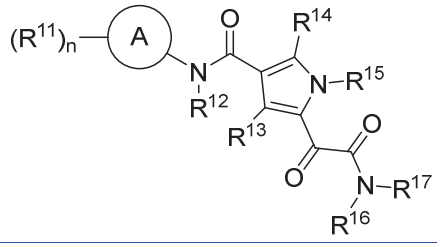
plays an important role in shuttling the RC DNA into the nucleus to initiate and maintain the cccDNA pools and may also play a role in regulating interferon sensitive gene expression. Thus, capsid modulators may have the unique ability to intervene at multiple points in the HBV lifecycle.

[0006] Several chemotype series of HBV capsid assembly modulators have been reported in the literature including: phenylpropenamides (PP) (e.g., AT-130), heteroarylpyrimidines (HAP) (e.g. Bay 41-4109), and sulfamoylbenzamides (SBA) (e.g. NVR 3-778). Capsid modulators exert their effects on the assembly process through one of two different mechanisms of action. The HAP series induces the aberrant assembly of large capsid aggregates that subsequently triggers the degradation of the core protein. The PP and SBA series, on the other hand, appear to accelerate capsid assembly resulting in the production of authentic empty capsid particles that have failed to incorporate pgRNA. Assembly modulators representing both mechanisms have demonstrated the ability to reduce HBV DNA levels in mouse models of infection. More recently, NVR 3-778 (SBA) demonstrated clinical proof-of-concept in a Phase 1b clinical trial, resulting in a -1.7 log10 reduction in HBV DNA following 600 mg bid dosing for 29 days.

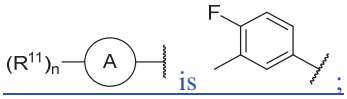
SUMMARY OF THE INVENTION

[0006a] In one aspect, provided herein is compound of Formula (I), or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof:



(I),

wherein:

 is ;

R^{12} is hydrogen or C_1-C_6alkyl;

R^{13} is hydrogen, halogen, -CN, -OH, -OR^a, -SH, -SR^a, -$S(=O)R^a$, -$S(=O)_2R^a$, -NO_2, -NR^bR^c, -$NHS(=O)_2R^a$, -$S(=O)_2NR^bR^c$, -$C(=O)R^a$, -$OC(=O)R^a$, -$C(=O)OR^b$, -$OC(=O)OR^b$, -$C(=O)NR^bR^c$, -$OC(=O)NR^bR^c$, -$NR^bC(=O)NR^bR^c$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^b$, C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, C_1-C_6aminoalkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, -C_1-C_6alkyl(aryl), -C_1-C_6alkyl(heteroaryl), -C_1-C_6alkyl(cycloalkyl), or -C_1-C_6alkyl(heterocycloalkyl); wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three R^3;

R^{14} is hydrogen, halogen, -CN, -OH, -OR^a, -SH, -SR^a, -$S(=O)R^a$, -$S(=O)_2R^a$, -NO_2, -NR^bR^c, -$NHS(=O)_2R^a$, -$S(=O)_2NR^bR^c$, -$C(=O)R^a$, -$OC(=O)R^a$, -$C(=O)OR^b$, -$OC(=O)OR^b$, -$C(=O)NR^bR^c$, -$OC(=O)NR^bR^c$, -$NR^bC(=O)NR^bR^c$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^b$, C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, C_1-C_6aminoalkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, -C_1-C_6alkyl(aryl), -C_1-C_6alkyl(heteroaryl), -C_1-C_6alkyl(cycloalkyl), or -C_1-C_6alkyl(heterocycloalkyl); wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three R^4;

R^{15} is hydrogen, -$S(=O)R^a$, -$S(=O)_2R^a$, -$S(=O)_2NR^bR^c$, -$C(=O)R^a$, -$C(=O)OR^b$, -$C(=O)NR^bR^c$, C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, C_1-C_6aminoalkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, -C_1-C_6alkyl(aryl), -C_1-C_6alkyl(heteroaryl), -C_1-C_6alkyl(cycloalkyl), or -C_1-C_6alkyl(heterocycloalkyl); wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three R^5;

R^{16} and R^{17} are each independently hydrogen, -CN, -OR^{20}, C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, C_1-C_6aminoalkyl, C_2-C_6alkenyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, -C_1-C_6alkyl(aryl), -C_1-C_6alkyl(heteroaryl), -C_1-C_6alkyl(cycloalkyl), or -C_1-C_6alkyl(heterocycloalkyl); wherein each alkyl, alkenyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three R^7;

or R^{16} and R^{17} are taken together with the nitrogen atom to which they are attached to form a heterocycloalkyl or a heterocycloalkenyl; each optionally substituted with one, two, or three R^8;

each R^{20} is independently hydrogen, C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, C_1-C_6aminoalkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three R^7;

each R^3, R^4, R^5, and R^8 is independently oxo, halogen, -CN, -OH, -OR^a, -SH, -SR^a, -$S(=O)R^a$, -$S(=O)_2R^a$, -NO_2, -NR^bR^c, -$NHS(=O)_2R^a$, -$S(=O)_2NR^bR^c$, -$C(=O)R^a$, -$OC(=O)R^a$, -$C(=O)OR^b$, -$OC(=O)OR^b$, -$C(=O)NR^bR^c$, -$OC(=O)NR^bR^c$, -$NR^bC(=O)NR^bR^c$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^b$, C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, C_1-C_6aminoalkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, -C_1-C_6alkyl(aryl), -C_1-C_6alkyl(heteroaryl), -C_1-C_6alkyl(cycloalkyl), or -C_1-C_6alkyl(heterocycloalkyl); wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three oxo, halogen, -CN, -OH, -OMe, -S(=O)Me, -$S(=O)_2$Me, -NH_2, -$S(=O)_2NH_2$,

-C(=O)Me, -C(=O)OH, -C(=O)OMe, C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, or C_1-C_6aminoalkyl;

each R^7 is independently oxo, halogen, -CN, -OH, -OR^a, -SH, -SR^a, -$S(=O)R^a$, -$S(=O)_2R^a$, -NO_2, -NR^bR^c, -$NHS(=O)_2R^a$, -$S(=O)_2NR^bR^c$, -$C(=O)R^a$, -$OC(=O)R^a$, -$C(=O)OR^b$, -$OC(=O)OR^b$, -$C(=O)NR^bR^c$, -$OC(=O)NR^bR^c$, -$NR^bC(=O)NR^bR^c$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^b$, C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, C_1-C_6aminoalkyl, C_2-C_6alkenyl, C_3-C_6alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, -C_1-C_6alkyl(aryl), -C_1-C_6alkyl(heteroaryl), -C_1-C_6alkyl(cycloalkyl), or -C_1-C_6alkyl(heterocycloalkyl); wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three R^{7a};

each R^{7a} is independently oxo, halogen, -CN, -OH, -OR^a, -NR^bR^c, -$C(=O)R^a$, -$C(=O)OR^b$, -$C(=O)NR^bR^c$, C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, or C_1-C_6aminoalkyl;

each R^a is independently C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, C_1-C_6aminoalkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three oxo, halogen, -CN, -OH, -OMe, -S(=O)Me, -$S(=O)_2$Me, -NH_2, -$S(=O)_2NH_2$, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, or C_1-C_6aminoalkyl; and

each R^b and R^c are independently hydrogen, C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, C_1-C_6aminoalkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three oxo, halogen, -CN, -OH, -OMe, -S(=O)Me, -$S(=O)_2$Me, -NH_2, -$S(=O)_2NH_2$, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, or C_1-C_6aminoalkyl;

or R^b and R^c are taken together with the nitrogen atom to which they are attached to form a heterocycloalkyl optionally substituted with one, two, or three oxo, halogen, -CN, -OH, -OMe, -S(=O)Me, -$S(=O)_2$Me, -NH_2, -$S(=O)_2NH_2$, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, or C_1-C_6aminoalkyl.

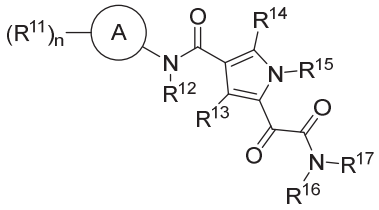
[0006b] In another aspect, provided herein is a pharmaceutical composition comprising a compound as described herein, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, and a pharmaceutically acceptable excipient.

[0006c] In another aspect, provided herein is a use of compound as described herein or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof in the manufacture of a medicament for the treatment of hepatitis B in a subject.

[0006d] In another aspect, provided herein is the compound as described herein, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof for use in therapy.

[0007] Described herein are compounds of Formula (I), (Ia)-(Id) that modulate the normal capsid assembly of hepatitis B core proteins to inhibit the hepatitis B lifecycle, and thus act as antiviral agents toward HBV.

[0008] Disclosed herein are compounds of Formula (I), or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof:



(I),

wherein:

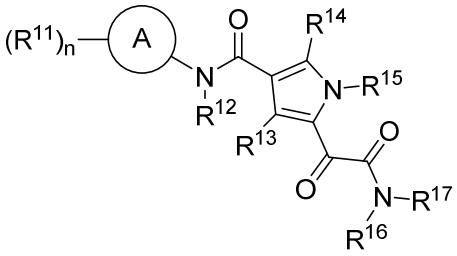
Ring A is aryl, heteroaryl, cycloalkyl, or heterocycloalkyl;

each R^{11} is independently halogen, -CN, -OH, -OR^a, -SH, -SR^a, -$S(=O)R^a$, -$S(=O)_2R^a$, -NO_2, -NR^bR^c, -$NHS(=O)_2R^a$, -$S(=O)_2NR^bR^c$, -$C(=O)R^a$, -$OC(=O)R^a$, -$C(=O)OR^b$, -$OC(=O)OR^b$, -$C(=O)NR^bR^c$, -$OC(=O)NR^bR^c$, -$NR^bC(=O)NR^bR^c$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^b$, C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, C_1-C_6aminoalkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, -C_1-C_6alkyl(aryl), -C_1-C_6alkyl(heteroaryl), -C_1-C_6alkyl(cycloalkyl), or -C_1-C_6alkyl(heterocycloalkyl); wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three R^1;

CLAIMS

WHAT IS CLAIMED IS:

1. A compound of Formula (I), or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof:

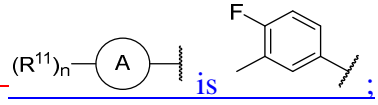


(I),

wherein:

~~Ring A is aryl, heteroaryl, cycloalkyl, or heterocycloalkyl;~~

~~each R^{11} is independently halogen, -CN, -OH, -OR^a, -SH, -SR^a, -$S(=O)R^a$, -$S(=O)_2R^a$, -NO_2, -NR^bR^e, -$NHS(=O)_2R^a$, -$S(=O)_2NR^bR^e$, -$C(=O)R^a$, -$OC(=O)R^a$, -$C(=O)OR^b$, -$OC(=O)OR^b$, -$C(=O)NR^bR^e$, -$OC(=O)NR^bR^e$, -$NR^bC(=O)NR^bR^e$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^b$, C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, C_1-C_6aminoalkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, -C_1-C_6alkyl(aryl), -C_1-C_6alkyl(heteroaryl), -C_1-C_6alkyl(cycloalkyl), or -C_1-C_6alkyl(heterocycloalkyl); wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three R^1;~~

~~or two R^{11} on adjacent atoms are taken together with the atoms to which they are attached to form a cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; each optionally substituted with one, two, or three R^2;~~  is ;

R^{12} is hydrogen or C_1-C_6alkyl;

R^{13} is hydrogen, halogen, -CN, -OH, -OR^a, -SH, -SR^a, -$S(=O)R^a$, -$S(=O)_2R^a$, -NO_2, -NR^bR^c, -$NHS(=O)_2R^a$, -$S(=O)_2NR^bR^c$, -$C(=O)R^a$, -$OC(=O)R^a$, -$C(=O)OR^b$, -$OC(=O)OR^b$, -$C(=O)NR^bR^c$, -$OC(=O)NR^bR^c$, -$NR^bC(=O)NR^bR^c$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^b$, C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, C_1-C_6aminoalkyl,

C_2-C_6alkenyl, C_2-C_6alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, -C_1-C_6alkyl(aryl), -C_1-C_6alkyl(heteroaryl), -C_1-C_6alkyl(cycloalkyl), or -C_1-C_6alkyl(heterocycloalkyl); wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three R^3;

R^{14} is hydrogen, halogen, -CN, -OH, -OR^a, -SH, -SR^a, -$S(=O)R^a$, -$S(=O)_2R^a$, -NO_2, -NR^bR^c, -$NHS(=O)_2R^a$, -$S(=O)_2NR^bR^c$, -$C(=O)R^a$, -$OC(=O)R^a$, -$C(=O)OR^b$, -$OC(=O)OR^b$, -$C(=O)NR^bR^c$, -$OC(=O)NR^bR^c$, -$NR^bC(=O)NR^bR^c$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^b$, C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, C_1-C_6aminoalkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, -C_1-C_6alkyl(aryl), -C_1-C_6alkyl(heteroaryl), -C_1-C_6alkyl(cycloalkyl), or -C_1-C_6alkyl(heterocycloalkyl); wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three R^4;

R^{15} is hydrogen, -$S(=O)R^a$, -$S(=O)_2R^a$, -$S(=O)_2NR^bR^c$, -$C(=O)R^a$, -$C(=O)OR^b$, -$C(=O)NR^bR^c$, C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, C_1-C_6aminoalkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, -C_1-C_6alkyl(aryl), -C_1-C_6alkyl(heteroaryl), -C_1-C_6alkyl(cycloalkyl), or -C_1-C_6alkyl(heterocycloalkyl); wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three R^5;

~~or R^{14} and R^{15} are taken together to form a heterocycloalkyl optionally substituted with one, two, three, or four R^6;~~

R^{16} and R^{17} are each independently hydrogen, -CN, -OR^{20}, C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, C_1-C_6aminoalkyl, C_2-C_6alkenyl, ~~C_2-C_6alkynyl,~~ cycloalkyl, ~~cycloalkenyl,~~ heterocycloalkyl, ~~heterocycloalkenyl,~~ aryl, heteroaryl, -C_1-C_6alkyl(aryl), -C_1-C_6alkyl(heteroaryl), -C_1-C_6alkyl(cycloalkyl), or -C_1-C_6alkyl(heterocycloalkyl); wherein each alkyl, alkenyl, ~~alkynyl,~~ cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three R^7;

or R^{16} and R^{17} are taken together with the nitrogen atom to which they are attached to form a heterocycloalkyl or a heterocycloalkenyl; each optionally substituted with one, two, or three R^8;

each R^{20} is independently hydrogen, C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, C_1-C_6aminoalkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three R^7;

~~n is 0-4;~~

each ~~R^1, R^2,~~ R^3, R^4, R^5~~, R^6~~, and R^8 is independently oxo, halogen, -CN, -OH, -OR^a, -SH, -SR^a, -S(=O)R^a, -$S(=O)_2R^a$, -NO_2, -NR^bR^c, -$NHS(=O)_2R^a$, -$S(=O)_2NR^bR^c$, -C(=O)R^a, -OC(=O)R^a, -C(=O)OR^b, -OC(=O)OR^b, -C(=O)NR^bR^c, -OC(=O)NR^bR^c, -$NR^bC(=O)NR^bR^c$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^b$, C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, C_1-C_6aminoalkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, -C_1-C_6alkyl(aryl), -C_1-C_6alkyl(heteroaryl), -C_1-C_6alkyl(cycloalkyl), or -C_1-C_6alkyl(heterocycloalkyl); wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three oxo, halogen, -CN, -OH, -OMe, -S(=O)Me, -$S(=O)_2$Me, -NH_2, -$S(=O)_2NH_2$, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, or C_1-C_6aminoalkyl;

each R^7 is independently oxo, halogen, -CN, -OH, -OR^a, -SH, -SR^a, -S(=O)R^a, -$S(=O)_2R^a$, -NO_2, -NR^bR^c, -$NHS(=O)_2R^a$, -$S(=O)_2NR^bR^c$, ~~-B(OR^b)(OR^e),~~ -C(=O)R^a, -OC(=O)R^a, -C(=O)OR^b, -OC(=O)OR^b, -C(=O)NR^bR^c, -OC(=O)NR^bR^c, -$NR^bC(=O)NR^bR^c$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^b$, C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, C_1-C_6aminoalkyl, C_2-C_6alkenyl, ~~C_2~~C_3-C_6alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, -C_1-C_6alkyl(aryl), -C_1-C_6alkyl(heteroaryl), -C_1-C_6alkyl(cycloalkyl), or -C_1-C_6alkyl(heterocycloalkyl); wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three R^{7a};

each R^{7a} is independently oxo, halogen, -CN, -OH, -OR^a, -NR^bR^c, -C(=O)R^a, -C(=O)OR^b, -C(=O)NR^bR^c, C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, ~~C_1-C_6aminoalkyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each~~

~~alkyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three oxo, halogen, -CN, -OH, -OMe, -S(=O)Me, -S(=O)$_2$Me, -NH$_2$, -S(=O)$_2$NH$_2$, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C$_1$-C$_6$alkyl, C$_1$-C$_6$haloalkyl, C$_1$-C$_6$hydroxyalkyl, or C$_1$-C$_6$aminoalkyl;~~or C$_1$-C$_6$aminoalkyl;

each R^a is independently C$_1$-C$_6$alkyl, C$_1$-C$_6$haloalkyl, C$_1$-C$_6$hydroxyalkyl, C$_1$-C$_6$aminoalkyl, C$_2$-C$_6$alkenyl, C$_2$-C$_6$alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three oxo, halogen, -CN, -OH, -OMe, -S(=O)Me, -S(=O)$_2$Me, -NH$_2$, -S(=O)$_2$NH$_2$, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C$_1$-C$_6$alkyl, C$_1$-C$_6$haloalkyl, C$_1$-C$_6$hydroxyalkyl, or C$_1$-C$_6$aminoalkyl; and

each R^b and R^c are independently hydrogen, C$_1$-C$_6$alkyl, C$_1$-C$_6$haloalkyl, C$_1$-C$_6$hydroxyalkyl, C$_1$-C$_6$aminoalkyl, C$_2$-C$_6$alkenyl, C$_2$-C$_6$alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three oxo, halogen, -CN, -OH, -OMe, -S(=O)Me, -S(=O)$_2$Me, -NH$_2$, -S(=O)$_2$NH$_2$, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C$_1$-C$_6$alkyl, C$_1$-C$_6$haloalkyl, C$_1$-C$_6$hydroxyalkyl, or C$_1$-C$_6$aminoalkyl;

or R^b and R^c are taken together with the nitrogen atom to which they are attached to form a heterocycloalkyl optionally substituted with one, two, or three oxo, halogen, -CN, -OH, -OMe, -S(=O)Me, -S(=O)$_2$Me, -NH$_2$, -S(=O)$_2$NH$_2$, -C(=O)Me, -C(=O)OH, -C(=O)OMe, C$_1$-C$_6$alkyl, C$_1$-C$_6$haloalkyl, C$_1$-C$_6$hydroxyalkyl, or C$_1$-C$_6$aminoalkyl.

2. The compound of claim 1, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

R^{14} is hydrogen~~, halogen, -CN, -OH, -OR^a, -NR^{b}R^c, -C(=O)OR^b, -C(=O)NR^{b}R^c,~~ or C$_1$-C$_6$alkyl~~, C$_1$-C$_6$haloalkyl, or cycloalkyl~~.

3. The compound of claim 1~~ or 2~~, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

~~R^{14} is hydrogen or C$_1$-C$_6$alkyl.~~

~~4. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:~~

R^{14} is C_1-C_6alkyl.

5. The compound of any one of claims 1-4, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

R^{15} is hydrogen, $-S(=O)_2R^a$, $-S(=O)_2NR^bR^e$, $-C(=O)R^a$, $-C(=O)OR^b$, $-C(=O)NR^bR^e$, C_1-C_6alkyl, C_1-C_6haloalkyl, or C_1-C_6hydroxyalkyl, or cycloalkyl.

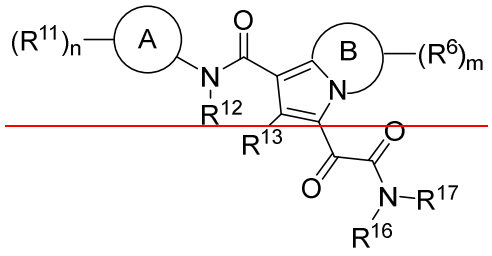
6. The compound of any one of claims 1-5, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

R^{15} is hydrogen, C_1-C_6alkyl, C_1-C_6haloalkyl, or C_1-C_6hydroxyalkyl.

7. The compound of any one of claims 1-6, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

R^{15} is C_1-C_6alkyl.

8.4. The compound of claim 1, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein the compound of Formula (I) is of Formula (Ia):



(Ia),

wherein:

Ring B is heterocycloalkyl;

each R^6 is independently oxo, halogen, $-CN$, $-OH$, $-OR^a$, $-SH$, $-SR^a$, $-S(=O)R^a$, $-S(=O)_2R^a$, $-NO_2$, $-NR^bR^e$, $-NHS(=O)_2R^a$, $-S(=O)_2NR^bR^e$, $-C(=O)R^a$, $-OC(=O)R^a$, $-C(=O)OR^b$, $-OC(=O)OR^b$, $-C(=O)NR^bR^e$, $-OC(=O)NR^bR^e$, $-NR^bC(=O)NR^bR^e$, $-NR^bC(=O)R^a$, $-NR^bC(=O)OR^b$, C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, $-C_1$-C_6alkyl(aryl), $-C_1$-C_6alkyl(heteroaryl), $-C_1$-C_6alkyl(cycloalkyl), or $-C_1$-C_6alkyl(heterocycloalkyl); and

m is 0-4.

9. The compound of claim 8, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

Ring B is a 5-, 6-, or 7-membered heterocycloalkyl.

10. The compound of claim 8 or 9, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

Ring B is a 5-membered heterocycloalkyl.

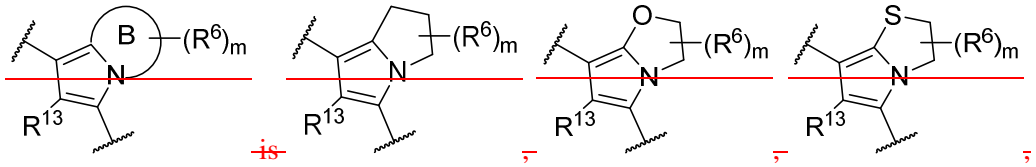
11. The compound of claim 8 or 9, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

Ring B is a 6-membered heterocycloalkyl.

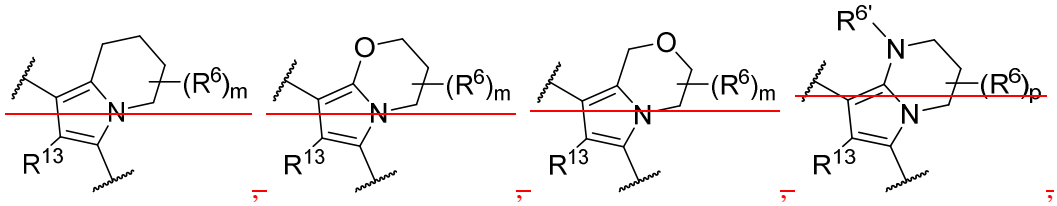
12. The compound of claim 8 or 9, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

Ring B is a 7-membered heterocycloalkyl.

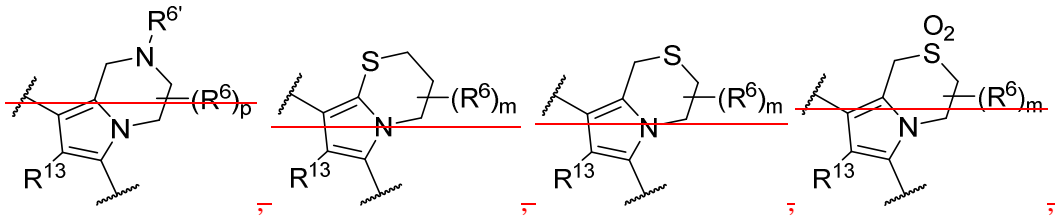
13. The compound of claim 8 or 9, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:



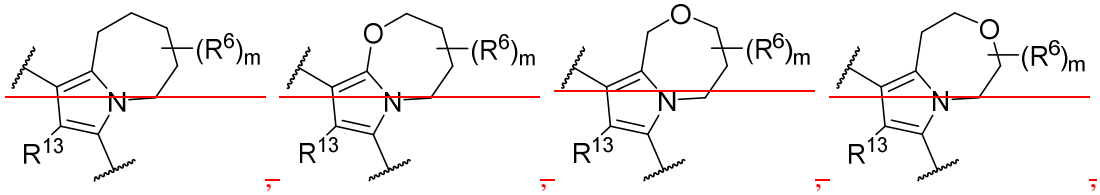
is , , , ;



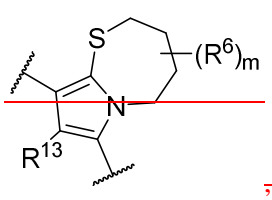
, , , , ;

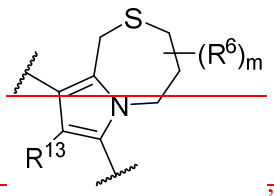


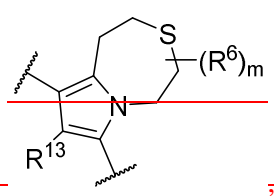
, , , , ;

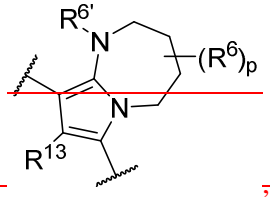


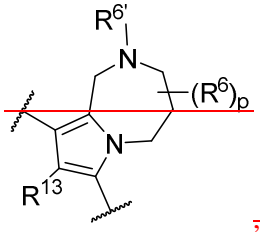
, , , , ;

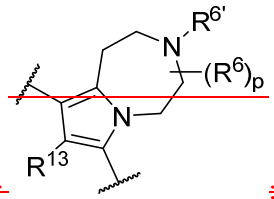


, 

, 

, 

, 

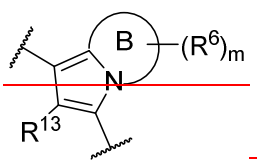


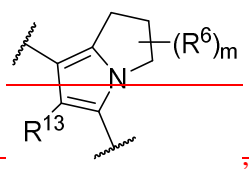
, or ; wherein

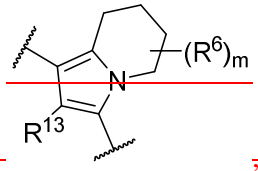
$R^{6'}$ is hydrogen, $S(=O)R^a$, $S(=O)_2R^a$, $S(=O)_2NR^bR^e$, $C(=O)R^a$, $C(=O)OR^b$, $C(=O)NR^bR^e$, C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, C_2-C_6alkenyl, C_2-C_6alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C_1-C_6alkyl(aryl), C_1-C_6alkyl(heteroaryl), C_1-C_6alkyl(cycloalkyl), or C_1-C_6alkyl(heterocycloalkyl); and

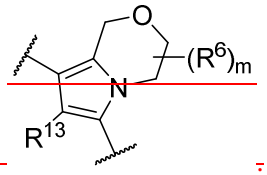
p is 0-3.

14. The compound any one of claims 8 or 9 or 13, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:



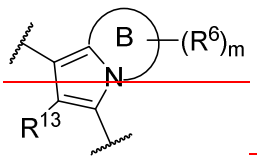
is 

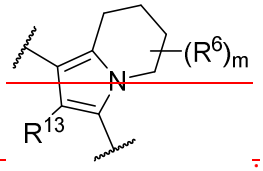
, 

, or 

.

15. The compound of any one of claims 8 or 9 or 13 or 14, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:



is 

.

16. The compound any one of claims 8-15, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

each R^6 is independently halogen, CN, OH, OR^a, NR^bR^e, $S(=O)_2R^a$, $S(=O)_2NR^bR^e$, $C(=O)R^a$, C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, or cycloalkyl.

17. The compound any one of claims 8-16, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

each R^6 is independently halogen, $S(=O)_2R^a$, $C(=O)R^a$, or C_1-C_6alkyl.

18. The compound of claim13, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

each R^6 is independently halogen, -CN, -OH, -OR^a, -NR^bR^e, -C_1-C_6alkyl, -C_1-C_6haloalkyl, -C_1-C_6hydroxyalkyl, or cycloalkyl; and

$R^{6'}$ is hydrogen, -$S(=O)_2R^a$, -$S(=O)_2NR^bR^e$, -$C(=O)R^a$, -C_1-C_6alkyl, -C_1-C_6haloalkyl, -C_1-C_6hydroxyalkyl, or cycloalkyl.

19. The compound of claim 13, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

each R^6 is independently halogen or -C_1-C_6alkyl; and

$R^{6'}$ is hydrogen, -$S(=O)_2R^a$, -$C(=O)R^a$, or -C_1-C_6alkyl.

20. The compound of claim 13, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

$R^{6'}$ is hydrogen or -C_1-C_6alkyl.

21. The compound any one of claims 8-20, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

m is 0-2.

22. The compound any one of claims 8-21, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

m is 0.

23. The compound of any one of claims 1-22, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

R^{12} is hydrogen or -C_1-C_6alkyl.

24. The compound of any one of claims 1-23, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

R^{13} is hydrogen, halogen, -CN, -OH, -OR^a, -NR^bR^e, -$C(=O)OR^b$, -$C(=O)NR^bR^e$, -C_1-C_6alkyl, -C_1-C_6haloalkyl, or cycloalkyl or C_1-C_6alkyl.

25. The compound of any one of claims claim 1-24, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

R^{13} is hydrogen, halogen, or -C_1-C_6alkyl.

26. The compound of any one of claims 1-25, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

R^{13} is hydrogen or -C_1-C_6alkyl.

27. The compound of any one of claims 1-26, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

~~R^{13} is C_1-C_6alkyl.~~

~~28. The compound of any one of claims 1-27, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:~~

~~Ring A is aryl or heteroaryl.~~

~~29. The compound of any one of claims 1-28, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:~~

~~Ring A is phenyl or pyridyl.~~

~~30. The compound of any one of claims 1-29, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:~~

~~Ring A is phenyl.~~

~~31. The compound of any one of claims 1-30, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:~~

~~each R^{11} is independently halogen, -CN, -OH, -OR^a, -NR^bR^c, -$C(=O)OR^b$, -$C(=O)NR^bR^c$, C_1-C_6alkyl, C_1-C_6haloalkyl, or cycloalkyl.~~

~~32. The compound of any one of claims 1-31, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:~~

~~each R^{11} is independently halogen, -CN, C_1-C_6alkyl, or C_1-C_6haloalkyl.~~

~~33. The compound of any one of claims 1-32, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:~~

~~each R^{11} is independently halogen or C_1-C_6alkyl.~~

~~34. The compound of any one of claims 1-33, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:~~

~~n is 0-3.~~

~~35. The compound of any one of claims 1-34, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:~~

~~n is 1.~~

~~36. The compound of any one of claims 1-35, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:~~

~~n is 2.~~

~~37. The compound of any one of claims 1-35, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:~~

~~n is 3.~~

~~38.~~5. ~~The compound of any one of claims 1-37~~, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

R^{16} is hydrogen or C_1-C_6alkyl.

~~39.~~6. The compound of ~~any one of claims~~claim 1~~-38~~, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

R^{16} is hydrogen.

~~40.~~7. The compound of ~~any one of claims~~claim 1~~-39~~, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

R^{17} is $-OR^{20}$, C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, C_1-C_6aminoalkyl, ~~C_2-C_6alkynyl,~~ cycloalkyl, ~~cycloalkenyl,~~ heterocycloalkyl, ~~heterocycloalkenyl,~~ aryl, heteroaryl, -C_1-C_6alkyl(aryl), -C_1-C_6alkyl(heteroaryl), -C_1-C_6alkyl(cycloalkyl), or -C_1-C_6alkyl(heterocycloalkyl); wherein each alkyl, ~~alkynyl,~~ cycloalkyl~~, cycloalkenyl~~, heterocycloalkyl, ~~heterocycloalkenyl,~~ aryl, and heteroaryl is independently optionally substituted with one, two, or three R^7.

~~41.~~8. The compound of ~~any one of claims~~claim 1~~-40~~, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

R^{17} is $-OR^{20}$, C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, C_1-C_6aminoalkyl, ~~C_2-C_6alkynyl,~~ cycloalkyl, ~~cycloalkenyl,~~ heterocycloalkyl, ~~aryl, heteroaryl,~~ -C_1-C_6alkyl(aryl), -C_1-C_6alkyl(heteroaryl), -C_1-C_6alkyl(cycloalkyl), or -C_1-C_6alkyl(heterocycloalkyl); wherein each alkyl, ~~alkynyl,~~ cycloalkyl, ~~cycloalkenyl,~~ heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three R^7.

~~42.~~9. The compound of ~~any one of claims~~claim 1~~-41~~, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

R^{17} is $-OR^{20}$, C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, cycloalkyl, heterocycloalkyl, -C_1-C_6alkyl(heteroaryl), or -C_1-C_6alkyl(cycloalkyl); wherein each alkyl, cycloalkyl, heterocycloalkyl, and heteroaryl is independently optionally substituted with one, two, or three R^7.

~~43.~~10. The compound of ~~any one of claims~~claim 1~~-42~~, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

R^{17} is C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, or cycloalkyl~~, or heterocycloalkyl~~; each optionally substituted with one, two, or three R^7.

~~44.~~11. The compound of ~~any one of claims~~claim 1~~-43~~, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

R^{17} is C_1-C_6alkyl or cycloalkyl; each optionally substituted with one, two, or three R^7.

~~45.~~12. The compound of ~~any one of claims~~claim 1~~-44~~, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

~~R^{17} is C_1-C_6alkyl optionally substituted with one, two, or three R^7.~~

~~46. The compound of any one of claims 1-45, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:~~

each R^7 is independently ~~oxo,~~ halogen, -CN, -OH, -OR^a, ~~-$S(=O)_2R^a$,~~ NR^bR^c, ~~-$NHS(=O)_2R^a$, -$S(=O)_2NR^bR^c$, -$B(OR^b)(OR^c)$,~~ $C(=O)R^a$, -$C(=O)OR^b$, -$C(=O)NR^bR^c$, ~~-$NR^bC(=O)R^a$,~~ C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, ~~C_1-C_6aminoalkyl,~~ cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl~~, alkenyl, alkynyl~~, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three R^{7a}.

~~47.~~13. The compound of ~~any one of claims~~claim 1~~-46~~, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

each R^7 is independently halogen, -CN, -OH, -OR^a, -NR^bR^c, -$C(=O)OR^b$, -$C(=O)NR^bR^c$, C_1-C_6alkyl, C_1-C_6haloalkyl, C_1-C_6hydroxyalkyl, cycloalkyl, or heteroaryl; wherein each alkyl, cycloalkyl~~, heterocycloalkyl~~, and heteroaryl is independently optionally substituted with one, two, or three R^{7a}.

~~48.~~14. The compound of ~~any one of claims~~claim 1~~-47~~, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:

each R^{7a} is independently halogen, -CN, -OH, -OR^a, -NR^bR^c, C_1-C_6alkyl, or C_1-C_6haloalkyl.

~~49. The compound of any one of claims~~claim 1~~-37, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:~~

~~R^{16} and R^{17} are taken together with the nitrogen atom to which they are attached to form a heterocycloalkyl optionally substituted with one, two, or three R^8.~~

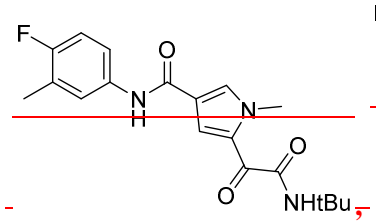
~~50. The compound of any one of claims 1-37 or 49, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:~~

~~each R^8 is independently oxo, halogen, -CN, -OH, -OR^a, -NR^bR^c, C_1-C_6alkyl, C_1-C_6haloalkyl, or C_1-C_6hydroxyalkyl.~~

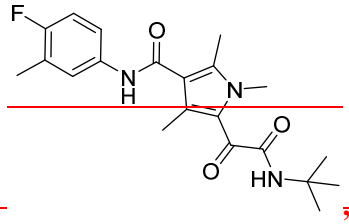
~~51. The compound of any one of claims 1-37 or 49 or 50, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, wherein:~~

~~each R^8 is independently –OH or C_1-C_6alkyl.~~

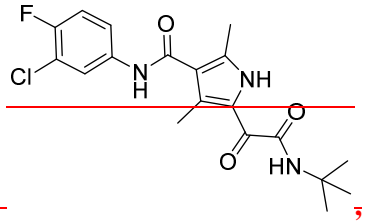
~~52.~~15. ~~A compound~~, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, selected from the group consisting of:



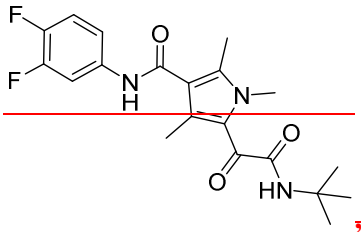
,



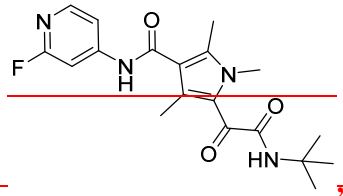
,



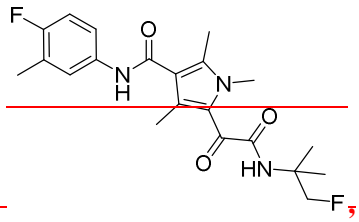
,



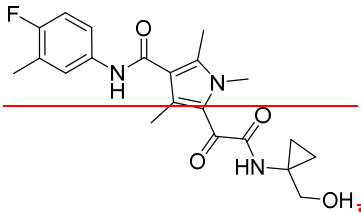
,



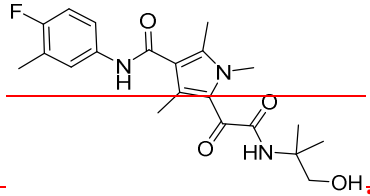
,



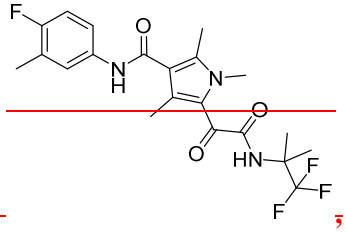
,



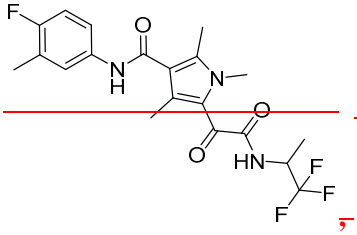
,



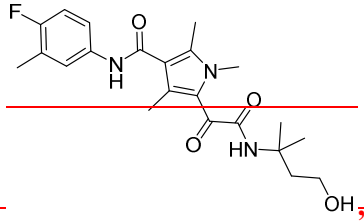
,



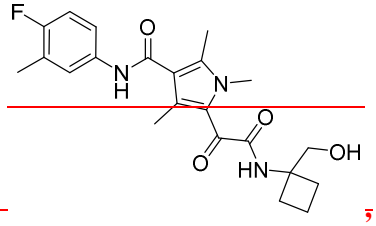
,



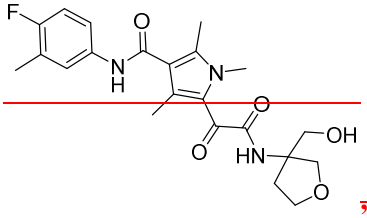
,



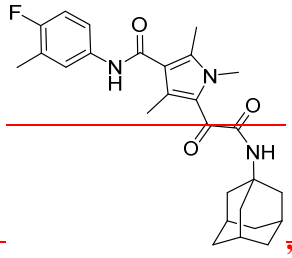
,



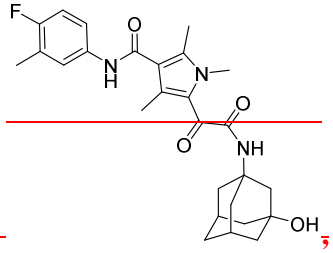
,



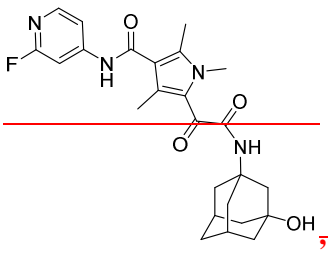
,



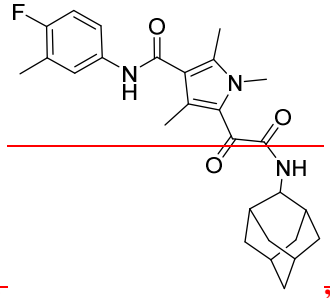
,



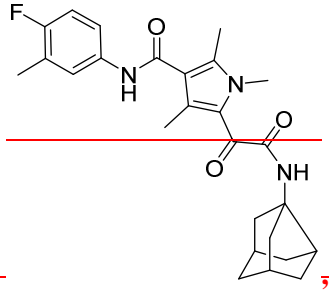
,



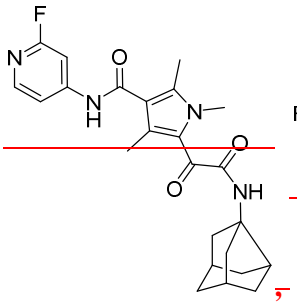
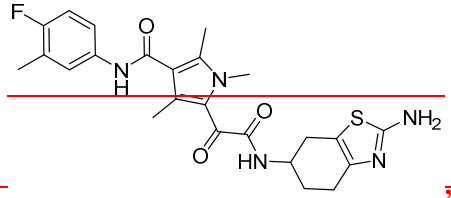
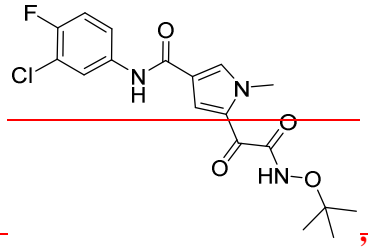
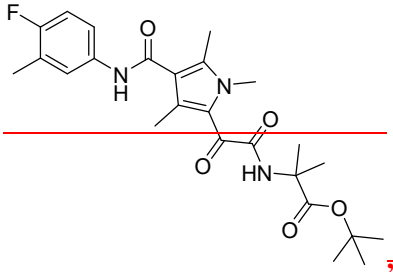
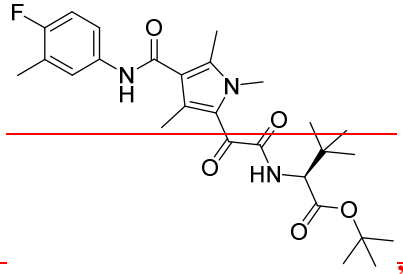
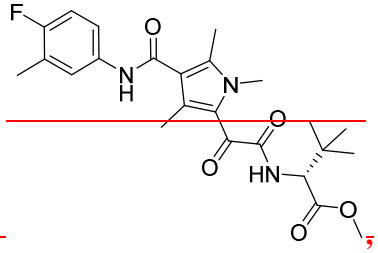
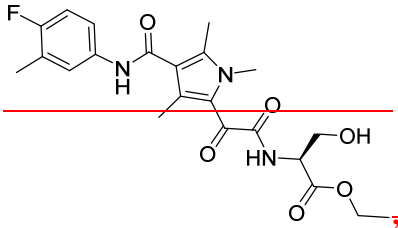
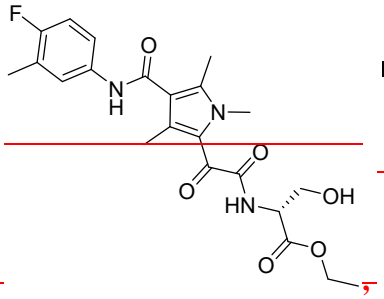
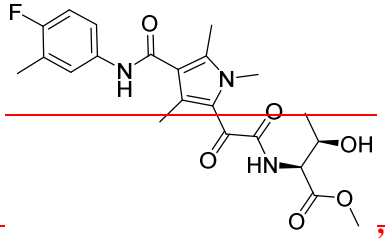
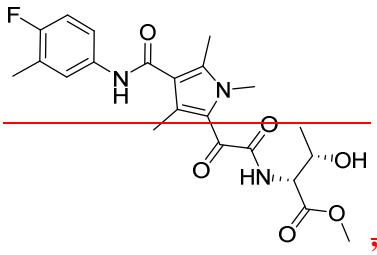
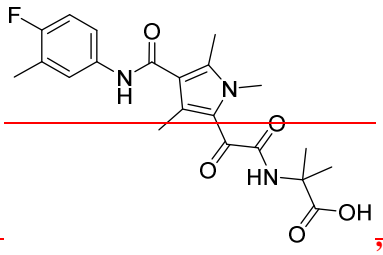
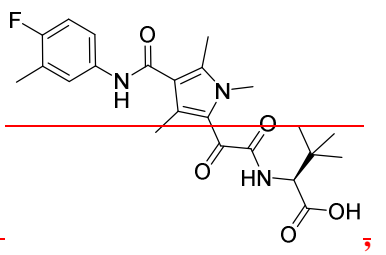
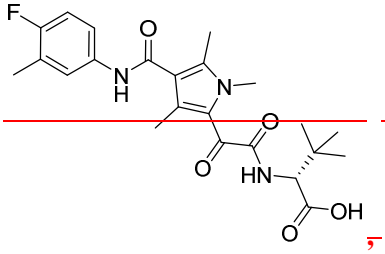
,

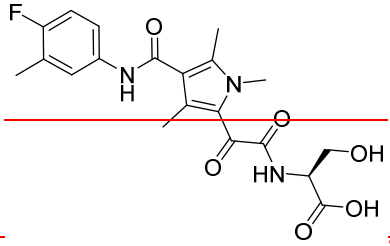


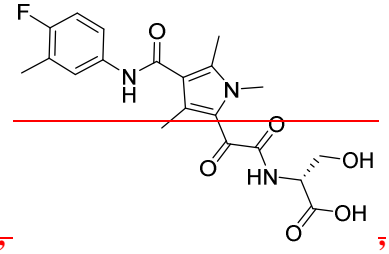
,

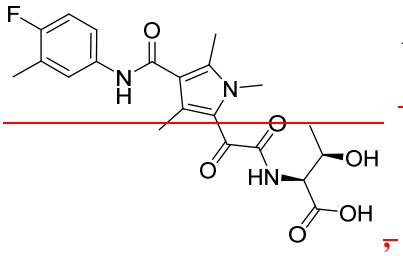
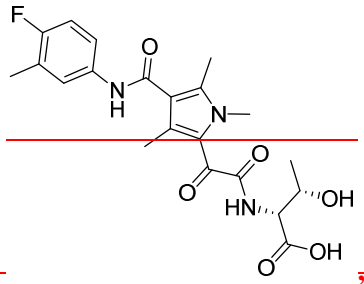
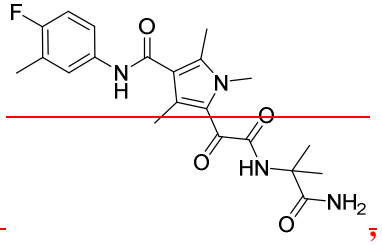
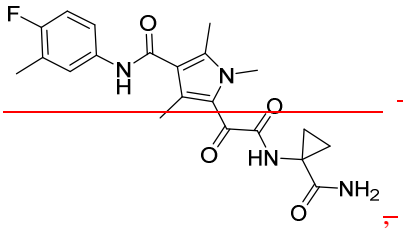
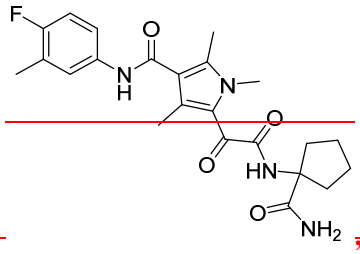
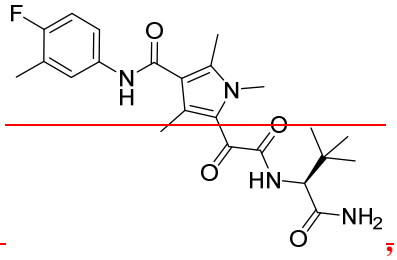
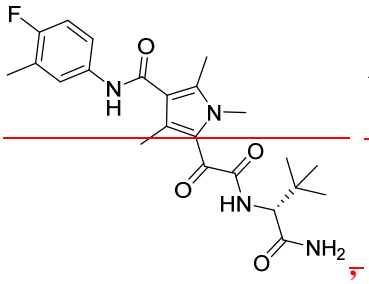
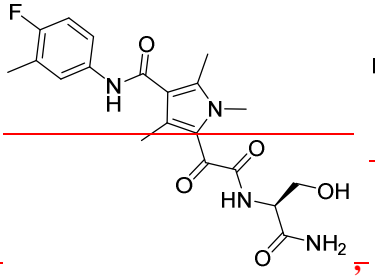
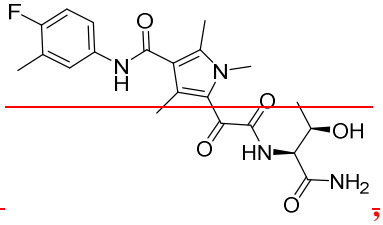
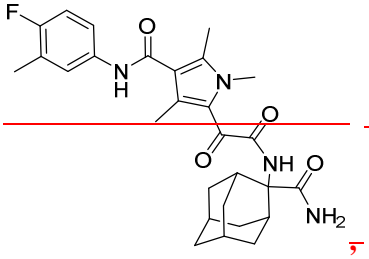
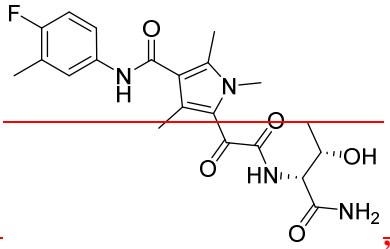
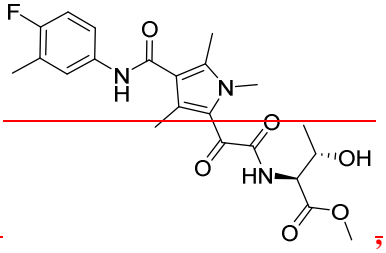
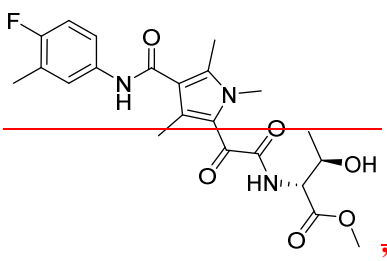
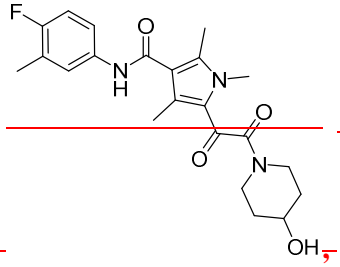
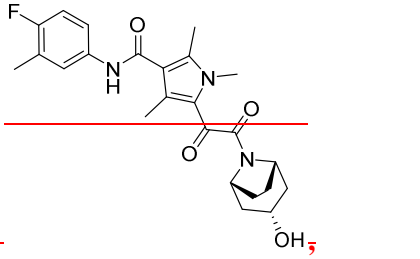
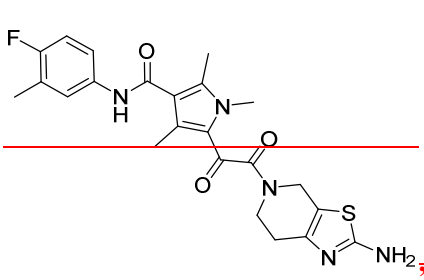
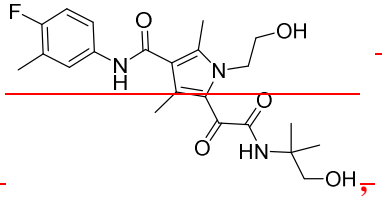
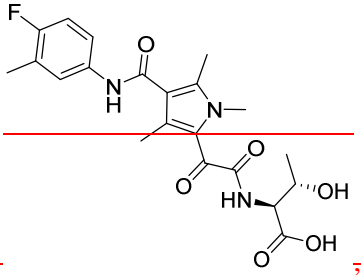


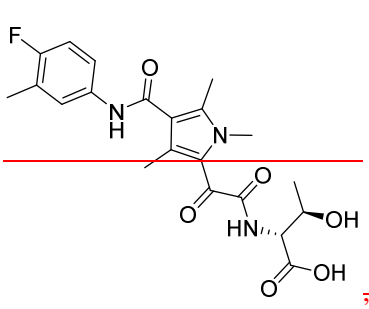
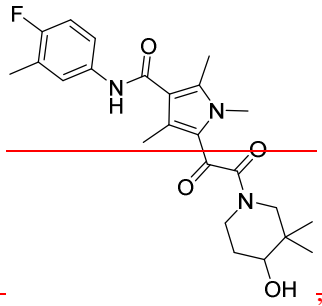
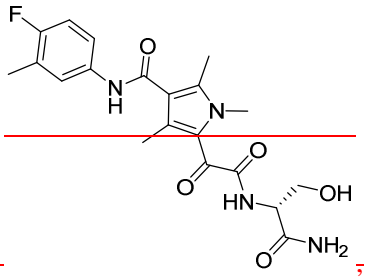
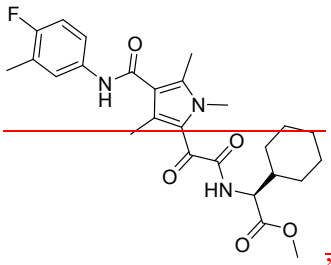
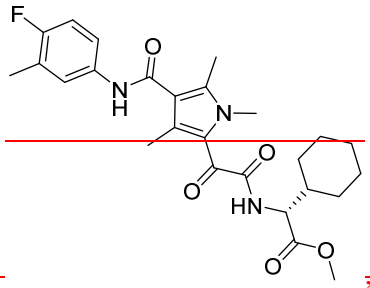
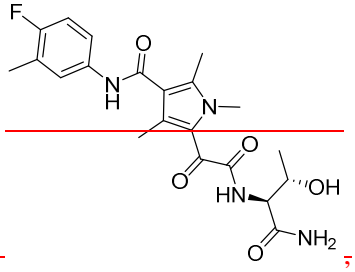
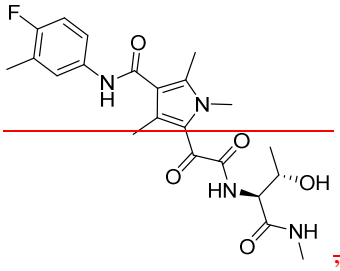
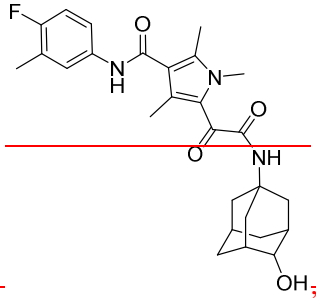
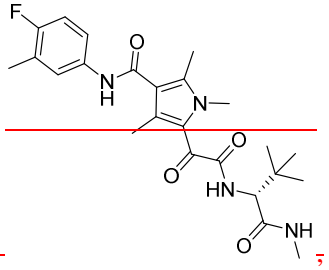
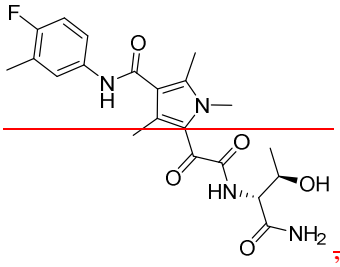
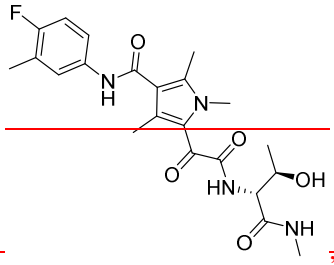
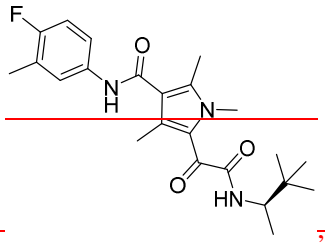
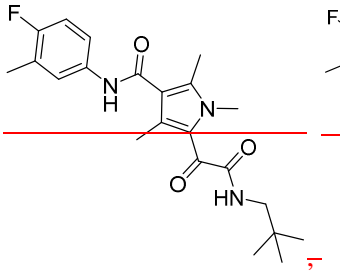
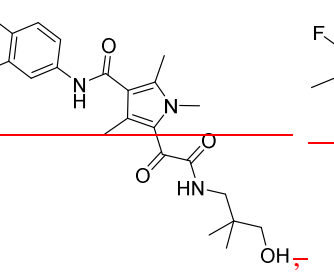
,






,

,

;

,

,

;

,

,

;

,

,

;

,

,

;

,

,

;

,

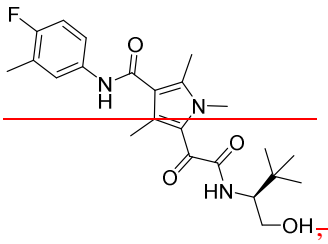
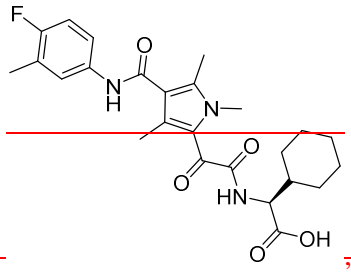
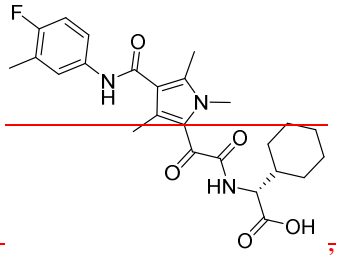
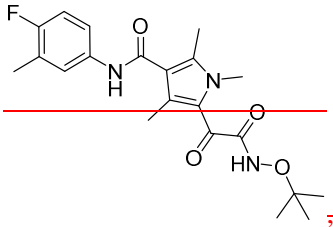
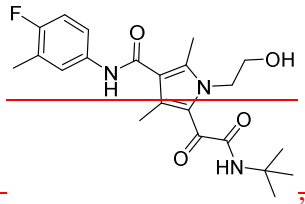
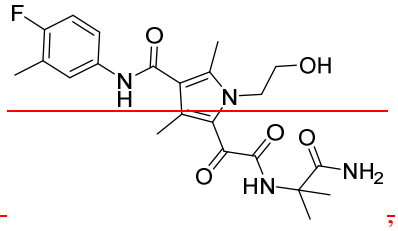
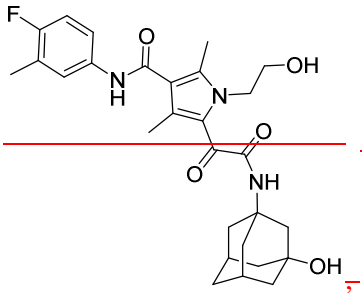
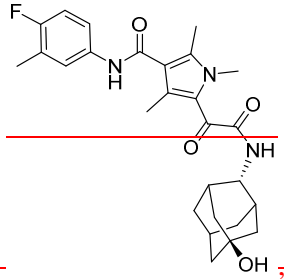
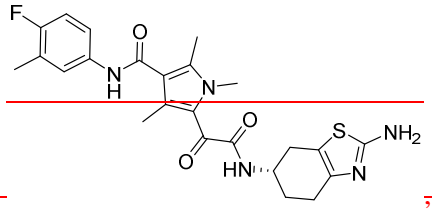
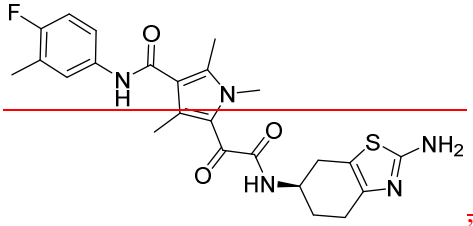
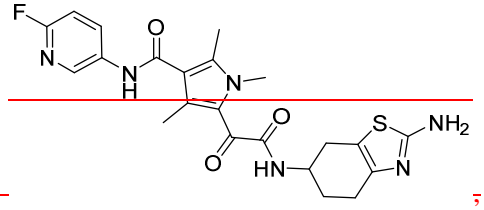
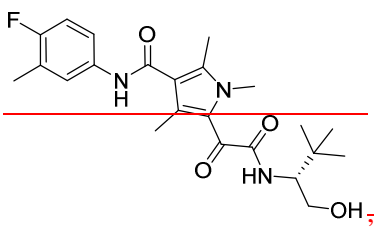
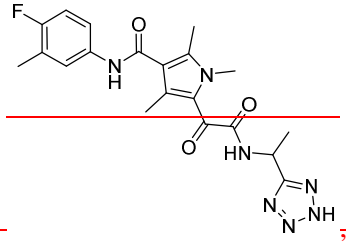
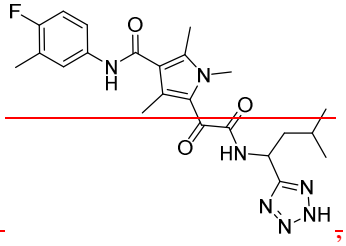
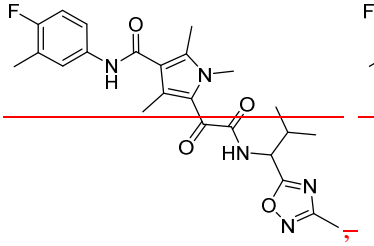
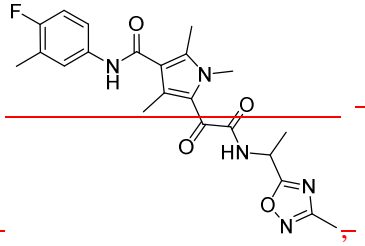
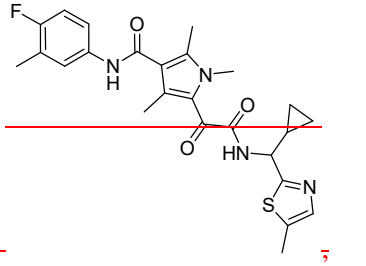
,

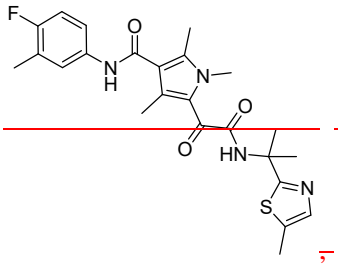
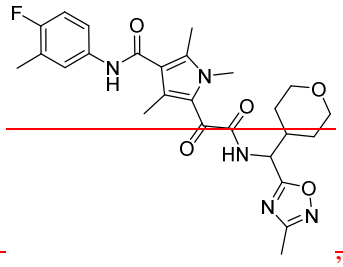
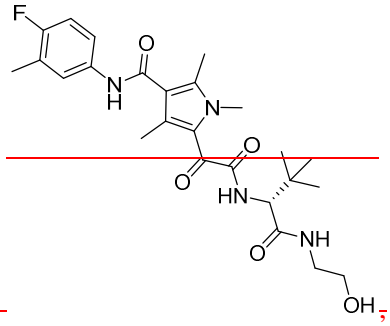
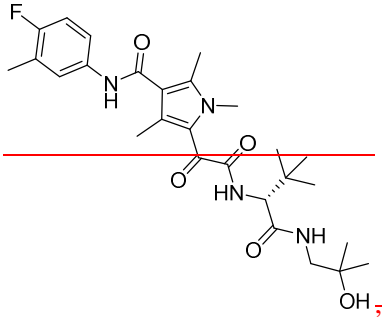
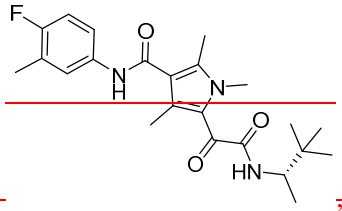
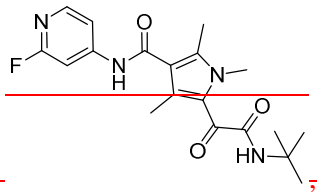
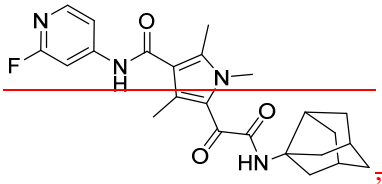
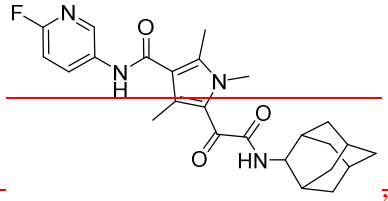
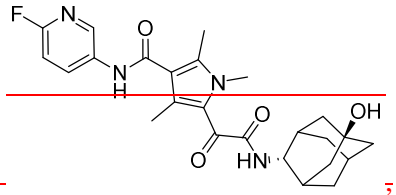
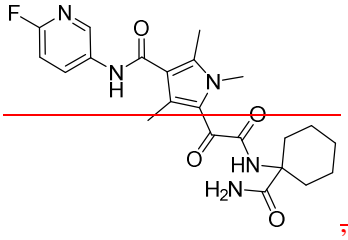
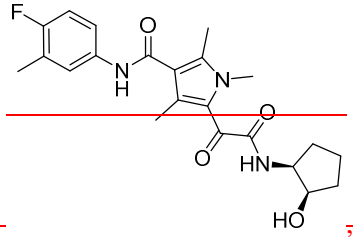
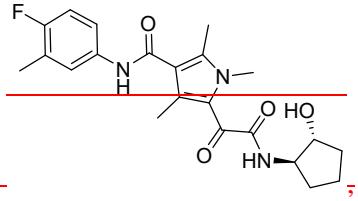
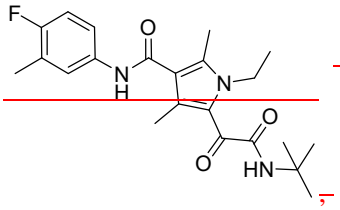
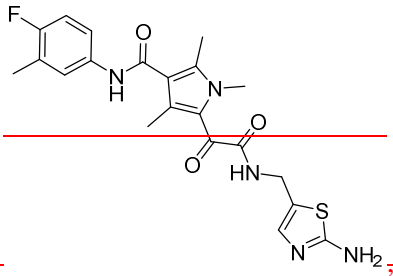
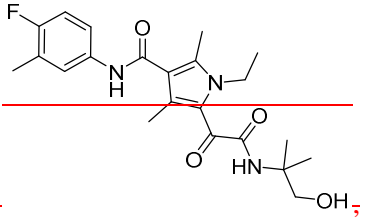
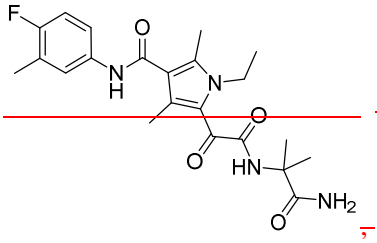
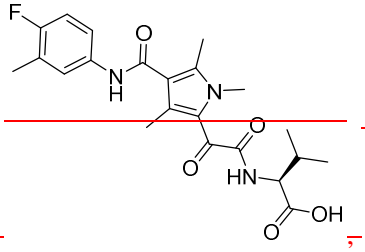
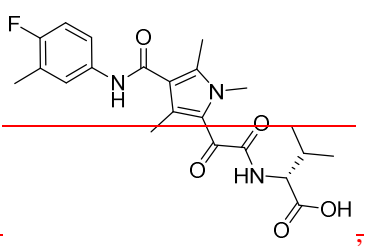
;

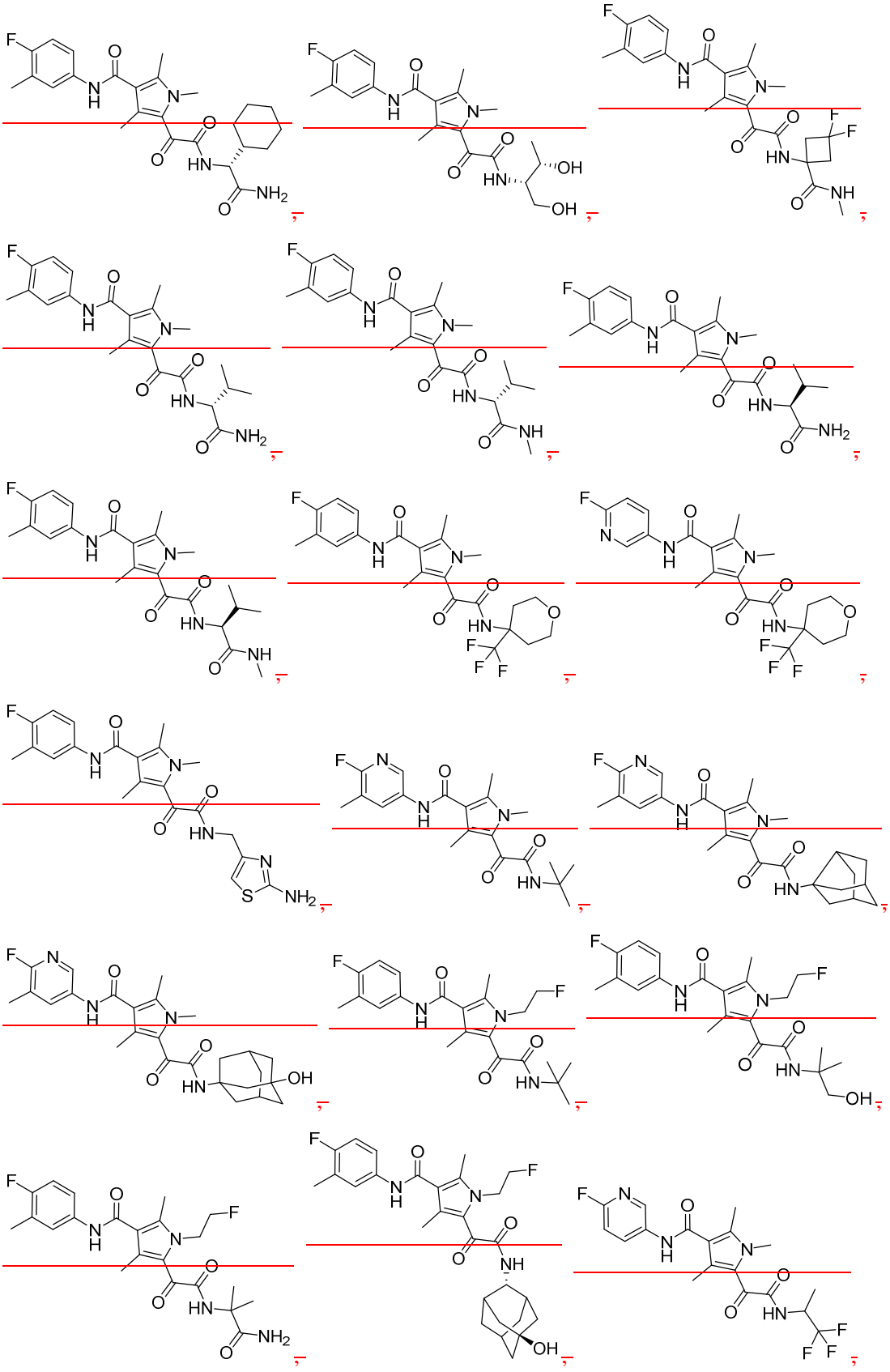
,

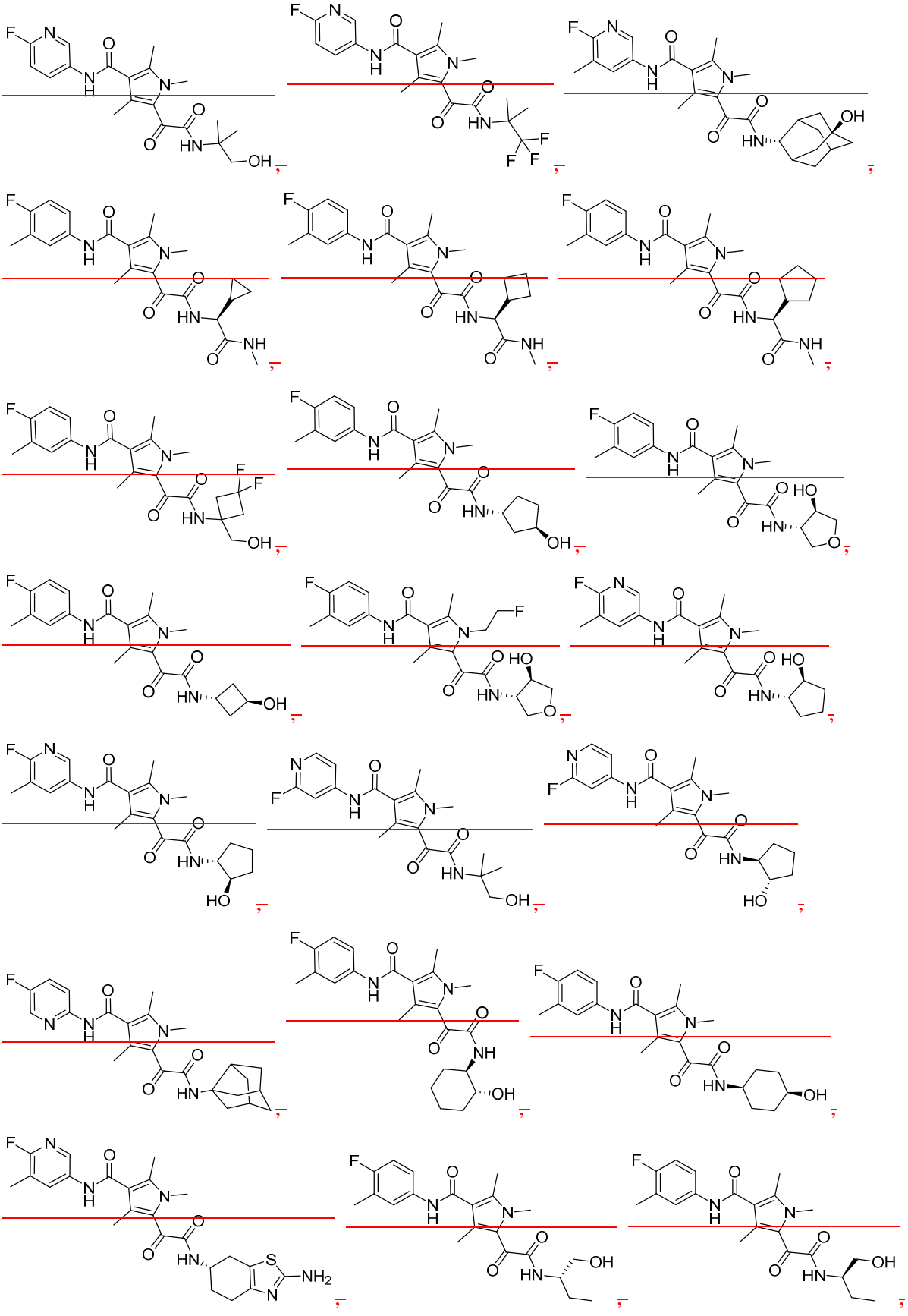
,

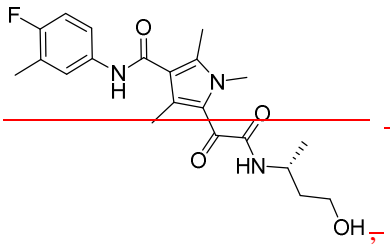
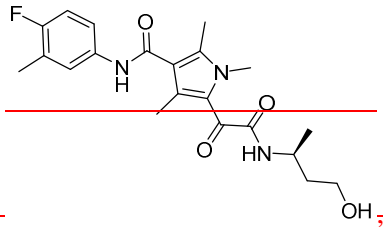
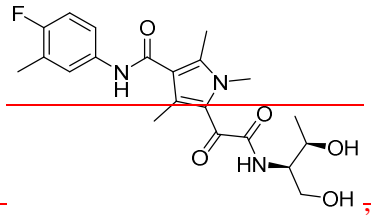
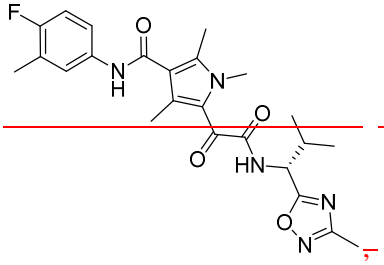
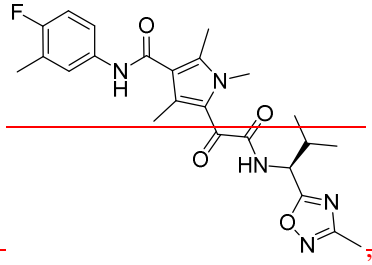
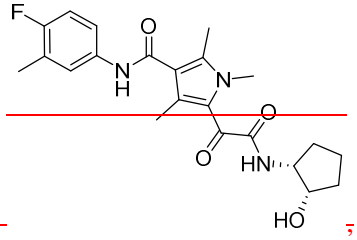
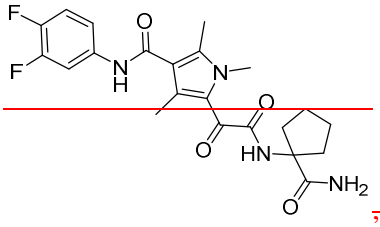
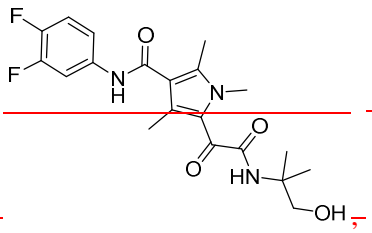
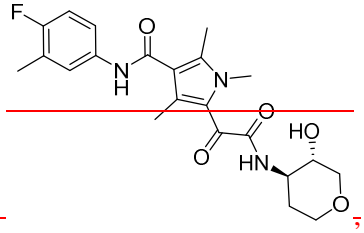
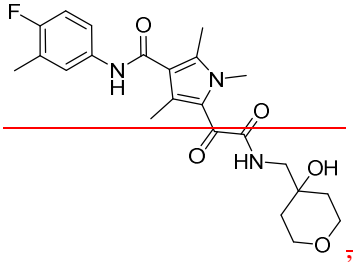
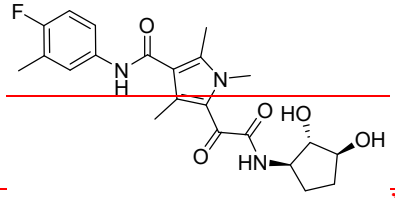
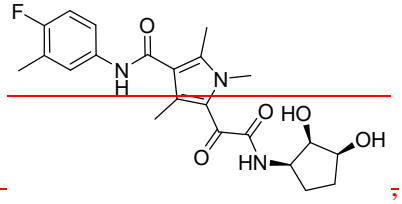
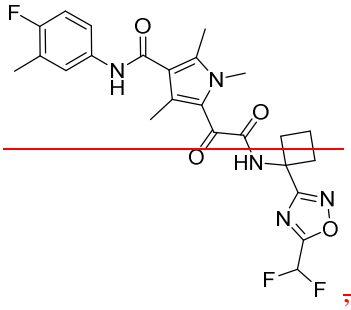
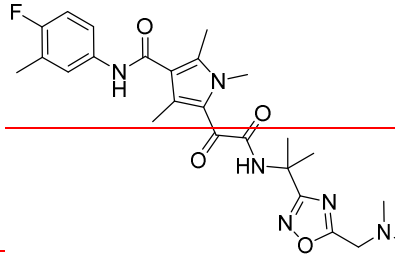
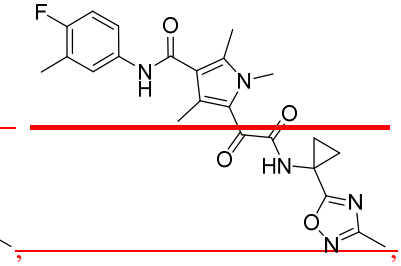
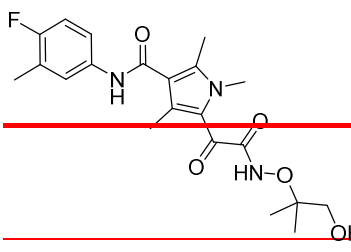
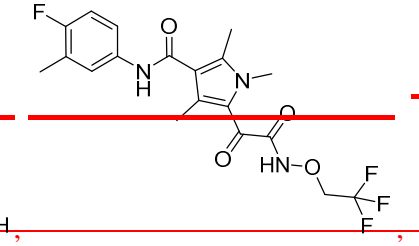
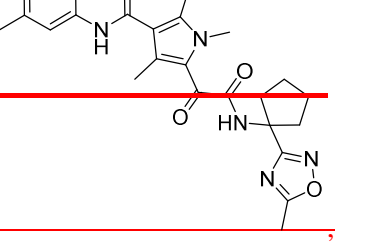
;

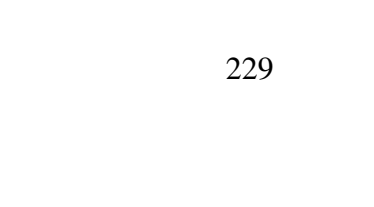

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

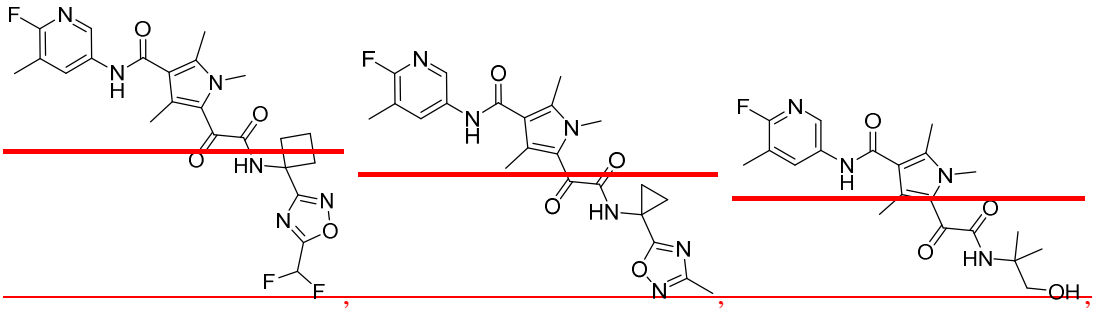



















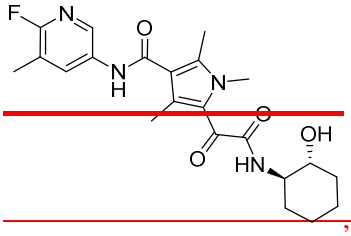
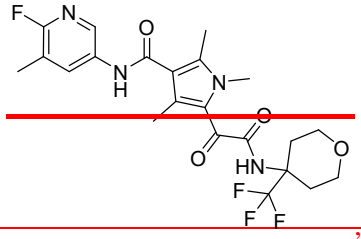
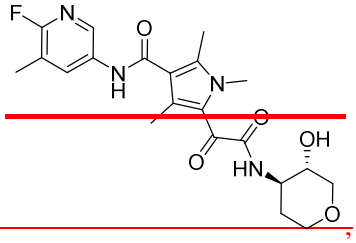
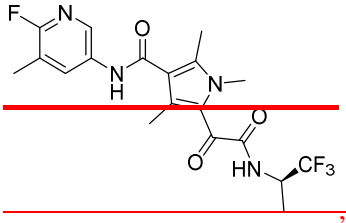
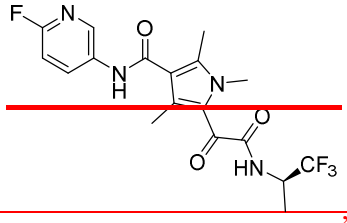
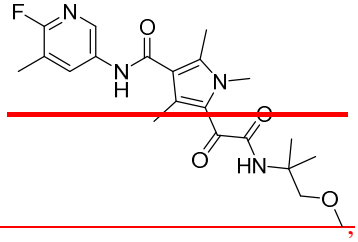
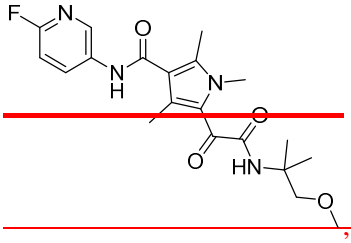
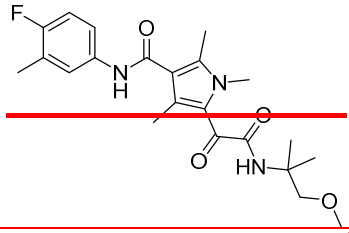
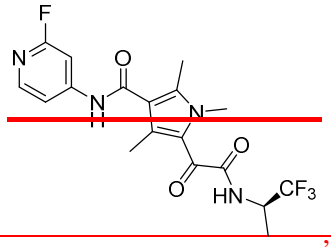
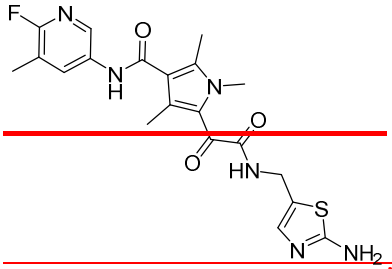
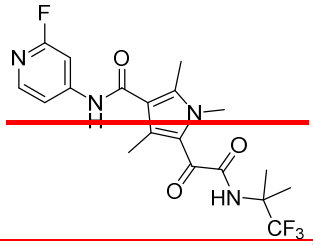
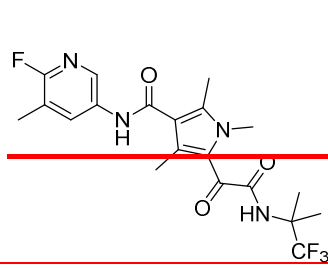
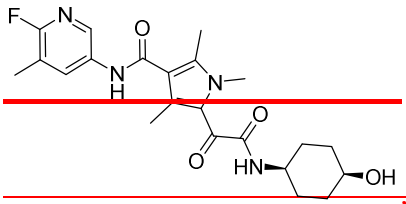
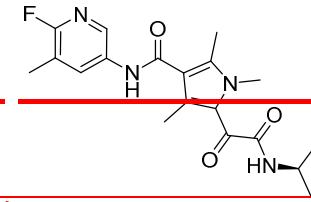
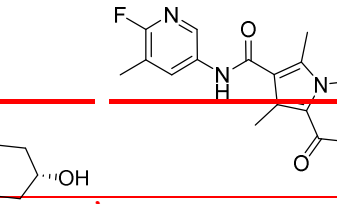


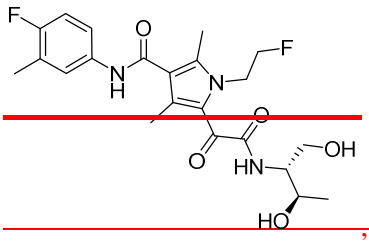
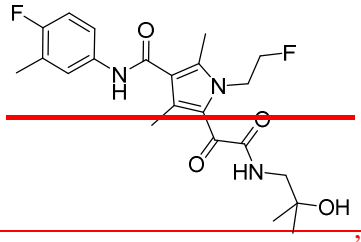
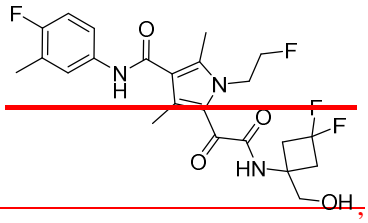
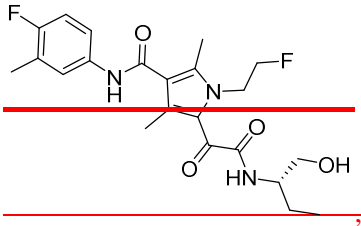
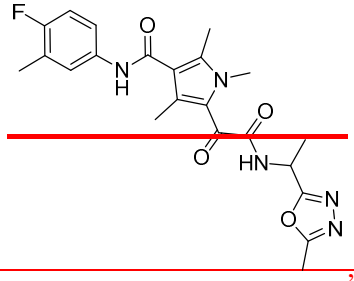
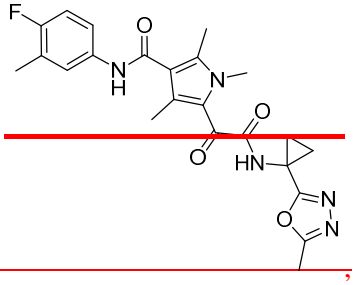
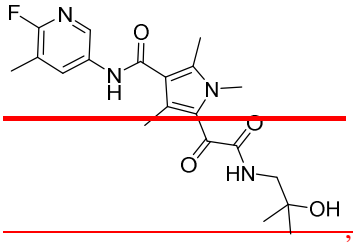
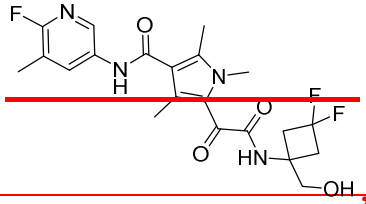
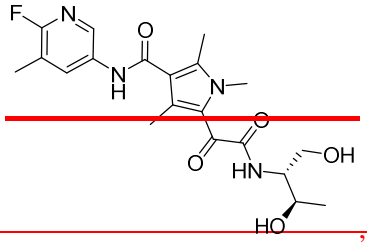
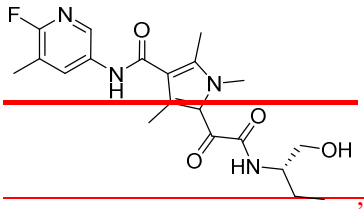
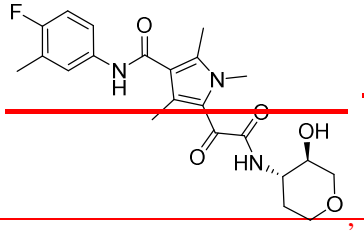
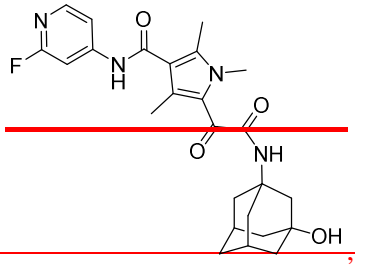




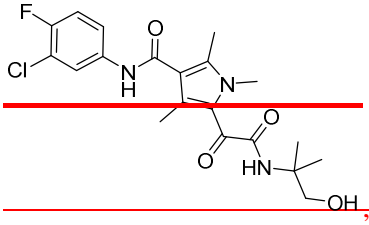
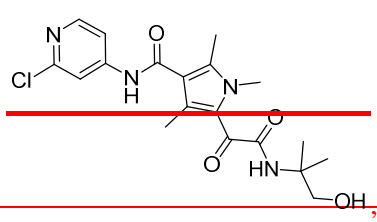
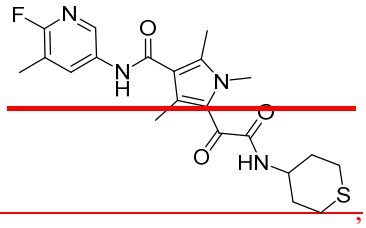
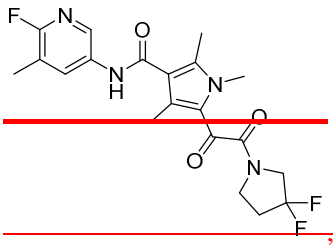
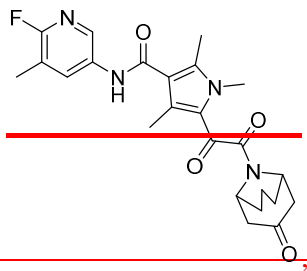
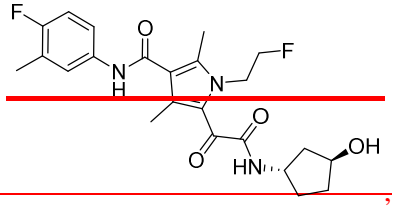


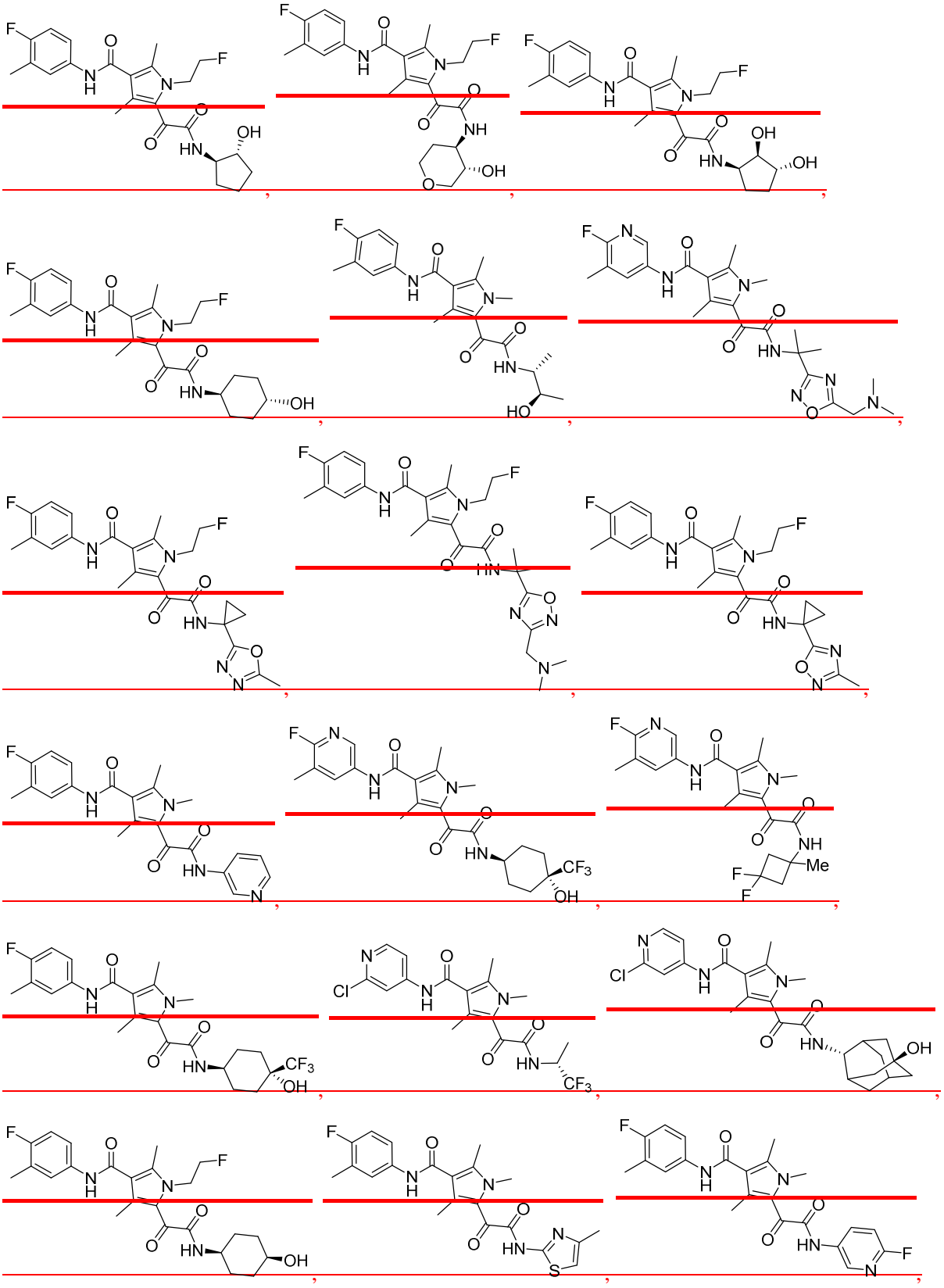
















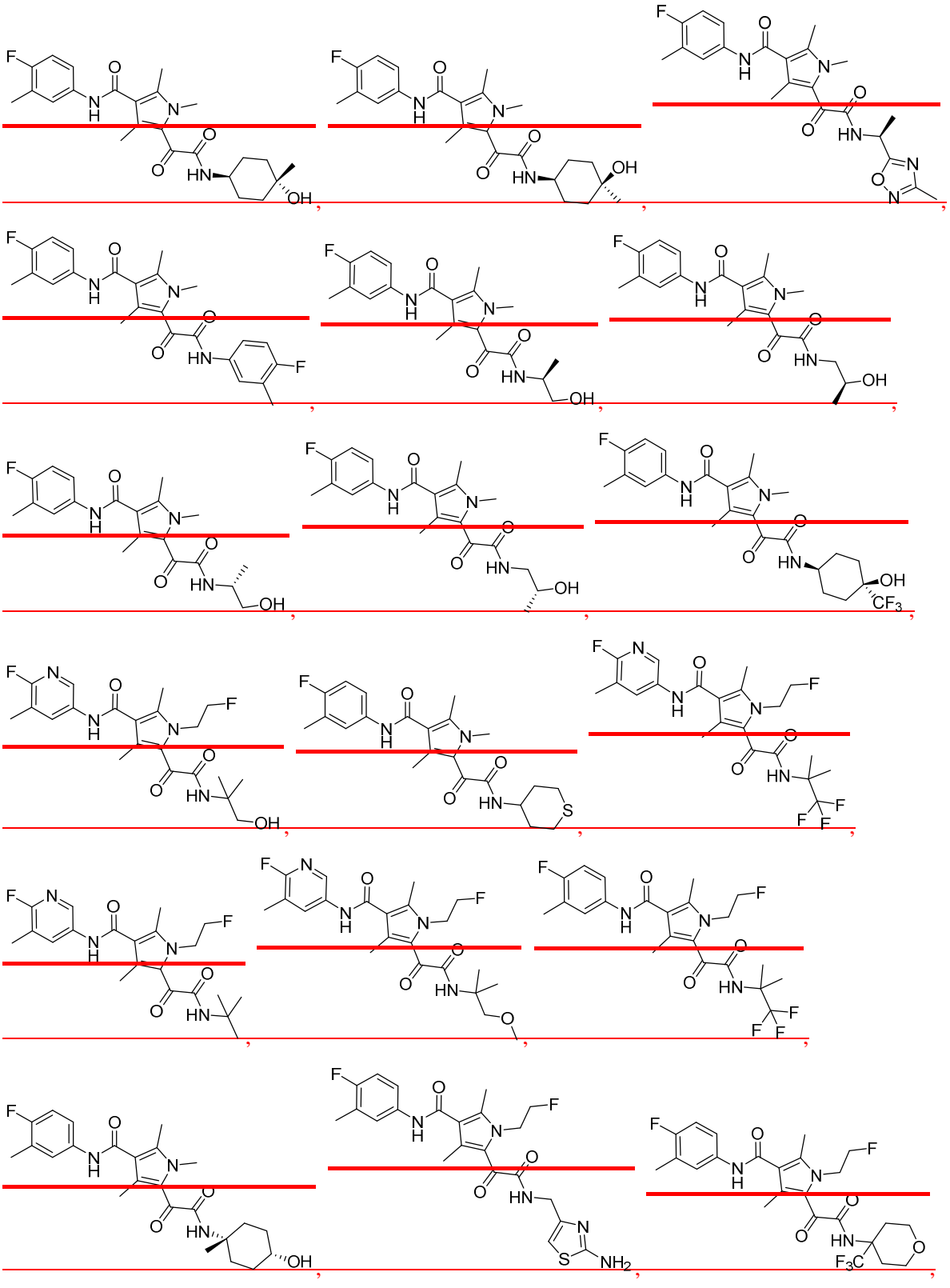

,

,

,

,

,

,

,

,

,

,

,

,

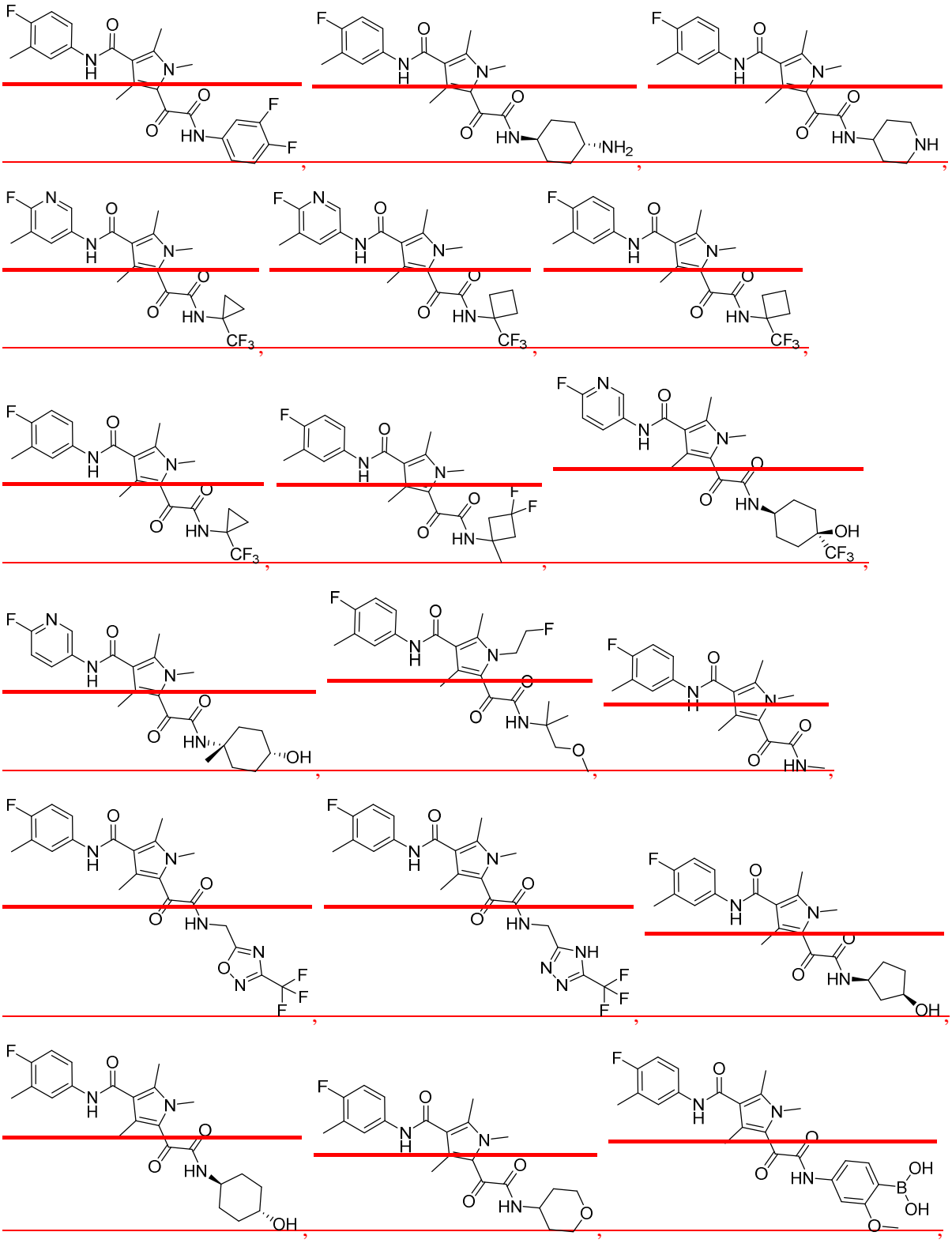
,

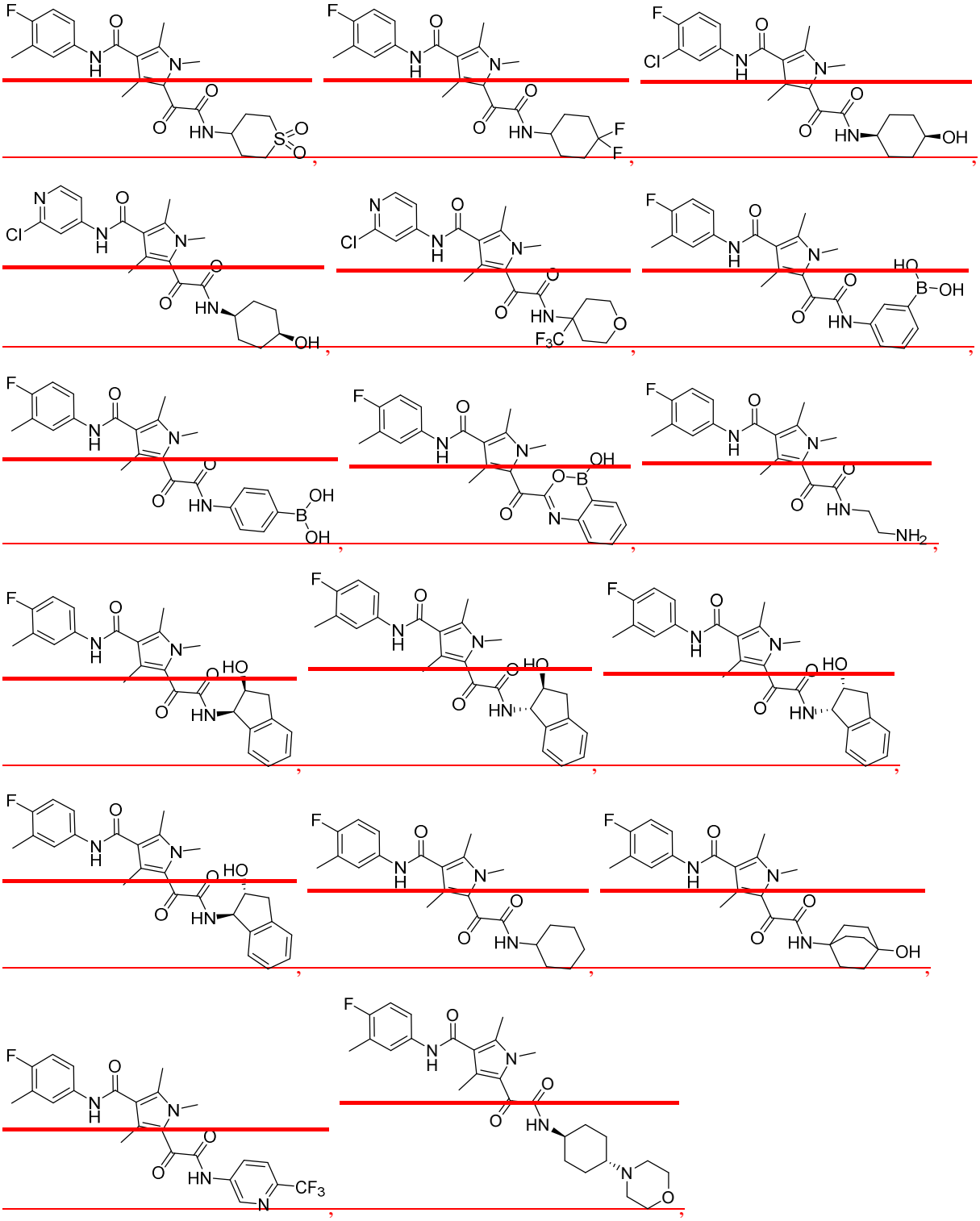
,

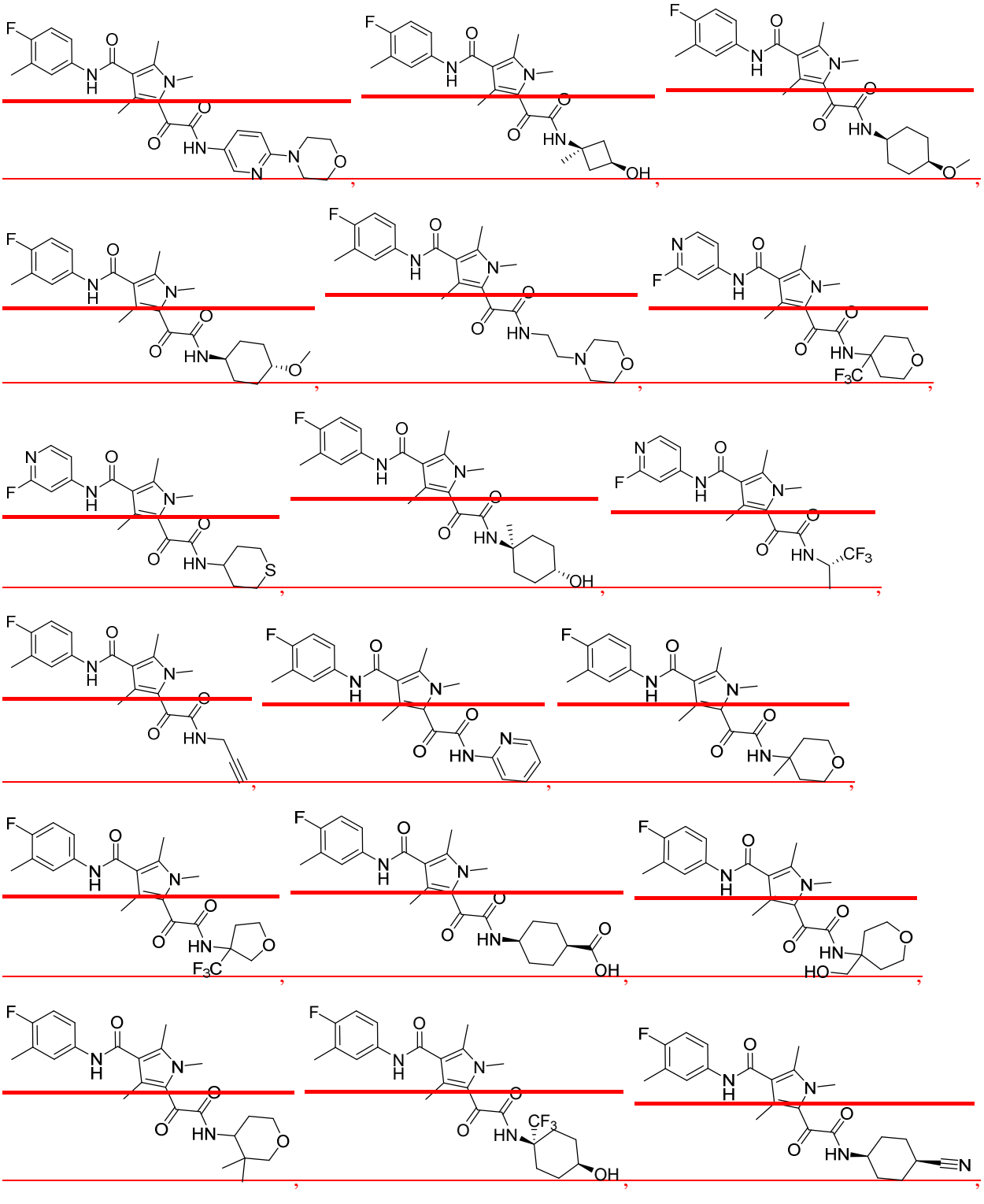
,

,

,

,

,

,

,

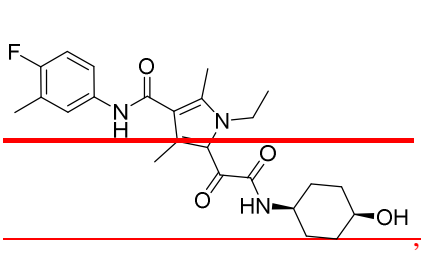
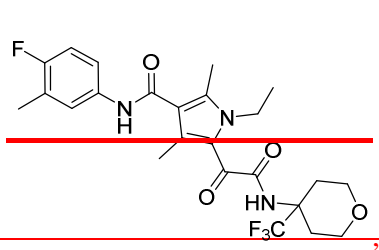
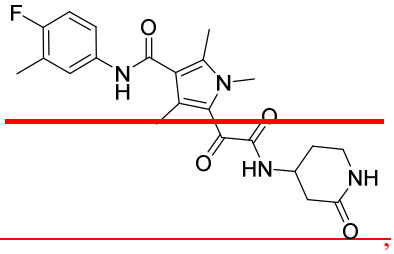
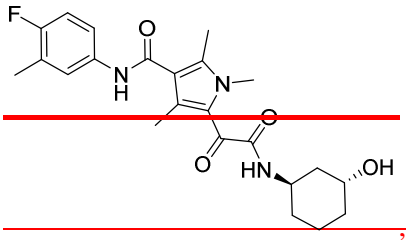
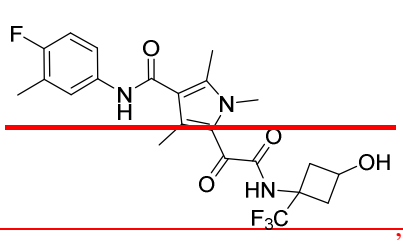
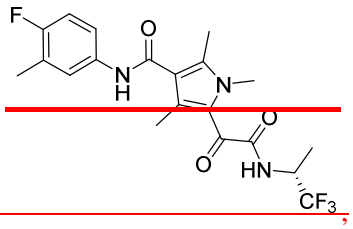
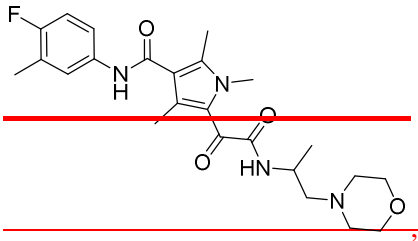
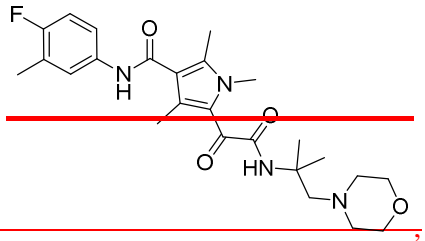
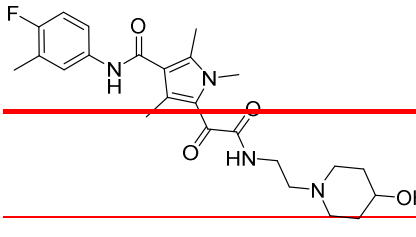
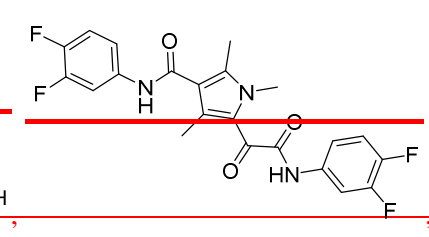


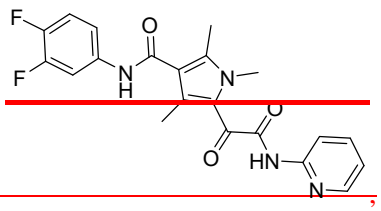
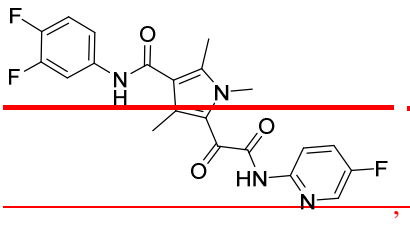
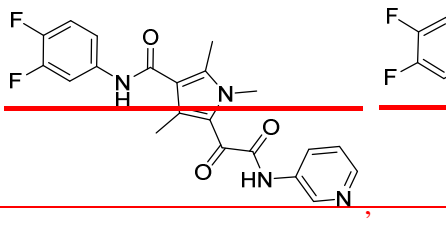
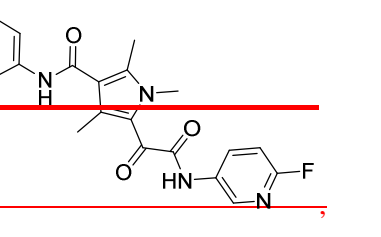
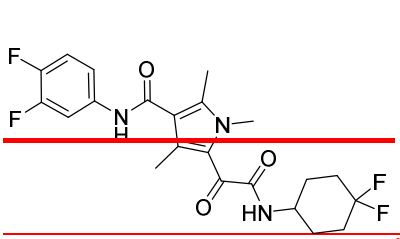
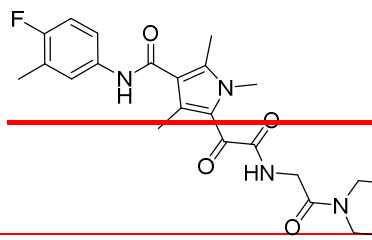


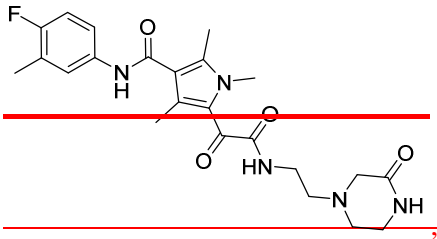
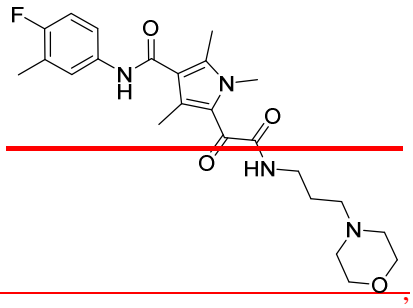
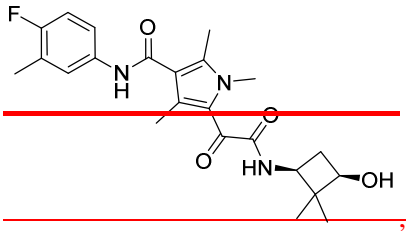
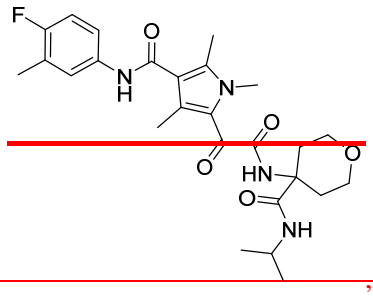
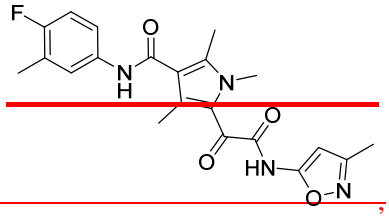
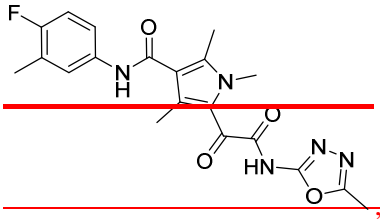
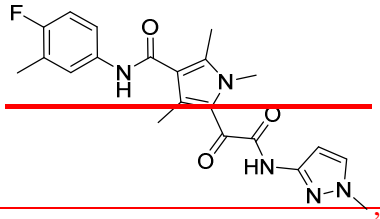
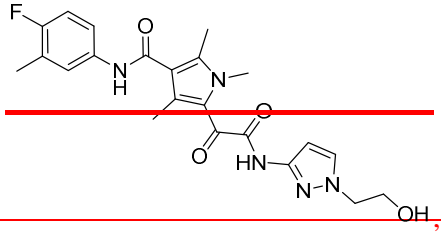
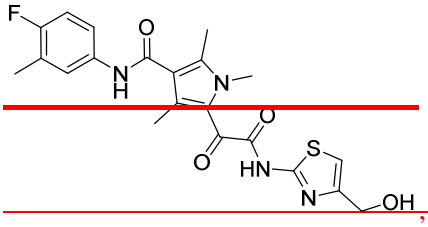
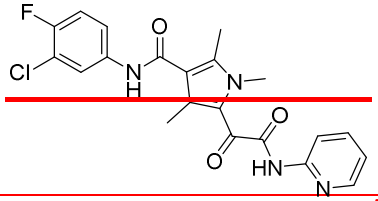
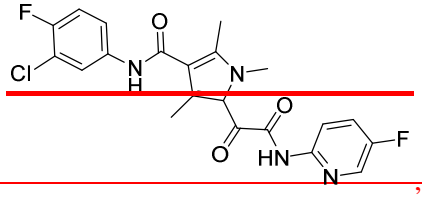
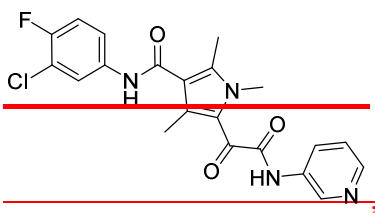
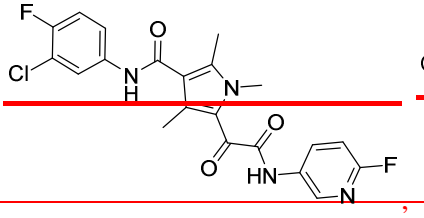
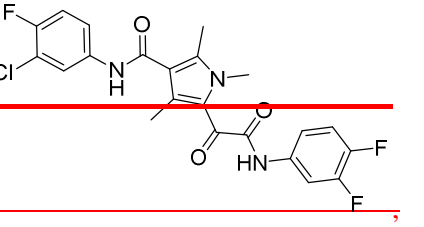
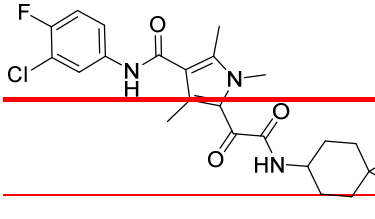
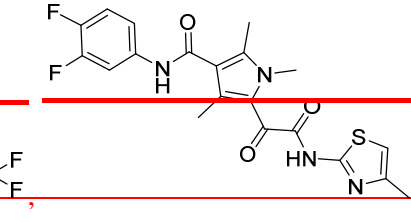
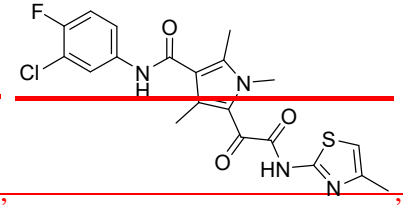


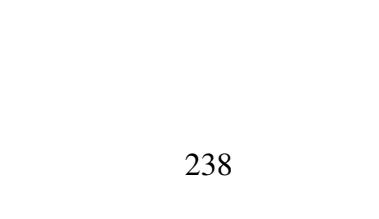




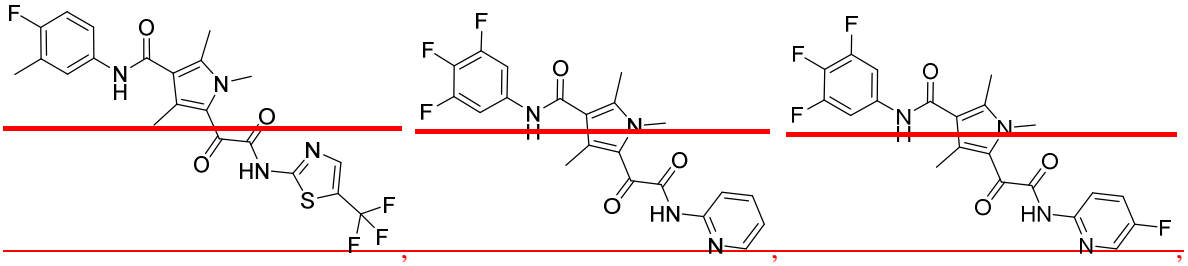











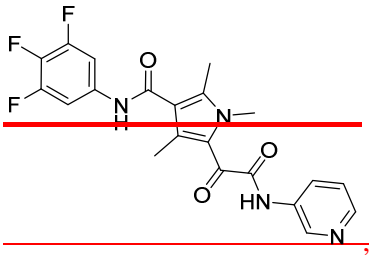
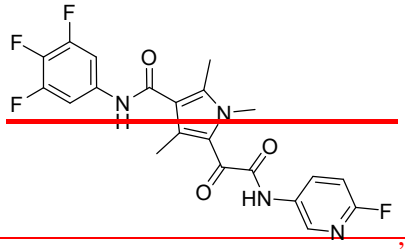
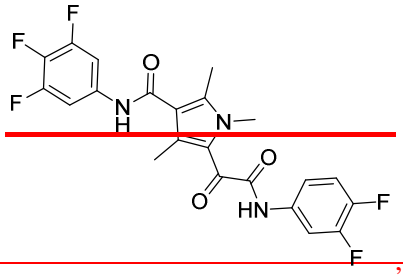
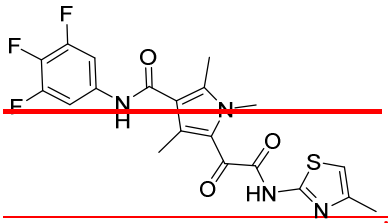
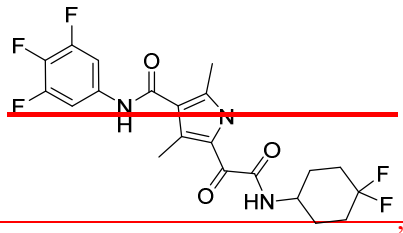
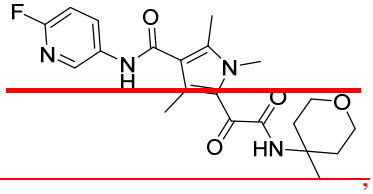
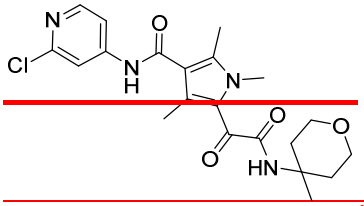
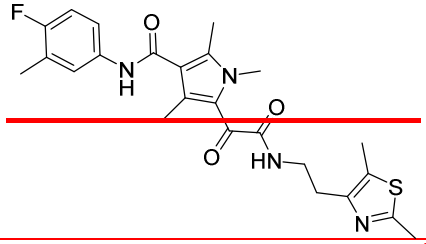
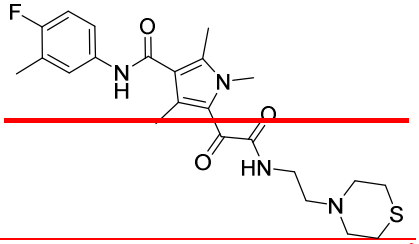
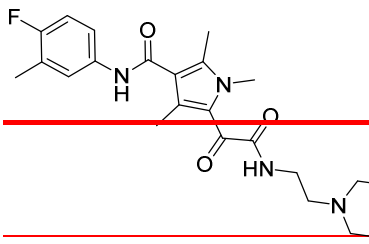







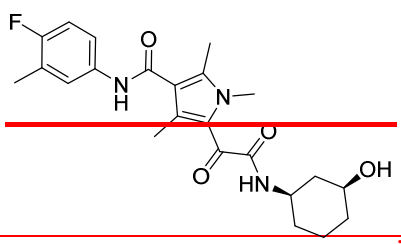
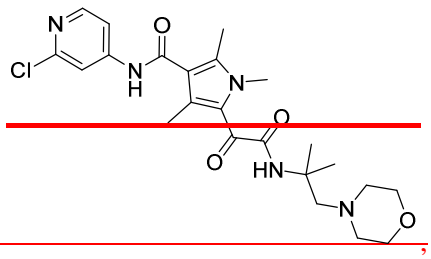
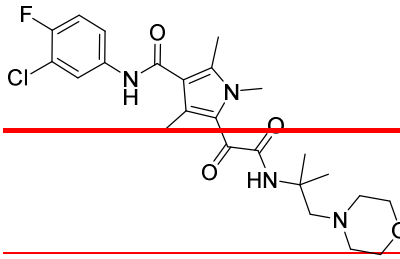
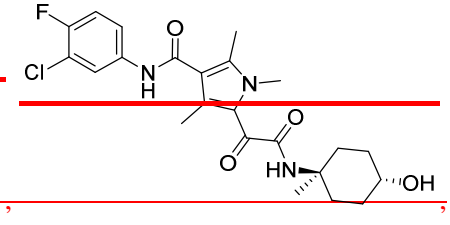


,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

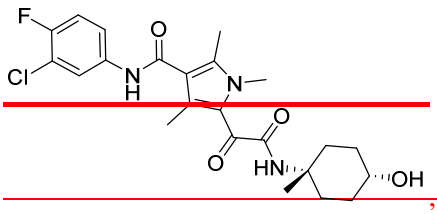
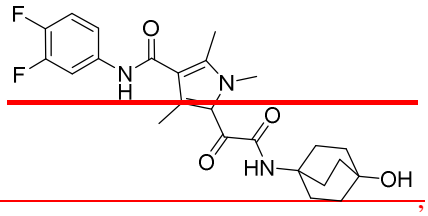
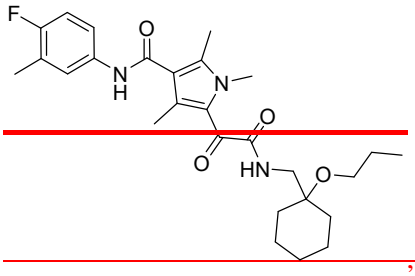
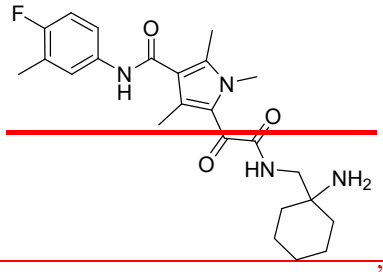
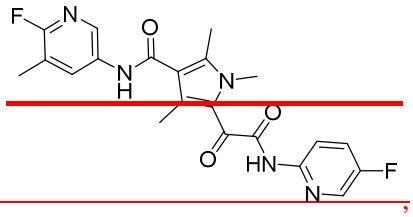
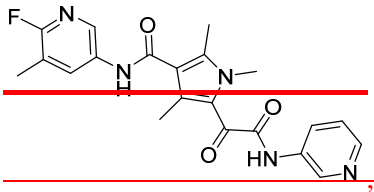
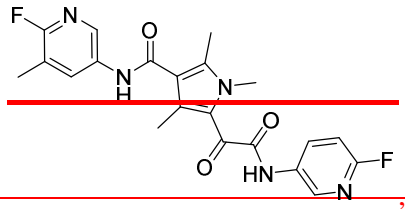
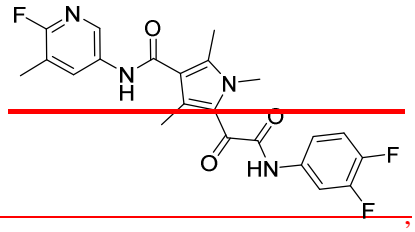
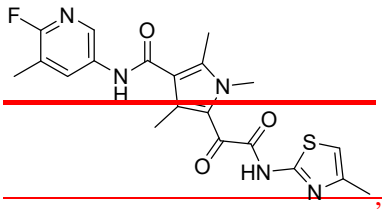
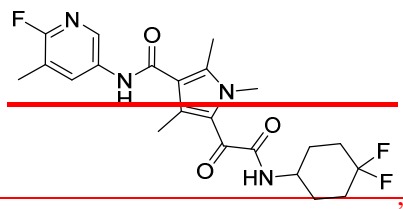
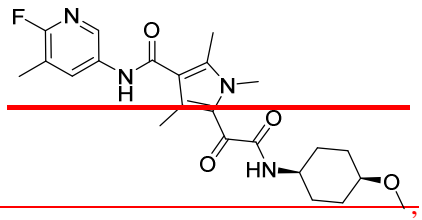
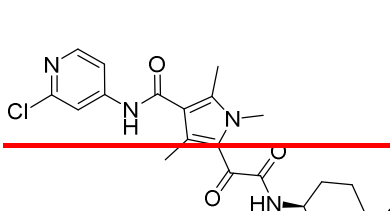
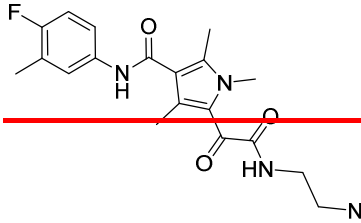
,

,

,



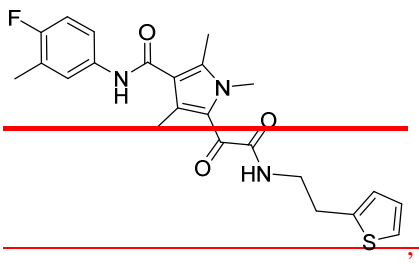
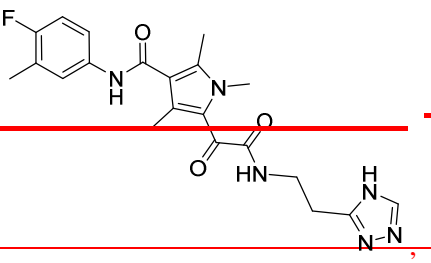






,

,

,

,

,

,

,

,

,

,

,

,

,

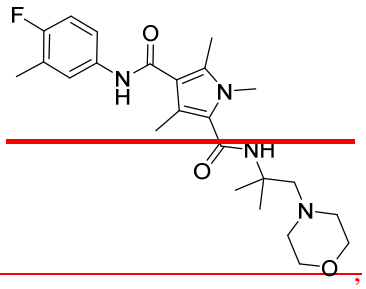
,

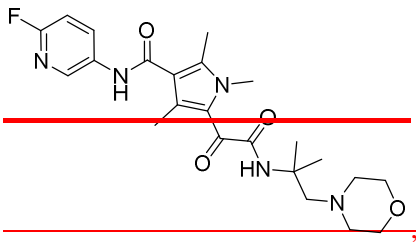
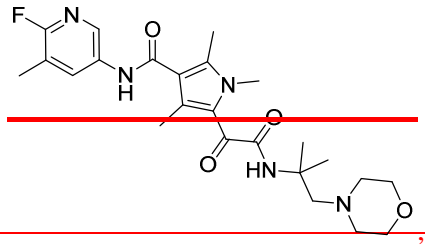
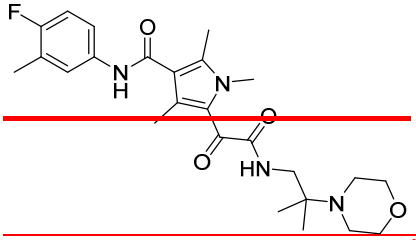
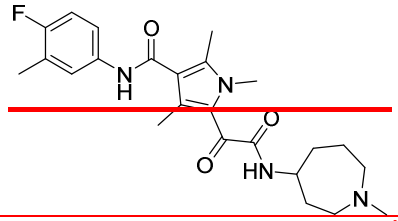
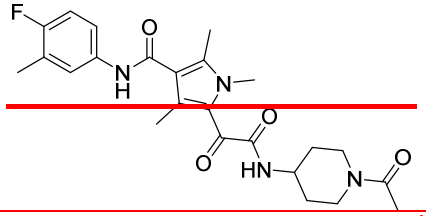
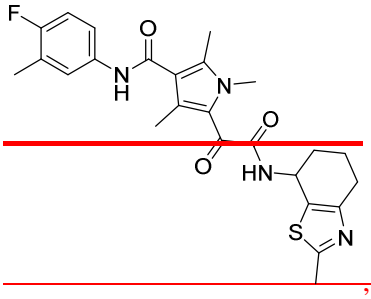
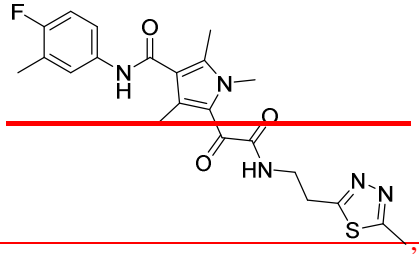
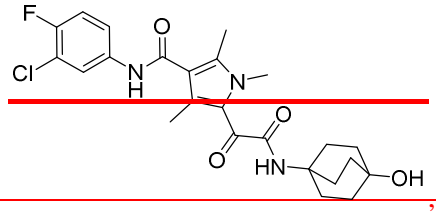
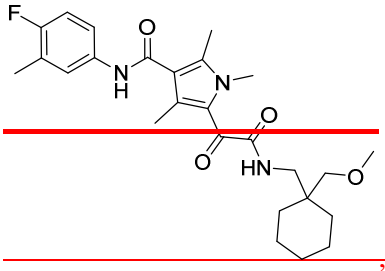
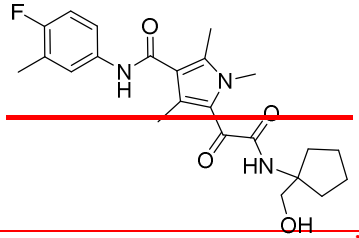
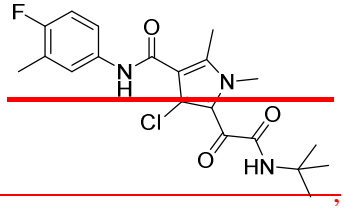
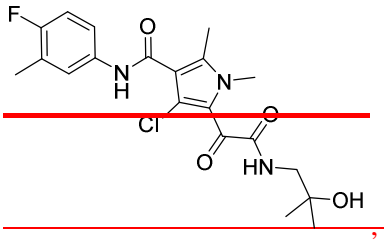
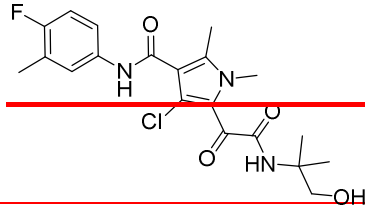
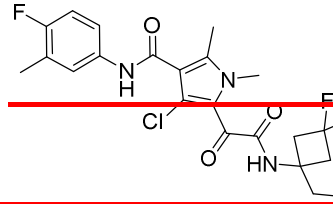
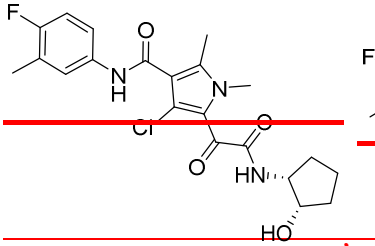
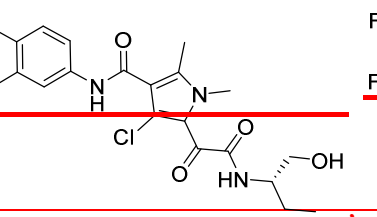
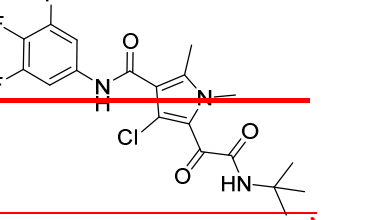
,

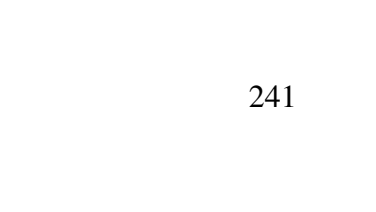
,

,

,

,

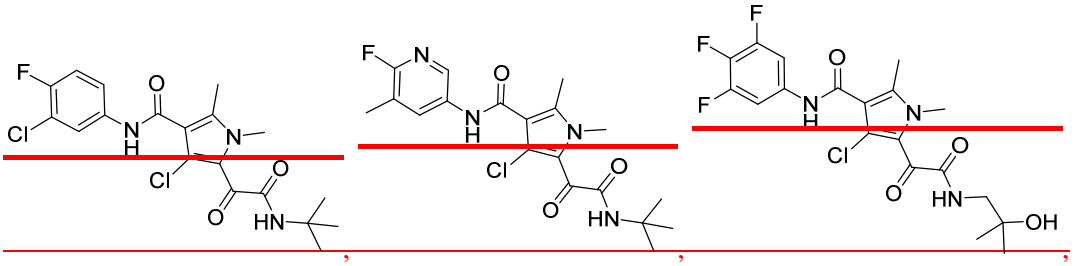
,

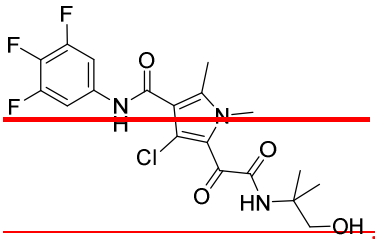
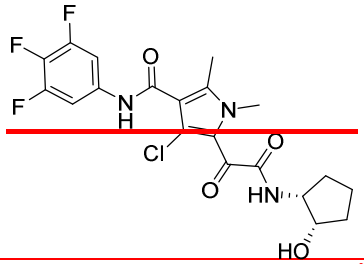
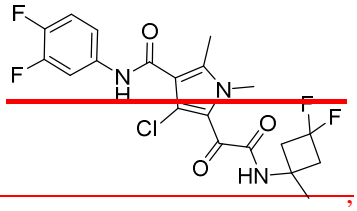
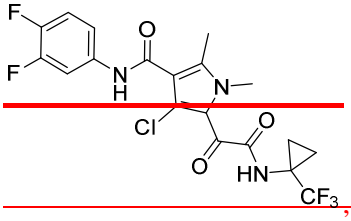
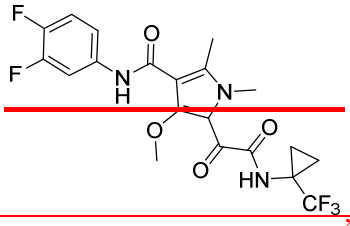
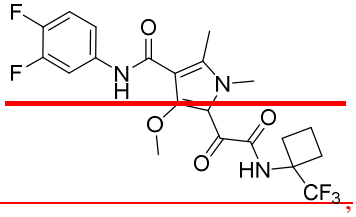
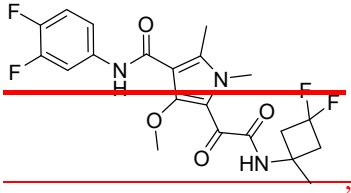
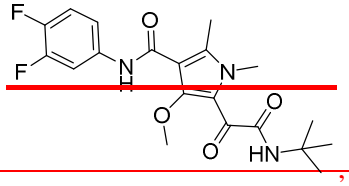
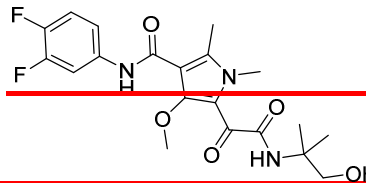
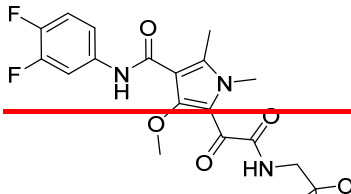
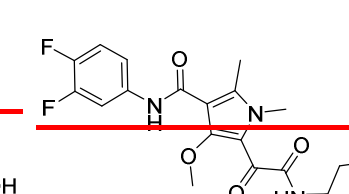
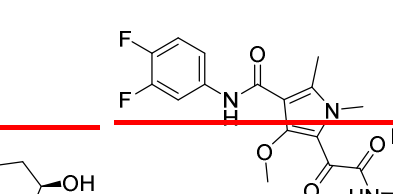
,

,

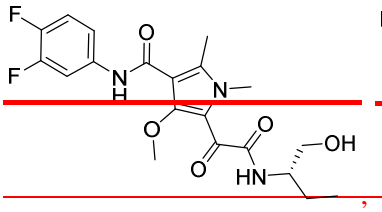
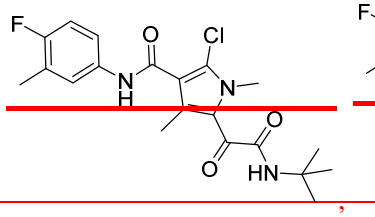
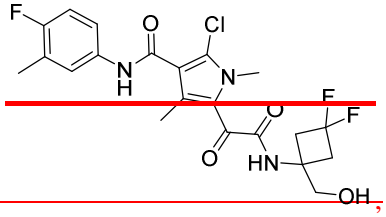

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

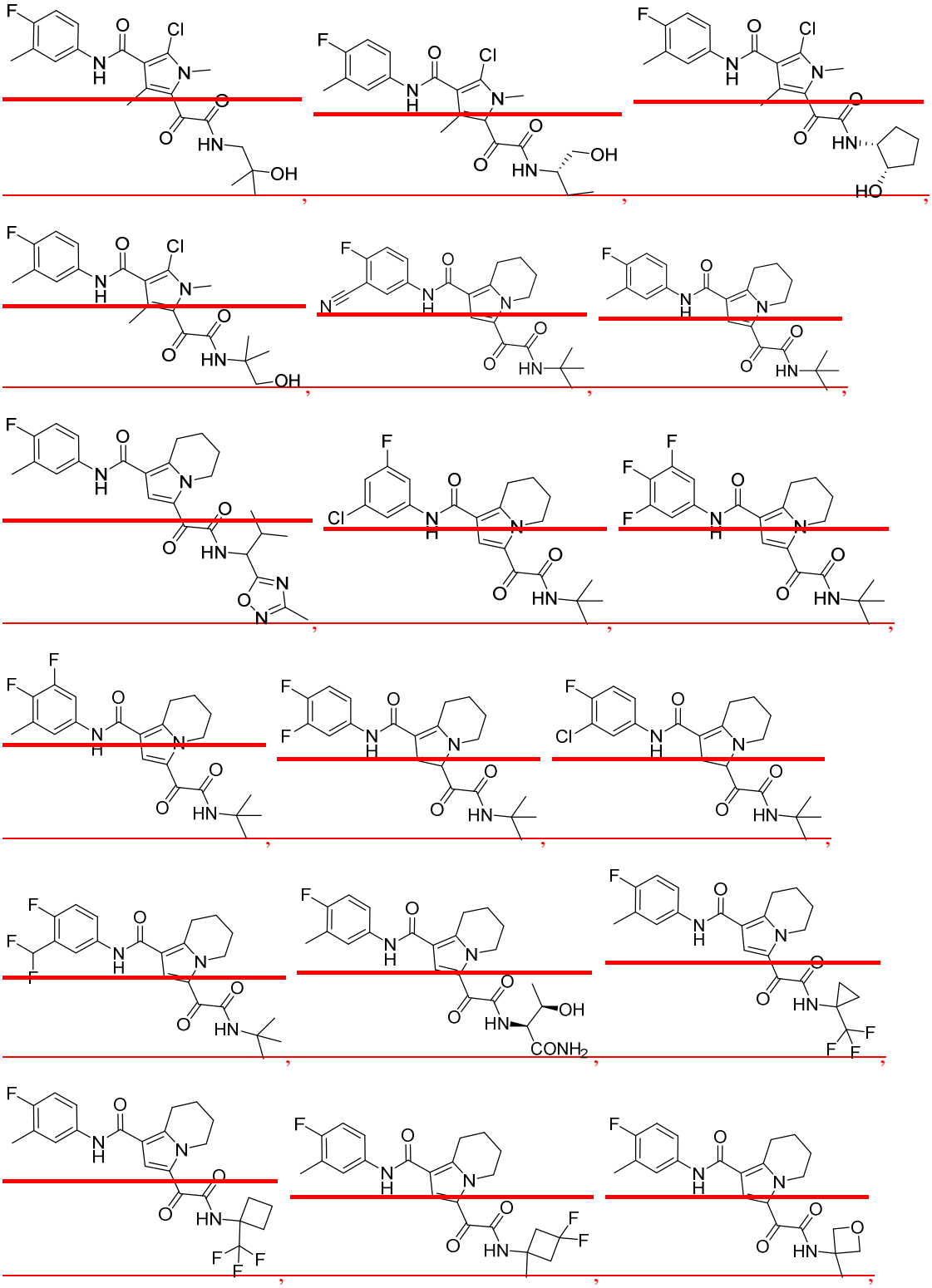
,

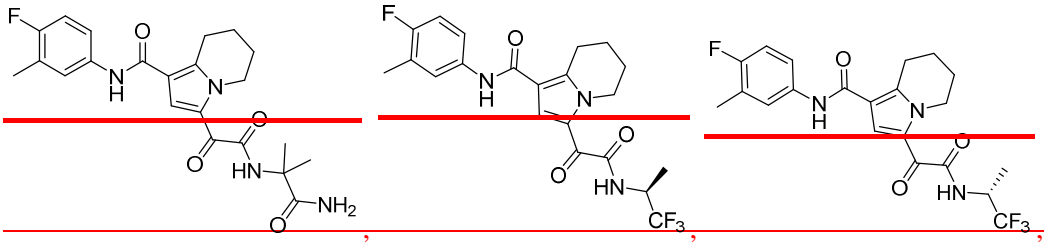


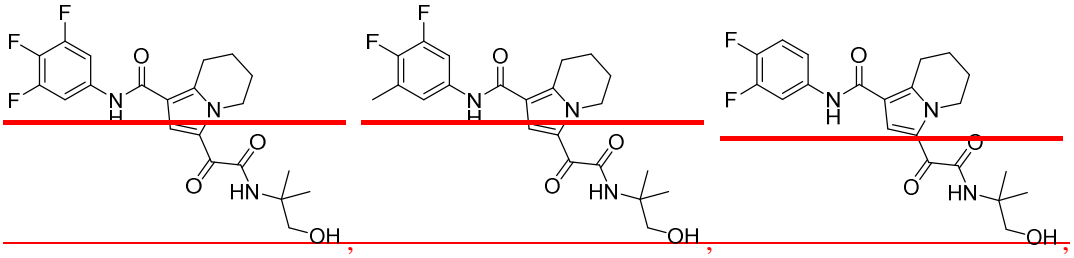













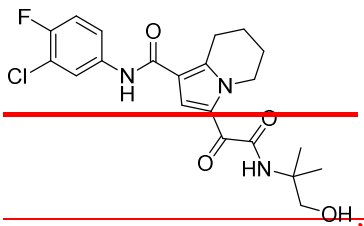
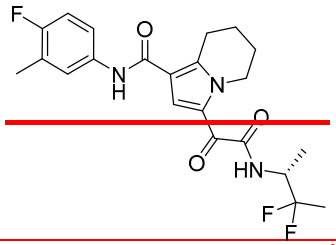
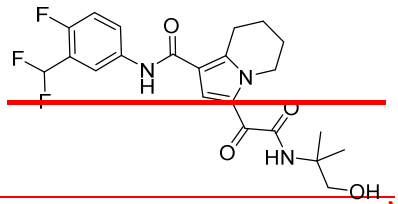
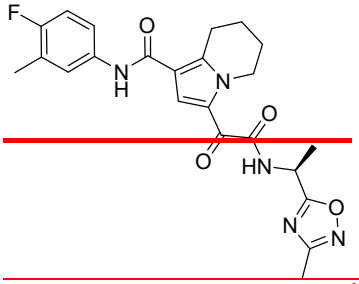
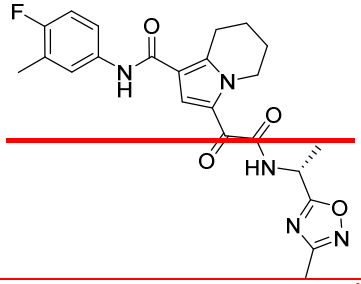
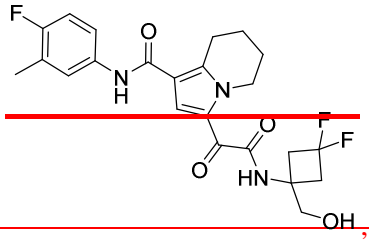
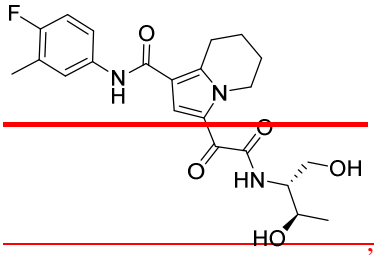
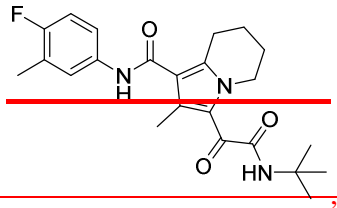
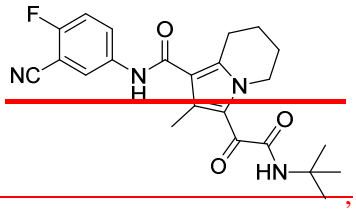
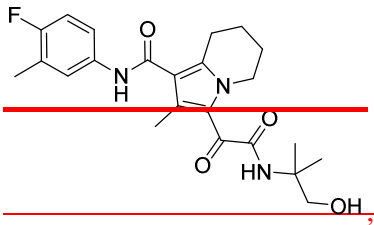
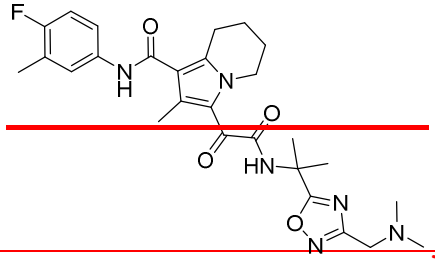
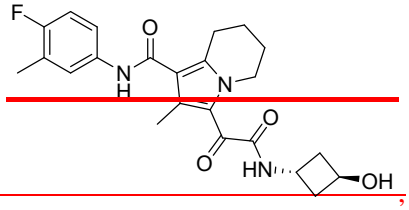
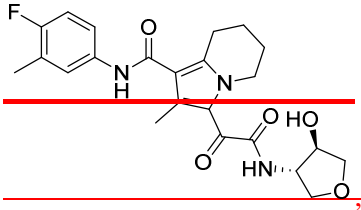
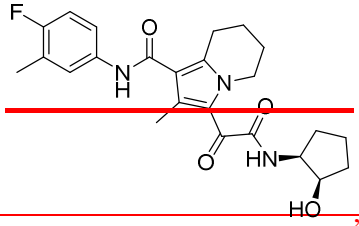
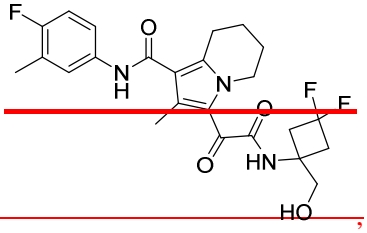




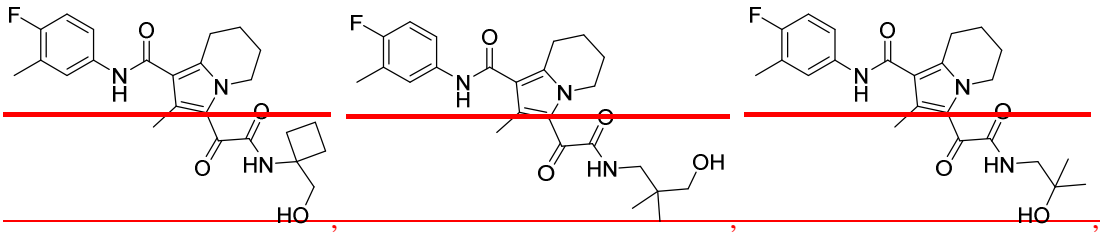


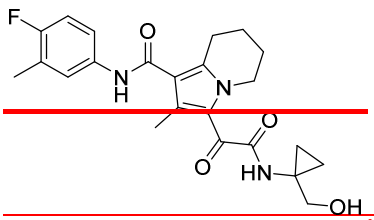
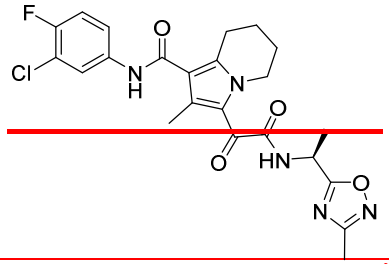
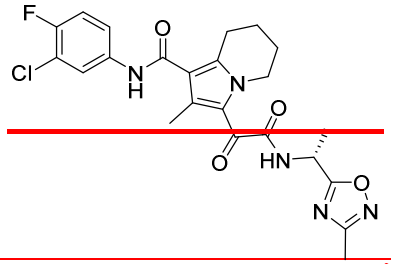
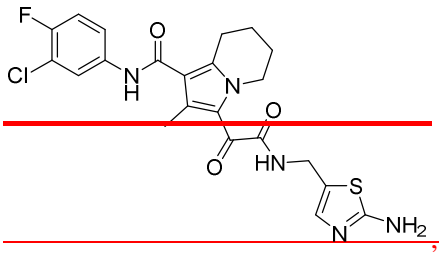
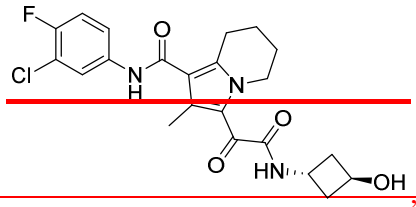
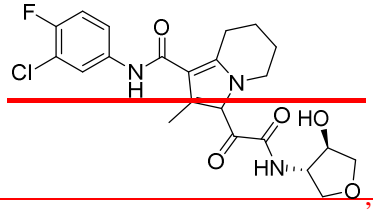
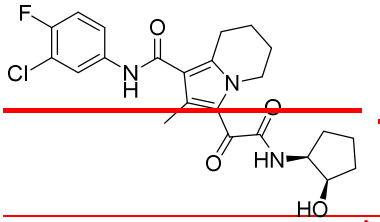
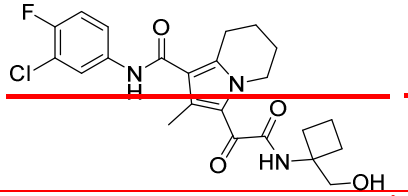
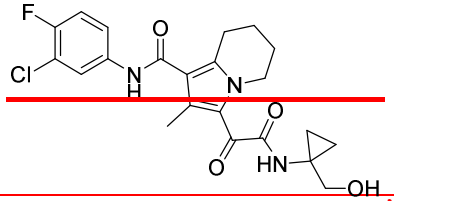
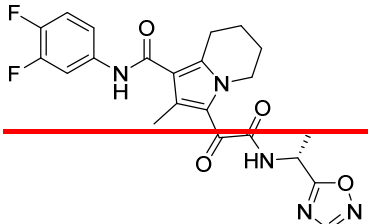
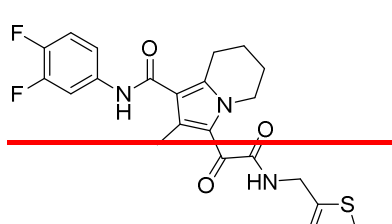
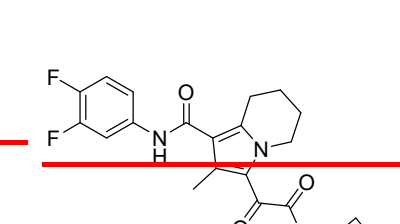
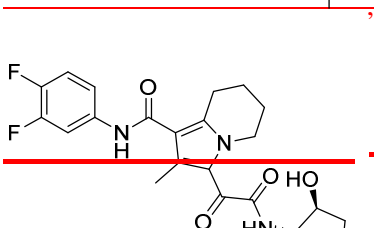
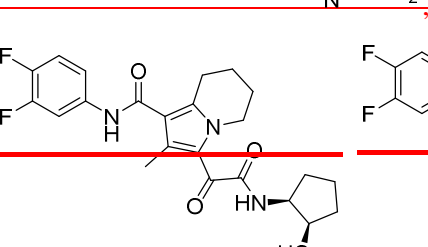
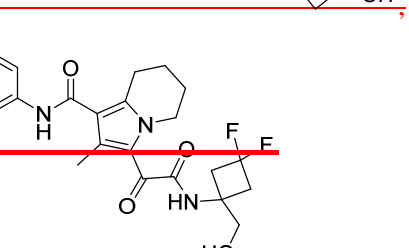


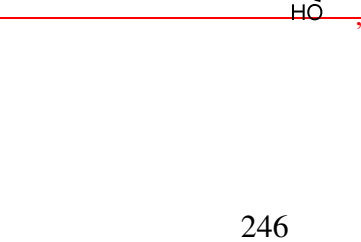
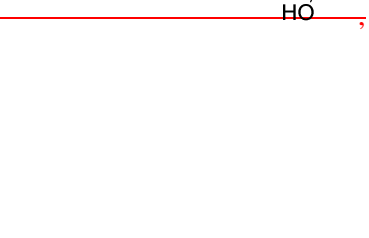


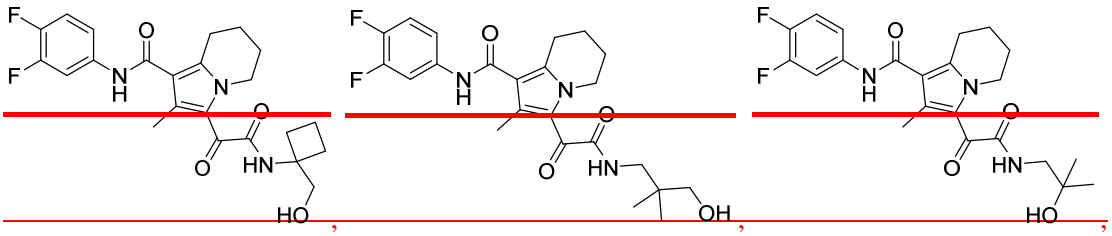


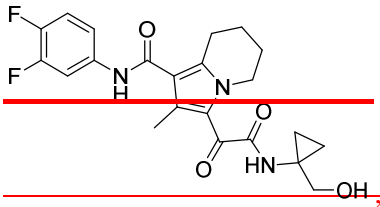
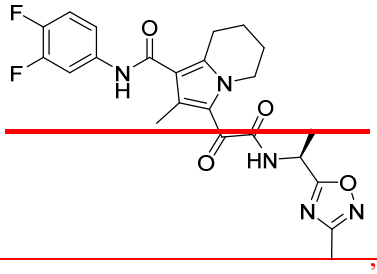
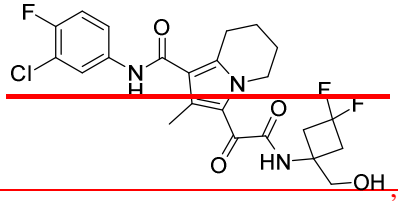
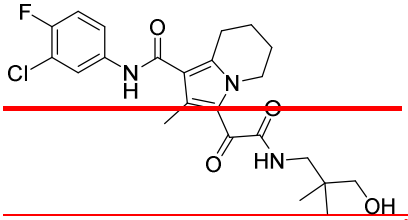
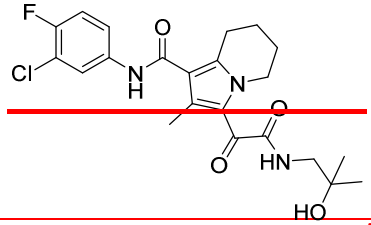
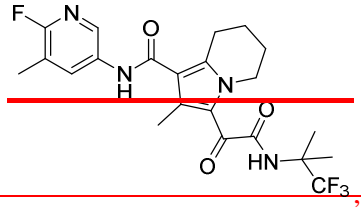
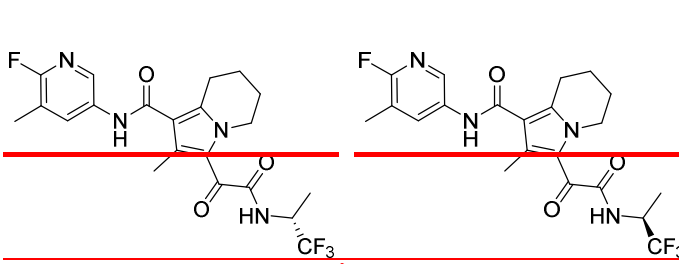
















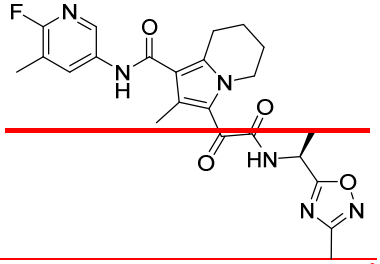
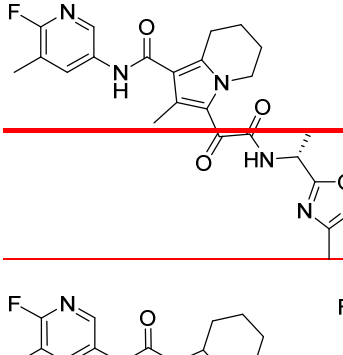
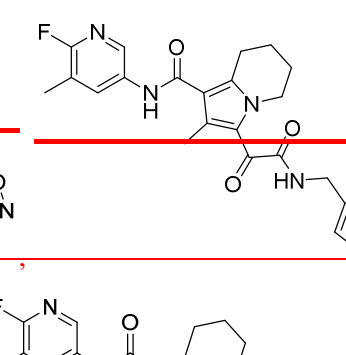


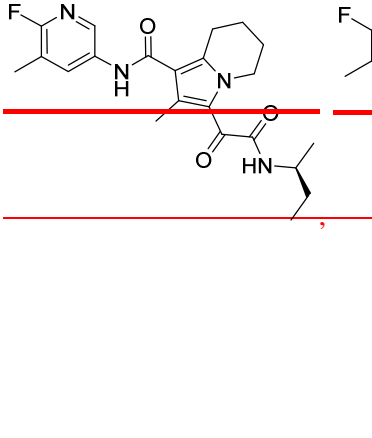
















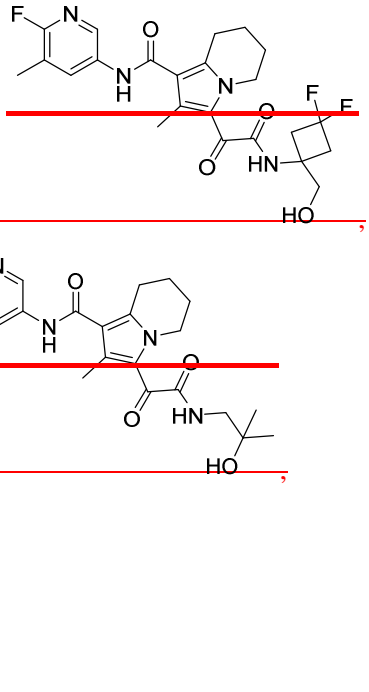



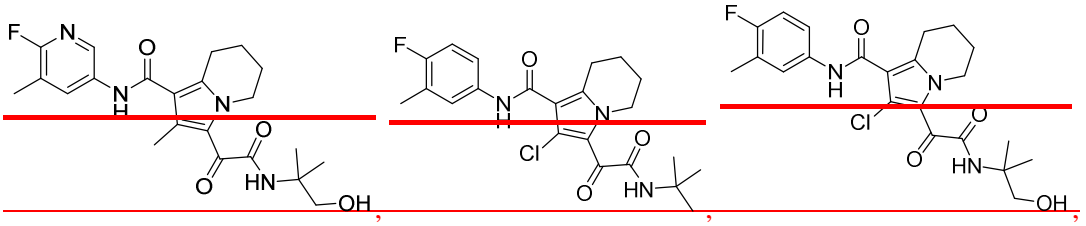


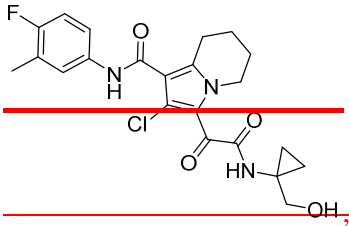
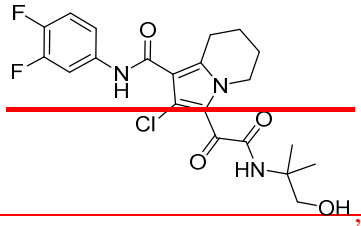
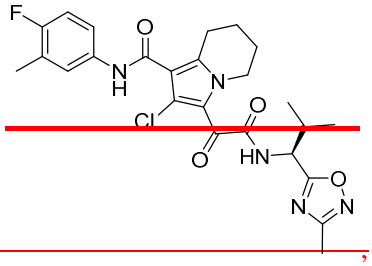
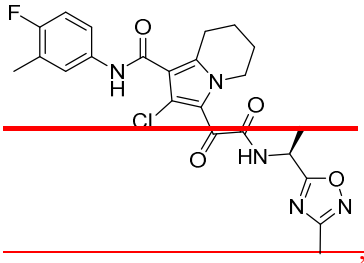
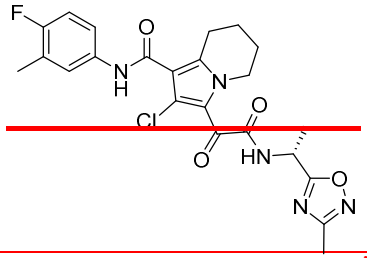
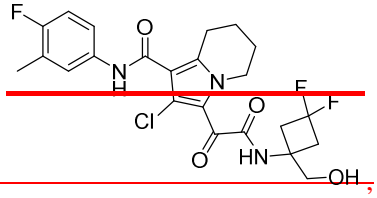
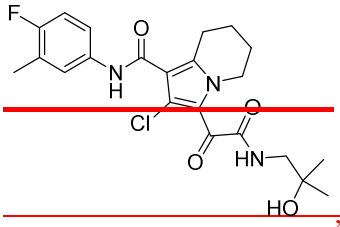
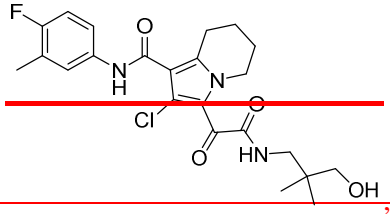
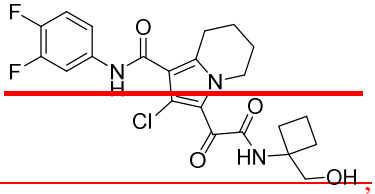
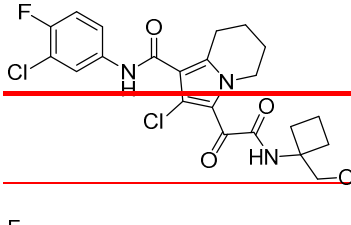
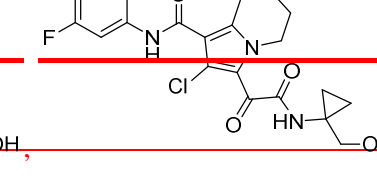
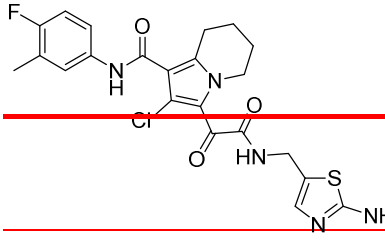
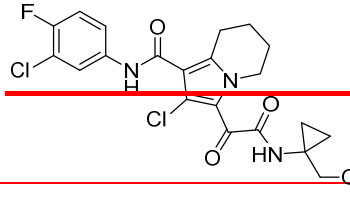








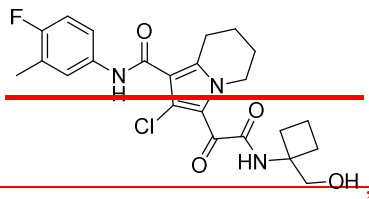
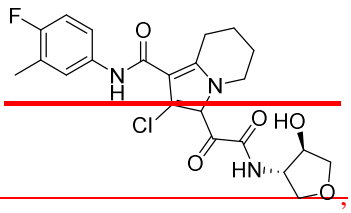




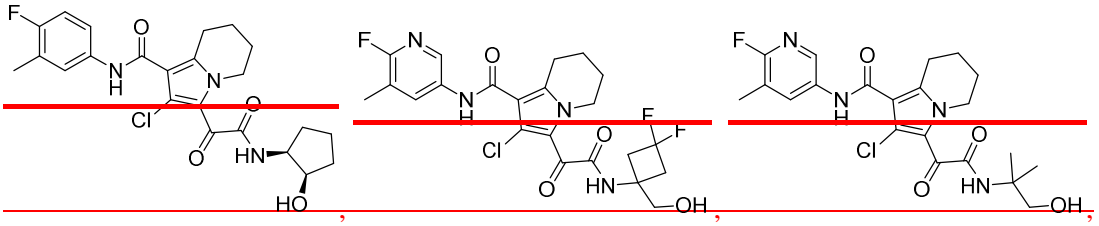


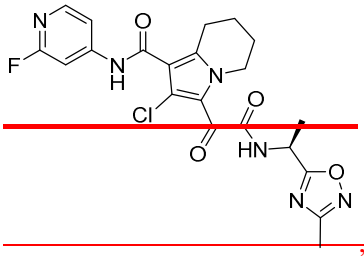
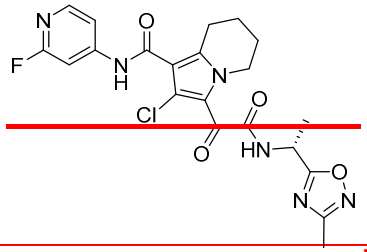
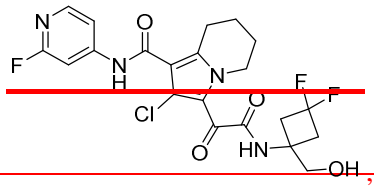
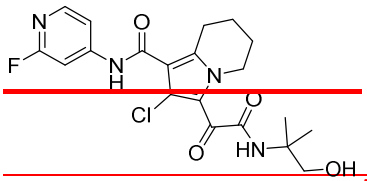
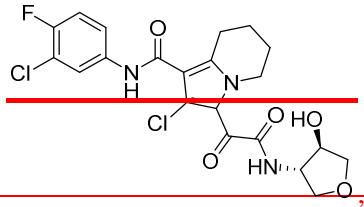
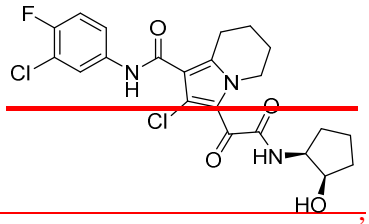
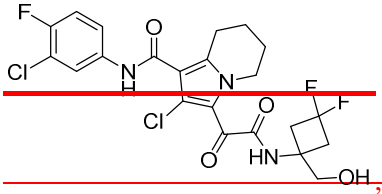
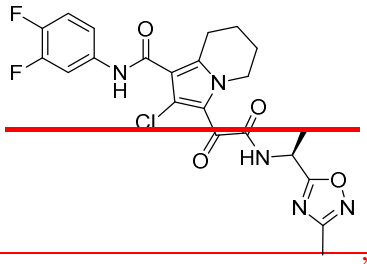
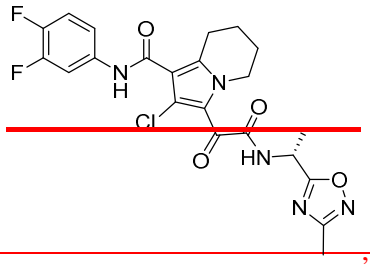
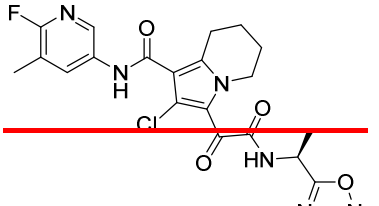


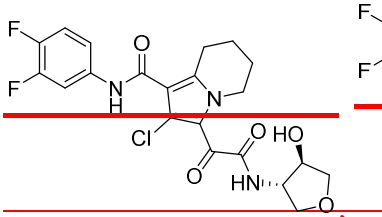


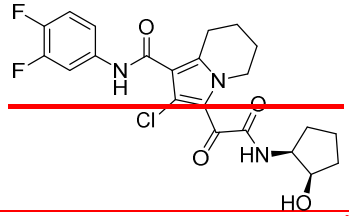
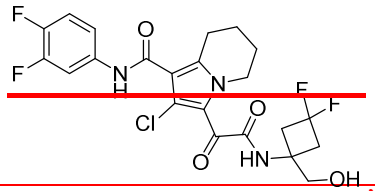














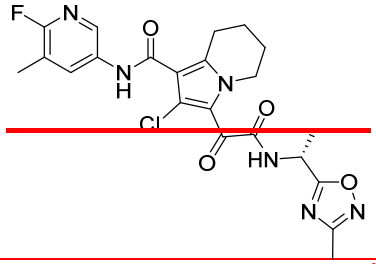
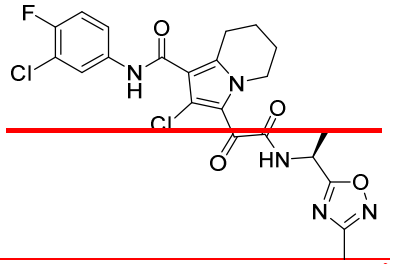



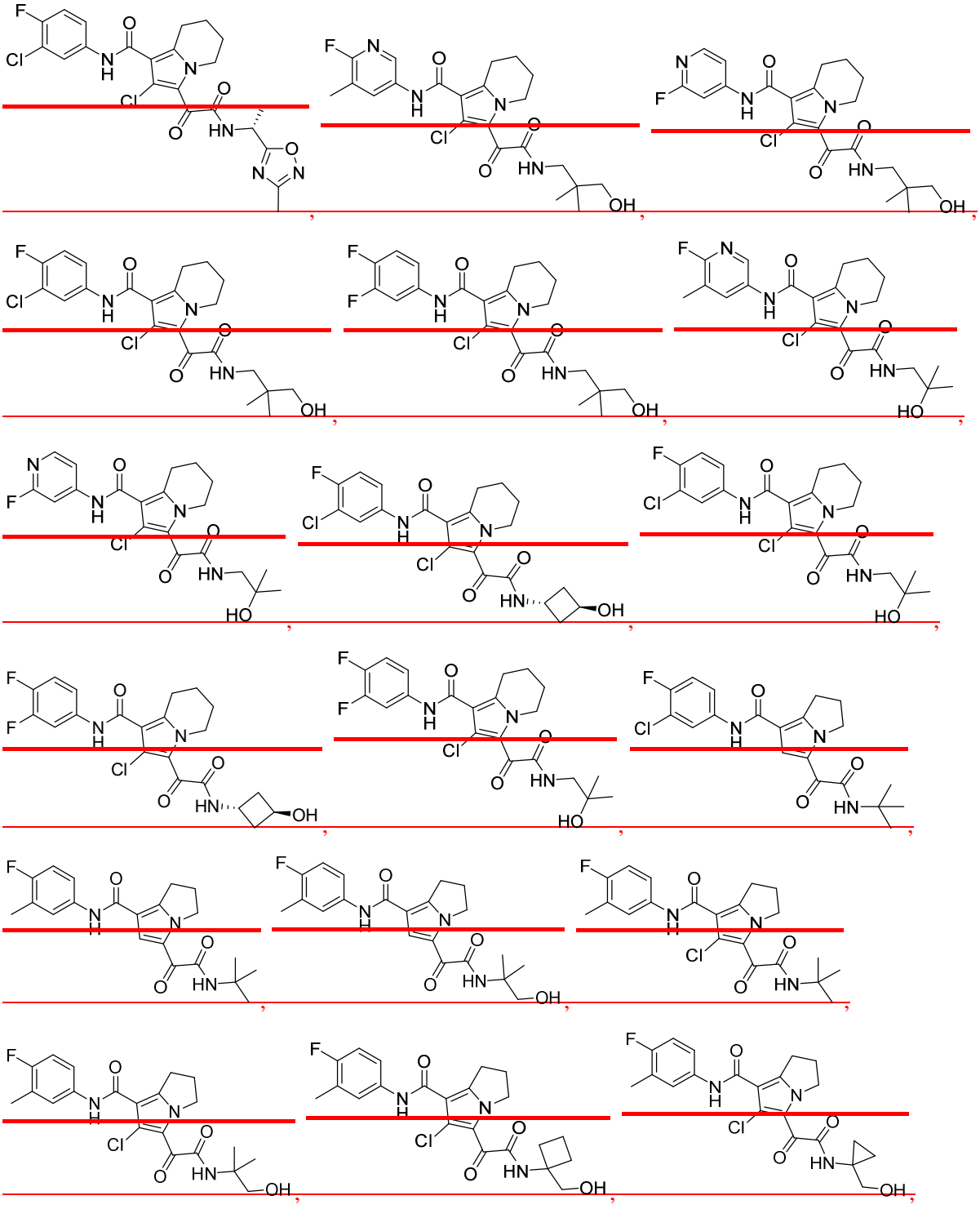


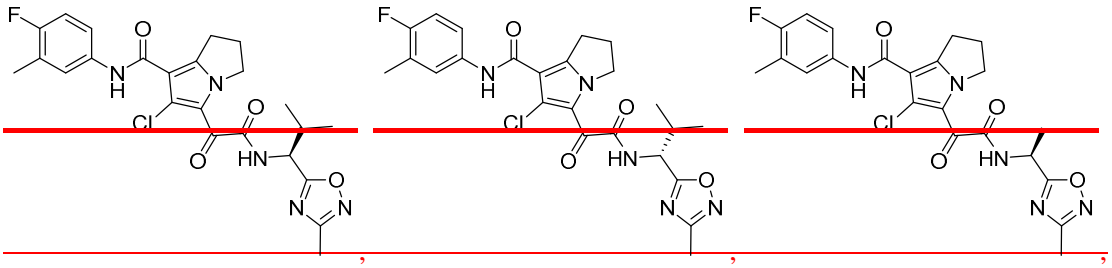











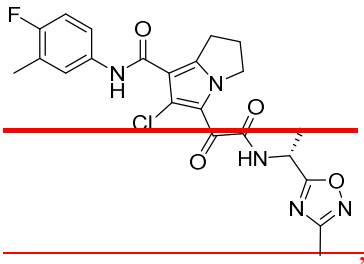
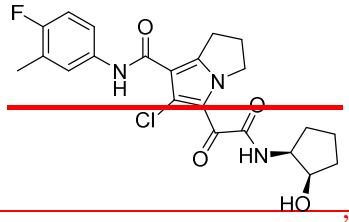
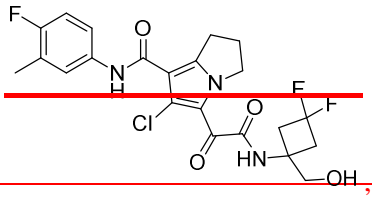
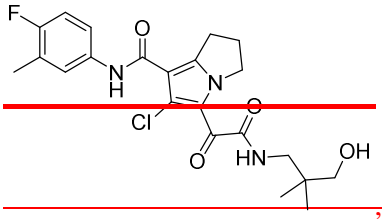
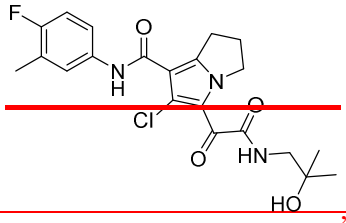
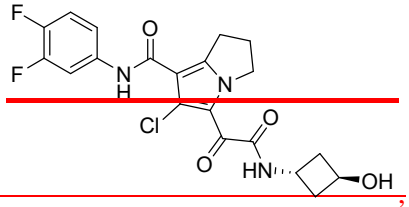
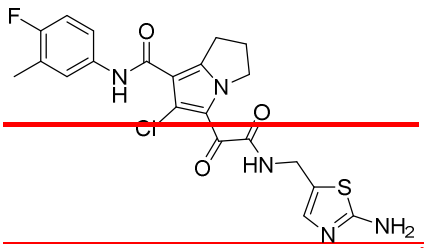
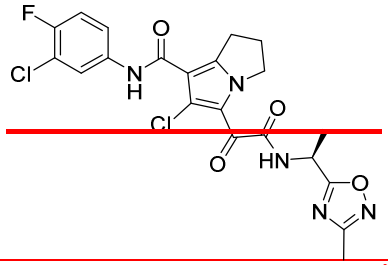
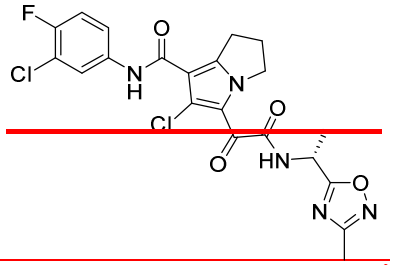
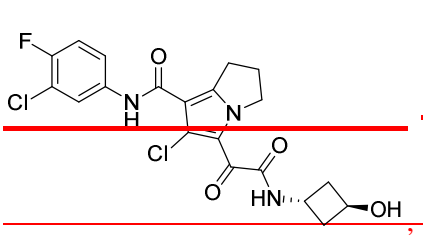
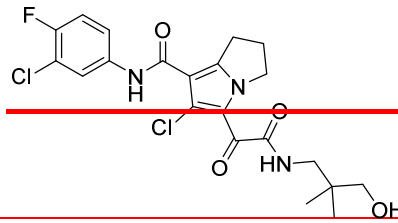
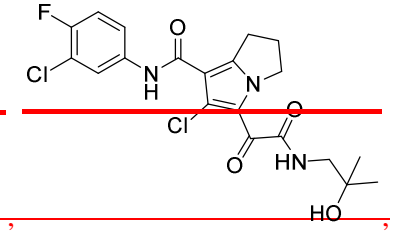
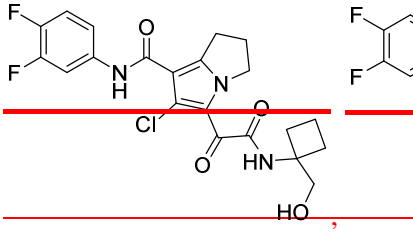
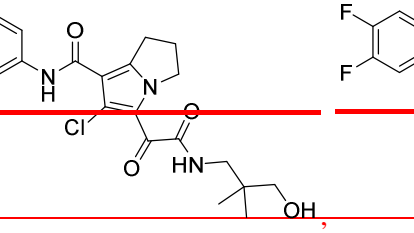
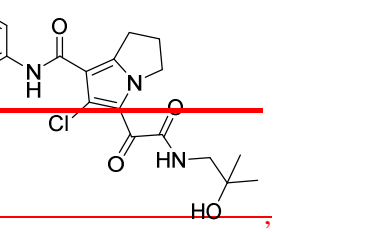


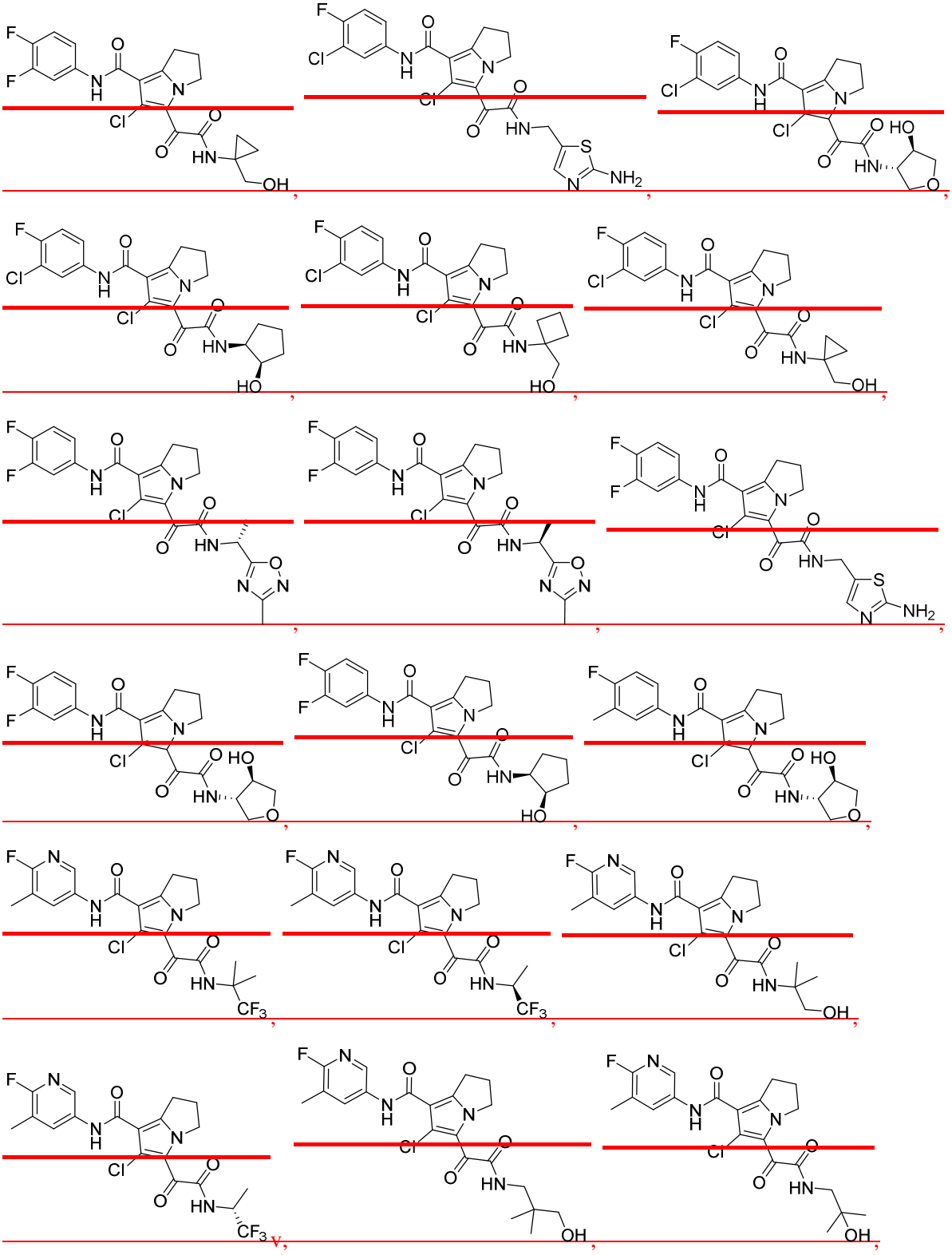



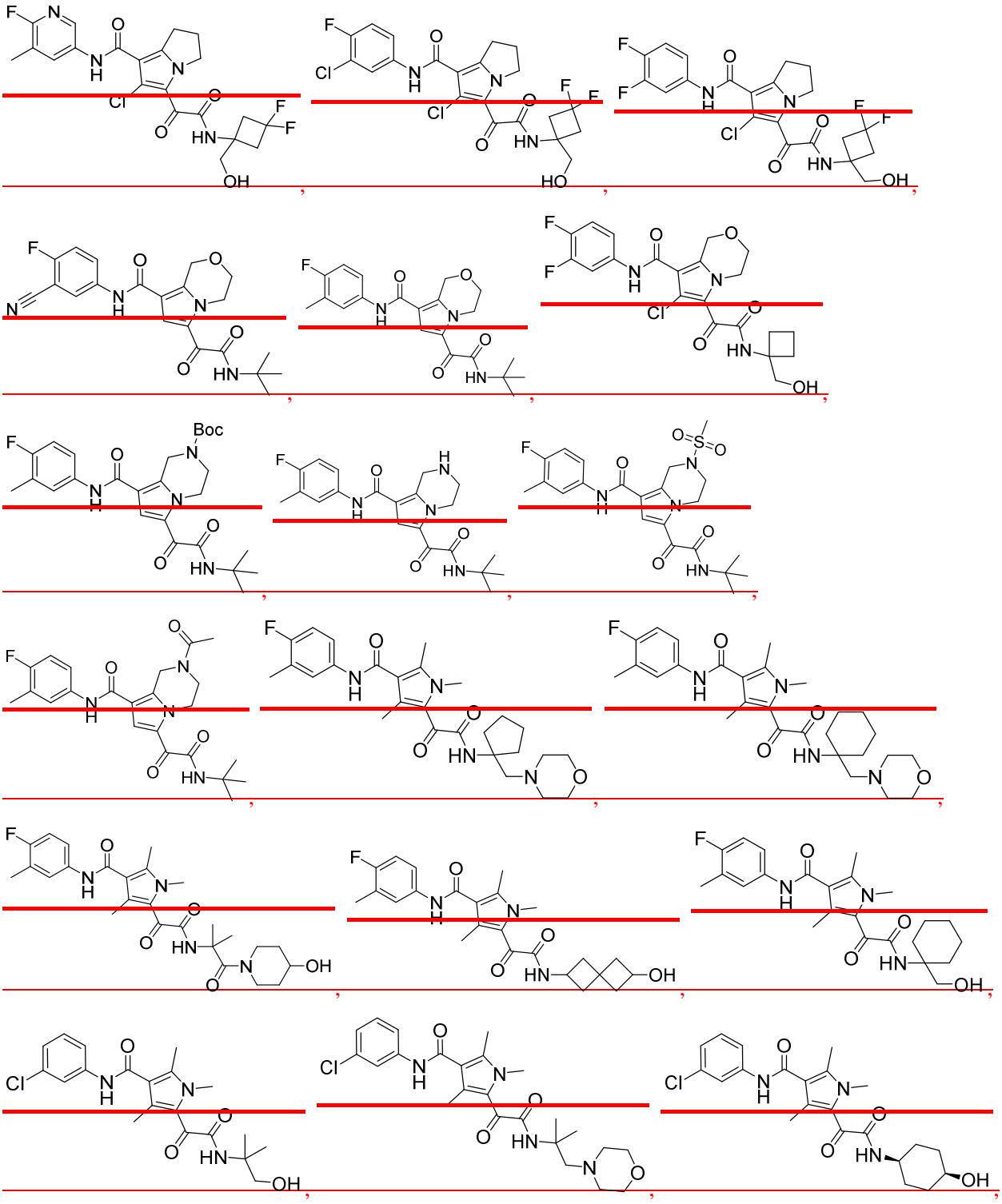


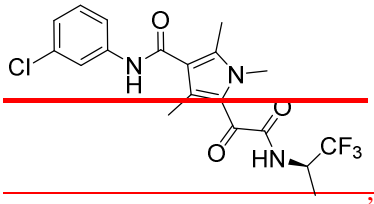
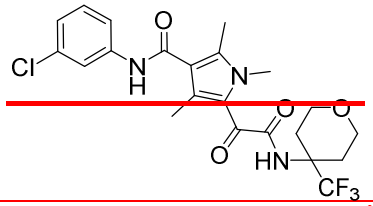
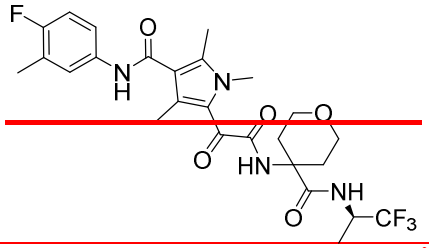
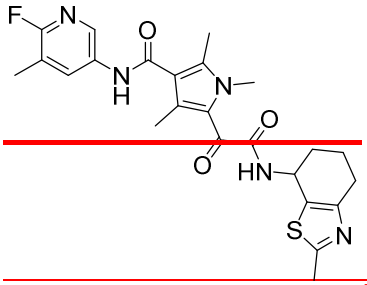
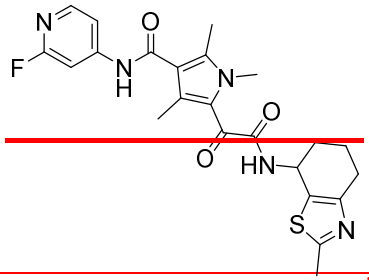
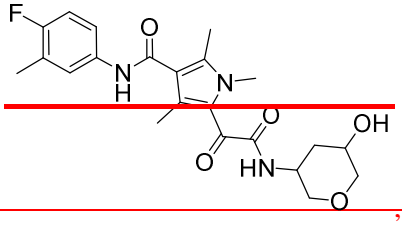
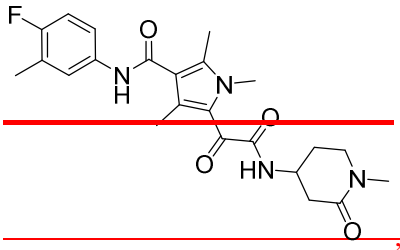
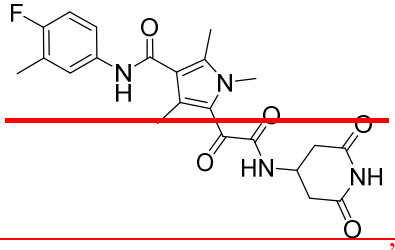
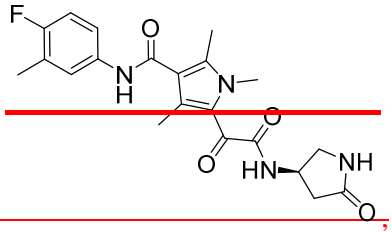
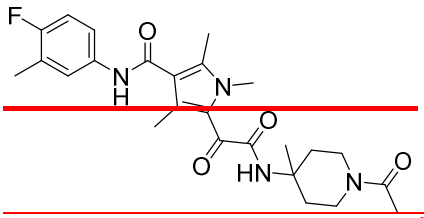
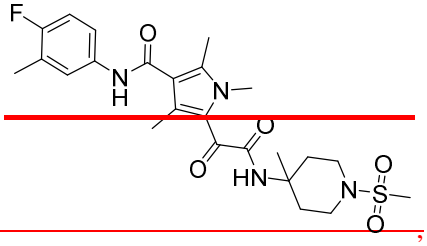
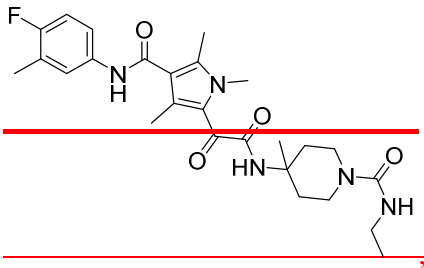
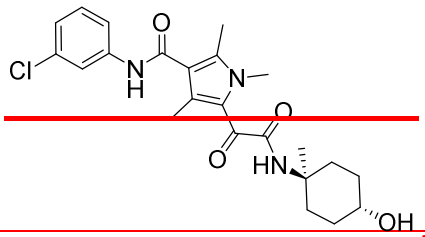
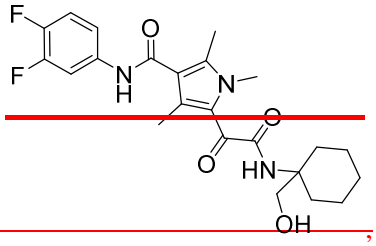
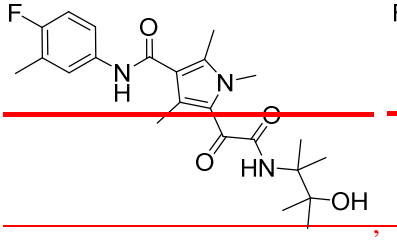
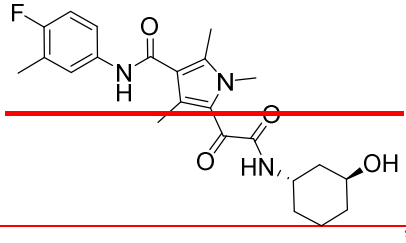
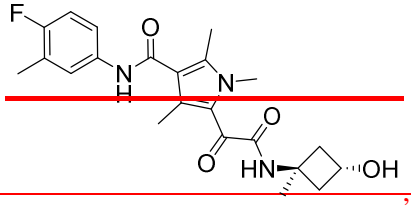


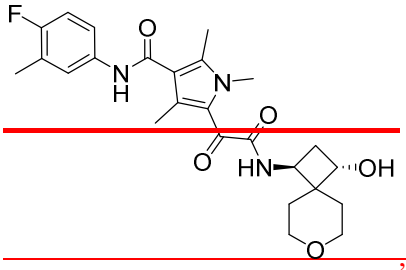
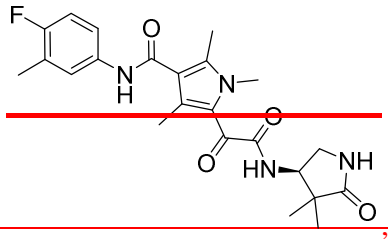
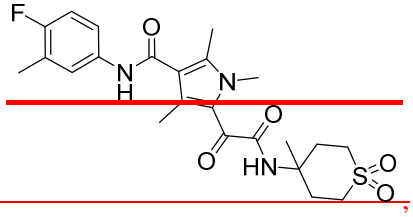
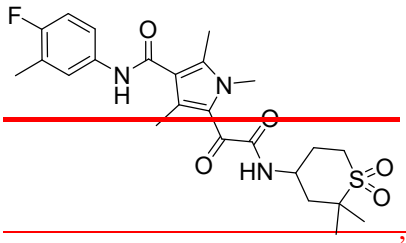
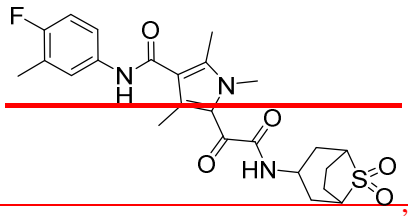
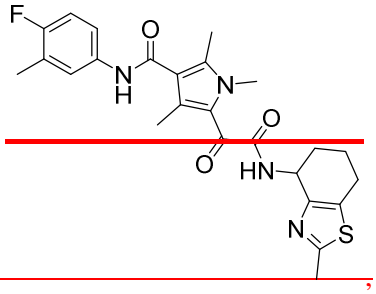
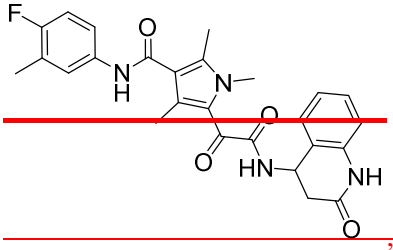
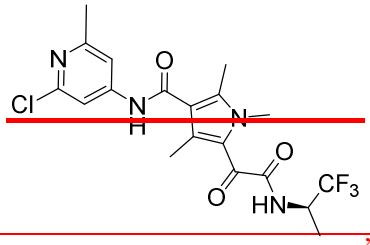
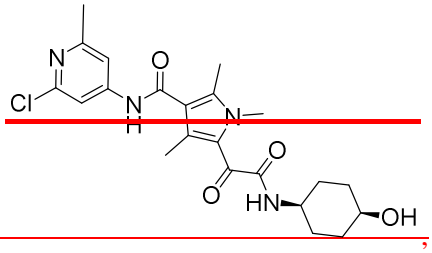
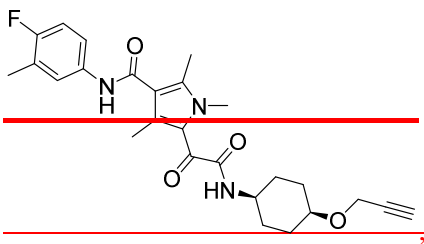
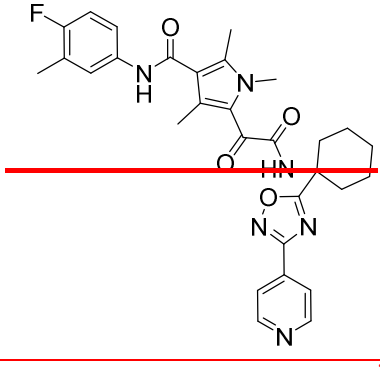
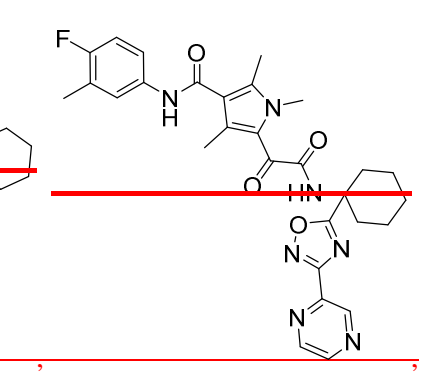
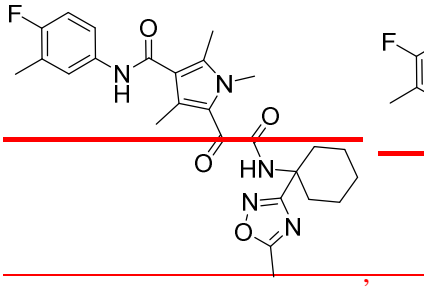
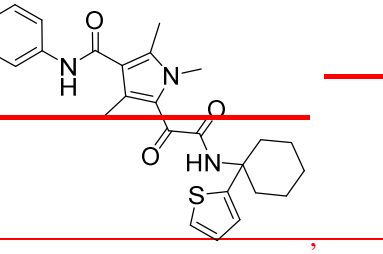


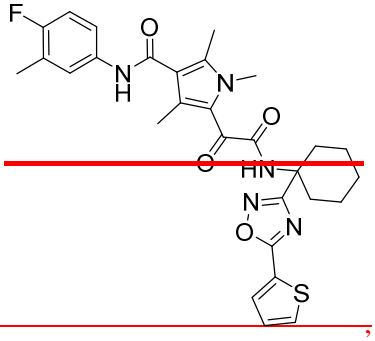


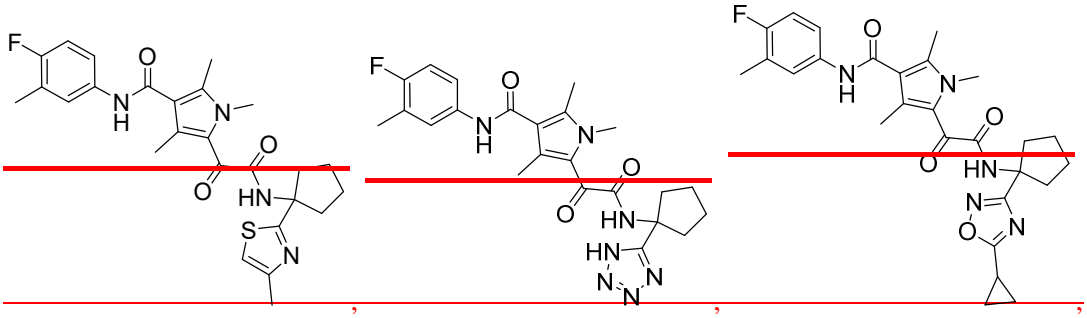


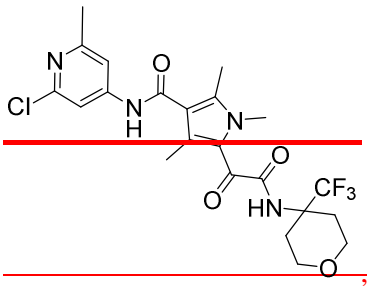
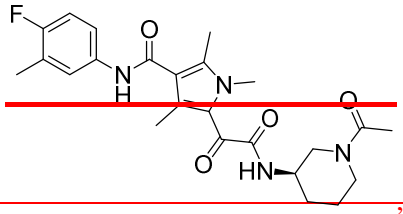
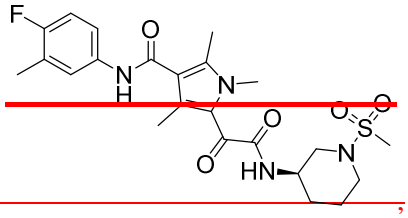
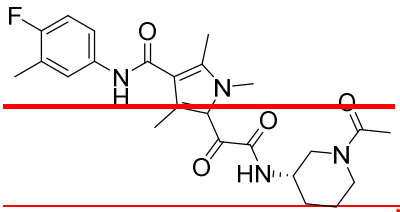
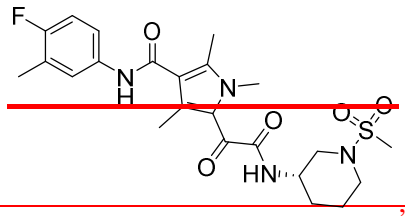
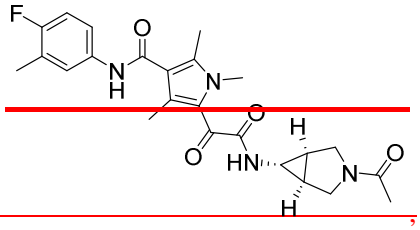
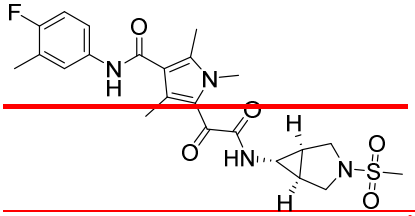
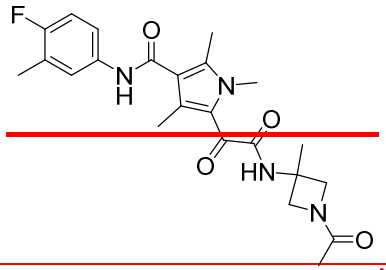
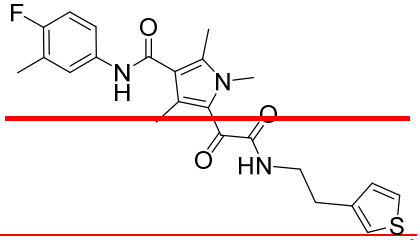
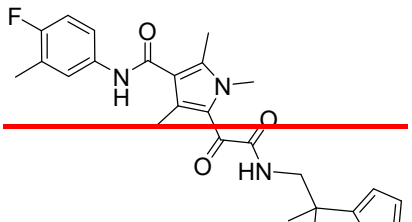


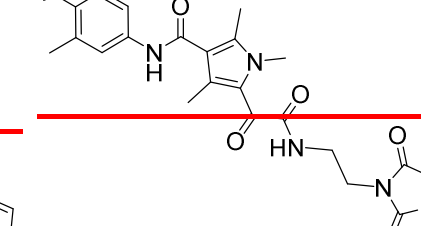















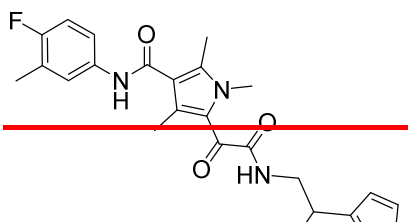



,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

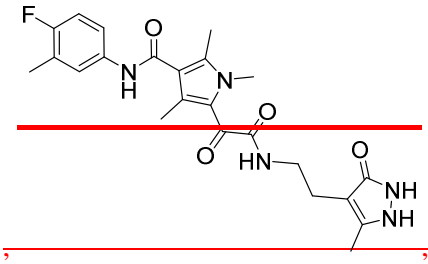
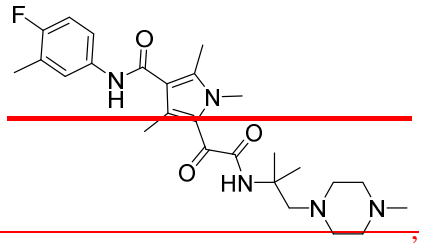
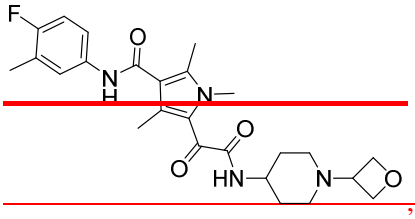
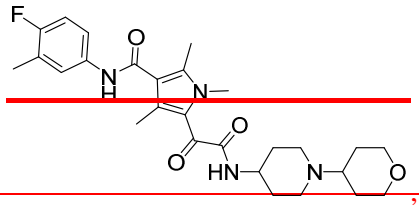
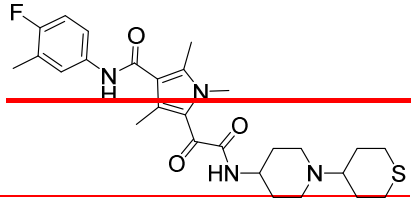
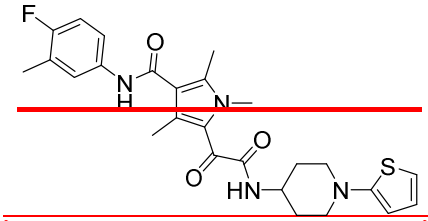
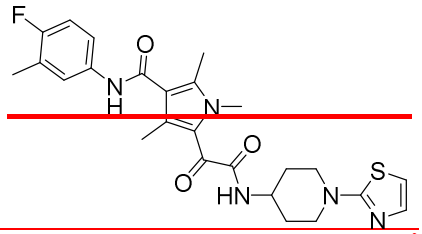
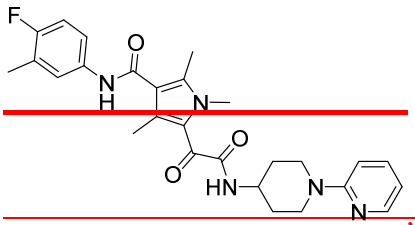
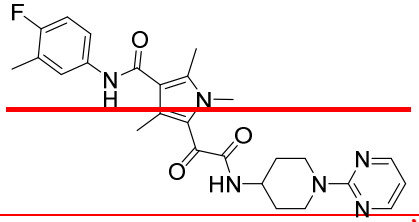
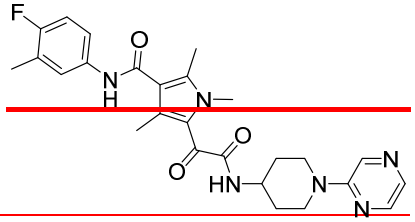
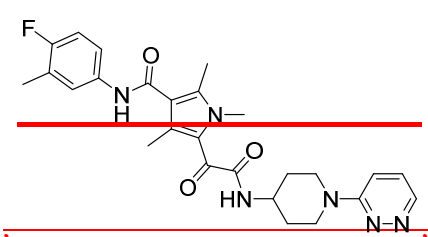
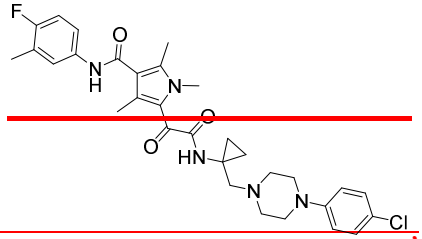
,

,

,

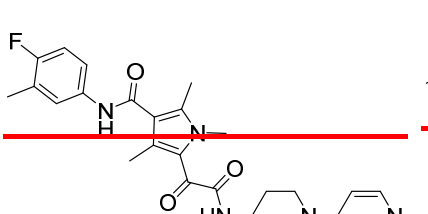
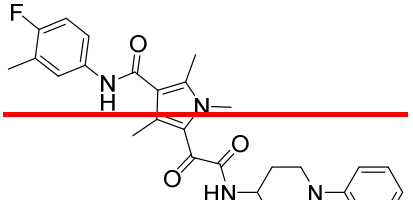
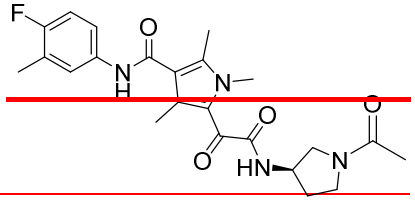
,

,

,

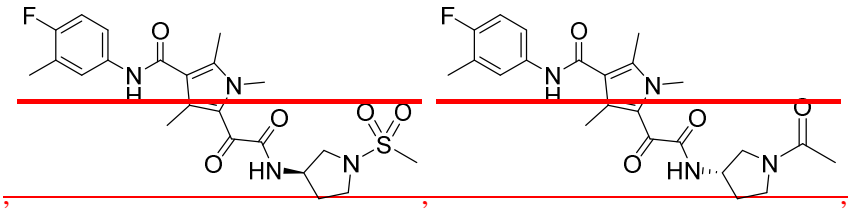

,

,

,

,


,

,

,

,


,

,

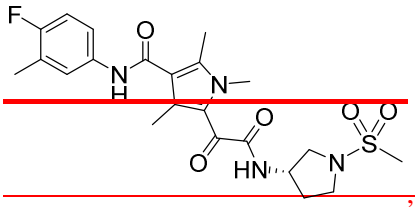
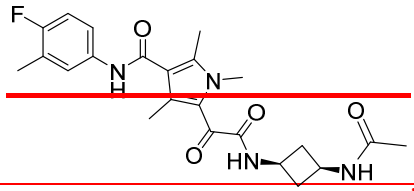
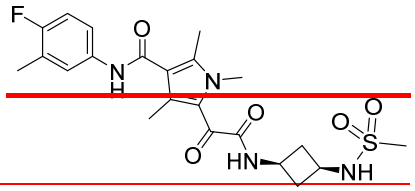
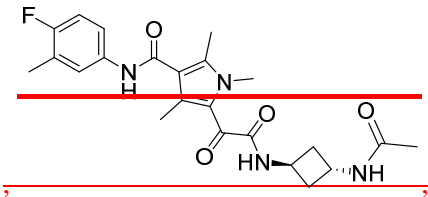
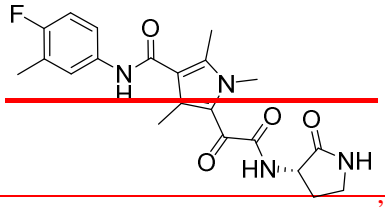
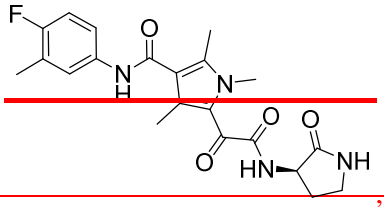
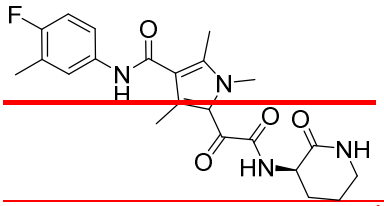
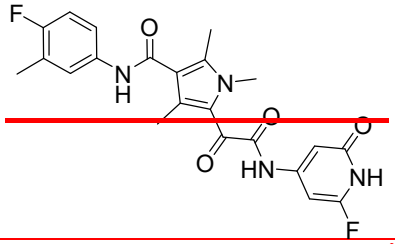
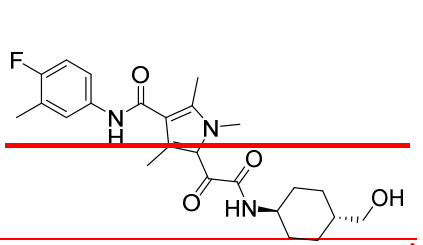
,

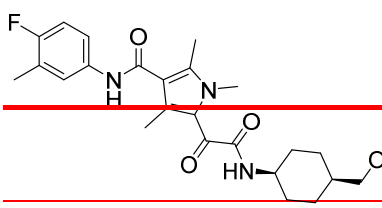
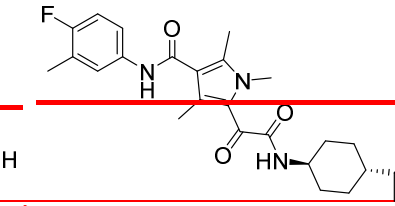
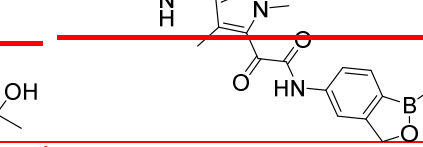
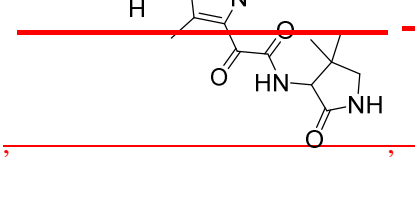
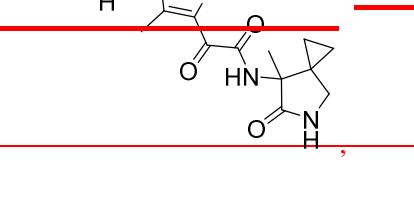
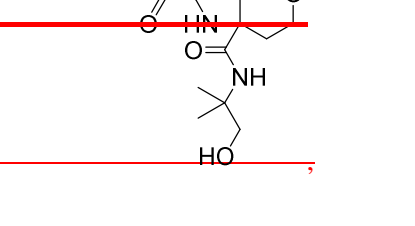
,

,

,


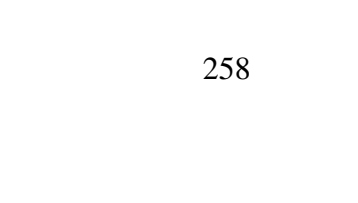
,

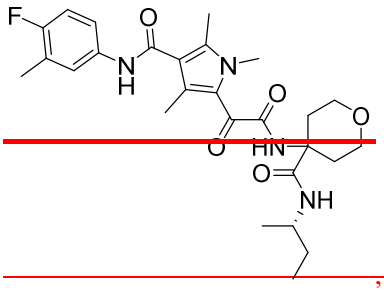
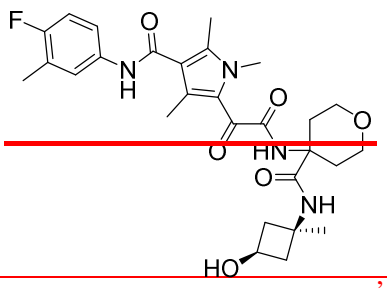
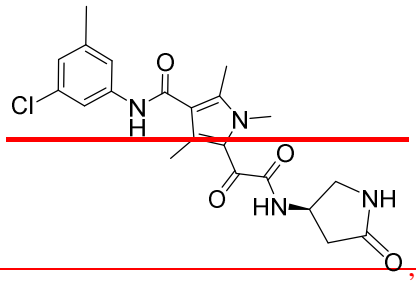
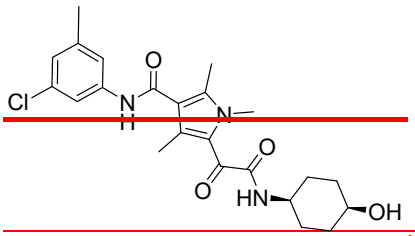
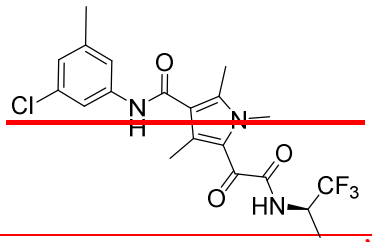
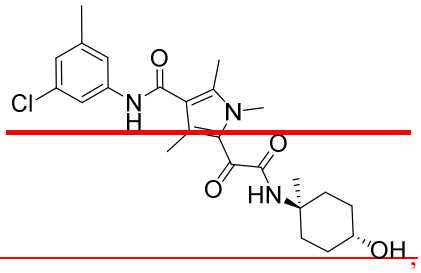
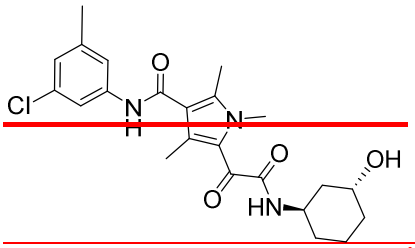
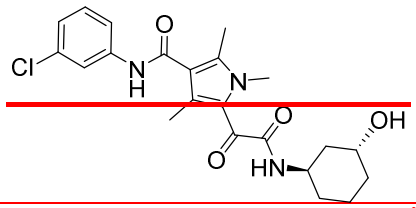
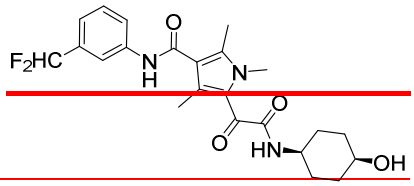
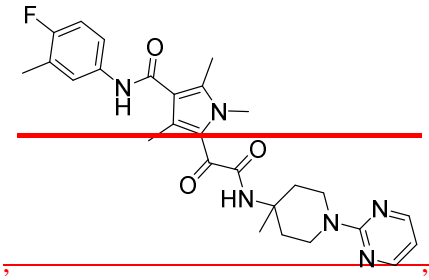
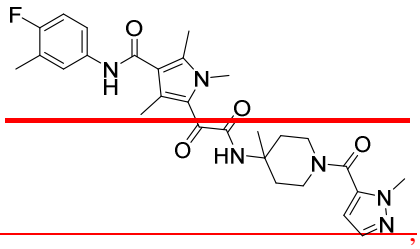
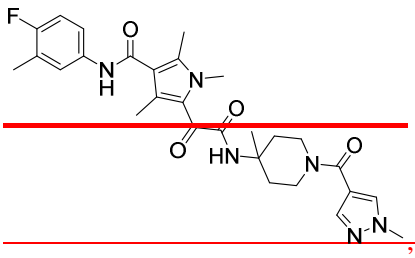
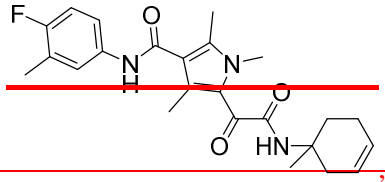
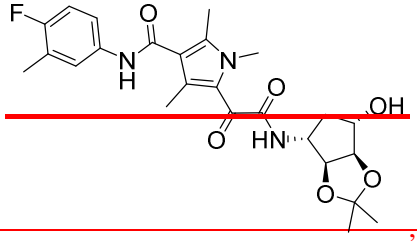
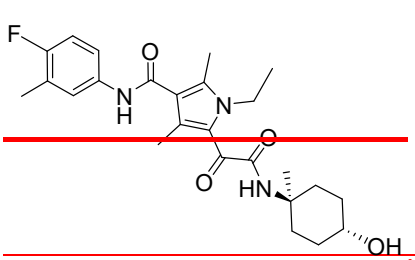
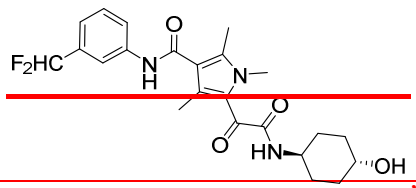
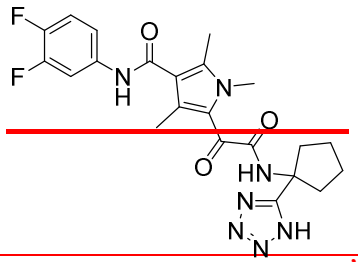
,



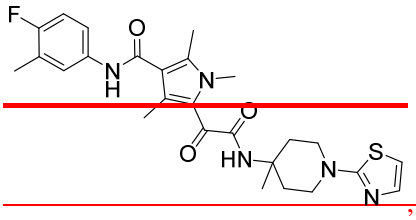
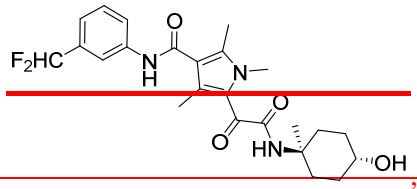
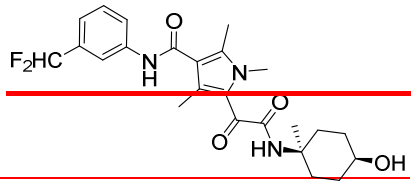
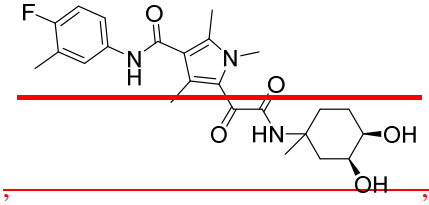
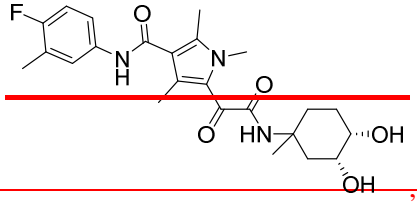
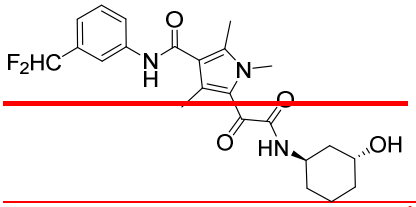
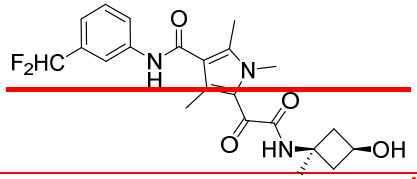
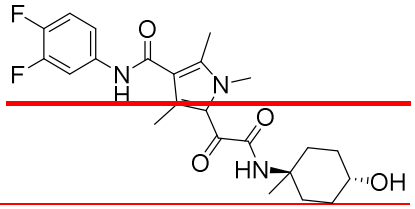
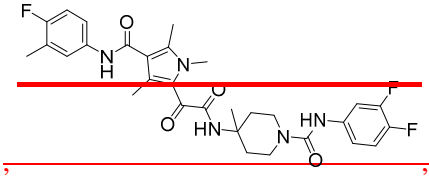
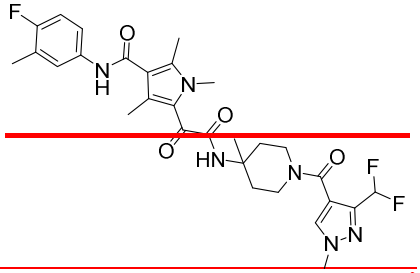
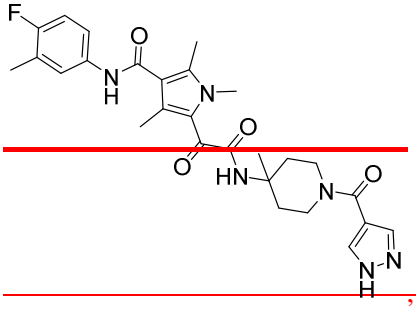
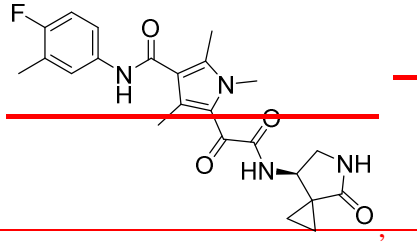
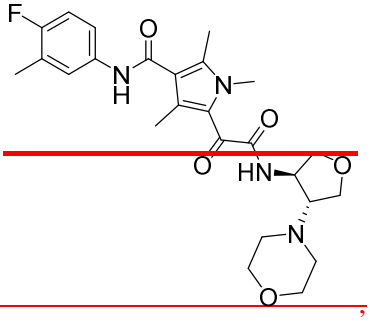
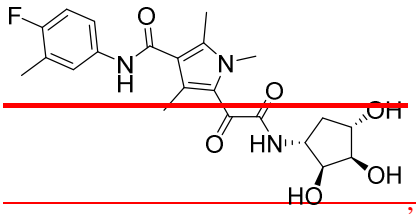
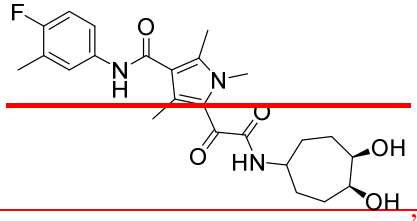
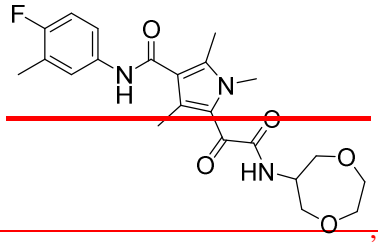


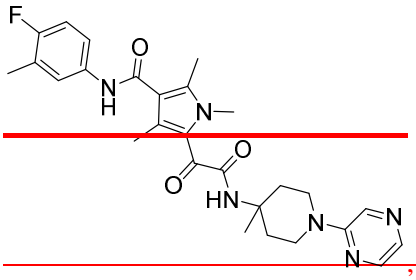
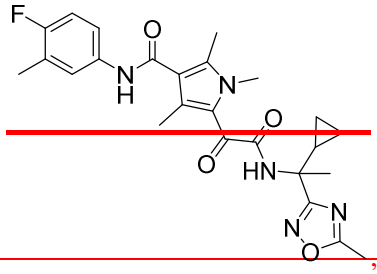
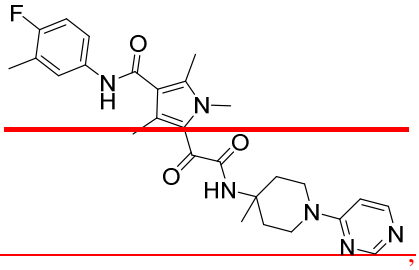
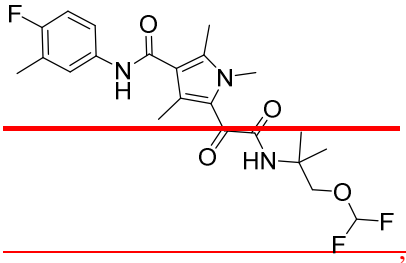
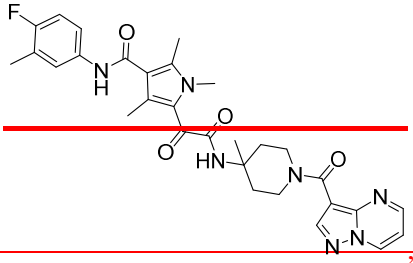
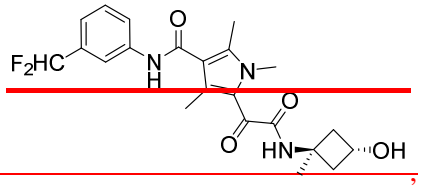
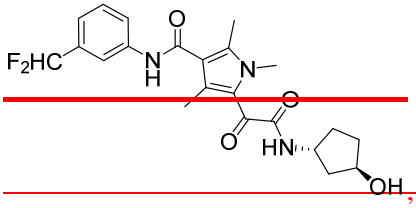
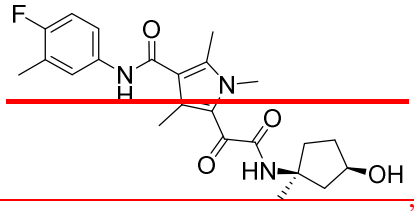
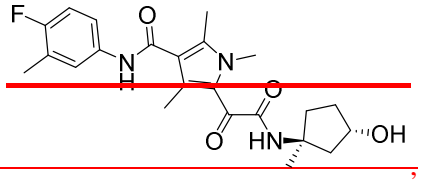
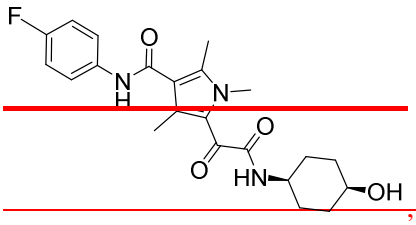
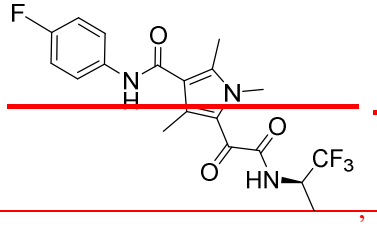

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

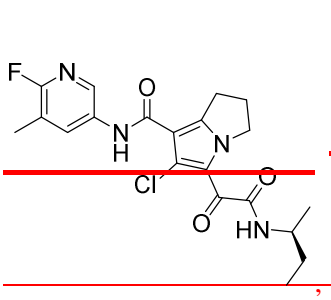
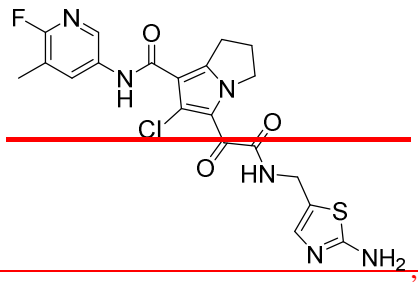
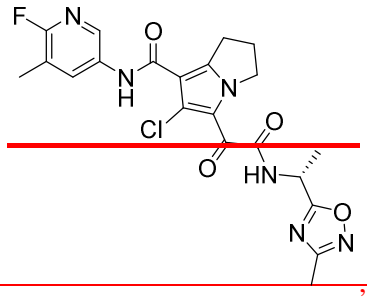
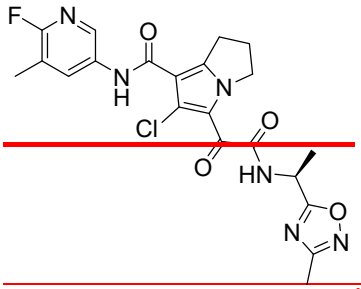
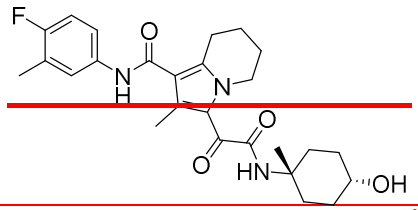
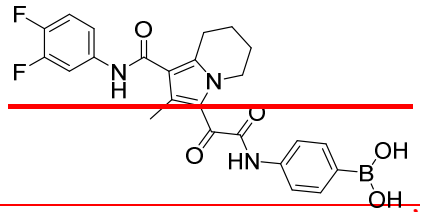
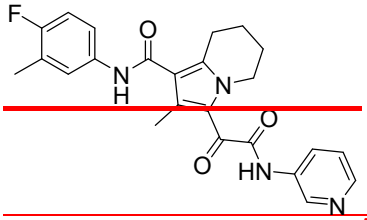
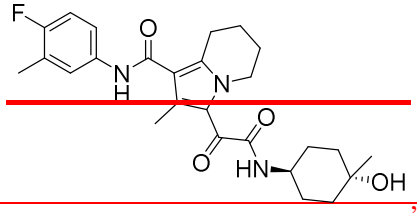
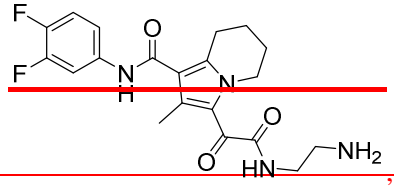
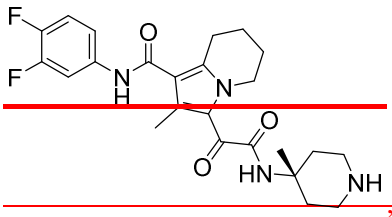
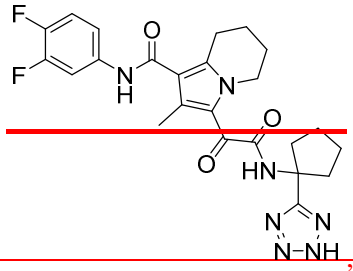
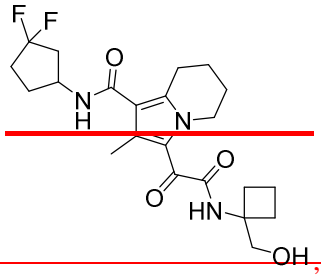
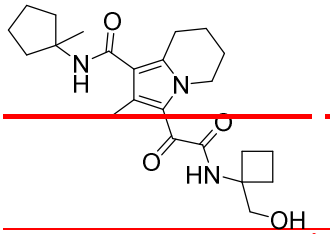
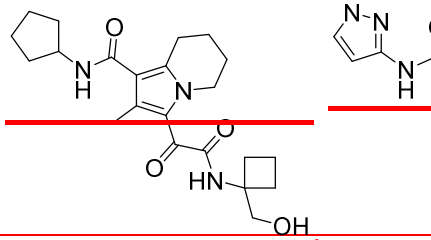
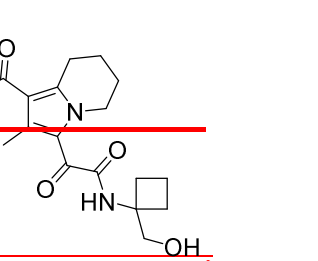
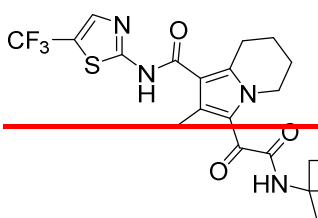
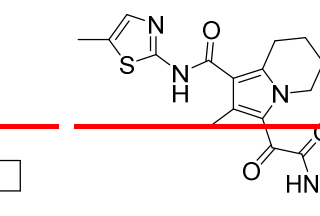
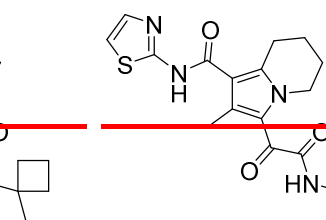
,

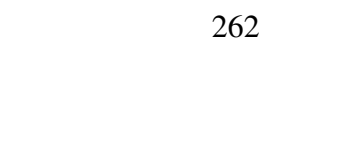
,

,

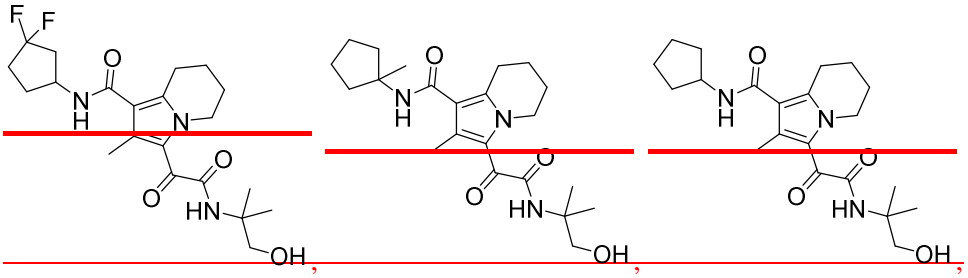

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

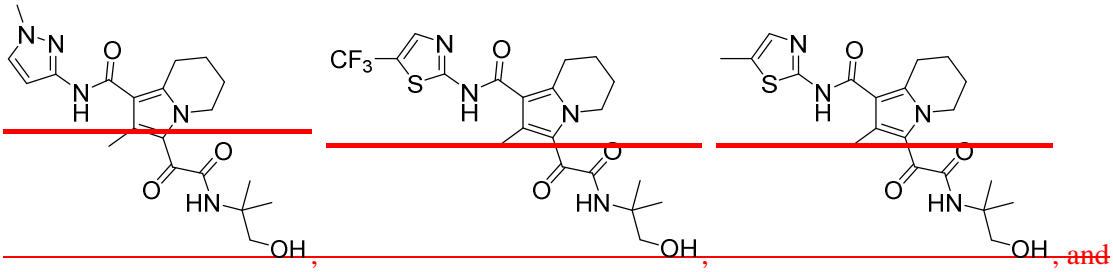

,

,

,

,

,

,

,

,

,

,

,

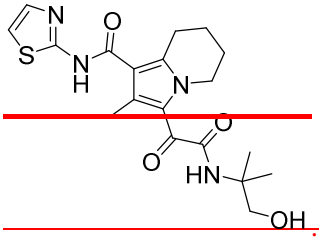

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

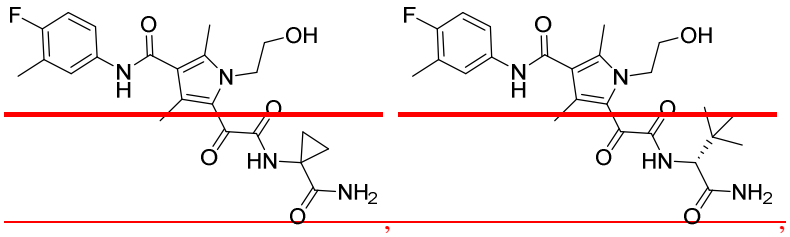
,

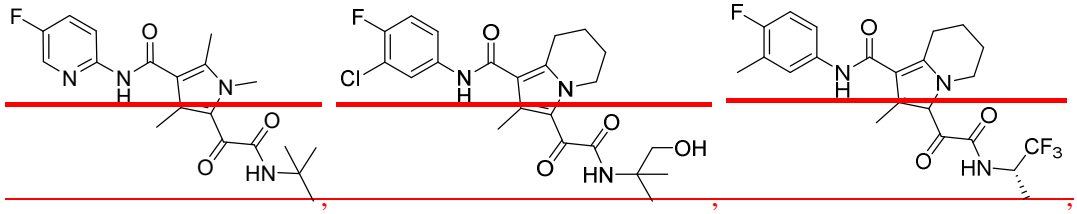


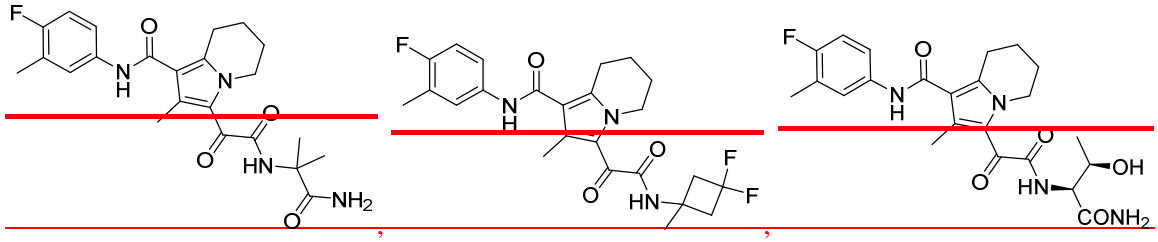


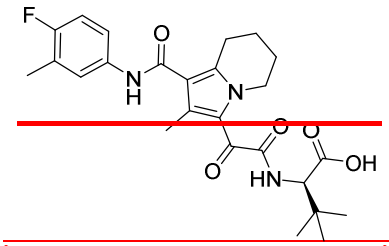
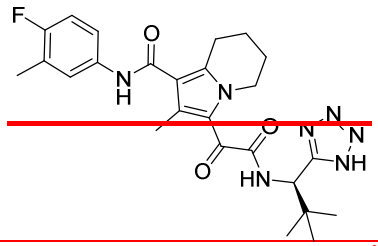
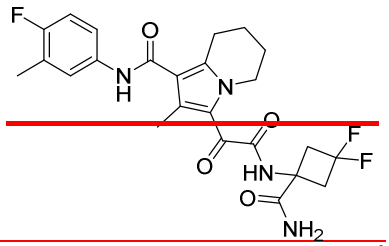
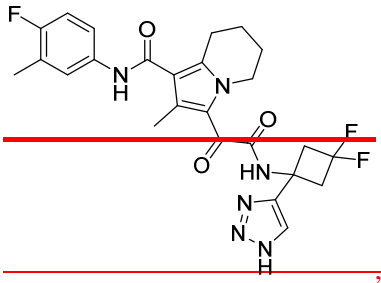
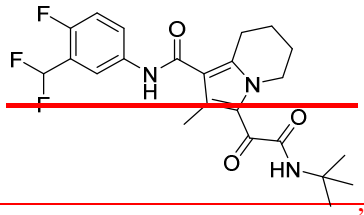
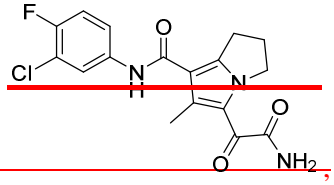
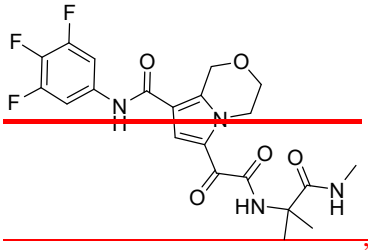
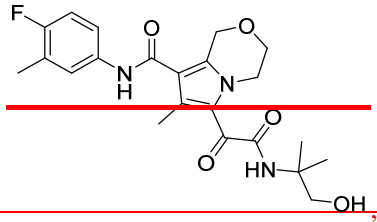
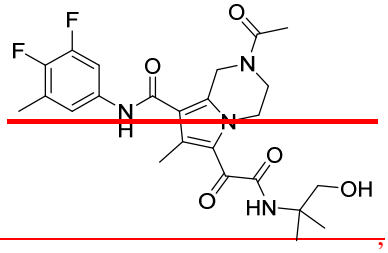
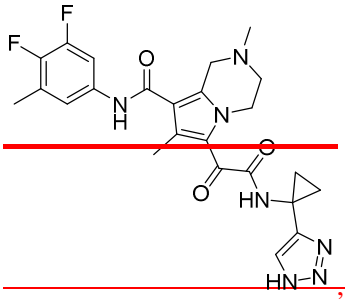
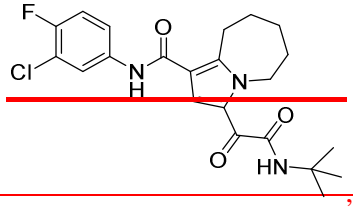
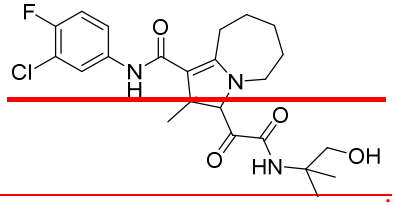


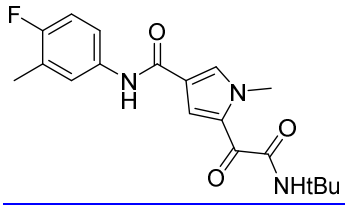
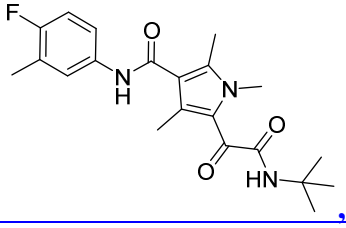
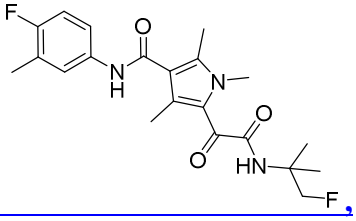
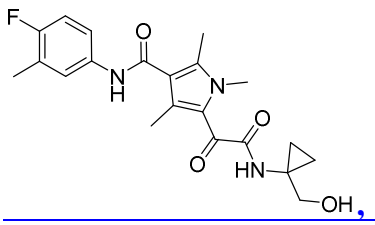
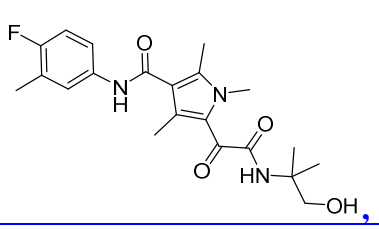
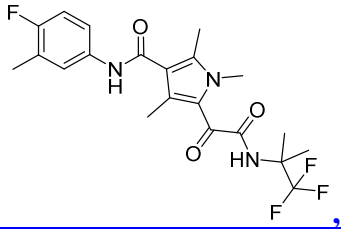
~~53. A compound, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, selected from the group consisting of:~~

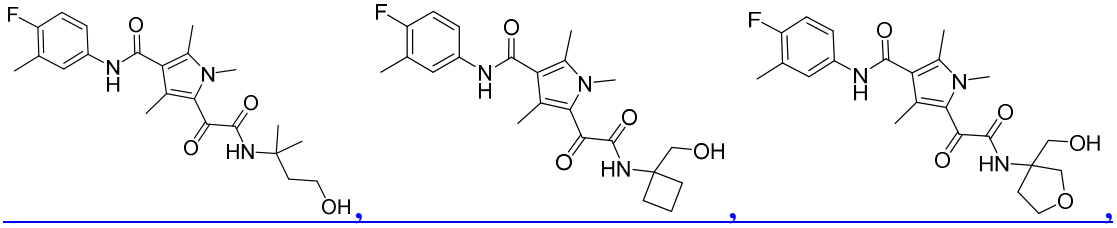


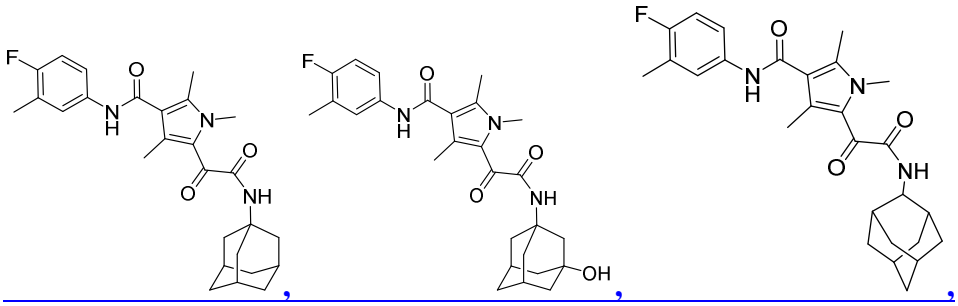


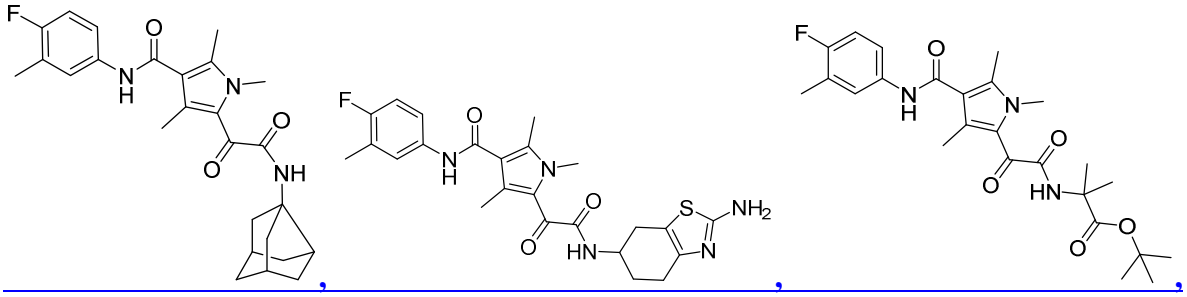


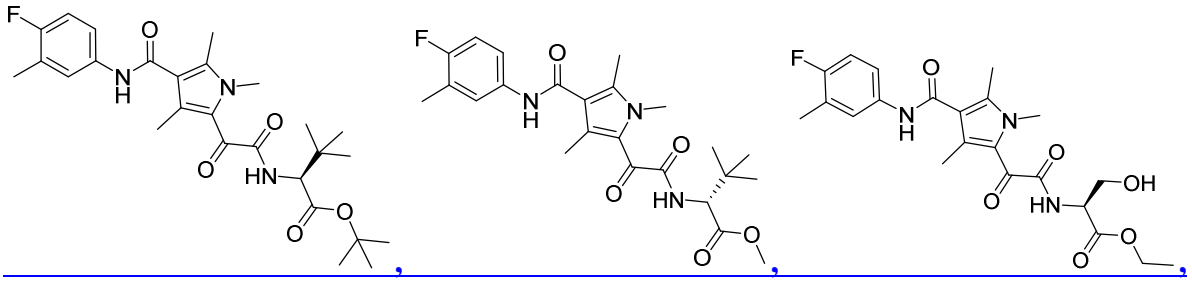













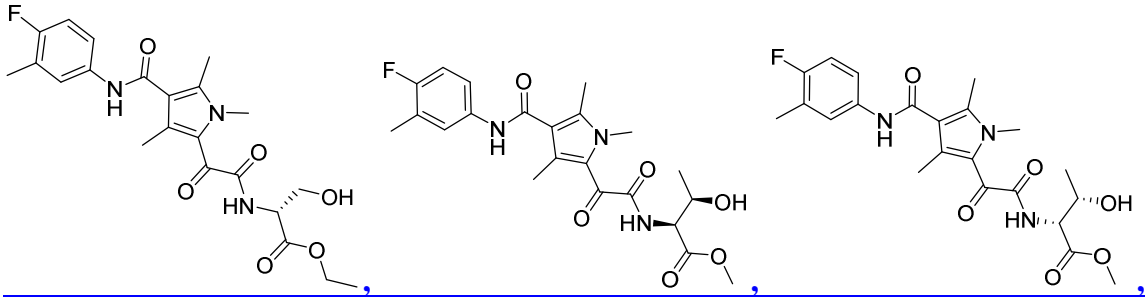







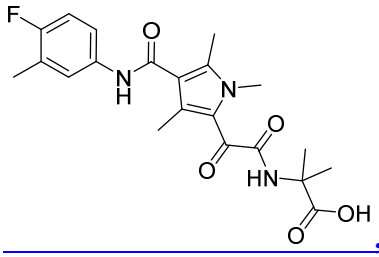
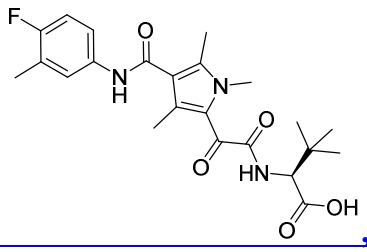
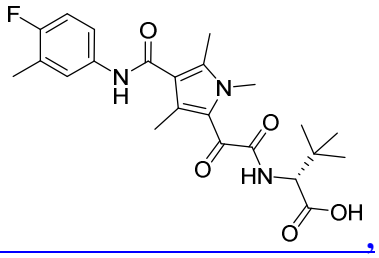
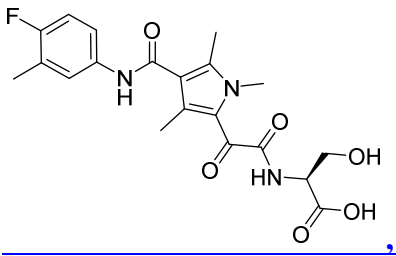
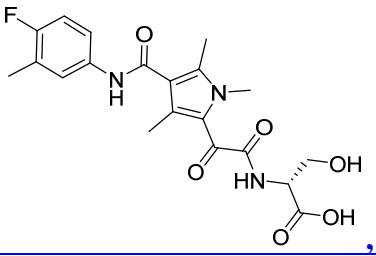
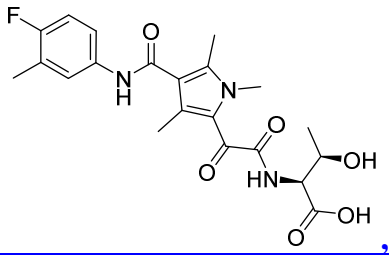
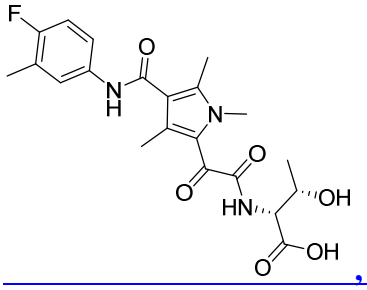
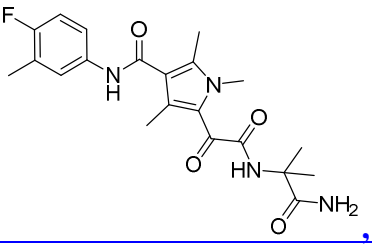
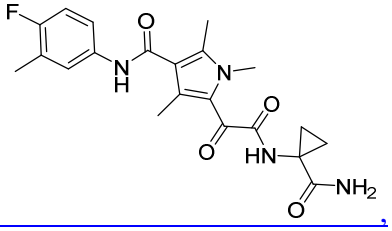
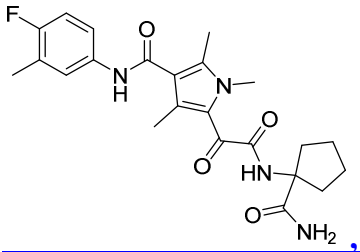
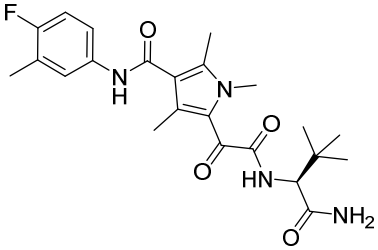
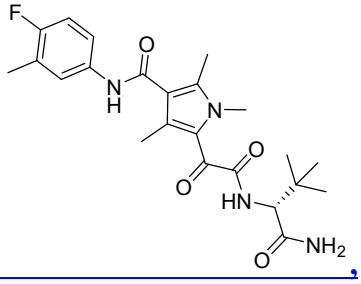
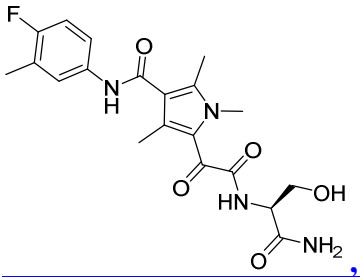
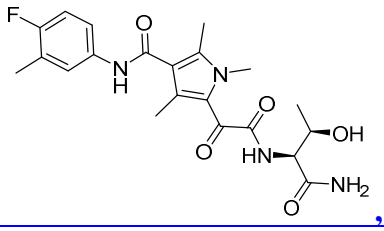
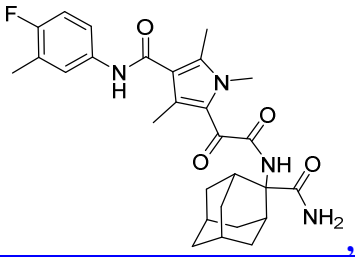
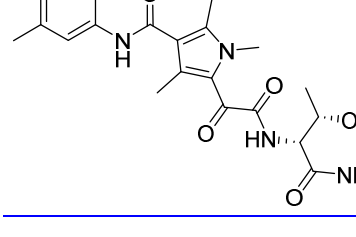
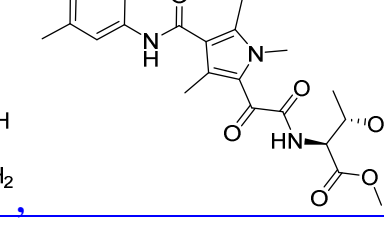


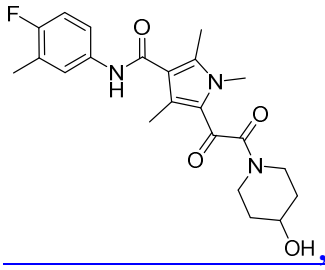
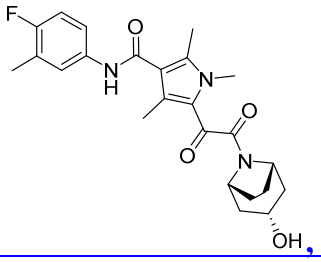
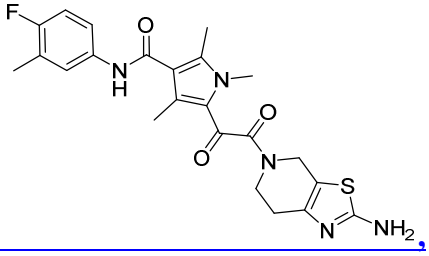
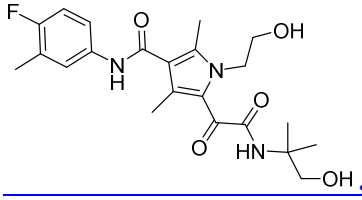
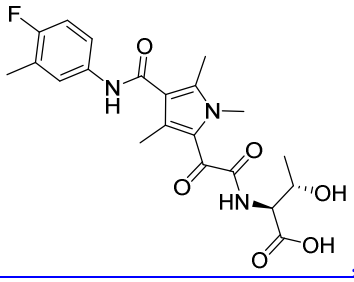
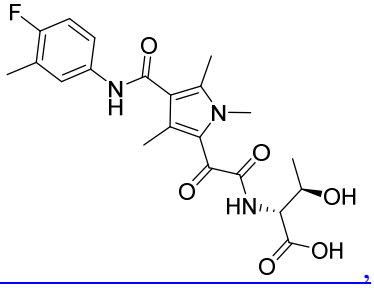
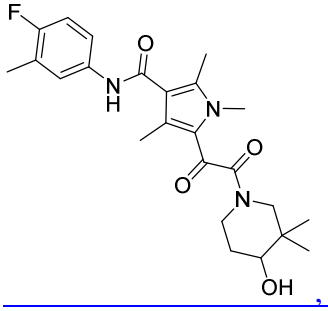
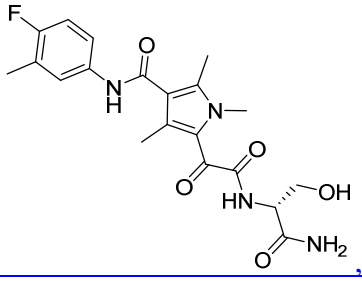
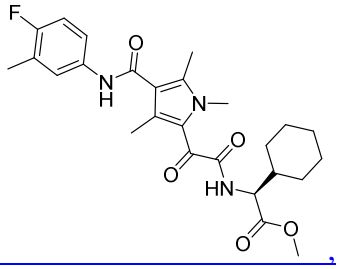
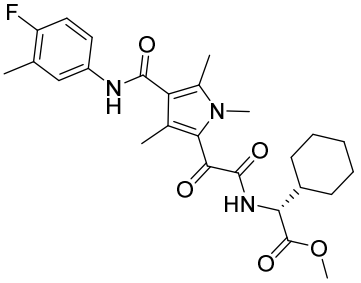
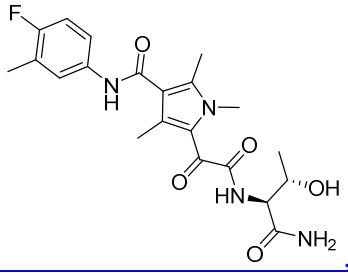
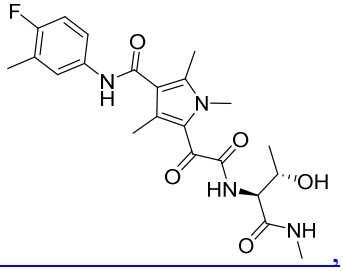
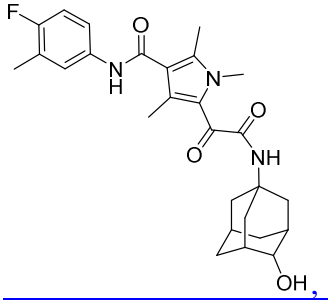
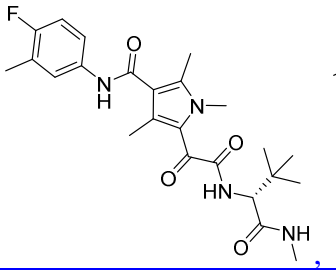
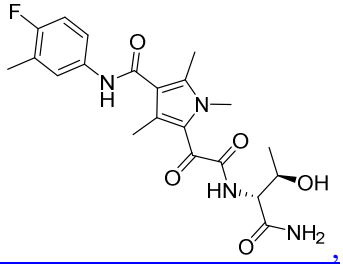


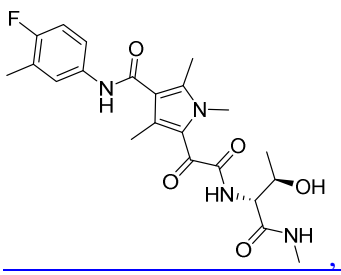
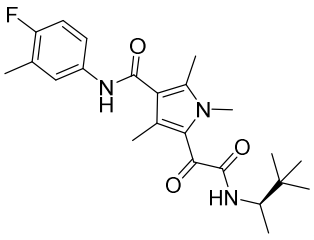
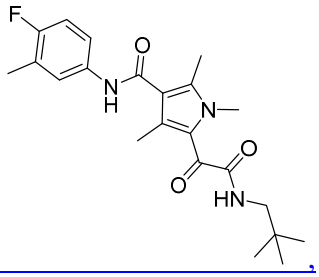


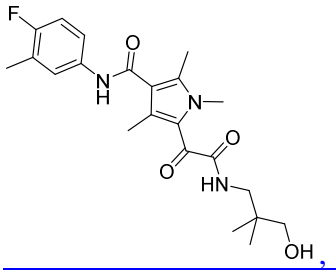
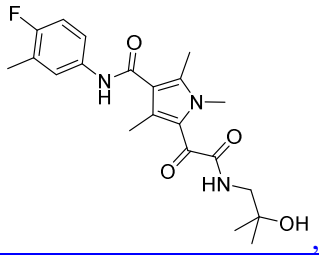
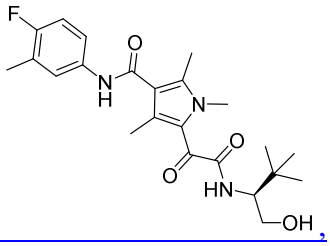


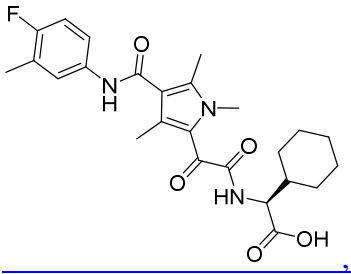
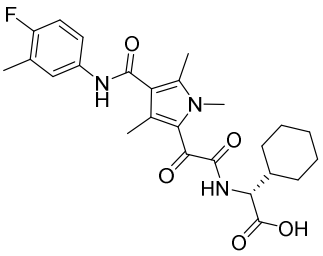
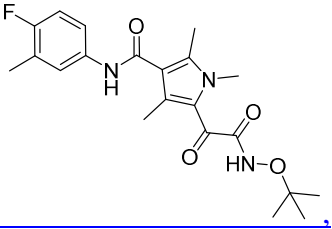


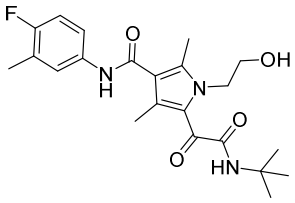
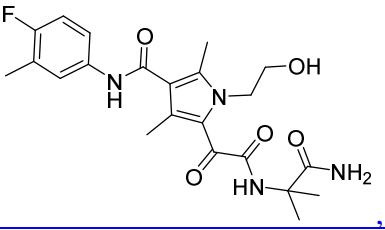
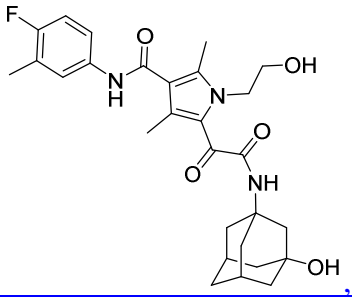


















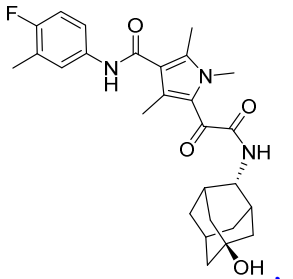
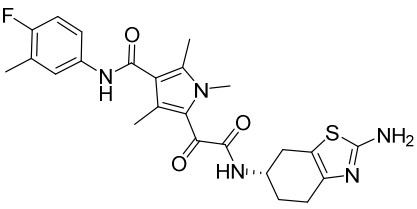
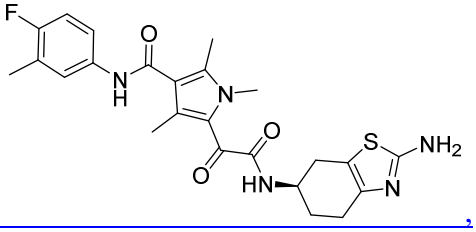
















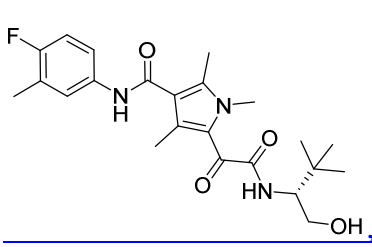
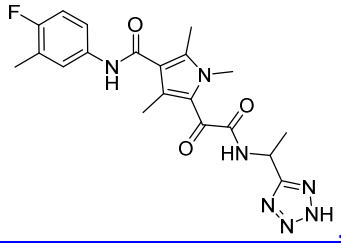
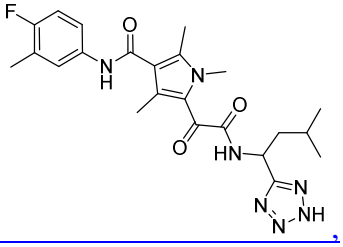
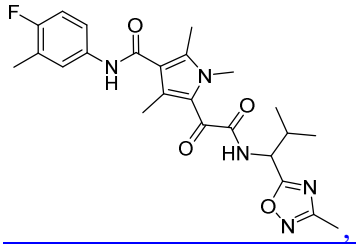
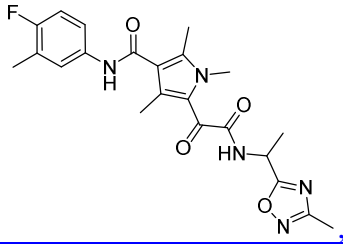
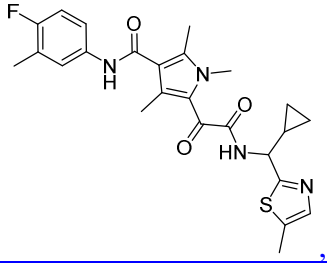
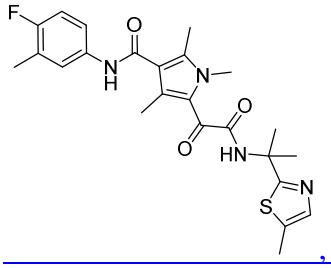
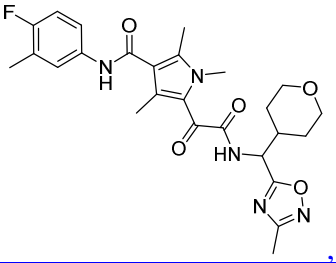
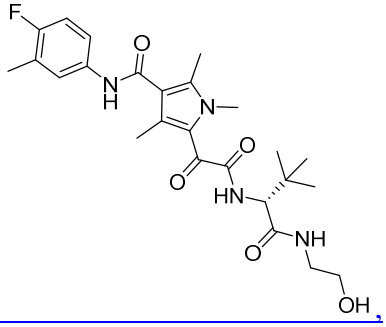
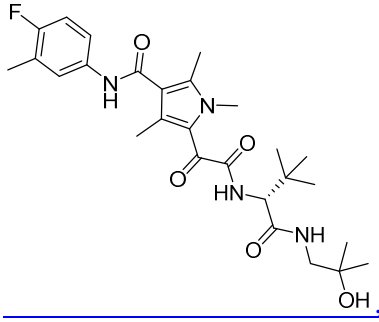
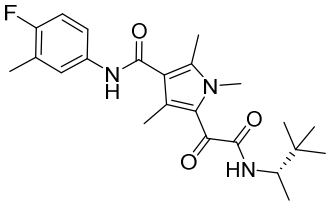
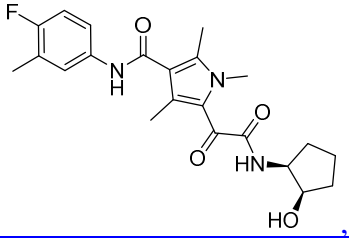
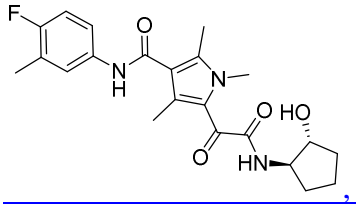
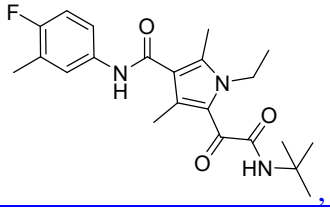
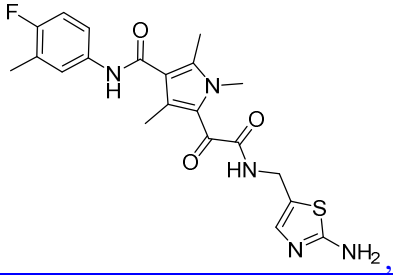




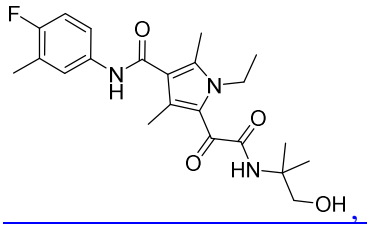
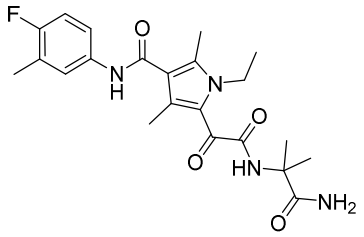
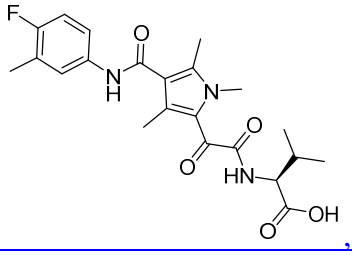
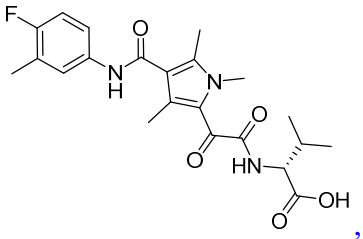
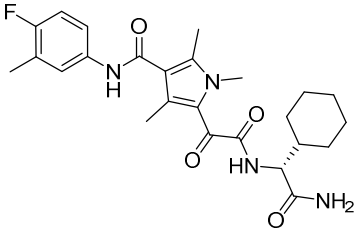
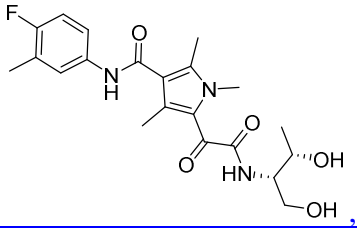
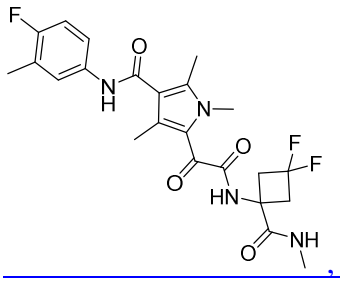
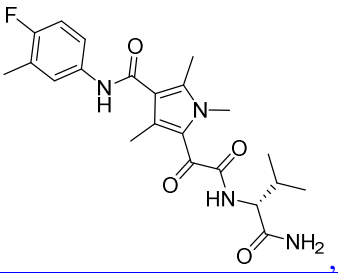
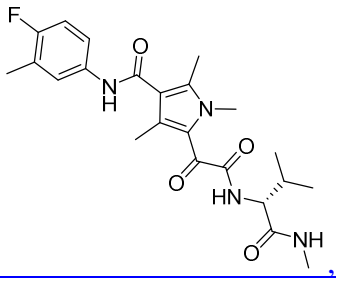
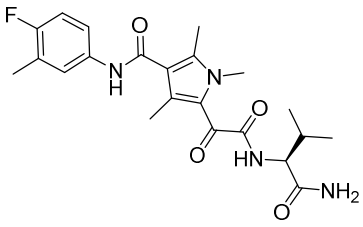
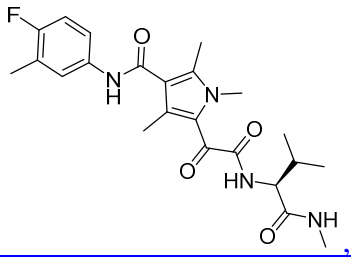
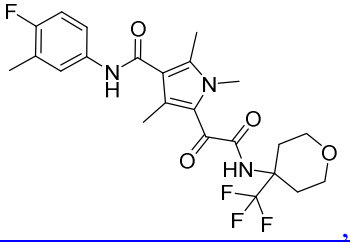
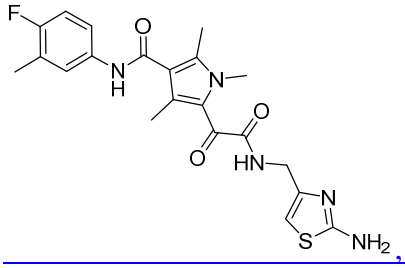
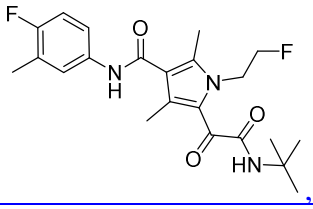
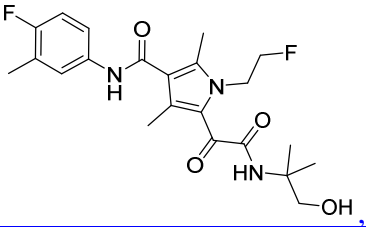
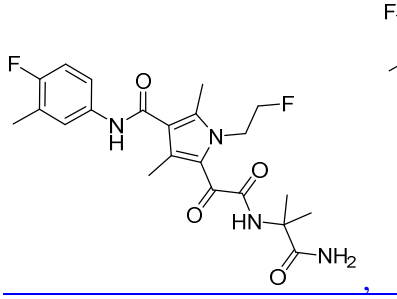
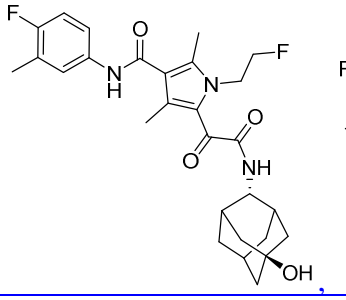




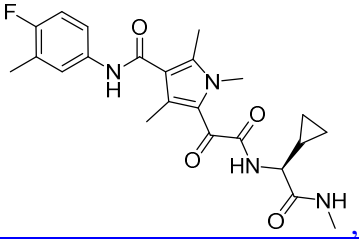




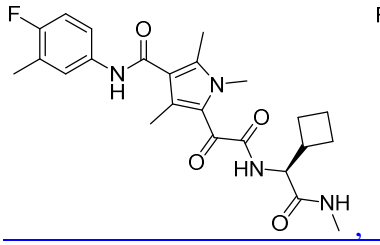
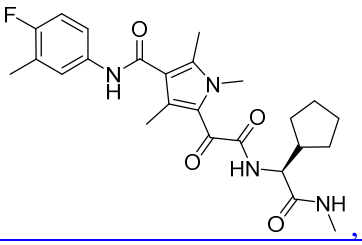
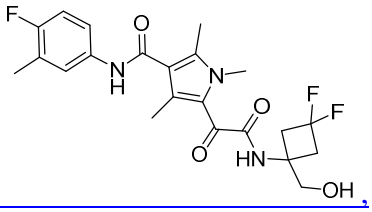
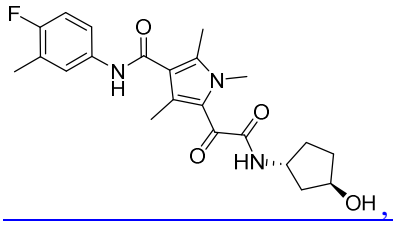
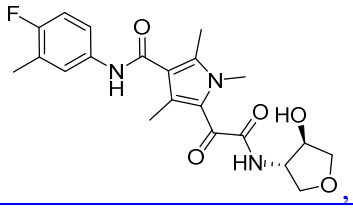
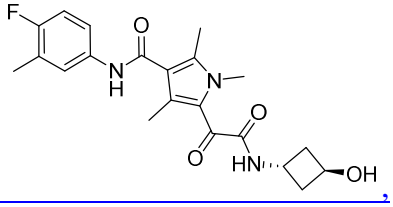
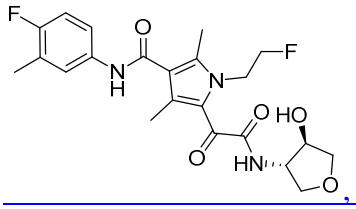
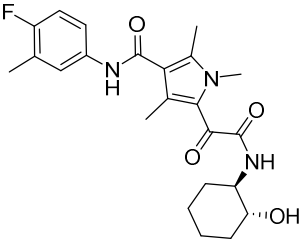
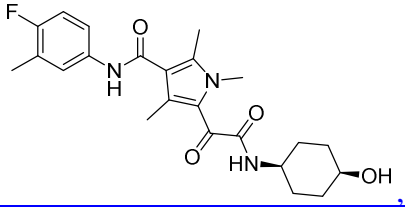
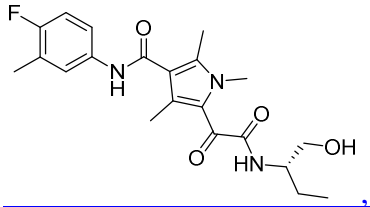
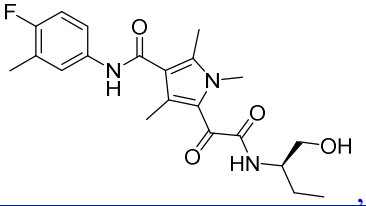
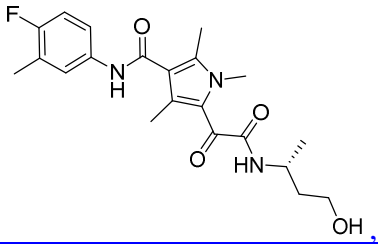
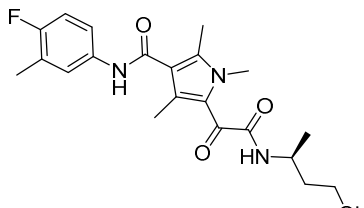
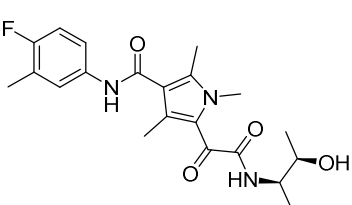
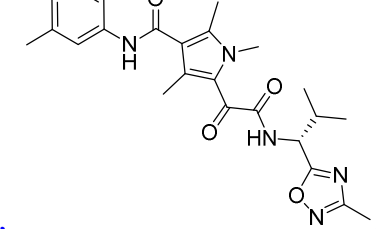
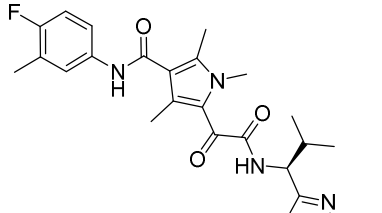
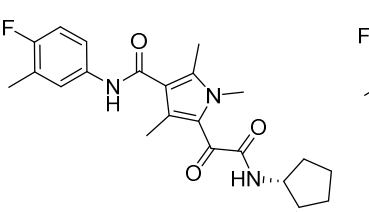
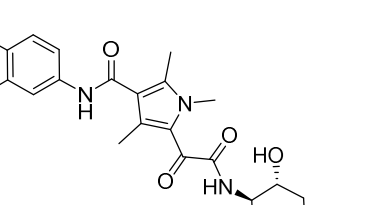

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,


,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

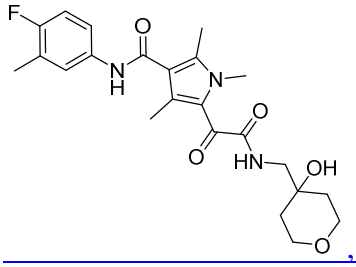
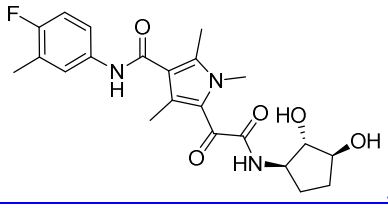
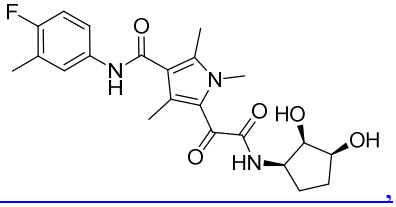
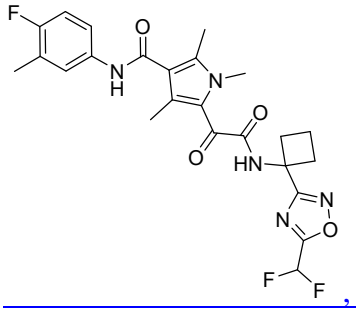
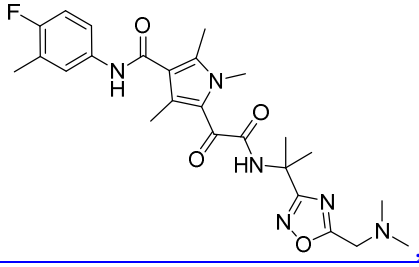
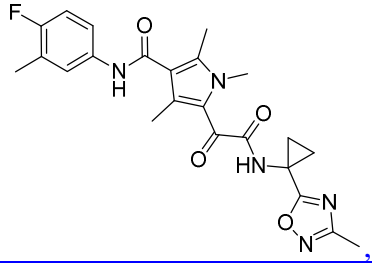
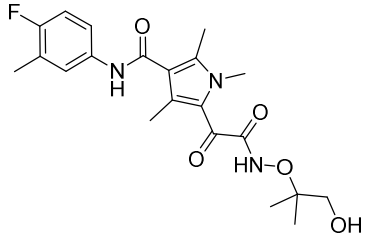
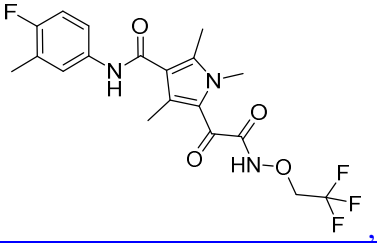
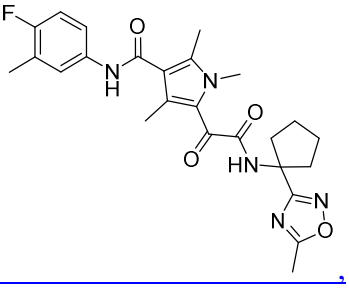
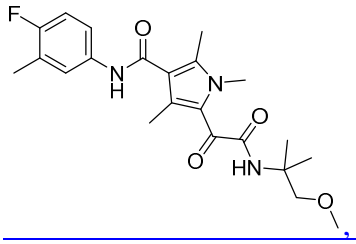
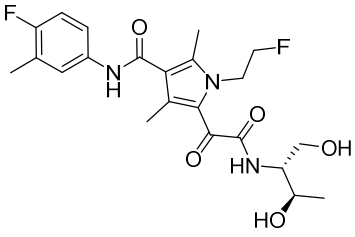
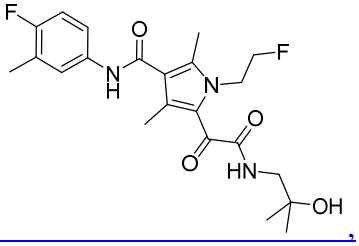
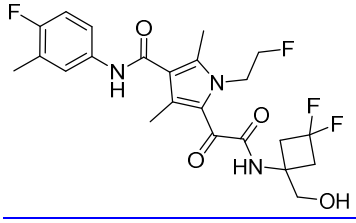
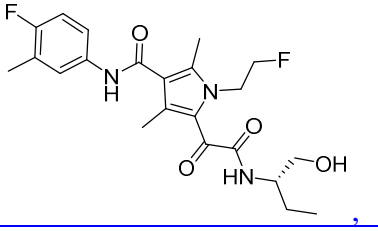
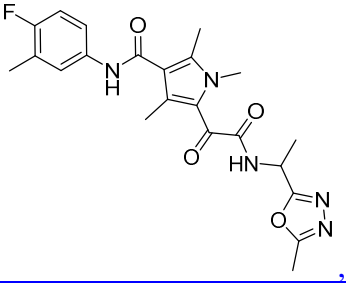
,

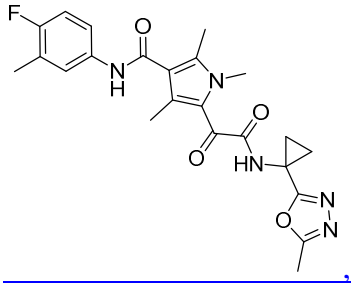
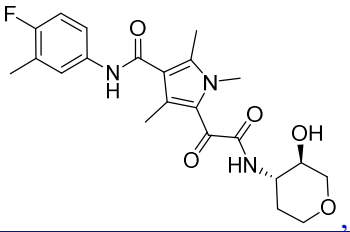
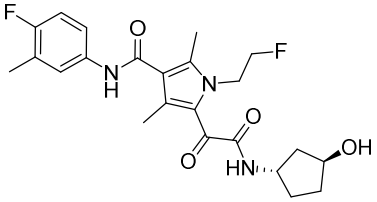
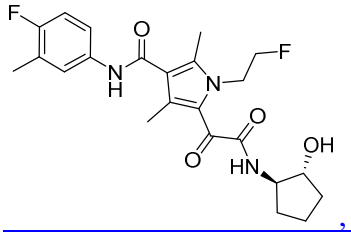
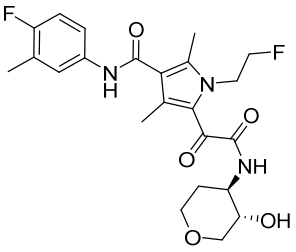
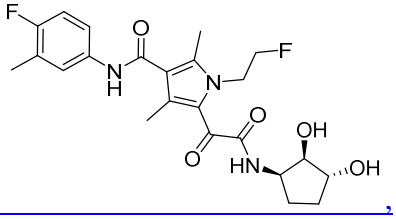
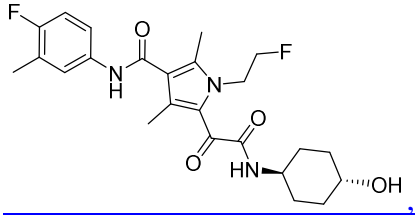
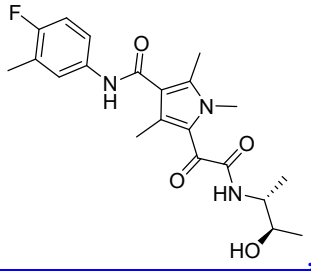
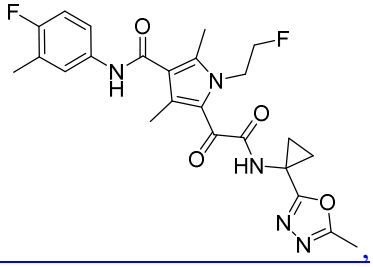
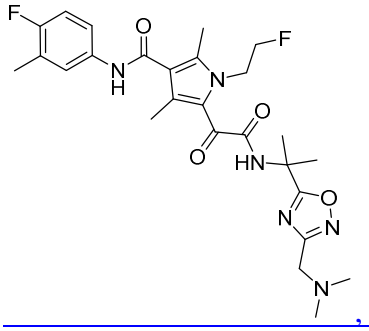
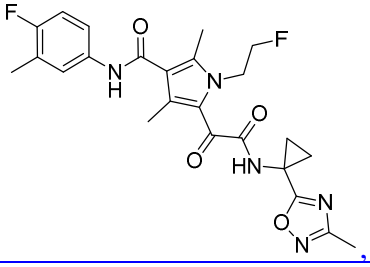
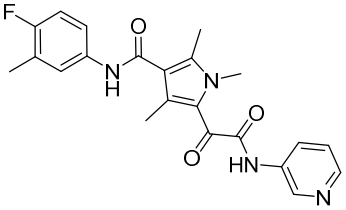
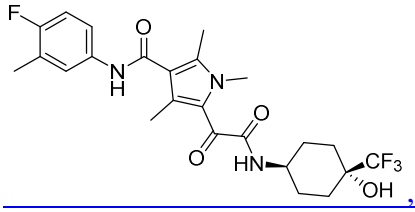
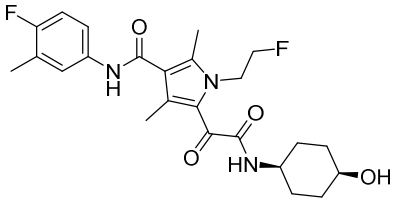
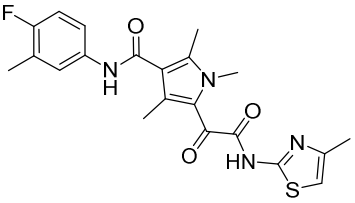
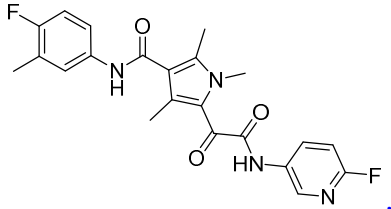
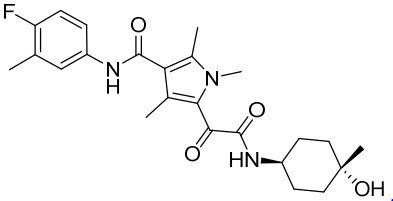
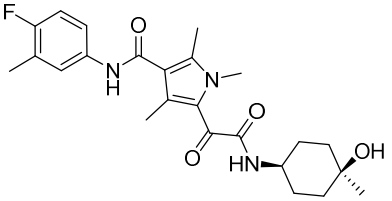
,

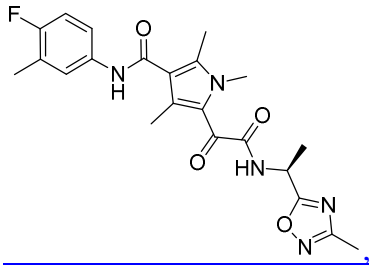
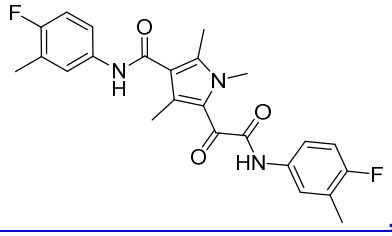
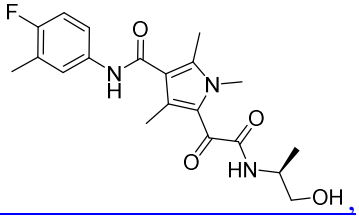
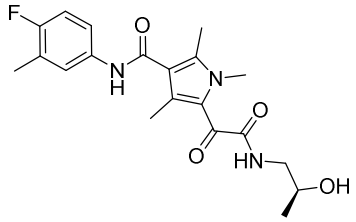
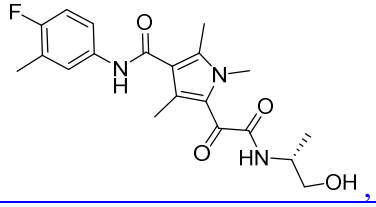
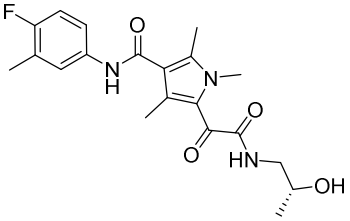
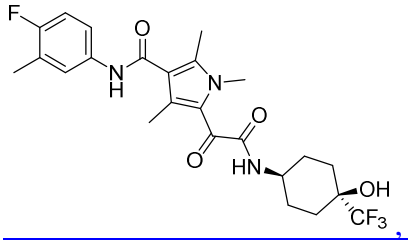
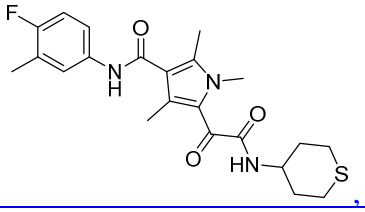
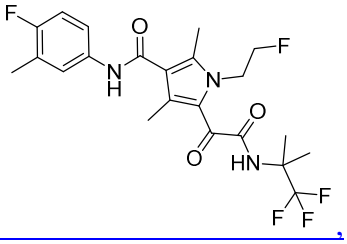
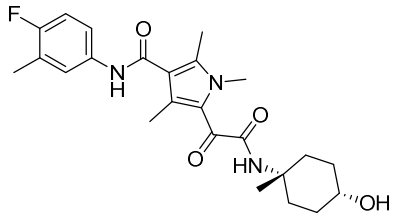
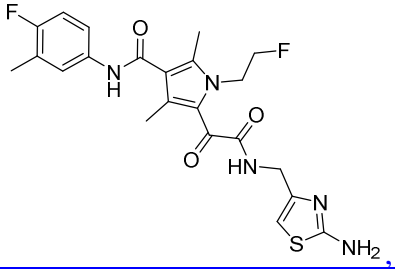
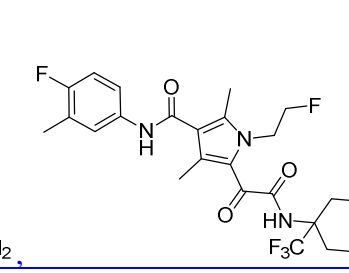
,

,

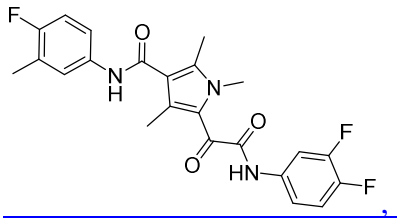
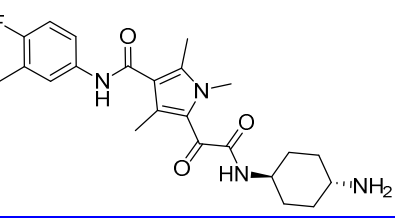
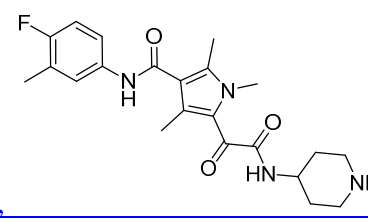
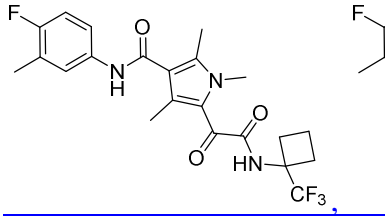
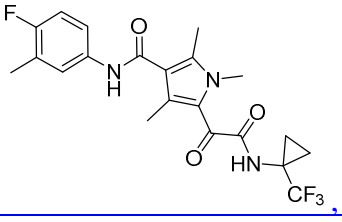
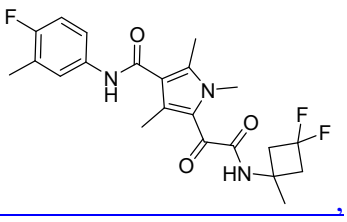



















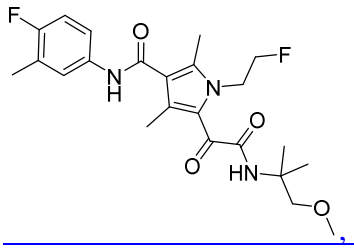
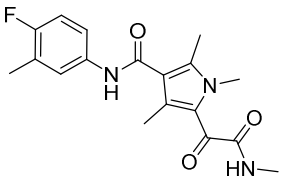
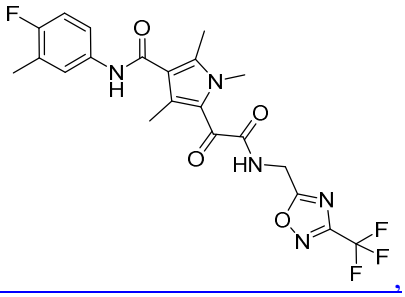
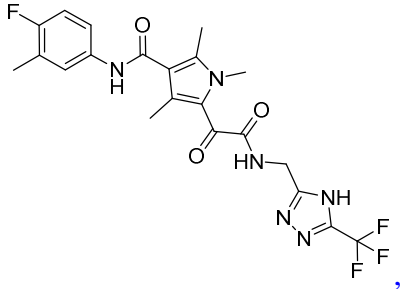
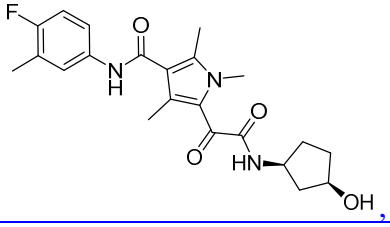
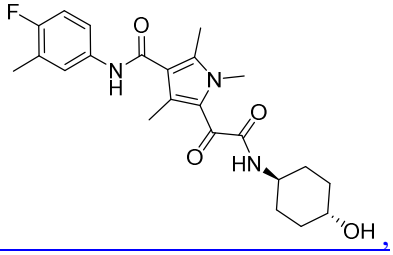
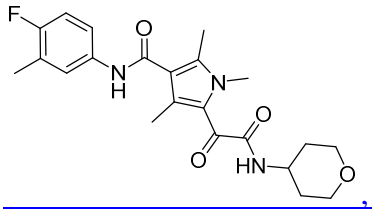
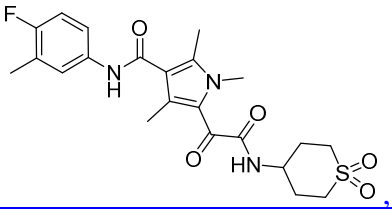
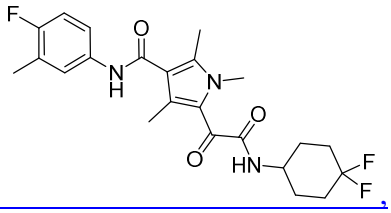
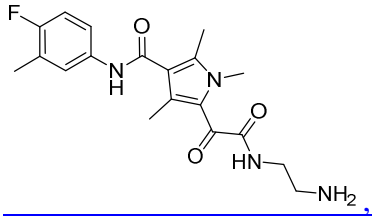
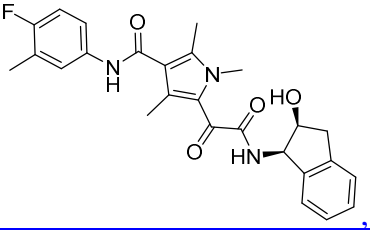
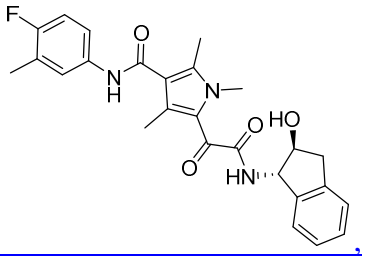
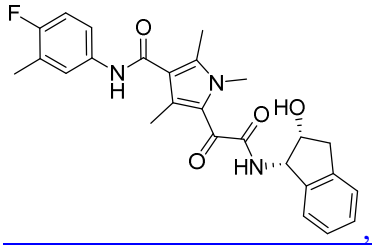
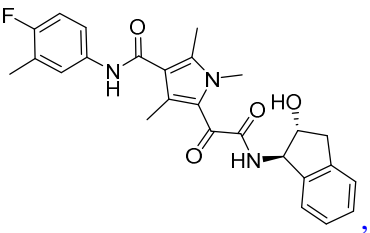
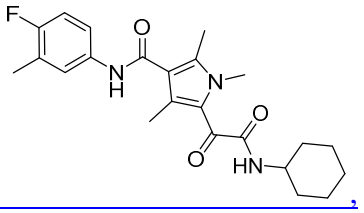
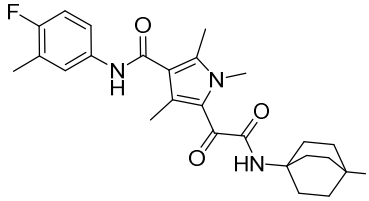
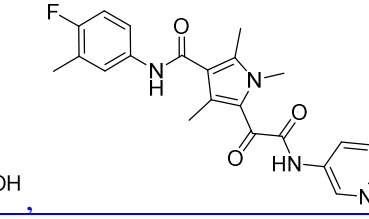



,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

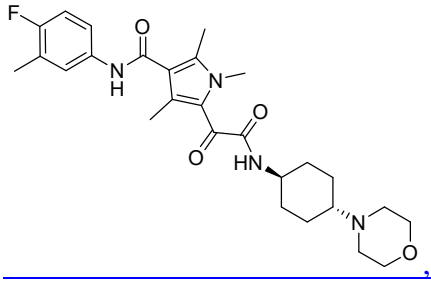
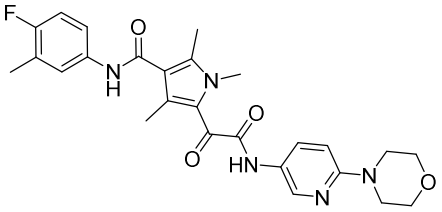
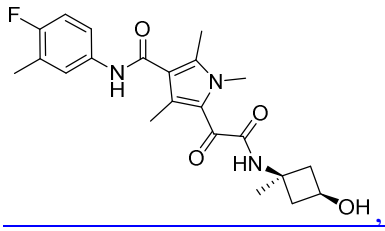
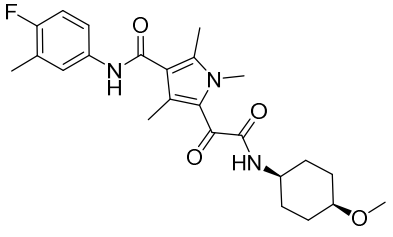
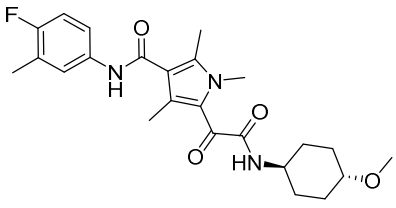
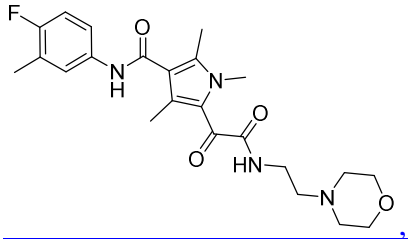
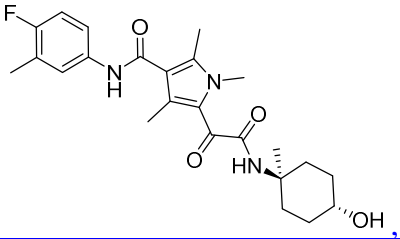
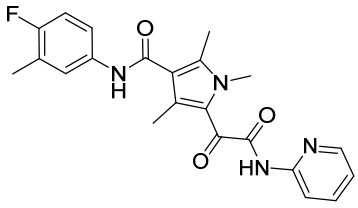
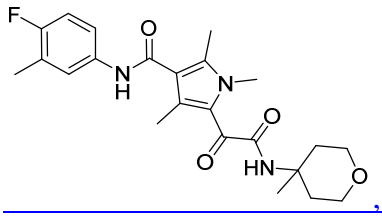
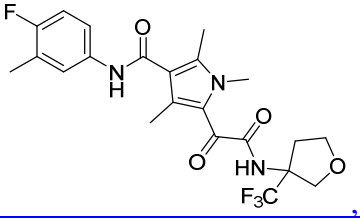
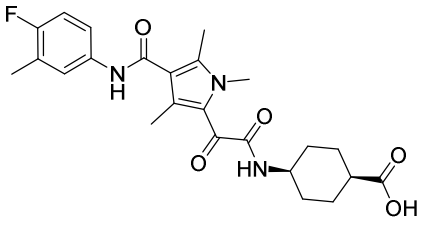
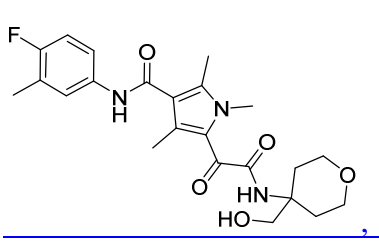
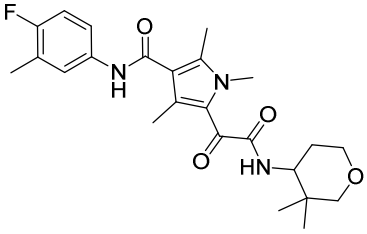
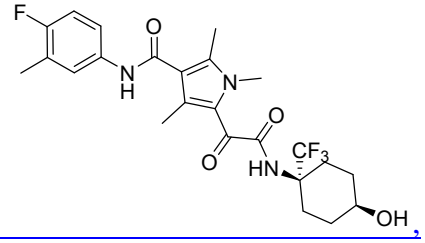
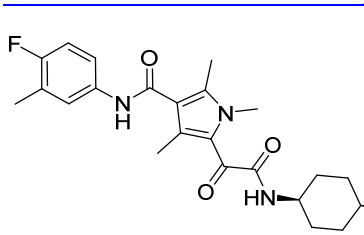
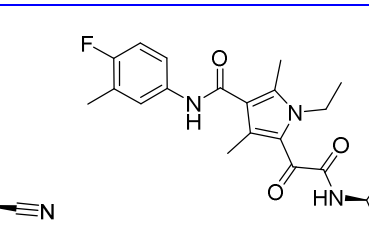
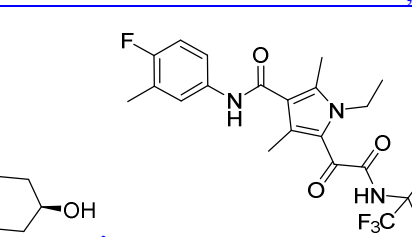

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

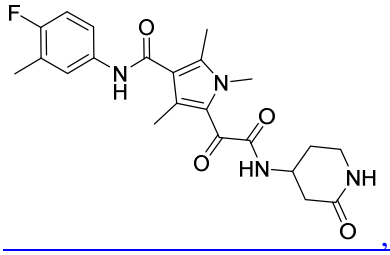
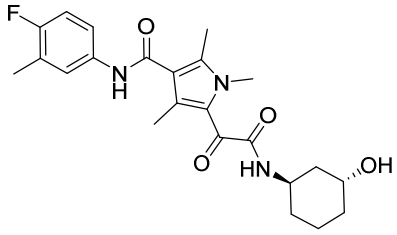
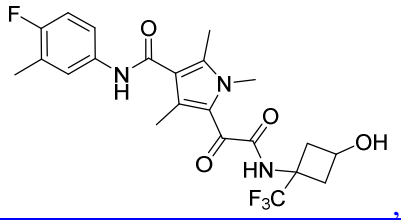
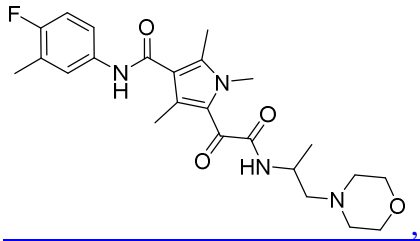
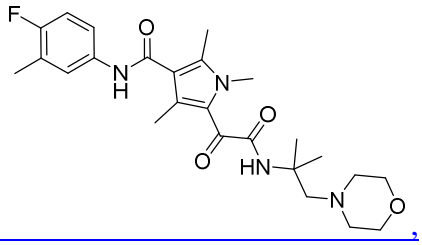
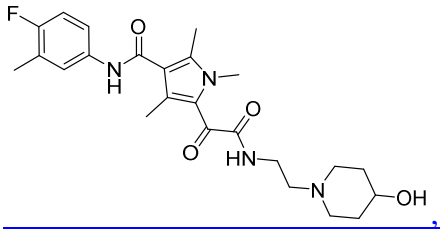
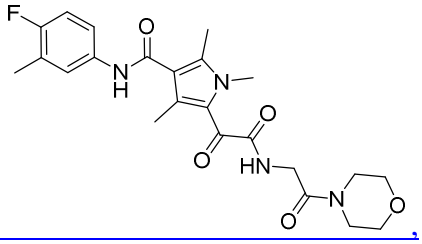
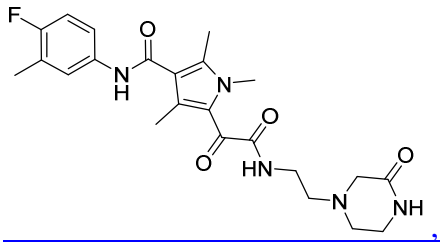
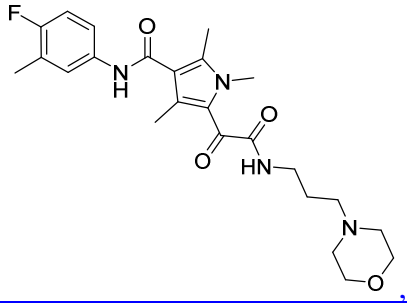
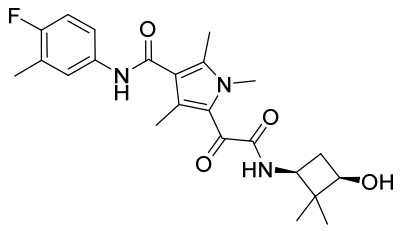
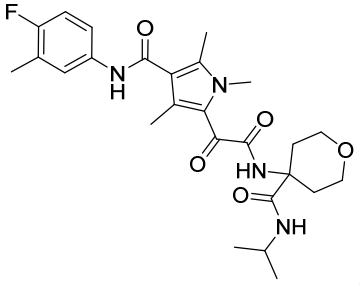
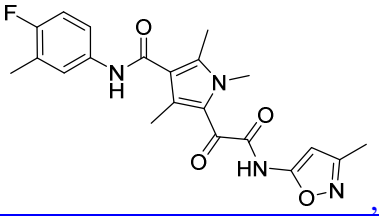
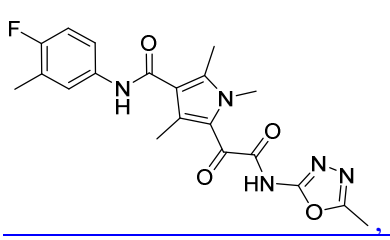
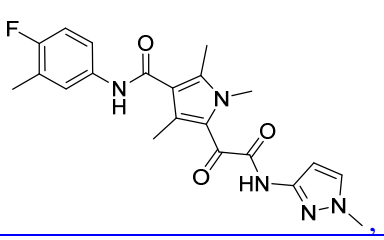
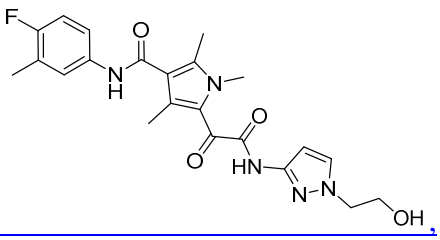







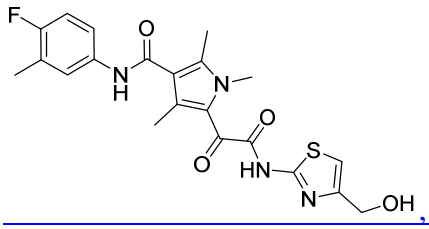
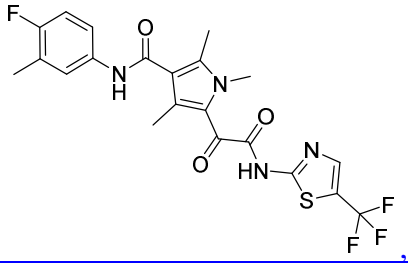
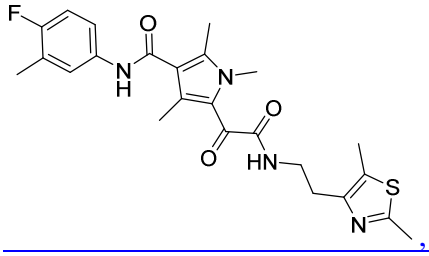
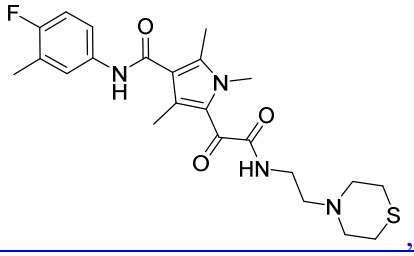
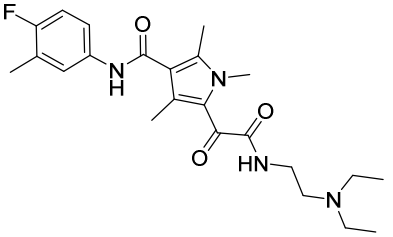
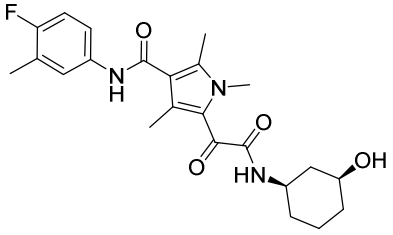
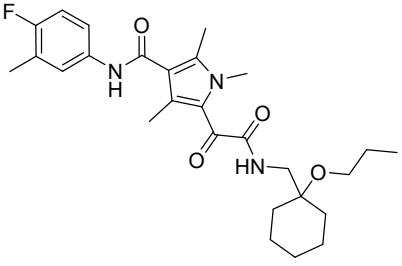
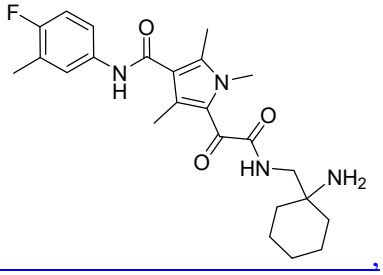
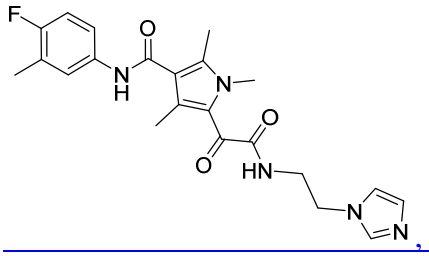
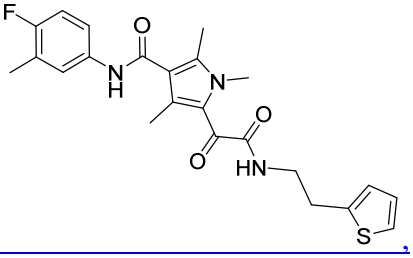
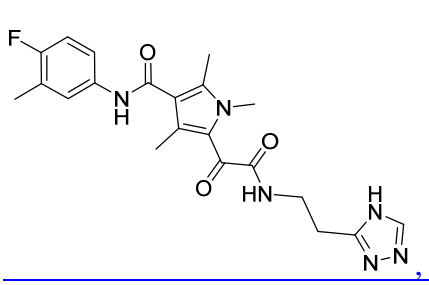
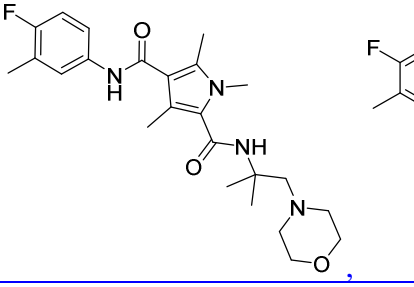


















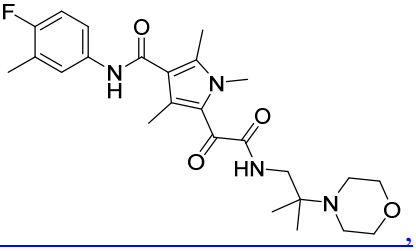


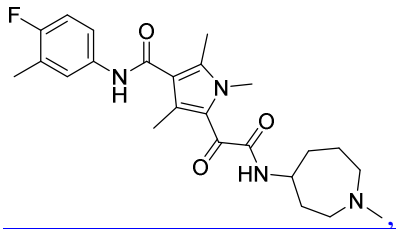
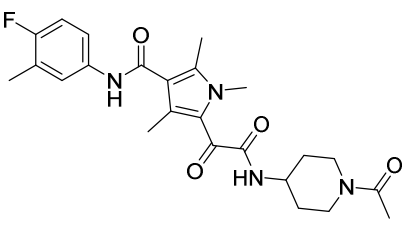
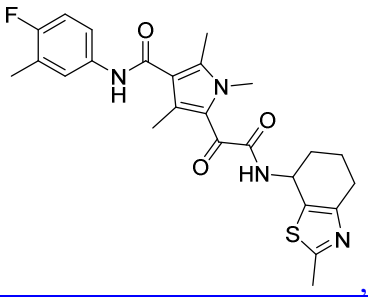
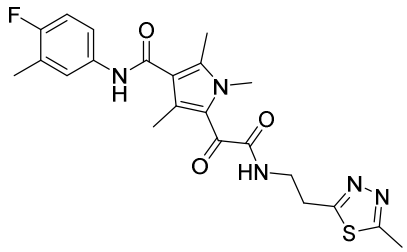
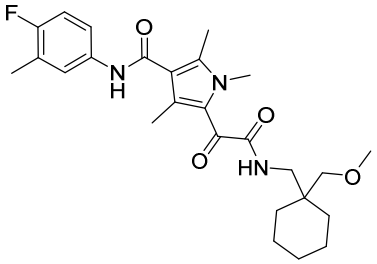
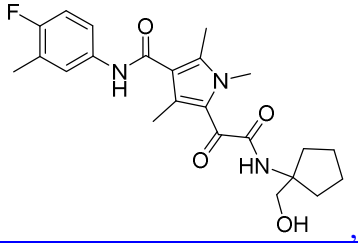
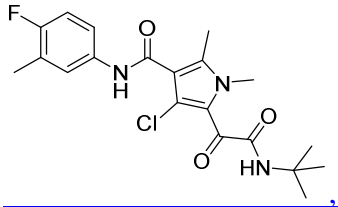
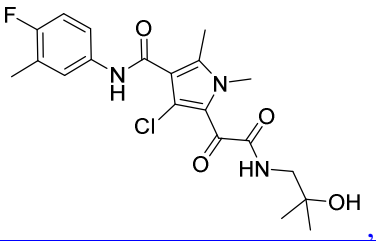
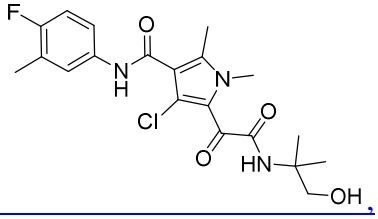
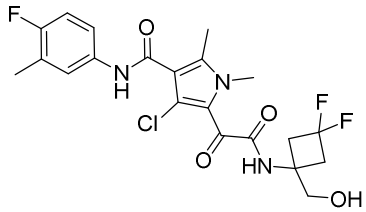
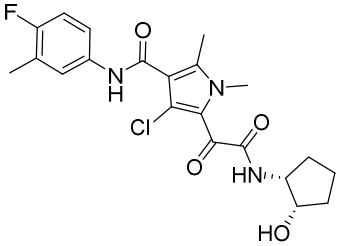
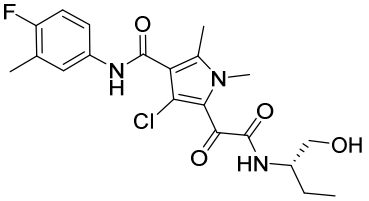
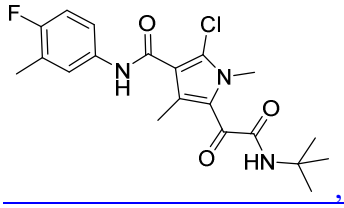
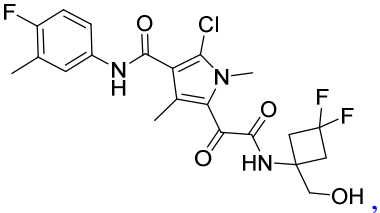
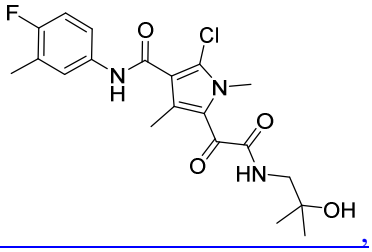
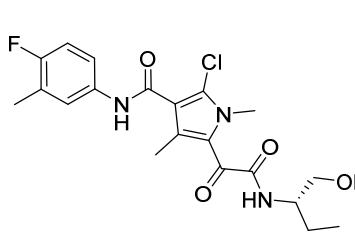
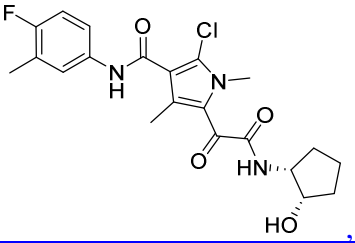



















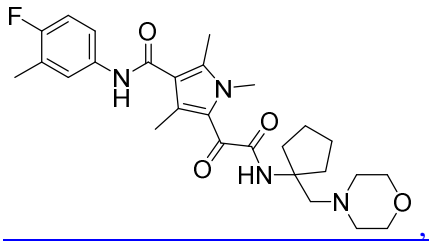
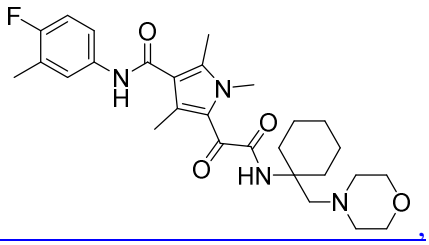
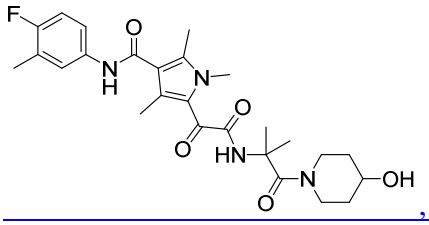
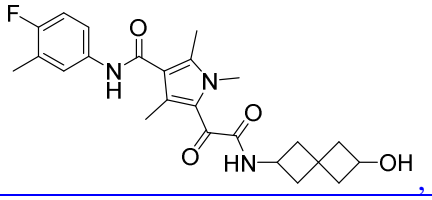
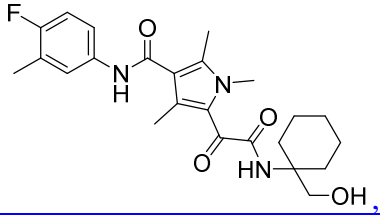
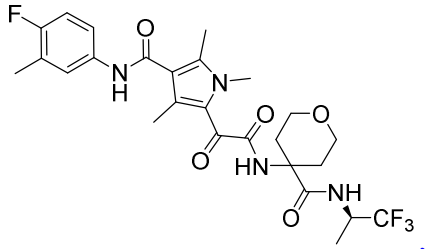
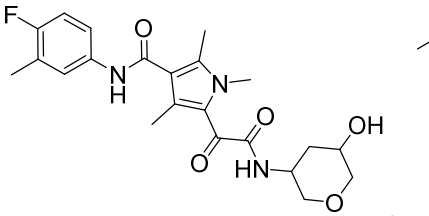
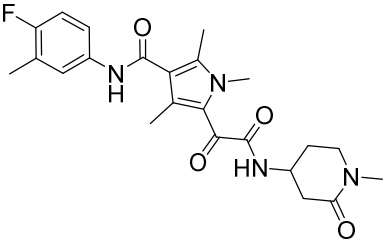
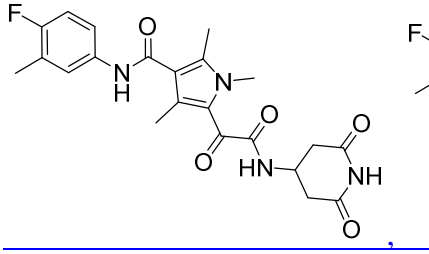
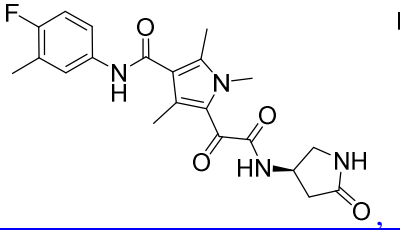
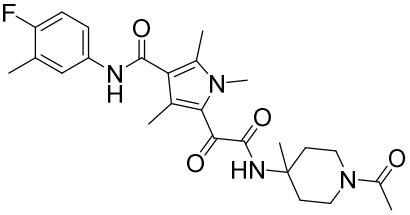
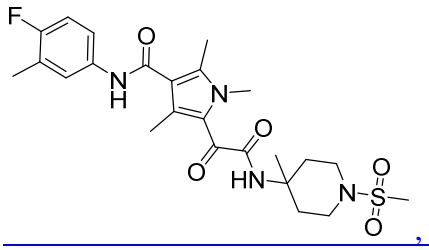
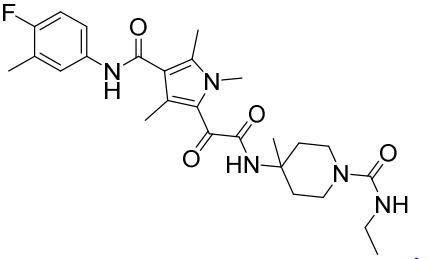
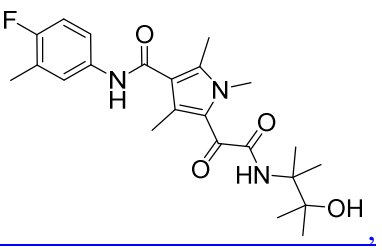
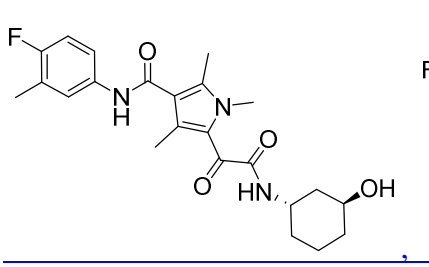
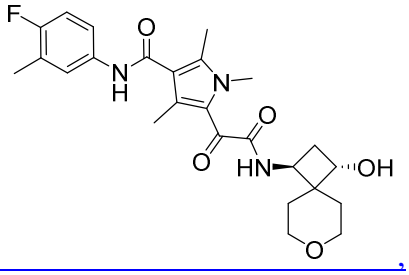


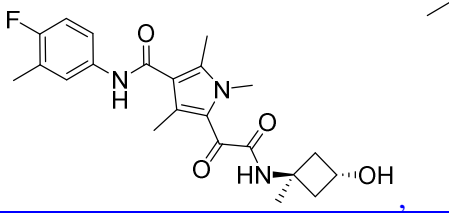

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

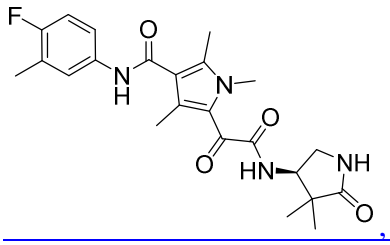
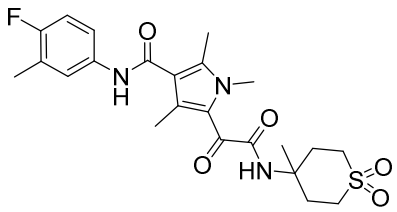
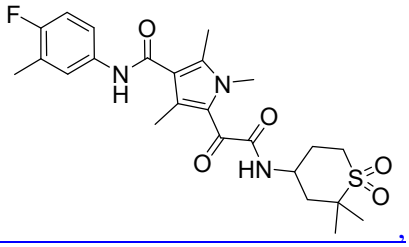
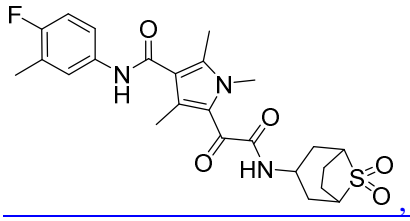
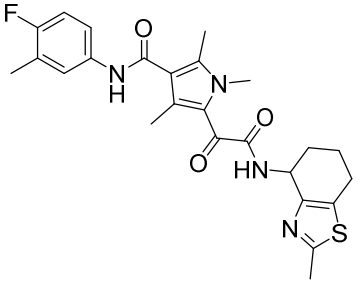
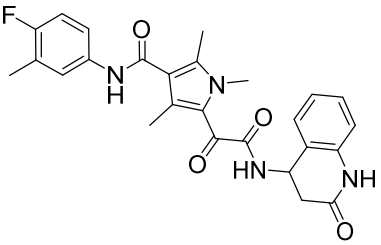
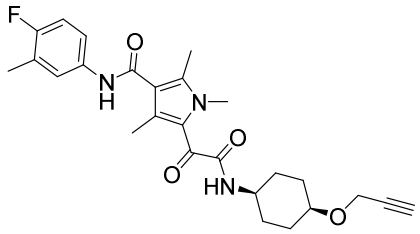
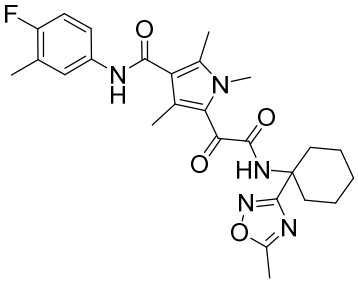
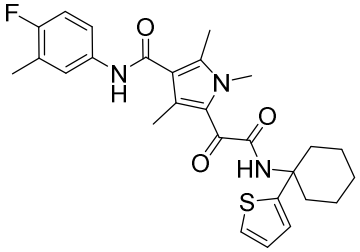
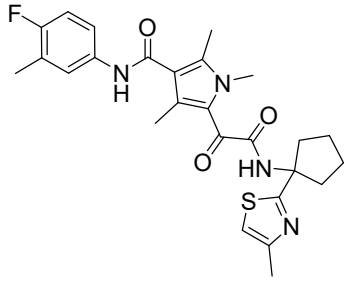
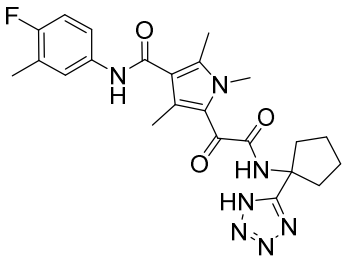
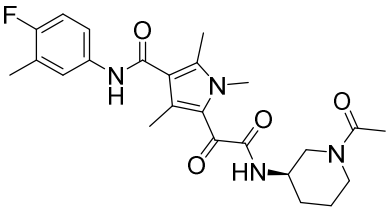
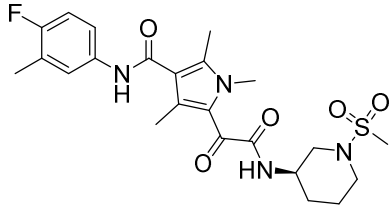
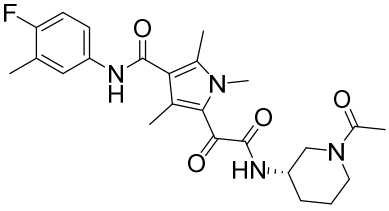
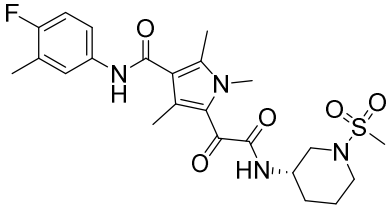
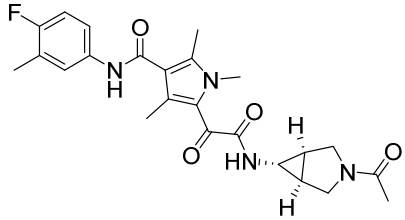
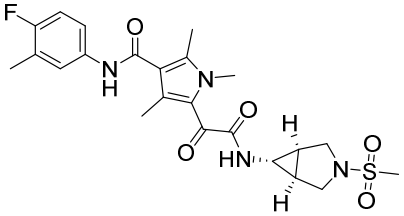
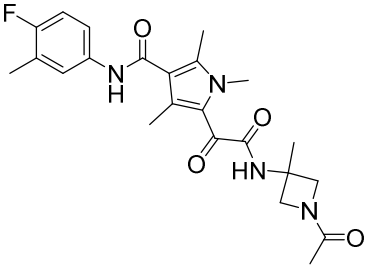













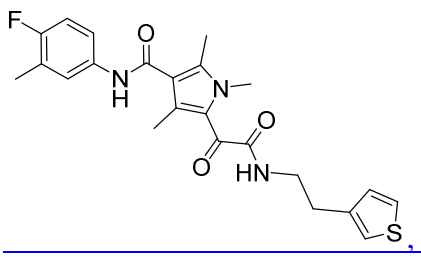
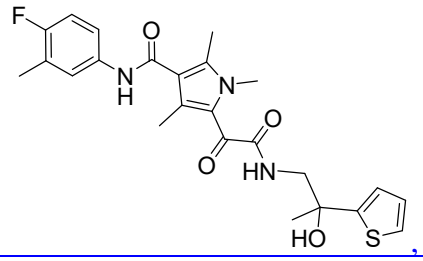
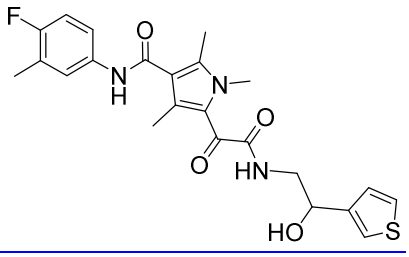
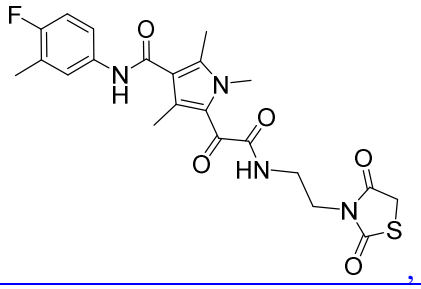
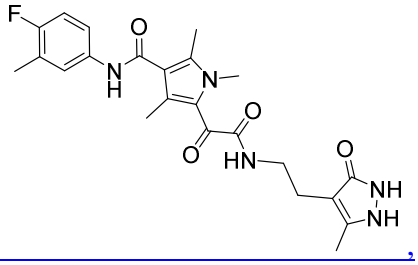
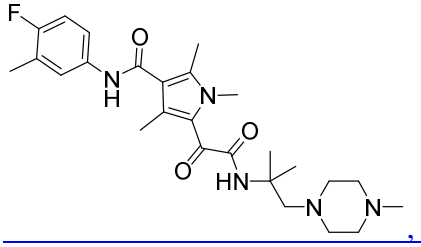
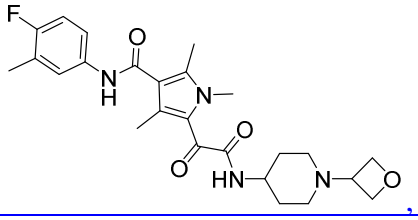
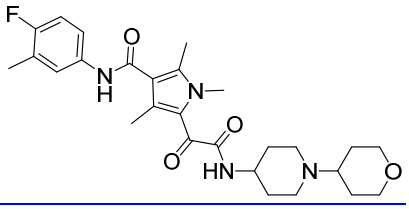
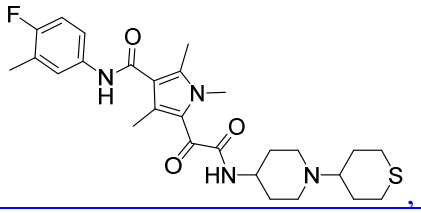
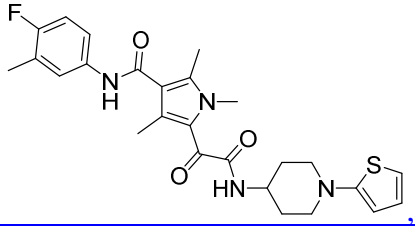
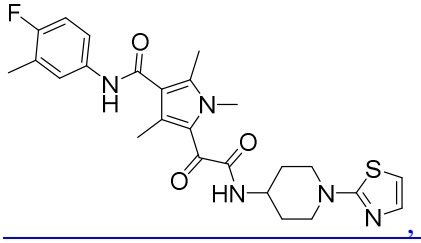
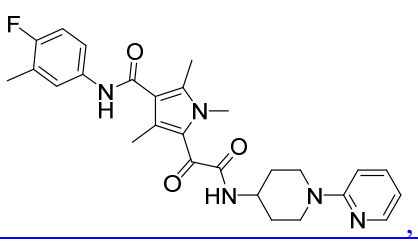
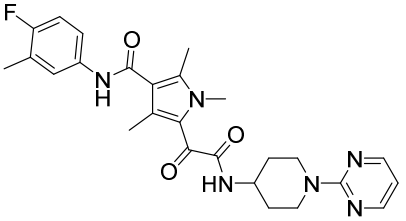
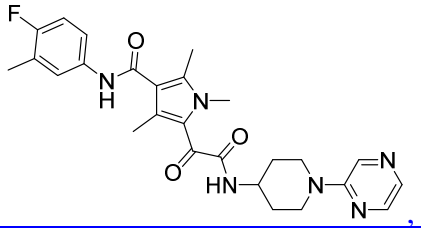
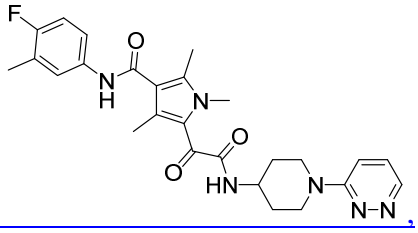


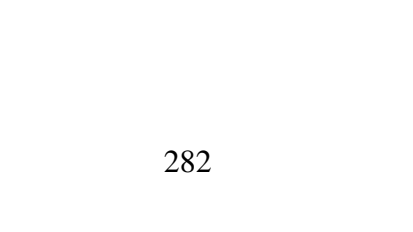


















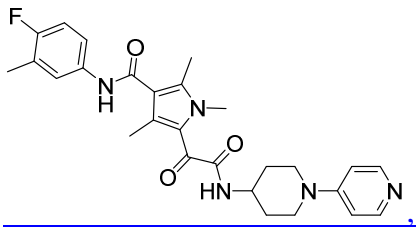
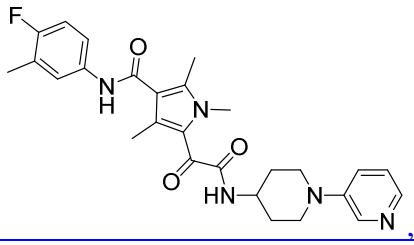
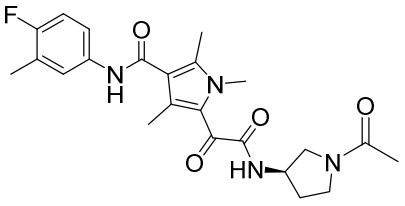
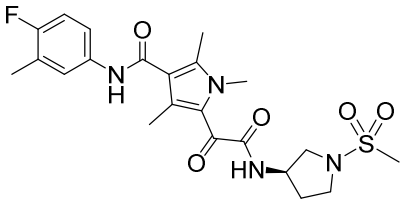
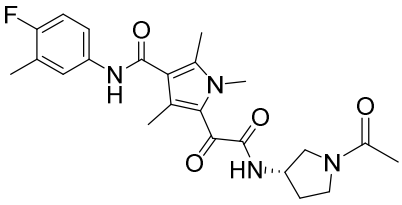
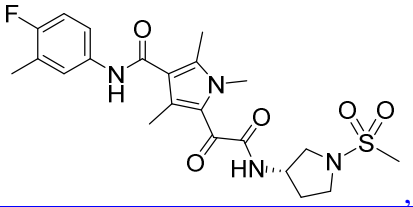
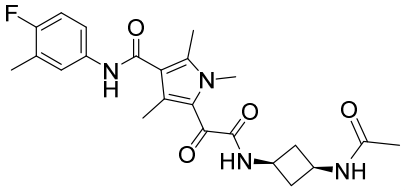
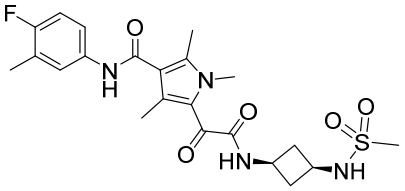
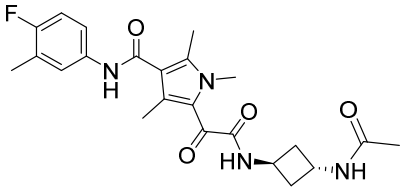
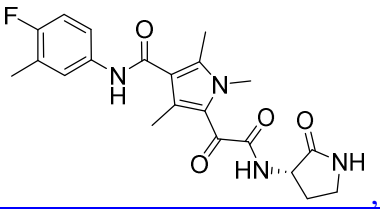
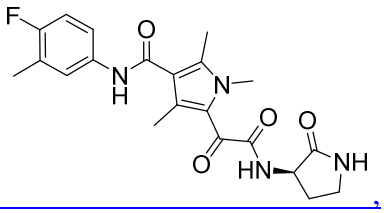
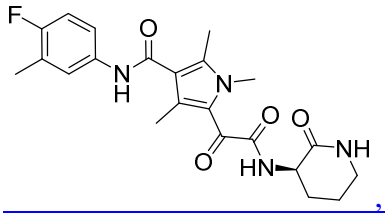
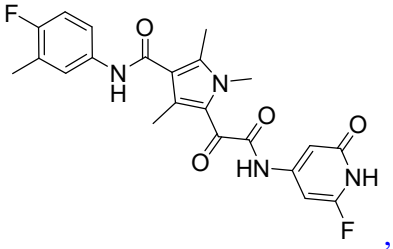
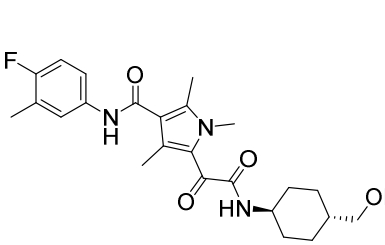
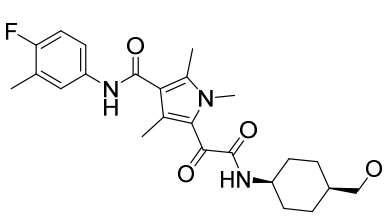
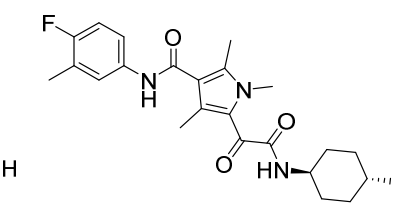
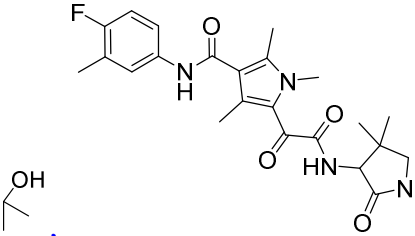



















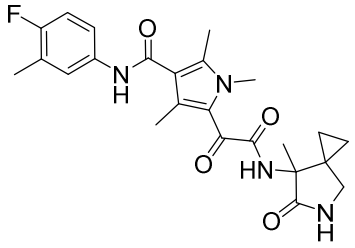
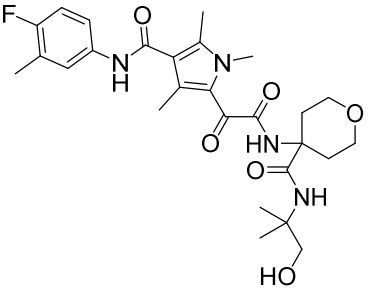
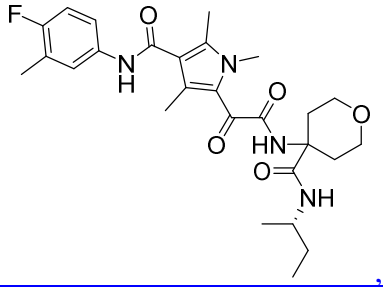
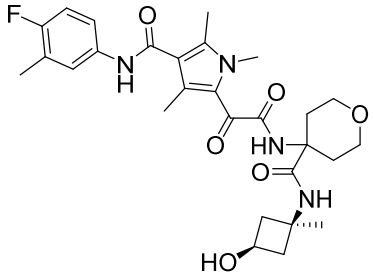
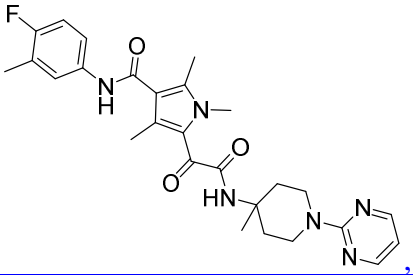
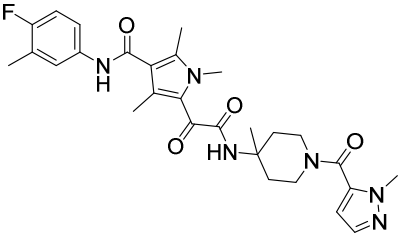
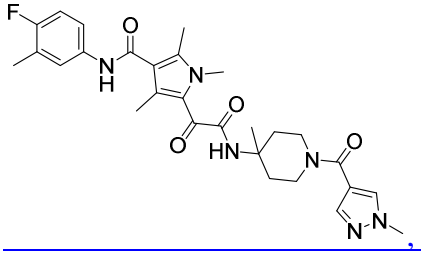
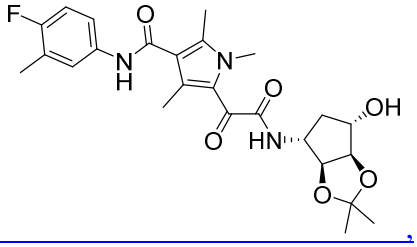
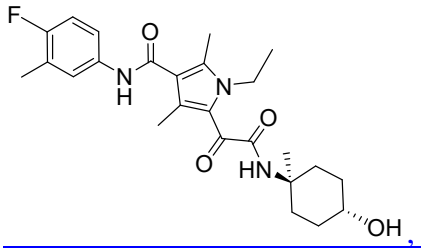
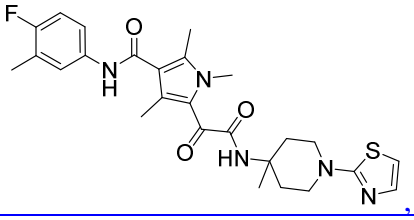
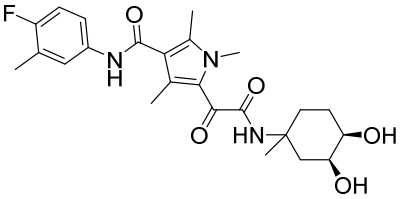
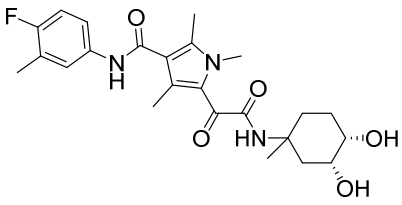
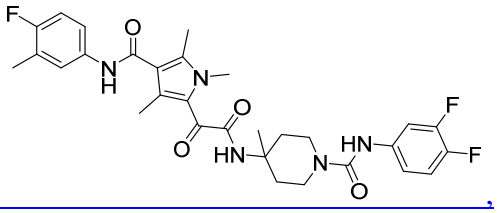
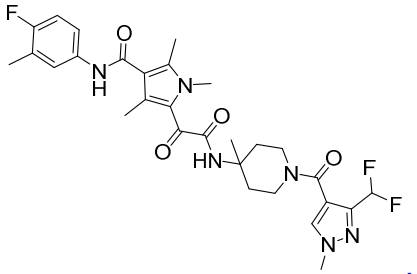
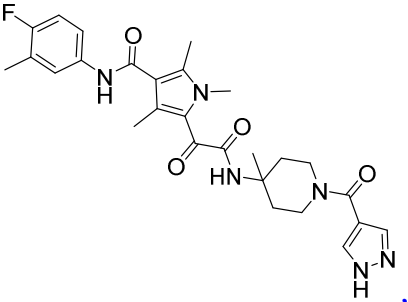
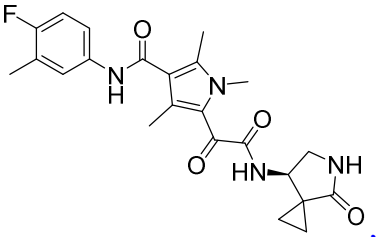


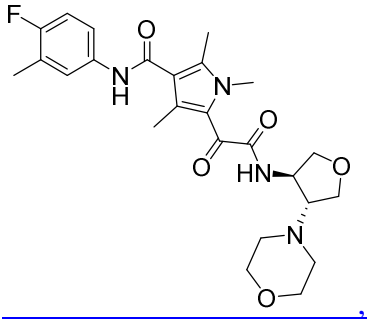
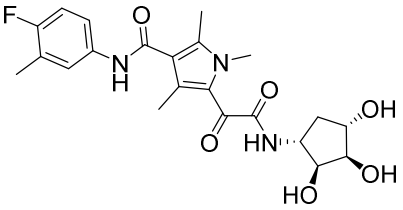
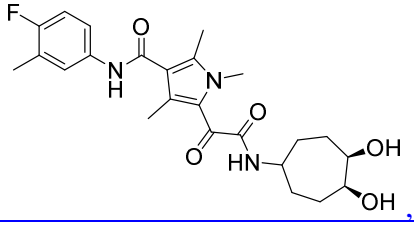

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

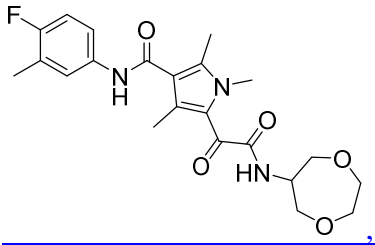
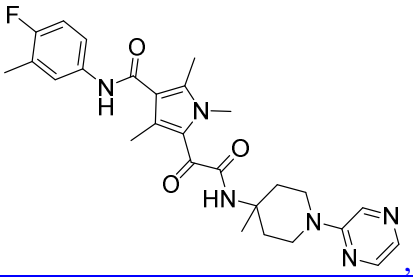
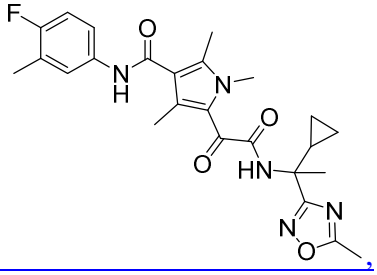
,

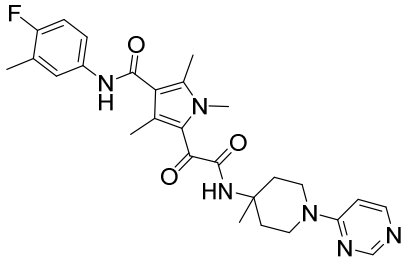
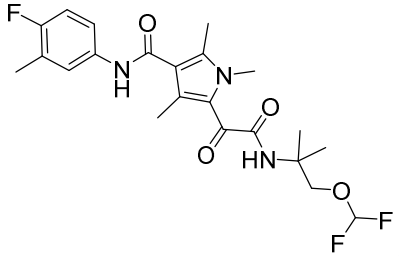
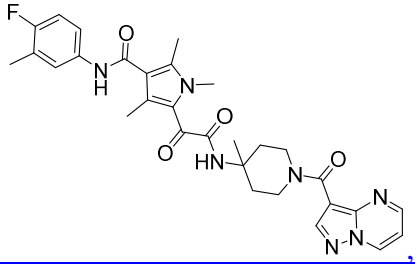
,

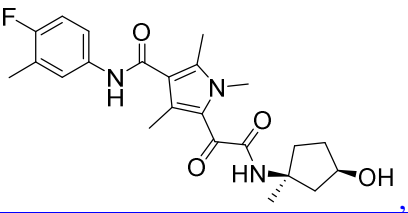
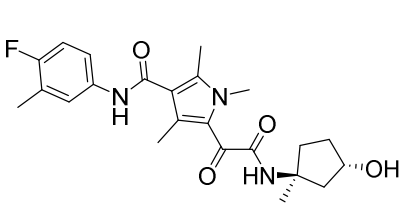
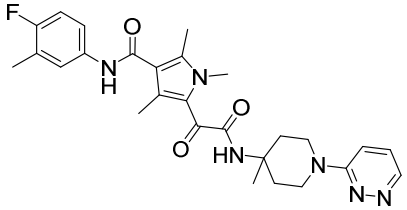
,

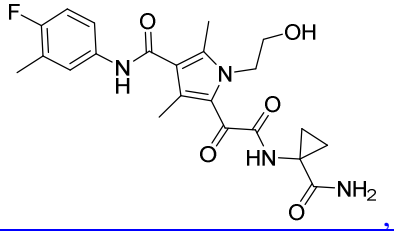
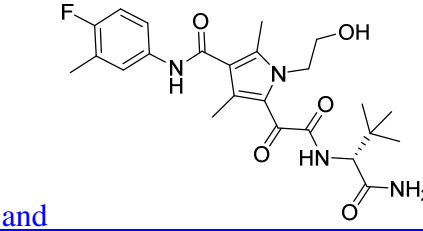

















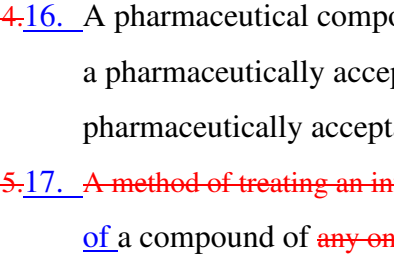
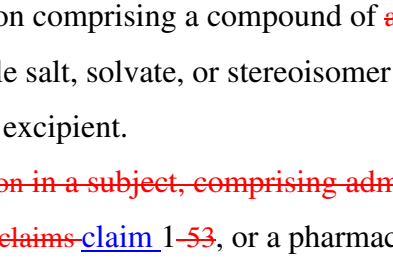

, 
, 
,


, 
, 
,


, 
, 
,


, 
, 
,


, 
,
,


, 
, and .

~~54.~~16. A pharmaceutical composition comprising a compound of ~~any one of claims~~claim 1~~-53~~, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, and a pharmaceutically acceptable excipient.

~~55.~~17. ~~A method of treating an infection in a subject, comprising administering to the subject~~ Use of a compound of ~~any one of claims~~ claim 1~~-53~~, or a pharmaceutically acceptable salt,

solvate, or stereoisomer thereof in the manufacture of a medicament for treating hepatitis B in a subject.

~~56. A method of treating an infection in a subject, comprising administering to the subject a pharmaceutical composition of claim 54.~~

~~57. The method of claim 55 or 56, wherein the infection is a viral infection.~~

~~58. The method of any one of claims 55-57, wherein the infection is caused by the hepatitis B virus.~~

~~59. The method of any one of claims 55-58, wherein the infection is hepatitis B.~~

18. The compound of claim 1, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof for use in therapy.