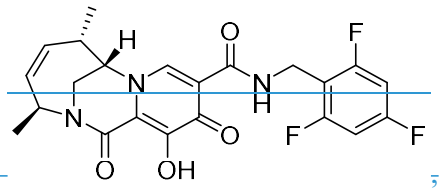
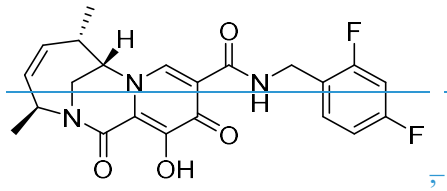
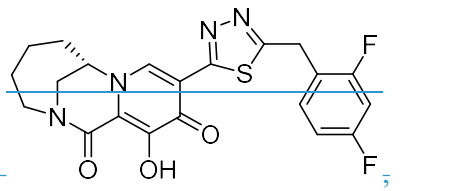
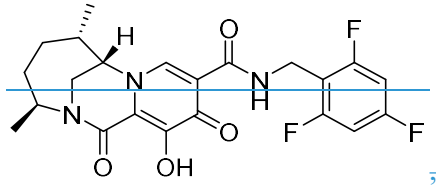
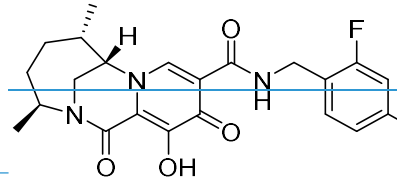

,


,

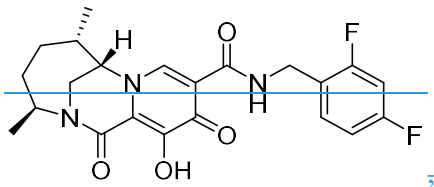
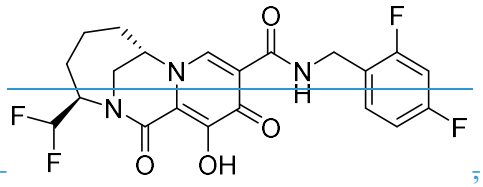
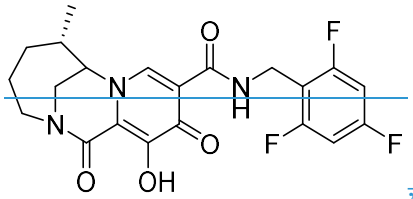
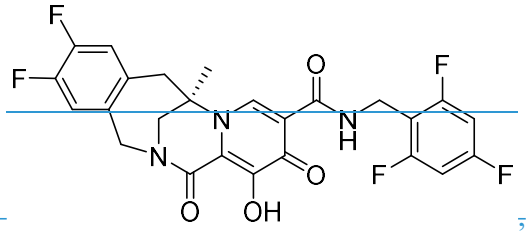
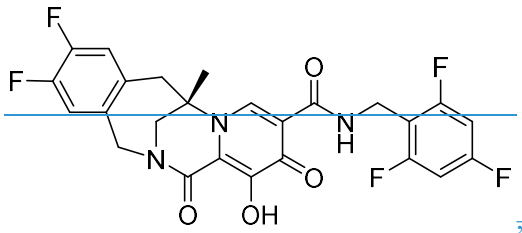
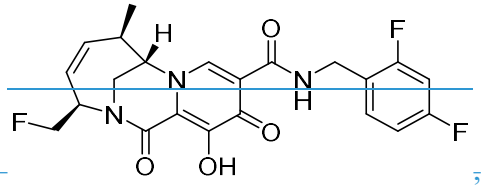
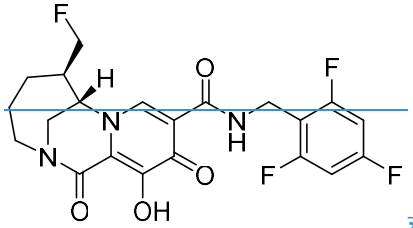
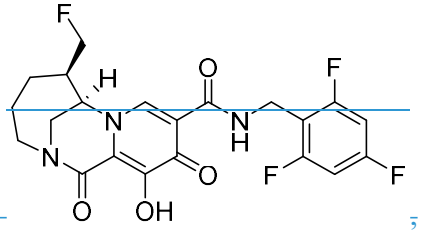
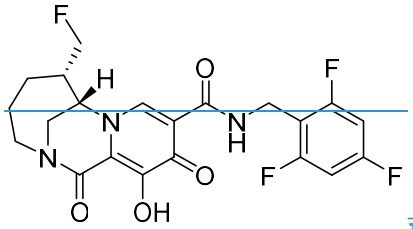
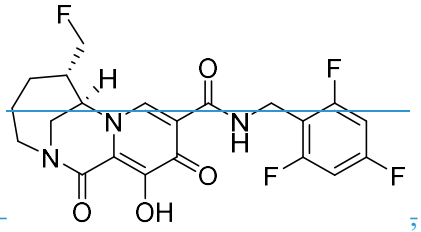
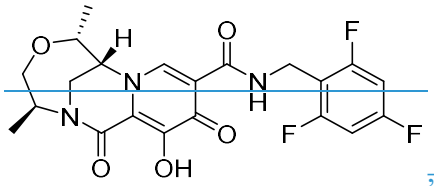
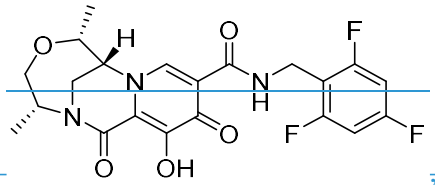
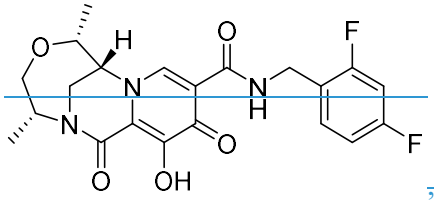

,


,


,




,

,

,

,

,

,

,

,

,

,

,

, and

, or a pharmaceutically acceptable salt thereof.

~~86.~~11. A pharmaceutical composition comprising a therapeutically effective amount of a compound of any one of claims 1-~~86~~10, or pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

12. The pharmaceutical composition of claim ~~87~~11, further comprising:

(i) ~~-~~one, two, three, or four additional therapeutic agents;~~.~~

(ii) one, two, three, or four additional therapeutic agents~~The pharmaceutical composition of claim 88~~, wherein the additional therapeutic agent or agents are anti-HIV agents.

(iii) one, two, three, or four additional therapeutic agents~~The pharmaceutical composition of claim 87 or 88~~, wherein the additional therapeutic agent or agents are HIV protease inhibitors, HIV non-nucleoside or non-nucleotide inhibitors of reverse transcriptase, HIV nucleoside or nucleotide inhibitors of reverse transcriptase, HIV capsid inhibitors, gp41 inhibitors, CXCR4 inhibitors, gp120 inhibitors, CCR5 inhibitors, latency reversing agents, capsid polymerization inhibitors, HIV bNAbs, TLR7 agonists, pharmacokinetic enhancers, other drugs for treating HIV, or combinations thereof; or~~.~~

(iv) one, two, three, or four additional therapeutic agents ~~The pharmaceutical composition of any one of claims 87-90~~, wherein the additional therapeutic agent or agents are abacavir, tenofovir alafenamide, tenofovir disoproxil, N-((*S*)-l-(3-(4-chloro-3-(methylsulfonamido)-l-(2,2,2-trifluoroethyl)-l*H*-indazol-7-yl)-6-(3-methyl-3-(methylsulfonyl)but-l-yn-l-yl)pyridin-2-yl)-2-(3,5-difluorophenyl)ethyl)-2-((3b*S*,4a*R*)-5,5-difluoro-3-(trifluoromethyl)-3b,4,4a,5-tetrahydro-l*H*-cyclopropa[3,4]cyclopenta[l,2-*c*]pyrazol-l-yl)acetamide, or a pharmaceutically acceptable salt thereof.

87.13. The pharmaceutical composition of ~~any one of~~ claim~~s 87-91~~11 or 12, wherein the pharmaceutical composition is for oral or parenteral administration.

~~88. A kit comprising a compound of any one of claims 1-86, or a pharmaceutically acceptable salt thereof, and instructions for use.~~

~~89. The kit of claim 93, further comprising one, two, three, or four additional therapeutic agent or agents.~~

~~90. The kit of claim 93 or 94, wherein the additional therapeutic agent or agents are anti-HIV agents.~~

~~91. The kit of any one of claims 93-95, wherein the additional therapeutic agent or agents are HIV protease inhibitors, HIV non-nucleoside or non-nucleotide inhibitors of reverse transcriptase, HIV nucleoside or nucleotide inhibitors of reverse transcriptase, HIV capsid inhibitors, gp41 inhibitors, CXCR4 inhibitors, gp120 inhibitors, CCR5 inhibitors, latency reversing agents, capsid polymerization inhibitors, HIV bNAbs, TLR7 agonists, pharmacokinetic enhancers, other drugs for treating HIV, or combinations thereof.~~

~~92. The kit of any one of claims 93-96, wherein the additional therapeutic agent or agents are abacavir, tenofovir alafenamide, tenofovir disoproxil, N-((*S*)-1-(3-(4-chloro-3-(methylsulfonamido)-1-(2,2,2-trifluoroethyl)-1*H*-indazol-7-yl)-6-(3-methyl-3-(methylsulfonyl)but-1-yn-1-yl)pyridin-2-yl)-2-(3,5-difluorophenyl)ethyl)-2-((3b*S*,4a*R*)-5,5-difluoro-3-(trifluoromethyl)-3b,4,4a,5-tetrahydro-1*H*-cyclopropa[3,4]cyclopenta[1,2-*c*]pyrazol-1-yl)acetamide, or a pharmaceutically acceptable salt thereof.~~

~~93. A method of treating an HIV infection in a human having or at risk of having the infection, comprising administering to the human a therapeutically effective amount of a compound of any one of claims 1-86 or pharmaceutically acceptable salt thereof, or a pharmaceutical composition of any one of claims 87-92.~~

(i) The method of claim 98, further comprising administering to the human a therapeutically effective amount of one, two, three, or four additional therapeutic agents.

(ii) The method of claim 99, wherein the additional therapeutic agent or agents are anti-HIV agents.

(iii) The method of claim 99 or 100, wherein the additional therapeutic agent or agents are HIV protease inhibitors, HIV non-nucleoside or non-nucleotide inhibitors of reverse transcriptase, HIV nucleoside or nucleotide inhibitors of reverse transcriptase, HIV capsid inhibitors, gp41 inhibitors, CXCR4 inhibitors, gp120 inhibitors, CCR5 inhibitors, latency reversing agents, capsid polymerization inhibitors, HIV bNAbs, TLR7 agonists, pharmacokinetic enhancers, other drugs for treating HIV, or combinations thereof.

(iv) The method of any one of claims 99-101, wherein the additional therapeutic agent or agents are abacavir, tenofovir alafenamide, tenofovir disoproxil, N-((*S*)-1-(3-(4-chloro-3-(methylsulfonamido)-1-(2,2,2-trifluoroethyl)-1*H*-indazol-7-yl)-6-(3-methyl-3-(methylsulfonyl)but-1-yn-1-yl)pyridin-2-yl)-2-(3,5-difluorophenyl)ethyl)-2-((3b*S*,4a*R*)-5,5-difluoro-3-(trifluoromethyl)-3b,4,4a,5-tetrahydro-1*H*-cyclopropa[3,4]cyclopenta[1,2-*c*]pyrazol-1-yl)acetamide, or a pharmaceutically acceptable salt thereof.

94. The method of any one of claims 98-102, wherein the administration is oral, intravenous, subcutaneous, or intramuscular.

95. Use of a compound of any one of claims 1-86, or pharmaceutically acceptable salt thereof, or a pharmaceutical composition of any one of claims 87-92, for treating an HIV infection in a human having or at risk of having the infection.

~~96. A compound of any one of claims 1-86, or pharmaceutically acceptable salt thereof, or a pharmaceutical composition of any one of claims 87-92, for use in medical therapy.~~

~~97. A compound of any one of claims 1-86, or pharmaceutically acceptable salt thereof, or a pharmaceutical composition of any one of claims 87-92, for use in treating an HIV infection.~~

14. Use of a compound of any one of claims 1-~~86~~10, or pharmaceutically acceptable salt thereof, ~~or a pharmaceutical composition of any one of claims 87-92,~~ in the manufacture of a medicament for treating an HIV infection in a human having or at risk of having the infection.

15. The use of claim 14, wherein the medicament further comprisies:

(i) one, two, three, or four additional therapeutic agents;

(ii) one, two, three, or four additional therapeutic agents, wherein the additional therapeutic agent or agents are anti-HIV agents;

(iii) one, two, three, or four additional therapeutic agents, wherein the additional therapeutic agent or agents are HIV protease inhibitors, HIV non-nucleoside or non-nucleotide inhibitors of reverse transcriptase, HIV nucleoside or nucleotide inhibitors of reverse transcriptase, HIV capsid inhibitors, gp41 inhibitors, CXCR4 inhibitors, gp120 inhibitors, CCR5 inhibitors, latency reversing agents, capsid polymerization inhibitors, HIV bNAbs, TLR7 agonists, pharmacokinetic enhancers, other drugs for treating HIV, or combinations thereof; or

(iv) one, two, three, or four additional therapeutic agents, wherein the additional therapeutic agent or agents are abacavir, tenofovir alafenamide, tenofovir disoproxil, N-((*S*)-l-(3-(4-chloro-3-(methylsulfonamido)-l-(2,2,2-trifluoroethyl)-l*H*-

indazol-7-yl)-6-(3-methyl-3-(methylsulfonyl)but-1-yn-1-yl)pyridin-2-yl)-2-(3,5-difluorophenyl)ethyl)-2-((3b*S*,4a*R*)-5,5-difluoro-3-(trifluoromethyl)-3b,4,4a,5-tetrahydro-1*H*-cyclopropa[3,4]cyclopenta[1,2-*c*]pyrazol-1-yl)acetamide, or a pharmaceutically acceptable salt thereof.

16. The use of claim 14, wherein the medicament is for co-administration with:

(i) a therapeutically effective amount of one, two, three, or four additional therapeutic agents;

(ii) a therapeutically effective amount of one, two, three, or four additional therapeutic agents, wherein the additional therapeutic agent or agents are anti-HIV agents;

(iii) a therapeutically effective amount of one, two, three, or four additional therapeutic agents, wherein the additional therapeutic agent or agents are HIV protease inhibitors, HIV non-nucleoside or non-nucleotide inhibitors of reverse transcriptase, HIV nucleoside or nucleotide inhibitors of reverse transcriptase, HIV capsid inhibitors, gp41 inhibitors, CXCR4 inhibitors, gp120 inhibitors, CCR5 inhibitors, latency reversing agents, capsid polymerization inhibitors, HIV bNAbs, TLR7 agonists, pharmacokinetic enhancers, other drugs for treating HIV, or combinations thereof; or

(iv) a therapeutically effective amount of one, two, three, or four additional therapeutic agents, wherein the additional therapeutic agent or agents are abacavir, tenofovir alafenamide, tenofovir disoproxil, N-((*S*)-1-(3-(4-chloro-3-(methylsulfonamido)-1-(2,2,2-trifluoroethyl)-1*H*-indazol-7-yl)-6-(3-methyl-3-(methylsulfonyl)but-1-yn-1-yl)pyridin-2-yl)-2-(3,5-difluorophenyl)ethyl)-2-((3b*S*,4a*R*)-5,5-difluoro-3-(trifluoromethyl)-3b,4,4a,5-tetrahydro-1*H*-

cyclopropa[3,4]cyclopenta[1,2-*c*]pyrazol-1-yl)acetamide, or a pharmaceutically acceptable salt thereof.

17. The use of any one of claims 14 to 16, wherein the medicament is formulated for oral, intravenous, subcutaneous, or intramuscular administration.