heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three oxo (when feasible), halogen, -OH, C_1-C_6 alkyl, or C_1-C_6 haloalkyl; and

each R^c and R^d is independently hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein the alkyl, alkenyl, alkynyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three oxo (when feasible), halogen, -OH, C_1-C_6 alkyl, or C_1-C_6 haloalkyl;

or R^c and R^d 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, C_1-C_6 alkyl, or C_1-C_6 haloalkyl.

[0006] Also disclosed herein are pharmaceutical compositions comprising a compound disclosed herein, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, and a pharmaceutically acceptable excipient.

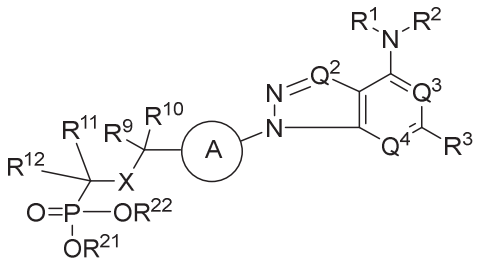
[0007] Also disclosed herein are methods of inhibiting CD73 comprising contacting CD73 with a compound disclosed herein, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof.

[0008] Also disclosed herein are methods of treating cancer in a subject, comprising administering to the subject a compound disclosed herein, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof or administering to the subject a pharmaceutical composition comprising a compound disclosed herein, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, and a pharmaceutically acceptable excipient.

[0009] Also disclosed herein are methods of treating an infection in a subject, comprising administering to the subject a compound disclosed herein, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof or administering to the subject a pharmaceutical composition comprising a compound disclosed herein, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, and a pharmaceutically acceptable excipient.

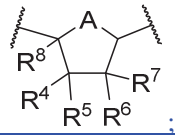
[0010] Also disclosed herein are methods of treating a neurodegenerative disease in a subject, comprising administering to the subject a compound disclosed herein, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof or administering to the subject a pharmaceutical composition comprising a compound disclosed herein, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, and a pharmaceutically acceptable excipient.

[0010a] Also disclosed herein is a compound of Formula (IV), or a pharmaceutically acceptable salt thereof:



Formula (IV);

wherein:

Ring A is 

;

Q^2 is N or CW;

Q^3 is N and Q^4 is CW;

or Q^3 is CW and Q^4 is N;

each W is independently hydrogen, halogen, -CN, $-OR^b$, NR^cR^d, C_1-C_6 alkyl, or C_1-C_6 haloalkyl;

A is -O- or $-CH_2-$;

X is -O-, -S-, $-S(=O)_2-$, $-NR^{17}-$, or $-C(R^{18})_2-$;

R^1 and R^2 are independently hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C_1-C_6 alkyl(aryl), C_1-C_6 alkyl(heteroaryl), C_1-C_6 alkyl(cycloalkyl), or C_1-C_6 alkyl(heterocycloalkyl); wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three R^{1a};

or R^1 and R^2 are taken together with the nitrogen atom to which they are attached to form a heterocycloalkyl optionally substituted with one, two, or three R^{1b};

each R^{1a} and R^{1b} is independently oxo (when feasible), halogen, -CN, $-OR^b$, $-SR^b$, $-S(=O)R^a$, $-NO_2$, $-NR^cR^d$, $-S(=O)_2R^a$, $-NR^bS(=O)_2R^a$, $-S(=O)_2NR^cR^d$, $-C(=O)R^a$, $-OC(=O)R^a$, $-C(=O)OR^b$, $-OC(=O)OR^b$, $-C(=O)NR^cR^d$, $-OC(=O)NR^cR^d$, $-NR^bC(=O)NR^cR^d$, $-NR^bC(=O)R^a$, $-NR^bC(=O)OR^b$, C_1-C_6 alkyl, C_1-C_6 fluoroalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C_1-C_6 alkyl(aryl), C_1-C_6 alkyl(heteroaryl), C_1-C_6 alkyl(cycloalkyl), or C_1-C_6 alkyl(heterocycloalkyl);

R^3 is hydrogen, halogen, -CN, $-OR^b$, $-SR^b$, $-NR^cR^d$, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, C_1-C_6 heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C_1-C_6 alkyl(aryl), C_1-C_6 alkyl(heteroaryl), C_1-C_6 alkyl(cycloalkyl), or C_1-C_6 alkyl(heterocycloalkyl); wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three R^{3a};

each R^{3a} is independently oxo (when feasible), halogen, -CN, $-OR^b$, $-NR^cR^d$, $-C(=O)R^a$, $-C(=O)OR^b$, $-C(=O)NR^cR^d$, C_1-C_6 alkyl, C_1-C_6 fluoroalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl;

R^4 and R^7 are independently hydrogen, halogen, $-OR^b$, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl;

R^5 and R^6 are independently hydrogen, halogen, $-OR^b$, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl;

R^8 is hydrogen, halogen, $-OR^b$, $-NR^cR^d$, C_1-C_6 alkyl, or C_1-C_6 haloalkyl;

R^9 and R^{10} are independently hydrogen, halogen, C_1-C_6 alkyl, or C_1-C_6 haloalkyl;

R^{11} is hydrogen, halogen, -CN, -OR^{13}, -SR^{13}, -S(=O)R^{14}, -NO_2, -$NR^{15}R^{16}$, -$S(=O)_2R^{14}$, -$NR^{13}S(=O)_2R^{14}$, -$S(=O)_2NR^{15}R^{16}$, -C(=O)R^{14}, -OC(=O)R^{14}, -C(=O)OR^{13}, -OC(=O)OR^{13}, -C(=O)$NR^{15}R^{16}$, -OC(=O)$NR^{15}R^{16}$, -NR^{13}C(=O)$NR^{15}R^{16}$, -NR^{13}C(=O)R^{14}, -NR^{13}C(=O)OR^{13}, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, 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^{11a};

R^{12} is halogen, -CN, -OR^{13}, -SR^{13}, -S(=O)R^{14}, -NO_2, -$NR^{15}R^{16}$, -$S(=O)_2R^{14}$, -$NR^{13}S(=O)_2R^{14}$, -$S(=O)_2NR^{15}R^{16}$, -C(=O)R^{14}, -OC(=O)R^{14}, -C(=O)OR^{13}, -OC(=O)OR^{13}, -C(=O)$NR^{15}R^{16}$, -OC(=O)$NR^{15}R^{16}$, -NR^{13}C(=O)$NR^{15}R^{16}$, -NR^{13}C(=O)R^{14}, -NR^{13}C(=O)OR^{13}, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, 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^{12a};

or R^{11} and R^{12} are taken together to form a cycloalkyl or heterocycloalkyl each optionally substituted with one, two, or three R^{11b};

each R^{11a}, R^{11b}, and R^{12a} is independently oxo (when feasible), halogen, -CN, -OR^{13}, -SR^{13}, -S(=O)R^{14}, -NO_2, -$NR^{15}R^{16}$, -$S(=O)_2R^{14}$, -$NR^{13}S(=O)_2R^{14}$, -$S(=O)_2NR^{15}R^{16}$, -C(=O)R^{14}, -OC(=O)R^{14}, -C(=O)OR^{13}, -OC(=O)OR^{13}, -C(=O)$NR^{15}R^{16}$, -OC(=O)$NR^{15}R^{16}$, -NR^{13}C(=O)$NR^{15}R^{16}$, -NR^{13}C(=O)R^{14}, -NR^{13}C(=O)OR^{13}, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 hydroxyalkyl, C_1-C_6 heteroalkyl, 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^{11c};

each R^{11c} is independently oxo (when feasible), halogen, -CN, -OR^{b}, -SR^{b}, -S(=O)R^{a}, -NO_2, -$NR^{c}R^{d}$, -$S(=O)_2R^{a}$, -$NR^{b}S(=O)_2R^{a}$, -$S(=O)_2NR^{c}R^{d}$, -C(=O)R^{a}, -OC(=O)R^{a}, -C(=O)OR^{b}, -OC(=O)OR^{b}, -C(=O)$NR^{c}R^{d}$, -OC(=O)$NR^{c}R^{d}$, -NR^{b}C(=O)$NR^{c}R^{d}$, -NR^{b}C(=O)R^{a}, -NR^{b}C(=O)OR^{b}, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C_1-C_6 alkyl(aryl), C_1-C_6 alkyl(heteroaryl), C_1-C_6 alkyl(cycloalkyl), or C_1-C_6 alkyl(heterocycloalkyl);

each R^{13} is independently hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, 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^{13a};

each R^{14} is independently C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, 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^{14a};

each R^{15} and R^{16} is independently hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, 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^{15a};

or R^{15} and R^{16} are taken together with the nitrogen atom to which they are attached to form a heterocycloalkyl optionally substituted with one, two, or three R^{15b};

each R^{13a}, R^{14a}, R^{15a}, and R^{15b} is independently oxo (when feasible), halogen, -CN, -OR^b, -SR^b, -$S(=O)R^a$, -NO_2, -NR^cR^d, -$S(=O)_2R^a$, -$NHS(=O)_2R^a$, -$S(=O)_2NR^cR^d$, -$C(=O)R^a$, -$OC(=O)R^a$, -$C(=O)OR^b$, -$OC(=O)OR^b$, -$C(=O)NR^cR^d$, -$OC(=O)NR^cR^d$, -$NR^bC(=O)NR^cR^d$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^b$, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C_1-C_6 alkyl(aryl), C_1-C_6 alkyl(heteroaryl), C_1-C_6 alkyl(cycloalkyl), or C_1-C_6 alkyl(heterocycloalkyl); wherein each alkyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three oxo (when feasible), halogen, -CN, -OR^b, -$S(=O)R^a$, -NO_2, -NR^cR^d, -$S(=O)_2R^a$, -$S(=O)_2NR^cR^d$, -$C(=O)R^a$, -$C(=O)OR^b$, -$C(=O)NR^cR^d$, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_2-C_6 alkenyl, or C_2-C_6 alkynyl;

R^{17} is hydrogen, -CN, -OR^b, -$S(=O)_2R^a$, -$C(=O)R^a$, -$C(=O)OR^b$, -$C(=O)NR^cR^d$, C_1-C_6 alkyl, C_1-C_6 fluoroalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C_1-C_6 alkyl(aryl), C_1-C_6 alkyl(heteroaryl), C_1-C_6 alkyl(cycloalkyl), or C_1-C_6 alkyl(heterocycloalkyl);

each R^{18} is independently hydrogen, halogen, -CN, -OR^b, -SR^b, -$S(=O)R^a$, -NO_2, -NR^cR^d, -$S(=O)_2R^a$, -$NHS(=O)_2R^a$, -$S(=O)_2NR^cR^d$, -$C(=O)R^a$, -$OC(=O)R^a$, -$C(=O)OR^b$, -$OC(=O)OR^b$, -$C(=O)NR^cR^d$, -$OC(=O)NR^cR^d$, -$NR^bC(=O)NR^cR^d$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^b$, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C_1-C_6 alkyl(aryl), C_1-C_6 alkyl(heteroaryl), C_1-C_6 alkyl(cycloalkyl), or C_1-C_6 alkyl(heterocycloalkyl);

R^{21} and R^{22} are independently hydrogen, C_1-C_{20} alkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C_1-C_6 alkyl(aryl), C_1-C_6 alkyl(heteroaryl), C_1-C_6 alkyl(cycloalkyl), C_1-C_6 alkyl(heterocycloalkyl); wherein each alkyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three R^{21a};

or R^{21} and R^{22} are taken together with the atoms to which they are attached to form a heterocycloalkyl optionally substituted with one, two, or three R^{21b};

each R^{21a} and R^{21b} is independently oxo (when feasible), halogen, -CN, -OR^b, -SR^b, -$S(=O)R^a$, -NO_2, -NR^cR^d, -$S(=O)_2R^a$, -$NHS(=O)_2R^a$, -$S(=O)_2NR^cR^d$, -$C(=O)R^a$, -$OC(=O)R^a$, -$C(=O)OR^b$, -$OC(=O)OR^b$, -$C(=O)NR^cR^d$, -$OC(=O)NR^cR^d$, -$NR^bC(=O)NR^cR^d$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^b$, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C_1-C_6 alkyl(aryl), C_1-C_6 alkyl(heteroaryl), C_1-C_6 alkyl(cycloalkyl), or C_1-C_6 alkyl(heterocycloalkyl);

each R^a is independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein the alkyl, alkenyl, alkynyl, heteroalkyl, cycloalkyl,

heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three oxo (when feasible), halogen, -OH, C_1-C_6 alkyl, or C_1-C_6 haloalkyl;

each R^b is independently hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein the alkyl, alkenyl, alkynyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three oxo (when feasible), halogen, -OH, C_1-C_6 alkyl, or C_1-C_6 haloalkyl; and

each R^c and R^d is independently hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein the alkyl, alkenyl, alkynyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three oxo (when feasible), halogen, -OH, C_1-C_6 alkyl, or C_1-C_6 haloalkyl;

or R^c and R^d 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, C_1-C_6 alkyl, or C_1-C_6 haloalkyl.

[0010b] Also disclosed herein is a use of a compound as described herein, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating cancer.

[0010c] Also disclosed herein is a compound as described herein, or a pharmaceutically acceptable salt thereof for use in therapy.

INCORPORATION BY REFERENCE

[0011] All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference for the specific purposes identified herein.

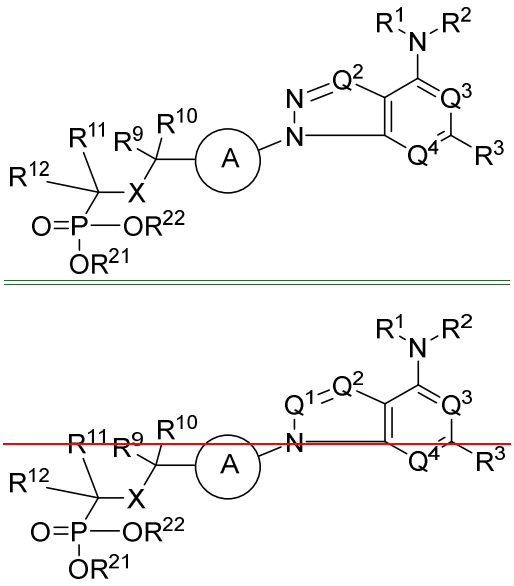
DETAILED DESCRIPTION OF THE INVENTION

[0012] CD73 is a glycosylphosphatidylinositol (GPI) anchored cell surface protein that catalyzes the hydrolysis of AMP to adenosine, and works in concert with CD39, which converts ATP into AMP. The resulting adenosine functions as a signaling molecule that activates the P1 receptors expressed on the cell

CLAIMS

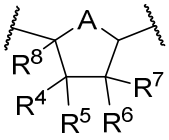
WHAT IS CLAIMED IS:

1. A compound of Formula (~~H~~IV), or a pharmaceutically acceptable salt~~, solvate, stereoisomer, or an isotopic variant~~ thereof:



Formula (~~H~~IV);

wherein:

Ring A is  ;

~~Q[1] is N and~~ Q^2 is N or CW ~~or Q^1~~;

Q^3 is N and ~~Q^2 is N;~~

~~Q^3 and~~ Q^4 ~~are independently N or~~ is CW; ~~provided that at least one of~~

or Q^3 ~~or~~is CW and Q^4 is N;

each W is independently hydrogen, halogen, -CN, $-OR^b$, NR^cR^d, C_1-C_6 alkyl, or C_1-C_6 haloalkyl;

A is -O~~;~~- or $-CH_2-$;

X is -O-, -S~~-~~-, $-S(=O)_2-$, $-NR^{17}-$, or -~~O~~$C(R^{18})_2$-;

R^1 and R^2 are independently hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C_1-C_6 alkyl(aryl), C_1-C_6 alkyl(heteroaryl), C_1-C_6 alkyl(cycloalkyl), or C_1-C_6 alkyl(heterocycloalkyl); wherein each

alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three R^{1a};

or R^1 and R^2 are taken together with the nitrogen atom to which they are attached to form a heterocycloalkyl optionally substituted with one, two, or three R^{1b};

each R^{1a} and R^{1b} is independently oxo (when feasible~~)~~, halogen, -CN, $-OR^b$, $-SR^b$, $-S(=O)R^a$, $-NO_2$, $-NR^cR^d$, $-S(=O)_2R^a$, $-NR^bS(=O)_2R^a$, $-S(=O)_2NR^cR^d$, $-C(=O)R^a$, $-OC(=O)R^a$, $-C(=O)OR^b$, $-OC(=O)OR^b$, $-C(=O)NR^cR^d$, $-OC(=O)NR^cR^d$, $-NR^bC(=O)NR^cR^d$, $-NR^bC(=O)R^a$, $-NR^bC(=O)OR^b$, C_1-C_6 alkyl, C_1-C_6 fluoroalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C_1-C_6 alkyl(aryl), C_1-C_6 alkyl(heteroaryl), C_1-C_6 alkyl(cycloalkyl), or C_1-C_6 alkyl(heterocycloalkyl);

R^3 is hydrogen, halogen, -CN, $-OR^b$, $-SR^b$, $-NR^cR^d$, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, C_1-C_6 heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C_1-C_6 alkyl(aryl), C_1-C_6 alkyl(heteroaryl), C_1-C_6 alkyl(cycloalkyl), or C_1-C_6 alkyl(heterocycloalkyl); wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three R^{3a};

each R^{3a} is independently oxo (when feasible), ~~halogen, -CN, $-OR^b$, $-NR^cR^d$, $-C(=O)R^a$, $-C(=O)OR^b$, $-C(=O)NR^cR^d$, C_1-C_6 alkyl, C_1-C_6 fluoroalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl;~~

~~R^4 and R^7 are independently hydrogen, halogen, $-OR^b$, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl;~~

~~R^5 and R^6 are independently hydrogen, halogen, $-OR^b$, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl;~~

~~R^8 is hydrogen, halogen, $-OR^b$, $-NR^cR^d$, C_1-C_6 alkyl, or C_1-C_6 haloalkyl;~~

~~R^9 and R^{10} are independently hydrogen, halogen, C_1-C_6 alkyl, or C_1-C_6 haloalkyl;~~

~~R^{11} is halogen, -CN, $-OR^{13}$, $-SR^{13}$, $-S(=O)R^{14}$, $-NO_2$, $-NR^{15}R^{16}$, $-S(=O)_2R^{14}$, $-NR^{13}S(=O)_2R^{14}$, $-S(=O)_2NR^{15}R^{16}$, $-C(=O)R^{14}$, $-OC(=O)R^{14}$, $-C(=O)OR^{13}$, $-OC(=O)OR^{13}$, $-C(=O)NR^{15}R^{16}$, $-OC(=O)NR^{15}R^{16}$, $-NR^{13}C(=O)NR^{15}R^{16}$, $-NR^{13}C(=O)R^{14}$, $-NR^{13}C(=O)OR^{13}$, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, 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^{11a};~~

R^{12} is hydrogen, halogen, $-CN$, $-OR^{13}$, $-SR^{13}$, $-S(=O)R^{14}$, $-NO_2$, $-NR^{15}R^{16}$, $-S(=O)_2R^{14}$, $-NR^{13}S(=O)_2R^{14}$, $-S(=O)_2NR^{15}R^{16}$, $-C(=O)R^{14}$, $-OC(=O)R^{14}$, $-C(=O)OR^{13}$, $-OC(=O)OR^{13}$, $-C(=O)NR^{15}R^{16}$, $-OC(=O)NR^{15}R^{16}$, $-NR^{13}C(=O)NR^{15}R^{16}$, $-NR^{13}C(=O)R^{14}$, $-NR^{13}C(=O)OR^{13}$, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, 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^{12a};

or R^{11} and R^{12} are taken together to form a cycloalkyl or heterocycloalkyl each optionally substituted with one, two, or three R^{11b};

each R^{11a}, R^{11b}, and R^{12a} is independently oxo (when feasible), halogen, $-CN$, $-OR^{13}$, $-SR^{13}$, $-S(=O)R^{14}$, $-NO_2$, $-NR^{15}R^{16}$, $-S(=O)_2R^{14}$, $-NR^{13}S(=O)_2R^{14}$, $-S(=O)_2NR^{15}R^{16}$, $-C(=O)R^{14}$, $-OC(=O)R^{14}$, $-C(=O)OR^{13}$, $-OC(=O)OR^{13}$, $-C(=O)NR^{15}R^{16}$, $-OC(=O)NR^{15}R^{16}$, $-NR^{13}C(=O)NR^{15}R^{16}$, $-NR^{13}C(=O)R^{14}$, $-NR^{13}C(=O)OR^{13}$, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 hydroxyalkyl, C_1-C_6 heteroalkyl, 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^{11c};

each R^{11c} is independently oxo (when feasible), halogen, $-CN$, $-OR^b$, $-SR^b$, $-S(=O)R^a$, $-NO_2$, $-NR^cR^d$, $-S(=O)_2R^a$, $-NR^bS(=O)_2R^a$, $-S(=O)_2NR^cR^d$, $-C(=O)R^a$, $-OC(=O)R^a$, $-C(=O)OR^b$, $-OC(=O)OR^b$, $-C(=O)NR^cR^d$, $-OC(=O)NR^cR^d$, $-NR^bC(=O)NR^cR^d$, $-NR^bC(=O)R^a$, $-NR^bC(=O)OR^b$, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C_1-C_6 alkyl(aryl), C_1-C_6 alkyl(heteroaryl), C_1-C_6 alkyl(cycloalkyl), or C_1-C_6 alkyl(heterocycloalkyl);

each R^{13} is independently hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, 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^{13a};

each R^{14} is independently C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, 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^{14a};

each R^{15} and R^{16} is independently hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, 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^{15a};

or R^{15} and R^{16} are taken together with the nitrogen atom to which they are attached to form a heterocycloalkyl optionally substituted with one, two, or three R^{15b};

each R^{13a}, R^{14a}, R^{15a}, and R^{15b} is independently oxo (when feasible), halogen, -CN, $-OR^b$, $-SR^b$, $-S(=O)R^a$, $-NO_2$, $-NR^eR^d$, $-S(=O)_2R^a$, $-NR^bS(=O)_2R^a$, $-S(=O)_2NR^eR^d$, $-C(=O)R^a$, $-OC(=O)R^a$, $-C(=O)OR^b$, $-OC(=O)OR^b$, $-C(=O)NR^eR^d$, $-OC(=O)NR^eR^d$, $-NR^bC(=O)NR^eR^d$, $-NR^bC(=O)R^a$, $-NR^bC(=O)OR^b$, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C_1-C_6 alkyl(aryl), C_1-C_6 alkyl(heteroaryl), C_1-C_6 alkyl(cycloalkyl), or C_1-C_6 alkyl(heterocycloalkyl); wherein each alkyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three oxo (when feasible), halogen, -CN, $-OR^b$, $-S(=O)R^a$, $-NO_2$, $-NR^eR^d$, $-S(=O)_2R^a$, $-S(=O)_2NR^eR^d$, $-C(=O)R^a$, $-C(=O)OR^b$, $-C(=O)NR^eR^d$, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_2-C_6 alkenyl, or C_2-C_6 alkynyl;

R^{21} and R^{22} are independently hydrogen, C_1-C_{20} alkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C_1-C_6 alkyl(aryl), C_1-C_6 alkyl(heteroaryl), C_1-C_6 alkyl(cycloalkyl), C_1-C_6 alkyl(heterocycloalkyl); wherein each alkyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three R^{21a};

or R^{21} and R^{22} are taken together with the atoms to which they are attached to form a heterocycloalkyl optionally substituted with one, two, or three R^{21b};

each R^{21a} and R^{21b} is independently oxo (when feasible), halogen, -CN, $-OR^b$, $-SR^b$, $-S(=O)R^a$, $-NO_2$, $-NR^eR^d$, $-S(=O)_2R^a$, $-NR^bS(=O)_2R^a$, $-S(=O)_2NR^eR^d$, $-C(=O)R^a$, $-OC(=O)R^a$, $-C(=O)OR^b$, $-OC(=O)OR^b$, $-C(=O)NR^eR^d$, $-OC(=O)NR^eR^d$, $-NR^bC(=O)NR^eR^d$, $-NR^bC(=O)R^a$, $-NR^bC(=O)OR^b$, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C_1-C_6 alkyl(aryl), C_1-C_6 alkyl(heteroaryl), C_1-C_6 alkyl(cycloalkyl), or C_1-C_6 alkyl(heterocycloalkyl);

each R^a is independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein the alkyl, alkenyl, alkynyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three oxo (when feasible), halogen, -OH, C_1-C_6 alkyl, or C_1-C_6 haloalkyl;

each R^b is independently hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein the alkyl, alkenyl, alkynyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three oxo (when feasible), halogen, -OH, C_1-C_6 alkyl, or C_1-C_6 haloalkyl; and

each R^e and R^d is independently hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein the alkyl, alkenyl, alkynyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally

substituted with one, two, or three oxo (when feasible), halogen, –OH, C_1-C_6 alkyl, or C_1-C_6 haloalkyl;

or R^e and R^d 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, C_1-C_6 alkyl, or C_1-C_6 haloalkyl.

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

Q^1 is N; and

Q^2 is CW.

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

Q^1 is N; and

Q^2 is N.

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

Q^3 is N and Q^4 is CW.

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

Q^4 is N and Q^3 is CW.

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

Q^3 is N and Q^4 is N.

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

each W is independently hydrogen, halogen, or C_1-C_6 alkyl.

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

each W is hydrogen.

9. The compound of any one of claims 1-8, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

R^3 is halogen, $-OR^b$, C_1-C_6 alkyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, or C_1-C_6 heteroalkyl; wherein each alkyl and alkynyl is independently optionally substituted with one, two, or three R^{3a}.

10. The compound of any one of claims 1-9, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

R^3 is halogen, $-OR^b$, C_2-C_6 alkynyl, or C_1-C_6 hydroxyalkyl; wherein each alkyl and alkynyl is independently optionally substituted with one, two, or three R^{3a}.

11. The compound of any one of claims 1-10, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

R^3 is halogen.

12. The compound of any one of claims 1-11, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

R^1 is C_1-C_6 alkyl, C_1-C_6 haloalkyl, cycloalkyl, heterocycloalkyl, C_1-C_6 alkyl(aryl), C_1-C_6 alkyl(heteroaryl), C_1-C_6 alkyl(cycloalkyl), or C_1-C_6 alkyl(heterocycloalkyl); wherein each alkyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three R^{1a}.

13. The compound of any one of claims 1-12, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

R^1 is C_1-C_6 alkyl, cycloalkyl, C_1-C_6 alkyl(aryl), or C_1-C_6 alkyl(cycloalkyl); wherein each alkyl, cycloalkyl, and aryl is independently optionally substituted with one, two, or three R^{1a}.

14. The compound of any one of claims 1-13, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

R^1 is cycloalkyl optionally substituted with one, two, or three R^{1a}.

15. The compound of any one of claims 1-14, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

each R^{1a} is independently oxo (when feasible) halogen, -CN, $-OR^b$, C_1-C_6 alkyl, or C_1-C_6 fluoroalkyl.

16. The compound of any one of claims 1-15, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

each R^{1a} is independently halogen or C_1-C_6 alkyl.

17. The compound of any one of claims 1-16, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

R^2 is hydrogen or C_1-C_6 alkyl.

18. The compound of any one of claims 1-17, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

R^2 is hydrogen.

19. The compound of any one of claims 1-18, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

R^8 is hydrogen or C_1-C_6 alkyl.

20. The compound of any one of claims 1-19, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

R^8 is hydrogen.

21. The compound of any one of claims 1-20, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

R^9 and R^{10} are independently hydrogen or C_1-C_6 alkyl.

22. The compound of any one of claims 1-21, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

R^9 and R^{10} are hydrogen.

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

A is O.

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

X is O.

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

R^5 and R^6 are independently hydrogen, halogen, OR^b, C_1-C_6 alkyl, or C_1-C_6 haloalkyl.

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

R^5 and R^6 are hydrogen.

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

R^4 and R^7 are independently hydrogen, halogen, OR^b, C_1-C_6 alkyl, or C_1-C_6 haloalkyl.

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

R^4 and R^7 are independently hydrogen, halogen, or OH.

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

R^4 and R^7 are independently halogen or OH.

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

R^4 and R^7 are independently hydrogen or OH.

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

R^4 and R^7 are –OH.

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

R^{21} and R^{22} are hydrogen.

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

R^{12} is hydrogen, halogen, $-OR^{13}$, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, C_2-C_6 alkynyl, or C_1-C_6 heteroalkyl; wherein each alkyl and alkynyl is independently optionally substituted with one, two, or three R^{12a}.

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

R^{12} is hydrogen, C_1-C_6 alkyl, C_1-C_6 hydroxyalkyl, or C_2-C_6 alkynyl; wherein each alkyl and alkynyl is independently optionally substituted with one, two, or three R^{12a}.

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

R^{12} is hydrogen.

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

R^{11} is halogen, –CN, $-OR^{13}$, $-NR^{15}R^{16}$, $-S(=O)_2R^{14}$, $-C(=O)OR^{13}$, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three R^{11a}.

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

R^{11} is –CN, $-S(=O)_2R^{14}$, $-C(=O)OR^{13}$, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, C_2-C_6 alkynyl, or heteroaryl; wherein each alkyl, alkynyl, and heteroaryl is independently optionally substituted with one, two, or three R^{11a}.

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

R^{11} is –CN, $-S(=O)_2R^{14}$, $-C(=O)OR^{13}$, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, or heteroaryl; wherein each alkyl and heteroaryl is independently optionally substituted with one, two, or three R^{11a}.

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

R^{11} is C_1-C_6 alkyl optionally substituted with one, two, or three R^{11a}.

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

R^{11} is C_1-C_6 alkyl substituted with one R^{11a}.

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

each R^{11a} is oxo (when feasible), halogen, -CN, $-OR^{13}$, $-SR^{13}$, $-S(=O)R^{14}$, $-NR^{15}R^{16}$, $-S(=O)_2R^{14}$, $-NR^{13}S(=O)_2R^{14}$, $-S(=O)_2NR^{15}R^{16}$, $-C(=O)R^{14}$, $-C(=O)OR^{13}$, $-C(=O)NR^{15}R^{16}$, $-OC(=O)NR^{15}R^{16}$, $-NR^{13}C(=O)R^{14}$, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, C_1-C_6 heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three R^{11e}.

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

each R^{11a} is independently oxo (when feasible), halogen, $-OR^{13}$, $-SR^{13}$, $-NR^{15}R^{16}$, $-S(=O)_2R^{14}$, $-NR^{13}S(=O)_2R^{14}$, $-S(=O)_2NR^{15}R^{16}$, $-C(=O)OR^{13}$, $-OC(=O)NR^{15}R^{16}$, $-NR^{13}C(=O)R^{14}$, heterocycloalkyl, aryl, or heteroaryl; wherein each heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three R^{11e}.

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

each R^{11a} is independently $-OR^{13}$.

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

R^{11} and R^{12} are taken together to form a cycloalkyl or heterocycloalkyl each optionally substituted with one, two, or three R^{11b}.

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

each R^{13} is independently hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three R^{13a}.

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

each R^{13} is independently C_1-C_6 alkyl, C_1-C_6 haloalkyl, or cycloalkyl; wherein each alkyl and cycloalkyl is independently optionally substituted with one, two, or three R^{13a}.

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

each R^{13} is independently C_1-C_6 alkyl.

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

each R^{14} is independently C_1-C_6 alkyl.

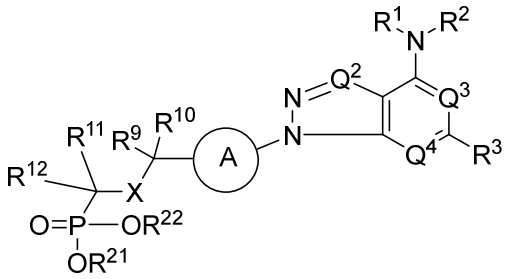
49. The compound of any one of claims 1-48, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

each R^{15} and R^{16} is independently hydrogen or C_1-C_6 alkyl.

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

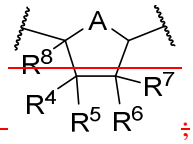
R^{15} and R^{16} are taken together with the nitrogen atom to which they are attached to form a heterocycloalkyl.

51. A compound of Formula (IV), or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof:



Formula (IV);

wherein:

Ring A is  ;

Q^2 is N or CW;

Q^3 is N and Q^4 is CW;

or Q^3 is CW and Q^4 is N;

each W is independently hydrogen, halogen, -CN, $-OR^b$, $-NR^eR^d$, C_1-C_6 alkyl, or C_1-C_6 haloalkyl;

A is -O- or $-CH_2-$;

X is -O-, -S-, $-S(=O)_2-$, $-NR^{17}-$, or $-C(R^{18})_2-$;

R^1 and R^2 are independently hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C_1-C_6 alkyl(aryl), C_1-C_6 alkyl(heteroaryl), C_1-C_6 alkyl(cycloalkyl), or C_1-C_6 alkyl(heterocycloalkyl); wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three R^{1a};

~~or R^1 and R^2 are taken together with the nitrogen atom to which they are attached to form a heterocycloalkyl optionally substituted with one, two, or three R^{1b};~~

~~each R^{1a} and R^{1b} is independently oxo (when feasible) halogen, -CN, $-OR^b$, $-SR^b$, $-S(=O)R^a$, $-NO_2$, $-NR^cR^d$, $-S(=O)_2R^a$, $-NR^bS(=O)_2R^a$, $-S(=O)_2NR^cR^d$, $-C(=O)R^a$, $-OC(=O)R^a$, $-C(=O)OR^b$, $-OC(=O)OR^b$, $-C(=O)NR^cR^d$, $-OC(=O)NR^cR^d$, $-NR^bC(=O)NR^cR^d$, $-NR^bC(=O)R^a$, $-NR^bC(=O)OR^b$, C_1-C_6 alkyl, C_1-C_6 fluoroalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C_1-C_6 alkyl(aryl), C_1-C_6 alkyl(heteroaryl), C_1-C_6 alkyl(cycloalkyl), or C_1-C_6 alkyl(heterocycloalkyl);~~

~~R^3 is hydrogen, halogen, -CN, $-OR^b$, $-SR^b$, $-NR^cR^d$, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, C_1-C_6 heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C_1-C_6 alkyl(aryl), C_1-C_6 alkyl(heteroaryl), C_1-C_6 alkyl(cycloalkyl), or C_1-C_6 alkyl(heterocycloalkyl); wherein each alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three R^{3a};~~

~~each R^{3a} is independently oxo (when feasible)~~ halogen, -CN, $-OR^b$, $-NR^cR^d$, $-C(=O)R^a$, $-C(=O)OR^b$, $-C(=O)NR^cR^d$, C_1-C_6 alkyl, C_1-C_6 fluoroalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl;

R^4 and R^7 are independently hydrogen, halogen, $-OR^b$, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl;

R^5 and R^6 are independently hydrogen, halogen, $-OR^b$, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl;

R^8 is hydrogen, halogen, $-OR^b$, $-NR^cR^d$, C_1-C_6 alkyl, or C_1-C_6 haloalkyl;

R^9 and R^{10} are independently hydrogen, halogen, C_1-C_6 alkyl, or C_1-C_6 haloalkyl;

R^{11} is hydrogen, halogen, -CN, $-OR^{13}$, $-SR^{13}$, $-S(=O)R^{14}$, $-NO_2$, $-NR^{15}R^{16}$, $-S(=O)_2R^{14}$, $-NR^{13}S(=O)_2R^{14}$, $-S(=O)_2NR^{15}R^{16}$, $-C(=O)R^{14}$, $-OC(=O)R^{14}$, $-C(=O)OR^{13}$, $-OC(=O)OR^{13}$, $-C(=O)NR^{15}R^{16}$, $-OC(=O)NR^{15}R^{16}$, $-NR^{13}C(=O)NR^{15}R^{16}$, $-NR^{13}C(=O)R^{14}$, $-NR^{13}C(=O)OR^{13}$, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, 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^{11a};

R^{12} is ~~hydrogen,~~ halogen, -CN, $-OR^{13}$, $-SR^{13}$, $-S(=O)R^{14}$, $-NO_2$, $-NR^{15}R^{16}$, $-S(=O)_2R^{14}$, $-NR^{13}S(=O)_2R^{14}$, $-S(=O)_2NR^{15}R^{16}$, $-C(=O)R^{14}$, $-OC(=O)R^{14}$, $-C(=O)OR^{13}$, $-OC(=O)OR^{13}$, $-C(=O)NR^{15}R^{16}$, $-OC(=O)NR^{15}R^{16}$, $-NR^{13}C(=O)NR^{15}R^{16}$, $-NR^{13}C(=O)R^{14}$, $-NR^{13}C(=O)OR^{13}$, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, C_2-C_6 alkenyl, C_2-C_6

alkynyl, C_1-C_6 heteroalkyl, 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^{12a};

or R^{11} and R^{12} are taken together to form a cycloalkyl or heterocycloalkyl each optionally substituted with one, two, or three R^{11b};

each R^{11a}, R^{11b}, and R^{12a} is independently oxo (when feasible), halogen, -CN, -OR^{13}, -SR^{13}, -$S(=O)R^{14}$, -NO_2, -$NR^{15}R^{16}$, -$S(=O)_2R^{14}$, -$NR^{13}S(=O)_2R^{14}$, -$S(=O)_2NR^{15}R^{16}$, -$C(=O)R^{14}$, -$OC(=O)R^{14}$, -$C(=O)OR^{13}$, -$OC(=O)OR^{13}$, -$C(=O)NR^{15}R^{16}$, -$OC(=O)NR^{15}R^{16}$, -$NR^{13}C(=O)NR^{15}R^{16}$, -$NR^{13}C(=O)R^{14}$, -$NR^{13}C(=O)OR^{13}$, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 hydroxyalkyl, C_1-C_6 heteroalkyl, 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^{11c};

each R^{11c} is independently oxo (when feasible), halogen, -CN, -OR^b, -SR^b, -$S(=O)R^a$, -NO_2, -NR^cR^d, -$S(=O)_2R^a$, -$NR^bS(=O)_2R^a$, -$S(=O)_2NR^cR^d$, -$C(=O)R^a$, -$OC(=O)R^a$, -$C(=O)OR^b$, -$OC(=O)OR^b$, -$C(=O)NR^cR^d$, -$OC(=O)NR^cR^d$, -$NR^bC(=O)NR^cR^d$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^b$, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C_1-C_6 alkyl(aryl), C_1-C_6 alkyl(heteroaryl), C_1-C_6 alkyl(cycloalkyl), or C_1-C_6 alkyl(heterocycloalkyl);

each R^{13} is independently hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, 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^{13a};

each R^{14} is independently C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, 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^{14a};

each R^{15} and R^{16} is independently hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, 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^{15a};

or R^{15} and R^{16} are taken together with the nitrogen atom to which they are attached to form a heterocycloalkyl optionally substituted with one, two, or three R^{15b};

each R^{13a}, R^{14a}, R^{15a}, and R^{15b} is independently oxo (when feasible), halogen, -CN, -OR^b, -SR^b, -$S(=O)R^a$, -NO_2, -NR^cR^d, -$S(=O)_2R^a$, -$NHS(=O)_2R^a$, -$S(=O)_2NR^cR^d$, -$C(=O)R^a$, -$OC(=O)R^a$, -$C(=O)OR^b$, -$OC(=O)OR^b$, -$C(=O)NR^cR^d$, -$OC(=O)NR^cR^d$, -$NR^bC(=O)NR^cR^d$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^b$, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C_1-C_6 alkyl(aryl), C_1-C_6 alkyl(heteroaryl), C_1-C_6 alkyl(cycloalkyl), or C_1-C_6 alkyl(heterocycloalkyl); wherein each alkyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three oxo (when feasible), halogen, -CN, -OR^b, -$S(=O)R^a$, -NO_2, -NR^cR^d, -$S(=O)_2R^a$, -$S(=O)_2NR^cR^d$, -$C(=O)R^a$, -$C(=O)OR^b$, -$C(=O)NR^cR^d$, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_2-C_6 alkenyl, or C_2-C_6 alkynyl;

R^{17} is hydrogen, -CN, -OR^b, -$S(=O)_2R^a$, -$C(=O)R^a$, -$C(=O)OR^b$, -$C(=O)NR^cR^d$, C_1-C_6 alkyl, C_1-C_6 fluoroalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C_1-C_6 alkyl(aryl), C_1-C_6 alkyl(heteroaryl), C_1-C_6 alkyl(cycloalkyl), or C_1-C_6 alkyl(heterocycloalkyl);

each R^{18} is independently hydrogen, halogen, -CN, -OR^b, -SR^b, -$S(=O)R^a$, -NO_2, -NR^cR^d, -$S(=O)_2R^a$, -$NHS(=O)_2R^a$, -$S(=O)_2NR^cR^d$, -$C(=O)R^a$, -$OC(=O)R^a$, -$C(=O)OR^b$, -$OC(=O)OR^b$, -$C(=O)NR^cR^d$, -$OC(=O)NR^cR^d$, -$NR^bC(=O)NR^cR^d$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^b$, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C_1-C_6 alkyl(aryl), C_1-C_6 alkyl(heteroaryl), C_1-C_6 alkyl(cycloalkyl), or C_1-C_6 alkyl(heterocycloalkyl);

R^{21} and R^{22} are independently hydrogen, C_1-C_{20} alkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C_1-C_6 alkyl(aryl), C_1-C_6 alkyl(heteroaryl), C_1-C_6 alkyl(cycloalkyl), C_1-C_6 alkyl(heterocycloalkyl); wherein each alkyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three R^{21a};

or R^{21} and R^{22} are taken together with the atoms to which they are attached to form a heterocycloalkyl optionally substituted with one, two, or three R^{21b};

each R^{21a} and R^{21b} is independently oxo (when feasible), halogen, -CN, -OR^b, -SR^b, -$S(=O)R^a$, -NO_2, -NR^cR^d, -$S(=O)_2R^a$, -$NHS(=O)_2R^a$, -$S(=O)_2NR^cR^d$, -$C(=O)R^a$, -$OC(=O)R^a$, -$C(=O)OR^b$, -$OC(=O)OR^b$, -$C(=O)NR^cR^d$, -$OC(=O)NR^cR^d$, -$NR^bC(=O)NR^cR^d$, -$NR^bC(=O)R^a$, -$NR^bC(=O)OR^b$, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6

alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, C_1-C_6 alkyl(aryl), C_1-C_6 alkyl(heteroaryl), C_1-C_6 alkyl(cycloalkyl), or C_1-C_6 alkyl(heterocycloalkyl);

each R^a is independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein the alkyl, alkenyl, alkynyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three oxo (when feasible), halogen, -OH, C_1-C_6 alkyl, or C_1-C_6 haloalkyl;

each R^b is independently hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein the alkyl, alkenyl, alkynyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three oxo (when feasible), halogen, -OH, C_1-C_6 alkyl, or C_1-C_6 haloalkyl; and

each R^c and R^d is independently hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein the alkyl, alkenyl, alkynyl, heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three oxo (when feasible), halogen, -OH, C_1-C_6 alkyl, or C_1-C_6 haloalkyl;

or R^c and R^d 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, C_1-C_6 alkyl, or C_1-C_6 haloalkyl.

~~52.~~2. The compound of claim ~~51~~1, or a pharmaceutically acceptable salt~~, solvate, stereoisomer, or isotopic variant~~ thereof, wherein:

Q^2 is CW.

~~53.~~3. The compound of claim ~~51~~1, or a pharmaceutically acceptable salt~~, solvate, stereoisomer, or isotopic variant~~ thereof, wherein:

Q^2 is N.

~~54.~~4. The compound of ~~any one of claims 51-53~~claim 1, or a pharmaceutically acceptable salt~~, solvate, stereoisomer, or isotopic variant~~ thereof, wherein:

Q^3 is N and Q^4 is CW.

~~55.~~5. The compound of ~~any one of claims 51-54~~claim 1, or a pharmaceutically acceptable salt~~, solvate, stereoisomer, or isotopic variant~~ thereof, wherein:

Q^4 is N and Q^3 is CW.

~~56.~~6. The compound of ~~any one of claims 51-55~~claim 1, or a pharmaceutically acceptable salt~~, solvate, stereoisomer, or isotopic variant~~ thereof, wherein:

each W is independently hydrogen, halogen, or C_1-C_6 alkyl.

~~57. The compound of any one of claims 51-56~~claim 1, or a pharmaceutically acceptable salt~~, solvate, stereoisomer, or isotopic variant thereof, wherein:~~

~~each W is hydrogen.~~

~~58.~~7. ~~The compound of any one of claims 51-57, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:~~ thereof, wherein:

R^3 is halogen, -OR^b, C_1-C_6 alkyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, or C_1-C_6 heteroalkyl; wherein each alkyl and alkynyl is independently optionally substituted with one, two, or three R^{3a}.

~~59.~~8. The compound of ~~any one of claims 51-58,~~claim 1 or a pharmaceutically acceptable salt~~, solvate, stereoisomer, or isotopic variant~~ thereof, wherein:

R^3 is halogen, -OR^b, C_2-C_6 alkynyl, or C_1-C_6 hydroxyalkyl; wherein each alkyl and alkynyl is independently optionally substituted with one, two, or three R^{3a}.

~~60. The compound of any one of claims 51-59~~claim 1, or a pharmaceutically acceptable salt~~, solvate, stereoisomer, or isotopic variant~~ thereof, wherein:

~~R^3 is halogen.~~

~~61.~~9. ~~The compound of any one of claims 51-60, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:~~

R^1 is C_1-C_6 alkyl, C_1-C_6 haloalkyl, cycloalkyl, heterocycloalkyl, C_1-C_6 alkyl(aryl), C_1-C_6 alkyl(heteroaryl), C_1-C_6 alkyl(cycloalkyl), or C_1-C_6 alkyl(heterocycloalkyl); wherein each alkyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three R^{1a}.

~~62.~~10. The compound of ~~any one of claims 51-61~~claim 9, or a pharmaceutically acceptable salt~~, solvate, stereoisomer, or isotopic variant~~ thereof, wherein:

R^1 is C_1-C_6 alkyl, cycloalkyl, C_1-C_6 alkyl(aryl), or C_1-C_6 alkyl(cycloalkyl); wherein each alkyl, cycloalkyl, and aryl is independently optionally substituted with one, two, or three R^{1a}.

11. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein:

each R^{1a} is independently halogen or C_1-C_6 alkyl.

12. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein:

R^2 is hydrogen or C_1-C_6 alkyl.

~~63.~~13. The compound of ~~any one of claims 51-62~~claim 12, or a pharmaceutically acceptable salt~~,~~ ~~solvate, stereoisomer, or isotopic variant~~ thereof, wherein:

R^2 is hydrogen.

~~R^1 is cycloalkyl optionally substituted with one, two, or three R^{1a}.~~

~~64.~~14. The compound of ~~any one of claims 51-63~~claim 1, or a pharmaceutically acceptable salt~~,~~ ~~solvate, stereoisomer, or isotopic variant~~ thereof, wherein:

~~each R^{1a} is independently oxo (when feasible) halogen, -CN, -OR^b, C_1-C_6 alkyl, or C_1-C_6 fluoroalkyl.~~

R^8 is hydrogen or C_1-C_6 alkyl.

~~65.~~15. The compound of ~~any one of claims 51-64~~claim 14, or a pharmaceutically acceptable salt~~,~~ ~~solvate, stereoisomer, or isotopic variant~~ thereof, wherein:

R^8 is hydrogen.

~~each R^{1a} is independently halogen or C_1-C_6 alkyl.~~

~~66.~~16. The compound of ~~any one of claims 51-65~~claim 1, or a pharmaceutically acceptable salt~~,~~ ~~solvate, stereoisomer, or isotopic variant~~ thereof, wherein:

R^9 and R^{10} are independently hydrogen or C_1-C_6 alkyl.

~~R^2 is hydrogen or C_1-C_6 alkyl.~~

~~67.~~17. The compound of ~~any one of claims 51-66~~claim 16, or a pharmaceutically acceptable salt~~,~~ ~~solvate, stereoisomer, or isotopic variant~~ thereof, wherein:

~~R^2 is hydrogen.~~

R^9 and R^{10} are hydrogen.

~~68.~~18. The compound of ~~any one of claims 51-67~~claim 1, or a pharmaceutically acceptable salt~~,~~ ~~solvate, stereoisomer, or isotopic variant~~ thereof, wherein:

~~R^8 is hydrogen or C_1-C_6 alkyl.~~

A is -O-.

~~69.~~19. ~~The~~A pharmaceutical composition comprising a compound of ~~any one of claims 51-68~~claim 1, or a pharmaceutically acceptable salt~~, solvate, stereoisomer, or isotopic variant~~ thereof, ~~wherein:~~ and a pharmaceutically acceptable excipient.

~~R^8 is hydrogen.~~

70.20. The Use of a compound of any one of claims 51-69 claim 1, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein: in the manufacture of a medicament for treating cancer.

R^9 and R^{10} are independently hydrogen or C_1-C_6 alkyl.

71. 21. The A compound of any one of claims 51-70 claim 1, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof for use in therapy., wherein:

R^9 and R^{10} are hydrogen.

72. The compound of any one of claims 51-71, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

A is -O-.

73. The compound of any one of claims 51-72, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

A is $-CH_2-$.

74. The compound of any one of claims 51-73, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

R^5 and R^6 are independently hydrogen, halogen, $-OR^b$, C_1-C_6 alkyl, or C_1-C_6 haloalkyl.

75. The compound of any one of claims 51-74, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

R^5 and R^6 are hydrogen.

76. The compound of any one of claims 51-75, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

R^4 and R^7 are independently hydrogen, halogen, $-OR^b$, C_1-C_6 alkyl, or C_1-C_6 haloalkyl.

77. The compound of any one of claims 51-76, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

R^4 and R^7 are independently hydrogen, halogen, or -OH.

78. The compound of any one of claims 51-77, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

R^4 and R^7 are independently halogen or -OH.

79. The compound of any one of claims 51-78, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

R^4 and R^7 are independently hydrogen or -OH.

80. The compound of any one of claims 51-79, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

R^4 and R^7 are -OH.

81. The compound of any one of claims 51-80, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

R^{21} and R^{22} are hydrogen.

82. The compound of any one of claims 51-81, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

R^{12} is hydrogen, halogen, $-OR^{13}$, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, C_2-C_6 alkynyl, or C_1-C_6 heteroalkyl; wherein each alkyl and alkynyl is independently optionally substituted with one, two, or three R^{12a}.

83. The compound of any one of claims 51-82, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

R^{12} is hydrogen, C_1-C_6 alkyl, C_1-C_6 hydroxyalkyl, or C_2-C_6 alkynyl; wherein each alkyl and alkynyl is independently optionally substituted with one, two, or three R^{12a}.

84. The compound of any one of claims 51-83, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

R^{12} is hydrogen.

85. The compound of any one of claims 51-84, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

R^{11} is halogen, $-CN$, $-OR^{13}$, $-NR^{15}R^{16}$, $-S(=O)_2R^{14}$, $-C(=O)OR^{13}$, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three R^{11a}.

86. The compound of any one of claims 51-85, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

R^{11} is $-CN$, $-S(=O)_2R^{14}$, $-C(=O)OR^{13}$, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, C_2-C_6 alkynyl, or heteroaryl; wherein each alkyl, alkynyl, and heteroaryl is independently optionally substituted with one, two, or three R^{11a}.

87. The compound of any one of claims 51-86, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

R^{11} is C_1-C_6 alkyl optionally substituted with one, two, or three R^{11a}.

88. The compound of any one of claims 51-87, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

R^{11} is C_1-C_6 alkyl substituted with one R^{11a}.

89. The compound of any one of claims 51-88, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

each R^{11a} is oxo (when feasible), halogen, -CN, $-OR^{13}$, $-SR^{13}$, $-S(=O)R^{14}$, $-NR^{15}R^{16}$, $-S(=O)_2R^{14}$, $-NR^{13}S(=O)_2R^{14}$, $-S(=O)_2NR^{15}R^{16}$, $-C(=O)R^{14}$, $-C(=O)OR^{13}$, $-C(=O)NR^{15}R^{16}$, $-OC(=O)NR^{15}R^{16}$, $-NR^{13}C(=O)R^{14}$, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 hydroxyalkyl, C_1-C_6 heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three R^{11e}.

90. The compound of any one of claims 51-89, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

each R^{11a} is independently oxo (when feasible), halogen, $-OR^{13}$, $-SR^{13}$, $-NR^{15}R^{16}$, $-S(=O)_2R^{14}$, $-NR^{13}S(=O)_2R^{14}$, $-S(=O)_2NR^{15}R^{16}$, $-C(=O)OR^{13}$, $-OC(=O)NR^{15}R^{16}$, $-NR^{13}C(=O)R^{14}$, heterocycloalkyl, aryl, or heteroaryl; wherein each heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three R^{11e}.

91. The compound of any one of claims 51-90, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

each R^{11a} is independently $-OR^{13}$.

92. The compound of any one of claims 51-91, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

R^{11} and R^{12} are taken together to form a cycloalkyl or heterocycloalkyl each optionally substituted with one, two, or three R^{11b}.

93. The compound of any one of claims 51-92, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

each R^{13} is independently hydrogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 heteroalkyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; wherein each alkyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl is independently optionally substituted with one, two, or three R^{13a}.

94. The compound of any one of claims 51-93, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

each R^{13} is independently C_1-C_6 alkyl, C_1-C_6 haloalkyl, or cycloalkyl; wherein each alkyl and cycloalkyl is independently optionally substituted with one, two, or three R^{13a}.

95. The compound of any one of claims 51-94, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

each R^{13} is independently C_1-C_6 alkyl.

96. The compound of any one of claims 51-95, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

each R^{14} is independently C_1-C_6 alkyl.

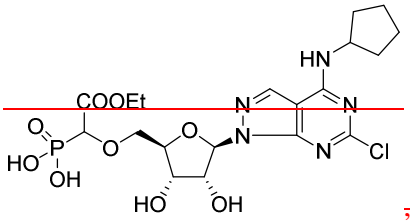
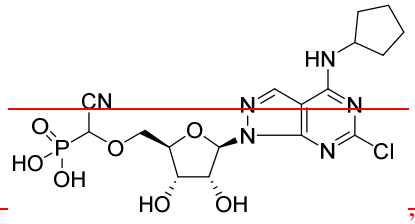
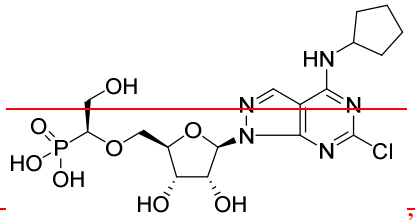
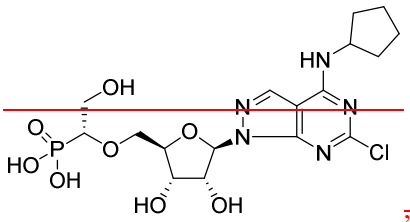
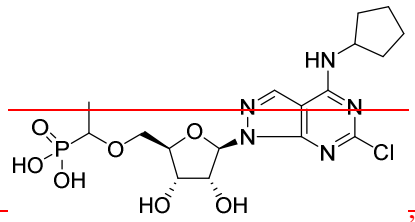
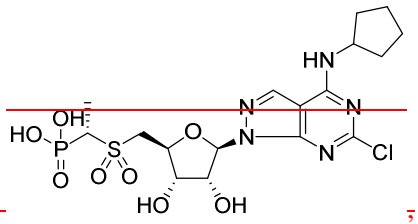
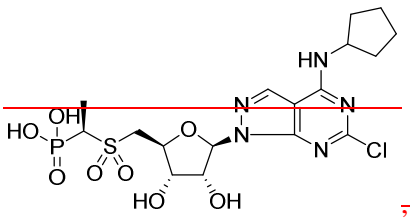
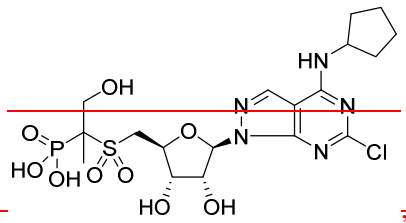
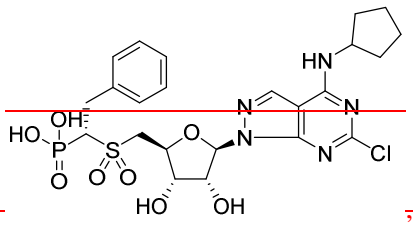
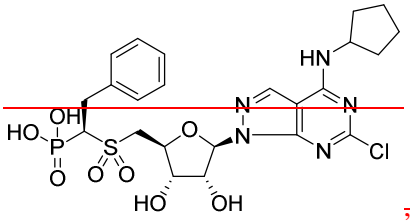
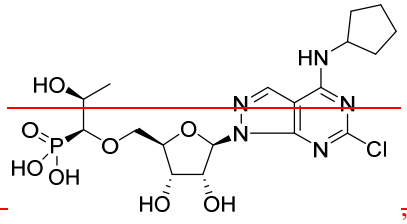
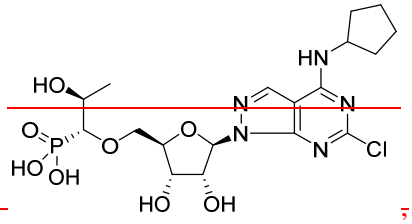
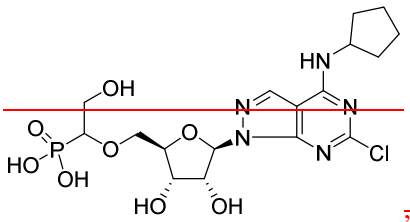
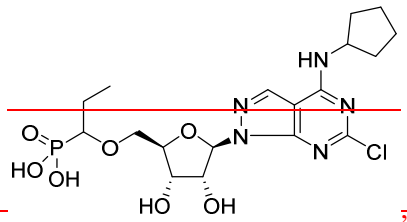
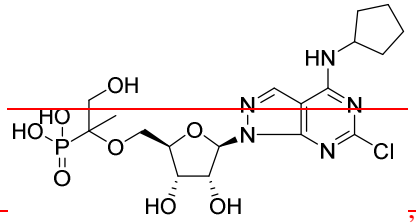
97. The compound of any one of claims 51-96, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

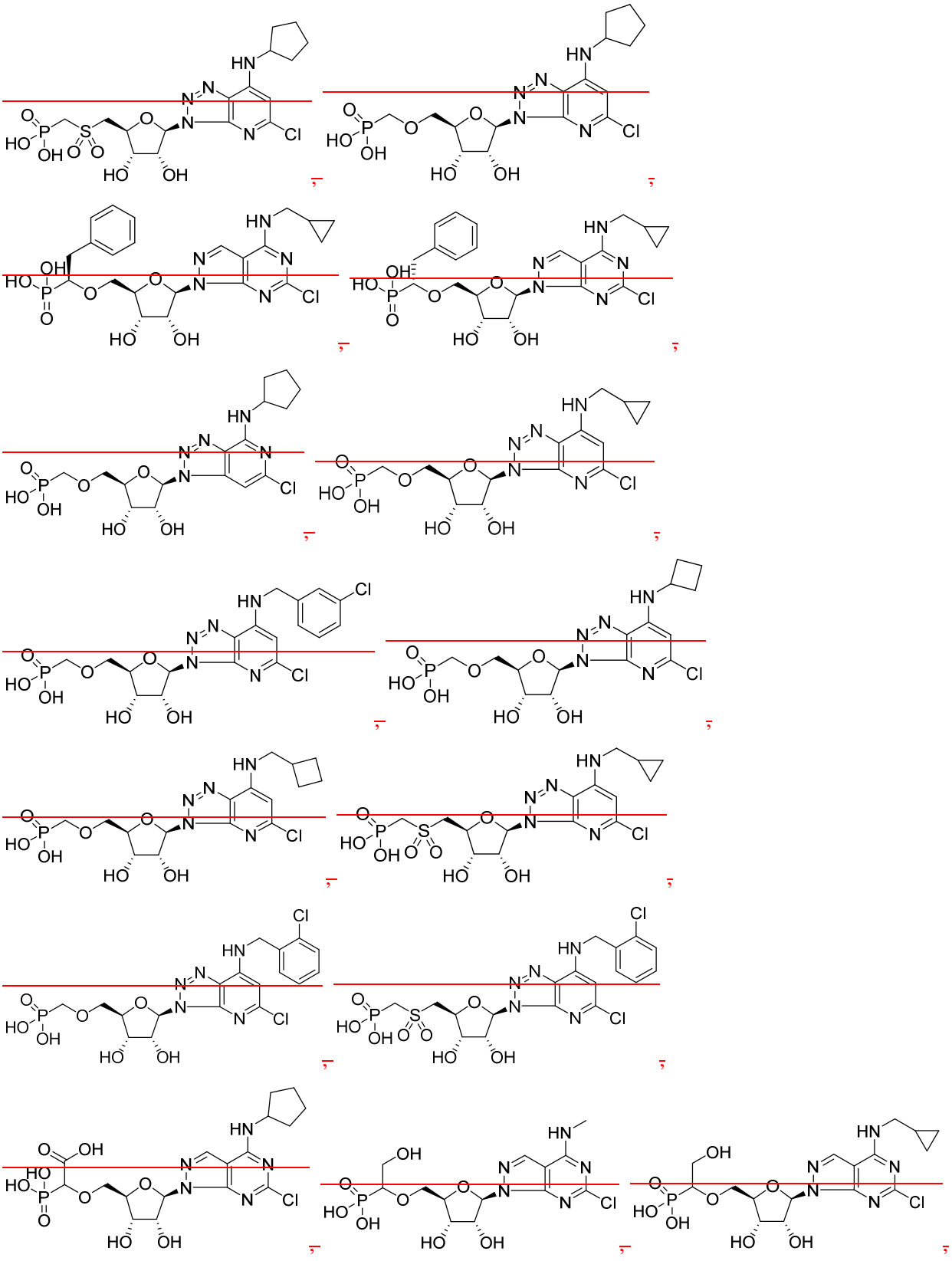
each R^{15} and R^{16} is independently hydrogen or C_1-C_6 alkyl.

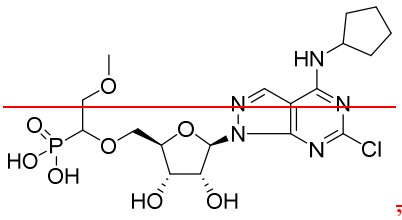
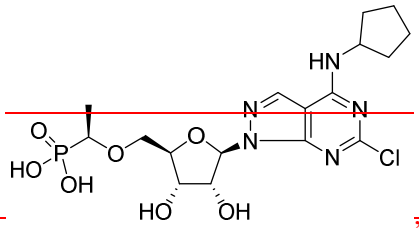
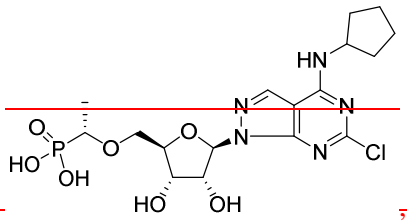
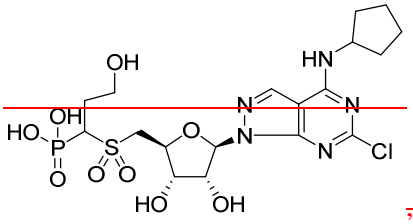
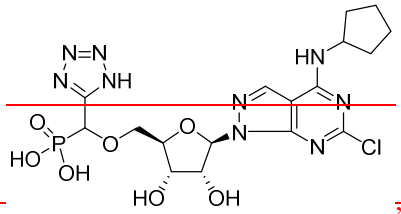
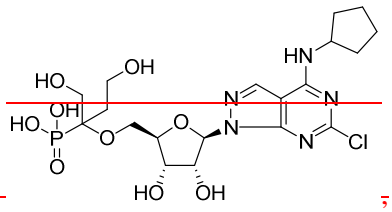
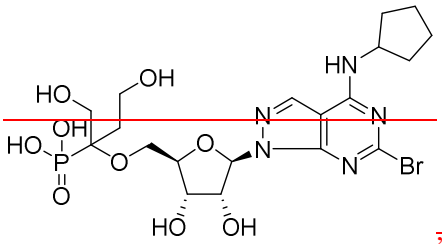
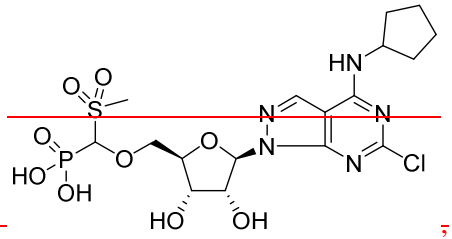
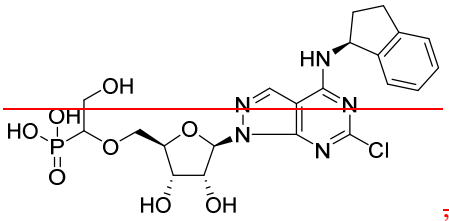
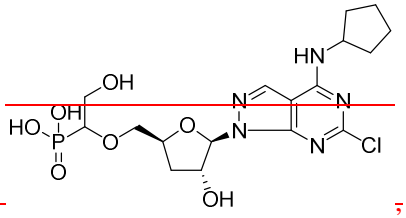
98. The compound of any one of claims 51-97, or a pharmaceutically acceptable salt, solvate, stereoisomer, or isotopic variant thereof, wherein:

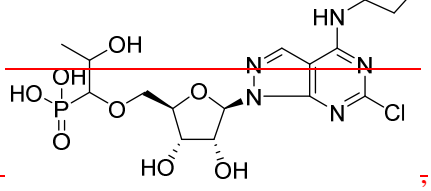
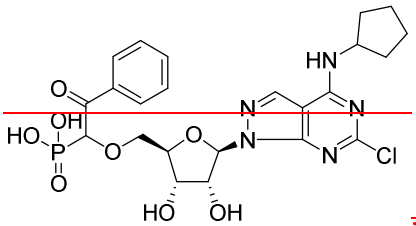
R^{15} and R^{16} are taken together with the nitrogen atom to which they are attached to form a heterocycloalkyl.

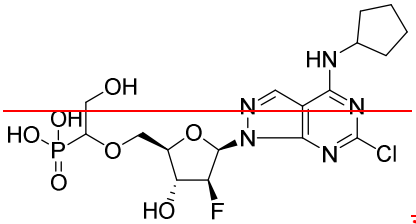
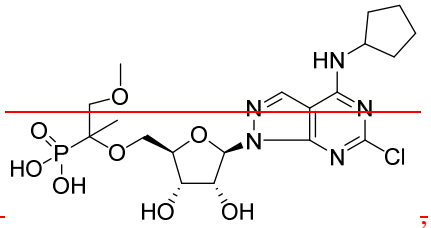
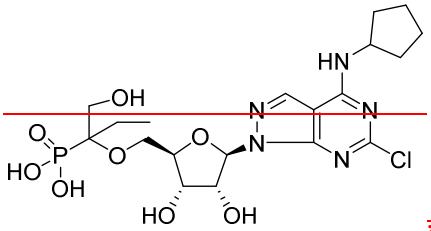
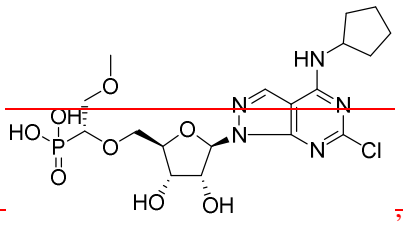
99. A compound selected from the group consisting of:

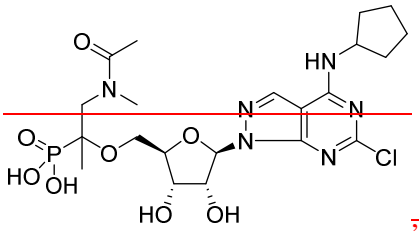

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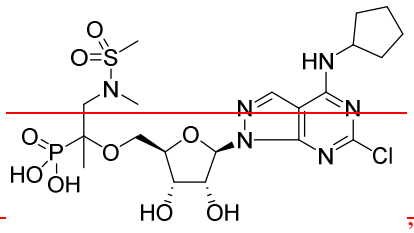


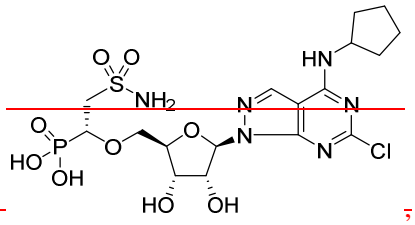











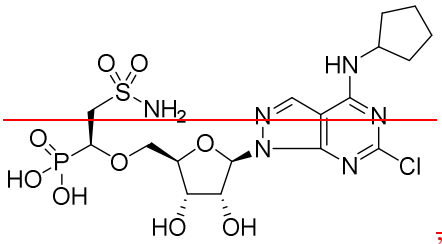



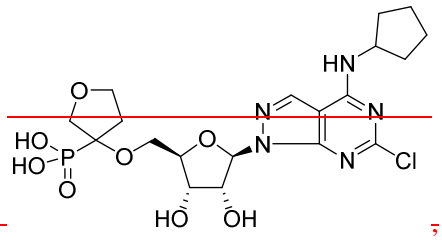





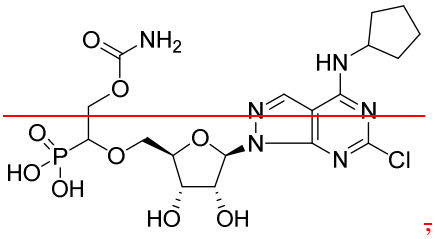


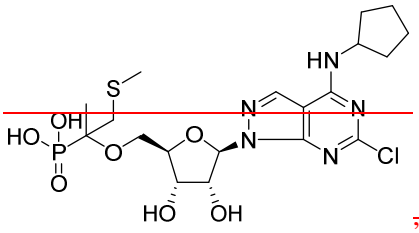


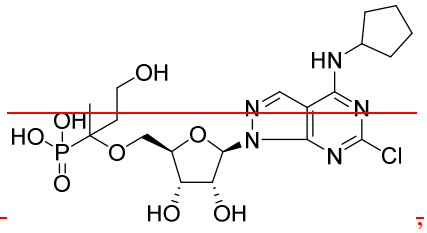


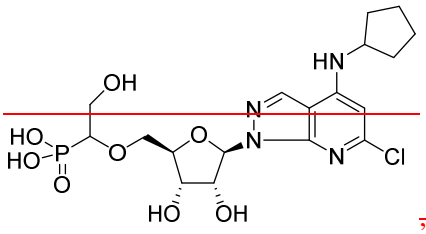


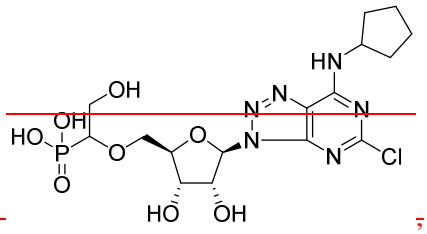


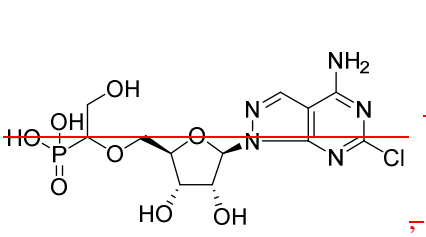


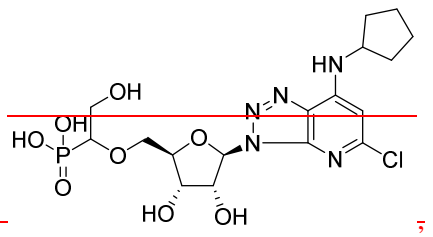


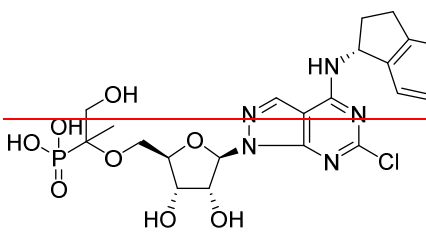


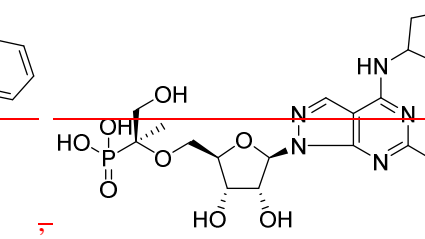


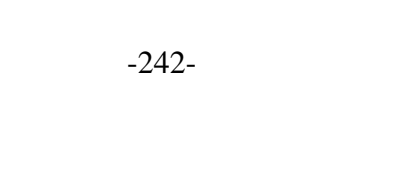


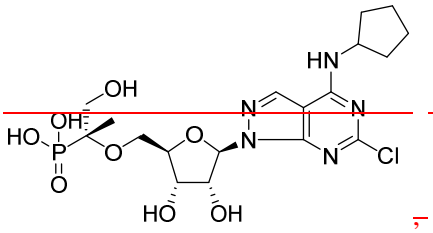
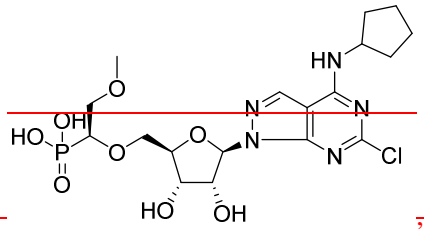
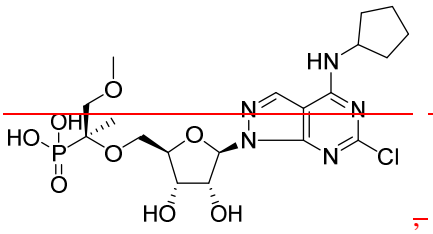
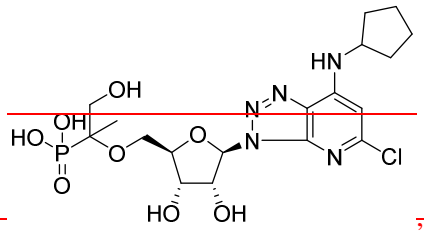
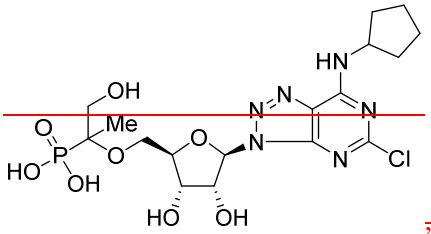
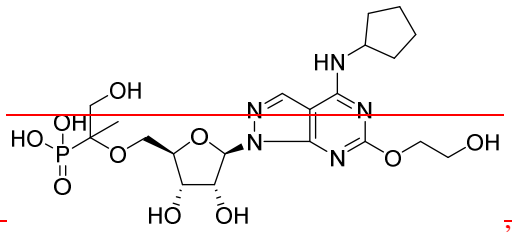
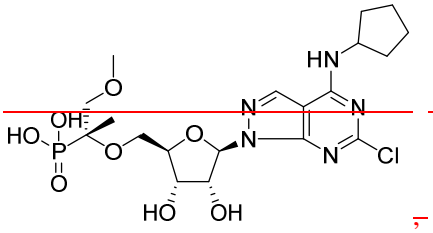
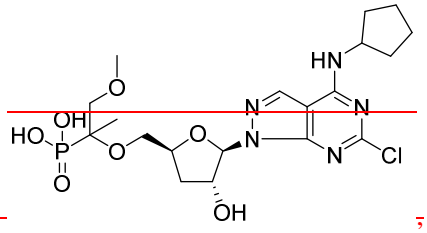
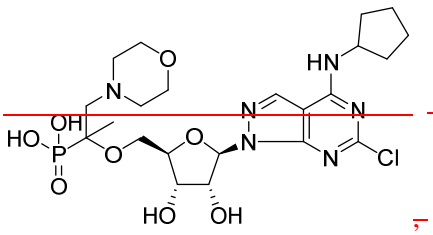
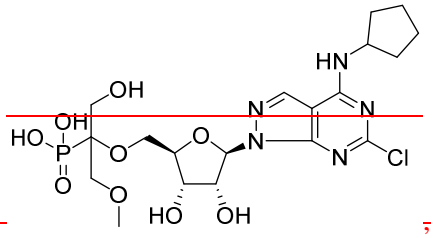
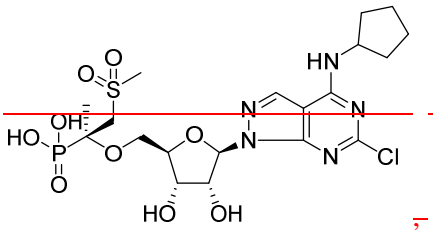
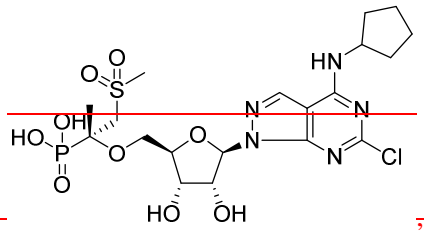
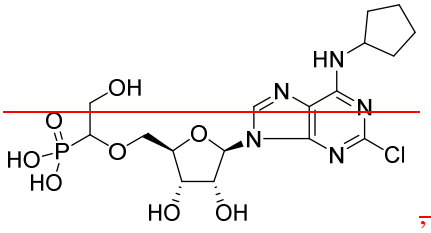
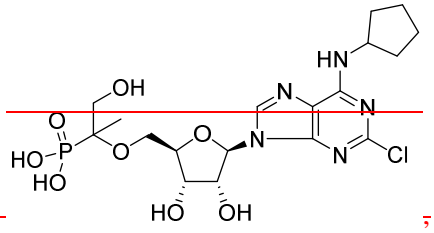


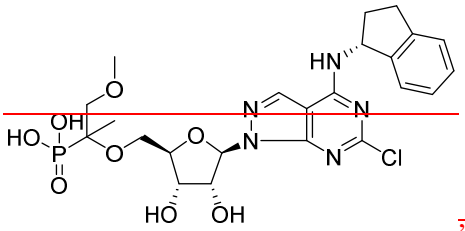
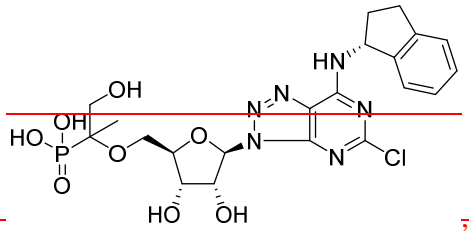
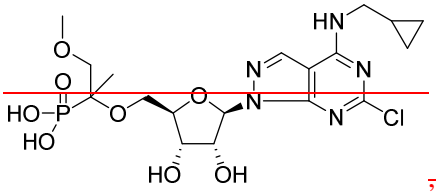
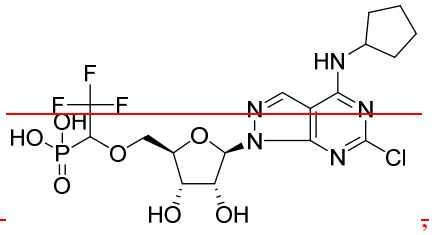
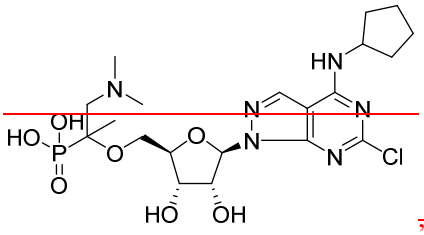
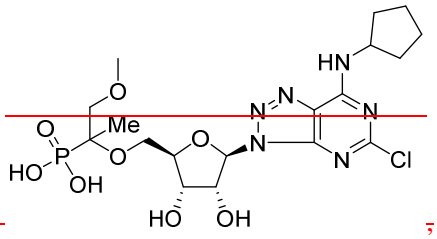
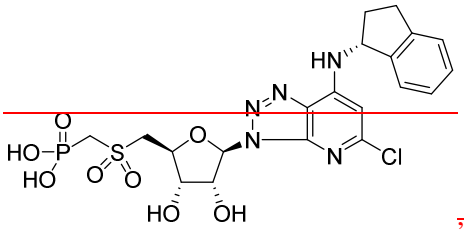
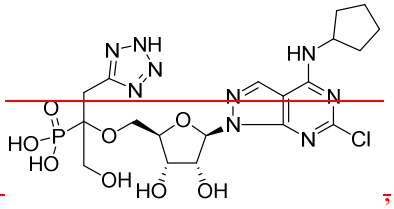
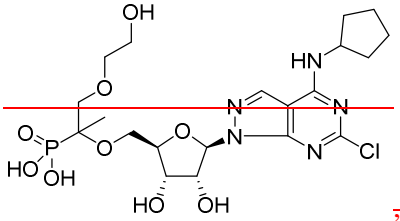
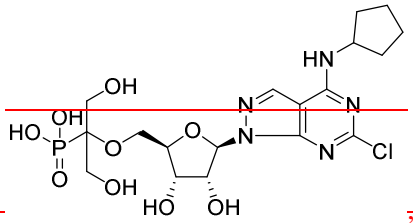
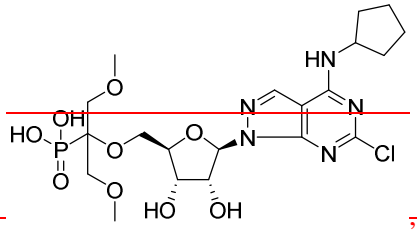
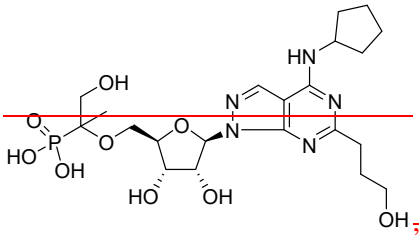
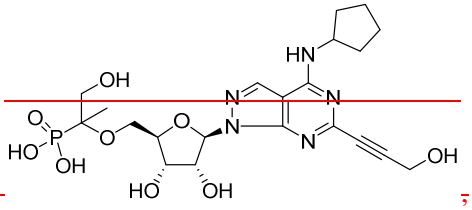
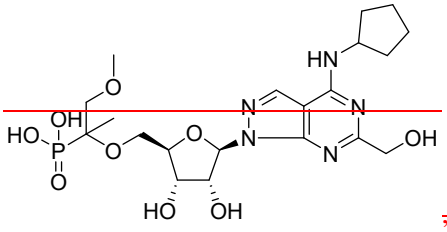
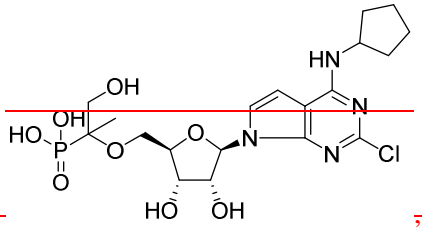






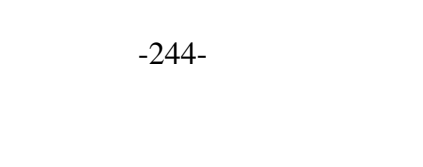


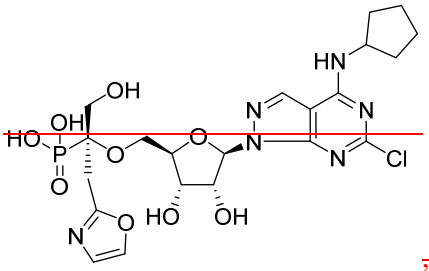
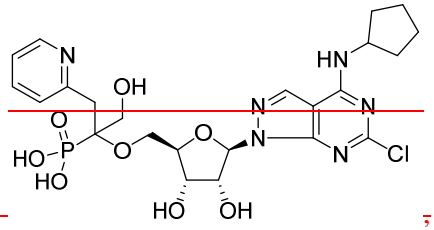
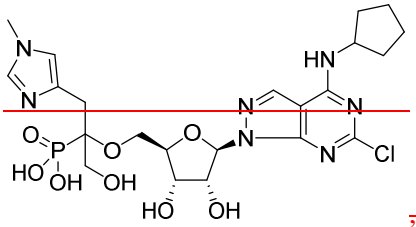
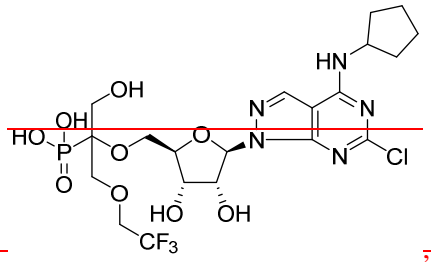
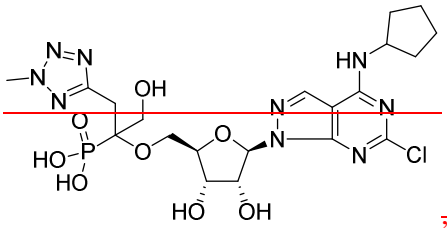
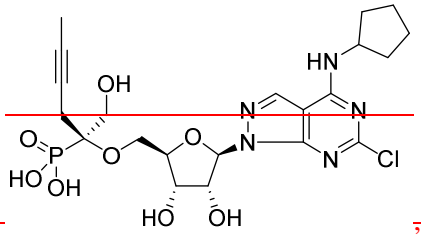
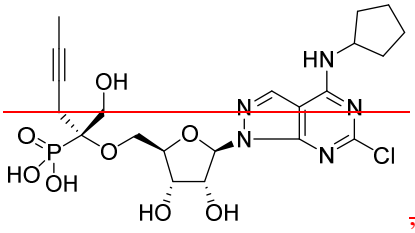
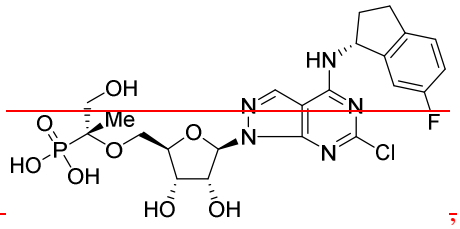
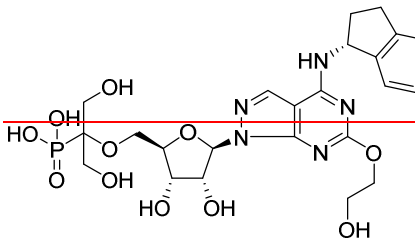
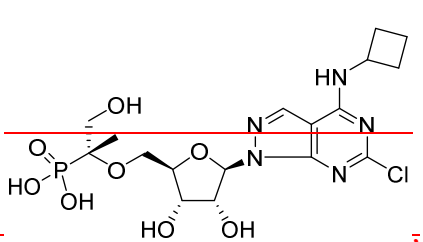
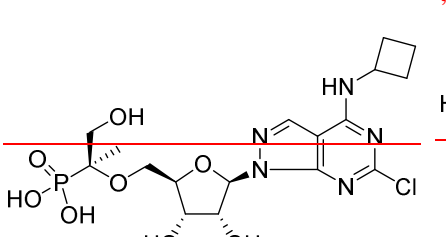

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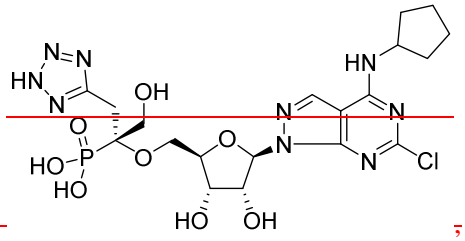

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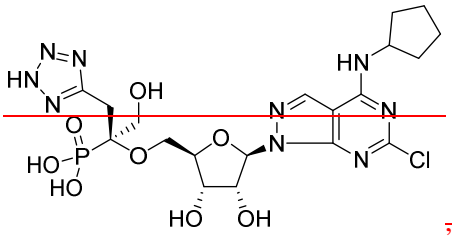
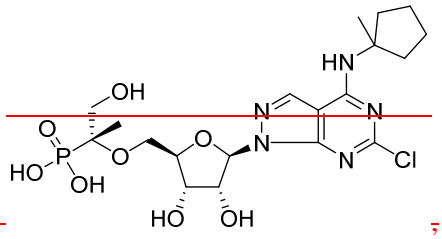
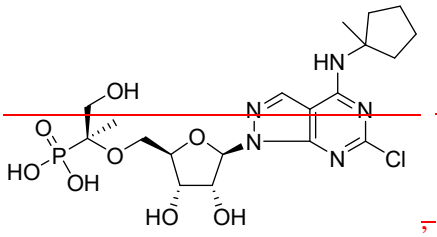
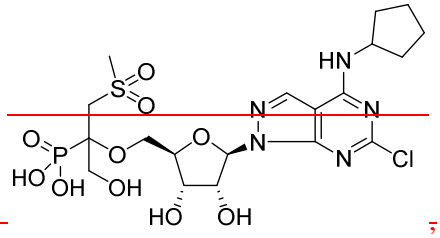
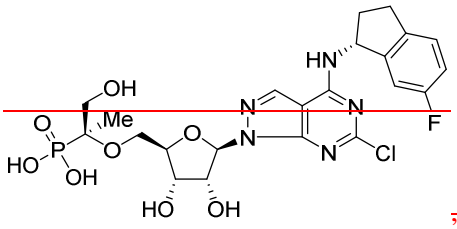
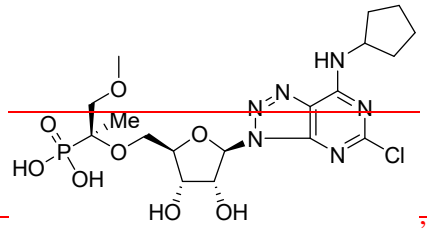
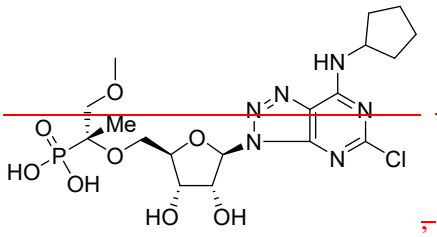
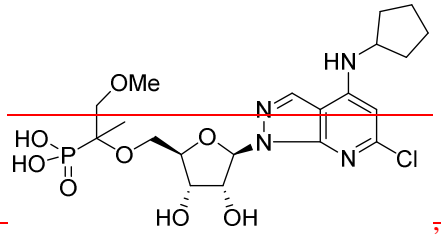
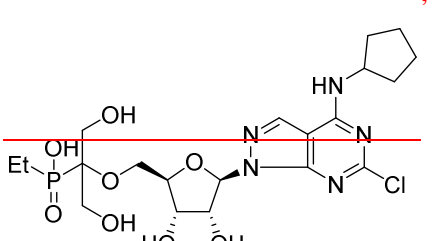
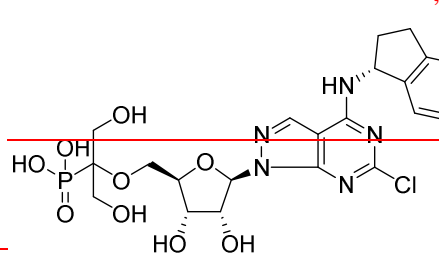
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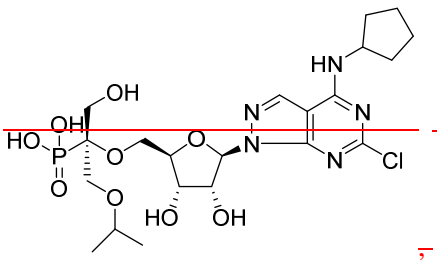
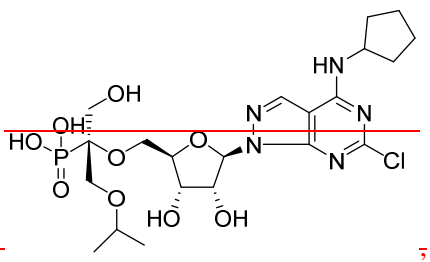
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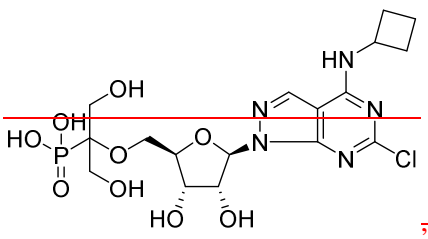
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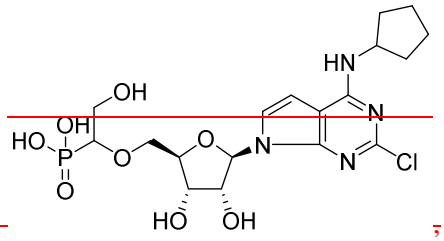












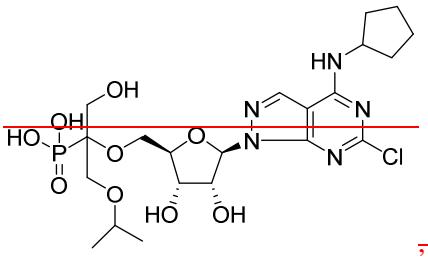


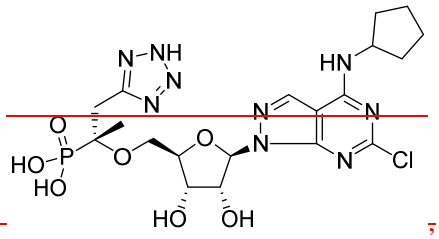











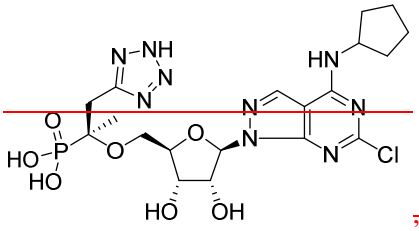



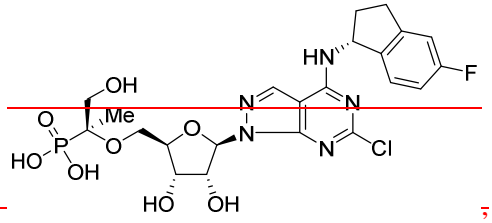


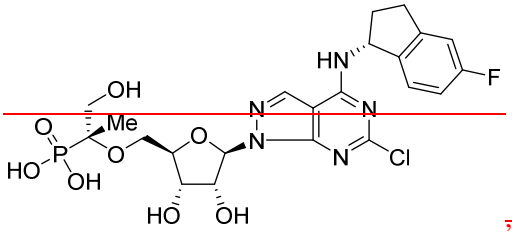


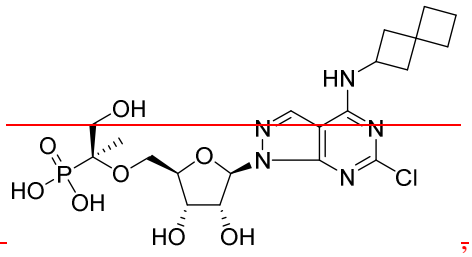


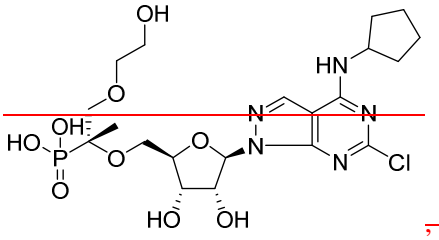


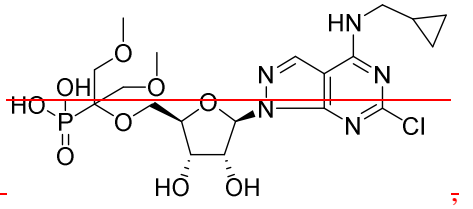


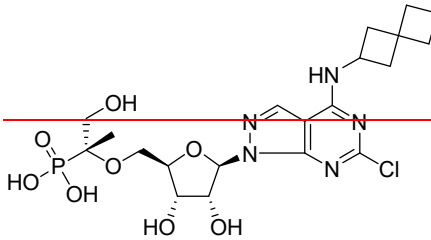


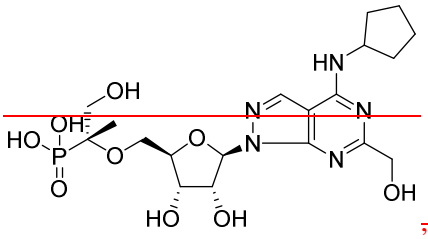
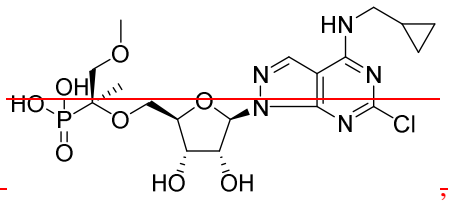
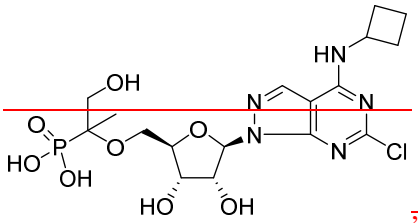
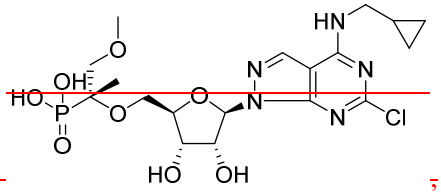
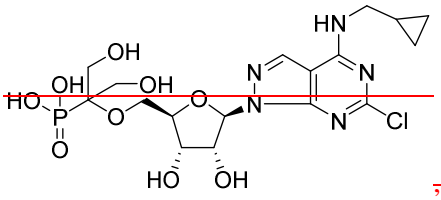
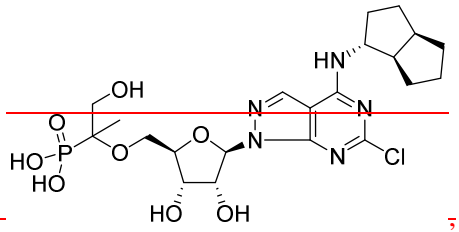
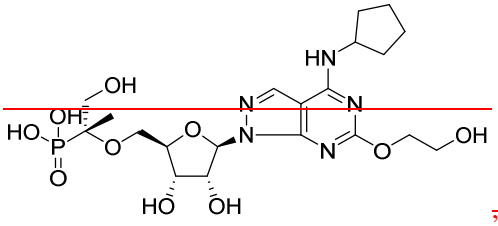
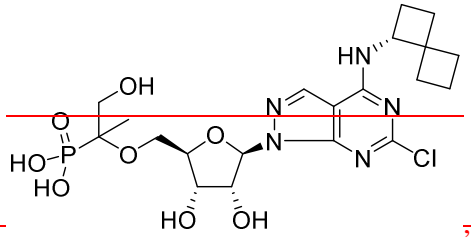
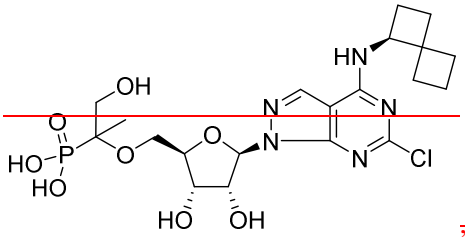
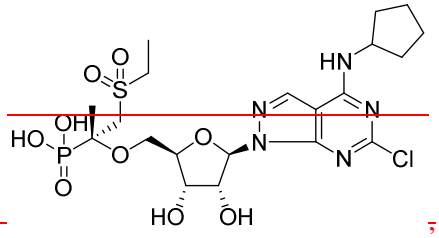
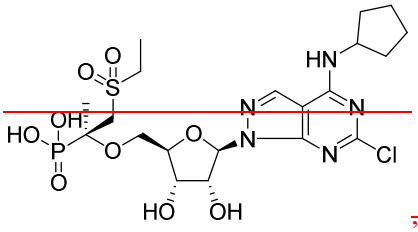
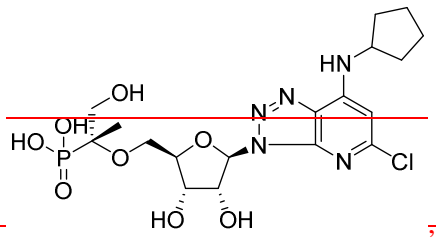
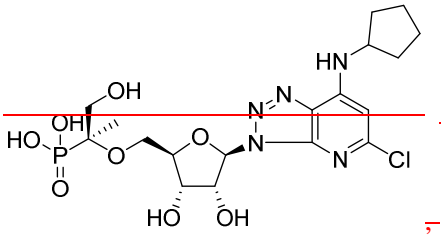
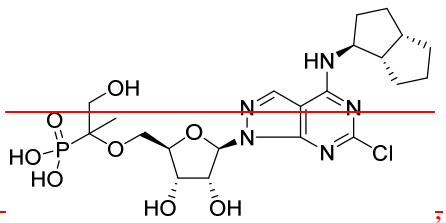


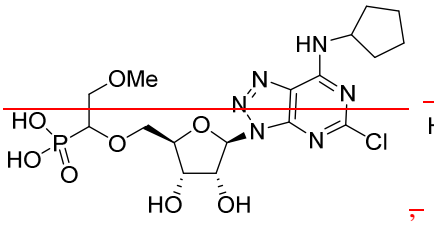
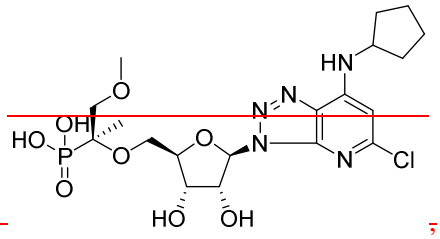
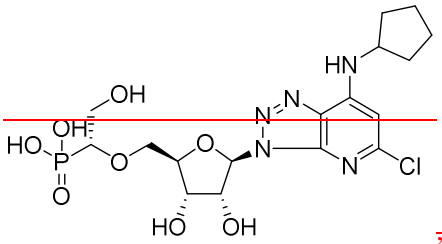
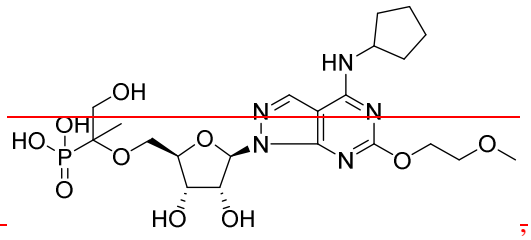
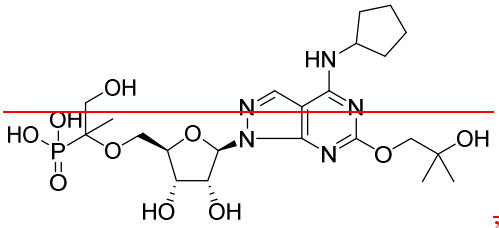
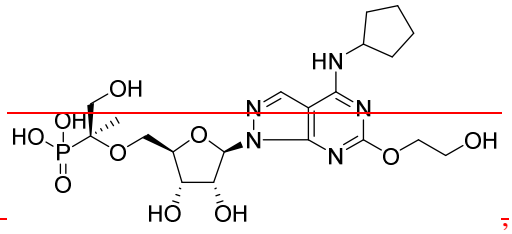
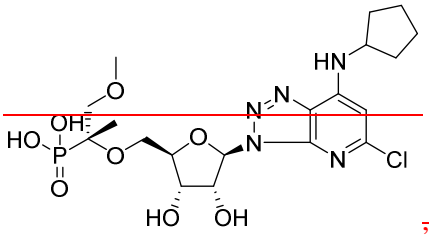
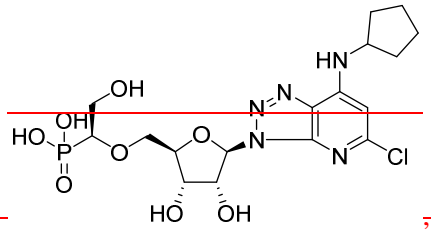
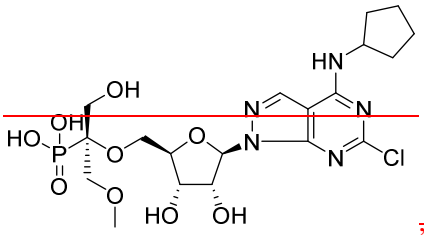
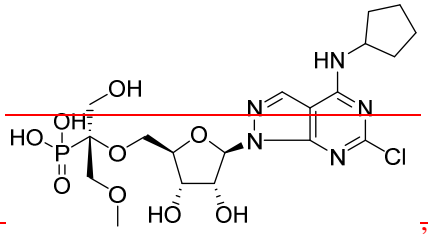
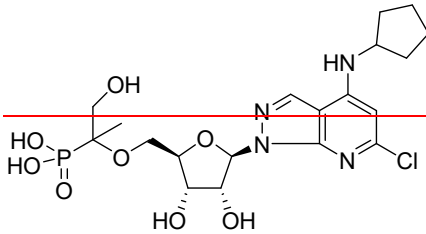
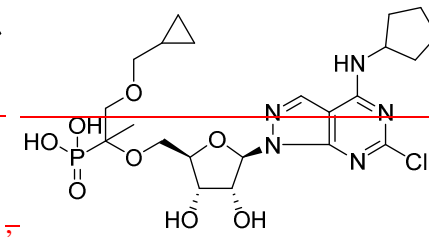
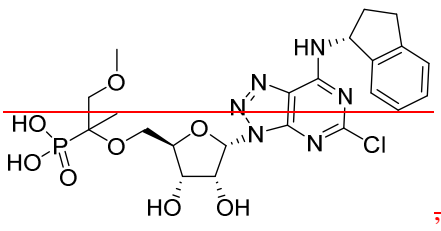
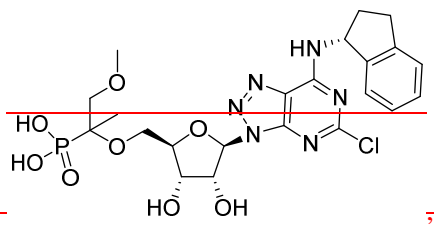


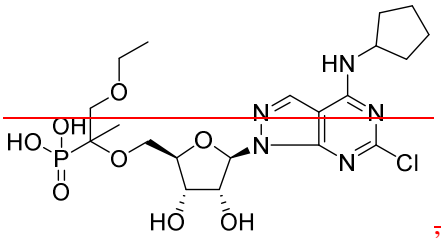
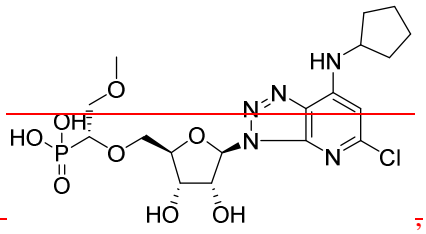
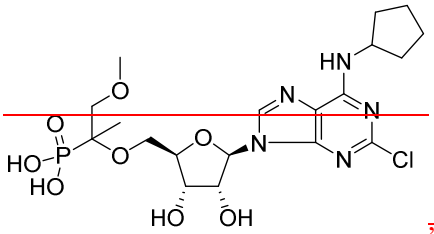
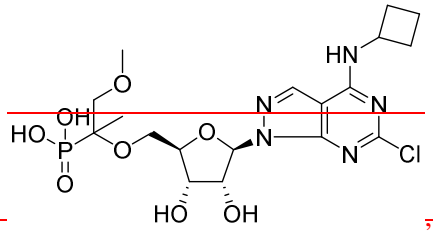
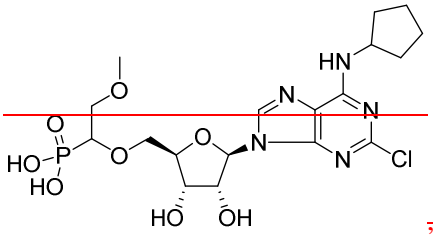
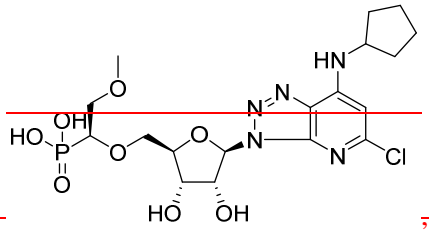
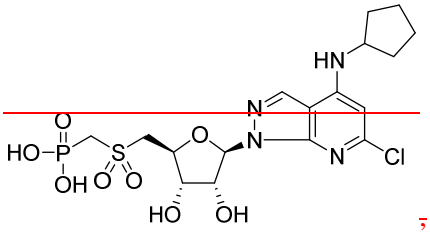
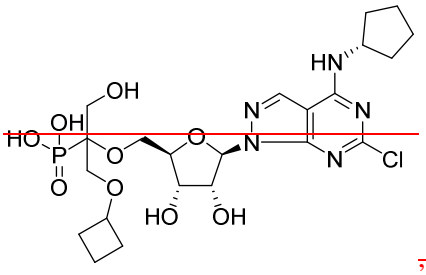
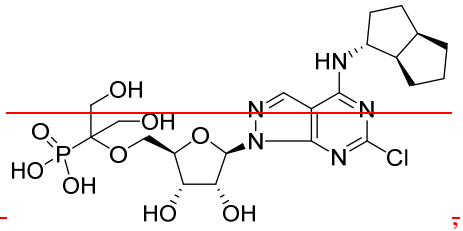
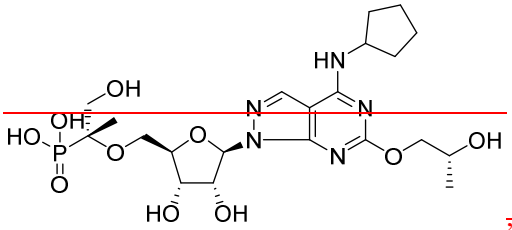
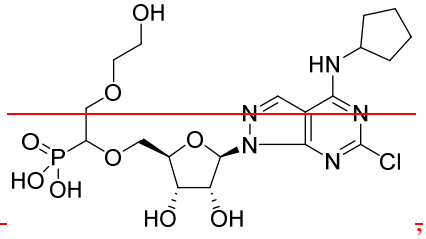


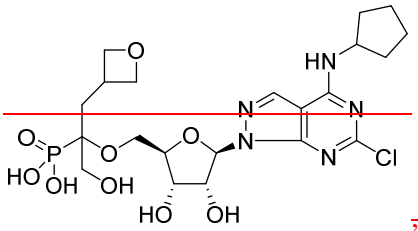
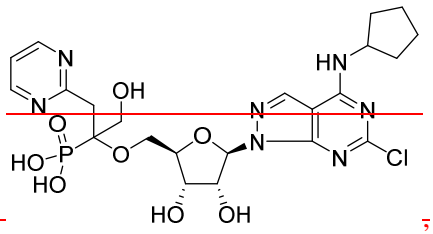


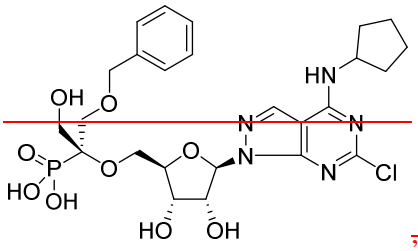
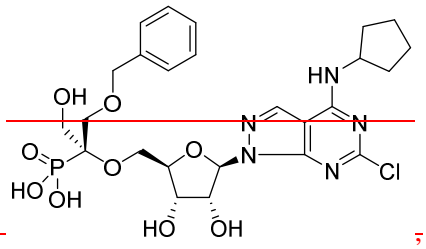
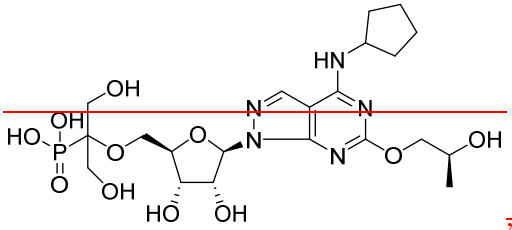
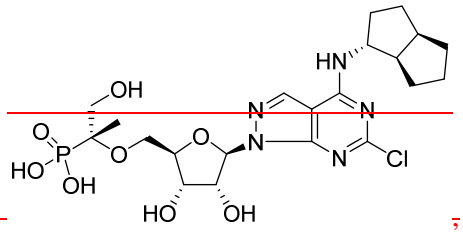
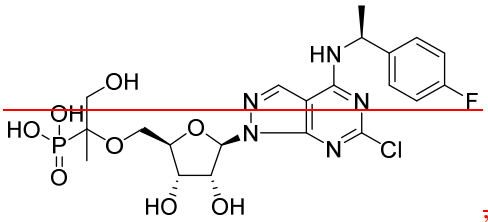
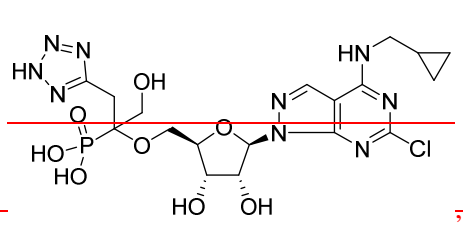
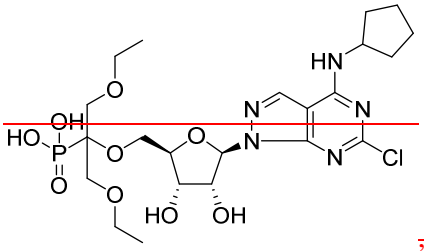
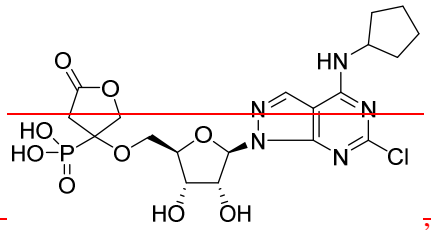
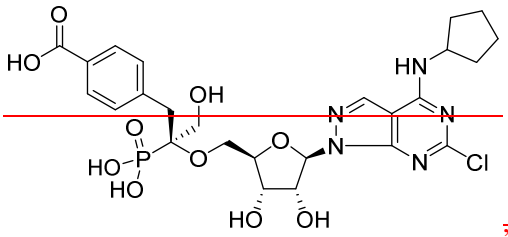
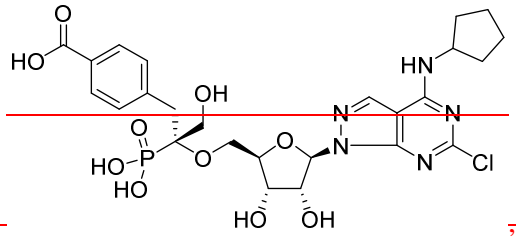


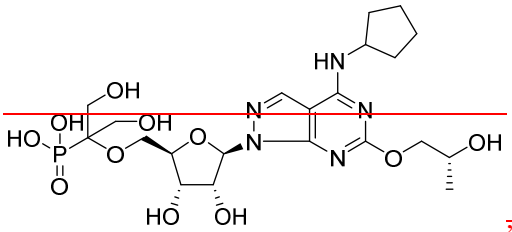
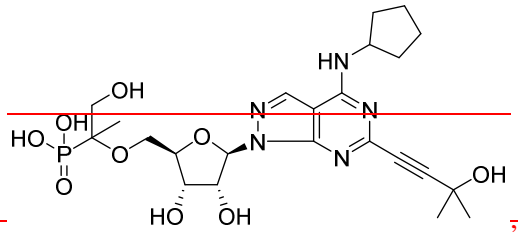
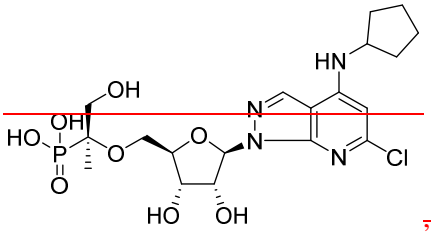
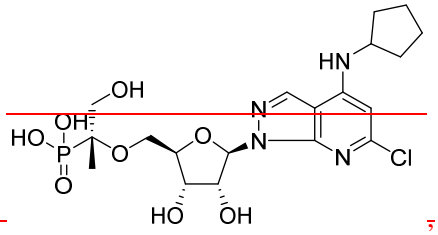
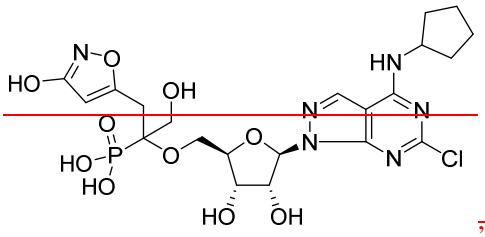
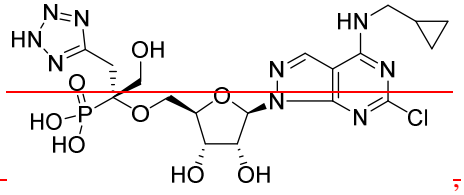
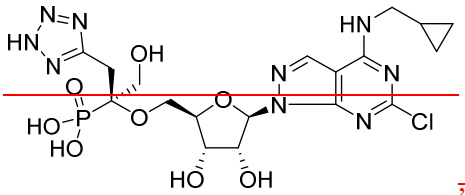
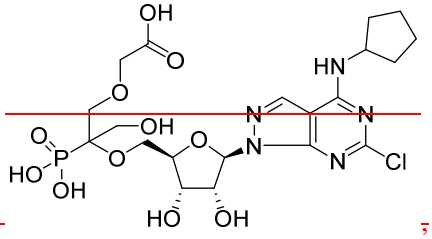
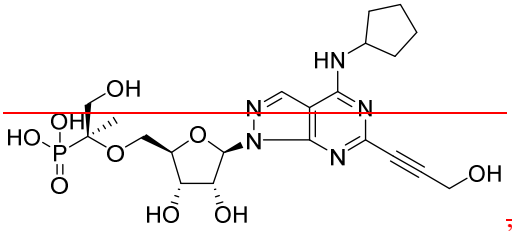
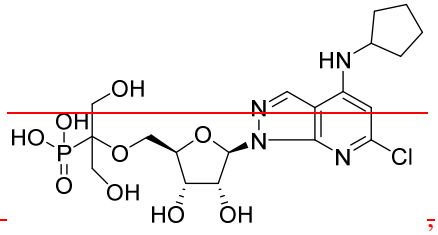
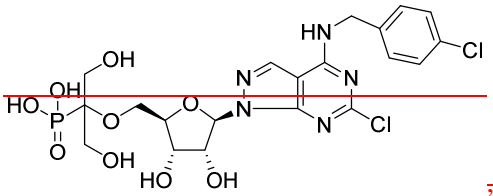
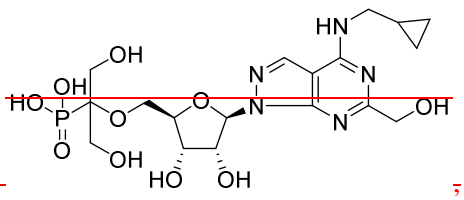
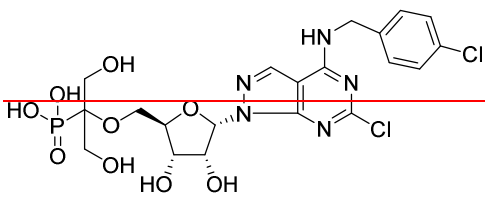
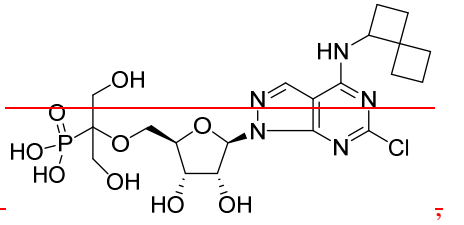

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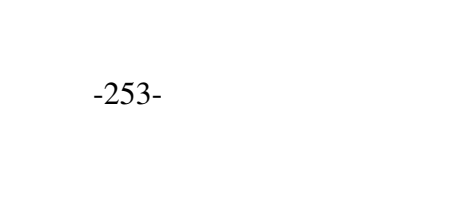















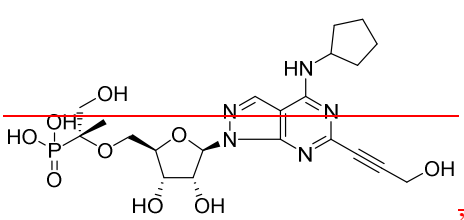
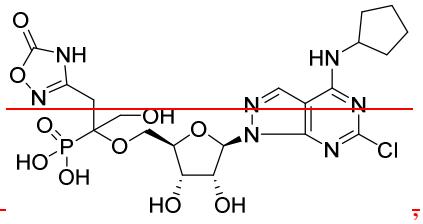
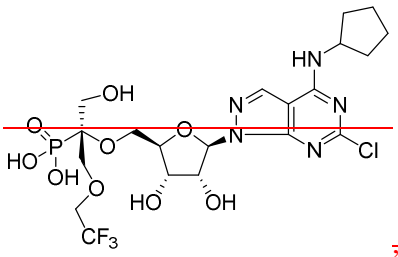
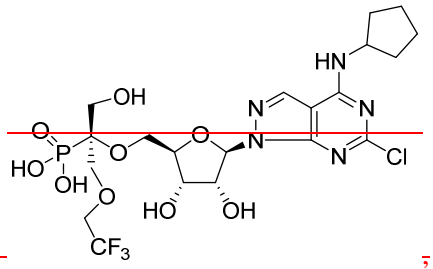
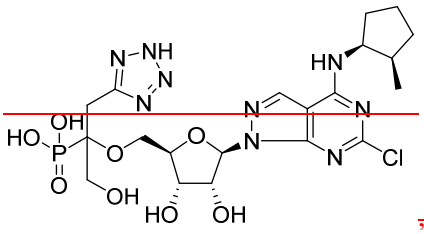
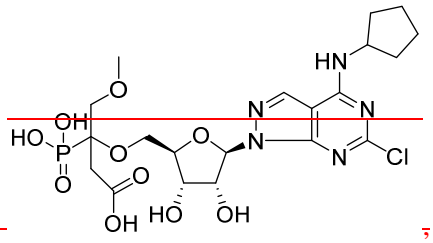
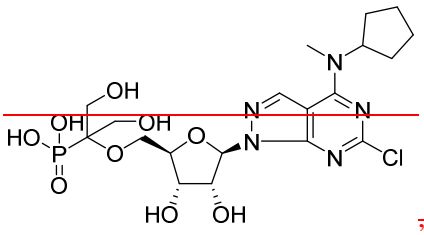
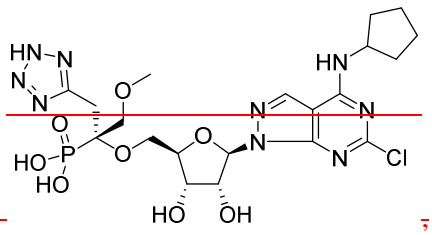
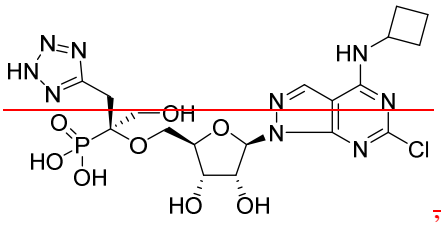
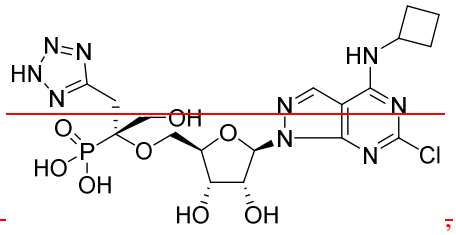
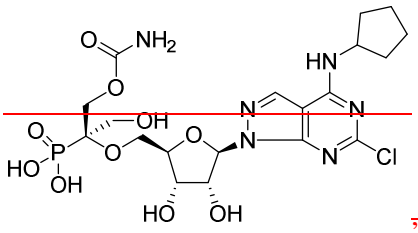
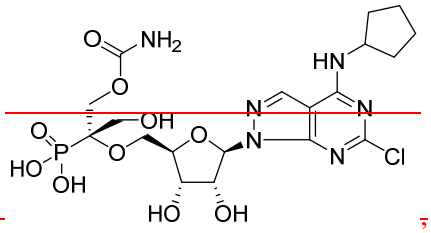
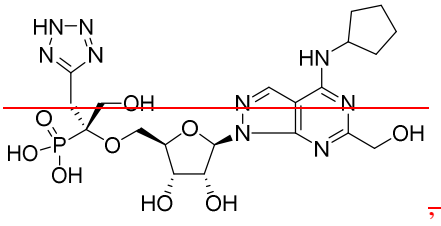
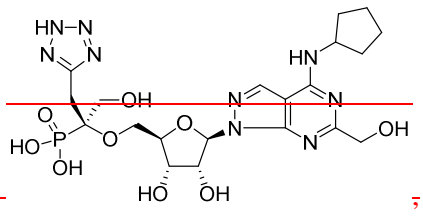

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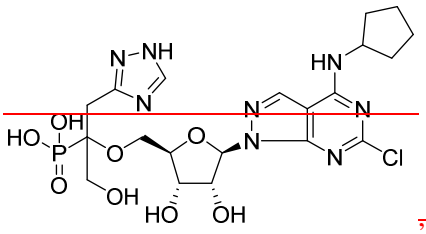
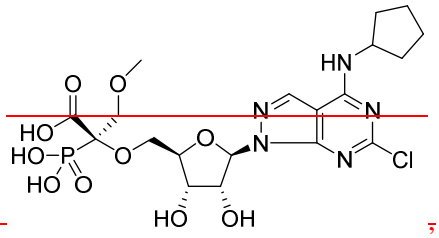
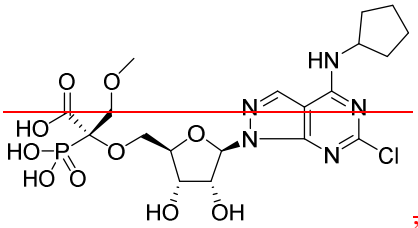
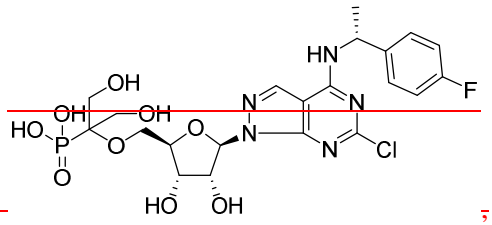
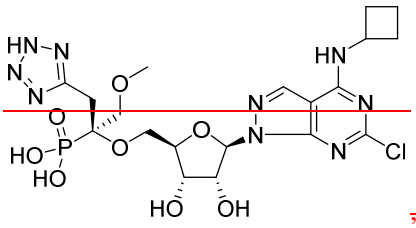
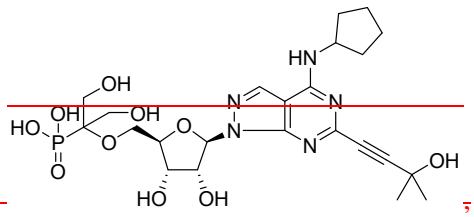
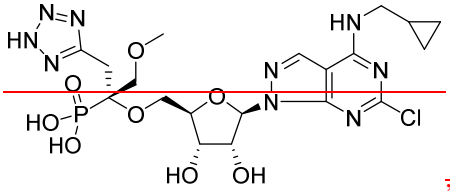
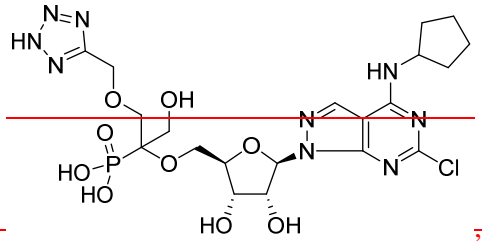
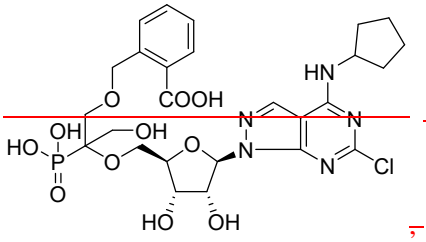
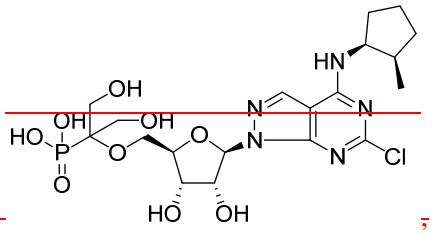
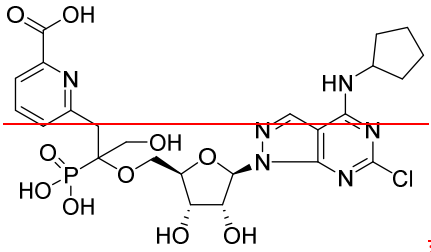
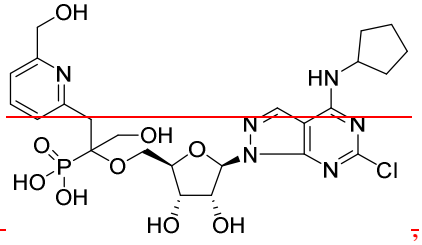




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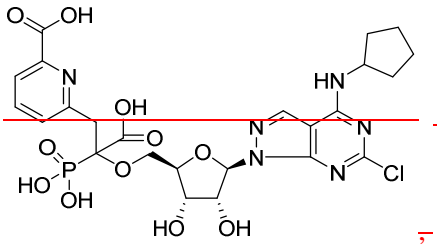
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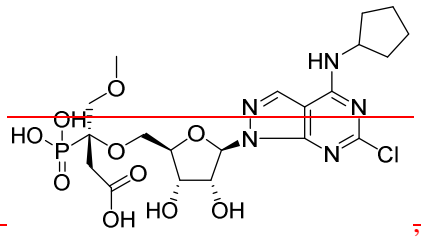

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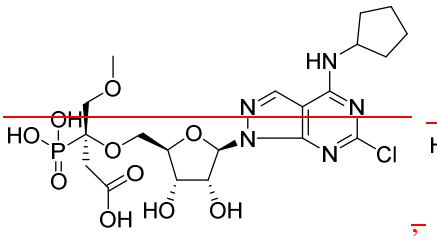

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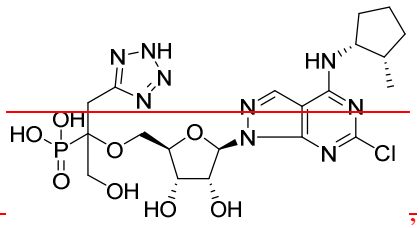
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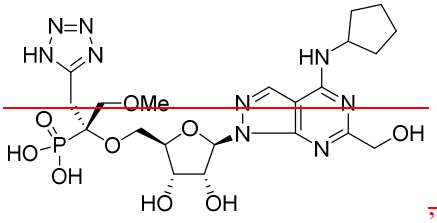
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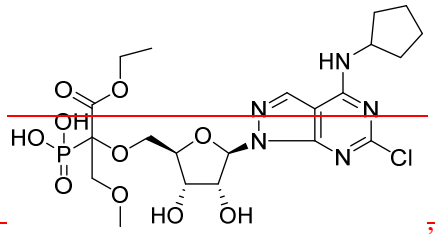


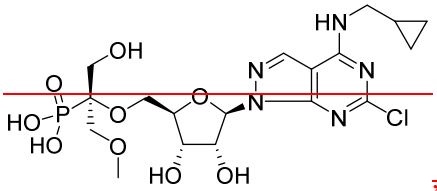


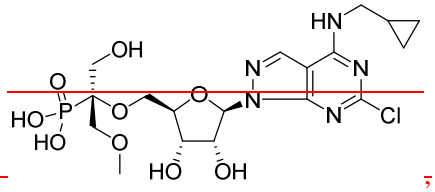


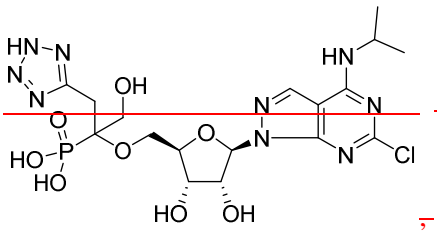


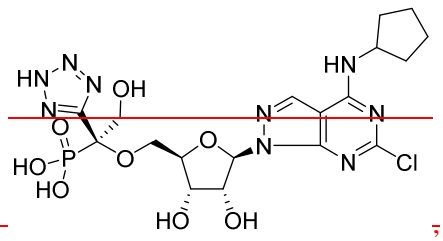


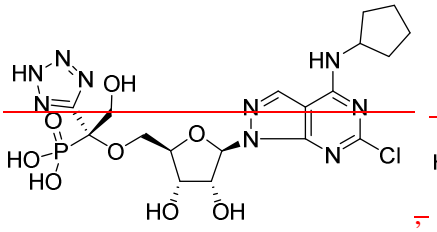


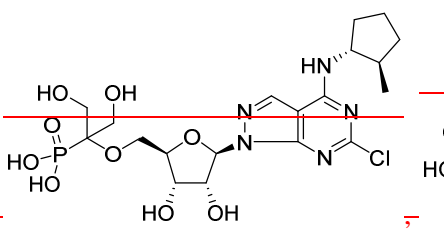


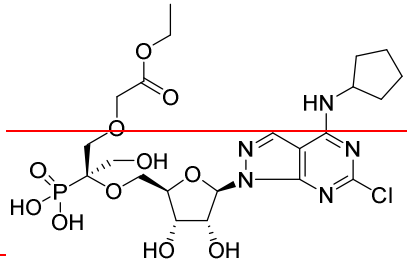


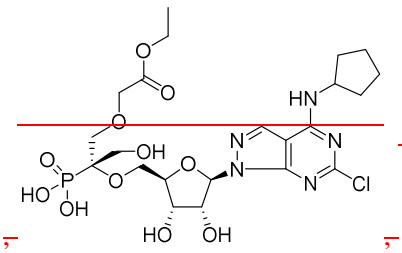
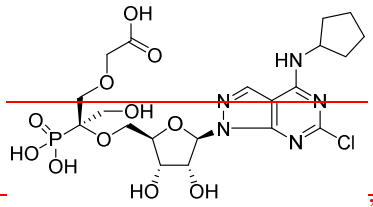
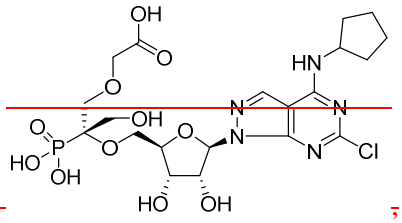
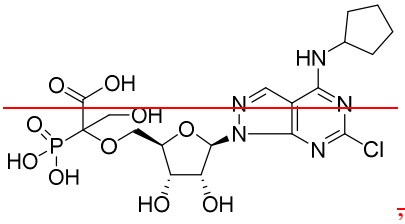
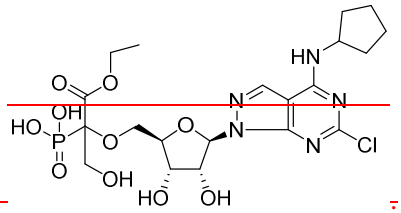










100. A pharmaceutical composition comprising a compound of any one of claims 1-99, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, and a pharmaceutically acceptable excipient.

101. A method of inhibiting CD73 comprising contacting CD73 with a compound of any one of claims 1-99, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof.

102. A method of treating cancer in a subject, comprising administering to the subject a compound of any one of claims 1-99, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof.

103. A method of treating subject, comprising administering to the subject a pharmaceutical composition of claim 100.

104. The method of either of claims 102 or 103, wherein the cancer is lung cancer, melanoma, breast cancer, ovarian cancer, colorectal cancer, gastric cancer, gallbladder cancer, prostate cancer, renal cancer, or a lymphoma.

105. The method of any one of claims 102-104, further comprising administering a second therapeutic agent.

106. The method of claim 105, wherein the second therapeutic agent is a chemotherapeutic agent or an immunotherapy agent.

107. A method of treating an infection in a subject, comprising administering to the subject a compound of any one of claims 1-99, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof.

108. A method of treating an infection in a subject, comprising administering to the subject a pharmaceutical composition of claim 100.

109. The method of either of claims 107 or 108, wherein the infection is a viral infection.

110. The method of either of claims 107 or 108, wherein the infection is a parasitic infection.

~~111. A method of treating a neurodegenerative disease in a subject, comprising administering to the subject a compound of any one of claims 1-99, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof.~~

~~112. A method of treating a neurodegenerative disease in a subject, comprising administering to the subject a pharmaceutical composition of claim 100.~~

~~113. The method of either of claims 111 or 112, wherein the neurodegenerative disease is Alzheimer's disease, Parkinson's disease, Huntington's disease, schizophrenia, or autism.~~